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The State of Cannabis Research Legislation in 2020

Ali J. Zarrabi, M.D., Jennifer K. Frediani, Ph.D., R.D., Joshua M. Levy, M.D., M.P.H.

Division of Palliative Medicine, Department of Family and Preventive Medicine (A.J.Z.), and the Department of Otolaryngology–Head and Neck Surgery (J.M.L.), Emory University School of Medicine, and the Nell Hodgson Woodruff School of Nursing, Emory University (J.K.F.) — both in Atlanta.

As growing numbers of Americans use federally unregulated cannabis products and develop complications — such as psychosis, cannabis use disorder, and electronic-cigarette, or vaping, product use–associated lung injury (EVALI) — the need to facilitate research on the products that our patients purchase from dispensaries is becoming increasingly pressing. Patients in our clinics routinely report using vape pens, dabs, waxes, edibles, and oils purporting to contain various concentrations of cannabinoids such as cannabidiol (CBD) and tetrahydrocannabinol (THC). Physicians register patients to obtain medicinal cannabis, counsel them on safe use of cannabis products, and monitor them for side effects of such products, yet they don't have access to reliable evidence on the effects of the products that patients are using.

Currently, if researchers plan to conduct clinical trials using cannabis, they must first seek separate approvals from the Food and Drug Administration (FDA) and the Drug Enforcement Administration (DEA).¹ Navigating this process can take a year or more. Once federal approval is granted, investigators can study cannabis obtained from only one government-authorized farm at the University of Mississippi, which contracts with the National Institute on Drug Abuse (NIDA) to cultivate cannabis for research purposes. The cannabis produced by this farm doesn't reflect the wide variety of products and cannabinoid formulations that patients obtain from commercial dispensaries. What's more, a lawsuit filed against the DEA alleged that the University of Mississippi product was contaminated with mold and of inconsistent quality. This lack of variety and alleged poor product quality limits the generalizability of potential findings from clinical trials.

The challenges associated with conducting high-quality research on cannabis were highlighted during a U.S. House Committee on Energy and Commerce Subcommittee on Health hearing on cannabis policy on January 15, 2020. In her opening statement, Representative Anna Eshoo (D-CA) described the “Catch-22” facing cannabis researchers: investigators cannot conduct research on cannabis until they demonstrate that it has medical use, and they cannot show that it has medical use until they conduct research.²

This dilemma was underscored by witnesses from federal agencies who testified before the House subcommittee. To date, 33 states and Washington, D.C., have legalized cannabis for

medicinal use. Other states, predominantly in the Southeast, have laws allowing people with certain medical conditions such as cancer to possess products that contain CBD and low concentrations of THC. The majority of Americans now live in a state where use of marijuana for medical or recreational purposes is legal, despite cannabis's designation as a Schedule I drug under the Controlled Substances Act, with no currently accepted medical use and a high potential for abuse.

In an August 2019 letter, NIH Director Francis Collins and then-Acting Commissioner of Food and Drugs Norman Sharpless emphasized the need to federally license additional entities to supply cannabis products. They added that both the NIH and the FDA support enabling researchers who hold a Schedule I license to study cannabis to obtain products from state-sanctioned dispensaries.³ Their recommendations, however, have not resulted in proposed legislation that would support researchers who want to conduct clinical trials using products obtained from dispensaries.

In the meantime, researchers from Yale University have circum-vented the process of obtaining cannabis from NIDA by forming a partnership with a Connecticut-based medical-marijuana producer and research firm to conduct clinical trials using plant-based cannabis. This firm, like other state-approved cannabis producers, is not licensed by the DEA to produce cannabis; however, the FDA approved a phase 1 clinical trial using its product, thereby paving a path forward for research involving commercial cannabis. Participants in this phase 1 trial obtain their cannabis directly from a designated dispensary, since researchers cannot legally purchase cannabis products from dispensaries, even with nonfederal funds. Whether research conducted in this manner can legally advance to phase 2 or 3 trials in the United States remains unknown.

Although Congress has yet to pass legislation advancing research on commercially available strains of cannabis, one proposed measure — the Medical Cannabis Research Act of 2019 — would increase the number of federally registered manufacturers allowed to supply cannabis for research purposes. This bill, a version of which was initially introduced in 2016, addresses the “overly burdensome registration process, redundant protocol reviews, lack of adequate research material and unnecessarily onerous security requirements”⁴ related to cannabis research. Although the DEA announced in 2016 that it would accept applications from additional growers intending to produce and distribute cannabis for research purposes, applications were stalled until 2019 when the DEA said it would instead propose new regulations for potential growers. These regulations have now been posted and are open for public comment until May 22, 2020 (www.federalregister.gov/documents/2020/03/23/2020-05796/controls-to-enhance-the-cultivation-of-marihuana-for-research-in-the-united-states). NIDA also recently invited input from the scientific community for establishing a standard THC dose for research purposes.

The state of cannabis research policy in 2020 resembles that of the previous decade: there is still only a single grower officially allowed by the DEA to produce cannabis for research purposes, and researchers lack appropriate access to commercially available products for clinical trials. We believe that it is important to facilitate research on cannabis products that patients are currently using in order to mitigate potential harms. To expedite such research,

we recommend two policy changes. First, in states where medical or recreational cannabis is legal, the federal government could accept applications from academic institutions for Schedule I licenses pertaining only to cannabis research. We believe that this measure is needed because the current process required for an individual investigator to become authorized to study cannabis is too burdensome. This burden could be alleviated quickly, and allowing multiple investigators to work under a single institutional license would increase the amount and quality of cannabis-related research. The government could take this step without removing appropriate controls on cannabis access and distribution.

Second, academic institutions with a Schedule I license could be broadly permitted to contract with state-sanctioned dispensaries and manufacturers to investigate products that are sold to patients. Building an infrastructure in which federal agencies regulate the quality of commercially available products could take years. Instead, we propose that close ties be established between state-sanctioned dispensaries and academic institutions. Such partnerships would ideally require manufacturers to ensure a consistent product with adequate supply for trials.

There are myriad potential clinical trials that could be conducted using cannabis products found in commercial dispensaries. Our observations from clinical practice suggest that one type of trial could assess the benefits and harms of THC oils when used for treating spasticity related to multiple sclerosis. Another could compare the effects of various strains of vaporized cannabis on chemotherapy-induced nausea and vomiting while also investigating the potential for respiratory complications in people with cancer. Finally, the effects of edible cannabis products on opioid craving in patients with opioid use disorder could be studied.

Many clinician-investigators see their patients use state-sanctioned cannabis products and bear witness to both the benefits and potential harms of such products. Although the campaign for rigorous research involving clinical trials of commercial products is moving in the right direction, progress has been slow. In the meantime, our patients continue to use various state-sanctioned cannabis products marketed as medicines in the absence of evidence to support their benefits or define their harms. We believe that the federal government should create prompt and practical ways for investigators to study the products that patients are using. We cannot wait for another public health disaster like the EVALI outbreak to push us forward.

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