RICE UNIVERSITY'S BAKER INSTITUTE FOR PUBLIC POLICY

REPORT 04.15.19

Marijuana as Medicine

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INTRODUCTION

Thirty-four states have laws permiting the use of marijuana—properly called cannabis—for specified medical purposes. Currently more than half the U.S. population has access to marijuana for medical use, and an estimated 2.6 million people are using it for relief.[1] States differ in stipulating what medical cannabis is, who can use it, and how they can get it. Most states with legal medical cannabis authorize licensed dispensaries. States that do not have dispensaries—as well as many that do—allow patients to grow their own marijuana plants.

A June 2018 University of Texas/Texas Tribune poll indicated that 53 percent of Texans would legalize it for any purpose, at least in small amounts, and 31 percent would legalize it for medical purposes only. Only 16 percent say marijuana should remain illegal under any circumstance.[2]

In the summer of 2018, both major Texas political parties passed by overwhelming majorities platform planks that reflect these views. The Republican version calls on legislators "to allow doctors to determine the appropriate use of cannabis to certified patients" and its Democratic counterpart urges "the immediate legalization of medical cannabis use."[3]

Texas legislators have heard the call and are considering 64 cannabis bills in the current session, 17 dealing only with medical cannabis, so many that Rep. Senfronia Thompson, D-Houston, chairwoman of the Public Health Committee, has created a Subcommittee on Medical Marijuana just to deal with these bills.

Several of these bills follow a recent trend of laws that allow for access to strains of marijuana that are high in CBD, the nonpsychoactive compound touted for its medical properties, but with little or no THC, the component that causes the "high." These laws have attracted support, particularly in southern states, because they are seen as a way to provide patients with some of the main medicinal qualities of the marijuana plant but without any psychoactive effects. As one observer put it, "They don't mind if you take medicine, as long as it doesn't make you happy." A key drawback of CBD-only laws is that they typically place strict limits on the number and types of qualifying medical conditions. In 2015, Texas passed the Compassionate Use Act (CUA), which allows Texans with intractable epilepsy to access low-THC (less than .5 percent) CBD oil, but that law has been criticized for its narrow scope (see below). Several bills introduced this session are attempts to expand the CUA. The two drawing most attention are House Bill 1365,[4] authored by Rep. Eddie Lucio III, D-Brownsville, and Senate Bill 90,[5] authored by Sen. José Menéndez, D-San Antonio. Though differing in some respects, both add substantially to the number of diseases or conditions that qualify for treatment, remove the cap on the amount of THC than can be legally dispensed or possessed, and provide detailed regulation of dispensaries and testing facilities, and myriad other details that are necessary parts of the lawmaking process.

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THE ENDOCANNABINOID SYSTEM

The chemical structure of cocaine, derived from the coca plant, was understood and described in the 1890s; that of morphine, derived from opium, came in the 1920s. The first serious attempt to analyze the structure and components of cannabis did not begin until the early 1960s, when Dr. Raphael Mechoulam, then an organic chemist at the Weizmann Institute of Science in Rehovot, Israel, applied to the U.S. National Institutes of Health for a grant to isolate and identify the psychoactive component of the marijuana plant. That first attempt was rejected, with the explanation that marijuana was used mostly in Mexico and South America and was not a problem in the United States. A year later, as the buds of the 1960s began to flower in profusion, the NIH called back, beginning decades of support that would enable Mechoulam to gain the unofficial title of "Father of Cannabis Research." More than 50 years later, at age 88, he is still on the case and under his leadership Israel has been called "The Holy Land of Medical Marijuana," attracting a concentration of cannabis research and top-level researchers unmatched anywhere else in the world.[6]

In fewer than five years, Mechoulam and his colleagues isolated many of the more than 100 of the plant's components, which they dubbed "cannabinoids" after marijuana's scientific name, Cannabis sativa. The most notable of these was Delta-9-Tetrahydrocannabinol (THC), responsible for the "high" that made marijuana famous. The other headliner, currently drawing even more public attention, was cannabidiol (CBD), a substance capable of controlling or reducing inflammation, anxiety, epileptic seizures, and pain, among numerous other known or plausible beneficial effects.[7]

Two decades later, Mechoulam's team gained a breakthrough understanding of how and why cannabinoids do their work. In 1988 came evidence that a type of cannabinoid receptor (CB1) exists in the brain and throughout the central nervous system, ready for the appropriate cannabinoid to bind with it to produce its effect. As Mechoulam put it, "We assumed that a cannabinoid receptor is not formed in the brain for the sake of a plant constituent."[8] Therefore, they inferred and through careful experimentation demonstrated that the human body produces its own (endogenous) cannabinoids, molecules that act as "ligands" (from the Latin *legere*, to bind) that activate and bind to appropriate bimolecular receptors to produce physiological effects. They called this happy bond anandamide, from the Sanskrit word for "bliss" or "supreme joy." Less spiritually, the scientific literature often uses images of a key (the "endocannabinoid") and a lock (the CB receptor) or a bullet and a target.

Five years later (1993), a second receptor (CB2), different from the one in the brain and central nervous system, was found throughout the immune and gastrointestinal systems. In 1995, the Mechoulam team reported a new endocannabinoid, 2-arachidonoyl glycerol (2-AG), similar to anandamide. Over the past quarter century, they have identified at least 100 others.

Together, these receptors and cannabinoids constitute the "endocannabinoid system" (ECS). Though much is still to be learned, a key reason the ECS exists is to maintain homeostasis—keeping things on an even keel by offering relief from pain, reduction of inflammation, control of nausea, uplift from depression and anxiety, and preventing, moderating, or curing some diseases. As one article put it, "Essentially every physiological system identified in our bodies is in some way modulated by eCBs [endocannabinoids]."[9] The Scientist, the Canadian magazine for life science professionals, put it more breezily: "Your Body is Teeming with Weed Receptors."[10] When the endogenous system is not strong enough to handle such tasks on its own, the use of exogenous cannabinoids—extracted from cannabis plants or produced synthetically—can bind with CB1 or CB2 to help restore order.

Not surprisingly, pharmaceutical companies have sought to meet these needs by producing synthetic chemical equivalents of key cannabinoids or "limited editions" of extracts from cannabis plants. Prominent examples include dronabinol (trade name Marinol), a synthetic THC developed to control nausea produced by

chemotherapy. Its popularity has been limited because it lacks CBD and other chemicals that modulate the unpleasant effects of the "high." Nabiximols (trade name Sativex), produced by the UK company GW Pharmaceuticals, combines THC and CBD extracted from cannabis plants in a 1-to-1 ratio, and works to reduce neuropathic pain, spasticity, and other symptoms of multiple sclerosis and related conditions. Sativex has been moderately well received in Canada and most European countries, but is not available legally in the United States. Mechoulam places greater confidence in what he calls the "Entourage Effect"—the many components of this complex plant work better together than in isolation of only one or two ingredients.[11]

Increased understanding of the ECS has generated an explosion of research by thousands of scientists striving to learn more about how it works and the therapeutic possibilities offered by the cannabis plant and medicines that could mimic its processes. In fiscal year 2017, the NIH supported 330 projects totalling almost $140 million on cannabinoid research.[12] Inevitably, some efforts will prove more successful than others, and some will fail. A 2017 exhaustive review by an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine found "conclusive or substantial evidence that cannabis or cannabinoids are effective for the treatment of chronic pain in adults, nausea and vomiting related to cancer chemotherapy, and symptoms of spasticity associated with multiple sclerosis."[13] It also indicated potential benefits for a variety of other conditions and stressed the need for more and better quality research.

The 212-page January 2018 issue of *Neuropsychopharmacology Reviews*,[14] an official publication of the American College of Neuropsychopharmacology, comprised a series of articles summarizing current understanding of cannabis and cannabinoids and their medical potential. Among notable findings are the ability or likelihood of these interactions to reduce inflammation and cartilage degradation caused by rheumatoid and osteoarthritis, reduce the spasms of multiple sclerosis, and control or significantly ease neuropathic pain associated with migraines, diabetes, traumatic nerve injury, chemotherapy, and other conditions. Clearly, scientific research regarding cannabinoids is not being done to provide healthy 20-somethings with justification for using an alleged knee pain as a way to obtain legal pot. For additional proof of that, visit the website of the National Cancer Institute[15] for brief descriptions and links to hundreds of research investigations of the demonstrated or potential effects of cannabis and cannabinoids for cancer development and treatment, appetite stimulation, analgesia, anxiety, and sleep. Much of the research involves rodents or monkeys, but clinical studies and trials with humans, long blocked by the Food and Drug Administration (FDA), the National Institute on Drug Abuse (NIDA), and the Drug Enforcement Administration (DEA), are slowly becoming more common.

The justification for placing limits on cannabis research involves the Controlled Substances Act, passed by Congress in 1970, which placed various drugs into five categories, or "schedules," that ostensibly indicate their relative benefits and dangers as determined by the FDA and the DEA. Schedule I contains substances deemed to have "no currently accepted medical use in treatment in the United States" and "a high potential for abuse."[16] The list includes heroin, LSD, Ecstasy, Quaaludes, and cannabis.[17] Schedule II drugs, which have a high potential for abuse but also have recognized medical uses, include morphine, methadone, oxycodone, and fentanyl. Used to treat acute "breakthrough" pain, fentanyl is approximately 100 times more potent than morphine and is the major contributor to the deadly spike in overdose deaths in recent years. *No one has ever died from an overdose of marijuana.* Inexplicably, dronabinol (Marinol), the synthetic form of THC, the component most vilified by marijuana's critics, is in Schedule III, deemed to have moderate potential for abuse and dependence, but less dangerous than drugs in Schedules I and II.

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To claim that cannabis poses more of a threat than heroin or oxycodone or fentanyl defies reason. Given the voluminous and growing evidence that cannabis has substantial medicinal benefits and is "accepted medical treatment" in Israel, Canada, and several countries in both Western and Eastern Europe and South America, how can federal agencies continue to assert that cannabis has no medical use?[18] The answer is maddening: because those same agencies have for years refused to permit the scientific research needed to prove that it does or might have such use. Obtaining a government grant to fund research into the possible benefits of cannabis requires FDA approval, which is extremely difficult to get. And if permission is granted, the cannabis used for such research must come from the DEA-licensed and federally run farm on the campus of the University of Mississippi. Access to the Ole Miss pot farm is controlled by the National Institute on Drug Abuse (NIDA), which rarely shares its stash with anyone interested in finding beneficial uses for cannabis. The American Medical Association, the American College of Physicians, the Institute of Medicine, and a host of other medical and scientific groups in this country and internationally have called for more research into the therapeutic benefits of cannabis. NIDA has consistently declined to participate. As one spokesperson put it, "Our focus is primarily on the negative consequences of marijuana use. We generally do not fund research focused on the potential beneficial medical effects of marijuana." Some softening of that restriction has occurred quite recently, but the general policy appears still to stand.

PROVEN OR PROMISING RESULTS

For a better appreciation of marijuana's proven or promising therapeutic potential, consider four conditions of interest to Texans, many of whom have lobbied legislators and testified before committees in recent sessions.

Intractable Epilepsy

Millions of people have watched CNN's Dr. Sanjay Gupta as he evolved from a critic of cannabis to an ardent believer in its therapeutic value. The turning point for Gupta, and for hundreds of thousands who watched his August 2013 special,[19] came when he tracked the story of Charlotte Figi, a 5-year-old girl burdened from shortly after her birth with Dravet's Syndrome, an extreme form of epilepsy that was producing 300 seizures a week, at least two every hour. After available pharmaceutical options failed and doctors recommended putting her into a coma to let her brain and body rest lest the seizures finally kill her, the Figis agreed to try a cannabis solution that was 21 percent CBD and less than 1 percent THC. The results were immediate and seemed miraculous. After the first dose, placed under her tongue, Charlotte had no seizures for three days. She was soon down to one seizure per week. When Gupta met her three months later, she was walking, talking, riding a horse, and riding a bike on her own. Forty-one other children in Colorado were using the solution, produced by the Stanley Brothers farm and called Charlotte's Web. All were reporting far fewer seizures. Soon, families were moving to Colorado from states where legal cannabis is not available to them. As noted earlier, in 2015 the legislature passed the Texas Compassionate Use Act, which authorized production of a CBD oil, trade name Epidiolex, to treat only one condition, intractable epilepsy, with Dravet's Syndrome the primary example. That restriction was tightened even further by requiring that patients must first establish that at least two FDA-approved drugs have failed to control their condition, then convince two of 18 neurologists certified by the state to give them a prescription that can be filled in only three dispensaries in the state, one in Schulenburg and two in Austin,[20] none in the 576 miles between Austin and El Paso. This is a feeble effort to ease the suffering of an estimated 160,000 Texans with intractable epilepsy, of whom fewer than 600 have jumped through the hoops to receive the medicine they need. Both HB 1365 and SB 90 will greatly improve these regulations.

Post-traumatic Stress Disorder

Cannabis offers—and according to abundant anecdotal testimony, delivers—substantial relief to people suffering from post-traumatic stress disorder. PTSD can be triggered by exposure to actual or threatened death, serious injury, or sexual violation. Symptoms include re-experiencing the event through flashbacks or nightmares, insomnia, depression, the inability to talk about the memories, estrangement and isolation from family and friends, self-blame, irritability, anxiety, fear, hypervigilance, anger, aggression, and reckless or self-destructive behavior. A variety of experiences—rape, fires, floods, and other traumatizing events—can give rise to PTSD, but none is more likely to produce its symptoms than war. One tragic consequence has been the alarming number of veterans who have taken their own lives, at a rate estimated to be more than 20 per day. Polls have found that more than 40 percent of Iraq and Afghanistan veterans display signs of mental and emotional health problems characteristic of PTSD, often made worse by chronic pain. A 2013 Veterans Administration report said that more than 300,000 veterans of those two wars had sought treatment for PTSD in VA hospitals and Vet Centers. The typical treatment options include opioid painkillers, antidepressants, and sleeping pills, which veterans known to the authors say were "handed out like Skittles," turning them into "pilled-up zombies." In varied ways, sizable numbers of veterans began to find relief from smoking cannabis, many coming to find it not a gateway to using more dangerous illicit substances, but an exit route from serious overuse of alcohol and prescription drugs. Despite the risk it involved, they began to share their stories and press for legal access to their drug of choice.

Despite being the ideal institution to conduct research on the potential of cannabis to help with PTSD, given its access to veterans suffering from it, the VA declined to do so. That decision drew a scathing response from the 2 million member American Legion, which claimed 92 percent of veteran households favored such research, but the VA stood firm, explaining that it could not conduct research with an illegal substance or even refer veterans to research projects. In fact, before 2010, veterans would lose their right to VA health services if they were found to be using any illegal substance, including marijuana, and VA physicians were not allowed even to discuss cannabis with their patients. That year, at the urging of groups such as Veterans for Medical Cannabis Access, the VA issued a directive that vets who are registered patients in a state-sanctioned medical marijuana program can continue marijuana use without losing access to VA treatment or other benefits. In states like Texas that do not allow medical marijuana, vets are out of luck.[21]

In March 2015, the FDA, DEA, and NIDA agreed, after long deliberation, to allow and provide cannabis for a "gold-standard" randomized controlled trial of whole plant cannabis as a treatment for PTSD symptoms. The study was funded by a $2.156 million grant from the Colorado Department of Public Health and Education to the Multidisciplinary Association for Psychedelic Studies (MAPS) and led by Sue Sisley, M.D. Despite state funding and federal authorization, approval, and oversight, the Ole Miss farm took two years to provide Sisley with the requested drugs, and what she eventually received reminded her of "green talcum powder" and was considerably less potent than what veterans could obtain elsewhere, making it more difficult to extrapolate her findings beyond her study subjects. In addition, some samples were contaminated with mold. Rick Doblin, MAPS' director, said the episode "shows that NIDA is completely inadequate as a source of marijuana for drug development research. They're in no way capable of assuming the rights and responsibilities for handling a drug that we're hoping to be approved by the FDA as prescription medicine."[22] (The DEA said in 2016 that it would approve other qualified growers to produce cannabis for research purposes, but as of this date, that has not happened.) Sisley did, however, proceed with the study and the results will be reported later this year. Meanwhile, research on cannabis and PTSD proceeds without hindrance in Israel and

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cannabis is available to treat PTSD through medical marijuana programs in New Mexico, Oklahoma, Arkansas, and Louisiana, all four states surrounding Texas.

Texas Veterans for Medical Marijuana is an active force in lobbying for legal access to the plant that has helped vets find surcease from the horrors of war. As Maj. Dave Bass, one of the group's founders and effective advocates, observed, "When a guy has done four tours in Iraq, like some of our people, and been wounded in action, it's hard to look him in the eye and call him a slacker pothead."[23] To mobilize veterans and dramatize being denied the medicine they know has helped them instead of the pills provided by the VA, the group collected one empty pill bottle from 500 vets, placing a toy soldier in each one, along with a slip of paper that provided the name, branch, dates of service, and service-connected disabilities of each person. Dubbed Operation Trapped, these were displayed in custom-made cases at veterans' events and at the Capitol for a week during the 2016-17 Texas legislative session. In Operation Still Trapped, the campaign for the current session, the bottles are displayed in a wooden coffin made to resemble those common in the 1800s. Both efforts have drawn wide media coverage in Texas and nationally, leading more veterans to join their cause. The group also reached Gov. Greg Abbott, who acknowledged in a debate during the 2018 election campaign that he had been in "discussions with veterans [and others] who make a very strong, compelling case about the legalization of medical marijuana."[24]

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Autism

Another serious set of conditions with inadequate relief from existing medical treatments but abundant anecdotal testimony is autism—more properly autism spectrum disorder (ASD). The "core symptoms" include communication difficulties, social awkwardness, persistent difficulties with social communication, and restrictive, repetitive patterns of behavior, interests, or activities. Hypersensitivity to certain sounds is also common.[25]

Studies in the 1960s and 1970s estimated the prevalence of autism to be between 2 and 4 per 10,000 children. The rate currently published by the CDC is about 1 in 59, with boys outnumbering girls by 4 to 1.[26] Nearly 500,000 persons with autism live in Texas. There is general agreement that a significant factor in this astonishing apparent explosion is a widening of diagnostic criteria such that children now described as "on the spectrum" might have been seen as odd, "slow," or difficult to control in earlier decades, but there is no question that the prevalence of children (who eventually become adults) on the serious segment of the spectrum has greatly increased.

There is strong scientific consensus that vaccines do not cause ASD, and no vaccine exists to cure it. Antipsychotic drugs Abilify and Risperdal are given to autistic youth for "irritability" and are often prescribed for kids with tantrums, aggression, and self-injury behavior, but both carry "black box warnings" of devastating side effects, some fatal.[27]

Other pharmaceuticals, developed to treat other conditions but used "off label" may bring some improvement for a time, but there are currently no FDA-approved drugs for treating ASD's core symptoms.

Much of the research about ASD and cannabinoids has used dronabinol (synthetic THC) alone. Some has combined CBD as a way to inhibit or modulate intoxication, tachycardia, and other effects associated with THC while also increasing the overall efficacy—the entourage effect—but lacking the versatility of the whole plant.

Until recently, most research regarding cannabinoids and ASD has been preclinical (using animal but not human subjects). These have indicated a correlation between ASD and impairments of the ECS. New research, now conducted on humans, is clarifying that relationship. In 2018, Stanford University scientists reported finding significantly lower concentrations of blissful anandamide in 60 children with ASD than in a control group of 56 "neurotypical" children, all aged 3 to 12. This first clinical test to confirm the findings of animal studies "suggests that impaired anandamide signaling may be involved in the pathophysiology of ASD."[28] Even newer

(2019) research from Israeli researchers found that serum levels of the major endocannabinoid AEA and related compounds were significantly lower in 93 children with ASD than in a control group of 93 age- and gender-matched neurotypical children.[29]

Earlier preclinical research had already indicated that targeting various ECS deficiencies common to ASD with phytocannabinoids (derived from cannabis plants) shows encouraging potential for treating ASD in humans, in keeping with the anecdotal evidence.[30] A 2017 Chilean study using oral cannabis extracts found them to be "dramatically more effective than conventional medicines" for ASD patients and called for large randomized controlled trials. An Israeli study (January 2019) of data collected from 188 autistic patients treated with medical cannabis oil between 2015 and 2017 found substantial evidence of significant (30.1 percent) or moderate (53.7 percent) improvement in common symptoms of ASD.[32] A second Israeli study, of children with ASD receiving oral cannabis under the direction of their physicians, reported a notable reduction in typical symptoms in about two-thirds of the cases.[33] Worth mentioning is that the reported adverse side effects were mild sleepiness, reflux, and changes in appetite. No need for a black box warning.

In recent years, while federal agencies continue to thwart clinical studies in the U.S. that might confirm such research, uncounted but substantial numbers of parents have experimented with cannabis and found it to bring quicker and longer-lasting relief and improvement to their children than anything else they have tried. Despite the legal risk, many have formed advocacy organizations to publicize the need and implore their legislators to pass bills that will give their children legal access to cannabis. The most prominent and vigorous of these groups in Texas is Mothers Advocating Medical Marijuana for Autism—MAMMA USA, founded and led by Austinites Thalia Michelle and AmyLou Fawell, both of whom describe themselves as "Bible-believing, Pro Life, 2nd Amendment Conservative Republican *Voters*."[34]

Chronic Pain and Opioid Use Disorder

Less dramatic but of enormous importance in considering medical cannabis is its established ability to diminish pain. The Institute of Medicine has estimated that "more than 100 million Americans suffer from chronic pain." The aforementioned 2017 NAS review said that THC, CBD, and cannabinol (CBN), a third major component of cannabis, are all known to help relieve pain.[36]

Though often effective in dealing with chronic pain, cannabinoids alone are insufficient to handle acute pain such as that from surgery, burns, broken bones, or advanced cancer, but there is strong evidence that, used in combination with opioids, they can significantly reduce the amounts needed for acute pain and thereby lessen the chance of overdose.[37] Several studies have found that "when given access to cannabis, individuals currently using opioids for chronic pain decrease their use of opioids by 40–60 percent and report that they prefer cannabis to opioids," mentioning fewer side effects and a better quality of life.[38] Related to that finding, noted in the Summer 2017 issue of *Neuroscience Quarterly*, is that CBD can significantly reduce the consumption of alcohol and also the motivation to relapse and resume drinking.[39]

In addition to assisting patients and their families, legal medical cannabis can help states save money. Two studies by Ashley C. Bradford and W. David Bradford, a father-daughter research team at the University of Georgia, found that use of prescription opioids dropped by more than 3.7 million daily doses among Medicare D enrollees from 2007 to 2014 as patients substituted legal cannabis for FDA-approved prescription drugs. In a 2016 paper published in the journal Health Affairs, the authors estimated that if all states legalized medical cannabis, the savings to Medicare in 2014 would be ca. $468 million.[40] A 2018 paper in the Journal of the American Medical Association, Internal Medicine, examining Medicaid data, estimated that all-states medical legalization would produce national savings for fee-to-service Medicaid of ca. $1.01 billion; if Medicaid managed care were included, the estimated savings would be ca. $3.89 billion.[41]

FEARS AND FACTS

We favor prudent uses of medical cannabis that are supported by careful research, but we acknowledge and want to respond to some of the apprehensions and objections raised by opponents, skeptics, and even people simply worried about increased legal use of a long-maligned drug.

Medical Marijuana Laws and Adolescent Use

Increased marijuana use, especially among adolescents, is one of the primary concerns among opponents of medical marijuana reform. Medical marijuana laws (MMLs) could plausibly increase use rates in several ways: by increasing availability, especially if state law allows dispensaries to become commonplace; by labeling marijuana a medicine, thus increasing perceptions that it is a drug without risks; and by decreasing the stigma of marijuana use, thus signaling that it is acceptable behavior. These fears are exaggerated. Dispensaries are not allowed to sell to minors, and teens have consistently reported that pot was easy to obtain over the four decades of near-total prohibition. Emphasis on the medical use of marijuana could lead youth to perceive the drug as something for sick people rather than something to be consumed recreationally; and legalization could prompt schools, parents, the medical community, and the media to increase efforts to warn young people about the risks of marijuana use.

Using data from the CDC's Youth Risk Behavior Survey to compare marijuana use rates among high school students before and after the passage of MMLs in several states suggests that the overall impact on teen use so far is negligible or negative. In Nevada and Connecticut, current marijuana use among high-school students (defined as having smoked marijuana in the past 30 days) rose slightly in the first year or two after medical legalization began, then dropped to levels significantly below where the rates had been before the change. In Arizona, Maryland, Massachusetts, New Hampshire, Rhode Island, and Vermont, teen use rates have remained stable or declined since the implementation of medical marijuana programs.[42]

Peer-reviewed studies of the relationship between MMLs and use report mixed findings depending on variations in study designs, such as survey data used, years examined, and states included in the analysis. A well-designed study funded by NIDA and using data from Monitoring the Future, an annual survey of roughly 50,000 high school students, compared adolescent (8th, 10th, and 12th graders) marijuana use and attitudes toward marijuana in states that had legalized medical use and those that had not. Looking at survey data over a 24-year period (1991–2014), the authors found that adolescent use did not increase in states that passed MMLs. Adolescent use was higher in states that had passed MMLs compared to those that had not, but the differences were present before the laws were passed, suggesting that they should not be attributed to the changes in the laws. Among 8th graders, marijuana use decreased and its perceived harmfulness increased in states that passed MMLs. The authors hypothesize that this decline could be due to increased media attention to the harms of marijuana use and increased efforts by parents to warn young teens about these risks.[43]

In contrast to these findings, a study using data from the National Survey on Drug Use and Health (NSDUH), a nationwide annual survey of approximately 70,000 people ages 12 and older, for the time period 2004–2012 found that implementation of MMLs was "associated with a 4.72 percent increase in the probability that young adults perceived no or low health risk related to marijuana use."[44] Another study that relied on the NSDUH found that state adoption of MMLs was associated with an increase in past-month marijuana use among 12- to 17-year-olds in those states between 2004 and 2011.[45] They also found, however, that MMLs did not impact adolescent use of other illicit drugs. Greater alcohol use, however, was associated with higher use rates of both marijuana and other illicit drugs, highlighting the central role alcohol plays in other drug use behaviors.

Several studies have found that "when given access to cannabis, individuals currently using opioids for chronic pain decrease their use of opioids by 40–60 percent and report that they prefer cannabis to opioids."

Taken together, these findings make it difficult to draw firm conclusions about the relationship between MMLs and adolescent marijuana use. On balance, the data available so far suggest that factors other than implementation of MMLs have greater influence on whether teens use marijuana. Regardless of the relationship, the fact remains that adolescent marijuana use, especially when heavy and prolonged, can have significant adverse consequences and cannot be dismissed. Still, this is not a reason to deny access to medical marijuana for the millions of people who can benefit from it. Instead, states can and should take a long-term view of MMLs and implement them in such a way that addresses the needs of patients without encouraging use among adolescents and young adults. This may mean placing restrictions on medical marijuana programs, such as limiting the number of dispensaries or the amount of THC a product may contain (though not so low as to render the product ineffective), and increasing evidence-based public health campaigns to educate adolescents on the risks of marijuana use.

Marijuana Use and Adverse Health Effects

Like all drugs, marijuana carries some risks and side effects. Available evidence indicates that marijuana has fewer negative physiological effects than more common recreational drugs such as alcohol and tobacco, some adverse effects on short-term cognitive impairment, and potentially negative effects on some mental health outcomes, psychosis in particular.

The NAS review found limited to no evidence for an association between marijuana use and development of depression, anxiety, post-traumatic stress, or bipolar disorder. It did, however, find "substantial evidence of a statistical association between cannabis use and the development of schizophrenia or other psychoses, with the highest risk among the most frequent users."[46]

There is considerable evidence to suggest that marijuana, especially marijuana high in THC, can exacerbate schizophrenia. (In contrast, some studies have shown that marijuana rich in CBD can help alleviate some symptoms of schizophrenia.) Some researchers argue that heavy and early use can actually cause schizophrenia in people who would not have developed it otherwise. Critics of that claim have countered that researchers have not been able to rule out the possibility of a "shared vulnerability," by which people at risk for schizophrenia are also more likely to use marijuana while young, due to other mediating factors.[47] Regardless, people with schizophrenia or a history of psychotic episodes are a vulnerable population that should be discouraged from marijuana use. This can be achieved through increasing public awareness of the connection between psychosis and marijuana use, but it is not a reason to deny access to marijuana for the millions of Americans who do not have these vulnerabilities and would benefit from the plant's use.

Overall, cannabis is far safer than many widely advertised and used drugs. Listen carefully to the commercials for almost any drug touted on television, especially the words spoken swiftly at the end of the pitch. Or read the warnings that accompany the prescriptions you pick up at your trusted pharmacy. Or Google NSAIDs and discover they are responsible for thousands of deaths each year.[48] You might be frightened, but you are likely to take those drugs without much hesitation, deciding that the potential benefits outweigh the risks. Parents of children with Dravet's Syndrome or autism may know that cannabis poses a risk for brains not fully formed, but few would deny their children access to plant-derived medicine whose safety and efficacy are attested to by abundant anecdote, proven by scientific research, and sensibly regulated in legal regimes. Neither should the Texas Legislature, which by providing regulated and safe access to medical cannabis to people with demonstrated need can provided justified relief, help reduce the opioid epidemic, and save Texas millions of dollars.

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ENDNOTES

1. Marijuana Policy Project, Medical Marijuana Patient Numbers, December 3, 2018, http://bit.ly/2TUmwhH.

2. University of Texas/Texas Tribune Poll, June 2018, http://bit.ly/2TbiFIV .

3. Ibid. The Republican plank passed by 90 to 10 percent. The entire Democratic platform was accepted on a voice vote.

4. HB 1365 available at https://capitol.texas.gov/tlodocs/86R/billtext/html/HB01365I.htm.

5.SB 90 available at https://capitol.texas.gov/tlodocs/86R/billtext/html/SB00090I.htm.

6. See "The Holy Land of Medical Marijuana" at https://bit.ly/2o95kSF.

7. R. Gaoni and R. Mechoulam, "Isolation, Structure, and Partial Synthesis of an Active Constituent of Hashish," *Journal of the American Chemical Society*, 86, no. 8 (1964): 1646–1647. For Mechoulam's own brief survey of his career, see R. Mechoulam and Lumir Hanus, "Anandamide and More," in Julie Holland, ed., *The Pot Book—A Complete Guide to Cannabis* (Rochester, Vermont: Park Street Press, 2010), 63–72.

8. Mechoulam and Hanus, Anandamide, 70.

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10. See "Your body is teeming with weed receptors," http://bit.ly/2TY8vzC.

11. Entourage Effect, http://bit.ly/2UaVmnZ.

12. See NIH research on marijuana and cannabinoids at http://bit.ly/2HLSFBG.

13. See the National Academies' summary of a report on the health effects of cannabis and cannabinoids at https://bit.ly/2V2ojyJ.

14. See 2018 Neuropsychopharmacology Review at https://www.nature.com/collections/pgzvtchpmq.

15. See National Cancer Institute studies at http://bit.ly/2JmOEWV.

16. See a Scientific American account of how cannabis was put into Schedule I at http://bit.ly/2JxOhsC.

17. The chemical names are LSD–lysergic acid diethylamide; ecstasy–MDMA, or 4–methylenedioxymethamphetamine; Quaaludes–methaqualone.

18. See countries approving medical marijuana at http://bit.ly/2U6VLXx.

19. See a CNN special with Sanjay Gupta at https://www.youtube.com/watch?v=XUwkLiciY6Q.

20. Technically, one of the Austin-area dispensaries is in Manchaca, an unincorporated community ca. 10 miles southwest of downtown Austin.

21. These paragraphs draw heavily on William Martin, "War Without End," *Texas Monthly*, May 2014, http://bit.ly/2Y7zZSD.

22. Caleb Hellerman, "Scientists say the government's only pot farm has moldy samples," https://to.pbs.org/2FcCnyU.

23. Martin, "War Without End."

24. See http://bit.ly/2Yiqujt, in which Abbot is impressed by veterans.

25. For the core symptoms of autism, see http://www.researchautism.net/autism-issues/core-symptoms-of-autism.

26. See CDC autism data at https://www.cdc.gov/ncbddd/autism/data.html.

27. See side effects Abilify [aripiprazole] at http://bit.ly/2TSBMg2; side effects of Risperdal [risperidone] at https://wb.md/2FjbGJ1.

28. For more on lower anandamide in ASD children, see Karhson et al., Molecular Autism 9 (2018):18, https://doi.org/10.1186/s13229-018-0203-y.

29. For an Israeli study on lower EC levels, see http://bit.ly/2HTiDmG.

30. For more on the role of cannabinoids in ASD therapy, see http://bit.ly/2OdAN3Y.

31. For the Chilean study, see http://bit.ly/2Ol4gJ9.

32. For the Israeli study of 188 patients, see https://www.nature.com/articles/s41598-018-37570-y.

33. For more on parents administering oral drops to children, see http://bit.ly/2Yf6vT0.

34. We gratefully acknowledge being guided to some of this research by Mses. Michelle and Fawell and the MMAMMA's website, http://www.mammausa.org. Ms. Fawell's presentation at a Baker Institute

event can be viewed at https://www.bakerinstitute.org/videos/texas-ready-medical-marijuana/ beginning at ca. 51:00.

35. For more on the 100 million in chronic pain, see https://wb.md/2FsaDHW.

36. National Academies summary, https://bit.ly/2V2ojyJ.

37. "Legalizing Marijuana Decreases Fatal Opiate Overdoses, Study Shows," see https://bit.ly/2lWSasa.

38. For more on the role of cannabis in opioid use, see https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6135562/#B36.

39. "Inside Neuroscience: Tapping into the Cannabinoid System," http://bit.ly/2HIIFt8.

40. See Ashley and David Bradford Medicare study at http://bit.ly/2CyAVpX.

41. Ashley C. Bradford, et al., "Association Between U.S. State Medical Cannabis Laws and Opioid Prescribing in the Medicare Part D Population," *JAMA Internal Medicine*, 2018, DOI: 10.1001/jamainternmed.2018.0266.

42. Data for each these states regarding adolescent use after medical cannabis legalization can be found at https://nccd.cdc.gov/YouthOnline/App/Results.aspx?LID=NV. Filter data by using choices in top box, "Choose Table Content."

43. Deborah S. Hasin, et al., "Medical Marijuana Laws and Adolescent Marijuana Use in the USA from 1991 to 2014: Results from Annual, Repeated Cross-sectional Surveys," Lancet Psychiatry 2 (2015): 601-608.

44. Hefei Wen, Jason M. Hockenberry, and Benjamin G. Druss, "The Effect of Medical Marijuana Laws on Marijuana-Related Attitude and Perception among U.S. Adolescents and Young Adults," *Prevention Science* 20 (2019): 215-223.

45. Lisa Stolzenberg, Stewart J. D'Alessio, and Dustin Dariano, "The Effect of Medical Cannabis Laws on Juvenile Cannabis Use," *International Journal of Drug Policy* (2015): 1-8.

46. National Academies, https://bit.ly/2V2ojyJ.

47. Charles Ksir and Carl L. Hart, "Cannabis and Psychosis: A Critical Overview of the Relationship," *Current Psychiatry Report* 18 (2016): 1-12.

48. A commonly reported figure for NSAID deaths is 16,500 per year, but that is likely quite exaggerated (see http://bit.ly/2YiJQ8n), but there is consensus that the number is in the thousands.

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Cite as:
Martin, William and Katharine Harris Neill. 2019. *Marijuana as Medicine.* Baker Institute Report no. 04.15.19. Rice University's Baker Institute for Public Policy, Houston, Texas.