

1. Medical condition proposed:

Non-severe and non-chronic Pain.

2. Provide justification for why this medical condition should be included as a qualifying debilitating medical condition for the use of medical marihuana. Be specific as to why medical marihuana should be used for this condition.

The review panel has the ability to add any medical condition or treatment. The medical condition or treatment does not have to be severe, chronic or debilitating.

333.26423(b)(3) **Any other medical condition or its treatment** approved by the department, as provided for in section 6(k).

The MMMP lists severe and chronic pain as a qualifying condition.

<http://legislature.mi.gov/doc.aspx?mcl-333-26423>

LARA statistics show that 79.99% of the 218,556 MMMP patients in 2016 were registered to use marijuana for “severe and chronic pain”. As we know that the medical use of marijuana can treat “severe and chronic pain” already, it can and should be used to treat regular generic pain that is not severe and chronic.

https://www.michigan.gov/documents/lara/Medical_Marihuana_Act_-_FY_2016_Statistical_Report_MCL_333.26426_and_Program_Information_Section_507_546675_7.pdf

President Trump’s ONDCP task force on the opioid prescriptions crisis has recommended calling for a national emergency.

The first and most urgent recommendation of this Commission is direct and completely within your control. Declare a national emergency under either the Public Health Service Act or the Stafford Act. With approximately 142 Americans dying every day, America is enduring a death toll equal to September 11th every three weeks.

<https://www.whitehouse.gov/sites/whitehouse.gov/files/ondcp/commission-interim-report.pdf>

Due to the interim report, President Donald J. Trump has instructed his Administration to use all appropriate emergency and other authorities to respond to the crisis caused by the opioid epidemic. 8-10-2017

<https://www.whitehouse.gov/the-press-office/2017/08/10/president-donald-j-trump-directs-administration-use-all-appropriate>

By approving non-chronic and non-severe pain as a qualifying condition, you will help prevent another “September 11th every three weeks”.

Conditions such as arthritis, headaches, broken bone or torn muscle can cause severe, chronic and debilitating pain. The majority of pains that people are prescribed opioid painkillers for do not qualify under the current definition "A chronic or debilitating disease or medical condition or its treatment that produces ... severe and chronic pain" in the MMMA, because a broken bone or torn muscle are not chronic and may not be debilitating enough to meet the definition.

The non-toxic, non-addictive medical marijuana is a desperately required treatment option to replace the opiate-based prescriptions for pain relief. Americans die every day due to the toxic prescription and non-prescription NSAID analgesics. Would you rather have someone die from Oxycontin or Aspirin than let them use non-toxic medical marijuana under a physician's care to treat their pain?

In Medical Marijuana states, overdoses on opioid prescription painkillers are reduced by 25%.

Conclusions and Relevance Medical cannabis laws are associated with significantly lower state-level opioid overdose mortality rates.

The 25% reduction found in the study was based on current states with "severe pain" and/or "chronic pain". If physicians are approved to write recommendations for medical marijuana for general pain, the amount of people overdosing on opioid based prescription medications will drop further than the 25% observed. This is evidenced by the studies that show people who use marijuana in conjunction with opioid painkillers find that they can reduce the dosage of the opioids to get the same pain relief.

Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010 Marcus A. Bachhuber, MD^{1,2,3}; Brendan Saloner, PhD, Chinazo O. Cunningham, MD, MS; et al doi:10.1001/jamainternmed.2014.4005

Using data on all prescriptions filled by Medicare Part D enrollees from 2010 to 2013, we found that the use of prescription drugs for which marijuana could serve as a clinical alternative fell significantly, once a medical marijuana law was implemented.

<http://content.healthaffairs.org/content/35/7/1230>

The CDC has declared opioid prescription overdoses an epidemic.

<https://www.cdc.gov/drugoverdose/epidemic/index.html>

Drug overdose deaths and opioid-involved deaths continue to increase in the United States. The majority of drug overdose deaths (more than six out of ten) involve an opioid. Since 1999, the number of overdose deaths involving opioids (including prescription opioids and heroin)

quadrupled. From 2000 to 2015 more than half a million people died from drug overdoses. Americans die every day from an opioid overdose.

Similar to comments made by President Obama at the National Prescription Drug Abuse and Heroin Summit.

It's important to recognize that today we are seeing more people killed because of opioid overdose than traffic accidents.

<https://obamawhitehouse.archives.gov/the-press-office/2016/03/29/remarks-president-panel-discussion-national-prescription-drug-abuse-and>

As well as President Trump's plan to limit opioid prescriptions.

“Reduce the amount of Schedule II opioids (drugs like oxycodone, methadone and fentanyl) that can be made and sold in the U.S.”

<http://web.archive.org/web/20170103232128/https://www.donaldjtrump.com/press-releases/donald-j.-trump-addresses-the-drug-epidemic-in-the-united-states>

President Obama and President Trump have instructed the FDA and DEA to limit opioid based prescription painkillers.

<https://www.nytimes.com/2016/03/17/health/er-pain-pills-opioids-addiction-doctors.html>

<http://jamanetwork.com/journals/jama/fullarticle/2503508>

April 19, 2016 CDC Guideline for Prescribing Opioids for Chronic Pain—United States, 2016
Deborah Dowell, MD, MPH. Tamara M. Haegerich, PhD. Roger Chou, MD.
JAMA. 2016;315(15):1624-1645. doi:10.1001/jama.2016.1464

Unfortunately, all of the limits, burdens and tightening of the rules for doctors to prescribe and pharmacists to dispense pain medication have caused patients' quality of life to drop. Due to these new rules, patients have been dropped by physicians, denied prescriptions at pharmacies and have been forced to turn to heroin just to attain pain relief. Thousands of people have signed this petition to have some of these rules rescinded so they can get their medications back, to no avail.

The reports from people about how they were denied pain medications were posted to the change.org petition. The reports are heartbreaking. These people in pain need a replacement therapy after they have been denied prescription opioid analgesics by their physicians and pharmacists.

David Jasko Hackensack, NJ Apr 27, 2017

"Tired of being treated as a "drug seeker," when pain medications are requested. Since I have been in chronic pain, 9 of 10 doctors have refused pain medication, leaving me unable to walk 90% of the time."

Sharron Rishling Las Vegas, NV Apr 27, 2017

"My daughter had had this terrible pain disease CRPS (Chronic Reflex Pain Syndrome) which is debilitating. She is totally disabled and they are not letting her have her pain medication."

nathan luse Wyoming, MI May 14, 2017

"I have chronic lower back pain, and chronic pain in my feet, pain meds got taken away, and there is no surgery to fix me. shots have zero effect, had a specialist notarized this. only thing that works and gets me out of bed is medication. Been cut-off since december."

Susan Pare Otisville, MI Feb 1, 2017

"I have been in severe, chronic pain of one form or another since I was two years old. I will be 64+ later this year. There has been almost no time in that period where I have been free of pain. I recall having to beg my doctor to prescribe more than 15 days of Vicodin at a time and that had to last me SIX MONTHS. Granted this was 20 years ago, but suddenly it is like living that time all over again. Surely there must be a happy medium between me and the neighborhood dealer."

Ariel G Baraga, MI Jan 28, 2017

Signing this because I deal with pain everyday that doctors do not help because they think I'm a drug seeking addict.

Deborah Palomarios Onaway, MI Jan 2, 2017

I have sever pain. I have had 4 back surgeries. The last two I was only given 10 days of pain meds then no more. Its barbaric!

Scott Behler Ann Arbor, MI Dec 18, 2016

Dealing with chronic pain for the last 19 years. I am a restaurant manager by career, and often am walking, standing, for 12 hours a day. Had the ability to manage my pain, and be successful in my position until about a year ago, when my doctor of many years cut me way back, and every time I see him now, directs me to see a different orthopedic or pain management clinic, who continually suggest additional surgeries (I've already had 7 of them, one more painful and longer recovery time than the next), or more injections (I've had multiple spinal, steroid, cortisone, synvisk, etc., that have worked for very short periods). I understand the issues with recreational usage problems, but let the people who are in legitimate pain and need them to survive get them! Sad when some of us chronic pain patients start thinking about finding street drugs such as heroin just to be

able to live a somewhat "normal" life. I've also heard of chronic pain patients that just give up and commit suicide. This is something that my faith would forever restrict me from doing, but I can understand giving up on life because what kind of life is it when you are continually suffering?

<https://www.change.org/p/congress-ease-the-dea-s-grip-on-doctors-allowing-chronic-pain-patients-to-get-the-medications-we-need>

Governor Rick Snyder and Michigan Attorney Bill Schuette also are working to reduce opioid addiction, abuse and overdoses.

<http://www.michigan.gov/ag/0,4534,7-164-46849-365940--,00.html>

Doctors in Michigan are licensed by LARA and are trusted to prescribe opioid painkillers that many people overdose on each day. Why would the LARA director and the Michigan Medical Marijuana Review Panel question a doctor's ability to recommend medical marijuana? Medical marijuana is a non-toxic plant which has no overdose deaths and is currently used safely and effectively by 218,000+ patients in Michigan to treat chronic pain and other conditions.

Conclusions. Operational Medical Marijuana Laws are associated with reductions in opioid positivity among 21- to 40-year-old fatally injured drivers and may reduce opioid use and overdose.

<http://ajph.aphapublications.org/doi/abs/10.2105/AJPH.2016.303426>

LARA should also instruct physicians and patients on the research that shows a combination of medical marijuana can be used as an adjunct therapy with opioid based painkillers to shrink opioid prescription dosages while continuing to achieve effective pain relief.

Cannabis as an Adjunct to or Substitute for Opiates in the Treatment of Chronic Pain
Philippe Lucas, M.A Journal of Psychoactive Drugs, 44 (2), 125–133, 2012
Doi 10.1080/02791072.2012.684624

A study by Pingsger (2006) on the effects of nabilone (a synthetic cannabinoid) as an adjunct to existing chronic pain therapy resulted in reduced pain and improved quality of life. Although some mild to moderate side effects were noted, the majority of patients reported overall benefits when compared to their usual chronic pain treatment. A clinical study by Nurmikko (2007) examining the effects of Sativex as an adjunct to existing stable analgesia in patients suffering from peripheral neuropathic pain showed that 26% of participants reported more than 30%

reductions in pain intensity, compared with 15% in those using placebo. Adverse events were few and largely mild or moderate.

A randomized clinical study by Skrabek and colleagues (2008) on nabilone as an adjunct treatment for 15 patients affected by fibromyalgia reported significant benefits in pain and overall function. Mild side-effects were reported, including weight gain, but participants indicated overall increases in quality of life.

Narang and colleagues (2008) conducted a phase 1 and phase 2 study examining the efficacy of dronabinol as an adjunct to opioid therapy for the treatment of chronic pain. Both studies showed that dronabinol decreased pain intensity and increased quality of life compared to baseline opiate therapy. The findings also reported mild to moderate side effects including drowsiness, but patients also reported an improvement in the quality of sleep and overall satisfaction with the treatment compared to placebo.

Additionally, studies also show that cannabinoids can prevent the development of tolerance to and withdrawal from opiates (Cichewicz & Welch 2003), and can even rekindle opiate analgesia after a prior dosage has become ineffective (Russo 2008a; Cichewicz & McCarthy 2003). Furthermore, research by Blume and colleagues (2011) and Ramesh and colleagues (2011) suggests that cannabinoid receptors might interrupt signaling in the opioid receptor systems, affecting both cravings for opiates and withdrawal severity.

In 2011, LARA provided physicians with guidelines on recommending medical marijuana to patients. If this petition is approved adding pain as a qualifying condition, LARA and the Board of Medicine should issue guidelines to physicians to ensure that patients are educated on medical marijuana as an adjunct therapy to limit opioid dosage or complete replacement of opioid based painkillers.

https://www.michigan.gov/documents/lara/lara_Medical_Marihuana_Final_Written_Certification_Statement_8-15-11_376283_7.pdf

LARA can create new guidelines to instruct physicians on how to write medical marijuana recommendations for pain and how to rescind the recommendation by contacting LARA once the painful condition, such as a broken bone or twisted joint, heals. This procedure is prescribed by MMMA law, MCL 333.26426 (f).

(f) If a registered qualifying patient's certifying physician notifies the department in writing that the patient has ceased to suffer from a debilitating medical condition, the card shall become null and void upon notification by the department to the patient.

<http://legislature.mi.gov/doc.aspx?mcl-333-26426>

While MMMP cards expire within 2 years, there is no requirement that people continue medical marijuana treatment for that time. Many people have received a physician's recommendation to use medical marijuana, registered with the state, received their MMMP card, tried marijuana, found out that medical marijuana did not benefit them, and then stopped using medical marijuana and let their registrations lapse. Just like any other medication, if it does not benefit or alleviate a person's condition, they will discontinue use and try a different medication. Prescriptions and prescription refills expire, prescription medications expire, these are not valid reasons to forbid people from prescription medications. Nor is a 2 year card expiration date a valid reason to forbid a person from using a medication for a condition which lasts less than 2 years.

Medical Marijuana has no toxic side effects and no known lethal dose.

Pain medications lead the list of the most common substances implicated in adult poison exposures (20 years old or older, NPDS, 2015).

<http://www.poison.org/poison-statistics-national>

Adults aged 45–54 had the highest rate of drug overdose deaths in 2015.

<https://www.cdc.gov/nchs/products/databriefs/db273.htm>

With the current nationwide epidemic of opioid abuse, dependence, and fatalities, clinicians are being asked by federal agencies and professional societies to control their prescribing of narcotic medications for pain. Federal guidelines emphasize tapering, discontinuing, and limiting initiation of these drugs except in provision of end-of-life care. Reducing reliance on opioids, however, is a massive task. According to one estimate, more than 650 000 opioid prescriptions are dispensed each day in the United States. Unless the nation develops an increased tolerance to chronic pain, reduction in opioid prescribing leaves a vacuum that will be filled with other therapies.

Enter cannabis. As of August 2016, the District of Columbia and 25 states have legalized cannabis for medical use. Recreational use of cannabis has been legalized in 4 of these states and Washington, DC, and like initiatives are pending in other states. The mandated transition to limit use of opioids, paired with the current climate around liberalizing cannabis, may lead to patients' formal and informal substitution of cannabis

for opioids. Observational studies have found that state legalization of cannabis is associated with a decrease in opioid addiction and opioid-related overdose deaths

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5332546/>

3. Provide a summary of the evidence that the use of medical marijuana will provide palliative or therapeutic benefit for this medical condition or is a treatment for this condition.

1. [10.1002/phar.1187](https://pubmed.ncbi.nlm.nih.gov/10.1002/phar.1187/)

Various forms of medicinal cannabis have provided mostly positive responses for patients with different types of pain: neuropathic, chronic, postoperative, and that related to fibromyalgia, rheumatoid arthritis, multiple sclerosis, and cancer. In studies evaluating smoked cannabis compared to placebo, significant improvements in pain were observed. These studies included a small number of patients (15–56) and used cigarettes with varying THC contents. THC content varies based on the strain of cannabis plant that is used. In general, a higher THC content (up to 9.4%) appears to be more effective for pain relief.

2. [10.1093/rheumatology/kei183](https://pubmed.ncbi.nlm.nih.gov/10.1093/rheumatology/kei183/)

In the first ever controlled trial of a Cannabis Based Medicine in RA, a significant analgesic effect was observed and disease activity was significantly suppressed following Sativex treatment. Whilst the differences are small and variable across the population, they represent benefits of clinical relevance and show the need for more detailed investigation in this indication. The large majority of adverse effects were mild or moderate, and there were no adverse effect-related withdrawals or serious adverse effects in the active treatment group.

3. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3998228/>

Ninety-seven per cent of respondents used cannabis primarily for chronic pain. Average pain improvement on a 0–10 pain scale was 5.0 (from 7.8 to 2.8), which translates to a 64% relative decrease in average pain. Half of all respondents also noted relief from stress/anxiety, and nearly half (45%) reported relief from insomnia. Most patients (71%) reported no adverse effects, while 6% reported a cough or throat irritation and 5% feared arrest even though medical cannabis is legal in Hawai'i. No serious adverse effects were reported.

These results suggest that Cannabis is an extremely safe and effective medication for many chronic pain patients. Cannabis appears to alleviate pain, insomnia, and may be helpful in relieving anxiety. Cannabis has shown extreme promise in the treatment of numerous medical problems and deserves to be released from the current Schedule I federal prohibition against research and prescription.

4. <https://pubmed.ncbi.nlm.nih.gov/16855921/>

From the results, it is obvious that throughout the cross-over periods the nabilone treatment was superior: decrease of the average spinal pain intensity within the last 4 weeks, decrease of the current spinal pain intensity, decrease of the average headache intensity within the last 4

weeks, increase of the number of days without headache within the last 4 weeks, increase of the quality of life.

5. <https://www.ncbi.nlm.nih.gov/pubmed/17997224>

Cannabinoids are known to have analgesic properties. We evaluated the effect of oro-mucosal sativex, (THC: CBD), an endocannabinoid system modulator, on pain and allodynia, in 125 patients with neuropathic pain of peripheral origin in a five-week, randomised, double-blind, placebo-controlled, parallel design trial. Patients remained on their existing stable analgesia. A self-titrating regimen was used to optimise drug administration. Sixty-three patients were randomised to receive sativex and 62 placebo. The mean reduction in pain intensity scores (primary outcome measure) was greater in patients receiving sativex than placebo. Improvements in Neuropathic Pain Scale composite score, sleep NRS, dynamic allodynia, punctate allodynia, Pain Disability Index and Patient's Global Impression of Change were similarly greater on sativex vs. placebo. *An open-label extension study showed that the initial pain relief was maintained without dose escalation or toxicity for 52 weeks.*

6. Nabilone for the treatment of pain in fibromyalgia. Skrabek (2008)

A randomized, double-blind, placebo-controlled trial was conducted to determine the benefit of nabilone in pain management and quality of life improvement in 40 patients with fibromyalgia. There were significant decreases in the visual analog scale (VAS) for pain, and anxiety in the nabilone treated group at 4 weeks. There were no significant improvements in the placebo group. Nabilone appears to be a beneficial, well-tolerated treatment option for fibromyalgia patients, with significant benefits in pain relief and functional improvement.

7. <https://www.ncbi.nlm.nih.gov/pubmed/18088560>

Phase I of this 2-phase study was a randomized, single-dose, double-blinded, placebo-controlled, crossover trial in which subjects were randomly administered either 10 mg or 20 mg of dronabinol or identical placebo capsules over the course of three, 8-hour visits. Phase II was an extended open-label titrated trial of dronabinol as add-on medication to patients on stable doses of opioids. Results of the Phase I study showed that patients who received dronabinol experienced decreased pain intensity and increased satisfaction compared with placebo. In the Phase II trial, titrated dronabinol contributed to significant relief of pain, reduced pain bothersomeness, and increased satisfaction compared with baseline. The incidence of side effects was dose-related. Overall, the use of dronabinol was found to result in additional analgesia among patients taking opioids for chronic noncancer pain.

8. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2503660/>

Cannabinoid analgesics have generally been well tolerated in clinical trials with acceptable adverse event profiles. Their adjunctive addition to the pharmacological armamentarium for treatment of pain shows great promise.

9. <https://www.ncbi.nlm.nih.gov/pubmed/12604676>

The analgesic effects of opioids, such as morphine and codeine, in mice are enhanced by oral administration of the cannabinoid delta(9)-tetrahydrocannabinol (delta(9)-THC). All of the fixed-ratio combinations tested produced greater antinociception (synergy) than predicted from simple additivity. These findings suggest that the use of a low-dose combination of analgesics is a valid and effective approach for the treatment of pain and necessitates further study.

10. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3742578/>

Future studies may contribute to the development of novel cannabinoid-based therapeutics that provide clinicians an additional tool to support the recovery of opioid-dependent persons undergoing treatment.

11. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3728280/>

Cannabinoids may form a useful adjunct to current analgesic drugs in many conditions, especially in low doses incapable of inducing hyperalgesia or other side effects. They can also be used as rescue drugs when opioid analgesia is ineffective or inadequate, or as opioid sparing agent. They also appear to antagonize several side effects of opioids, and the opioid-cannabinoid combination may become a very useful agent in the long-term management of severe pain. Preclinical data also suggest a beneficial effect of cannabinoids on the disease process in HIV, cancer, and MS. While smoked marijuana tends to be a controversial territory, evidence points to significant multi-symptom relief from it especially in HIV patients.

12. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2950205/>

A single inhalation of 25 mg of 9.4% tetrahydrocannabinol herbal cannabis three times daily for five days reduced the intensity of pain, improved sleep and was well tolerated.

13. <https://harmreductionjournal.biomedcentral.com/articles/10.1186/1477-7517-2-18>

Data were available for 128 participants. Long term and regular medical cannabis use was frequently reported for multiple medical conditions including chronic pain (57%), depression (56%), arthritis (35%), persistent nausea (27%) and weight loss (26%). Cannabis was perceived to provide "great relief" overall (86%), and substantial relief of specific symptoms such as pain, nausea and insomnia.

Approximately three quarters of participants (71%) claimed to have experienced a return of their symptoms or condition on stopping cannabis, *especially: pain (53% of those who claimed a return of symptoms)*, depression or anxiety (30%), insomnia (11%), spasm (10%) and nausea/vomiting or lack of appetite (9%).

14. 10.1111/j.1742-1241.2004.00271.x

Medicinal cannabis use was reported by patients with chronic pain (25%), multiple sclerosis and depression (22% each), arthritis (21%) and neuropathy (19%).

15. <https://www.ncbi.nlm.nih.gov/pubmed/12185373>

Small doses of smoked cannabis may improve pain, mood and sleep in some patients with chronic pain.

16. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3673028/>

In general, chronic pain disorders were the most common diagnoses made by physicians, with nearly 60 percent (58.2%) of applicants being diagnosed with some sort of musculoskeletal or neuropathic chronic pain condition. Low back pain was diagnosed for over one quarter (26.2%) of patients seen during this three month period, with lumbar and cervical degenerative disc disease (together 21.8%) and arthritis (18%) the next most common diagnoses in the chronic pain group.

Non-prescription therapies tried by applicants seeking medicinal marijuana allowances included physical therapy (48.6%), chiropractic services (37.2%), surgery (21.9%), psychological counseling (20.7%), and acupuncture (19.6%). Thus, these data do not suggest that applicants immediately seek marijuana recommendations as the first strategy to deal with their symptoms. In many cases, these individuals tried more traditional forms of medicine.

17. [10.1345/aph.1G217](https://pubmed.ncbi.nlm.nih.gov/21345/)

Cannabinoids provide a potential approach to pain management with a novel therapeutic target and mechanism. Chronic pain often requires a polypharmaceutical approach to management, and cannabinoids are a potential addition to the arsenal of treatment options.

18. [10.1097/01.anes.0000286986.92475.b7](https://pubmed.ncbi.nlm.nih.gov/10109701/)

By 45 min after cannabis exposure, however, there was a significant decrease in capsaicin-induced pain with the medium dose and a significant increase in capsaicin-induced pain with the high dose.

This study suggests that there is a window of modest analgesia for smoked cannabis, with lower doses decreasing pain and higher doses increasing pain.

19. [10.1016/j.ejphar.2007.04.010](https://pubmed.ncbi.nlm.nih.gov/101016/)

In summary, the synergistic interaction of $\Delta 9$ -THC and morphine in arthritic rats, as well as the potency of $\Delta 9$ -THC in the CFA chronic pain condition, points to the possibility of the use of the combination, or to the use of a $\Delta 9$ -THC analog, to treat chronic pain conditions for which opioids alone are ineffective.

20. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4791148/>

Cannabinoids could be synergistic with opioids in the relief of pain. The safety profile of cannabis is acceptable, with side effects that are generally tolerable and short-lived.

21. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2683812/>

Thematic analysis revealed that these teens differentiated themselves from recreational users and positioned their use of marijuana for relief by emphasizing their inability to find other ways to deal with their health problems, the sophisticated ways in which they titrated their intake, and the benefits that they experienced. These teens used marijuana to gain relief from difficult feelings (including depression, anxiety and stress), sleep difficulties, problems with concentration and physical pain.

22. [10.1002/cbdv.200790150](https://doi.org/10.1002/cbdv.200790150)

In a Phase-II double-blind, randomized placebo-controlled five-week study of 56 rheumatoid arthritis patients with Sativex by Blake et al. , employing nocturnal treatment only, subjects received a maximum of 6 sprays each evening (16.2 mg THCp 15 mg CBD). In the final treatment week, many study measures favored Sativex over placebo: morning pain on movement, morning pain at rest , 28- joint disease activity score, and Short Form McGill Pain Questionnaire (SF-MPQ) pain at present. Sleep quality favored Sativex over placebo.

23. <https://www.ncbi.nlm.nih.gov/pubmed/15857739>

Following Ethics Committee approval, HIV-positive individuals attending a large clinic were recruited into an anonymous cross-sectional questionnaire study. Up to one-third (27%, 143/523) reported using cannabis for treating symptoms. Patients reported improved appetite (97%), *muscle pain* (94%), nausea (93%), anxiety (93%), *nerve pain* (90%), depression (86%), and paresthesia (85%).

24. <https://www.ncbi.nlm.nih.gov/pubmed/24095000>

Patients reported using cannabis to treat multiple symptoms, with sleep, pain, and anxiety being the most common. Cannabis was perceived to provide effective symptoms relief across medical conditions. Patterns of use were also consistent across medical conditions. Notable differences were observed with regard to modes of access.

25. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1654142/>

Cannabis, in herbal form, is widely used as self-medication by patients with diseases such as HIV/AIDS and multiple sclerosis suffering from symptoms including pain, muscle spasticity, stress and insomnia.

26. [10.1016/j.jns.2008.06.037](https://doi.org/10.1016/j.jns.2008.06.037)

The VAS evaluation of self-reported clinical modifications after cannabis medicinal use showed a wide range of improvement that was mainly perceived in sleep disturbances, pain, tremor, and muscle spasms

27. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4721313/>

Conversely, multiple potential therapeutic benefits are attributed to cannabis and supported by differing degrees of evidence ([Baker et al., 2003a](#), [Baker et al., 2003b](#), [Ben Amar, 2006](#), [Borgelt et al., 2013](#), [Hazekamp and Grotenhermen, 2010](#), [Kalant, 2001](#), [Leung, 2011](#), [Robson, 2001](#)). Various evidence points to cannabis' effects as an analgesic, especially for neuropathic pain ([Campbell et al., 2001](#), [Martín-Sánchez et al., 2009](#)).

28. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5165161/>

In addition, we have assessed the role of the cannabinoid system and marijuana constituents in neuroprotection as well as considered other beneficial effects of marijuana. Marijuana has been shown to improve nonmotor symptoms of PD such as depression, pain, sleep, and anxiety.

Moreover, components of cannabis have been demonstrated to have neuroprotective effect due to their anti-inflammatory, antioxidative, and antiexcitotoxic properties.

4.2. Analgesic Effect of Cannabinoids

Pain is a relevant and often underestimated nonmotor symptom of PD. Pain affects more than 50% of people with this disorder and can cause extreme physical, psychological, and social disorders and worsen Parkinsonian disability. Different treatment options are used to treat PD pain. However, these medications have significant side effects and do not provide universal efficacy. Cannabis is well known as a pain-relieving plant. The cannabinoid receptors in the central and peripheral nervous systems have been shown to modulate pain perception. Several clinical studies have been performed to investigate the effect of marijuana or cannabinoids on pain. Smoked cannabis significantly reduced neuropathic pain intensity as well as significantly improved mood disturbance, physical disability, and quality of life in HIV-patients. Cannabis was effective at ameliorating neuropathic pain in patients with central and peripheral neuropathic pain. Inhaled cannabis significantly reduced pain intensity (34%) compared to placebo in a clinical trial of painful distal symmetric polyneuropathy (DSPN). Whole plant extracts of *Cannabis sativa* produced statistically significant improvements on the mean pain severity score. Cannabis-based medicine significantly decreased chronic pain intensity as well as sleep disturbance in multiple sclerosis patients. Oromucosal nabiximols (1 : 1 combination of the THC and CBD) produced a reduction in pain intensity scores in patients with neuropathic pain.

These findings are consistent with other discoveries supporting the efficacy of cannabis in relieving pain. The analgesic effect of cannabinoids has been reviewed. The review of the literature suggests that marijuana and/or cannabinoids may be efficacious for pain relieving in various disease states including PD.

29. <https://www.ncbi.nlm.nih.gov/pubmed/26317379>

367 medical marijuana patients in Arizona were surveyed.

318 patients reported using medical marijuana for treatment of Chronic Pain.

General relief from Chronic Pain symptoms was 76.7%

Relief by medical marijuana compared to other medications was 73.5%

Less frequent use of other medications was 90.2%

106 patients reported using medical marijuana for treatment of Headaches.

General relief from Headaches was 68.9%

Relief by medical marijuana compared to other medications was 73.7%

Less frequent use of other medications was 93.8%

30. <https://www.ncbi.nlm.nih.gov/pubmed/28189912>

In regards to conditions, pain-related conditions were the most common, reported by 53% of participants (n = 144; chronic pain 36% (n = 98), arthritis 12% (n = 32), headache 5% (n = 14)).

The second most prominent class was mental health (eating disorder, PTSD & psychiatric

disorder), reported by 15% (n = 41). Other prominent conditions included gastrointestinal I disorders (11%, n = 29), insomnia (7%, n = 18) and multiple sclerosis (4%, n = 11). In regards to symptoms; the most highly endorsed were chronic pain (73%, n = 197), stress (60%, n = 162), insomnia (57%, n = 155), depression (46%, n = 126) and headache (32%, n = 87). Gastrointestinal (GI) issues also featured prominently, with 29% (n = 79) citing appetite loss and another 29% (n = 79) nausea. Cannabis was perceived to be very effective at symptom relief, with 95% (n = 257) reporting that it “often” or “always” helped alleviate their symptoms.

31. 10.1111/j.1742-1241.2004.00271.x

Medicinal cannabis use was reported by patients with chronic pain (25%), multiple sclerosis and depression (22% each), arthritis (21%) and neuropathy (19%)
The mean age of the 2969 subjects was 52.7 years (SD 12.7), of whom 1805 (60.7%) were female. MS was the most common disease, reported by 1753 subjects (59%), while 1280 reported neuropathy (43%), 1125 reported chronic pain (33%) and 777 reported arthritis (26%). There was considerable overlap among these conditions.

Overall Effectiveness. Of 948 reported users, 648 (68%) reported that cannabis made their symptoms overall much better, 256 (27%) said a little better, 36 (4%) said no difference and eight subjects said a little worse (four subjects) or much worse (four subjects).

Effectiveness Compared to Other Medications. When asked how cannabis compared to other medications overall, 412 of 916 subjects (45%) said it worked much better than prescribed medications, 261 (28%) said it was somewhat better and 45 (5%) said it was about the same; only 27 subjects said that prescription medicines worked better than cannabis (18 somewhat better and nine much better). One hundred and seventy-one (19%) subjects said it was impossible to tell.

Side Effects Compared to other Medications. When asked to compare the undesirable effects of cannabis to those of prescribed medicines, 872 subjects responded, of whom six found that cannabis produced much worse side effects, 23 found somewhat worse side effects and 54 said the side effects were about the same. Two hundred and sixty-four (30%) subjects stated that side effects of prescribed medicines were somewhat worse and 294 (34%) said they were much worse. Two hundred and thirty-one (26%) stated that it was impossible to tell.

Effects on Other Medication Use. Of the 909 subjects responding to this question, 374 stated that their use of

cannabis had changed their use of other medications, while 521 said it had not. Fourteen were not coded.

Return of Symptoms on Stopping. Of the 876 subjects responding, 673 said their symptoms returned or got worse when they stopped using cannabis, and 203 denied any worsening on stopping cannabis.

32 10.1111/dar.12323

Participants presented with the range of conditions that is generally consistent with surveys of CTP users, the most prominent conditions being pain (32%), mood (i.e. anxiety and depression; 18%), arthritis (15%), HIV (10%), gastrointestinal disorder (7%)

The high rate of substitution for prescribed substances, particularly among patients with pain-related conditions, suggests that further research into cannabis/ cannabinoids as a potentially safer substitute for or adjunct to opiates is justified, and adds to research suggesting this phenomenon is robust across samples [6,20].

We created a dichotomous pain condition variable by aggregating respondents who identified the primary condition treated with CTP as spinal pain, non-spinal pain, or arthritis (n = 220), and comparing these participants to an aggregation of all other conditions (n = 241). A large contingent of these non-pain respondents nonetheless endorsed pain among the symptoms for which they used CTP (71%, n = 171), therefore, we conducted supplementary analyses comparing those who endorsed treating pain with CTP among a list of symptoms (83%, n = 390) with those who did not endorse treating pain with CTP (17%, n = 82).

33. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5422566/>

We previously reported in an earlier survey that of 1,429 respondents, 61% reported using cannabis for managing pain, 58% reported using cannabis for anxiety and 50% reported using cannabis for depression. In the current analysis, these same conditions were also the most commonly reported conditions by respondents. Of the 1,040 participants reporting pain and/or intractable pain, 619 (59.52%) reported depression and anxiety as comorbidities. As such, the odds of reporting substituting cannabis for prescription drugs were more than one and a half times greater (OR, 1.66; 95% CI, 1.27–2.16) among those reporting using it to manage pain, anxiety and depression than among those using it to manage only one of the three conditions. This team previously reported that in a survey of 1,429 medical cannabis users, 61% reported cannabis use for pain, 58% reported cannabis use for anxiety and 50% reported using cannabis to manage depression.⁶ In 2016, Dale and Stacey reported that those using cannabis for pain were more likely to be substituting for prescription drugs. In 2017, Walsh et al published a review of medical cannabis and mental health to try to better understand how medical cannabis use may impact areas of potential concern for clinicians. “Relaxation and relief of anxiety” and “relief of negative mood” or depression were among the most widely reported conditions in 60 publications included in their analysis. Because it is common for chronic pain patients to be prescribed combinatorial pharmacotherapy to address comorbidity with depression and/or

anxiety, it is largely unknown how often patients may be discontinuing prescription medications when initiating cannabis use.

Taken with preclinical data on the role of the endocannabinoid system in stress, pain processing and immune homeostasis, it is clear that future investigation is warranted using controlled trials with human subjects to better understand the role that cannabis may play in treating pain, anxiety, depression and other conditions.

34. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4277530/>

Most of the respondents (from the clinic and online groups) reported that cannabis improved their mood, pain, muscle spasms, and sleep.

35. <https://www.ncbi.nlm.nih.gov/pubmed/11210205>

This article reports on an exploratory study of medical cannabis users. Interviews were completed with 50 self-identified medical cannabis users recruited through notices in newspapers and on bulletin boards. They reported using cannabis for a variety of conditions including HIV-AIDS-related problems, *chronic pain*, depression, anxiety, menstrual cramps, migraine, narcotic addiction as well as *everyday aches, pains*, stresses and sleeping difficulties.

36. <https://www.ncbi.nlm.nih.gov/pubmed/26749285>

MEASUREMENTS AND RESULTS:

The primary outcome was number of migraine headaches per month with medical marijuana use. Secondary outcomes were the type and dose of medical marijuana used, previous and adjunctive migraine therapies, and patient-reported effects. *Migraine headache frequency decreased from 10.4 to 4.6 headaches per month ($p < 0.0001$) with the use of medical marijuana.* Most patients used more than one form of marijuana and used it daily for prevention of migraine headache. Positive effects were reported in 48 patients (39.7%), with the most common effects reported being prevention of migraine headache with decreased frequency of migraine headache (24 patients [19.8%]) and aborted migraine headache (14 patients [11.6%]). Inhaled forms of marijuana were commonly used for acute migraine treatment and were reported to abort migraine headache. Negative effects were reported in 14 patients (11.6%); the most common effects were somnolence (2 patients [1.7%]) and difficulty controlling the effects of marijuana related to timing and intensity of the dose (2 patients [1.7%]), which were experienced only in patients using edible marijuana. Edible marijuana was also reported to cause more negative effects compared with other forms.

37. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2683812/>

Five teens indicated they used marijuana to obtain pain relief, and several others shared similar stories about other youth. *One male used marijuana to deal with pain associated with rehabilitation after a muscle injury, another used marijuana following an accident where he sustained 3rd degree burns and yet another because of plates in his back due to a car injury.* Others suggested that marijuana reduced muscle pain after a hard day of skiing and helped with headaches, and that girls used marijuana for menstrual cramps. One 17-year old male used it daily and explained that marijuana "numbs your systems or senses [and] relaxes your muscles."

4. Provide articles published in peer-reviewed scientific journals reporting the results of research on the effects of marihuana on the medical condition or treatment of the medical condition and supporting why the medical condition should be added to the list of debilitating medical conditions under the Medical Marihuana Act. Attach a copy of all articles that are discussed in this section. Please do not attach articles that are not discussed in this section.

See enclosed.

