Ohio Patient Network

www.OhioPatientsNetwork.org

Ohio Patient Network
PO Box 42042
Cincinnati, Ohio

Opioid Use Disorder Petition- Section 4

Evidence supporting the use of medical marijuana

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New York, Illinois, Pennsylvania & New Jersey now use medical marijuana for Opioid Use Disorder. Newer studies done in 2019 continue to show significant reduction in opioid prescriptions and usage in states with marijuana laws vs non marijuana states. In the numerous articles included you will find study's conclusions with links that show medical marijuana reduction on prescription rates and opioid overdoses. See uploaded file that includes recent 2019 information.
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Section 4 Narrative - <u>Evidence supporting the use of medical marijuana to treat or alleviate the disease or condition, including journal articles, peer-reviewed studies, and other types of medical or scientific documentation.</u>

New York, Illinois, Pennsylvania & New Jersey use medical marijuana for Opioid Use Disorder and conditions where they would have prescribed an opioid is a fact. Newer studies done in 2019 continue to show significant reduction in opioid prescriptions and usage in states with marijuana laws vs non marijuana states. In the numerous articles included you will find study's conclusions with links that show medical marijuana reduction on prescription rates and opioid overdoses.

One of the most interesting findings is the increase in treatment retention rates. It is well known that the longer one stays in a treatment program, the better their chances are for success. See references numbered 14 & 16. Also reference 15 (Solomon) contains a large survey of medical marijuana patients and supports what Ohio Patient Network (OPN) has heard from patients here in Ohio, since OPN was formed seventeen years ago in 2001. For example, an extremely common complaint Ohio Patients Network (OPN) hears from Pain Clinic Patients is being removed or threatened due to a drug test detecting marijuana. These patients have consistently said the more marijuana they have the less opioids they need to control their pain. Thus if more patients could use marijuana, more patients would remain in the various addiction treatment programs.

Included as a separate file due to file size are 1) A presentation by Dr. Ethan Russo on a "Historical Review of Cannabis for Pain Relief and Addiction Treatment" and 2) A Medical Cannabis Opioid Guide - How to Use Cannabis to Reduce and Replace Opioid Medications by Dr. Dustin Sulak.

Below is an introduction and listing of included the references to the Medical Journal Articles and reports.

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Note: Each subject area is separated by a dashed (-=-=) line and has Hyperlink(s) to the full/original article from which the summary quotes or relevant sections were obtained. Note if petition reviewers are use unable to use the Hyperlink provided to obtain the reference document, Ohio Patient Network can provide an original copy upon request. Also note any excerpts or copies of the referenced articles text are in *non bolded italics*. We have included the US National Library of Medicine National Institute of Health PUBMED.GOV link for studies 18-21 listed.

1. **An Introduction**
2. **Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain**
3. **Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010**
4. **Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use**
5. **Cannabis as an Adjunct to or Substitute for Opiates in the Treatment of Chronic Pain**
6. **Is Cannabis use associated with less opioid use among people who inject drugs?**
7. **Cannabis as a substitute for alcohol and other drugs**
8. **Cannabis in palliative medicine: Improving care and reducing opioid-related morbidity.**
9. **Association Between US State Medical Cannabis Laws and Opioid Prescribing in the Medicare Part D Population**
10. **Study Links Medical Marijuana Dispensaries to Reduced Mortality From Opioid Overdose**
11. **The Pennsylvania Department of Health approved medical marijuana to treat patients addicted to opioids.**
12. **State of NJ: Medical Marijuana Program. 2018. Patient FAQs New Jersey adds Opioid Use Disorder to the Medical Marijuana Program**
13. **Final Agency Decision under the New Jersey Medical Marijuana Program.**
14. **Intermittent Marijuana Use Is Associated with Improved Retention in Naltrexone Treatment for Opiate-Dependence**
15. **Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report**
16. **High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis.**
17. **A collection of Journal articles relating cannabis and addiction with publication references**
18. **Emerging Evidence for Cannabis' Role in Opioid Use Disorder (published in late 2018)**
19. **The effect of cannabis laws on opioid use (published in 2019)**
20. **Medical Cannabis: Effects on Opioid and Benzodiazepine Requirements for Pain Control. (published in 2019)**
21. **The impact of cannabis access laws on opioid prescribing. (published in 2019)**

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1 – Introduction

Last year the OPN's petition to include Opioid Use Disorder was rejected, since that time a report in the Journal PLoS ONE titled *"Association between medical cannabis laws and opioid overdose mortality has reversed over time" by Chelsea L. Shover, Corey S. Davis, Sanford C. Gordon, and Keith Humphreys in PNAS June 25, 2019 116 (26) 12624-12626; first published June 10, 2019 https://doi.org/10.1073/pnas.1903434116* **appeared to undermine the conclusion stated in last years petition submitted by OPN. That study had numerous flaws that are identified in the indented rebuttal below this paragraph.** ***OPN stands by our petition that the inclusion of Opioid Use Disorder as a Qualifying condition for the Ohio Medical Marijuana Control program is in the best interest of public health for those under conventional treatment particularly in the Pain Clinics in Ohio.***

We have added newer studies/reports done in 2019 along with the studies OPN submitted last year. **Below is a rebuttal of the Shover study's conclusion.**

> ***The belief that expanding cannabis access plays a role in mitigating opioid use and abuse by the study failure to replicate observational findings initially documenting the trend. Both studies employed similar methodology. Investigators evaluated whether the passage of medical cannabis legislation was associated with later changes in opioid-related mortality. The first study, published in the "Journal of the American Medical Association" in 2014, reported that opioid overdose deaths fell significantly in the years following marijuana liberalization. By contrast, the most recent paper reports that this effect reversed over time. Authors also failed to identify a similar decline in opioid-related mortality in states that have more recently enacted medical marijuana-related laws.***
>
> ***Why the disparate results? One factor likely has to do with the differing inclusion criteria utilized in the two studies. While the 2014 paper assessed trends exclusively in states with operational medical marijuana access programs, investigators writing in PLoS ONE did not. Rather, they categorized numerous states with non-traditional medical marijuana laws — such as those jurisdictions that simply exempt specific patients who obtain black market CBD products from criminal prosecution — as "medical cannabis states."***
>
> ***In other cases, states that have codified medical marijuana legislation, but have yet to establish regulated cannabis production or sales, were also included. Predictably, these states with only limited, or in some cases, no medical cannabis access whatsoever, failed to experience any statistically significant trends.***

But before jumping to any conclusions based upon the findings of any single paper, it is important to acknowledge that dozens of additional peer-reviewed studies exist on this topic. Most, but not all, of this literature supports the cannabis substitution theory.

What's even more important, is that longitudinal studies evaluating opioid use patterns in specific patient populations provide clear and consistent evidence of this phenomenon. In contrast to observational, population-based studies (such as those summarized above), which only seek to identify whether an association exists between the passage of medical cannabis laws and opioid use trends in the general population — this data explicitly assesses individual patients' relationship with opioids following their registration in state-sponsored access programs.

In virtually all cases, these studies conclude that patients diagnosed with chronic pain and other debilitating conditions typically reduce, or in some cases, eliminate their use of opioids following their enrollment in state-sanctioned programs.

For example, researchers writing in the May 2019 edition of the journal Annals of Pharmacotherapy evaluated the use of opioids in 77 intractable pain patients newly enrolled in the Minnesota Medical Cannabis Program. Researchers reported "a statistically significant decrease in MME (milligram morphine equivalents) from baseline to both three and six months."

{Note the core of the above rebuttal was primarily written by Paul Armentano.}

Introduction continued

Although Opioid Use Disorder has only recently been specifically recognized as a qualifying condition for medical cannabis in any US medical marijuana states, the medical community is becoming increasingly aware of the correlation between medical cannabis use and lower rates of opiate use and opiate overdose death rates in medical marijuana states, as referenced in studies #2 and #3. In effect, when physicians recommend medical cannabis for other qualifying medical conditions in which the prescription of opioids is part of the medically accepted treatment, they are witnessing their patients using lower dosages of opiate medications or discontinuing opiate use completely.

An important consideration is the time that a patient stays in treatment for opiate dependence. The Raby and Socías study (item 14 & 16) demonstrate that the intermittent use of marijuana was linked to improvement in treatment retention rates.

The very fact that Ohio's Medical Marijuana Program has chronic and severe pain or intractable pain as a qualifying condition supports that medical marijuana is a potential alternative to opiates in general.

Therefore Ohio Patient Network's contention is that Opioid Use Disorder / Opiate Addiction itself should be recognized as a qualifying condition for the Ohio Medical Marijuana Control Program, the opiate epidemic in Ohio could be more effectively addressed through this process of harm reduction for users of both prescription and illicit opiates.

Below is a list of articles from peer-reviewed scientific journals along with a brief excerpt from abstracts, conclusions, or results. A hyperlink and/or DOI reference number to the original documents are provided. There are literally dozens more peer-reviewed journal articles that could be used to support this petition; we are happy to provide the petition reviewers access to Ohio Patient Network reports spreadsheet.

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2. Source: Kevin F. Boehnke, Evangelos Litinas, Daniel J. Clauw. 2016. *Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain.* The Journal of Pain, Volume 17, Issue 6, 739 - 744.

Highlights:

• Cannabis use was associated with 64% lower opioid use in patients with chronic pain.
• Cannabis use was associated with better quality of life in patients with chronic pain.
• Cannabis use was associated with fewer medication side effects and medications used.

Abstract: Opioids are commonly used to treat patients with chronic pain (CP), though there is little evidence that they are effective for long term CP treatment. Previous studies reported strong associations between passage of medical cannabis laws and decrease in opioid overdose statewide. Our aim was to examine whether using medical cannabis for CP changed individual patterns of opioid use. Using an online questionnaire, we conducted a cross-sectional retrospective survey of 244 medical cannabis patients with CP who patronized a medical cannabis dispensary in Michigan between November 2013 and February 2015. Data collected included demographic information, changes in opioid use, quality of life, medication classes used, and medication side effects before and after initiation of cannabis usage. Among study participants, medical cannabis use was associated with a 64% decrease in opioid use (n = 118), decreased number and side effects of medications, and an improved quality of life (45%). This study suggests that many CP patients are essentially substituting medical cannabis for opioids and other medications for CP treatment, and finding the benefit and side effect profile of cannabis to be greater than these other classes of medications. More research is needed to validate this finding.

Abstract – http://www.jpain.org/article/S1526-5900(16)00567-8/abstract
Full Text – http://www.jpain.org/article/S1526-5900(16)00567-8/fulltext

References – http://www.jpain.org/article/S1526-5900(16)00567-8/references

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3. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. 2014. *Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States 1999-2010*. JAMA Internal Medicine.

"Results: Three states (California, Oregon, and Washington) had medical cannabis laws effective prior to 1999. Ten states (Alaska, Colorado, Hawaii, Maine, Michigan, Montana, Nevada, New Mexico, Rhode Island, and Vermont) enacted medical cannabis laws between 1999 and 2010. States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, −37.5% to −9.5%; P = .003) compared with states without medical cannabis laws. Examination of the association between medical cannabis laws and opioid analgesic overdose mortality in each year after implementation of the law showed that such laws were associated with a lower rate of overdose mortality that generally strengthened over time: year 1 (–19.9%; 95% CI, −30.6% to −7.7%; P = .002), year 2 (−25.2%; 95% CI, −40.6% to −5.9%; P = .01), year 3 (−23.6%; 95% CI, −41.1% to −1.0%; P = .04), year 4 (−20.2%; 95% CI, −33.6% to −4.0%; P = .02), year 5 (−33.7%; 95% CI, −50.9% to −10.4%; P = .008), and year 6 (−33.3%; 95% CI, −44.7% to −19.6%; P < .001). In secondary analyses, the findings remained similar."

And

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

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***4.* National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Health Sciences Policy; Committee on Pain Management and Regulatory Strategies to Address Prescription Opioid Abuse; Phillips JK, Ford MA, Bonnie RJ, editors. 2017*. Pain Management and the Opioid Epidemic: Balancing Societal and Individual Benefits and Risks of Prescription Opioid Use.* Pain Management and the Opiate Epidemic.**

"while further testing needs to be done, medical marijuana may be advocated as part of a comprehensive package of policies to reduce the population risk of opioid analgesics."

Abstract (3): http://archinte.jamanetwork.com/article.aspx?articleid=1898878#Abstract
Full Text (3): https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/1898878
Full Text (4): https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4392651/

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5. Lucas, Philippe. 08 June 2012. *Cannabis as an Adjunct to or Substitute for Opiates in the Treatment of Chronic Pain*. Journal of Psychoactive Drugs.

Abstract: There is a growing body of evidence to support the use of medical cannabis as an adjunct to or substitute for prescription opiates in the treatment of chronic pain. When used in conjunction with opiates, cannabinoids lead to a greater cumulative relief of pain, resulting in a reduction in the use of opiates (and associated side-effects) by patients in a clinical setting. Additionally, cannabinoids can prevent the development of tolerance to and withdrawal from opiates, and can even rekindle opiate analgesia after a prior dosage has become ineffective. Novel research suggests that cannabis may be useful in the treatment of problematic substance use. These findings suggest that increasing safe access to medical cannabis may reduce the personal and social harms associated with addiction, particularly in relation to the growing problematic use of pharmaceutical opiates. Despite a lack of regulatory oversight by federal governments in North America, community-based medical cannabis dispensaries have proven successful at supplying patients with a safe source of cannabis within an environment conducive to healing, and may be reducing the problematic use of pharmaceutical opiates and other potentially harmful substances in their communities.

Full Text:
https://www.researchgate.net/publication/230652616_Cannabis_as_an_Adjunct_to_or_Substitute_for_Opiates_in_the_Treatment_of_Chronic_Pain

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6. Kral AH, Wenger L, Novak SP, Chu D, Corsi KF, Coffa D, Shapiro B, Blumenthal RN. 2015. *Is Cannabis use associated with less opioid use among people who inject drugs?* Drug Alcohol Dependence.

Conclusions: There is a statistical association between recent cannabis use and lower frequency of nonmedical opioid use among people who inject drugs (PWID). This may suggest that PWID use cannabis to reduce their pain and/or nonmedical use of opioids. However, more research, including prospective longitudinal studies, is needed to determine the validity of these findings.

Full Text: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4509857/

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7. Reiman, A. 2009. *Cannabis as a substitute for alcohol and other drugs*. Harm Reduction Journal.

Conclusion: The substitution of one psychoactive substance for another with the goal of reducing negative outcomes can be included within the framework of harm reduction. Medical cannabis patients have been engaging in substitution by using cannabis as an alternative to alcohol, prescription and illicit

drugs.

Full Text: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2795734/

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8. Carter GT, Flanagan AM, Earleywine M, Abrams DI, Aggarwal SK, Grinspoon L. 2011. *Cannabis in palliative medicine: Improving care and reducing opioid-related morbidity.* American Journal of Hospice and Palliative Medicine.

Abstract: Unlike hospice, long-term drug safety is an important issue in palliative medicine. Opioids may produce significant morbidity. Cannabis is a safer alternative with broad applicability for palliative care. Yet the Drug Enforcement Agency (DEA) classifies cannabis as Schedule I (dangerous, without medical uses). Dronabinol, a Schedule III prescription drug, is 100% tetrahydrocannabinol (THC), the most psychoactive ingredient in cannabis. Cannabis contains 20% THC or less but has other therapeutic cannabinoids, all working together to produce therapeutic effects. As palliative medicine grows, so does the need to reclassify cannabis. This article provides an evidence-based overview and comparison of cannabis and opioids. Using this foundation, an argument is made for reclassifying cannabis in the context of improving palliative care and reducing opioid-related morbidity.

Full Text:
https://www.researchgate.net/publication/50891411_Cannabis_in_Palliative_Medicine_Improving_Care_and_Reducing_Opioid-Related_Morbidity

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9. Ashley C. Bradford, W. David Bradford, Amanda Abraham, Grace Bagwell Adams, et al. 2018. *Association Between US State Medical Cannabis Laws and Opioid Prescribing in the Medicare Part D Population*. JAMA Internal Medicine.
And also found in
Bradford AC, Bradford WD. 2016. *Medical Marijuana Laws Reduce Prescription Medication Use in Medicare Part D.* Health Affairs 35, no.7.

Question: What is the association between US state implementation of medical cannabis laws and opioid prescribing under Medicare Part D?

Findings: This longitudinal analysis of Medicare Part D found that prescriptions filled for all opioids decreased by 2.11 million daily doses per year from an average of 23.08 million daily doses per year when a state instituted any medical cannabis law. Prescriptions for all opioids decreased by 3.742 million daily doses per year when medical cannabis dispensaries opened.

Abstract: Legalization of medical marijuana has been one of the most controversial areas of state policy change over the past twenty years. However, little is known about whether medical marijuana is being

used clinically to any significant degree. 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. National overall reductions in Medicare program and enrollee spending when states implemented medical marijuana laws were estimated to be $165.2 million per year in 2013. The availability of medical marijuana has a significant effect on prescribing patterns and spending in Medicare Part D.

Multiple Sources
https://www.healthaffairs.org/doi/abs/10.1377/hlthaff.2015.1661
https://jamanetwork.com/journals/jamainternalmedicine/article-abstract/2676999
http://www.ouramazingworld.org/uploads/4/3/8/6/43860587/bradford2016.pdf

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10. Eric Sarlin, M.Ed., M.A. 2016. *Study Links Medical Marijuana Dispensaries to Reduced Mortality From Opioid Overdose.* National Institute of Drug Abuse.

"The most striking finding was that legally protected marijuana dispensaries (LMDs) were associated with lower rates of dependence on prescription opioids, and deaths due to opioid overdose."

"Dr. Powell and his co-investigators compared rates of opioid-related treatment admissions and mortality rates in states with and without LMDs using data from the annually compiled Treatment Episodes Data Set (TEDS) and the National Vital Statistics System, respectively. Their analysis revealed that states with LMDs had lower opioid-overdose mortality rates and fewer admissions to treatment for opioid addiction than they would have had without the dispensaries. The estimated sizes of the reductions were 16 to 31 percent in mortality due to prescription opioid overdoses, and 28 to 35 percent in admissions for treatment of opioid addiction. This latter reduction was steeper, up to 53 percent, among patients who entered treatment independently of the criminal justice system. The researchers also noted a trend whereby the longer LMDs were in place, the more the incidence of opioid-related problems declined."

This work was supported by NIH grant DA032693.

NIDA Article website source citations

- **National Bureau of Economic Research. 2015. *Do Medical Marijuana Laws Reduce Addictions and Deaths Related to Pain Killers?* Cambridge, MA: National Bureau of Economic Research.**
- **Pacula, R.L.; Powell, D.; Heaton, P. et al. 2015. *Assessing the effects of medical marijuana laws on marijuana use: The devil is in the details*. Journal of Policy Analysis and Management 34(1):7-31.**
- **Sevigny, E.; Pacula, R.L.; and Heaton, P. 2014. *The effects of medical marijuana laws on potency.* International Journal of Drug Policy.**

Full Text: https://www.drugabuse.gov/news-events/nida-notes/2016/05/study-links-medical-marijuana-dispensaries-to-reduced-mortality-opioid-overdose

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11- Governor Tom Wolf: governor.pa.gov. 2018. ***Wolf Administration Approves Eight Universities as Certified Medical Marijuana Academic Clinical Research Centers.***

The Pennsylvania Department of Health approved medical marijuana to treat patients addicted to opioids

Earlier this year the Pennsylvania Department of Health approved medical marijuana to treat patients addicted to opioids May 14th 2018. The Pennsylvania Secretary of Health Dr Levine said "By adding opioid-use disorder as an approved medical condition under the program, we not only give physicians another tool for treatment of this devastating disease, but we allow for research to be conducted on medical marijuana's effectiveness in treatment" Additionally Dr Levine said "It's important to note that medical marijuana is not a substitute for proven treatments for opioid-use disorder. In Pennsylvania, medical marijuana will be available to patients if all other treatment fails, or if a physician recommends that it be used in conjunction with traditional therapies."

Full Text: https://www.governor.pa.gov/wolf-administration-approves-eight-universities-certified-medical-marijuana-academic-clinical-research-centers/

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12. State of NJ: Medical Marijuana Program. 2018. ***Patient FAQs.*** **State of NJ: Department of Health.**

Question: "I have Opiod Use disorder. Am I eligible to get medicinal marijuana?"
Answer: "Yes, opioid use disorder resulting from the treatment of chronic pain with opioids was added under condition "chronic pain related to musculoskeletal disorders." The Department received a petition seeking to add opioid use disorder (MMP-063) as a qualifying medical condition under the Medicinal Marijuana Program."

Full Text: https://www.nj.gov/health/medicalmarijuana/pat_faqs.shtml#2

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13- State of New Jersey: Department of Health. 2018. ***Letter to Petitioners from the New Jersey Department of Health : Final Agency Decision to Establish Additional Debilitating Medical Condition under the New Jersey Medical Marijuana Program*****.**

NOTE: Along with other approved conditions, Opioid Use Disorder is included.

Letter Full Text link:
https://www.nj.gov/health/medicalmarijuana/documents/MMP_FinalAgencyDecisionGrantingPetitions.pdf
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14- Wilfrid Noel Raby, PhD, MD, Kenneth M. Carpenter, PhD, Jami Rothenberg, PhD, Adam C. Brooks, PhD, Huiping Jiang, PhD, Maria Sullivan, MD, Adam Bisaga, MD, Sandra Comer, PhD, Edward V. Nunes, MD. 2018. *Intermittent Marijuana Use Is Associated with Improved Retention in Naltrexone Treatment for Opiate-Dependence.*
American Academy of Addiction Psychiatry: The American Journal on Addictions, 18: 301–308.

Pertinent Excerpts from the discussion

“The present study replicates a previous surprising finding that intermittent cannabis use is associated with improved retention in naltrexone treatment among opioid dependent patients…”

“Intermittent cannabis use was also associated with improved adherence to naltrexone pill-taking. The data comparing cannabis use levels before versus after treatment entry suggest patients either stay at the same level, or advance to a higher level of cannabis use after starting naltrexone, consistent with a process of self-medication. These findings are of interest, because they suggest the hypothesis that moderate cannabis use may be exerting a beneficial pharmacological effect improving the tolerability of naltrexone in the early weeks after induction, and that cannabinoid agonists might have promise for improving the effectiveness of naltrexone treatment for opioid dependence.”

Full Text:
https://www.ncbi.nlm.nih.gov/pubmed/19444734

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15- Perry Solomon, MD, Amanda Reiman Phd, Mark Welty, Phd. 2017. *Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report.* Cannabis and Cannabinoid Research Vol. 2, No. 1.

Abstract: Prescription drug overdoses are the leading cause of accidental death in the United States. Alternatives to opioids for the treatment of pain are necessary to address this issue. Cannabis can be an effective treatment for pain, greatly reduces the chance of dependence, and eliminates the risk of fatal overdose compared to opioid-based medications. Medical cannabis patients report that cannabis is just as effective, if not more Than opioid-based medications for pain. Materials and Methods: The current study examined the use of cannabis as a substitute for opioid-based pain medication by collecting survey data from 2897 medical cannabis patients.

Discussion: Thirty-four percent of the sample reported using opioid-based pain medication in the past 6 months. Respondents overwhelmingly reported that cannabis provided relief on par with their other medications, but without the unwanted side effects. Ninety-seven percent of the sample "strongly agreed/agreed" that they are able to decrease the amount of opiates they consume when they also use cannabis, and 81%"strongly agreed/agreed" that taking cannabis by itself was more effective at treating their condition than taking cannabis with opioids. Results were similar for those using cannabis with non opioid-based pain medications.

Conclusion: Future research should track clinical outcomes where cannabis is offered as a viable substitute for pain treatment and examine the outcomes of using cannabis as a medication assisted treatment for opioid dependence.

Full Text:
https://doi.org/10.1089/can.2017.0012

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16-Socías ME, Wood, Lake, Nolan, Fairbairn, Hayashi, Shulh , Liu, Kerr, Milloy MJ
High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis.
Sources
https://www.ncbi.nlm.nih.gov/pubmed/30238568
https://onlinelibrary.wiley.com/doi/epdf/10.1111/add.14398
doi:10.1111/add.14398

BACKGROUND AND AIMS: Cannabis use is common among people on opioid agonist treatment (OAT), causing concern for some care providers. However, there is limited and conflicting evidence on the impact of cannabis use on OAT outcomes. Given the critical role of retention in OAT in reducing opioid-related morbidity and mortality, we aimed to estimate the association of at least daily cannabis use on the likelihood of retention in treatment among people initiating OAT. As a secondary aim we tested the impacts of less frequent cannabis use.

DESIGN: Data were drawn from two community-recruited prospective cohorts of people who use illicit drugs (PWUD). Participants were followed for a median of 81 months (interquartile range = 37-130).

SETTING: Vancouver, Canada.

PARTICIPANTS: This study comprised a total of 820 PWUD (57.8% men, 59.4% of Caucasian ethnicity, 32.2% HIV-positive) initiating OAT between December 1996 and May 2016. The proportion of women was higher among HIV-negative participants, with no other significant differences.

MEASUREMENTS: The primary outcome was retention in OAT, defined as remaining in OAT (methadone or buprenorphine/naloxone-based) for two consecutive 6-month follow-up periods. The primary explanatory variable was cannabis use (at least daily versus less than daily) during the same 6-month period. Confounders assessed included: socio-demographic characteristics, substance use patterns and social-structural exposures.

FINDINGS: In adjusted analysis, at least daily cannabis use was positively associated with retention in OAT [adjusted odds ratio (aOR) = 1.21, 95% confidence interval (CI) = 1.04-1.41]. Our secondary analysis showed that compared with non-cannabis users, at least daily users had increased odds of retention in OAT (aOR = 1.20, 95% CI = 1.02-1.43), but not less than daily users (aOR = 1.00, 95% CI = 0.87-1.14).

CONCLUSIONS: Among people who use illicit drugs initiating opioid agonist treatment in Vancouver, at least daily cannabis use was associated with approximately 21% greater odds of retention in treatment compared with less than daily consumption.

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17. A collection of Journal articles relating cannabis and addiction with publication citations
* (Note: some citations may be partial repeats or different quotes from the previous 17 *items*)

"The endocannabinoid system also participates in the common mechanisms underlying relapse to drug-seeking behavior by mediating the motivational effects of drug-related environmental stimuli and drug re-exposure."
Rafael Maldonado, Olga Valverde, Fernando Berrendero. 2006. ***Involvement of the Endocannabinoid System in Drug Addiction.***

"History of cannabis use… did not negatively impact the methadone induction process. Pilot data also suggested that objective ratings of opiate withdrawal decrease in MMT patients using cannabis during stabilization."
Jillian L. Scavone PhD, Robert C. Sterling PhD, et. al. 2013 ***Impact of Cannabis Use During Stabilization on Methadone Maintenance Treatment.***

"We have concluded that improvements in state medical cannabis legislation and regulations could increase program enrollment and save lives."
Americans for Safe Access. 2017. ***Medical Cannabis as a Tool to Combat Pain and the Opiod Crisis.***

"Medical marijuana policies were significantly associated with reduced OPR-related hospitalizations but had no associations with marijuana-related hospitalizations."
Yuyan Shi. 2017. ***Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever***

"Legally protected marijuana dispensaries (LMDs) were associated with lower rates of dependence on prescription opioids, and deaths due to opioid overdose, than would have been expected based on prior trends"
Eric Sarlin, M.Ed., M.A. 2016. ***Study Links Medical Marijuana Dispensaries to Reduces Mortality From Opiod Overdose.***

"States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate (95% CI, −37.5% to −9.5%; P = .003) compared with states without medical cannabis laws. Examination of the association between medical cannabis laws and opioid analgesic overdose mortality in each year after implementation of the law showed that such laws were associated with a lower rate of overdose mortality that generally strengthened over time."
Marcus A. Bachhuber, MD; Brendan Saloner, PhD; Chinazo O. Cunningham, MD; et al. 2014. ***Medical Cannabis Laws and Opioid Analgesic Overdose Mortality in the United States, 1999-2010.***

"Intermittent cannabis users showed superior retention in naltrexone treatment (median days retained = 133; mean = 112.8, SE = 17.5), compared to abstinent (median = 35; mean = 47.3, SE = 9.2) or consistent users (median = 35; mean = 68.3, SE = 14.1) (log rank = 12.2, df = 2, p = .002). The effect remained significant in a Cox model after adjustment for baseline level of heroin use and during treatment level of cocaine use. Intermittent cannabis use was also associated with greater adherence to naltrexone pill-taking."
Raby WN1, Carpenter KM, Rothenberg J, Brooks AC, Jiang H, Sullivan M, Bisaga A, Comer S, Nunes EV. 2009. ***Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence.***

"Medical marijuana legalization was associated with 23% (p = 0.008) and 13% (p = 0.025) reductions in hospitalizations related to opioid dependence or abuse and OPR overdose, respectively; lagged effects were observed after policy implementation... Medical marijuana polices had no associations with marijuana-related hospitalizations."
Yuyan Shi. 2017. ***Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever.***

"CBD attenuated context-induced and stress-induced drug seeking without tolerance, sedative effects, or interference with normal motivated behavior. Following treatment termination, reinstatement remained attenuated up to ≈5 months although plasma and brain CBD levels remained detectable only for 3 days. CBD also reduced experimental anxiety and prevented the development of high impulsivity in rats with an alcohol dependence history."
Gustavo Gonzalez-Cuevas, Remi Martin-Fardon ,Tony M. Kerr, et al. 2018. ***Unique treatment potential of cannabidiol for the prevention of relapse to drug use: preclinical proof of principle***

"Preclinical animal models have long demonstrated that, in addition to reducing the rewarding properties of opioid drugs and withdrawal symptoms, CBD directly reduces heroin-seeking behavior. Importantly, these effects are related to conditioned cue-induced reinstatement of heroin-seeking behavior, an effect that was evident weeks after CBD was initially administered. This long-lasting effect is an important consideration in developing practical strategies for substance use disorders..."
Yasmin L.Hurd. 2017. ***Cannabidiol: Swinging the Marijuana Pendulum From 'Weed' to Medication to Treat the Opioid Epidemic***

"Our results suggest that cannabidiol interferes with brain reward mechanisms responsible for the expression of the acute reinforcing properties of opioids, thus indicating that cannabidiol may be clinically useful in attenuating the rewarding effects of opioids."
Vicky Katsidoni; Ilektra Anagnostou; George Panagis. 2012. ***Cannabidiol inhibits the reward-facilitating effect of morphine: involvement of 5-HT1A receptors in the dorsal raphe nucleus.***

"Among people who use illicit drugs initiating opioid agonist treatment in Vancouver, at least daily cannabis use was associated with approximately 21% greater odds of retention in treatment compared with less than daily consumption."
Maria Eugenia Socías; EvanWood; Stephanie Lake; et al. 2018. ***High-intensity cannabis use is associated with retention in opioid agonist treatment: a longitudinal analysis*.**

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18. Emerging Evidence for Cannabis' Role in Opioid Use Disorder

In Conclusion

Conclusion: The compelling nature of these data and the relative safety profile of cannabis warrant further exploration of cannabis as an adjunct or alternative treatment for OUD.

Abstract

Introduction: The opioid epidemic has become an immense problem in North America, and despite decades of research on the most effective means to treat opioid use disorder (OUD), overdose deaths are at an all-time high, and relapse remains pervasive. Discussion: Although there are a number of FDA-approved opioid replacement therapies and maintenance medications to help ease the severity of opioid withdrawal symptoms and aid in relapse prevention, these medications are not risk free nor are they successful for all patients. Furthermore, there are legal and logistical bottlenecks to obtaining traditional opioid replacement therapies such as methadone or buprenorphine, and the demand for these services far outweighs the supply and access. To fill the gap between efficacious OUD treatments and the widespread prevalence of misuse, relapse, and overdose, the development of novel, alternative, or adjunct OUD treatment therapies is highly warranted. In this article, we review emerging evidence that suggests that cannabis may play a role in ameliorating the impact of OUD. Herein, we highlight knowledge gaps and discuss cannabis' potential to prevent opioid misuse (as an analgesic alternative), alleviate opioid withdrawal symptoms, and decrease the likelihood of relapse. Conclusion: The compelling nature of these data and the relative safety profile of cannabis warrant further exploration of cannabis as an adjunct or alternative treatment for OUD.

Source

Cannabis Cannabinoid Res. 2018 Sep 1;3(1):179-189. doi: 10.1089/can.2018.0022. eCollection 2018.
Emerging Evidence for Cannabis' Role in Opioid Use Disorder.
Wiese B1,2, Wilson-Poe AR2.
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US National Library of Medicine National Institute of Health PUBMED.GOV link
https://www.ncbi.nlm.nih.gov/pubmed/30221197

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19. The effect of cannabis laws on opioid use, Flexon JL, Stolzenberg L, D'Alessio SJ.
Int J Drug Policy. 2019 Dec;74:152-159. doi: 10.1016/j.drugpo.2019.09.013. Epub 2019 Oct 4.

In conclusion study 19 states that....

> **"In conclusion, the present study found that in MML (Medical Marijuana Law) states some displacement is occurring away from opioids toward medicinal cannabis, but misuse of opioids is neither increasing nor decreasing owning to the policy."**

and goes on the conclude

> **"Since recent research has suggested that MMLs (Medical Marijuana Laws) do influence the negative outcomes associated with opioid reliance, such as reducing premature death from overdose (Bachhuber et al., 2015), and there does not appear to be a concern that enacting MMLs increases opioid misuse directly, medicinal cannabis may be one avenue to combat the consequences of the opioid epidemic...."**

Source
Int J Drug Policy. 2019 Dec;74:152-159. doi: 10.1016/j.drugpo.2019.09.013. Epub 2019 Oct 4.
The effect of cannabis laws on opioid use.
Flexon JL1, Stolzenberg L2, D'Alessio SJ3.
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US National Library of Medicine National Institute of Health PUBMED.GOV link
https://www.ncbi.nlm.nih.gov/pubmed/31590091

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20. Medical Cannabis: Effects on Opioid and Benzodiazepine Requirements for Pain Control.
In conclusion study 20 states that....

> **Conclusion and Relevance: Over the course of this 6-month retrospective study, patients using medical cannabis for intractable pain experienced a significant reduction in the number of MMEs available to use for pain control.**

Abstract

Background: There is currently little evidence regarding the use of medical cannabis for the treatment of intractable pain. Literature published on the subject to date has yielded mixed results concerning the efficacy of medical cannabis and has been limited by study design and regulatory issues. Objective: The objective of this study was to determine if the use of medical cannabis affects the amount of opioids and benzodiazepines used by patients on a daily basis. Methods: This single-center, retrospective cohort study evaluated opioid and benzodiazepine doses over a 6-month time period for patients certified to use medical cannabis for intractable pain. All available daily milligram morphine equivalents (MMEs) and daily diazepam equivalents (DEs) were calculated at baseline and at 3 and 6 months. Results: A total of 77 patients were included in the final analysis. There was a statistically significant decrease in median MME from baseline to 3 months (-32.5 mg; P = 0.013) and 6 months (-39.1 mg; P = 0.001). Additionally, there was a non-statistically significant decrease in median DE at 3 months (-3.75 mg; P = 0.285) and no change in median DE from baseline to 6 months (-0 mg; P = 0.833).

Source

Ann Pharmacother. 2019 Nov;53(11):1081-1086. doi: 10.1177/1060028019854221. Epub 2019 May 25.
Medical Cannabis: Effects on Opioid and Benzodiazepine Requirements for Pain Control.
O'Connell M1, Sandgren M2, Frantzen L3, Bower E4,5, Erickson B5.
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US National Library of Medicine National Institute of Health PUBMED.GOV link
https://www.ncbi.nlm.nih.gov/pubmed/31129977

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21 The impact of cannabis access laws on opioid prescribing.

Note the state results of the study

> **Analyzing a dataset of over 1.5 billion individual opioid prescriptions between 2011 and 2018, which were aggregated to the individual provider-year level, we find that recreational and medical cannabis access laws reduce the number of morphine milligram equivalents prescribed each year by 11.8 and 4.2 percent, respectively.**

J Health Econ. 2019 Dec 14;69:102273. doi: 10.1016/j.jhealeco.2019.102273. [Epub ahead of print]
The impact of cannabis access laws on opioid prescribing.
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Abstract

While recent research has shown that cannabis access laws can reduce the use of prescription opioids, the effect of these laws on opioid use is not well understood for all dimensions of use and for the general United States population. Analyzing a dataset of over 1.5 billion individual opioid prescriptions between 2011 and 2018, which were aggregated to the individual provider-year level, we find that recreational and medical cannabis access laws reduce the number of morphine milligram equivalents prescribed each year by 11.8 and 4.2 percent, respectively. These laws also reduce the total days' supply of opioids prescribed, the total number of patients receiving opioids, and the probability a provider prescribes any opioids net of any offsetting effects. Additionally, we find consistent evidence that cannabis access laws have different effects across types of providers, physician specialties, and payers.

Source

J Health Econ. 2019 Dec 14;69:102273. doi: 10.1016/j.jhealeco.2019.102273. [Epub ahead of print]
The impact of cannabis access laws on opioid prescribing.
McMichael BJ1, Van Horn RL2, Viscusi WK3.
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3 University Distinguished Professor of Law, Economics, and Management, Vanderbilt University Law School. 131 21st Avenue South, Nashville, TN, 37203, United States. Electronic address: kip.viscusi@vanderbilt.edu.

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