

O’Shaughnessy’s

The Journal of Cannabis in Clinical Practice

Autumn 2018

Logical response to a public health emergency—

Cannabis enables pain patients to cut opiate use; Availability would reduce ER visits and OD deaths

By Dustin Sulak, DO

In the late 1990s, Purdue Pharmaceuticals aggressively marketed OxyCodone, advising physicians that their new semi-synthetic opioid was less addicting than true opiates such as codeine. Similar claims were made by other opioid manufacturers, including Johnson & Johnson/Janssen, Glaxo, and Abbott Laboratories.

Between 1999 and 2010, the sales of prescription opioids quadrupled—and so did the rate of opioid overdose deaths.

Enough opioids were prescribed in 2010 to give a one-month supply of five milligrams of hydrocodone (Vicodin, a semi-synthetic made by Abbot) every four hours to every adult in the U.S.

The epidemic that began largely in the doctor’s office could not be contained there.

By 2010, one in 20 Americans over the age of 12 had used an opioid medication non-medically, or used it other than as prescribed. The epidemic that began largely in the doctor’s office could not be contained there.

Heroin as a cause of opioid overdose began rising sharply in 2011. Nearly 80 percent of heroin users reported using prescription opioids before initiating heroin use.

The number of deaths involving fentanyl, a synthetic opioid, rose from 3,000 in 2013 to 20,000 in 2016.

In 2016 some 64,000 Americans died of drug overdose deaths—more than died during all the years of the Vietnam War. In 2017 the number had risen to 72,000—higher than deaths from car crashes.

US Americans account for five percent of the world’s population and consume 80 percent of the world’s opioids. We’re using opioids to such an extent that some countries have trouble accessing opioids for essential needs like post-surgical or end-of-life treatment. Even US hospitals are now reporting shortages of morphine and hydromorphone.

According to a 2014 report by Express Scripts, 50 percent of people who took prescription opioids for more than 30 days in their first year of use continued to use opioids for three years or longer. Half of them were being prescribed short-acting opioids such as Vicodin, which are most likely to lead to addiction and abuse. Nearly 60 percent of the patients were taking opioids in combination with drugs that are known to make opioids more dangerous and an overdose more likely.



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in Maine and Massachusetts.

Sulak has helped more than 18,000 patients use cannabis as medicine. He educates patients and fellow clinicians via the Healer.com website and frequent conference presentations. This article is based on talks given in response to the US opioid epidemic. (New England is one of the regions hardest hit.)

Despite the widespread prescribing of opioids for chronic pain, the evidence that opioids actually help with this condition is surprisingly weak. A review in the *Annals of Internal Medicine* in 2015 summarized, “Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain in function.”

The authors analyzed 34 studies on adults with chronic pain who had been using opioids for more than three months. They were unable to find a single study that assessed outcomes longer than one year of use related to pain, function, or quality of life!

They did, however, find increased risk of serious harm associated with long-term opioid use: overdose, abuse, fractures, heart attacks, and sexual dysfunction. And a high number of people using prescription opioids end up abusing heroin.

Finally recognizing this gap in the scientific literature, a study published in the *Journal of the American Medical Association* compared long-term opioid with non-opioid treatment (such as NSAIDs, antidepressants, neuroleptics) in 265 patients with chronic pain. Researchers found no significant difference in pain-related function over 12 months, but the pain intensity was significantly reduced in the non-opioid group. As expected, adverse medication-related symptoms were significantly more

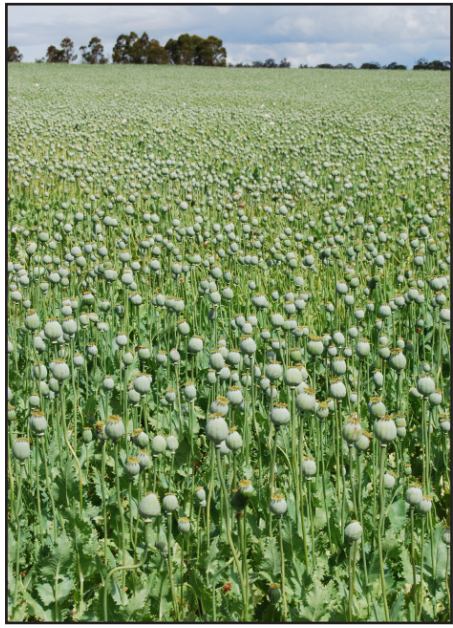


PAPAVER SOMNIFERUM (“the sleep-inducing poppy” in poster at left) produces opium in its seed pod. The milky opium may consist of four to 20 percent morphine and other pain-reducing alkaloids. Semisynthetic opioids contain small amounts of natural alkaloids.

common in the opioid group.

The doctors’ dilemma

We clinicians see people coming in with chronic pain, and we feel obligated to do something to help them. After patients fail respond to more conservative and often in-



POPPIES GROWN FOR MEDICAL USE IN TASMANIA by international agreement are bred so that thebaine, not morphine, is the dominant opioid. A Johnson & Johnson subsidiary, Tasmanian Alkaloids, was producing about half the world’s legal supply as of 2016.

effective treatments, most doctors turn to opioid medications because they’re out of alternatives—or so they think.

Thankfully, there is an alternative, an option that has been proven safe and effective in the treatment of chronic pain: cannabis.

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Even in ‘progressive’ California

Medical Boards’ Restrictive Practice Guidelines Challenged by Society of Cannabis Clinicians

By Fred Gardner

Physicians in the United States are licensed by state medical boards. Licenses can be suspended or revoked when a board deems physicians guilty of serious infractions.

Typically, members of a state medical board have been appointed to a two-year term by the governor. (Many have contributed money to the governor’s party.) They meet quarterly and vote on policy matters.

The board’s business is conducted by career bureaucrats and gun-carrying “peace officers” who investigate complaints against physicians. We, the people, count on them to identify and expel quacks, sexual predators, incompetents and profiteers—important, meaningful work.

Some infractions by physicians are gross and readily provable. Others are subtle and subject to interpretation, such as “failure to conduct a good-faith examination.” Physicians who approve cannabis use by patients have frequently been the target of medical board investigations in California and other states.

Being investigated is a costly, time-consuming process that involves hiring a lawyer. Zealous undercover investigators can frame physicians by feigning symptoms.

In 2015 an obscure but powerful bureaucratic entity called the Federation of State Medical Boards (FSMB) took aim at Cannabis Approving Doctors (CADs).

The FSMB, a non-profit that employs 80 people in Eulis, Texas, and six lobbyists in Washington, D.C., developed “model guidelines” that would trigger investigations of CADs based on how many patients

they authorize to use cannabis, the percentage of approvals issued to patients under age 30, and the number of plants they authorize patients to grow.

The FSMB also sought to prevent clinicians who approve use by patients from using cannabis as medicine themselves.

At the FSMB convention in San Diego in April 2016, delegates from all 50 states and 20 US Territories agreed unanimously that their medical boards should take steps to adopt the federation’s guidelines. Voting “aye” for the California board were Executive Director Kimberly Kirchmeyer and Howard Krauss, MD, a Los Angeles ophthalmologist who has never approved cannabis use by a patient.

FSMB president Humayun Chaudhry, DO and two co-authors then published an

“The use of medicinal cannabis is not prima facie evidence of impairment or abuse.”

—Stephen Robinson, MD

article entitled “Medical Board Expectations for Physicians Recommending Marijuana” in the prestigious *Journal of the American Medical Association (JAMA)*. Their “viewpoint” essay ran online June 16 and in the print edition August 9.

The Society of Cannabis Clinicians (SCC, a doctors’ group founded in 2000 by Tod Mikuriya, MD) urged the Medical Board of California (MBC) to reject the federation’s approach.

At a July 2016 meeting of the Califor-

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STEPHEN ROBINSON, MD, representing the Society of Cannabis Clinicians at a meeting of the Medical Board of California, warned that proposed “model guidelines” would lead to specialists being targeted by the board’s Enforcement Division and pressured to not use cannabis as medicine themselves. At right, board members Katherine Feinstein and Michael Bishop, MD.

Cannabis/Opioids from page 1

But most doctors don’t know about that option. They find themselves face-to-face with patients who say, “My pain is worse. The opioids aren’t working, I need more. If I don’t get them I’m not going to be able to go to work, I’m not going to be able to support my family, I’m not going to be able to function...” It’s hard for clinicians to say ‘no,’ because they don’t have another tool.

Cannabis can prevent opioid tolerance-building and the need for dose escalation. Cannabis can treat the symptoms of opioid withdrawal. And cannabis is safer than other harm-reduction options for people who are addicted to or dependent on opioids.

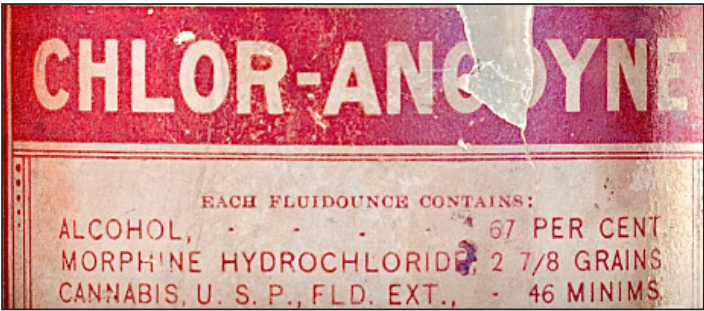
My goal is to carry the message that there is another tool. Cannabis can replace and reduce the dose of opioid medications needed to control pain. Cannabis can prevent opioid tolerance-building and the need for dose escalation. Cannabis can treat the symptoms of opioid withdrawal. And cannabis is safer than other harm-reduction options for people who are addicted to or dependent on opioids.

Randomized, placebo-controlled trials —RCTs, considered the gold-standard by medical scientists—show that cannabis can be used to treat chronic pain.

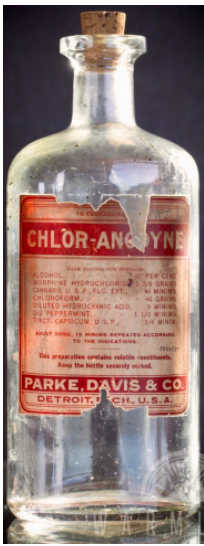
In contrast to the *Annals of Internal Medicine* article that found no evidence supporting the use of long-term opioids, a June 2015 review article by Mary Lynch and Mark Ware in the *Journal of Neuroimmune Pharmacology* evaluated 11 randomized clinical trials published in 2010-2014. “The quality of the trials was excellent,” they wrote. “Seven of the trials demonstrated a significant analgesic effect.

“Several trials also demonstrated improvement in secondary outcomes (e.g., sleep, muscle stiffness and spasticity). Adverse effects most frequently reported, such as fatigue and dizziness, were mild to moderate in severity and generally well tolerated. This review adds further sup-

Cannabinoid-opioid pharmaceutical



MANUFACTURED BY PARKE, DAVIS, Chlor-Anodyne was one of the most popular compound drugs of the 19th century. It combined morphine, cannabis, and capsicum, taking advantage of the interplay among our three receptor systems that control pain (endorphin, endocannabinoid, and vanilloid), and likely providing better outpatient pain relief than anything available in the pharmacy today.



port that currently available cannabinoids are safe, modestly effective analgesics that provide a reasonable therapeutic option in the management of chronic non-cancer pain.”

Seventeen of 10 animal studies had what Nielsen called an “opioid-sparing effect.”

Cannabinoid-Opioid Synergy

Cannabinoids and opioids have a few things in common. Both are derived from plants with thousands of years of historical medical use. Both mimic substances our bodies produce: endocannabinoids and endorphins. And both change the way we experience pain. Is there a basis for using these two classes of medication together?

Opioid and cannabinoid receptors are present in pain areas of the brain. (Receptors can be thought of as antennae or little keyholes. When an opioid or cannabinoid fits into its receptor, it has some effect on the cell, changing its physiology.)

Both opioid and cannabinoid receptors are also present in areas that influence addiction and reward-seeking behavior. Not only are the two receptor types co-localized in these nerve cells, they’ve been show to interact with each other, seemingly working together in the great symphony of our human physiology.

Pain medicines that combine cannabinoids and opioids to take advantage of these overlapping receptor system are, in fact, nothing new. One of the most popular compound drugs of the 19th century, Chlor-Anodyne combined morphine, cannabis, and capsicum, taking advantage of the interplay among our three receptor systems that control pain (endorphin, endocannabinoid, and vanilloid), and likely providing better outpatient pain relief than anything available in the pharmacy today,

Researchers using rodent models of pain have been demonstrating since the late 1990s that administering opioids and cannabinoids together results in a greater-than-additive anti-pain effect. A team at the Medical College of Virginia determined that a dose of 20 milligrams-per-kilogram-of-body-weight of either morphine or THC achieved 30 percent of the maximum possible pain-reducing effect. But the two drugs given together resulted in maximum pain reduction (100%). This demonstrated a synergy between opioids and cannabinoids, since 30 plus 30 equaled 100 in terms of pain relief. Using morphine alone, 100mg/kg dose was required for maximum relief.

In 2017 an Australian group led by Suzanne Nielsen published a meta-analysis of animal studies that examined the effects of cannabinoid-opioid co-administration. Seventeen of 19 studies demonstrated what Nielsen calls an “opioid-sparing effect.” When combined with THC, the effective dose of morphine was 3.6 times lower and the effective dose of codeine 9.5 times lower. But does this translate to the human experience?

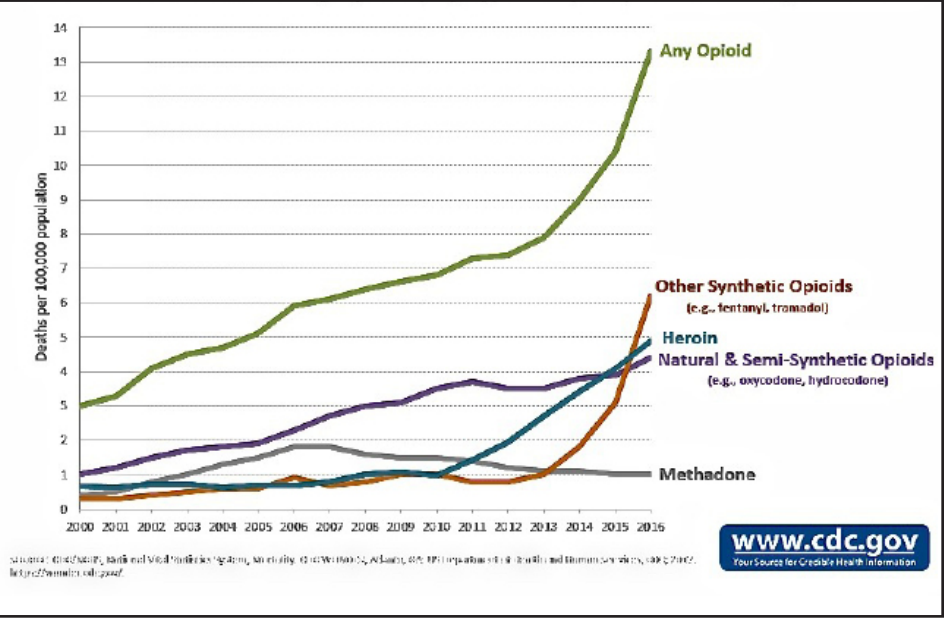
In a 2011 study, Donald Abrams, MD, added a low dose of vaporized cannabis to the regimen of 21 patients who were using high-dose opioids (ineffectively) to treat chronic pain in a hospital setting. The cannabis, provided by the National Institute on Drug Abuse, contained 3.56 percent THC —very low potency, given what’s available to US consumers.

Patients vaporizing three times daily reported a significant decrease in pain —27 percent. Perhaps more potent cannabis and/or a different delivery method would have led to even greater relief. Several subsequent studies have also demonstrated significant pain relief from adding cannabis in patients with chronic pain that is refractory to opioid drugs.

A 2018 study from Ziva Cooper, PhD, examined the pain-relieving effects of various combinations of cannabis (placebo or 5.6% THC delivered via a joint) and oxycodone (placebo, 2.5 mg, and 5 mg capsules) on healthy volunteers using the “cold pressor test.” (Subjects submerged their hand in ice water, rating the time until the onset of pain, the time until they could no longer tolerate the pain, and the intensity of the pain.) Cooper also evaluated whether cannabis increased the degree to which subjects liked the oxycodone and wanted to take it again.

Cooper’s findings confirm the extensive preclinical literature: administered alone, only the 5 mg dose of oxycodone increased pain threshold and tolerance compared to

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OPIOID OVERDOSES AS A CAUSE OF DEATH BETWEEN 2000 AND 2016 rose from five per 100,000 Americans abpve age 12 to more than 13 per 100,000. In 2011 prescription opioids (natural and semi-synthetic) were responsible for more than twice as many deaths as heroin and fentanyl combined. By 2015 heroin and fentanyl each exeeded prescription opioids as the cause of OD fatalities.

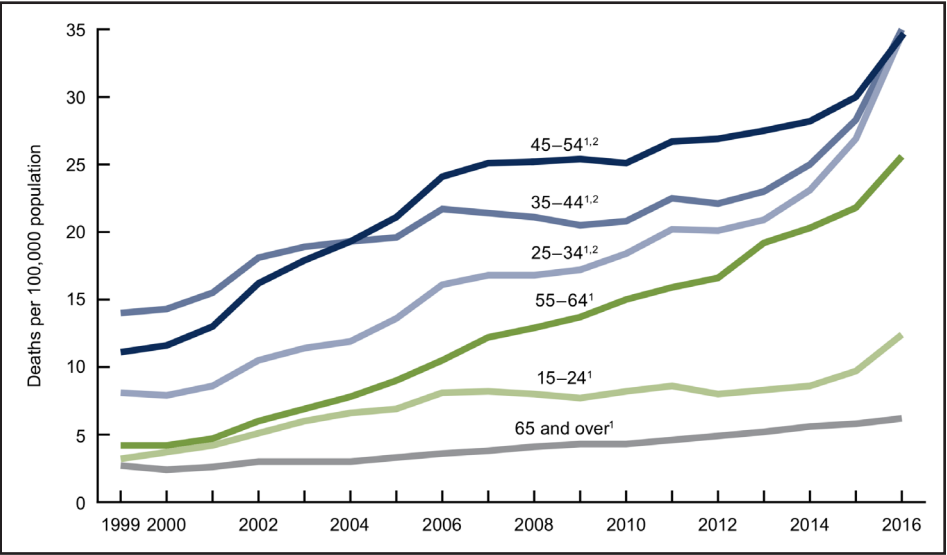
In 2011 prescription opioids (natural and semi-synthetic) were responsible for more than twice as many deaths as heroin and illicit fentanyl combined. By 2015 heroin and fentanyl each exeeded prescription opioids as the cause of OD fatalities.

Semisynthetic opioids contain small amounts of the natural alkaloids made by the poppy plant. Hydrocodone contains codeine. Oxycodone contains thebaine. Hydro-morphone contains morphine.

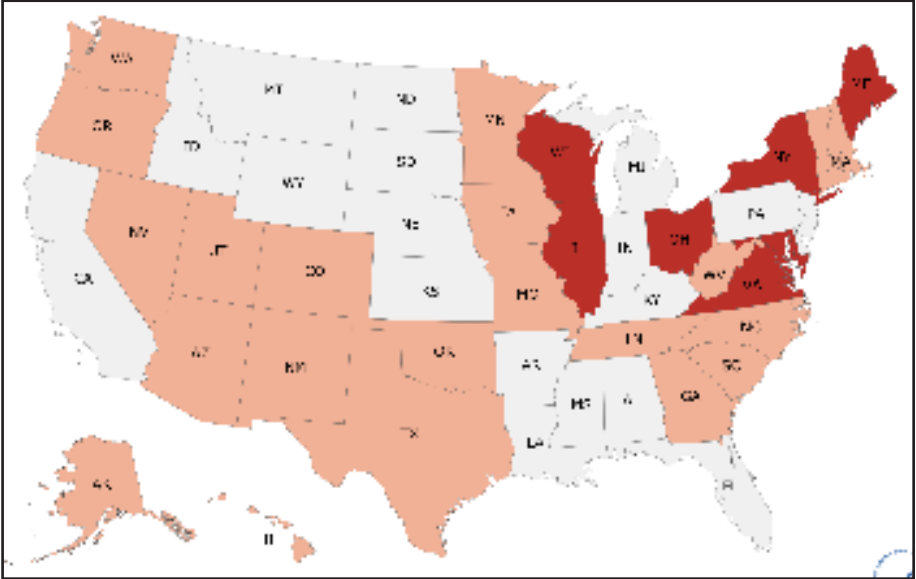
Synthetics—Fentanyl, Demerol, Dilaudid, Norco, Lortab, Atarax, Methadone, Buprenorphine— are designed in the laboratory by chemists who look to the molecular structure of natural alkaloids for inspiration.

“Opiate” is a term reserved for compounds produced by the plant, such as morphine, codeine, thebaine, and papaverine. (Just as *Cannabis* plants make numerous chemically distinct cannabinoid acids, *Papaver somniferum* plants make numerous, distinct opium alkaloids.)

Opioids cause death by suppressing the central nervous system, which is respon-



DEATHS FROM PRESCRIPTION-OPIOD OVERDOSES IN US BY AGE, 1999-2016. Vertical scale shows deaths per 100,000 population. The sharpest rise in recent years has been in the 25-to-34 and 35-42 age groups. Source: NCHS, National Vital Statistics System, Mortality



DEATHS FROM PRESCRIPTION-OPIOD OVERDOSES BY STATE IN 2015-2016. Overdose deaths caused by prescription drugs continued to rise in some states (red). Orange indicates states with prescription-opioid death rates near the national average.

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placebo – 2.5 mg of oxycodone did not change these measures.

When combined with active cannabis, however, the 2.5 mg dose of oxycodone did increase the pain threshold and tolerance compared to placebo and active cannabis alone. In other words, adding cannabis made an ineffective dose of oxycodone into an effective dose.

Furthermore, adding cannabis to the 2.5 mg oxycodone dose increased the degree to which subjects liked the capsule and wanted to take it again. Cooper notes that adding cannabis to oxycodone not only potentiates the analgesia, it may also increase its efficacy as a harm reduction strategy — and its abuse liability.

While cannabis amplifies the analgesic effect of opioids, it in no way amplifies their dangerous effects.

Treating Chronic Pain

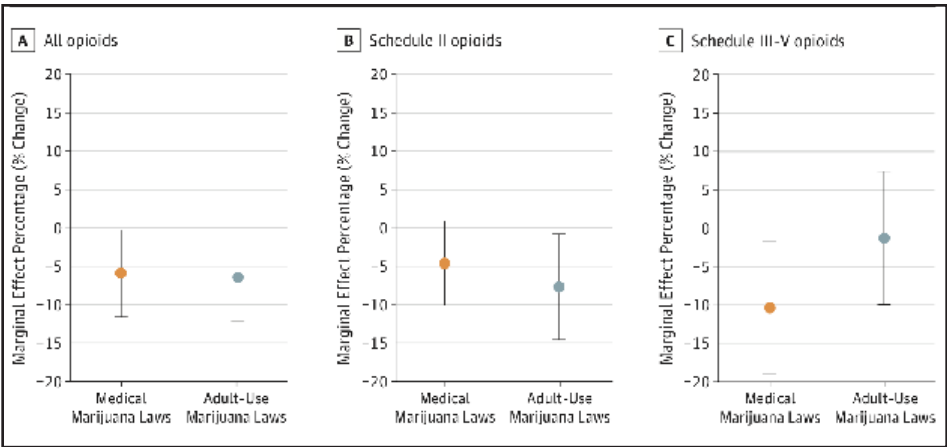
A study conducted in Israel by Simon Haroutounian and colleagues at Hadassah-Hebrew University Medical Center, published in 2016, looked at 176 patients with chronic pain, 73 of whom were on opioids at baseline. They were all given 20 grams of cannabis per month and a choice of how to ingest it: smoked, in cookies, or in an olive oil extract.

Patients were encouraged to decrease their other medications for treating pain if they could. They were given titration instructions — basically “start low, gradually increase dosage, use it three times daily.” And by the seven-month mark, 44 percent of those who were on opioids at baseline had completely discontinued their opioid therapy.

Also in 2016, a survey of 244 pain patients by Kevin Boehnke and colleagues at University of Michigan’s School of Public Health found that medical cannabis use was associated with an overall 64 percent decrease in opioid use, a decrease in the number and severity of side effects from other medications, and a 45% improvement on a scale assessing quality of life.

In a 2017 cohort study from Jacob Vigil and colleagues at the University of New Mexico, 37 habitual opioid-using, chronic pain patients enrolled in New Mexico’s medical cannabis program were compared to 29 non-enrolled patients. In the medical cannabis group, 84 percent of patients (31) reduced their opioid dose and 41 percent (15) ceased using the drugs.

In the non-cannabis group, 45 percent (13) reduced their opioid dose and only one patient ceased using opioids. There was a clear trend of opioid dose reduction in the cannabis group and opioid dose escalation in the non-cannabis group. The medical cannabis group also experienced marked improvements in quality of life, social life,



ASSOCIATION BETWEEN MEDICAL AND ADULT-USE MARIJUANA LAWS on Medicaid-covered opioid prescribing rate were graphed by Wen and Hockenberry. Schedule 2 opioids include Oxycodone, hydrocodone, fentanyl, morphine, and codeine. Schedule 3 narcotics include: combination products containing less than 15 milligrams of hydrocodone per dosage unit (Vicodin), products containing not more than 90 milligrams of codeine per dosage unit (Tylenol with codeine), and buprenorphine (Suboxone).

activity level, and concentration.

A paper by Wen and Hockenberry in JAMA Internal Medicine April 2 looked at pain drugs and opioid prescribing between 2011 and 2016. Eight states implemented medical cannabis programs during that time frame: Connecticut, Delaware, Illinois, Maryland, Massachusetts, Minnesota, New Hampshire, and New York. Four states legalized adult use: Alaska, Colorado, Oregon, and Washington.

Just by having medical cannabis laws, states achieved a six percent decrease in opioid prescriptions! Adult use marijuana laws were associated with a 9.78% decrease.



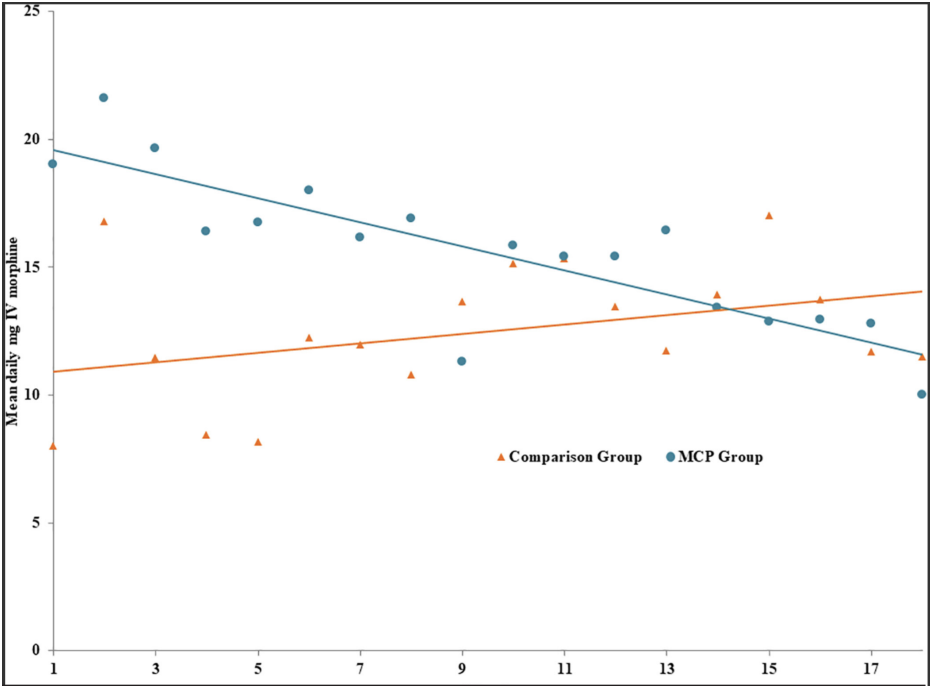
Given more than 67 million Medicaid participants, the potential savings to the federal government are enormous.

Note that the researchers were tabulating the number of opioid prescriptions for which Medicaid reimbursed —not morphine equivalents. Number of prescriptions tells more about opioid cessation than it does about reduction of use.

In the clinic, If I’m prescribing someone 80 milligrams of morphine three times a day, and I get him down to 10 milligrams of morphine three times a day, that’s a huge improvement. But he’s filling the same number of prescriptions.

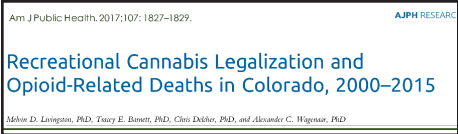
People are decreasing their dose —that’s what I’m seeing in the clinic.

So a reduction in number of prescriptions is not showing the taper, it’s showing discontinuation. That’s a great ultimate goal, but not always what we can do.



IN STUDY BY VIGIL ET AL, MEAN PRESCRIBED DAILY OPIOID DOSE declined over the course of 18 months among chronic pain patients enrolled in New Mexico’s Medical Cannabis Program (blue). Daily opioid dose rose among patients in a comparison group (orange). Vertical scale shows mean daily dose in morphine equivalents. Lines show the trends.

many lives could be saved with a program and education? We can’t wait around for this, it has to happen now.



Colorado’s legalization of recreational cannabis sales and use in 2014 led to a 0.7% decrease in opioid-related deaths per month, according to a paper in the American Journal of Public Health. A graph of opiod deaths per month between 2000 and 2015 shows the trend beginning to reverse.

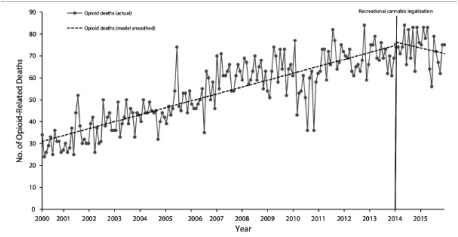


FIGURE 1—Changes in Monthly Opioid-Related Deaths Following Recreational Cannabis Legalization in Colorado, 2000–2015

Imagine if we had rescheduling and federal legalization! How many fewer people would be dying every day?

Safety and Efficacy

While cannabis amplifies the analgesic effect of opioids, it does not amplify their most dangerous effects. Opioids stimulate receptors in the cardio-respiratory centers —the part of the brainstem that controls heart rate and breathing. Too many opioids will shut down these essential functions.

Since there are virtually no cannabinoid receptors present in those areas, cannabis does not share these potentially lethal side effects. By adding cannabinoids to opioids in the treatment of pain, we produce a greater therapeutic index: the lethal dose of the opioid treatment stays the same, but the effective dose goes way down. So it’s actually safer for patients to use the combination than opioids alone.

One of the biggest problems with long-term opioid treatment is that it stops working. People build up tolerance to opioids. They come back every three to six months saying, “I want more, I need more.”

I saw this in my medical training, especially during residency. It was the bane of the primary-care provider’s existence. What to do about these patients for whom we don’t have a better solution?

Every once in a while I would see a patient who came in on a stable dose of opioids —for example five milligrams of oxycodone three times a day— and never asked for a dosage increase. I started to wonder, ‘Why are these patients so different from all the other patients that are taking opioids?’ And I started to ask them directly and was surprised to learn that these patients had a clear understanding of their strategy to prevent opioid tolerance and dose escalation.

I was told, “This is what I’m doing, Doc. I’m using cannabis in combination with the pills and it makes them more powerful, it makes it so I don’t need more.” I remember one patient in particular that pulled his cannabis out of his pocket and insisted that I smell the answer to my question.

When I looked at the primary literature, I found that my patient’s strategy had a valid scientific basis. Diana Cichewicz and colleagues reported that animals treated with combination THC and morphine avoid tolerance to the opioid, maintain analgesic efficacy, and actually

I don’t make a sharp distinction between “adult use” and “medical use.” A study in Colorado of people buying cannabis for “recreational use” found many were using it for help getting to sleep. There’s a continuum. People defining their use as recreational may be enhancing their quality of life and less likely to use other drugs, which is a medical result.

I completely agree with the authors’ conclusion: “Marijuana liberalization alone cannot solve the opioid epidemic. It is but one potential aspect of a comprehensive package to tackle the epidemic.”



The same issue of JAMA Internal Medicine contained an article by Ashley Bradford and University of Georgia co-authors (including her father) looking at Medicare Part D prescribing associated with state-level medical cannabis laws. They found a 14.4 percent reduction in states that allowed dispensaries and a 6.9 percent reduction in states that only allowed home cultivation.

Bradford et al documented significant decreases in hydrocodone and morphine prescriptions. They were looking at prescriptions by drug name and did not convert the doses into morphine equivalents. So, again, we’re not looking at dosage-reduction data, which would reveal a lot. People are decreasing their dose —that’s what I’m seeing in the clinic.

Bear in mind that medical cannabis laws are associated with people getting off opioids even with no specific program helping them do so. The states offer no education, no encouragement to use cannabis to reduce opioid use. In most states with medical marijuana laws, Opioid Use Disorder is not even a qualifying condition

There are more than 115 people dying of opioid overdose in the US every day. How

Medical Cannabis Dispensary Open	
Hydrocodone	-17.4
Oxycodone	9.1
Fentanyl	-9.7
Morphine	-20.7
Methadone	1.3
Other opioid	-12.8
Medical Cannabis Home Cultivation Allowed	
Hydrocodone	-9.4
Oxycodone	9.3
Fentanyl	-3.0
Morphine	-8.5
Methadone	5.1
Other opioid	-5.8

DAILY DOSES PRESCRIBED FOR OPIOIDS through Medicare Part D went down after states passed medical cannabis laws. Bradford et al reported a 14.4% reduction in states that allowed dispensaries (top half of table) and a 6.9% reduction in states that only allowed home cultivation (bottom half).

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Cannabis/Opioids from previous page

have increased numbers of opioid receptors in the spinal cord.

This is the opposite of what happens when they're treated with morphine alone. The dose of THC needed to preserve the effectiveness of morphine was so low that it produced no significant analgesia on its own.

Harm Reduction

While we would like to imagine that everyone with addiction problems can successfully avoid all potentially addicting substances, the medical community has finally recognized that that's not practical. While the path of abstinence is effective for certain individuals, it just does not work for everyone.

Mainstream medicine employs two opioid drugs as harm-reduction alternatives in treating opioid dependence: Methadone and Buprenorphine

Instead of insisting on abstinence, we can replace a harmful substance with a safer one. This approach is known as "harm reduction." Mainstream medicine employs two opioid drugs as harm-reduction alternatives in treating opioid dependence: Methadone and Buprenorphine (synthetic opioids that hardly cause a high).

Buprenorphine combined with an opioid blocking drug called Naloxone, is sold as Suboxone. These two drugs are the cornerstone of "Medication Assisted Treatment," an approach to opioid abuse that combines FDA-approved drugs (courtesy of the same industry that started this problem) with counseling and behavioral therapies.

How effective are Methadone and Suboxone? A 2014 review by the Cochrane Database on the efficacy of these harm-reduction options found that only high-dose buprenorphine (16 mg) was more effective than placebo in suppressing illicit opioid use. Methadone was found to have equal efficacy in suppressing illicit use, and was superior to Buprenorphine in retaining people in treatment.

It's important to note that while suppressing illicit opioid use is the goal, retaining people in treatment may alone be a helpful outcome. Conversely, many critics point out that Suboxone is effective at suppressing the most unpleasant aspect of opioid addiction and abuse — the withdrawal symptoms— which simply allows addicts to feel well until they can get another dose of their drug of choice.

Both drugs can lead to overdose deaths. Methadone was responsible for about one-

third of opioid overdose deaths in 2009, according to the CDC.

While Suboxone is safer than methadone, it can still cause a fatal overdose, especially if taken with other drugs that suppress cardio-respiratory function, such as a benzodiazepines, which are often prescribed to treat anxiety and sleep disturbance right alongside the Suboxone.

Cannabis has a lower risk of dependence than any other psychoactive substance.

How does cannabis compare to methadone and Suboxone as a potential harm reduction agent?

It has a lower risk of dependence than any other psychoactive substance. Most people who stop using cannabis are able to do so without any formal treatment. And cannabis has a low risk for abuse and diversion, especially in non-smoked forms such as tinctures and sprays. The slower onset makes the cannabis less rewarding and thus less prone to abuse.

For example, in more than 30,000 patient years of randomized control trial data of nabiximols (Sativex), a standardized cannabis extract from GW Pharmaceuticals, there has been no evidence of abuse or diversion.

In 2014, Marcus Bachhuber and colleagues published a study in the *Journal of the American Medical Association* that evaluated various attempts to reduce opioid dependence and overdose deaths. One approach was a prescription-drug monitoring program adopted by most states that enables a medical provider to log in, look up a patient, and find out which controlled substances they've been prescribed, where and when the prescriptions were filled, and so forth. The monitoring program was not associated with decreased opioid overdose deaths.

Laws requiring or allowing a pharmacist to request patient identification were found to have no association with the rate of opioid overdose deaths. Increased state oversight of pain management clinics also demonstrated no significant impact.

But states that simply passed a medical cannabis law, reduced opioid overdose deaths by 24.8 percent on average!

The paper by Bachhuber et al inspired "replication studies" by a RAND Corporation group led by Rosalie Liccardo Pacula. They reported in the *Journal of Health Economics* that access to legal cannabis dispensaries was the key factor in driving down opioid-related mortality.

Pacula reported a corollary finding:

States with the most restrictions on patients' access to cannabis achieved the least reduction in opioid-related mortality.

states with the most restrictions on patients' access to cannabis achieved the least reduction in opioid-related mortality.

Other studies have shown that medical and adult use cannabis laws are associated with less opioid prescribing/dispensing, fewer opioid-related emergency room visits, and significant cost savings for states and the federal government.

In 2016 the U.S. Centers for Disease Control released new guidelines for prescribing opioids to patients with chronic pain. Their goal was to restrain clinicians' irresponsible prescribing practices and target the source of the opioid problem. Perhaps, in a small acknowledgment of the potential of cannabis to help with the opioid problem, the section on urine drug testing stated: "Clinicians should not test for substances which would not affect patient management or for which implications for patient management are unclear. For example, experts noted that there might be uncertainty about the clinical implications of a positive urine drug test for Tetrahydrocannabinol (THC)."

The CDC seemed to be advising doctors that opioid users should not be discouraged from also using cannabis. Unfortunately, this sensible advice has not been widely heeded. Cannabis clinicians frequently encounter patients who report, "my pain management doctor found THC in my urine, and they kicked me out of their practice." Or, "they cut off my prescriptions with no taper."

This punitive approach makes no sense. It is well documented that cannabis is a good replacement for both illegal and prescription drugs. A survey of 473 medical cannabis patients in British Columbia found 87 percent were using cannabis as a substitute for something else — 80.3 percent using it as a substitute for prescription drugs; 51 percent for alcohol; 32 percent for illicit substances. The reasons they gave were: more effective, fewer and less severe side effects, lower risk of dependence and addiction.

Several other studies have shown similar results.

Patients with "Opioid Use Disorder"

There is strong evidence that cannabis can be safely used to reduce and replace opioid medications in patients with chronic pain. What about patients with "Opioid Use Disorder" who don't have chronic pain?

Unfortunately, the clinical evidence is scant, but some data plus the anecdotal reports of patients and clinicians on the front lines supports more research in this area.

Naltrexone, a drug that blocks the opioid receptor, is another medication-assisted approach to opioid abuse, but in this case, a way to support opioid abstinence. Cannabis use has been associated with improved Naltrexone treatment retention.

A 2009 study from Wilfrid Raby and colleagues at Columbia University in New York found that intermittent cannabis users were staying in a treatment program for 113 days, on average, whereas people who didn't use cannabis at all only lasted 47 days. The investigators also found that intensive behavioral therapy helped the consistent cannabis users but didn't help the non-users at all.

Other studies have shown that THC reduces opioid withdrawal symptoms and cannabis users are more likely to come back for a second injection of long-acting naltrexone, and that opioid injectors who use cannabis have lower monthly injections than their non-cannabis using peers.

Cannabis can not only keep people in treatment, replace and reduce opioid in-

take, improve the pain relief that opioids provide, prevent opioid dose escalation and tolerance —it can also treat the symptoms of opioid withdrawal: nausea, vomiting, diarrhea, abdominal cramping, muscle spasms, anxiety, agitation, restlessness, insomnia, runny nose and sweating — all symptoms that cannabis is well-known to ameliorate.

Cannabinoids have repeatedly been shown to promote neuroplastic changes in the brain —structural alterations related to new patterns of thought, perception, and behavior. In animal models of anxiety, psychosis, depression, and memory impairment, cannabinoid-induced neurogenesis is associated with behavioral improvement. These are precisely the types of changes needed to get someone out of the cycle of addiction and into a new phase in their life. Perhaps this is another reason why some cannabis users are more likely to find success in treatment for Opioid Use Disorder.

Pain worsens depression and anxiety

In a paper published in *Addictive Behavior*, Marian Wilson and colleagues at Washington State University reported that frequency of cannabis use heightened the associations between pain and depression and pain and anxiety.

Wilson's team interviewed 150 patients being treated for Opium Use Disorder at a medication-assisted treatment clinic. "Results from the current study," they wrote, "may indicate that cannabis use interferes with one's ability to unbundle one's existing symptoms. Cannabis may decrease confidence for managing emotions, or diminished ability to manage symptoms may increase frequency of cannabis use."

Why do my patients consistently report and demonstrate enhanced confidence? They specifically tell me that they're better able to unbundle their symptoms. Without cannabis it's "one big ball of suffering"; but in that cannabis state of consciousness they can say, "Okay, that's the sensation, and here's the judgment. I call that pain. And here's the anxiety about that pain."

That unbundling is extremely therapeutic. Why are my patients different from the patients in the cohort of the study?

I think there may be a selection bias in that the people coming to me are motivated. They are early medical cannabis adopters. They want to use cannabis to get off opioids.

Self-efficacy is the belief in one's ability to succeed at a given task, a 'can-do' attitude, a sense of optimism and control over one's environment.

Wilson and colleagues also published an abstract this year in the *Journal of Pain*, with a different cohort: 150 people with opioid use disorder, and another 150 people with persistent pain.

This time they controlled for "self-efficacy." They found that cannabis users had more confidence, better sleep quality and less pain intensity.

"Self efficacy" is the belief in one's ability to succeed at a given task, a 'can-do' attitude, a sense of optimism and control over one's environment. It determines whether or not one can rise up after being knocked down. Improving self-efficacy is an important goal, because people with higher levels of self-efficacy tend to be more successful reducing opioid use by using cannabis —and more successful overall.

Might a certain dose and frequency of cannabis use enhance self-efficacy, while a higher dose and frequency reduce it (by fostering reliance on cannabis instead of

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PRINCE ROGERS NELSON, a brilliant musician who lived with chronic pain (and had a valid medical diagnosis), died of an opioid overdose in April 2016. He did not know that the Vicodin that an associate obtained for him had been laced with fentanyl.

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one’s self)?

In cannabinoid medicine we see many bi-directional effects —cannabis producing one result or the opposite result, depending on dose, frequency, and “set and setting,” meaning the attitude of the person and the environment in which they use it.

If you take the same dose of cannabis on your couch with a friend, versus at the oral surgeon’s office, you’re going to have a different experience with it. Could there be a way to approach cannabis use that would enhance self-efficacy? I believe the answer is yes, especially if we give it to patients with that intention.

There are big populations of people who haven’t heard about using cannabis to reduce opioid use. They have low self-efficacy. They don’t love or know about cannabis. They’re not fed up with the medical system. They still trust the people giving them methadone. What can we learn from our patients, our successes, and help apply that to the rest of the population?

When we get to the roots of the opioid problem, we’re getting to the roots of many other problems that are leading to morbidity, mortality, and more healthcare spending.

If we want to solve a problem that’s killing 115 Americans a day, we have to get to the roots of it. And when we get to the roots of the opioid problem, we’re getting to the roots of many other problems that are leading to morbidity, mortality, and more healthcare spending.

The CBD Era

The medical cannabis movement has led to a whole new set of cannabis users —patients who want symptom relief. They want the medical benefits, but they don’t want to get high or impaired. Fortunately, in 2008 the advent of analytical labs enabled growers to identify cannabis strains in which non-impairing cannabidiol —CBD, a sister molecule of THC— was the predominant

Field-grown plants vs. synthetic and processed alternatives



Tobacco is a healing herb. Tobacco products are the leading cause of morbidity, mortality, and healthcare spending.



Poppies yield natural opioids. Oxycontin is a semi-synthetic derived from thebaine.



Organic vegetables are available at Farmers Markets for a fortunate fraction of the US population. Supermarket aisles are filled with processed foods.



cannabinoid.

CBD been shown to reduce the side effects of THC and to enhance its benefits. It has minimal side effects and toxicity, and

reduces anxiety, a component of abuse and relapse. CBD has been shown to reduce the rewarding properties of opioid drugs and opioid withdrawal symptom. It reduces

heroin-seeking behavior in animals, and reduces heroin-related cue-induced craving in human heroin abusers. And it can do all this without any of its own rewarding properties, so it has no abuse liability.

Laws need to change so the medical community can start using cannabis as an adjunctive treatment for opioid use disorder.

What is to be done?

Doctors and patients need better access to medical cannabis, especially standardized, dependable formulations containing both CBD and THC. Laws need to change so the medical community can start using cannabis as an adjunctive treatment for opioid use disorder. We’re thankful that we have a great medical cannabis system in Maine, for example, but as of September 2018, CHECK THIS, I am still not allowed to use cannabis to treat patients with opioid use disorder unless they have chronic pain that’s failed to respond to six months of conventional therapy. There are still many parts of the country and the world where cannabis is still completely illegal.

Some addiction experts are concerned that liberalizing the cannabis laws will encourage adolescents to perceive it as safe and to start using at a younger age.

A 2015 paper in *Lancet Psychiatry* provided reassuring data. “There is no evidence of a differential increase in past month use in youths that can be attributed to state medical marijuana laws,” it concluded.

And a paper in *The International Journal of Drug Policy* found “the results of this study showed no evidence for an increase in adolescent marijuana use after the passage of state laws permitting use of marijuana for medical purposes. Concerns that increased marijuana use is an unintended effect of state marijuana laws seems unfounded.”

Cannabis dosing to support opioid reduction

Cannabis can be used in so many different ways to individually tailor a treatment depending on one’s needs. Could specific approaches to dosing further increase the effectiveness and reduce the potential harm of cannabis in the setting of opioid dependence? Here are the guidelines I provide to my patients in Maine:

1. Always take a small dose of cannabis, preferably using a non-inhaled delivery method, with every dose of opioids. Many people make the mistake of thinking they should choose one or the other, but it’s clear for all the reasons discussed in this article that the combination works best. In most people, only a low dose of THC is needed to augment the effects of the opioids, so I instruct my patients to start at one-to-two milligrams of THC per dose and gradually increase until they notice the opioid pills are starting to feel much stronger. Once reaching this dose of THC, many will begin tapering the opioid drugs by cutting tablets in half and/or taking them less frequently.
2. Use inhaled cannabis to manage breakthrough symptoms and to reduce cravings. The rapid onset of vaporized or smoked cannabis makes it perfect for addressing these challenges that so often interfere with successful opioid tapering. I encourage my patients to reserve inhaled cannabis for when it’s needed most, ideally three times daily or less, and to use the lowest effective dose, taking one or two puffs and repeating every five minutes as needed, to prevent building tolerance to cannabis.
3. Use cannabis to promote regular sleep patterns. Reducing and discontinuing opioid drugs is a challenge at every level of our being: physical, mental/emotional, and spiritual. There is no medication or herb that can make this easy, and people dedicated to this change need every ounce of strength, determination, and resilience they can muster. This is why restorative sleep is essential and should be addressed at the beginning of this process. Only sedating strains of cannabis should be used in the evening, and an oral dose of cannabis (e.g. capsule) should be taken before bed if needed. While proper use of cannabis is often enough for most people to achieve healthy sleep, the cannabis can also be safely used in conjunction with other natural and pharmaceutical sleeping aids.
4. Use cannabis to enhance health-promoting activities such as exercise, meditation, prayer, journaling and reflecting, and counseling or behavioral therapies. As mentioned above, the enhanced neuroplasticity of the endocannabinoid system can help these essential components of a healing plan work even more powerfully. Many of my patients find themselves more likely to participate in these activities when they’re combined with cannabis. So when using inhaled cannabis to treat breakthrough symptoms or cravings (suggestion 2), I tell my patients to take a walk outside, try some of my free exercises and meditations on Healer.com/wellness, or sit down with their

Case Report: Cannabis Replacing Opioids for Chronic Pain

A 43-year-old man with chronic pain, victim of a hit-and-run motor vehicle-pedestrian accident at age 25, resulting in spinal disc herniation. When he first came in he had already tried cortisone injections, chiropractic, physical therapy, and prescription medications. He did not have satisfactory improvement. He saw an orthopedic specialist who recommended surgery based on the patient’s physical exam, which included weakness in one of his legs that was affecting his gait and posture. The patient did not want surgery at age 43; he wanted to postpone it as long as possible.

He was a high school graduate and worked at an electronics store. He had a 15-month old, first-born child. He came in with an average pain level of 6-7 out of 10. He had a little cannabis history, had tried it at age 16, but hadn’t used it in 20 years. He didn’t have any history of adverse affects with cannabis. He simply wasn’t using it. He was on muscle relaxants, two anti-inflammatories, two opioid pain relievers (tramadol and hydrocodone), an anti-nausea drug because the pain relievers cause nausea, blood pressure medication, and cholesterol medication. He had previously tried gabapentin (an anti-convulsant often used to treat pain) and Lyrica, which is in that same category.

At a return visit six months after cannabis certification, he reported started using edible cannabis in the form of cookies – not something I typically recommend. I prefer products that enable you to know how many drops you’re taking or how many milligrams. The patient was also smoking cannabis two to three times weekly, just taking two to three puffs for breakthrough symptoms. Initially he had an adverse affect from the edible —he ate too much— but once he adjusted the dosage he was able to use the cookies without any side effect.

At six months, he had stopped hydrocodone and tramadol, the two opioids, and also stopped one of the anti-inflammatories. The anti-muscle-spasm medication that he had been using daily was now needed only once a month. His average level was down to 3-4 on the pain scale. He had a significant decrease in muscle spasms.

His physical exam revealed improvement. He had normal strength in his lower extremities and was actually walking normally. Perhaps that’s because he had improved function, or because the muscle spasms had been under control for so long his spine was able to get back into alignment, or because cannabis has anti-inflammatory properties and reduced the inflammation that was pressing on that nerve root. Probably all of the above. He reported that he was able to carry his son, was able to enjoy fatherhood. And that’s an incredible result!

When I was in my medical training, if I would have seen that happen, I would have thought I was in some alternate reality. How did this patient get such good results? How did he actually come off of all his opioids and medications? This is normal for us now. We see this all the time. —Dustin Sulak, D.O.