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## The Implications of Marijuana Legalization in Colorado

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**The legalization of marijuana** in Colorado has had complex effects on the health of its citizens. Physicians have the responsibility to present a balanced perspective, identifying both the potential health benefits and risks associated with marijuana use. In this Viewpoint, we discuss the history of marijuana policy in Colorado and the expected and unexpected effects of increased marijuana availability. Other states considering marijuana policy liberalization may learn from the experiences in Colorado.

### History of Colorado Marijuana Policy

In November 2000, the Colorado state constitution was amended to allow for the use of medical marijuana by patients with “chronic debilitating medical conditions.”<sup>1</sup> Few patients used medical marijuana until October 2009, when the US Attorney General distributed guidelines for federal prosecution of the possession and use of marijuana, ceding jurisdiction of marijuana law enforcement to state governments. The combination of permissive local law and the federal policy change effectively liberalized the sale and use of medical marijuana in Colorado. Anyone with one of the conditions outlined by Colorado law could be issued a medical marijuana license with no expiration date. The number of licenses increased from 4819 on December 30, 2008, to 116 287 on September 30, 2014.

In November 2012, Amendment 64, which legalized the retail sale, purchase, and possession of marijuana for state residents and visitors older than 21 years, was approved by 55% of voters. During the following year, the state legislature appointed policy advisors to

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determine a tax structure, outline dispensary regulations, and determine the public health implications of the legalization. Retail marijuana stores began sales to consumers on January 1, 2014. Medical and retail marijuana products are the same, although regulations vary between the 2 marketplaces. For example, there is no minimum age restriction, and only state residents can legally buy medical marijuana in Colorado. As of November 3, 2014, 497 medical marijuana dispensaries and 292 retail dispensaries were licensed in Colorado.<sup>2</sup>

## Expected Health System Effects of Legalization

Increased availability led to increased health care utilization related to marijuana exposure.<sup>3</sup> Exacerbation of chronic health conditions was expected. Tetrahydrocannabinol (THC) is associated with psychosis, anxiety, and depression symptoms, making exacerbation of underlying psychiatric disorders inevitable. However, it is difficult to fully quantify the scope of this increased health care utilization because marijuana use is often coincident with other behaviors that contribute to health care visits. For example, the combination of marijuana plus ethanol increases the risk of motor vehicle collisions more than either substance alone. Serum THC concentrations are not readily available, so assessing causality is difficult.

However, there has been an increase in visits for pure marijuana intoxication. These were previously a rare occurrence, but even this increase is difficult to quantify. Patients may present to emergency departments (EDs) with anxiety, panic attacks, public intoxication, vomiting, or other nonspecific symptoms precipitated by marijuana use. The University of Colorado ED sees approximately 2000 patients per week; each week, an estimated 1 to 2 patients present solely for marijuana intoxication and another 10 to 15 for marijuana-associated illnesses.

## Medical Marijuana Use

Patients with some seizure disorders may benefit from the cannabidiol component in marijuana, and several clinical trials will soon enroll patients (NCT02224690, NCT02224560, NCT02224703, NCT02091375, NCT02224573). Marijuana likely has anti-inflammatory effects<sup>4</sup> and may benefit some patients with inflammatory bowel disease.<sup>5</sup> Marijuana may have a safer therapeutic window than opioids for pain control, and an observational study found fewer opioid-related deaths in states with liberal marijuana laws.<sup>6</sup> However, it is unlikely that marijuana is effective for the wide range of health problems approved under Colorado law.<sup>1</sup>

Legalization of marijuana has increased opportunities for clinician scientists to study the positive health effects of marijuana due to increased availability; however, federal designation of marijuana as a Schedule I drug continues to limit investigators' ability to conduct high-quality, nationally funded clinical trials. The use of medical marijuana for a wide range of disorders is inconsistent with the science supporting its effectiveness, highlighting the need for high-quality research.

## Unexpected Health System Effects of Legalization

Experimentation with new ways to use and produce THC products has resulted in unexpected health effects, including an increased prevalence of burns, cyclic vomiting syndrome, and health care visits due to ingestion of edible products.

The University of Colorado burn center has experienced a substantial increase in the number of marijuana-related burns. In the past 2 years, the burn center has had 31 admissions for marijuana-related burns; some cases involve more than 70% of body surface area and 21 required skin grafting. The majority of these were flash burns that occurred during THC extraction from marijuana plants using butane as a solvent.

The frequent use of high THC concentration products can lead to a cyclic vomiting syndrome. Patients present with severe abdominal pain, vomiting, and diaphoresis; they often report relief with hot showers. A small study at 2 Denver-area hospitals revealed an increase in cyclic vomiting presentations from 41 per 113 262 ED visits to 87 per 125 095 ED visits (prevalence ratio, 1.92) after medical marijuana liberalization (A. A. Monte, MD, unpublished data, December 2014).

The most concerning health effects have been among children. The number of children evaluated in the ED for unintentional marijuana ingestion at the Children's Hospital of Colorado increased from 0 in the 5 years preceding liberalization to 14 in the 2 years after medical liberalization.<sup>3</sup> This number has increased further since legalization; as of September 2014, 14 children had been admitted to the hospital this year, and 7 of these were admitted to the intensive care unit. The vast majority of intensive care admissions were related to ingestion of edible THC products.

## Challenges of Edible Marijuana Products

Edible products are responsible for the majority of health care visits due to marijuana intoxication for all ages. This is likely due to failure of adult users to appreciate the delayed effects of ingestion compared with inhalation. Prolonged absorption complicates dosing, manufacturing inconsistencies lead to dose variability, and the appealing product forms lead to unintentional ingestion by children.

Smoking marijuana results in clinical effects within 10 minutes, peak blood concentrations occur between 30 and 90 minutes, and clearance is complete within 4 hours of inhalation.<sup>7</sup> Oral THC does not reach significant blood concentration until at least 30 minutes, with a peak at approximately 3 hours, and clearance approximately 12 hours after ingestion.<sup>7</sup>

Ten to 30 mg of THC is recommended for intoxication depending on the experience of the user; each package, whether it is a single cookie or a package of gummy bears, theoretically contains 100 mg of THC. Because many find it difficult to eat a tenth of a cookie, unintentional overdosing is common. Furthermore, manufacturing practices for marijuana edible products are not standardized. This results in edible products with inconsistent THC concentrations, further complicating dosing for users. According to a report in the *Denver*

*Post*, products described as containing 100 mg of THC actually contained from 0 to 146 mg of THC.<sup>8</sup>

Initially, nonmedical edible products were required to be sold in a childproof package, although medical marijuana did not have this requirement. Childproof packaging requirements are now consistent across both retail and medical products, but there is no dosing recommendation for medical marijuana. To complicate matters further, the packaging is inconsistently effective and not applied to a dosing unit. This means that a product may be sold in a childproof container, but once the package is opened, the product is readily accessible to children. Although ingestion of 100 mg of THC in an adult may result in delirium or severe physiologic impairment, this dose is unlikely to cause respiratory arrest, which may occur in children at this dose.

Edible or capsule formulations may be a preferable route of administration when compared with inhalation for individuals with legitimate medical indications for the drug. However, there is no reason these products should be packaged in a manner that is appealing to children or makes them easily confused with nonmarijuana products. Furthermore, the concentration of THC must be systematically measured and reported. No one would tolerate a medication that contained a variable amount of the active ingredient. Standardizing the production and premarket testing of edible products may help limit inadvertent overdoses.

## Conclusions

While many users feel they have benefited from marijuana legalization in Colorado, there have also been untoward adverse health effects. The risks of use must be consistently communicated through health care practitioners and public health officials, especially for edible products that pose unique risks for exposed adults and children. Ultimately, additional research is needed to quantify the benefits and risks of marijuana utilization so health care professionals can have well-informed discussions with medical and recreational users.

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