From: noreply@pharmacy.ohio.gov
To: MedicalMarijuana@med.ohio.gov
Subject: Condition Petition for Robert Ryan
Date: Tuesday, December 31, 2019 1:43:27 PM

This message was sent from the Condition page on medicalmarijuana.ohio.gov.

Box was check regarding file size being too large to upload. Action needed!

Name: Robert Ryan
Address: 9514 Conklin Ave, Cincinnati, OH, 45242
Phone: (513) 207-3964
Email: rryan@ohiopatientsnetwork.org

Specific Disease or Condition:
Opioid Use Disorder

Information from experts who specialize in the disease or condition.
Opioid Use Disorder is the physical and psychological reliance on opioids found in prescription pain medications and illegal drugs like heroin and fentanyl derivatives. Addiction occurs when dependence interferes with daily life. Symptoms include uncontrollable cravings and inability to control opioid use. People may experience whole body craving, sweating, euphoria or general angst. Some common effects are constipation, nausea, and death due to overdose. See uploaded file.

Relevant medical or scientific evidence pertaining to the disease or condition.
Included in the attached Section 2 PDF file is a variety of government reports detailing the relevant medical evidence of Opioid Use Disorder with reference links to the original reports. The documents address the scope and the science of addiction, including a commentary by Nora D. Volkow, M.D., Director, NIDA and more. The attachment also includes the most recent report from the National Center for Health Statistics listing Ohio as the second highest in the nation for overdoses.

Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition.
Opioid Use Disorder is a complex condition that is not easily treated successfully. The patient usually has other associated mental and/or physical issues. According to NIDA the relapse rate for patients going through drug addiction treatment ranges from 40% to 60%. Twelve Step Facilitation programs have mixed success and are not well documented. The indisputable fact that we have such a tremendous number of overdose deaths indicates that conventional medical therapies are insufficient.

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.
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.

Letters of support provided by physicians with knowledge of the disease or condition. This may include a letter provided by the physician treating the petitioner, if applicable.
Attached are letters supporting adding Opioid Use Disorder/Opiate Addiction as a qualifying condition. Note Dr. Ethan Russo, is a neurologist with drug development experiences and leadership positions in international research medical organizations; Dr. Blatman, an Ohio based pain practitioner; Dr . Sawyer, certified in Suboxone therapy and others. Dr. Thress is also included. Also noted are 22 doctors who have supported the Leeds and Rosenberger 2018 petition.

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Opioid Use Disorder Petition- Section 1

Information from experts who specialize in the study of the disease or condition

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Opioid Use Disorder is the physical and psychological reliance on opioids found in prescription pain medications and illegal drugs like heroin and fentanyl derivatives. Addiction occurs when dependence interferes with daily life. Symptoms include uncontrollable cravings and inability to control opioid use. People may experience whole body craving, sweating, euphoria or general angst. Some common effects are constipation, nausea, and death due to overdose. See uploaded file.

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Section 1 Narrative

<u>Information from experts who specialize in the study of the disease or condition</u>

Opioid Use Disorder is the physical and psychological reliance on opioids, found in various prescription pain medications and illegal drugs such as heroin and fentanyl derivatives. Addiction occurs when dependence interferes with daily life and becomes the focus of obtaining the next dose. This excessive reliance can easily lead one down a spiraling negative path in life.

Symptoms of addiction include uncontrollable cravings and inability to control opioid use even though it's having negative effects on personal relationships, finances and/or law abiding behaviors. People may experience whole body craving or sweating, euphoria or general angst. Some common effects are constipation, nausea, and death due to overdose.

The material is from experts who have specialized in the study of addiction. Information from the American Psychiatric Association DSM-5 Criteria for Diagnosis of Opioid Use Disorder and Dr. Marc A. Schuckit as published in the New England Journal of Medicine.

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 obtain an original copy upon request. Also note any excerpts or copies of the referenced articles text are in *non bolded italics***.**

=-=

1- Mark A. Schuckit, M.D. 2016. *Treatment of Opioid-Use Disorders.* New England Journal of Medicine

- *Use of an opioid in increased amounts or longer than intended Persistent wish or unsuccessful effort to cut down or control opioid use*

- *Excessive time spent to obtain, use, or recover from opioid use*
- *Strong desire or urge to use an opioid*
- *Interference of opioid use with important obligations*
- *Continued opioid use despite resulting interpersonal problems, social problems (e.g., interference with work), or both*
- *Elimination or reduction of important activities because of opioid use*
- *Use of an opioid in physically hazardous situations (e.g., while driving)*
- *Continued opioid use despite resulting physical problems, psychological problems, or both*
- *Need for increased doses of an opioid for effects, diminished effect per dose, or both*
- *Withdrawal when dose of an opioid is decreased, use of drug to relieve withdrawal, or both*

Full Text: https://www.nejm.org/doi/full/10.1056/NEJMra1604339
-=

2- The American Psychiatric Association. 2013. Criteria for Diagnosis of Opioid Use Disorder. Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, page 541.

DSM-5 Criteria for Diagnosis of Opioid Use Disorder

1. *Opioids are often taken in larger amounts or over a longer period of time than intended.*
2. *There is a persistent desire or unsuccessful efforts to cut down or control opioid use.*
3. *A great deal of time is spent in activities necessary to obtain the opioid, use the opioid, or recover from its effects.*
4. *Craving, or a strong desire to use opioids.*
5. *Recurrent opioid use resulting in failure to fulfill major role obligations at work, school or home.*
6. *Continued opioid use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of opioids.*
7. *Important social, occupational or recreational activities are given up or reduced because of opioid use.*
8. *Recurrent opioid use in situations in which it is physically hazardous*
9. *Continued use despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by opioids.*
10. **Tolerance, as defined by either of the following: (a) a need for markedly increased amounts of opioids to achieve intoxication or desired effect (b) markedly diminished effect with continued use of the same amount of an opioid*
11. **Withdrawal, as manifested by either of the following: (a) the characteristic opioid withdrawal syndrome (b) the same (or a closely related) substance are taken to relieve or avoid withdrawal symptoms*

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Opioid Use Disorder Petition- Section 2

Relevant medical or scientific evidence of Opioid Use Disorder

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Included in the attached Section 2 PDF file is a variety of government reports detailing the relevant medical evidence of Opioid Use Disorder with reference links to the original reports. The documents address the scope and the science of addiction, including a commentary by Nora D. Volkow, M.D., Director, NIDA and more. The attachment also includes the most recent report from the National Center for Health Statistics listing Ohio as the second highest in the nation for overdoses.

-=-=-=-= End of 500 character limit website form -=-=-=-=-=-=-

<u>Relevant medical or scientific evidence of Opioid Use Disorder</u>

Included in this Section 2 of the petition is a variety of government reports detailing the relevant medical evidence of Opioid Use Disorder with reference links to the original reports. The documents address the science of addiction, including a commentary by Nora D. Volkow, M.D., Director, NIDA and more. Dr Volkow clearly states that of Opioid Use Disorder / Opiate Addiction is a medical condition.

This attachment also includes the most recent report from the National Center for Health Statistics listing Ohio as the second highest in the nation for overdoses. A report on the deaths from the Center for Disease Control and the science of addiction. With enhanced controls and restriction on Prescription Drugs and reporting via the Ohio Automated Rx Reporting System (OARRS), prescription related deaths have decreased while other opiate related deaths have increased dramatically.

Below is a list of the relevant medical or scientific evidence pertaining to Opioid Use Disorder / Opiate Addiction included in this section.

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 obtain an original copy upon request. Also note any excerpts or copies of the referenced articles text are in *non bolded italics***.**

1. **Opioid-Related Overdose Deaths**
2. **Drug Overdose Deaths in the United States, 1999–2017 report by the Center for Disease Control and Prevention**
3. **Assessing and Addressing Opioid Use Disorder from the Center for Disease Control**

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4. **Drugs, Brains, and Behavior: The Science of Addiction, Nora D. Volkow, M.D., Director, National Institute on Drug Abuse**
5. **Drug Misuse and Addiction from National Institute of Drug Abuse**
6. **Addiction Science from National Institute of Drug Abuse**
7. **2017 Ohio Drug Overdose Data: General Findings (Ohio Department of Health)**

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1 - National Institute on Drug Abuse. 2018. Ohio Opioid Summary. Opioid Summaries by State. Opioid-Related Overdose Deaths

Ohio is among the top five states with the highest rates of opioid-related overdose deaths. In 2016, there were 3,613 opioid-related overdose deaths--- in Ohio—a rate of 32.9 deaths per 100,000 persons and more than double the national rate of 13.3 deaths per 100,000. Since 2010, the rate has tripled from 10 deaths per 100,000. In the same period, the number of heroin-related deaths increased from 355 to 1,478 deaths, and deaths related to synthetic opioids rose from 175 to 2,296 deaths.

Source: **https://www.drugabuse.gov/drugs-abuse/opioids/opioid-summaries-by-state/ohio-opioid-summary**

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2 - Holly Hedegaard, M.D., Arialdi M. Miniño, M.P.H., and Margaret Warner, Ph.D. 2018. *Drug Overdose Deaths in the United States, 1999–2017.*Center for Disease Control and Prevention: National Center for Health Statistics
NCHS Data Brief No. 329, November 28th 2018

The most recent report from the CDC ranks Ohio as #2 in the nation in overdose deaths, some key findings are

- *In 2017, there were 70,237 drug overdose deaths in the United States.*
  The age-adjusted rate of drug overdose deaths in 2017 (21.7 per 100,000) was 9.6% higher than the rate in 2016 (19.8).
- *Adults aged 25–34, 35–44, and 45–54 had higher rates of drug overdose deaths in 2017 than those aged 15–24, 55–64, and 65 and over.*
- *West Virginia (57.8 per 100,000), Ohio (46.3), Pennsylvania (44.3), and the District of Columbia (44.0) had the highest age-adjusted drug overdose death rates in 2017.*

Deaths from drug overdose continue to be a public health burden in the United States (1–5). This report uses the most recent final mortality data from the National Vital Statistics System (NVSS) to update

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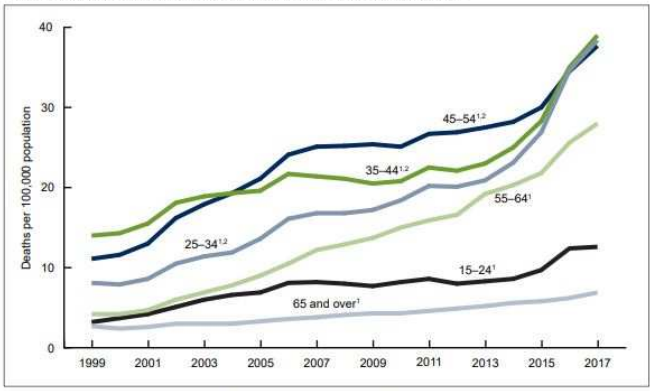
trends in drug overdose deaths, describe demographic and geographic patterns, and identify shifts in the types of drugs involved.

Figure 2. Drug overdose death rates, by selected age group: United States, 1999–2017



[1]Significant increasing trend from 1999 through 2017 with different rates of change over time, $p < 0.005$.
[2]2017 rates were significantly higher for age groups 25–34, 35–44, and 45–54 than for age groups 15–24, 55–64, and 65 and over, $p < 0.05$. The rate for age group 35–44 was significantly higher than the rate for age group 45–54 and statistically the same as the rate for age group 25–34.
NOTES: Deaths are classified using the *International Classification of Diseases, 10th Revision*. Drug-poisoning (overdose) deaths are identified using underlying cause-of-death codes X40–X44, X60–X64, X85, and Y10–Y14. Access data table for Figure 2 at: https://www.cdc.gov/nchs/data/databriefs/db329_tables-508.pdf#2.
SOURCE: NCHS, National Vital Statistics System, Mortality.

Above is Figure 2 from the CDC report of overdose death rates

Source Links
https://www.cdc.gov/nchs/products/databriefs/db329.htm
https://www.cdc.gov/nchs/data/databriefs/db329-h.pdf

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3 - Center for Disease Control. Assessing and Addressing Opioid Use Disorder (OUD)
Center for Disease Control

Opioid Misuse in the United States
Here's what we know about opioid misuse:

- *In 2016, 11.5 million people self-reported that they had personally misused prescription opioids during the previous year.*
- *The most commonly-reported reason that opioids were misused was to relieve physical pain (62.3 %).*
- *The misused prescription opioids were obtained:*
  - *From a friend or relative (53.0 %)*
  - *Through prescription(s) or stealing from a healthcare provider (37.5 %), typically through one doctor*
  - *From a drug dealer or stranger (6.0 %)*

OUD is defined in the DSM-5 as a problematic pattern of opioid use leading to clinically significant impairment or distress.

OUD was previously classified as Opioid Abuse or Opioid Dependence in DSM-IV.
OUD has also been referred to as "opioid addiction."

Full Text
https://www.cdc.gov/drugoverdose/training/oud/accessible/index.html
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4 - Dr Nora D. Volkow, M.D. 2018. *Drugs, Brains, and Behavior: The Science of Addiction*. National Institute on Drug Abuse

Preface excerpts (Full article at link below)

How Science Has Revolutionized the Understanding of Drug Addiction
For much of the past century, scientists studying drugs and drug use labored in the shadows of powerful myths and misconceptions about the nature of addiction. When scientists began to study addictive behavior in the 1930s, people addicted to drugs were thought to be morally flawed and lacking in willpower. Those views shaped society's responses to drug use, treating it as a moral failing rather than a health problem, which led to an emphasis on punishment rather than prevention and treatment.

Today, thanks to science, our views and our responses to addiction and the broader spectrum of substance use disorders have changed dramatically. Groundbreaking discoveries about the brain have revolutionized our understanding of compulsive drug use, enabling us to respond effectively to the problem.

As a result of scientific research, we know that addiction is a medical disorder that affects the brain and changes behavior. We have identified many of the biological and environmental risk factors and are beginning to search for the genetic variations that contribute to the development and progression of the disorder. Scientists use this knowledge to develop effective prevention and treatment approaches that reduce the toll drug use takes on individuals, families, and communities.

Despite these advances, we still do not fully understand why some people become addicted to drugs or how drugs change the brain to foster compulsive drug use. This booklet aims to fill that knowledge gap by providing scientific information about the disorder of drug addiction, including the many harmful consequences of drug use and the basic approaches that have been developed to prevent and treat substance use disorders.

At the National Institute on Drug Abuse (NIDA), we believe that increased understanding of the basics of addiction will empower people to make informed choices in their own lives, adopt science-based policies and programs that reduce drug use and addiction in their communities, and support scientific

research that improves the Nation's well-being.

Full Text
https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/preface

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5 - National Institute of Drug Abuse. 2018. *Drug Misuse and Addiction*

Excerpts (Full article at link below)

Addiction is defined as a chronic, relapsing disorder characterized by compulsive drug seeking and use despite adverse consequences. It is considered a brain disorder, because it involves functional changes to brain circuits involved in reward, stress, and self-control, and those changes may last a long time after a person has stopped taking drugs.11

Addiction is a lot like other diseases, such as heart disease. Both disrupt the normal, healthy functioning of an organ in the body, both have serious harmful effects, and both are, in many cases, preventable and treatable. If left untreated, they can last a lifetime and may lead to death.

Full Text
https://www.drugabuse.gov/publications/drugs-brains-behavior-science-addiction/drug-misuse-addiction
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6 - Source National Institute of Drug Abuse. Addiction Science

Brief Description

Many people don't understand why or how other people become addicted to drugs. They may mistakenly think that those who use drugs lack moral principles or willpower and that they could stop their drug use simply by choosing to. In reality, drug addiction is a complex disease, and quitting usually takes more than good intentions or a strong will. Drugs change the brain in ways that make quitting hard, even for those who want to. Fortunately, researchers know more than ever about how drugs affect the brain and have found treatments that can help people recover from drug addiction and lead productive lives.

Full Text
https://www.drugabuse.gov/related-topics/addiction-science

Additional References

1. Koob, G. F. & Volkow, N. D. Neurocircuitry of addiction. Neuropsychopharmacology 35, 217–238 (2010).
2. Koob, G. F. Negative reinforcement in drug addiction: the darkness within. Curr. Opin. Neurobiol. 23, 559–563 (2013).
3. Volkow, N. D., Koob, G. F. & Baler, R. Biomarkers in substance use disorders. ACS Chem. Neurosci. 6, 522–525 (2015).

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7 - Ohio Department of Health. 2017. *2017 Ohio Drug Overdose Data: General Findings.*

Selected Quotes

> *Prescription opioid-related overdose deaths accounted for 523 of Ohio's total 4,854 unintentional overdose deaths in 2017, compared to 564 of 4,050 total deaths in 2016. Combating prescription opioid abuse continues to be critical to Ohio's overall efforts to fight drug abuse, addiction and overdose because prescription opioids abuse is a key risk factor for the use of illicit drugs like fentanyl and related drugs, according to the Centers for Disease Control and Prevention (CDC).*
>
> *Illicit fentanyl and related drugs like carfentanil continued to drive an increase in Ohio's unintentional overdose deaths in 2017, with 70.7 percent involving these drugs compared to 58.2 percent in 2016, 37.9 percent in 2015, and 19.9 percent in 2014. Carfentanil was involved in 29.4 percent of deaths attributed to fentanyl and related drugs in 2017 (Figure 7).*

Source

https://odh.ohio.gov/wps/portal/gov/odh/know-our-programs/violence-injury-prevention-program/media/2017_OhioDrugOverdoseReport

Full text PDF direct link

https://odh.ohio.gov/wps/wcm/connect/gov/5deb684e-4667-4836-862b-cb5eb59acbd3/2017_OhioDrugOverdoseReport.pdf?MOD=AJPERES&CONVERT_TO=url&CACHEID=ROOTWORKSPACE.Z18_M1HGGIK0N0JO00QO9DDDDM3000-5deb684e-4667-4836-862b-cb5eb59acbd3-moxPbu6

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Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition.

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Opioid Use Disorder is a complex condition that is not easily treated successfully. The patient usually has other associated mental and/or physical issues. According to NIDA the relapse rate for patients going through drug addiction treatment ranges from 40% to 60%. Twelve Step Facilitation programs have mixed success and are not well documented. The indisputable fact that we have such a tremendous number of overdose deaths indicates that conventional medical therapies are insufficient.
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<u>Consideration of whether conventional medical therapies are insufficient to treat or alleviate the disease or condition.</u>

Opioid Use Disorder is a complex condition that is not easily treated successfully. The patient usually has other mental and/or physical issues associated with the condition. According to NIDA the relapse rate for patients going through drug addiction treatment ranges from 40% to 60%. A popular treatment method is the replacement of one opiate with a different one (i.e. Methadone, Suboxone, and Buprenorphine). These carry their own risk of addiction, problematic withdrawal, illicit distribution and even overdoses. Twelve Step Facilitation programs have mixed success and are not well documented.

The fact that we continue to have the increasing number of overdose deaths despite the existence of conventional therapies suggests that conventional medical therapies remain insufficient in addressing the complexities associated with opioid use disorder.

One aspect of this condition is that for many people, opioid use disorder represents a chronic lifelong condition. Therefore for many, opioid use disorder / opiate addiction is a condition which requires strategies that are long term, and perhaps life-long. The longer one is in some form of treatment, the more likely the addicted individual will be successful in dealing with the negative effects of their addiction.

Below are a series of conventional therapies used today with mixed success.

- **Medication assisted treatments: Methadone, Suboxone and Subutex (agonist/partial agonist therapies); Naltrexone and Vivitrol (antagonist therapies).**
- **Varying levels of care ranging from inpatient detoxification, residential treatment, intensive outpatient treatment and outpatient treatment.**
- **The legal system administered programs including drug court programs.**
- **Sober support programs including 12 step programs and faith-based programs.**

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Medication Assisted Treatments

Methadone treatment for addiction is only available through strictly regulated opioid treatment programs accredited by the Substance Abuse and Mental Health Services Administration (SAMHSA). Persons with OUDs initially attend the opioid treatment program daily before receiving take-home doses.

"According to the National Institute on Drug Abuse publication Principles of Drug Addiction Treatment: A Research-Based Guide – 2012, the length of methadone treatment should be a minimum of 12 months. Some patients may require treatment for years. Even if a patient feels that they are ready to stop methadone treatment, it must be stopped gradually to prevent withdrawal"

Reference Source: Substance Abuse and Mental Health Services Administration. 2015. Medication and Counseling Treatment: Methadone. https://www.samhsa.gov/medication-assisted-treatment/treatment/methadone).

-=-=- and from Mattick et al -=-=-

Due to the nature of how Methadone works it places patients in a situation where they are essentially committed to a daily-dose, long-term replacement program. If an individual chooses to go off Methadone, the withdrawal syndrome persists for an extended period of time and is mentally and physically taxing. Patients come off of their Methadone for numerous reasons, and the associated physical and psychological withdrawal symptoms serve as significant relapse triggers leading some patients back to the dangerous behaviors associated with heroin use. Hence, having insight as to who will be compliant with a Methadone program from those who will not commit to the requirements of a Methadone program, is important and carries important safety implications. Many opt not to consider Methadone as a treatment alternative because of these limitations, making this option insufficient in meeting the overall needs of those with Opioid Use Disorder.

BACKGROUND:
Methadone maintenance was the first widely used opioid replacement therapy to treat heroin dependence, and it remains the best-researched treatment for this problem. Despite the widespread

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use of methadone in maintenance treatment for opioid dependence in many countries, it is a controversial treatment whose effectiveness has been disputed.

MAIN RESULTS:
Eleven studies met the criteria for inclusion in this review, all were randomized clinical trials, two were double-blind. There were a total number of 1969 participants. The sequence generation was inadequate in one study, adequate in five studies and unclear in the remaining studies. The allocation of concealment was adequate in three studies and unclear in the remaining studies. Methadone appeared statistically significantly more effective than non-pharmacological approaches in retaining patients in treatment and in the suppression of heroin use as measured by self report and urine/hair analysis (6 RCTs, RR = 0.66 95% CI 0.56-0.78), but not statistically different in criminal activity (3 RCTs, RR=0.39; 95%CI: 0.12-1.25) or mortality (4 RCTs, RR=0.48; 95%CI: 0.10-2.39).

AUTHORS' CONCLUSIONS:
Methadone is an effective maintenance therapy intervention for the treatment of heroin dependence as it retains patients in treatment and decreases heroin use better than treatments that do not utilise opioid replacement therapy. It does not show a statistically significant superior effect on criminal activity or mortality.

Reference Source:
Mattick RP1, Breen C, Kimber J, Davoli M.
Author Info : National Drug and Alcohol Research Centre, University of New South Wales, National Drug and Alcohol Research Centre, University of New South Wales, Sydney, New South Wales, Australia, 2052. 2009. Methadone maintenance therapy versus no opioid replacement therapy for opioid dependence.
Cochrane Database Syst Rev.;(3):CD002209.
doi: 10.1002/14651858.CD002209.pub2.
https://www.ncbi.nlm.nih.gov/pubmed/19588333

=-=-=-=- and from NIDA =-=-=-=-

"Relapse rates for addiction resemble those of other chronic diseases such as diabetes, hypertension, and asthma."

Reference Source #2
2- National Institute of Drug Abuse. 2018. How effective is drug addiction treatment? Principles of Drug Addiction Treatment: A Research-Based Guide (Third Edition)
https://www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third-edition/frequently-asked-questions/how-effective-drug-addiction-treatment

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Suboxone

The use of Suboxone to help patients with Opioid Use Disorder has become very common and with this replacement therapy comes some understandable and predicted problems associated with misuse, abuse and diversion. Johanson, Arfkena, di Menza and Schuster (2012) describe the abuse potential with Suboxone; they comment on how abuse and diversion problems grow in parallel with the increasing number of prescriptions written for Suboxone. This conclusion was supported by earlier work that appeared in the British Journal of Addiction.

While Suboxone has provided a tool for physicians to help patients with Opioid Use Disorder it faces similar challenges comparable to those faced by the Methadone programs.

Abstract

Background: Since 2003, buprenorphine has been approved for the treatment of opioid dependence in office-based practice. Diversion and abuse can be a threat to its continued approval under these conditions.

Methods: As part of a national post marketing surveillance program, applicants to substance abuse treatment and physicians certified to prescribe buprenorphine were surveyed about their perceptions of buprenorphine/naloxone diversion and abuse. These surveys were supplemented by information from national databases. Availability of buprenorphine/naloxone was measured by number of tablets dispensed.

Results: Measures of diversion and abuse of buprenorphine/naloxone increased from 2005 to 2009. The results from the applicant survey showed that the perceptions of the extent of diversion and abuse were lower than positive controls, methadone, oxycodone and heroin, but higher than the negative control, amitriptyline. By 2009, 46% of the physicians believed that buprenorphine /naloxone was diverted but 44% believed illegal use was for self-management of withdrawal and 53% believed the source of the medication was substance abuse patients. Other measures from national databases showed similar results. When adjusted for millions of tablets sold per year, slopes for measures of diversion and abuse were reduced.

CONCLUSIONS:
The increases in diversion and abuse measures indicate the need to take active attempts to curb diversion and abuse as well as continuous monitoring and surveillance of all buprenorphine products. However, these increases parallel the increased number of tablets sold. Finding a balance of risk/benefit (i.e. diversion and abuse versus expanded treatment) remains a challenge.

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Reference Source
Diversion and abuse of buprenorphine: findings from national surveys of treatment patients and physicians.
Drug Alcohol Depend. 2012 Jan 1;120(1-3):190-5. Epub 2011 Aug 21.
Johanson CE , Arfken CL, di Menza S, Schuster CR.
https://www.ncbi.nlm.nih.gov/pubmed/21862241
DOI 10.1016/J.DRUGALCDEP.2011.07.019

-=-= and from the British Journal of Addiction -=-=

Summary
Buprenorphine has been described as a potent analgesic with low abuse potential. Sporadic reports in the world literature would seem to contradict this view. A retrospective study of all opiate addicts first presenting over a 12-month period showed an increasing level of buprenorphine abuse.

Reference Source
2 - Buprenorphine Abuse Among Opiate Addicts
British Journal of Addiction Volume 83, Issue 9
JOHN J. O'CONNOR M.B., M.R.C.Psych. EAMONN MOLONEY M.B. RAYMOND TRAVERS M.B. AISLING CAMPBELL M.B.
https://doi.org/10.1111/j.1360-0443.1988.tb00536.x

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Vivitrol and Naltrexone

Vivitrol is one of the newest medical interventions to assist with treating Opioid Use Disorder. Unlike the opiate-based agonists, Vivitrol is an injectable form of Naltrexone that works as an antagonist, or "opiate blocker." Vivitrol has shown to be of value in helping patients avoid relapse on opiates (Sullivan, 2012). It appears that Vivitrol is superior to oral dose naltrexone with respect to treatment compliance, as measured by retention rates in treatment (Tucker, Ritter, Maher & Jackson, 2004; Chang et. al, 2018).

Some significant concerns and limitations facing both oral dose and injectable forms of Naltrexone (Vivitrol) have to do with initiation and subsequent adherence. The addicted heroin user must first go through withdrawal and be opiate free before beginning treatment with either form of Naltrexone. This deters some from considering this as an option.

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Interestingly, Raby et al. (2009) found that patients who used marijuana while also being treated with Naltrexone remained in treatment an average of 100 days longer. This novel approach to treating Opioid Use Disorder is an alternative and a promising strategy in helping individuals recover from their dependency to opiates.

Reference Sources

CHANG, G. et al. Adherence to extended release naltrexone: Patient and treatment characteristics. American Journal on Addictions, [s. l.], v. 27, n. 6, p. 524–530, 2018.
https://onlinelibrary.wiley.com/doi/abs/10.1111/ajad.12786

RABY, W. N. et al. Intermittent Marijuana Use Is Associated with Improved Retention in Naltrexone Treatment for Opiate-Dependence. American Journal on Addictions, [s. l.], v. 18, n. 4, p. 301–308, 2009.
https://www.tandfonline.com/doi/abs/10.1080/10550490902927785
Online DOI: 10.1080/10550490902927785

SULLIVAN, M. A. et al. Naltrexone treatment for opioid dependence: Does its effectiveness depend on testing the blockade? Drug & Alcohol Dependence, [s. l.], v. 133, n. 1, p. 80–85, 2013.
https://www-sciencedirect-com.proxy.libraries.uc.edu/science/article/pii/S0376871613002160
https://doi.org/10.1016/j.drugalcdep.2013.05.030

TUCKER, T. K. et al. Naltrexone maintenance for heroin dependence: uptake, attrition and retention. Drug & Alcohol Review, [s. l.], v. 23, n. 3, p. 299–309, 2004.
https://www.ncbi.nlm.nih.gov/pubmed/15370010
DOI: 10.1080/09595230412331289464

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Drug Courts/ Compulsory Treatment

Results
Of an initial 430 potential studies identified, nine quantitative studies met the inclusion criteria. Studies evaluated compulsory treatment options including drug detention facilities, short (i.e. 21-day) and long-term (i.e., 6 months) inpatient treatment, community-based treatment, group-based outpatient treatment, and prison-based treatment. Three studies (33%) reported no significant impacts of compulsory treatment compared with control interventions. Two studies (22%) found equivocal results but did not compare against a control condition. Two studies (22%) observed negative impacts of compulsory treatment on criminal recidivism. Two studies (22%) observed positive impacts of compulsory inpatient treatment on criminal recidivism and drug use.

Conclusion
There is limited scientific literature evaluating compulsory drug treatment. Evidence does not, on the whole, suggest improved outcomes related to compulsory treatment approaches, with some studies suggesting potential harms. Given the potential for human rights abuses within compulsory treatment

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settings, non-compulsory treatment modalities should be prioritized by policymakers seeking to reduce drug-related harms.

Reference Source
D Werb, A Kamarulzaman, MC Meacham, C Rafful, B Fisher, SA Strathdee, and E Wood. 2016.
THE EFFECTIVENESS OF COMPULSORY DRUG TREATMENT: A SYSTEMATIC REVIEW.
International Journal of Drug Policy.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4752879/

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12 step programs

One of the more difficult "therapies" to discuss are the 12 step programs. At a basic level they are not scientific or medicine based, but some have more of a moral basis underpinning. Thus there is a lot of heated rhetoric and blowback when the effectiveness is assessed or challenged.

Below are some examples of some of the critical evaluation. Note these are primarily based on the alcohol, but note the Narcotics Anonymous is based upon the same basic model.

A 2006 Cochrane systematic review reviewed studies published between 1966 and 2005 that investigated the efficacy of AA and twelve step facilitation (TSF) found no significant difference between the results of AA and twelve-step participation compared to other treatments, stating that "experimental studies have on the whole failed to demonstrate their effectiveness in reducing alcohol dependence or drinking problems when compared to other interventions." This conclusion was based on a meta-analysis of the results of eight trials involving a total of 3,417 individuals.

Source Ferri, Marcia; Amato, Laura; Davoli, Marina. 2006. Alcoholics Anonymous and other 12-step programmes for alcohol dependence. Cochrane Database of Systematic Reviews (3): CD005032. *https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD005032.pub2/full*

-=-=- And by Gabrielle Glaser. -=-=-=

Dr. Lance Dodes, a retired psychiatry professor from Harvard Medical School, book "The Sober Truth: Debunking the Bad Science Behind 12-Step Programs and the Rehab Industry" looked at Alcoholics Anonymous's retention rates along with studies on sobriety and rates of active involvement (attending meetings regularly and working the program) among AA members. Based on these data, he put AA's actual success rate somewhere between 5 and 8 percent.

The late G. Alan Marlatt, a respected addiction researcher at the University of Washington, commented on the controversy in a 1983 article in American Psychologist. "Despite the fact that the basic tenets of [AA's] disease model have yet to be verified scientifically," Marlatt wrote, "advocates of the disease

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model continue to insist that alcoholism is a unitary disorder, a progressive disease that can only be arrested temporarily by total abstention.

Source: Gabrielle Glaser. 2015. *The Irrationality of Alcoholics Anonymous.* The Atlantic.
https://www.theatlantic.com/magazine/archive/2015/04/the-irrationality-of-alcoholics-anonymous/386255/

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Opioid Use Disorder Petition- Section 4

Evidence supporting the use of medical marijuana

=-=- 470 characters for the 500 character limited website section portion -=-=-=
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.
-=-=-=-=-=-=-=- End of 500 character entry for website =-=-=-=-=-=-=-=

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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Opioid Use Disorder Petition- Section 4

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.

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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.

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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.

-=

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.
Author information
1 Department of Psychology, University of Missouri-St. Louis, St. Louis, Missouri.
2 Department of Anesthesiology, Pain Center, Washington University School of Medicine, St. Louis, Missouri.

Ohio Patient Network
PO Box 42042
Cincinnati, Ohio

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.
Author information
1 Department of Criminology and Criminal Justice, Green School of International and Public Affairs, Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-366A, Miami, FL 33199, USA. Electronic address: flexonj@fiu.edu.
2 Department of Criminology and Criminal Justice, Green School of International and Public Affairs, Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-253A, Miami, FL 33199, USA. Electronic address: stolzenb@fiu.edu.
3 Department of Criminology and Criminal Justice, Green School of International and Public Affairs. Florida International University, Modesto A. Maidique Campus, 11200 SW 8th Street, PCA-263B, Miami, FL 33199, USA. Electronic address: dalessi@fiu.edu.

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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.
Author information
1 HealthEast St Joseph's Hospital, Ann Arbor, MI, USA.
2 HealthEast Woodwinds Health Campus, Woodbury, MN, USA.
3 HealthEast St Joseph's Hospital, St Paul, MN, USA.
4 HealthEast Rice Street Clinic, Maplewood, MN, USA.
5 HealthEast Pain Center, Maplewood, MN, USA.

US National Library of Medicine National Institute of Health PUBMED.GOV link
https://www.ncbi.nlm.nih.gov/pubmed/31129977

-=-

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.
McMichael BJ1, Van Horn RL2, Viscusi WK3.
Author information
1 Assistant Professor of Law, University of Alabama School of Law, Box 870382, 101 Paul W. Bryant Drive East, Tuscaloosa, AL, 35487, United States. Electronic address: bmcmichael@law.ua.edu.

2 Associate Professor of Management and Law, Executive Director of Health Affairs, Owen Graduate School of Management, Vanderbilt University, 401 21st Avenue South, Nashville, TN, 37203, United States. Electronic address: larry.vanhorn@owen.vanderbilt.edu.
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.

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.
Author information
1 Assistant Professor of Law, University of Alabama School of Law, Box 870382, 101 Paul W. Bryant Drive East, Tuscaloosa, AL, 35487, United States. Electronic address: bmcmichael@law.ua.edu.
2 Associate Professor of Management and Law, Executive Director of Health Affairs, Owen Graduate School of Management, Vanderbilt University, 401 21st Avenue South, Nashville, TN, 37203, United States. Electronic address: larry.vanhorn@owen.vanderbilt.edu.
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.

US National Library of Medicine National Institute of Health PUBMED.GOV link
https://www.ncbi.nlm.nih.gov/pubmed/?term=impact+of+cannabis+access+laws+on+opioid+prescribing
https://www.sciencedirect.com/science/article/pii/S0167629618309020?via%3Dihub

Ohio Patient Network

www.OhioPatientsNetwork.org

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PO Box 42042
Cincinnati, Ohio
45242

Opioid Use Disorder Petition- Section 5

Letters of support provided by physicians with knowledge of the disease or condition

-=-=-=-466 characters of 500 character website entry-=-=-=--=
Attached are letters supporting adding Opioid Use Disorder/Opiate Addiction as a qualifying condition. Note Dr. Ethan Russo, is a neurologist with drug development experiences and leadership positions in international research medical organizations; Dr. Blatman, an Ohio based pain practitioner; Dr . Sawyer, certified in Suboxone therapy and others. Dr. Thress is also included. Also noted are 22 doctors who have supported the Leeds and Rosenberger 2018 petition.
=-=-=-500 character website entry-=-=-=--=

Section 5 – Letters of support provided by physicians with knowledge of the disease or condition

Included in this PDF are letters supporting adding Opioid Use Disorder as a qualifying condition. One is from Dr. Ethan Russo, a neurologist with drug development experiences and leadership positions in international research medical organizations; Dr. Blatman, an Ohio based pain practitioner; Dr. Sawyer, certified in Suboxone therapy and others.

List of letters of support

- **Dr. Thress (Added for 2019 petition)**
- **Dr. Russo ***
- **Dr. Blatman ****
- **Dr. Sawyer ****
- **Dr. Austin ***
- **Dr. Kollman ***
- **Dr. Simmons ***
- **Dr. Mooney ***

*** Originally listed in 2018 petition with continued support of petition in 2019**
**** email continued support for 2019**

In addition to the Doctors listed above, below are 17 more physicians found in Dr. Leeds' 2018 Petition from Wright State University and Rosenberger 2018 Petition

Margaret M. Dunn, M.D., M.B.A., FACS
Dean, Professor of Surgery

S. Bruce Binder, M.D., Ph.D.
Chair and Associate Professor
Department of Family Medicine

Peter Reynolds,M.D., FAAFP

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Director, Family Medicine Residency Program
Associate Professor Department of Family Medicine

Joy Forcier, LISW
Behavioral Health Consultant
Wright State Physicians, Family Medicine

F. Stuart (Skip) Leeds, M.D., M.S.
Assistant Professor, Family Medicine
WSU Boonshoft School of Medicine

Anand Dugar, MD
CEO Green Health Docs – greenhealthdocs.com
215-287-3607 (Cell)
adugar12@yahoo.com (Email)

Supporting Doctors found in 2018 Rosenberger Petition

Martha Hackett, MD
Peter Howison, MD
Sharrie Ann Ray, MD
Cynthia L. Dietrich, DO
Solomon Zaraa, DO
Nora McNamara, MD
Noah Miller, MD
Paul Y. Song, MD
Anand Dugar, MD
Oscar B. Cataldi, Jr., MD
Timothy Thress, MD

Also included at the end of this attachment is from state house news "The Hannah Report" quotes from Dr. Soin at the June 8th 2017 Medical Marijuana Advisory Board Meeting.

-=-=-=-=-=-

Pot Could Wean People Off Opioids, Medical Board President Says
Story originally published in The Hannah Report on June 8, 2017
THE HANNAH COLLECTION
Capitol Connection | Hannah Report | ActionTRACK™
Ohio News Wire | The Complete Statehouse | State Health Clips
21 West Broad Street, Suite 1000 (10th Floor) Columbus, OH 43215

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45242

Opioid Use Disorder Petition- Section 5

Many doctors see medical marijuana as an opportunity to transition patients away from opioid use, State Medical Board of Ohio (SMBO) President Amol Soin said Thursday.

"If that occurs, I think that would be beneficial -- significantly," Soin told members of the Medical Marijuana Advisory Committee (MMAC) during the panel's meeting in the Riffe State Office Tower.

"What I've realized is at the end of the day, when someone's been suffering from chronic pain for a really long time, it doesn't matter what treatment modality it is -- whether it's an opioid, physical therapy, surgical option or potentially cannabis -- if their pain score gets lower they're obviously satisfied, right?" Soin told Hannah News after the meeting, noting that most patients are most interested in relieving pain, not getting high on opioids.

He said the addition of medical marijuana as an option for treating chronic pain could reduce the number of opioid overdoses in Ohio, which currently has the highest drug overdose death toll in the country. An overdose from marijuana has never been reported, according to a fact sheet on the U.S. Drug Enforcement Administration's (DEA) website.

"So if the cannabis allows you to get out of pain, I think there's a huge opportunity to wean or stop opioids on those patients," said Soin, a pain management physician. "In fact … I just think about the patients in my practice now that I talk to that I think may benefit from cannabis as a means to get them off of addicting painkillers."

The following pages without OPN letterhead contain the letters of support from the various doctors that support Ohio Patient Network Petition to add Opioid Use Disorder to the list of Qualifying Conditions to the Ohio Medical Marijuana Control Program.

rryan@ohiopatientsnetwork.org

From: TIM THRESS <tthress@aol.com>
Sent: Monday, December 30, 2019 4:32 PM
To: rryan@ohiopatientsnetwork.org
Subject: New qualifications

I have been seeing patients for one and a half years as far as recommending cannabis. During that time I have seen a large amount of patients with chronic pain and opioid abuse disorder. These patients have been coming back for renewals. One of the questions asked is “Have you been able to wean off your opioids ?” The majority have been able to either eliminate or reduce the amount of opioids used. I believe medical cannabis helps patients with opioid abuse disorder wean off their opioids Dr Thress

Sent from my iPhone

rryan@ohiopatientsnetwork.org

From: Hal Blatman <hblatman@me.com>
Sent: Monday, December 30, 2019 8:25 PM
To: Robert Ryan
Cc: Kim McCutcheon
Subject: Re: Letter of support for Opioid Use Disorder qualifying condition for the Ohio Medical Marijuana program

12-30-2019

Rob, Please pass this letter to the Medical Board:

Medical Board of Ohio,

I am writing in support of adding "Opioid Use Disorder" as a qualifying diagnosis for eligibility in the state medical marijuana program.

The main medications for this are methadone and suboxone. In my pain practice, both of these medications are more dangerous or addictive than marijuana.

Marijuana is a better alternative, less dangerous, and not physically addictive. Lack of supply does not induce a physical withdrawal as with opioids.

Thank you for taking another look at this difficult issue.

Sincerely,

Hal S Blatman

Hal S Blatman, MD, FAAO APT, ABIHM, ABOIM, DAIPM
Past Chair, Integrative Medicine Consortium
Past President, American Holistic Medical Association
Affiliated Faculty, Bastyr University, Seattle
Medical Director, Blatman Health and Wellness Center
www.BlatmanHealthAndWellness.com
Author: Winners' Guide to Pain Relief
Office: 513-956-3200
Fax: 513-956-3202

> On Dec 30, 2019, at 6:21 PM, rryan@ohiopatientsnetwork.org wrote:
>
> Hal,
>
> Could you write a short supportive email letter for the Ohio Medical Board to consider adding Opioid Use Disorder as a qualifying condition for the Ohio medical marijuana program?

I attached your letter from last year for your reference. I am dropping the words [Opiate addiction] from the petition since it is not a DSM/medical code and using Opioid Use Disorder as the official condition nomenclature.

Best wishes,
Rob
<Dr Hal Blatman.pdf>

rryan@ohiopatientsnetwork.org

From: dr.will@fuse.net
Sent: Monday, December 30, 2019 10:31 PM
To: Mark Welty
Cc: ethan russo; Ethan Russo; Trent Austin; sfgsfb@gmail.com; Robert Ryan
Subject: Re: Opioid Use Disorder - Petition

Perhaps the medical and pharmacy boards will finally accept this is another solution to the OUD epidemic in Ohio!

Thank you for helping to "spread the word not the germs"!

Dr. Will

Will Sawyer, MD

Sharonville Family Medicine
(O) 513-769-4951

or

Henry the Hand Foundation (501c3)

O: 513.769.HAND(4263)

www.henrythehand.com

The 4 Principles of Hand Awareness:

1. WASH your hands when they are dirty and BEFORE eating.

2. DO NOT cough into your hands.

3. DO NOT sneeze into your hands.

4. Above all, DO NOT put your fingers into your eyes, nose, or mouth.

The 4 Principles of Hand Awareness have been endorsed by the AMA and AAFP.

From: "Mark Welty" <weltyma@gmail.com>
To: "ethan russo" <ethan.russo@icci.science>, "Ethan Russo" <ethanrusso@comcast.net>, "dr will" <dr.will@fuse.net>, "Trent Austin" <t.austin.accudoc@gmail.com>, sfgsfb@gmail.com
Cc: "Robert Ryan" <rryan@ohiopatientsnetwork.org>
Sent: Monday, December 30, 2019 10:00:11 PM
Subject: Opioid Use Disorder - Petition

Dear Doctors Russo, Blatman, Sawyer, Austin and Mooney,

I want to thank you for your time today and for your continued support of the petition for the inclusion of Opioid Use Disorder as a qualifying condition of Ohio's Medical Marijuana Control Program. I am on the Ohio Patient Network board and Rob Ryan with the Ohio Patient Network will be submitting this petition by tomorrow's deadline. Please know that Doctors Kollman and Simmons provided letters of support last year but I was not able to reach them for this year's petition. We will reach out to them tomorrow to ensure that they too wish to be included as part of the petition. Again, thank you for your dedication to helping improve the quality of care to patients.

Sincerely,

Mark Welty, Ph.D., LPCC-S, LSW
OPN

Ethan Russo, MD
Hal Blatman, MD (e-mail address not available)
William Sawyer, MD

Trent Austin, MD (voicemail left inquiring about continuing support based on last year's letter of support)

Steve Mooney, MD
Paul Kollman, MD **
Joel R. Simmons, MD **

ICCI

ETHAN RUSSO, MD | DIRECTOR OF RESEARCH AND DEVELOPMENT
+1-206-304-4344 | ethan.russo@icci.science |

International Cannabis and Cannabinoids Institute
Jachymova 26/2 | CZ 110 00 Prague 1 | Czech Republic| EU

url | facebook | twitter

December 7, 2018

Regarding: **Qualifying Conditions for Ohio Medical Marijuana Control Program**

Dear Colleagues,

I am writing this letter to support strongly the inclusion of cannabis-based treatment for opioid use disorder and addiction in the Ohio state program.

In order to provide some perspective on my support for such treatment, it may be pertinent to present my qualifications. I was a Psychology major at the University of Pennsylvania, and am a diplomate of the American Board of Psychiatry and Neurology, with certification in Neurology with Special Qualification in Child Neurology. I was a neurologist in private practice for 20 years in Missoula, MT, USA and was medical director for a hospital-based chronic pain treatment program. During that time, I held faculty positions as Adjunct Associate Professor, Department of Pharmaceutical Sciences, University of Montana, and Clinical Assistant Professor, University of Washington School of Medicine. Also during this interval, I became deeply involved in the study of medicinal plant and cannabinoids, and authored/edited several books and many peer-reviewed academic journal articles on this and related subjects in psychopharmacology. In 2003, I became Senior Medical Advisor to GW Pharmaceuticals www.gwpharm.com, a British research and development company, and remained in that position through 2014, as a liaison to basic scientists and clinicians focusing on various therapeutic applications of cannabis-based medicines, and managing as Study Physician and Medical Monitor various Phase I-III clinical trials in treatment of intractable cancer pain, multiple sclerosis for Sativex/nabiximols and Epidiolex/cannabidiol for epilepsy. I am past chairman of the International Association for Cannabinoid Medicines, and am past president of the International Cannabinoid Research Society, the world's premier organization devoted to the study of the endocannabinoid system that is germane to investigation and treatment of pain, epilepsy, addiction, and various psychiatric conditions. From 2015-2017, I was Medical Director of PHYTECS www.phytecs.com, a research and development company focusing on the endocannabinoid system. From October 2017 to the present, I have been the Director of Research and Development for the International Cannabis and Cannabinoids Institute

https://www.icci.science/en/ based in Prague, Czechia, a European center of excellence promoting research in cannabis and cannabinoids.

I am very familiar with the particulars of cannabinoid treatment of opioid use disorder and addiction and have published several times on this subject (articles attached). The ability of cannabis to produce opioid sparing and treat opioid addiction has been known and documented in this country and elsewhere since the 19th century. Given current epidemiological evidence that availability of cannabis medically reduces opioid overdose mortality, reduces numbers and costs of opioid prescriptions and basic science and controlled trial evidence of opioid sparing, there is no rational nor scientific reason to deny its availability for these conditions. With 72,000 deaths due to opioid overdose in the USA in 2017, it is painfully apparent that current therapeutic interventions are woefully insufficient. It would be unconscionable to deny this potentially life-saving treatment to the people of Ohio.

I urge responsible individuals to pursue the only reasonable course, and include cannabis as an approved treatment for the conditions of opioid use disorder and addiction.

Sincerely,

Ethan B. Russo, MD Home address: 20402 81st Avenue SW, Vashon, WA 98070 USA,

Mobile phone: +1-206-304-4344

Personal Email: ethanrusso@comcast.net

BLATMAN
HEALTH AND WELLNESS CENTER

Tel. 513 956 3200
Fax. 513 956 3202

Support of adding Opioid Use Disorder to medical marijuana control program for State of Ohio

12/8/18

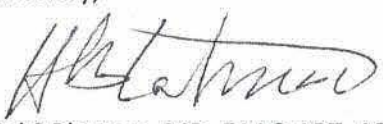
Medical Board of Ohio,

I am a solo physician in a pain and rehabilitation practice for 30 years in Blue Ash, Ohio, a suburb of Cincinnati. I am certified for suboxone therapy and am licensed for CTR medicinal cannabis in Ohio. During my years of practice, I have treated many patients and their families for opiate abuse disorder/addiction disorders. Since initiation of this state's medical marijuana program I have seen the clinical benefits of cannabis as an integral therapy for opiate use disorder. In addition, there is good medical evidence for using medical marijuana as part of an opiate addiction program. As a pain practitioner, I have seen patients willing to discontinue use of more dangerous substances when medical marijuana is available.

Adding this condition as a treatment option with medicinal cannabis will have a significant impact on the opiate epidemic and reducing harm from this chronic disease in Ohio.

I thank you in advance for adding OUD/addiction to the list of qualifying conditions for Ohio Medical Marijuana program.

Sincerely,



Hal S Blatman, MD, FAAO APT, ABIHM, ABOIM, DAIPM
Affiliated Faculty, Bastyr University
Past Chair, Integrative Medicine Consortium
Past President, American Holistic Medical Association
Medical Director, Blatman Health and Wellness Center
www.BlatmanHealthAndWellness.com
Author: Winners' Guide to Pain Relief
Office: 513-956-3200
Fax: 513-956-3202
Home: 513-677-3787

SHARONVILLE FAMILY MEDICINE

11714 U.S. Route 42
Cincinnati, Ohio 45241
(513) 769-4951

William P. Sawyer, M.D.

To: Medical Board of Ohio
From: William P Sawyer, MD
Subject: Letter in Support of adding Opioid Use Disorder to medical marijuana control program for Ohio
Date: 12/8/18

I am a solo Family Medicine physician for 32 years in Sharonville, Ohio, a suburb of Cincinnati and still practicing. I am certified for suboxone therapy and am licensed for CTR medicinal cannabis in Ohio. I have treated many patients and their families who have or had opiate use disorder/addiction and have seen the clinical benefits to cannabis as an integral therapy for opiate use disorder. When patients and their families have the trust and confidence in their personal physician, the patients open up to what THEY are taking to improve their situation, by reducing withdrawal symptoms, their associated anxiety and modulates the triggers/cravings for many with OUD/addiction. In my additional studies since becoming licensed for CTR medicinal cannabis in Ohio, I have learned more about the neurochemistry of the patient's clinical results I have seen as a clinician in both the acute care and chronic care of addiction/OUD.

Adding this condition as a treatment option with medicinal cannabis will have a significant impact on the opiate epidemic and harm reduction of this chronic disease in Ohio.

I thank you in advance for adding OUD/addiction to the list of qualifying conditions for Ohio Medical Marijuana program.

Sincerely,

William P Sawyer, MD
Sharonville Family Medicine
11714 US Rte. 42
Cincinnati, Ohio 45241
513-769-4951
Dr.will@fuse.net
Ohio license: 35.048348CTR

To: Whom it concerns at the Medical Board of Ohio
From: Paul Kollman, MD
Subject: Opioid Use Disorder addition to medical marijuana control program
Date: 12/9/18

I have been treating patients in Ohio since 1965, but it is only recently that I have become aware of the positive potential for medical marijuana. I am a U.S. Army veteran and a member of the American Legion and part of the team of veterans that developed a resolution regarding the Veterans Administration policy towards the use of medical marijuana. In the process of developing the American Legion's resolution, I became more educated about the impact of medical marijuana laws has had on reducing overdose death in other states.

Our resolution passed at the local Post level, the county level, the state level and eventually the National level of the American Legion. It has helped changed VA policy and replaced an older policy that forbid VA doctors from even talking about medical marijuana. There is more to do at the VA level, but is currently constrained by Federal laws. I am encouraged that Ohio has started to recognize the potential benefits of marijuana.

I am aware of the various conditions that medical marijuana can be used for, but it misses an important one that is having a huge negative impact. That is heroin addiction. I support adding opioid use disorder as condition that enables physicians to make recommendation for the use of medical marijuana. In my opinion, this is another tool in the physician's toolbox to save lives.

Sincerely,

Paul Kollman MD

Paul Kollman, MD
7648 Fairwind Dr
Cincinnati, Ohio
45242
Ohio Medical License 35.028375

To: Medical Board of Ohio
From: Dr. Trent Austin
Subject: Letter of Support to add Opioid Use Disorder to medical marijuana control program
Date: 12/7/18

I have been treating patients in Ohio and Indiana for over 14 years. I am passionate about helping patients support their health with natural options for chronic illnesses. Opiate use disorder is a very serious chronic illness that is effecting both Ohio and Indiana.

Medical cannabis in a therapeutic setting and application has the possibility to address opioid addiction on a number of fronts. The first is the immediate effects of withdrawal.

Fortunately cannabis is effective in mitigating those withdrawal symptoms. Once the dire threat of withdrawal symptoms is eliminated or minimized the underlying condition can be treated.

States which have legalized medical cannabis have seen a marked decrease in opioid prescriptions and use, typically around 30 %.

I urge you to add opioid addiction to the list of qualifying conditions for Ohio Medical Marijuana program.

Sincerely,

Trent Austin, MD
4212 E. County Road 1400 N
Batesville, In, 47006-8662
Email: t.austin.accudoc@gmail.com
Telephone: 812-212-2969
Medical License 35.125199CTR

Opioid Use Disorder / Opiate Addiction
Letter of Support

Dear Ohio Medical Marijuana Control Program:

This letter is in support of the Ohio Patient Network's (OPN) submission to add Opioid Use Disorder / Opiate Addiction to the list of qualifying conditions for medical marijuana in the state of Ohio. I hope you will find the supporting evidence provided in Section 4 of the OPN submission as compelling as I have when it comes to the potential benefit of marijuana in treating this condition. This would be a welcome addition to our program and an extremely helpful tool in the fight against opioid abuse epidemic.

Thanks for your consideration.

12/9/18

Joel R. Simmons, MD
Medical Director

Date

Ohio Herbal Clinic
1830 E Broad St
Columbus, OH 43203
614-914-5224
email: info@ohioherbalclinic.com
web: www.OhioHerbalClinic.com

December 18, 2018

To: State Medical Board of Ohio; Ohio Medical Marijuana Control Program; The State of Ohio Board of Pharmacy
From: Stephen B. Mooney MD, Medical Director
Thrive Healthcare Center LLC

Dear Medical and Pharmacy Colleagues,

The intent of this letter of support is to serve as acknowledgement of my professional and clinical support for the inclusion of Opioid Use Disorder as a qualifying condition for Ohio's Medical Marijuana Control Program. As a licensed Medical Doctor, in the State of Ohio, who closely follows scientific research and published data relating to Medical Marijuana efficacy, I am aware of the existence of research that supports the use of Medical Marijuana in the care of certain types of patients diagnosed with Opioid Use Disorder. Of special interest is the fact that Medical Marijuana may be particularly valuable during the process of opioid withdrawal. Moreover, convincing data also exists suggesting that Medical Marijuana has the promising potential to be part of the ongoing care, which may include other medically-approved, medication-assisted therapies, for patients diagnosed with Opioid Use Disorder.

Sincerely,

Stephen B. Mooney MD

Thrive Healthcare Center LLC

204 2nd Street NE

New Philadelphia, Ohio 44663

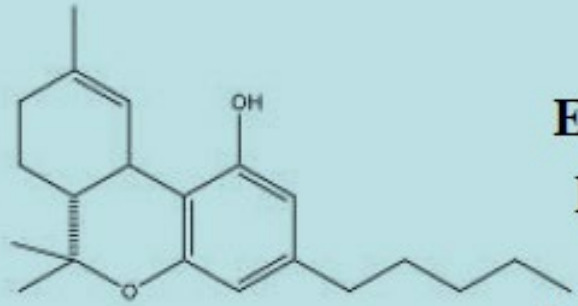
Office: (234) 801-2500

Cell: (330) 491-7927

Email: thrivehealthcare420@gmail.com

Historical Review of Cannabis for Pain Relief and Addiction Treatment

Cannabis sativa (EBR)



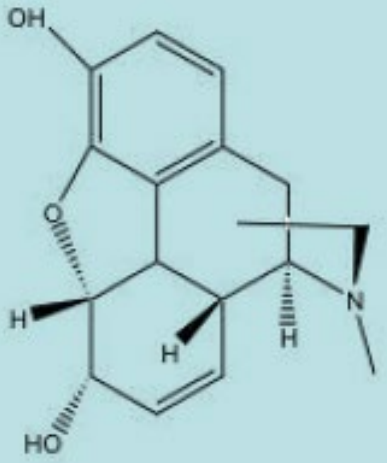
delta-9-tetrahydrocannabinol (THC)

Ethan Russo, MD

Director of Research and Development

International Cannabis and Cannabinoids Institute (ICCI

Papaver somniferum (EBR)



Morphine

ethanrusso@comcast.net

Facts and Figures

- 2016 deaths from opioid overdose topped 64,000 in USA (NYT, 9/2/17), mostly fueled by fentanyl (540% increase in 3 years)
- 2.5 million Americans have opioid use disorder (Hurd 2017)
- 80 die each day from OD
- 80% start by misusing prescription opioids
- 200 million opioid prescriptions/year

Sumerian: A.ZAL.LA

Akkadian: *azallu*

Hieroglyphic: *shemshemet*

Chinese *kanji: ma*

Sanskrit: *bhang*

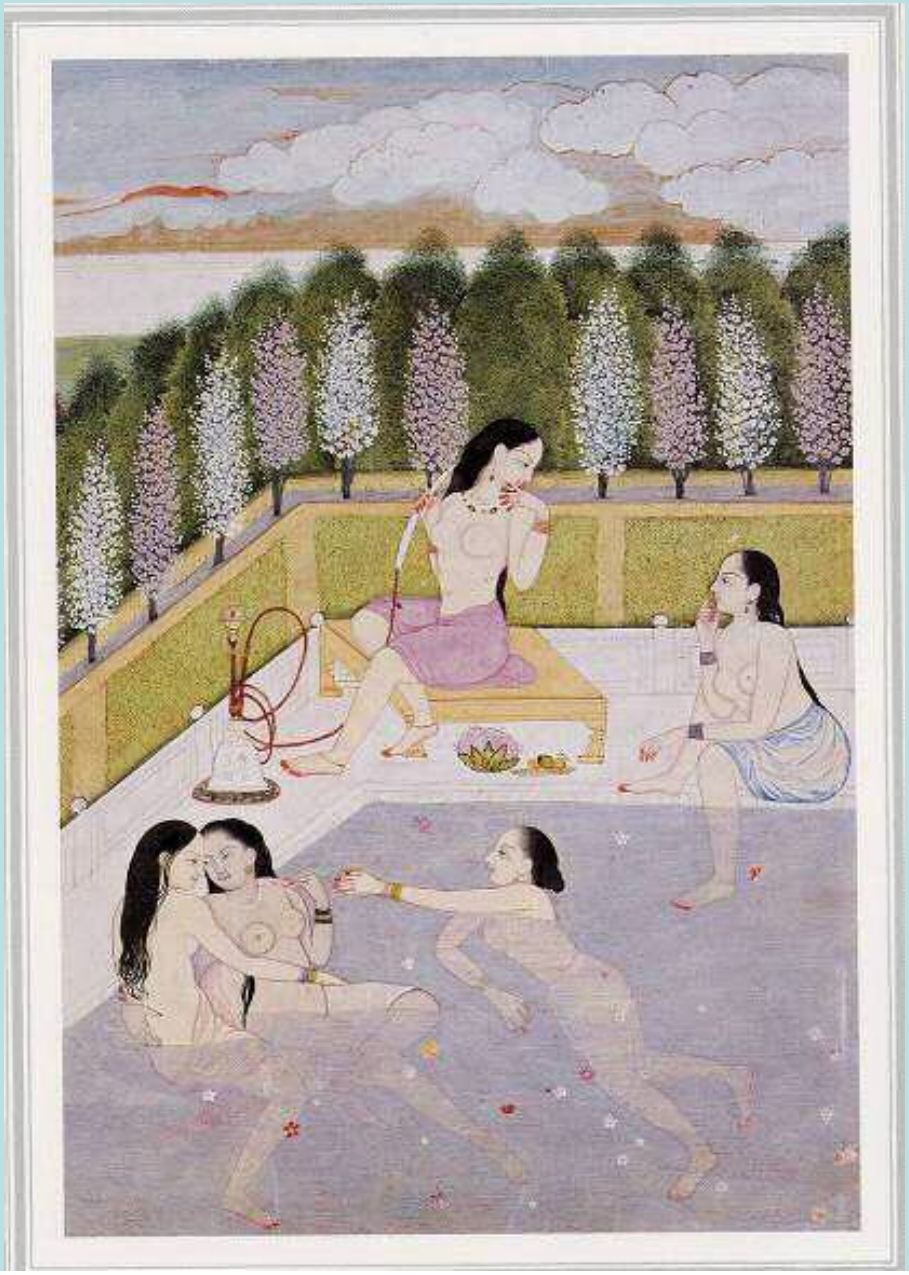
Persian: *shadanaj*

Hebrew: *kaneh bosem*

Greek: cannabis

Russo EB. History of cannabis and its preparations in saga, science an sobriquet. *Chemistry & Biodiversity.* 2007;4(8):2624-4

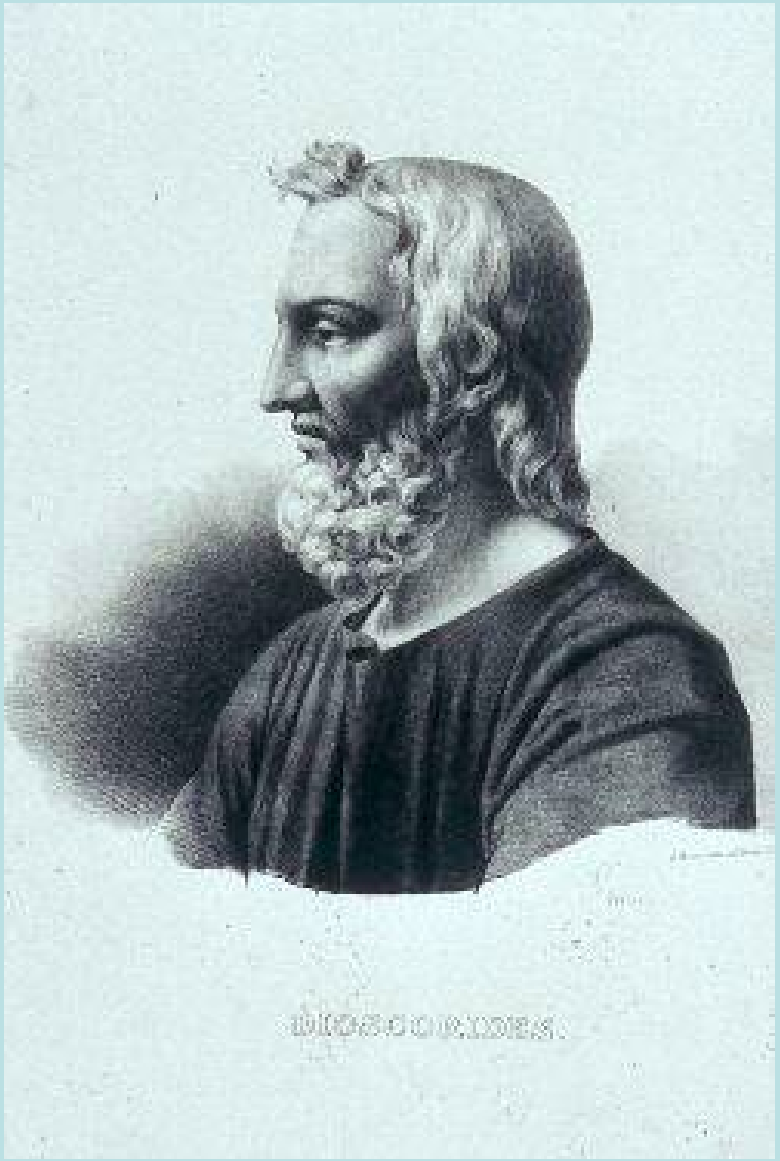
yurvedic Medicine, India 4th-3rd Centu BCE



Used in folk medici as an aphrodisiac (tantric yoga), and a a treatment for gynecological pain (Dwarakanath 1965

Perfumed Garden, as translated by Sir Richard Burton, Park St. Press:Rochester, VT, 1992, p. 26.

Dioscorides, 1st century.



Cannabis is a plant of much use this life for ye twistings of very strong ropes, it bears leaves like the Ash, of a bad scent, long stalks, empty, a **round seed, which being eaten of much do quench geniture, but being juiced when it is green is good for the pains of the ears.**

Materia Medica.

Pliny the Elder, 1st Century

"Hempseed, it is said, renders men impotent: the juice of this seed will extract worms from the ears, or any insect which may have entered them, though at the cost of producing head-ache. The virtues of hemp, it is said, are so great, that an infusion of in water will cause it to coagulate: hence, it is, if taken in water, it will arrest looseness in beasts of burden. **A decoction of the root in water, relaxes contractions of the joints, and cures gout and similar maladies. It is applied raw to burns,** but it must be frequently changed, so as to not let it dry."

Natural History (Pliny 1951)

(Book XX, Ch. 97, p.298)

Galen, 2nd century.

The leaves of this plant rcannabisl cure flatus - Some people squeeze the fresh (seeds) for use in ear-aches. I believe that it is us in chronic pains.

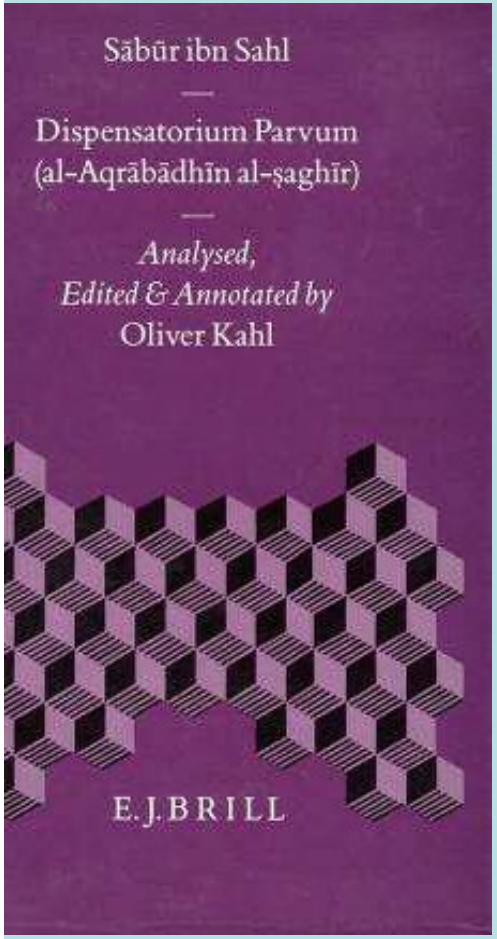
De facultatibus alimentoru

Hua-tho in the *Kou-kín-i-tong*, China, 2nd century.

He gave to the sick person a preparation of hemp (Ma-yo), and a few moments, he became so insensible that it were as if he was plunged into rapture of loss of life Then, following this instance, he practiced some overtures, incision amputations, and removed the cau of the malady; then he repaired th tissues with suture points, and app liniments. [translation EBR]

Julien, M.S. 1849. *Chirugie Chinoi Substance anesthétique employée Chine, dans le commencement du ieme siècle. Comptes Rendus Hebdomadaires de l'Académie de Sciences* 28: 195-198.

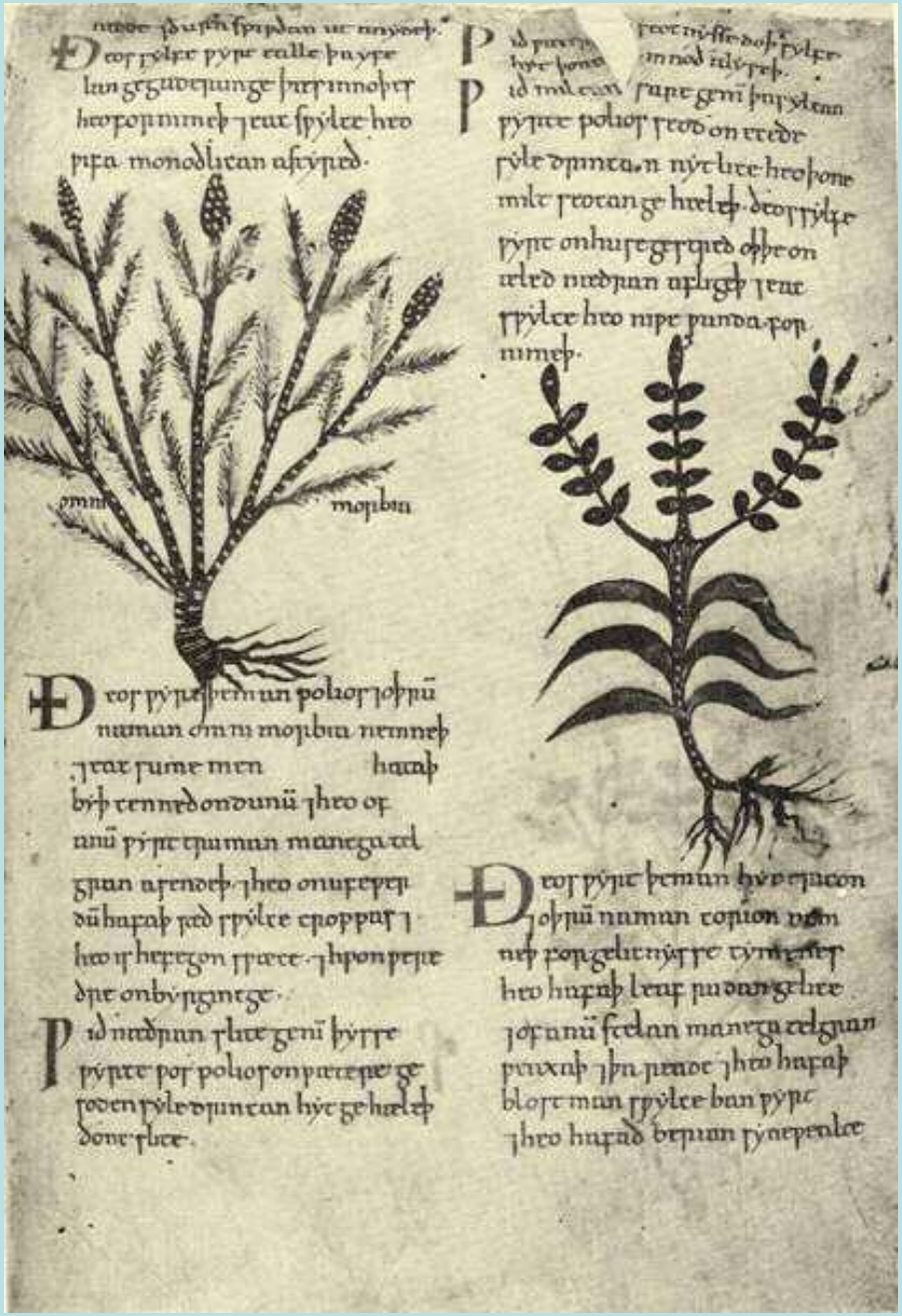
Sabur ibn Sahl, Persia, 9th Century



وشعر الغول وأصول الهندباء وكشت بر كشت[a] من كلّ واحد وزن درهميْن
وتُرَاب المُرَبَّعَات[143] وزن درهميْن وحبّ المحلب وأصول الخردل الأبيض
وعيدان البلسان من كلّ واحد وزن درهميْن وماء السوسن وماء الشَوْك وزن
درهم وعُقَد التِبْن الّذي في الحِيطان وزن سبعة دراهم وخُرْء الثعلب وزن
نصف درهم وهزارجشان وششبندان من كلّ واحد وزن أربعة الدراهم
[٣٣ب] وقشور أصول الكبر وزن نصف درهم تجمع هذه الأدوية مسحوقة
منخولة بحريرة وينقع منها ما آنْتُقِعَ بالشراب الصافي وهو الأصل أو
الجمهوري أو المثلّث ويرفع في إناء ويستعمل بعد ستّة أشهُر الشربة منه
كَالحِمَّصَة بماء قشور أصول الرازيانج والكرفس ويسعط منه بقدر حَبَّة
الحِنْطَة بماء الشهدانج أو بماء المرزنجوش وَلْيُتَّخَذْ في أيّام طُلُوع كَلْب
الجَبَّار[144] إن شاء اللّه.

n intranasal base preparation of juice from cannabis flowers was mixed with a variety of other herbs to treat migraine, calm uterine pains, prevent miscarriage, and preserve fetuses in their mothers' abdomens.

Old English Herbarium, 11th Century



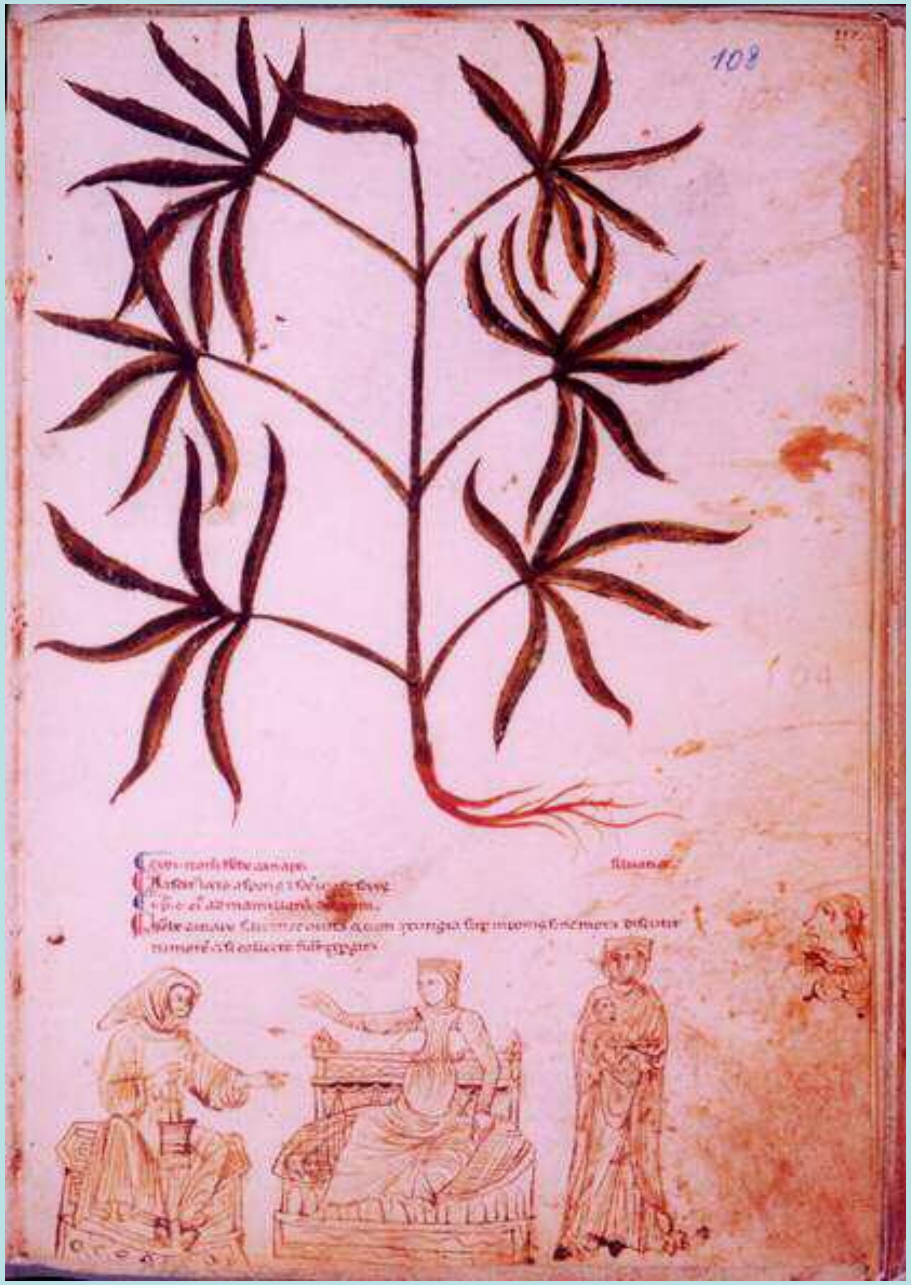
"---for pain of the innards take the same plant [*haenep,* hemp], give it to drink, it takes away the pain."

Hildegard von Bingen

"**Whoever has an empty brain and head pains may eat it and the head pains will be reduced.** Though he who is healthy and full of brains shall not be harmed by it. – He who has an empty brain shall be caused pain by indulging in hemp. A healthy head and a full brain will not be harmed."

Physica ~ 1158

Codex Vindobonensis 93, Österreichische Nationalbibliothek Vienna, Austria, 13th century



The Latin inscription describes the use of cannabis mixed into an ointment and rubbed on the breasts to reduce swelling and pain.

Leonhart Fuchs, *New Kreuterbuch, 1542*

Hemp root, boiled in water, an wrapped---is also good for gou The raw root, pounded and wrapped, is good for the burn. The wild hemp, boiled and wrapped, alleviates and splits the tumour.
(Translation courtesy of Franjo Grotenhermen)

FUCHS, L. 1999. The great herbal of Leonhart Fuchs : De historia stirpium commentarii insignes, 1542 , Stanford, CA, Stanford University Press.

François Rabelais, 1546

Si promptement voulez guerir une bruslure, soit d'eaue, soit de feu, applicquez y du Pantagruelion crud, c'est à dire tel qui naist de terre, sans aultre appareil ne composition. Et ayez esguard de le changer ainsi que le voirez deseichant sus le mal.
Livre III, Chapitre 51

If you want to cure a burn, no matter whether it be from boilin water or burning wood, just rub on raw Pantgruelion [hemp], ju as it comes out of the earth, without doing anything else. Bu be careful to change the dressin when you see it drying out on th wound.

RABELAIS, F. 1990. Gargantu and Pantagruel, New York, Norton. Book III, Chapter 51, page 371

Li Shih-Chen, *Pen T'sao Kang Mu (Bencao Gang Mu)*, 1596

Cannabis flowers were recommended for menstrual disorders. Seed kernels were employed fo postpartum dificulties. It was also observed (p. 91) "The juice of the root is - thought to have a beneic action in retained placent and post-partum hemorrhage."

John Parkinson, 1640.

Hempe is cold and dry --- the *Dutch* as one sai doe make an Emulsion out of the seede, --- f openeth the obstructions of the gall, and cau digestion of choller therein: --- **the Emulsio decoction of the seede**, stayeth laskes and fluxes that are continuall, **easeth the paines the collicke:** and allayeth the troublesome humours in the bowels: --- **The decoction, o the roote is sayd to allay inflammations in head or any other part, the herbe it selfe, the distilled water thereof performeth the effect; the same decoction of the rootes, easeth the paines of the goute, the hard tumours, or knots of the joynts, the paines and shrinking of the sinewes, and other th like paines of the hippes: it is good to be u for any place that hath beene burnt by fir the fresh juyce be mixed with a little oyle butter.**

Theatrum botanicum: The theater of plants; or herball of a large extent. London: Tho. Cote

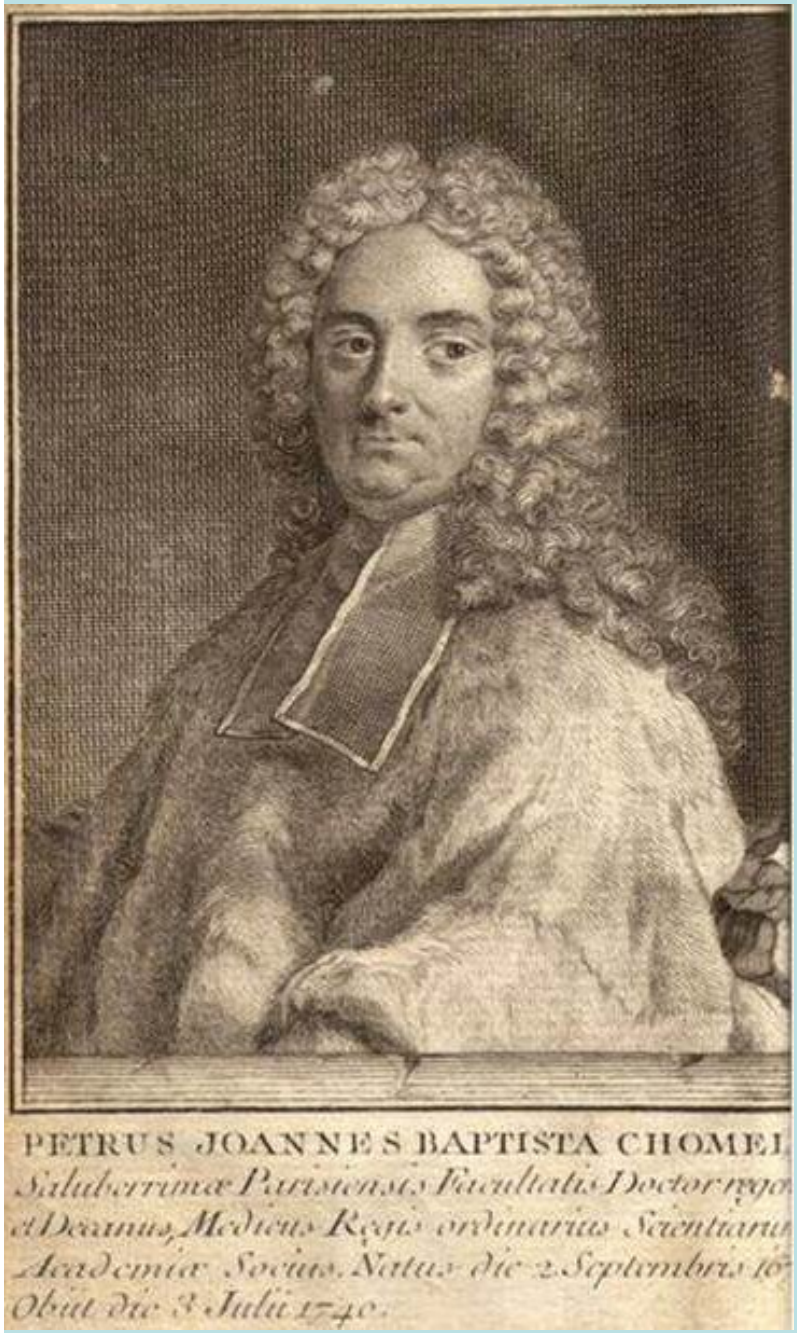
Georg Everhard Rumpf, 17th century

"The Indians [loose term for peoples of the East] deem this Fool's-Herb to be their *Nepenthe* which serves to drive away sorrow and bring them jollity."

also described use in gonorrhea, **pleuritic chest pain and hernia**

E.M. Beekman (Ed.). *The Poison Tree: Selected Writings of Rumphius on the Natural Histor of the Indies.* Amherst: Univ. of Massachusetts.

Pierre-Jean-Baptiste Chomel, 1712.

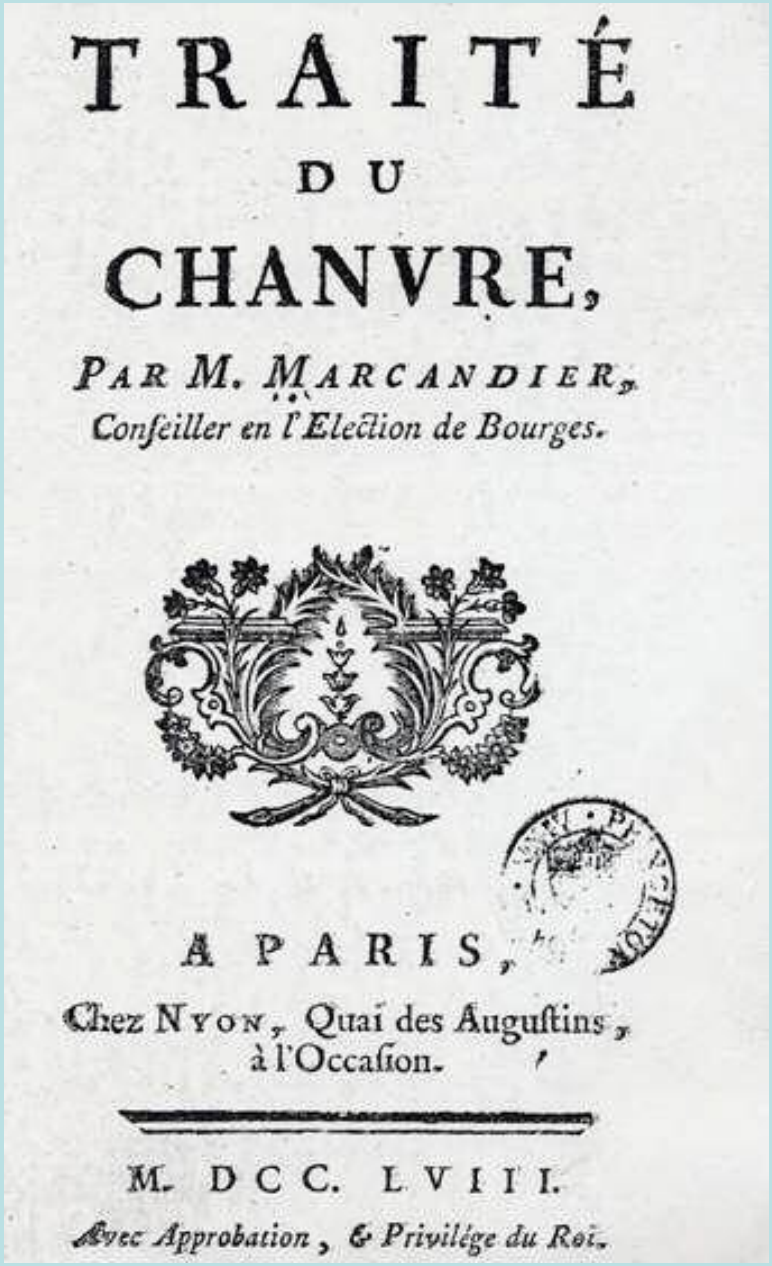


The leaves of hemp and its se crushed and applied in a cataplasm, are strongly resolutive; one employs them the country for scrofula and scirrhous tumours.

This oil mixed with a little melted wax, is a good remed for burns, from which it appeases the pain. [translatio EBR]

Abrégé de l'histoire des plante usuelles. Pp. 369-370. Paris: Librairies Associés.

Marcandier 1758



TRAITÉ
DU
CHANVRE,
PAR M. MARCANDIER,
Conseiller en l'Election de Bourges.

A PARIS,
Chez NYON, Quai des Augustins,
à l'Occasion.

M. DCC. LVIII.
Avec Approbation, & Privilége du Roi.

"The seed and the green leaves, crushed and applied in the form of cataplasm, to painful tumors, appear to b strongly resolutive and intoxicating."

(translation EBR, p. 38).

Carolinus Linnaeus, 1772.

"narcotica, phantastica, dementans,

anodyna,

repellens."

Materia medica per regna tria naturae. Lipsiae et Erlangae: Wolfgang Waltherum.

William O'Shaughnessy, 1839.

Employed successfully in rheumatic disorders among many others.

ON THE PREPARATIONS OF THE INDIAN HEMP, OR GUNJAH

(CANNABIS INDICA):

THEIR EFFECTS ON THE ANIMAL SYSTEM IN HEALTH, AND THEIR UTILITY IN THE TREATMENT OF TETANUS AND OTHER CONVULSIVE DISEASES

By W. B. O'SHAUGHNESSY, M.D.,

Assistant-Surgeon, and Professor of Chemistry, &c.

In the Medical College of Calcutta.

Presented October, 1839.

The narcotic effects of Hemp are popularly known in the south of Africa, South America, Turkey, Egypt, Asia Minor, India, and the adjacent territories of the Malays, Burmese, and Siamese. In all these countries Hemp is used in various forms, by the dissipated and depraved, as the ready agent of a pleasing intoxication, In the popular medicine of these nations, we find it extensively employed for a multitude of affections. But in Western Europe, its use either as a stimulant or as a remedy, is equally unknown. With the exception of the trial, as a frolic, of the Egyptian 'Hasheesh,' by a few youths in Marseilles, and of the clinical use of the wine of Hemp by Mahneman, as shewn in a subsequent extract, I have been unable to trace any notice of the employment of this drug in Europe.

Much difference of opinion exists on the question, whether the Hemp so abundant in Europe, even in

Clendinning, J. 1843. Observation on the medicinal properties of *Cannabis sativa* of India. *Medico-Chirurgical Transactions* 26:188-210.

Noted marked success in treating rheumatic conditions, neuropathic pain and migraine with cannabis in 3 cases, **including one complicated by morphine withdrawal symptoms.**

Michael Donovan, Dublin, 1845

Treated many patients with headache and neuralgias, who persisted in use of Indian hemp, even in the face of side effects, and with marked improvement in sleep, even in a case of sciatica.

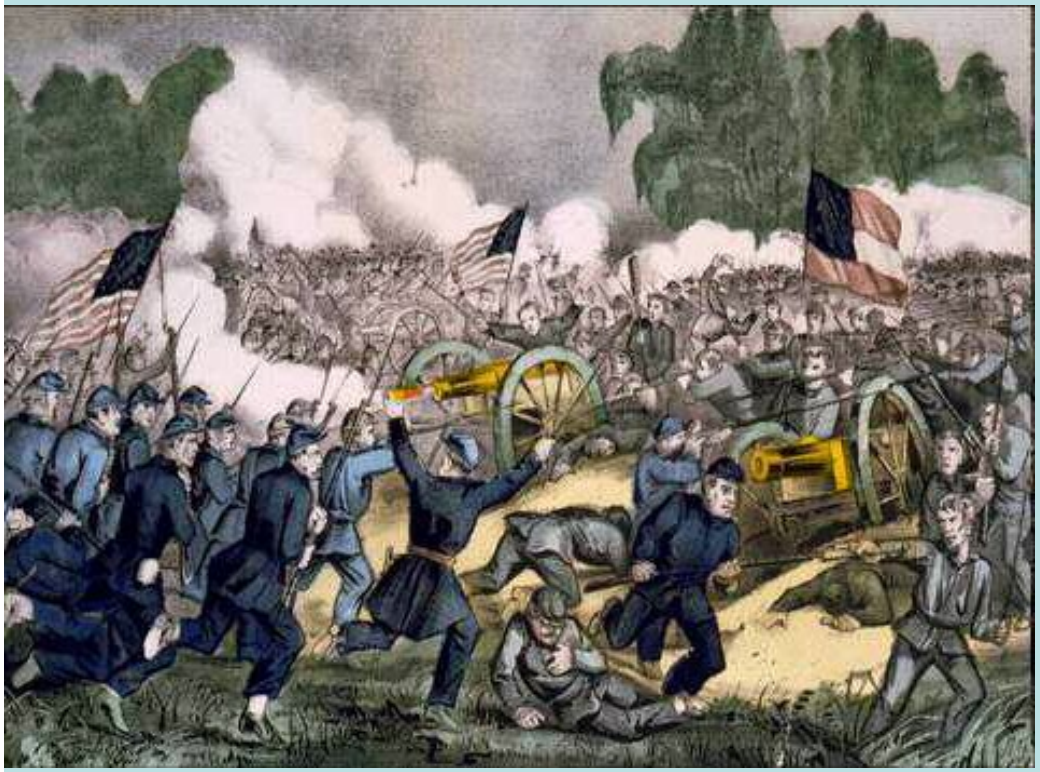
Donovan, M. 1845. On the physical and medicinal qualities of Indian hemp (Cannabis indica); With observations on the best mode of administration, and cases illustrative of its powers. *Dublin Journal of Medical Science* 26:368-402, 459-461.

Robert Christison, 1848.

"**Indian hemp** has been used as antispasmodic in hydrophobia, tetan malignant cholera, and infantile convulsions, with marked relief in repeated instances. Some cases of tetanus appear to have been cured in the East-Indies by it; **---It has also been employed with success as an anodyne in chronic rheumatism, toothache, and other varieties of neuralgia. I have used it a good de and with decided success, in disea at large, to obtain sleep."**

Christison, R. A dispensatory o commentary on the pharmacopoeias of Great Brita and the United States. Philadelphia: Lea and Blanchard; 1848. (p 974)

American Civil War, 1860s



Cannabis was employed to treat war injuries, and combined with opium to treat fluxes, such as dysentery.

The Medical and Surgical History of the Civil War, Vol. 4, Broadfoot Pub. Co., Wilmington, NC, 1992.

Sir John Russell Reynolds, 1868.

This medicine [cannabis] appear capable of reducing over-activi of the nervous centres without interfering with any one of the functions of organic, or vegetal life. **The bane of many opiate and sedatives is this, that the relief of the moment, the hou or the day, is purchased at th expense of to-morrow's miser In no one case to which I hav administered Indian hemp, h I witnessed any such results.**

Therapeutical uses *and toxic effe of Cannabis Indica*, *Lancet* 1:6 638.

Silas Weir Mitchell, 1874.

It is necessary at times to do somethin to give immediate relief to the too prolonged pain [of migraine], and **in these cases a combination of cannabis indica and morphia answers very well; but in a disease so wearisome and long, it is well to be more than cautious in ordering narcotics**

Headaches, from heat-stroke, from fevers, after meningitis, from over use of brain, from eye strain. *Medical and Surgical Reporter* 31(July 25, August 1):67-70, 81-84.

Edouard Seguin, 1877.

"Briefly stated my thesis is THAT BY THE LONG-CONTINUED USE OF CANNABIS INDICA, MIGRAINE OR SICK-HEADACH MAY BE CURED, MUCH RELIEVED, OR MITIGATED IN SEVERITY.

I never allow my patients to take opium or morphia themselves in this disease.

The principle of the treatment is to keep the nervous system steadily under a slight influen of cannabis for a long period of time; ---

I usually obtain a promise from the patient th he will regularly take the pills for a period of three months.---

The majority of patients relieved have obtain months of freedom from attacks while taking remedy."

Contribution to the therapeutics of migraine. *Medical Record* 12:774-776.

Hobart Hare, 1887.

CANNABIS INDICA has been before the profession for many years as a remedy to be used in combating almost all forms of pain, yet, owing to the variations found to exist as to its activity, it has not received the confidence which I think it now deserves.

... The advantages in its use over opium consist chiefly in the absence of prostratio and nausea after its ingestion, and in the partial lack of soporific power which it possesses compared to the opiate, for in certain cases sleep is not always desirable when pain is to be removed. That cannabi indica has, however, marked powers as a soporific is not to be denied. Added to these advantages is the fact of its failure t produce serious symptoms even if very large doses be taken, although I have found the efficient dose of a pure extract o hemp to be as powerful in relieving pain a the corresponding dose of the same preparation of opium. (p. 225-226)

Clinical and physiological notes on the action *Cannabis indica*, *Therapeutic Gazette*, 2:225 228.

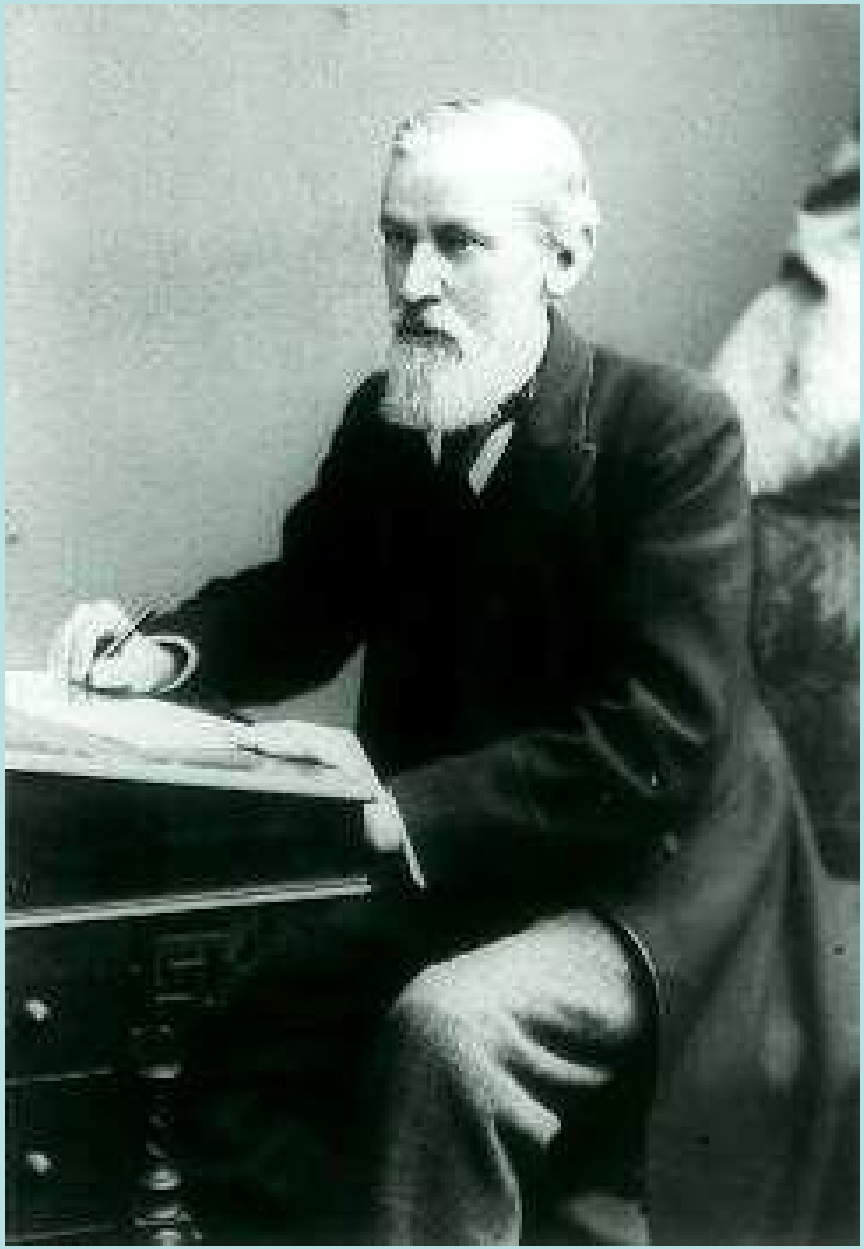
Richard Greene, 1888

"Since 1872 I have often prescribed it [cannabis] , and I have yet to meet with a case in which at least some improvement does not follow the careful and continuous use of the drug."

"It should be noted that the treatment her advocated afresh is not merely a palliativ one during the paroxysm, like the use of guarana, caffeine, hypodermic morphine or nitrite of amyl inhalations, but is ofte curative and nearly always gives some lasting relief."

Greene, R. 1888. The treatment of migraine with Indian hemp. *Practitioner* 41:35-38. (36)

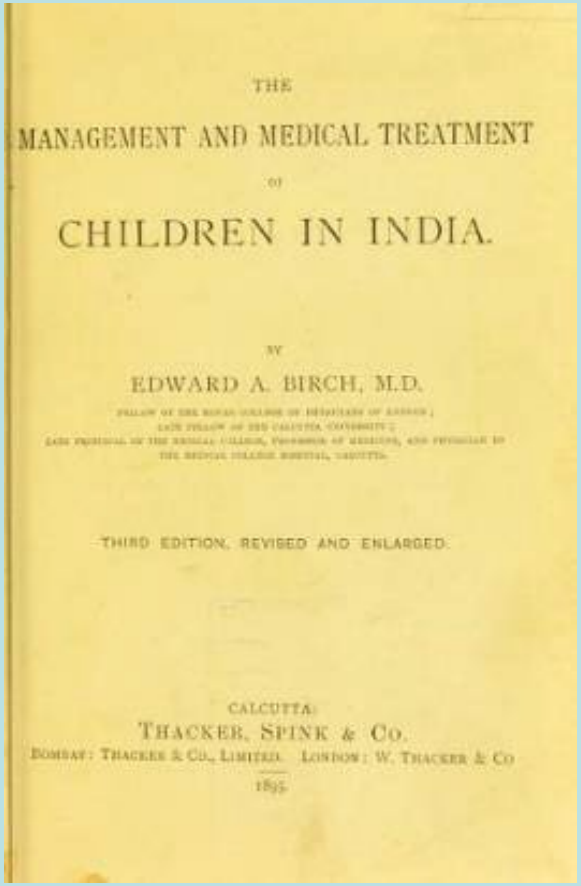
Sir William Gowers, 1888.



Sedatives are very uncertain in their influence [on headaches]. **Opium a morphia are seldom useful, and often do more harm than good, in consequence of the indirect effect the constipation that is produced.** Gelsemium and Indian hemp frequently lessen the pain, the form chiefly in neuralgic forms about the front of the head, the latter not only neuralgic, but in anaemic, and also other ill-defined forms of headache.

A Manual of Diseases of the Nervous System, Philadelphia: Blakiston.

Edward Alfred Birch, 1840-1912


THE
MANAGEMENT AND MEDICAL TREATMENT
OF
CHILDREN IN INDIA.
BY
EDWARD A. BIRCH, M.D.
THIRD EDITION, REVISED AND ENLARGED.
CALCUTTA:
THACKER, SPINK & CO.
BOMBAY: THACKER & CO., LIMITED. LONDON: W. THACKER & CO
1895

After serving in the China War, he joined the Indian Medical Service in Bengal at the Calcutta Medical College. He successfully treated a laudanum addict described as resembling "an exhumed corpse," who after thrice daily administration of cannabis extract recovered suficiently over

J.B. Mattison, 1891.

Employed cannabis in treatin addiction to cocaine, chloral hydrate and opiates:

"In these, often, it has proved an eficient substitute for the poppy."

Cannabis indica as an anodyne and hypnotic, *St. Louis Med. Surg J* 61:265-271.

J.B. Mattison, 1891.

"In headache, periodical or long continued, one half to two grains solid extract may be given each hour or two till the attack is arrested, and then continued in a similar dose, morning and night, for weeks or months. It is important not to quit the drug during a respite from pain. ---

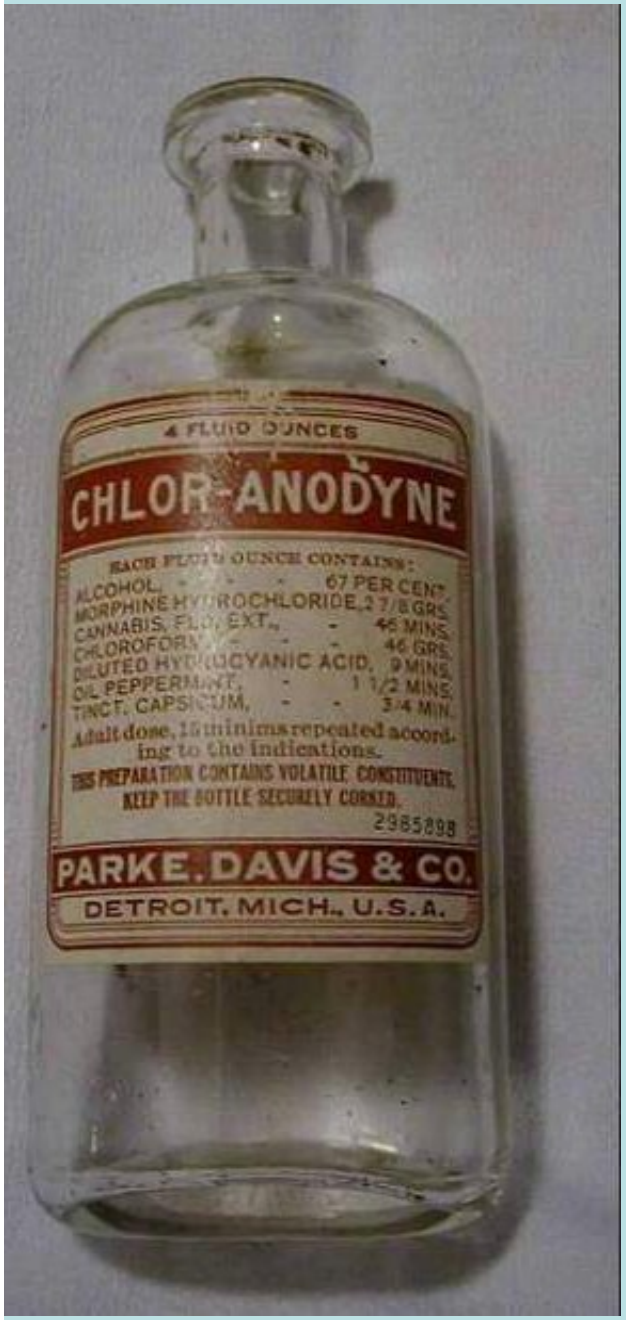
Recollect that hemp eases pain without disturbing stomach an secretions so often as opium, a that competent men think it no only calmative, but curative."

Cannabis indica as an anodyne an hypnotic, *St. Louis Med. Surg J* 61:265-271.

Thomas D. Crothers, *Morphinism and Narcomanias from Other Drugs*. W.B. Saunders, Philadelphia, 1902.

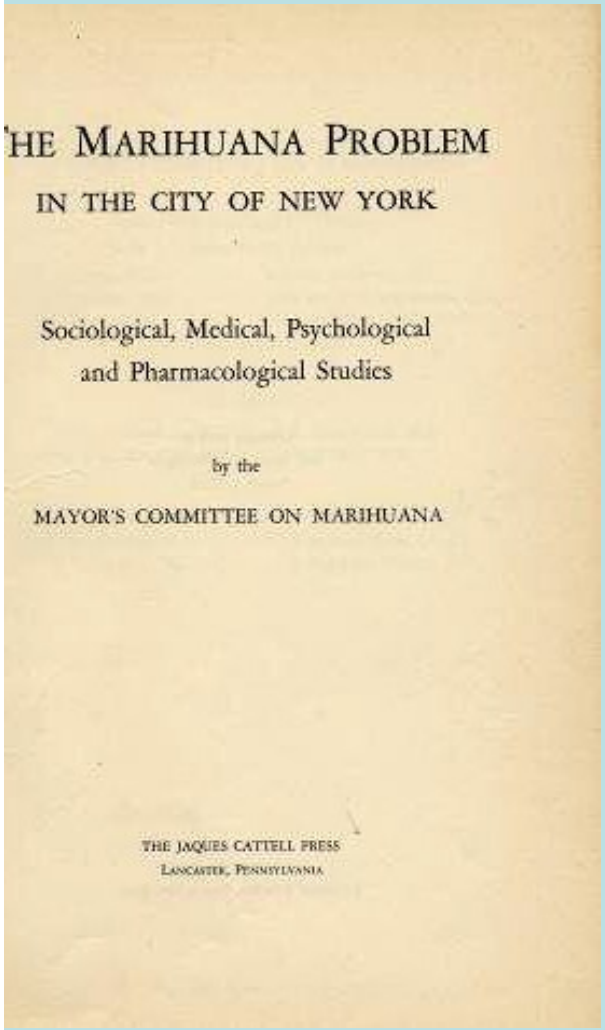
"Cannabis indica can often be used with very good effect [in treating morphinism], especiall for the temporary removal of the worst symptoms."
(p. 182)

Empirical Medicine of the 19th Century



- Combined morphine, cannabis, and capsicum
- Provided a phyto-opioid, phytocannabinoid, and phytovanillo in one preparation
- Affected the 3 known endogenous biochemical systems mediating pai endorphin/enkephalin, endocannabinoid, vanilloid
- Arguably may have provided better outpatient pain relief than is current available in the 21st century

LaGuardia Commission, 1944



'HE MARIHUANA PROBLEM

IN THE CITY OF NEW YORK

Sociological, Medical, Psychological
and Pharmacological Studies

by the

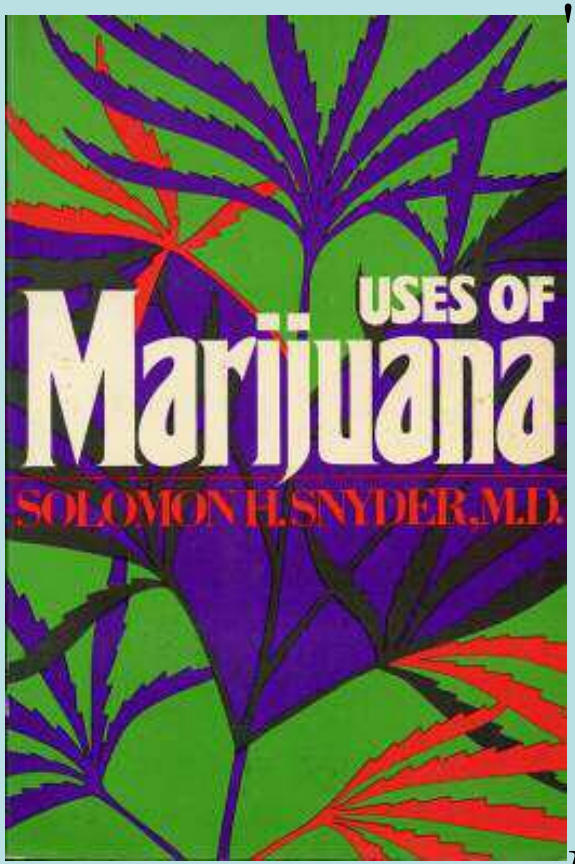
MAYOR'S COMMITTEE ON MARIHUANA

THE JAQUES CATTELL PRESS
LANCASTER, PENNSYLVANIA

At the Riker's Island Penitentiary observations were made on inmates who were addicted to morphine or heroin. Two grou were selected, the addicts in each being matched with those in t other group as to age, physical condition, duration and intensity habit, and number of previous attempts at cure. The subjects in o group received no treatment or were given Magendie's soluti according to the usual hospital regimen, while those in the oth group were treated with 15 mg. of tetrahydrocannabinol three tim daily with or without placebo (subcutaneous water injection). A attempt was made to evaluate the severity of the withdrawal sig and symptoms. The impression was gained that those who receiv tetrahydrocannabinol had less severe withdrawal symptoms and l the hospital at the end of the treatment period in better conditi than those who received no treatment or who were treated wi Magendie's solution. The ones in the former group maintained th appetite and in some cases actually gained weight during the wit drawal period.

p.
147

Solomon Snyder, 1971.



"For there are many condition such as migraine headaches o menstrual cramps, where something as mild as aspirin gives insuficient relief and opiates are too powerful, not mention their potential for addiction. Cannabis might conceivably fulill a useful ro in such conditions."

Uses of marijuana. New York: Oxford University.

Tod Mikuriya, 1973

Published a historical compendium of cannabis articles from the 19th century including treatment of addictions.

MIKURIYA, T. H. 1973. Marijuana: Medical papers, 1839-1872, Oakland, CA, Medi-comp Press.

Studies in Pain (Noyes 1975)

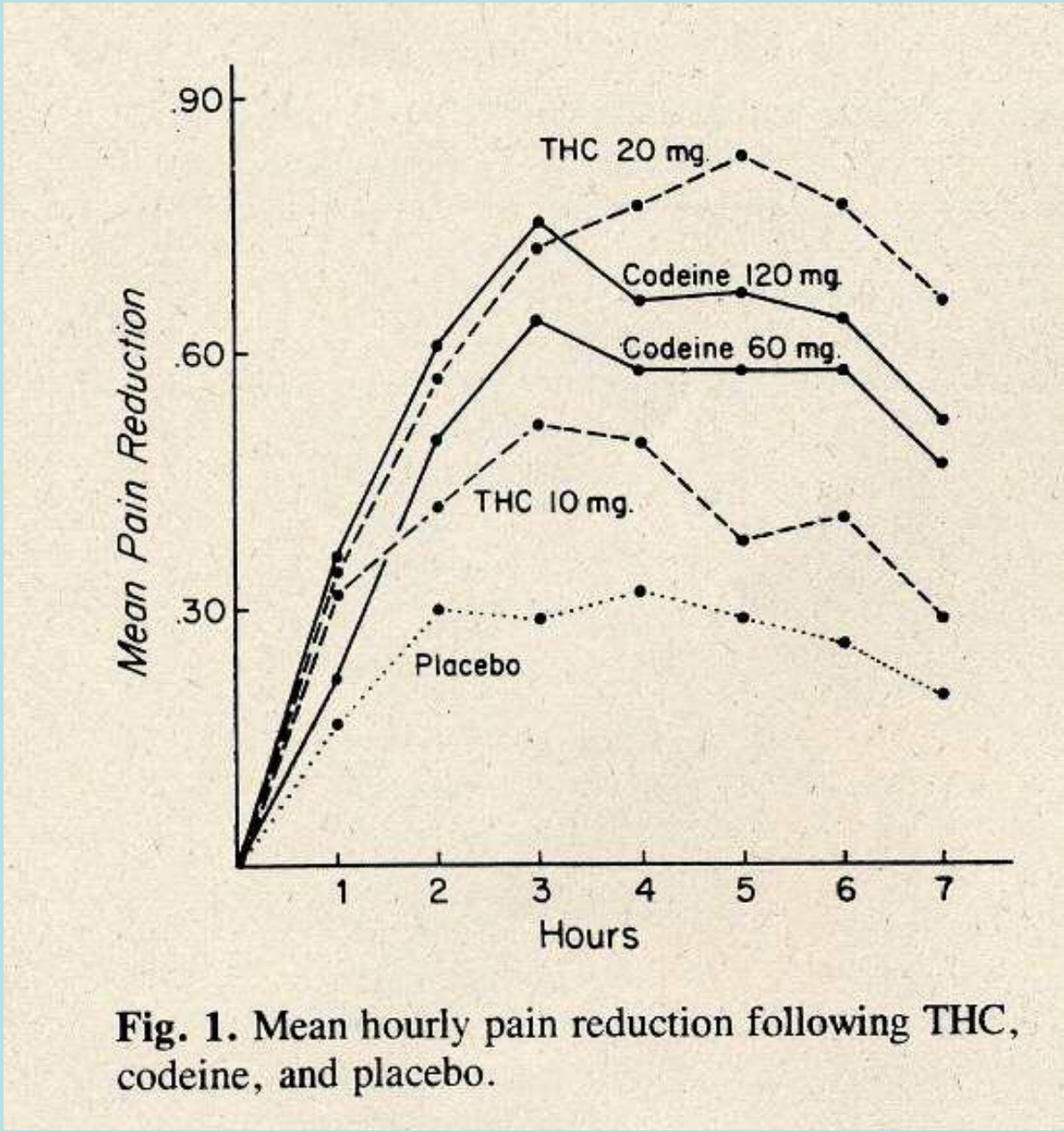


Fig. 1. Mean hourly pain reduction following THC, codeine, and placebo.

Reiman, A. (2009). Cannabis as a substitute for alcohol and other drugs. *Harm Reduct J, 6*, 35.

Many pa'ents use medical cannabis in a harm4reduc'on paradigm

Philippe Lucas, Victoria, BC

Man lauded for providing medical marijuana

A Victoria judge who praised an advocate for the medical use of marijuana says that either Parliament or the Supreme Court must resolve the legal issues surrounding the therapeutic use of the illegal drug. Provincial Court Judge Robert Higinbotham granted an absolute discharge to Philippe Lucas, who had pleaded guilty to possessing about 3 kg of marijuana. Higinbotham said Lucas had merely "provided that which the government was unable to provide: a safe and high-quality supply of marijuana to those needing it for medicinal purposes."

Philippe Lucas: show some compassion

Lucas runs the Vancouver Island Compassion Society (see *CMAJ* 1999;161[8]:1024), which provides marijuana to about 250 members who have been referred by their doctors. Higinbotham lauded Lucas' motives, transparency and meticulous record-keeping in operating the club, a registered nonprofit society (www.thevics.com). The judge also cited the measures the club has taken to prevent redistribution of the marijuana by members.

Lucas' troubles began when he called police after a burglary at the Compassion Society. He says the club had enjoyed a good relationship with the police since it opened in 1999. The thief was caught, but Lucas was charged with possession of marijuana. Since the court decision was announced, Lucas has seen a surge in requests for information about the club, and the doctors supporting him "have been extremely buoyed by the decision. There are many doctors in Victoria who would rather send patients to us than go through the legal Health Canada program [www.hc-sc.gc.ca/hecs-sesc/ocma/index.htm], and I think that is very telling." About 80 physicians refer patients to the club, which verifies all referrals. Most of the patients have AIDS, hepatitis or cancer.

Lucas, who has a legal exemption to use the drug because of hepatitis C contracted via a blood transfusion, hopes the court decision will spur federal action. — *Heather Kent*, Vancouver

Lucas, P. (2012). Cannabis as an adjunct to or substitute for opiates in the treatment of chronic pain. *J Psychoactive Drugs, 44*(2), 125-133.

Cannabinoid Analgesia

- The ECS is active in tonic fashion in control of pain (Richardson 1997)
- ECS functions in nociceptive areas of CNS:
- Integrative control of pain in PAG (Walker 1999)
- **VPL where CBs 10-fold more potent than morphine in WDR neurons mediating pain (Martin 1996)**
- ECS active in spinal cord pain mechanisms including NMDA (Hohmann 1995, Richardson 1998) wind-up (Strangman 1999), and allodynia (Rahn 2007)
- ECS also active in periphery on pain, inflammation, hyperalgesia (Richardson 1998), contact dermatitis and pruritis (Karsak 2007)

Russo, E.B. 2008. Cannabinoids in management of difficult to control pain. *Therapeutics & Clinical Risk Management* 4(1):345-259.

Cannabinoids - Mechanisms of action are distinct from opioids

- THC and CBD have analgesic eficacy in animal models
- Mechanisms are due to activity at CB1 and CB2 receptors (THC), and at TRPV1 receptors (CBD).
- CBD has anti-inflammatory properties in vitro
- Opioid eficacy related to activity at mu opioid receptors
- CB receptors are scarce in cardiorespiratory centres in contrast to opioid receptors

BUT

- Cannabinoids enhance release of endogenous opioids
- CB receptors may co-localize with mu opioid receptors

AND

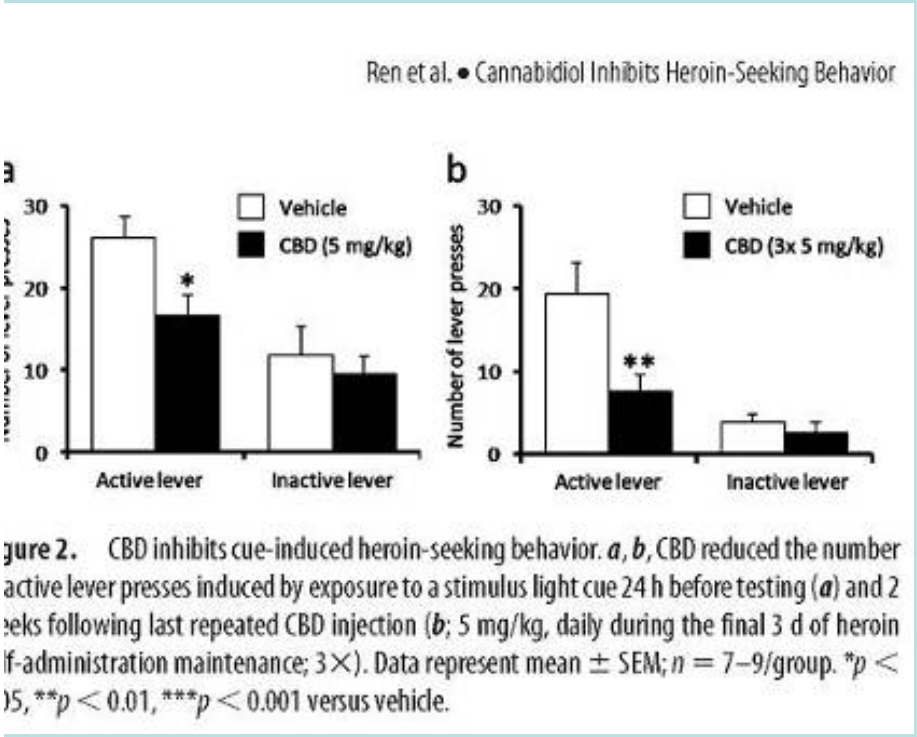
No evidence of clinically relevant adverse drug-drug interaction between cannabinoids and opioids

Cannabinoid-Opioid Interactions

- THC stimulates beta-endorphin production (Wiegant 1987; Manzanares 1998)
- THC interacts with endogenous opioids in periaqueductal gray matter (Meng 1998)
- THC may allow clinical "opiate sparing" (Cichew[redacted] 1999)
- THC prevents development of tolerance to and withdrawal from opiates (Cichewicz 2002)
- THC rekindles opiate analgesia (Cichewicz 2003)

+

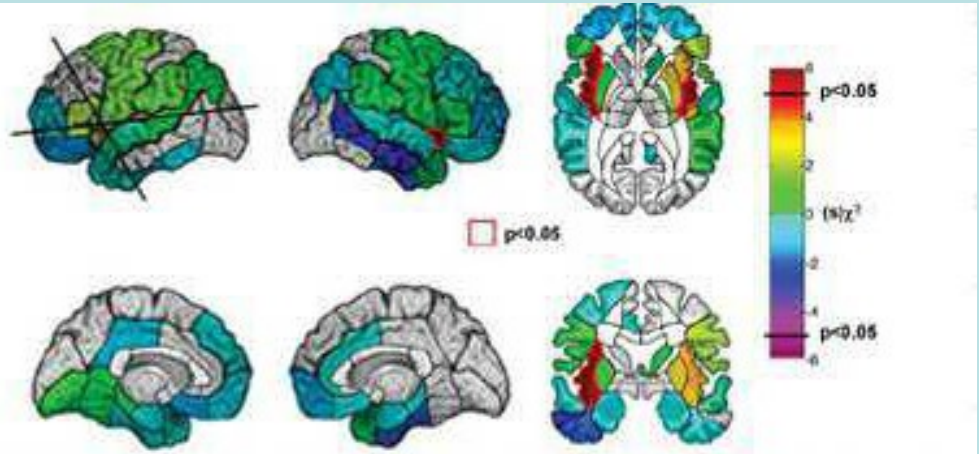
en, Y et al. (2009) Cannabidiol, a nonpsychotropic component of cannabis, inhib cue-induced heroin seeking and normalizes discrete mesolimbic neuronal disturbances. *J Neurosci* ***29***(47)***:*** 14764-14769.



gure 2. CBD inhibits cue-induced heroin-seeking behavior. *a*, *b*, CBD reduced the number active lever presses induced by exposure to a stimulus light cue 24 h before testing (*a*) and 2 eks following last repeated CBD injection (*b*; 5 mg/kg, daily during the final 3 d of heroin lf-administration maintenance; 3×). Data represent mean ± SEM; $n = 7–9$/group. $^{*}p <$ 05, $^{**}p < 0.01$, $^{***}p < 0.001$ versus vehicle.

- CBD 5 mg/kg/d in rats attenuated heroin-seeking behaviour reinstated by conditioned stimuli, even 24 to 2 wks later.
- CBD reversed changes in AMPA GluR1 and CB1R expression in NAc induced b heroin
- Authors proposed CBD at Tx. for heroin craving and relapse

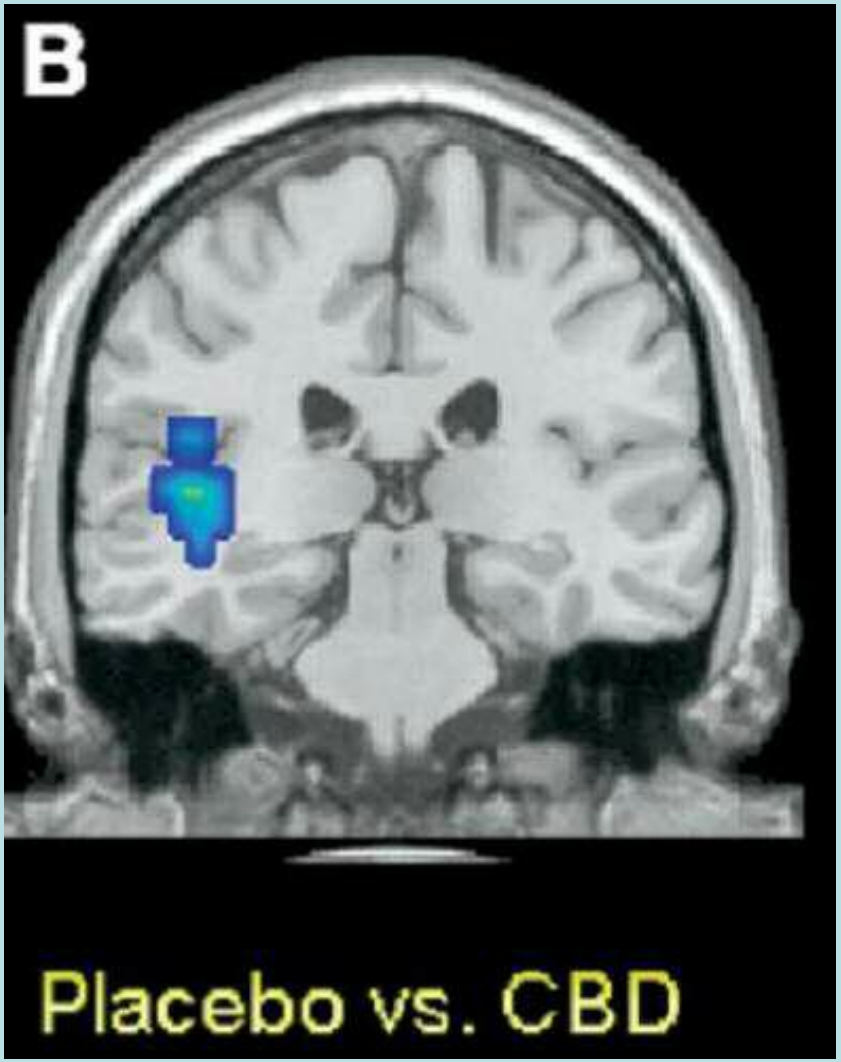
Naqvi, NH et al. (2007) Damage to the insula disrupts addiction to cigarette smoking. *Science* **315**(5811)**:** 531-534.



3. Whole-brain region-by-region logistic regression analysis. The color of each region ponds to a χ^2 statistic given the sign of regression coefficient obtained from the logistic ssion analysis. The only regions that were assigned a color were those for which the number of nts was sufficient to detect a statistically significant effect (Materials and Methods). Regions hich there was a statistically significant association between a lesion and a disruption of ing addiction ($P < 0.05$, uncorrected) are highlighted in red. The insula is the only region on r side of the brain where a lesion was significantly associated with a disruption of smoking tion. There were nonsignificant effects in regions on the left side that are adjacent to the ; however, patients with damage in these regions also tended to have damage in the insula rials and Methods). The likelihood of having a disruption of smoking addiction was not ased after damage in the orbitofrontal cortex.

- Patients with damage in the insula (e.g., CVA) were able to quit smoking tobacco without relapse or urges.
- The insula appears to be a critical neural center mediating nicotine addiction
- Urge for drugs further localized to insula for cocaine, EtOH, heroin (Naqvi 2009, 2010)

Borgwardt SJ et al. Neural basis of Delta-9-tetrahydrocannabinol and cannabidiol: effects during response inhibition. *Biol Psychiatr* 2008 64(11):966-73.



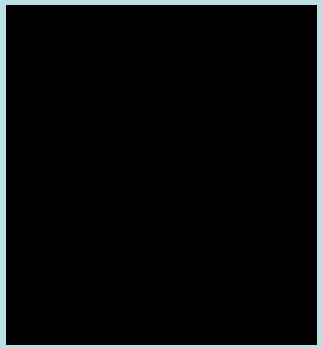
CBD 600 mg po functionally deactivated the left insula in human volunteers vs. placebo ($p<0.01$), without accompanying sedation or other psychoactive changes.

Xi, Z. X., et al. 2011. Brain cannabinoid CB(2) receptors modula cocaine's actions in mice. *Nat Neurosci* 14 (9):1160-6.

CB2 is expressed in VTA and NAc dopaminergic neurons

Activation of CB2 by JWH133 (systemically, intranasal or microinjection in NAc) inhibited DA release, and cocaine self-administration in mice.

(Caryophyllene probably acts similarly)



Johnson, JR, et al. An Open-Label Extension Study to Investigate the Long-Term Safety Tolerability of THC/CBD Oromucosal Spray and Oromucosal THC Spray in Patients W Terminal Cancer-Related Pain Refractory to Strong Opioid Analgesics. *J PainSympto Management.* 2012.

"Notably in this population with terminal disease, study medication **[Sativex] was taken for more than six months by 10% of patients and for more than a year by 5% without requiring dose escalation."** In summary, the findings show that **some patients will continue to obtain relief of cancer-related pain with long-term use of THC/CBD spray, without increasing their dose of this or other pain-relieving medications over time**, (from page 11)

An MS patient

- Previously disabled wi intractable pain
- Now employs solely Sativex® with low dos amitriptyline (150 mg — 25 mg)
- Has returned to full-tim employment in an MS Centre

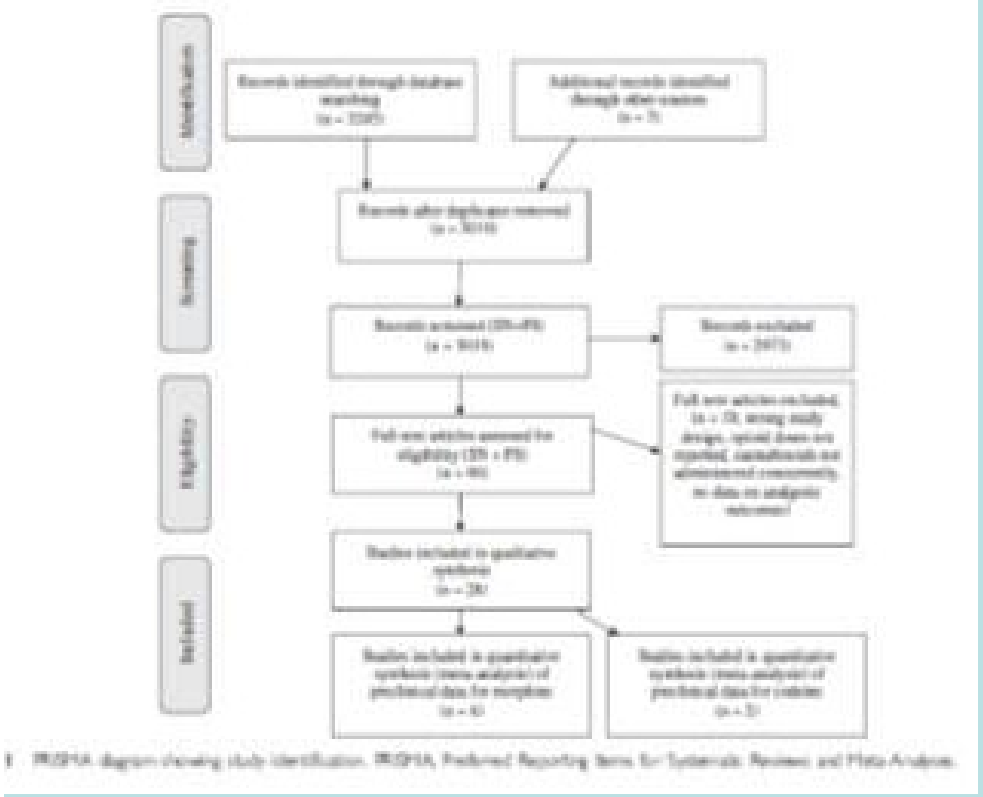
A sciatica patient

- Has reduced MS-Contin® dose from 180 to 30 mg a day on Sativex®
- Pain has diminishe from 9/10 to 4/10.

Use of Cannabis in Cannabis or Opioid Use Disorder

- Cannabis can be used concomitantly with opioids, even in those with medical dependency. Close follow-up is mandatory.
- After an interval in which pain reduction is achieved, a judicious dose-reduction or tapering schedule from the opioids should be initiated.
- The medical patient who fulfills diagnostic criteria of cannabis use disorder or displays tolerance to high doses should undergo a desensitization regimen, as outlined by Dustin Sulak, DO: www.healer.com

Nielsen, S., et al. 2017. Opioid-Sparing Effect of Cannabinoids: A Systematic Review and Meta-Analysis *Neuropsychopharmacology* 42: 1752-65.



- 17/19 (90%) of preclinical studies showed cannabinoid-opioid analgesic synergy
- ED50 of morphine with THC is 3.6X lower than when used alone ($p<0.001$)
- Most clinical studies have not been designed or powered to demonstrate opioid-sparing.

Boehnke, K. F. et al. 2016. Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain *J Pain* 17: 739-44.

Outcome of Interest	Entire Set of Questionnaires (N = 244)
[redacted]M score	9.23 (5.52)
[redacted]pioid use change	–63% (46%)
[redacted]egree to which side effects of medication affect daily function (before using medical cannabis); scale from 1 to 10	6.44 (2.91)
Degree to which side effects of medication affect daily function (after using medical cannabis); scale from 1 to 10	2.77 (2.35)
Number of medication classes used (before cannabis use)	2.35 (1.43)
[redacted]mber of medication classes used (after cannabis use)	1.82 (.94)
[redacted]ality of life change	45% (28%)

In study 118 patients, cannabis use led to a 64% reduction in opioids and a 45% increase in QOL measures (possibly due to fewer opioid-associated AEs

Gruber, S. A., et al. 2017. The Grass Might Be Greener: Medical Marijuana Patients Exhibit Altered Brain Activity and Improved Executive Function after 3 Months of Treatment *Front Pharmacol* 8: 983.

TABLE 4 | Mood and health ratings at pre-treatment and after 3 months of MMJ use (post-treatment).

Rating scale	Visit 1 Pre-treatment Mean (SD)	Visit 2 Post-treatment Mean (SD)	ANOVA	
			F	*p* (η^2)
Clinical ratings				
Profile of Mood States (POMS)[a]				
Vigor	16.86 (6.19)	16.14 (6.53)	0.140	0.235 (0.026)
Anger	8.68 (10.33)	8.59 (8.21)	0.000	0.477 (<0.001)
Confusion	8.00 (6.38)	6.73 (4.92)	2.748	0.056 (0.116)
Tension	12.69 (9.98)	12.05 (9.97)	0.152	0.350 (0.007)
Fatigue	9.91 (7.29)	8.77 (7.24)	1.946	0.089 (0.085)
Depression	15.18 (16.78)	14.14 (10.86)	0.217	0.323 (0.010)
[redacted]	26.50 (51.08)	34.14 (46.89)	0.055	0.409 (0.003)
[redacted]ession Inventory (BDI)[a]				
[redacted]	15.77 (12.00)	8.73 (11.00)	**8.559**	**0.003 (0.313)***
[redacted]ety Inventory (BAI)[a]				
[redacted]	10.55 (10.37)	9.73 (9.93)	0.237	0.319 (0.011)
[redacted]pulsiveness Scale (BIS-11)[a]				
[redacted]n	16.59 (5.77)	16.59 (5.47)	0.000	0.500 (0.000)
Motor	23.00 (3.43)	21.23 (5.37)	**12.521**	**0.001 (0.374)***
[redacted]lanning	25.41 (6.53)	25.50 (6.50)	0.077	0.392 (0.004)
[redacted]	65.00 (16.08)	61.41 (14.64)	1.626	0.108 (0.072)
[redacted] **quality of life ratings**				
[redacted] Sleep Quality Index (PSQI)[b]				
[redacted]	8.26 (4.46)	6.05 (3.26)	**7.167**	**0.008 (0.265)***
[redacted] functioning	71.59 (21.40)	71.82 (26.03)	0.001	0.480 (<0.001)
[redacted]tations (physical)	44.32 (43.60)	56.82 (44.44)	**3.915**	**0.031 (0.157)***
[redacted]tations (emotional)	63.64 (43.52)	60.61 (45.58)	0.006	0.380 (0.005)
[redacted]fatigue	42.73 (25.36)	51.36 (21.67)	**10.736**	**0.002 (0.339)***
[redacted]al well-being	67.64 (26.18)	68.82 (27.33)	0.821	0.187 (0.036)
[redacted]functioning	62.50 (28.12)	68.75 (25.36)	1.819	0.096 (0.080)
[redacted]	52.73 (7.06)	58.30 (26.36)	0.918	0.174 (0.042)
[redacted] health	57.50 (19.75)	60.91 (19.56)	1.668	0.106 (0.074)

Clinical rating scales (POMS, BDI, BAI), lower scores reflect lower levels of clinical symptoms; BIS-11, lower scores indicate lower levels of self reported impulsivity; PSQI, lower scores reflect improved sleep quality; SF-36, higher scores indicate higher quality of life. [a]df = 1,21; [b]df = 1,18; *bolded results are significant at $p \leq 0.05$; italicized results approach significance at $p \leq 0.10$.

- No mood or health ratings worsened with treatment.
- Significant improvements were noted on depression (BDI), impulsivity (BIS-11), sleep (PSQI) and quality of life (SF-36), especially for energy and fewer physical limitations
- **Patients on opioids reduced intake 47.69%**, benzodiazepines 46.91%, antidepressants 22.35%, and mood stabilizers 28.57% afte 3 months of cannabis treatment

Cooper, Z. D., et al. 2018. Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability *Neuropsychopharmacology*.

Achieving analgesia with lower opioid oses may also decrease adverse effects elated to opioid use that diminish their herapeutic utility, including constipation, espiratory depression, and the evelopment of opioid tolerance and ependence."

This potential for cannabinoids to ecrease the abuse liability of opioids has rofound implications for the most ignificant adverse effects of opioids; that s, the risk of opioid use disorders and ssociated fatalities." (p. 2)

- 18 cannabis smokers with cold pressor testing
- 5 mg oxycodone with cannabis increased pain tolerance (p<(0.05), as did cannabis plus previously inactive 2.5 mg oxycodone, an opioid-sparing effect
- Benefits were obtained without concomitant increase in the drug abuse liability of cannabis (drug liking)

Habib, G., and S. Artul. 2018. Medical Cannabis for the Treatment of Fibromyalgia *J Clin Rheumatol*

TABLE 3. Meds Consumed Prior to and Under MC Treatment

Medication	Prior to MC Treatment No. Patients (%)	Under MC Treatment No. Patients (%)	*P*
Simple analgesics	12 (~46)	3 (~15)	0.000
NSAIDs	19 (~73)	2 (~8)	0.000
[illegible]ple opiates	4 (~15)	0 (0)	0.055
[illegible]abalin	7 (~27)	0 (0)	0.005
[illegible]ng opiates	20 (~77)	5 (~19)	0.000
[illegible]zodiazepines	7 (~27)	1 (~5)	0.027
[illegible]yclics	4 (~15)	0	0.055
Other antidepressants	8 (~31)	3 (~12)	0.107

NSAIDs indicates nonsteroidal anti-inflammatory drugs.

- **26 pts. in Israel getting mean dose of 26 g. of cannabis/month (<1 g/d)**
- 46% reported increase in work capacity or return to work
- **Substantial opioid sparing and decreased use of adjunctive drugs was noted.**

Bar-Lev Schleider, L., et al. 2018. Prospective analysis of safety and efficacy of medical cannabis in large unselected population of patients with cancer *Eur J*

Table 2
Concomitant medications use at the baseline and six month follow up.

	Intake	Change at six month follow-up					
cation family	Total	I stopped taking this medication	Dosage decreased	Has not changed	Dosage increased	Other	New medication
ids, n (%)	344	124 (36.0)	34 (9.9)	176 (51.1)	4 (1.1)	6 (1.7)	32
analgesics and antipyretics, n (%)	177	56 (31.6)	15 (8.4)	102 (57.6)	–	4 (2.2)	2
lytics, n (%)	155	37 (23.8)	3 (1.9)	113 (72.9)	1 (0.6)	1 (0.6)	5
otics and sedatives, n (%)	114	29 (25.4)	7 (6.1)	76 (66.6)	–	2 (1.7)	3
Corticosteroids for systemic use, plain, n (%)	85	27 (31.7)	6 (7.0)	49 (57.6)	–	3 (3.5)	7
Antiemetics and antinauseants, n (%)	49	33 (67.3)	1 (2.0)	15 (30.6)	–	–	–
Laxatives, n (%)	38	12 (31.5)	2 (5.2)	23 (60.5)	–	1 (2.6)	2

Of 344 patients (33.9%) on opioids at onset, 36% were able to discontinue them, 9,9% decreased their dose, only 1.1% increased and 51% continued on a stable dosage.

Krebs, E. E., et al. 2018. Effect of Opioid vs Nonopioid Medications on Pain-Related Function in Patients With Chronic Back Pain or Hip or Knee Osteoarthritis Pain: The SPACE Randomized Clinical Trial. *JAMA* 319 (9):872 882.

- 240 patients randomized to receive opioid vs. non-opioid regimen
- After 1 year, NSD in pain on Brief Pain Inventory (BPI) interference
- Pain intensity was significantly better in the non-opioid group (p=0.03)!
- AEs were significantly more common in opioid group (p=0.03)!
- 'Treatment with opioids was not superior to treatment with non-opioid medications for improving pain-related function over 12 months."

HEALER

Medical Cannabis Opioid Guide

How to Use Cannabis to Reduce and Replace Opioid Medications

By Dr. Dustin Sulak, Co-founder Healer

www.Healer.com

Thousands of people have used cannabis to help them reduce and replace opioid medications, as demonstrated in numerous recent scientific papers[1-4] and strongly supported by animal research. [5] If you or your loved one is considering this, congratulations!

I conducted a survey of my patients in 2016. Of the 542 opioid users who added cannabis, 39% were able to completely stop opioid use, and 39% used cannabis to reduce their opioid dosage. Adding cannabis reduced pain by more than 40% in nearly half the patients and improved function in 80%. In 87% of patients, it improved quality of life!

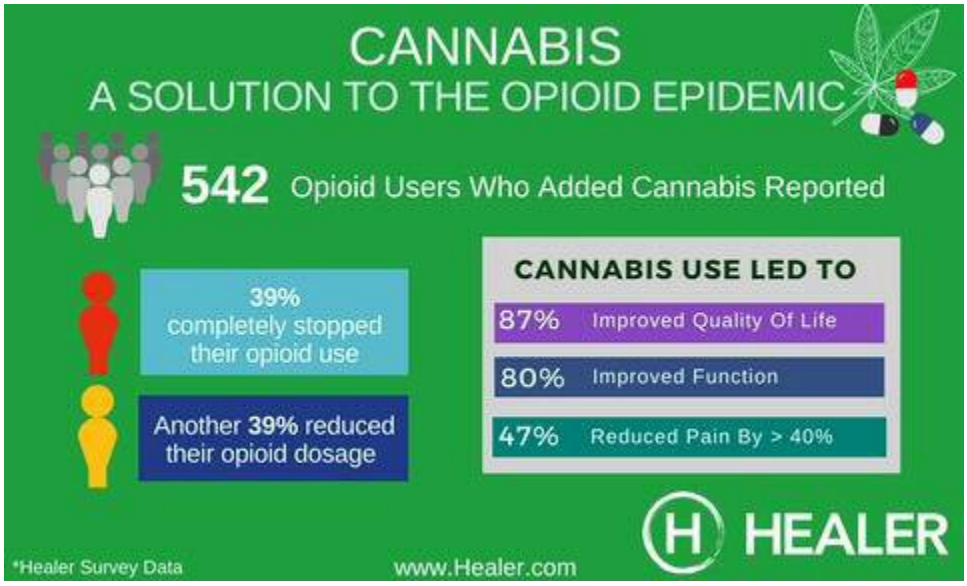


Chart 1: Healer Survey Data 2016

The following guidelines are based on my experience treating chronic pain with cannabis in 8 years of clinical practice, conferring with my colleagues, and closely following the scientific literature. These guidelines apply to patients from any walk of life, including those with chronic pain, PTSD (post-traumatic stress disorder), addiction, non-medical use of opioids, etc.

Advantages of Adding Cannabis

- Cannabis enhances pain relief and other medical effects of opioids.[5]
- Taking cannabis with opioids can make the opioids safer by widening their therapeutic window (the window between the effective dose and the lethal dose). An ineffective dose of an opioid drug can become effective when it's combined with cannabis.[6]
- In addition to reducing pain, cannabis conveys holistic benefits, such as improving sleep,[7] reducing anxiety,[8] relaxing muscles, giving perspective on life's challenges, etc.
- Cannabis relieves the symptoms of opioid withdrawal.[9]
- In dealing with opioid addiction, cannabis can be safer than other harm reduction options like methadone and Suboxone. It does not have the risk of a fatal overdose and has a lower risk of dependence and problematic use than other psychoactive substances.[10] Cannabis can be used in combination with methadone or Suboxone to enhance the benefits and support a taper of these drugs.
- Some studies have shown that cannabis users are more successful adhering to other forms of opioid addiction treatment, such as long-acting naltrexone.[9]

Basic Principles of Use

1. Take a low dose of cannabis with every dose of opioids.
    a. Even at low doses that do not cause impairment or adverse effects, cannabis can enhance the effects of opioid medications.
    b. Always use the lowest effective dose of cannabis to avoid building tolerance. (To find your optimum dose, new and experienced cannabis users can follow the Healer.com dosage programs.)
2. For longer acting effects, oral delivery, such as a tincture or oil absorbed through the blood vessel in the mouth or a capsule swallowed and absorbed in the intestine, is optimal. Both methods allow for a measurable dose in milligrams of THC (tetrahydrocannabinol) and CBD (cannabidiol).
3. Only use inhaled cannabis to reduce cravings and for breakthrough symptoms (severe pain, flashbacks, panic attacks, withdrawal symptoms, etc.).
4. Use cannabis to promote restorative sleep.
5. Use cannabis to enhance the enjoyment and benefits of therapeutic activities (exercise, meditation, prayer, journaling, counseling, etc.). (See Healer.com/Wellness for some simple but powerful wellness practices.)

Specific Dosing Information

- I recommend my patients start with a liquid cannabis preparation (tincture or oil) that's administered under the tongue. This allows for intermediate onset of benefits and easy dosage adjustments. The oral preparation should give a specific milligram (amount of drug) per milliliter (amount of liquid) potency (mg/ml), allowing you to accurately dose using drops or an oral syringe.
- The cannabis tincture should be taken 3 to 4 times daily or with every administration of an opioid drug.
- The content of CBD and THC is important. For most of my patients, a CBD:THC ratio of approximately 1:1 is broadly effective and well tolerated.
    - People who are very sensitive to THC can reduce potential unwanted effects by using a CBD:THC ratio of 4:1 or higher.
    - If you don't have access to cannabis preparations containing CBD, you can still succeed using THC-dominant preparations.

- **Recommended starting dose: CBD 1 mg + THC 1 mg.**
  - This dose is too low to have a noticeable effect in many patients, but some do report benefits.
  - Every day, increase your individual THC dose by 1 to 2 mg (and the appropriate corresponding amount of CBD depending on your selected CBD:THC ratio). If your Day 1 dose is CBD 1 mg + THC 1 mg (with no discernible effect), on Day 2 increase the dose to CBD 2 mg + THC 2 mg.
  - Most patients achieve good results at 2 to 15 mg of THC per dose.

- **How will I know when I reach my optimal dose?**
  - Use Healer's Inner Inventory, located in Healer.com/programs to identify the dose that creates a therapeutic effect (reduced pain, reduced anxiety, etc.).
  - If you find that cannabis makes the effects of the opioid feel stronger or last longer, or if you are able to take less of the opioid drugs, you've reached an effective dose.
  - You can maintain consistent benefits without building tolerance for years or decades if you stay at your optimal dose of cannabis. If you've developed tolerance by regularly exceeding your optimal dose, complete Healer's Sensitization Protocol as soon as possible to recover the full benefits of cannabis.
  - You've likely exceeded your optimal dose if you experience:
    - A reduction in the effects (it was working, but now it's not)
    - An increase in unwanted side effects (such as confusion, lightheadedness, fatigue).
  - Many patients find that they are able to decrease their opioid dosage by 50% to 80% in the first 2 weeks after adding cannabis at the optimal dose, and then they continue to reduce opioids more slowly thereafter. I encourage you to take advantage of this 2-week window of opportunity. Other people do not experience this rapid reduction at first but find they are able to taper their opioid medications slowly and consistently.

- **When using inhaled cannabis for cravings and breakthrough symptoms:**
  - Use a vaporizer or pipe with cannabis flowers, if possible.
  - Take 1 inhalation, wait 5 to 10 minutes, then repeat if necessary.
  - Avoid concentrates (hash, dabs, shatter, etc.) and high potency vape pens unless 3 to 5 inhalations of herbal cannabis are ineffective. Concentrates are more likely to cause you to build tolerance to cannabis, and most vape pens fail to convey the full range of compounds that produce the desired medical benefits.
  - Select cannabis strains that correlate with your specific goals. For example, one strain for sleep, one for pain, one for cravings, etc. See Healer's Cannabis Shopping Guide for more guidance about strains and their associated benefits.

For Patients New to Cannabis or Not Currently Using Cannabis:

- Refer to Healer's Introduction to Cannabis program for more specific step-by-step dosing guidance.

Introduction to Cannabis
4 Day Program

https://healer.com/programs/introduction-to-cannabis/

For Experienced Cannabis Users:

- Before starting to taper opioids, it's essential that you reverse any tolerance to cannabis to ensure you get best results. I strongly suggest beginning with Healer's 6-day Sensitization Protocol.
- If you are not experienced with oral dosing of cannabis liquid medicines or capsules, familiarize yourself with this delivery method and find your optimal dosage before starting to taper your opioid drugs. See Healer's Switching from Inhalation to Tincture program for more details.

Sensitization Protocol
6 Day Program

https://healer.com/programs/sensitization-protocol/

Switching From Inhalation
to Tincture

https://healer.com/programs/switching-from-inhalation-to-tincture/

If Low-Dose Cannabis Is Ineffective:

- For a small percentage of my patients, low-to-moderate-dose cannabis (≤60mg of THC daily) is not sufficient to help them reduce opioid medications. If you see no response (improved symptoms and ability to decrease opioids) after using cannabis for 30 days at low doses, then it may be time to switch to a high-dose protocol that typically uses cannabis concentrate taken by mouth or high potency edibles.
- Gradually work up to very high doses. For example, start at 20 mg of THC three times daily and gradually, over 1 to 4 weeks, work up to 100 to 500 mg of THC per dose. Gradual titration is important to prevent the unpleasant side effects of cannabis overdose.

CAUTIONS

1. Discuss your intention to use cannabis for this purpose with your health care provider and collaborate to achieve your goals. Do not adjust the dosage of prescribed opioid medications without discussing it with your provider. If your health care provider is uncomfortable with a THC-positive urine drug screen, please note that the Centers for Disease Control and Prevention (CDC) recommends against urine testing for THC in patients prescribed opioids for chronic pain.[11]
2. Work with an experienced cannabis clinician who can monitor and provide feedback on your use of cannabis.
3. Inhaled THC-dominant cannabis has rewarding effects that trigger the pleasure centers in the brain. While this can be useful in combating cravings for more dangerous drugs, it can also trigger a desire for more strongly rewarding substance and behaviors. Please limit your use of inhaled cannabis to cravings and breakthrough symptoms, as described above.

Those who are most successful in using cannabis to replace opioid drugs always use a combination of pharmacologic and behavioral interventions. No medication is powerful enough to accomplish this goal on its own. By prioritizing and organizing the proper resources for sleep, exercise, counseling, support groups, and social support, you can ensure your success!

I want to learn from your experiences. Please go to http://www.healer.com/programs/feedback

References

1. Haroutounian S, et al. The effect of medicinal cannabis on pain and quality-of-life outcomes in chronic pain: A prospective open-label study. Clin J Pain. 2016;32(12):1036-1043.
2. Boehnke KF, Litinas E, Clauw DJ. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. J Pain. 2016;17(6):739-744.
3. Lucas P, Walsh Z. Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. Int J Drug Policy. 2017;42:30-35.
4. Piper BJ, et al. Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. J Psychopharmacol. 2017;31(5):569-575.
5. Nielsen S, et al. Opioid-sparing effect of cannabinoids: A systematic review and meta-analysis. Neuropsychopharmacology. 2017;42(9):1752.
6. Cooper ZD, et al. Impact of co-administration of oxycodone and smoked cannabis on analgesia and abuse liability. Neuropsychopharmacology. 2018:1.
7. National Academies of Sciences, Engineering, and Medicine. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: National Academies Press; 2017.
8. Walsh Z, et al. Medical cannabis and mental health: A guided systematic review. Clin Psych Rev. 2017;51:15-29.
9. Bisaga A, et al. The effects of dronabinol during detoxification and the initiation of treatment with extended release naltrexone. Drug Alcohol Depend. 2015;154:38-45.
10. Anthony JC, Warner LA, Kessler RC. Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey. Exp Clin Psychopharmacol. 1994;2(3):244.
11. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. JAMA. 2016;315(15):1624-1645.