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WHY MARIJUANA **WILL NOT** FIX THE OPIOID EPIDEMIC

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Why Marijuana Will Not Fix the Opioid Epidemic

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MARIJUANA HAS BEEN USED for reported medical purposes for thousands of years when the plant at that time had THC content of 0.5-3%. Currently, the most common reported medical use is for pain. As of this writing there are 30 states and the District of Columbia have some form of legalized marijuana, with eight states having legalized for recreational use. The United States is currently in the grips of an opioid epidemic which has been growing over the last 20 years and began with “pain” being termed the “5th vital sign.” At the time, it was reported that people in pain did not become addicted to opioids, and the number of opioid prescriptions started to increase over time, followed by an increase in opioid overdose deaths.¹

There has been a lot of discussion about how the use of cannabis will help curb the opioid epidemic.² It has been reported that medical cannabis laws are associated with significantly lower opioid overdose mortality rates, and others have suggested that legalization may result in less opioid overdose deaths.³ Other studies have reported that medical marijuana laws were associated with a decrease in Medicare prescriptions, saving millions of dollars.⁴ The same authors followed up with another report suggesting that medical cannabis laws are associated with significant reductions in opioid prescribing in the Medicare Part D population.⁵ Cost savings in this day and age of health care is very important, but it was noted that “the researchers themselves cannot say if people switched from opioid prescriptions to using a medical marijuana product.” It is difficult to translate population-level analyses to individual marijuana-opioid substitutions, and this patient population is a rather small percentage



of people who may be using opioids and/or medical marijuana. In 2017 Colorado had a record number of opioid overdose deaths from any opioid, including heroin and Colorado has had a medical marijuana program since 2001.⁶

In the face of the opioid crisis, the medical providers should utilize other ways for people to avoid the use of opioids. Treatments such as physical therapy, acupuncture, chiropractic, massage, and cognitive-behavioral therapies are some of the standard treatments in the management of people with pain. Other naturopathic remedies have been suggested and tried but not proven.⁷

There is some evidence that there are components of the marijuana plant which may have therapeutic medical value.⁸ Cannabinoid and opioid receptors belong to the rhodopsin subfamily of G-protein-coupled receptors and are synergistic.⁹ Both are localized primarily at the presynaptic terminals and when activated, reduce cellular levels of cyclic adenosine monophosphate (cAMP) by inhibition of adenylyl cyclase,

which effects neurotransmission. Receptor activation of both also modifies the permeability of sodium, potassium, and calcium channels and receptors of both systems co-exist in the central nervous system, with overlapping distribution in the brain, brainstem, and spinal cord.¹⁰

Both receptors co-localize on GABAergic neurons with potential coupling to second messenger systems, and receptor stimulation can suppress inhibition, suppress excitation, as well as inhibit the release of several neurotransmitters, including L-glutamate, GABA, norepinephrine, serotonin, dopamine, and acetylcholine, therefore modulating pain pathways and potentially provide antinociception. Opioids and cannabinoids share pharmacologic profiles and both can cause sedation, hypotension, hypothermia, decreased intestinal motility, drug-reward enforcement, and antinociception.

There are several reasons as to why any reported benefit will be outstripped by lack of benefit and increased risk of harm, and why cannabis is contributing to ongoing opioid

use, and subsequently, the opioid epidemic. There is evidence in animal models showing adolescent rats exposed to THC will develop enhanced heroin self-administration as adults¹¹ which may be due to activation of mesolimbic transmission of dopamine by a common mu opioid receptor mechanism.^{11,12} More than 90% of heroin users report a prior history of marijuana use compared to a prior history of painkiller use (47%).¹³ Prospective twin studies demonstrated that early cannabis use was associated with an increased risk of other drug abuse.¹⁴ This particular study was conducted when the THC content was much lower than today's products which can reach 95% THC.

The currently accepted body of evidence supporting use of cannabis in pain consists of 28 studies comprised of 63 reports and 2,454 patients.¹⁵ Additional articles rely on this primary paper's misleading statement that "there is substantial evidence that cannabis is an effective treatment for chronic pain in adults."¹⁶ Both articles noted that products typically studied are not available in the United States (nabiximols, Sativex) or were with available synthetic agents (dronabinol, nabilone), and were studied in less common pain conditions: neuropathic and cancer pain. Currently there is no widely available or accepted medical literature showing any benefit for pain with dispensary cannabis in common pain conditions.¹⁷

Dispensary cannabis is a generic substance containing multiple components which may have physiologic activity in the body. The College of Family Physicians of Canada outlined potential prescribing guidelines of medical cannabinoids in primary care.¹⁸ They strongly recommended against use for acute pain, headache, osteoarthritis, and back pain, and also discouraged smoking.

There is currently a large and growing body of evidence showing that cannabis use increases, rather than decreases non-medical prescription opioid use and opioid use disorder, based on follow-up of more than 33,000 people.¹⁹ Concurrent use of cannabis and opioids by patients with chronic pain appears to indicate a higher risk of opioid misuse.²⁰ Closer monitoring for opioid-related aberrant behaviors is indicated in this group of patients and it suggests that cannabis use is a predictor of aberrant drug behaviors in patients receiving chronic opioid therapy.

Inhaled cannabis in patients with chronic low back pain does not reduce overall opioid use, and those patients are more likely to meet the criteria for substance abuse disorders, and are more likely to be non-adherent with their prescription opioids.²¹ It has been found that patients with chronic pain participating in an interdisciplinary pain rehabilitation program and using cannabis may be at higher risk for substance related negative outcomes, and were more likely to report a past history of illicit substance, alcohol, and tobacco use.²² A more recent study of 57,000 people showed that medical marijuana users are more likely to use prescription drugs medically and non-medically, and included pain relievers, stimulants, tranquilizers, and sedatives.²³ There is also evidence that states that medical marijuana laws lead to the probability people will make Social Security Disability claims.²⁴

There is sufficient and expanding evidence demonstrating that medical marijuana use will not curb the opioid epidemic. There is

further evidence that marijuana is a companion drug rather than substitution drug and that marijuana use may be contributing to the opioid epidemic rather than improving it. Although there are patients who have successfully weaned off their opioids and use marijuana instead, the evidence that marijuana will replace opioids is simply not there.

Medical provider and patient awareness, utilization of prescription drug monitoring programs, widespread availability and use of naloxone, and increasing coverage for atypical opioids and abuse deterrent formulations are only some of the other factors which hopefully will be contributing to any impact on the opioid crisis. Education and prevention efforts as well as medication assisted therapies will be additional benefits to impact the opioid epidemic. Physicians should continue to monitor their patients closely, perform random drug testing to detect opioid misuse or aberrant behavior, and intervene early with alternative therapies when possible. Marijuana alone is certainly not the answer. ■

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