

Cannabis: A Solution to the Opioid Epidemic?

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- The opioid problem
- Cannabis can replace and reduce opioids.
- Adding cannabis makes opioids safer.
- Cannabis prevents opioid-tolerance and the need for dose escalation.
- Cannabis can treat the symptoms of opioid withdrawal.
- Cannabis compared to other harm reduction options
- How to use cannabis to decrease and discontinue opioids

Public Health Impact of Opioid Prescriptions



- 44 people in the United States die every day from prescription painkiller overdose.
- Almost 7,000 people are treated in emergency departments every day for using prescription opioids in a manner other than as directed.
- One in 20 people in the United States, ages 12 and older, used prescription painkillers non-medically in 2010.

Data from cdc.gov

Public Health Costs of Opioid Prescriptions: Federal CDC Data



- Sales of opioids quadrupled between 1999 and 2010.
- Between 2000 and 2014 the rates of death from prescription-opioid overdose nearly quadrupled.
- Enough opioids were prescribed in 2010 to medicate every American adult with a standard pain treatment dose of 5 mg of hydrocodone taken every 4 hours for a month.

Data from cdc.gov

Opioid Abuse





Castlight Health "The Opioid Crisis in America's Workforce"

Prescription Opioids in America



- While America claims less than 5% of the world's population, it consumes roughly 80% of the world's opioid supply (Manchikanti & Singh, 2008)
- Nearly 50% of patients who took opioids for more than 30 days in the first year of use continued to use them for three years or longer.
 - Nearly 50% were taking only short-acting opioids, putting them at higher risk of addiction.
 - Nearly 60% of patients using opioids were taking a combination of drugs that are dangerous and potentially fatal

(Express Scripts report: A Nation In Pain, 2014)





79.5% of heroin users report using prescription opioids before initiating heroin use.

Muhuri et al., 2013

Do Opioids Help Chronic Pain?



"Evidence is insufficient to determine the effectiveness of longterm opioid therapy for improving chronic pain and function."

- 34 studies analyzed, \geq 18yo, \geq 3months chronic pain and opioid Rx
- No studies evaluated long-term (>1 year) outcomes related to pain, function, or quality of life:
 - opioid vs. placebo, opioid vs. no opioid therapy, opioid vs. nonopioid therapy
- Increased risk for serious harms associated with long-term opioid therapy: overdose, opioid abuse, fractures, myocardial infarction, and markers of sexual dysfunction

Chou et al., Ann Intern Med. 2015

J Neuroimmune Pharmacol DOI 10.1007/s11481-015-9600-6

INVITED REVIEW

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Cannabinoids for the Treatment of Chronic Non-Cancer Pain: An Updated Systematic Review of Randomized Controlled Trials

M. E. Lynch^{1,3} & Mark A. Ware²

- 11 RCTs published 2010-14, n=1185 met inclusion criteria.
- Excellent quality of trials (mean 7 on Modified Oxford Scale, range 5–7)
- 7 studies demonstrated cannabinoid exhibited an analgesic effect that was significantly better than the control.
- Drug related adverse effects primarily fatigue, dizziness, dry mouth, nausea and disturbances in cognition
 - mild to moderate, transient and generally well tolerated
- Findings consistent with those from the previous review (Lynch and Campbell 2011)
- Total of 22 of 29 RCTs demonstrating that cannabinoids demonstrate a modest analgesic effect and are safe in the management of chronic pain.



Heroin Addiction and Overdose Deaths are Climbing



Opioid overdoses driving increase in drug overdoses overall



Prescription Opioid vs. Heroin Overdose Deaths





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Cannabinoid-Opioid Synergy





Cannabinoid-Opioid Synergy

- Opioid and cannabinoid receptors are both present in pain signaling regions of the brain and spinal cord.
- Opioid and cannabinoid signaling pathways interact with each other.
- Administering cannabinoids with opioids results in a greater than additive antinociceptive (anti-pain) effect.

reviewed in Cichewicz, 2004

Cannabinoid-Opioid Synergy:

20mg/kg THC = 30% MPE 20mg/kg morphine = 30% MPE 20mg/kg THC + 20mg/kg morphine = 100% MPE

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THC 20mg/kg + morphine morphine-only



Smith et al. 1998

Opioid-sparing Effect of Cannabinoids: A Systematic Review and Meta-analysis



- 17 of 19 pre-clinical studies demonstrated synergistic effects from opioid-cannabinoid co-administration.
- The ED₅₀ of morphine administered in combination with THC is 3.6 times lower than the ED₅₀ of morphine alone (95% Cl 1.95, 6.76; n = 6).
- The ED_{50} for codeine administered in combination with THC was 9.5 times lower than the ED_{50} of codeine alone. (95% CI 1.6, 57.5, n = 2)

Cannabinoid-Opioid Synergy Human Trial



- 21 patients with chronic pain on sustained release opioids
 - Oxycodone mean 62mg BID or morphine mean 53mg
 BID
- Cannabis (NIDA supplied, 3.56% THC) vaporized 3x daily, inpatient setting
- Pain significantly decreased: 27% (95% CI 9,46)

(Abrams et al. 2011)



Can Cannabis Be Used To Replace Opioids in Chronic Pain Patients?

Cannabis For Treatment-Resistant Chronic Pain



- Open-label, longitudinal ~7 months, n=176
 - 73 on opioids at baseline
- 20g cannabis monthly: smoked, cookies, or olive oil extract
- Patients given titration instructions up to 3x/day
- Subjects encouraged to attempt gradual dose reduction of other analgesics, especially opioids
- Results:
 - Improvements in pain and pain-related quality of life scores
 - 44% of those taking opioids discontinued

Haroutounian et al., 2016

Medical Cannabis Associated With Decreased Opioid Use in Chronic Pain Patients

- Cross-sectional retrospective survey of 244 medical cannabis patients with chronic pain in Michigan
- Medical cannabis use associated with
 - 64% decrease in opioid use (n=118)
 - Decreased number and side effects of medications
 - Improved quality of life (45%)

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Survey Data: Integr8 Maine 2016 n=542 cannabinoid-opioid cotreatment:

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- 39% stopped opioids completely
 73% for >1 year
- 39% reduced dose
- 47% reported \geq 40% pain reduction
- 80% reported improved function
- 87% reported improved quality of life





RESEARCH ARTICLE

Associations between medical cannabis and prescription opioid use in chronic pain patients: A preliminary cohort study

Jacob M. Vigil¹*, Sarah S. Stith², Ian M. Adams³, Anthony P. Reeve³

 University of New Mexico, Department of Psychology, Albuquerque, New Mexico, United States of America, 2 University of New Mexico, Department of Economics, Albuquerque, New Mexico, United States of America, 3 Industrial Rehabilitation Clinics, Albuquerque, New Mexico, United States of America Associations Between Medical Cannabis and Prescription Opioid Use in Chronic Pain Patients: a Preliminary Cohort Study (Vigil et al., 2017)



Fig 1. Mean prescribed daily opioid dosage by month. Notes: Month "1" represents the first month postenrollment for the MCP patients (n = 37) and the fourth month of observation for the comparison group (n = 29). The time trends add a linear representation of the relative change in prescribed daily opioid dosage starting with the time of treatment (enrollment in the MCP).

Table 1. Effect of MCP enrollment on opioid prescription patterns (Means comparison).

Variable (N = 66)	Comparison (N = 29)	МСР (N = 37)	P Value
Ceased opioid prescriptions {0,1}	3.4% (1)	40.5% (15)	<0.001
Reduced prescribed daily opioid dosage {0,1}	44.8% (13)	83.8% (31)	0.001





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Fig 2. Effects of medical cannabis on quality of life, social interactions, activity levels and concentration. Notes: These survey questions were administered as a follow-up survey to 23 of the 37 MCP patients with frequent use of prescription opioids. No "extremely negative" impacts were reported by any patient, and a "negative impact" was reported by one patient for *Activity* levels and by two patients for *Concentration*.

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https://doi.org/10.1371/journal.pone.0187795.g002

Average numbers of daily doses filled for prescription drugs annually per physician in states with a medical marijuana law, by condition categories studied, compared to the average numbers in states without a law





Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D

Bradford & Bradford, 2016

Medical Cannabis Laws a

Changes associated with a state's having a medical marijuana law prescriptions for drugs used to treat conditions with medical m



Healer.com © 2016 Bradford & Bradford, 2017

Estimated federal and individual states' 2014 savings associated with having a medical marijuana law in Medicaid prescription drug spending on drugs used to treat conditions with medical marijuana indications

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	Estimated savings (\$)		
State	State's share	Federal share	
AK	1,944,311	1,944,311	
AZ	72,101	147,921	
CA	98,007,503	98,007,503	
CO	14,429,495	14,429,495	
CT	20,713,760	20,713,760	
DE	4,303,530	5,326,208	
DC	1,213,247	2,830,910	
HI	3,913	4,214	
IL	16,748,519	16,748,519	
ME	3,432,821	5,495,192	
MD	6,125,628	6,125,628	
MA	10,666,546	10,666,546	
MI	15,964,564	31,436,160	
MN	4,696,356	4,696,356	
MT	1,672,696	3,295,216	
NV	3,770,236	6,447,206	
NH	350,141	350,141	
NU	800/121	800 / 21	
NM	118,849	267,024	
NY	7,681,603	/,6031,603	
OR	5,033,148	8,621,622	
RI	132,468	133,052	
VT	3,105,997	3,813,132	
WA	2,327,151	2,327,151	



The pot compon

debate





Is marijuana safe and effective as medicine?

Research Report Series

Though none of these studies are definitive, they cumulatively suggest that medical marijuana products may have a role in reducing the use of opioids needed to control pain. More research is needed to investigate this possibility.

https://www.drugabuse.gov/publications/marijuana/marijuana-safe-effective-medicine



Recommendations and Reports / Vol. 65 / No. 1

Morbidity and Mortality Weekly Report

March 18, 2016

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CDC Guideline for Prescribing Opioids for Chronic Pain — United States, 2016

previously (30). Clinicians should not test for substances for which results would not affect patient management or for

which implications for patient management are unclear. For example, experts noted that there might be uncertainty

about the clinical implications of a positive urine drug test for tetrahyrdocannabinol (THC). In addition, restricting



Is It Safe To Use Cannabis and Opioids Together?







(Terry et al. 2010)

Is It Safe To Use Cannabinoids and Opioids Together?

- Opioid and cannabinoid receptors are co-distributed in pain centers.
- Cannabinoid receptors have low density in brainstem cardiorespiratory centers.
- Combination increases
 therapeutic index of opiates!

opioid alone Effective Lethal dose dose opioid + cannabis

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(reviewed in Cichewicz, 2004)

Retention of Efficacy



Combination-treated animals demonstrated:

- Upregulation of opioid receptor proteins in the spinal cord.
- Avoidance of tolerance to the opioid with retention of the antinociceptive effect.

(reviewed in Cichewicz, 2004)

How to Treat Opioid Addiction?







NDC 12496-1208-3 30 pouches each containing 1 sublingual film

need emergency medical care. Keep SUBOXONE

out of the reach of children.

Suboxone (buprenorphine and naloxone) sublingual film 8 mg/2 mg Rx only Children who accidentally take SUB0XONE will

suboxone.com



OUTPATIENT VS. INPATIENT DRUG REHAB CENTERS

Which is Right for You?

Outpatient and inpatient drug rehab programs both have pros and cons, but which is best for your particular needs?



1 EVALUATION 2 STABILIZATION 3 DETOXIFICATION 4 REHABILITATION

Current Harm Reduction Options

- Buprenorphine (e.g. Suboxone)
 - Only high dose \geq 16 mg was more effective than placebo in suppressing illicit opioid use (3 studies, n=729).
 - (SMD) -1.17; 95% CI -1.85 to -0.49
 - Low-dose (2 studies, n=487) and medium-dose (2 studies, n=463) did not suppress illicit opioid use better than placebo.
- Methadone is superior to buprenorphine in retaining people in treatment, and methadone equally suppresses illicit opioid use.

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Cannabis for Harm Reduction



- Better safety profile than methadone or Suboxone
- Lower risk of dependence than any other psychoacitve substance
- Low risk for abuse and diversion
 - Standardized oral preparations even safer
 - 30,000 patient years with nabiximols showed no evidence of abuse or diversion (Russo et al., 2015)
- Most people who stop using cannabis do so without formal treatment.

CBD for Opioid Addiction?



- Non-rewarding
- Minimal side effects and toxicity
- Reduces anxiety, a component of abuse and relapse
- Reduces the rewarding properties of opioid drugs and withdrawal symptoms
- Reduces heroin-seeking behavior in animals
- Reduces heroin-related cue-induced craving in heroin abusers

reviewed in Hurd, 2017

Medical Cannabis Law and Opioid Abuse



States with medical cannabis laws had a 24.8% lower mean annual opioid overdose mortality rate compared with states without medical cannabis laws. (Bachhuber et al., 2014)

able. Association Between Medical Cannabis Laws and State-Level Opioid Analgesic Overdose Mortality Rates in the United States, 1999-2010					
	Percentage Difference in Age-Adjusted Opioid Analgesic Overdose Mortality in States With vs Without a Law				
	Primary Analysis	Secondary Analyses			
Independent Variable ^a	Estimate (95% CI) ^b	Estimate (95% CI) ^c	Estimate (95% CI) ^d		
Medical cannabis law	-24.8 (-37.5 to -9.5) ^e	-31.0 (-42.2 to -17.6) ^f	-23.1 (-37.1 to -5.9) ^e		
Prescription drug monitoring program	3.7 (-12.7 to 23.3)	3.5 (-13.4 to 23.7)	7.7 (-11.0 to 30.3)		
Law requiring or allowing pharmacists to request patient identification	5.0 (-10.4 to 23.1)	4.1 (-11.4 to 22.5)	2.3 (-15.4 to 23.7)		
Increased state oversight of pain management clinics	-7.6 (-19.1 to 5.6)	–11.7 (–20.7 to –1.7) ^e	-3.9 (-21.7 to 18.0)		
Annual state unemployment rate ⁹	4.4 (-0.3 to 9.3)	5.2 (0.1 to 10.6) ^e	2.5 (-2.3 to 7.5)		

Medical Cannabis Law and Opioid Abuse Medical cannabis laws had a 23% less hospitalizations related to opioid abuse and 13% less hospitalizations related to opioid pain reliever overdose. (Shi, 2017)

Y. Shi / Drug and Alcohol Dependence 173 (2017) 144–150

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Table 1

Associations between Medical Marijuana Policies and State-Level Hospitalizations Rates Related to Marijuana and Opioid Pain Reliever, State Inpatient Databases 1997–2014.

State-level Explanatory Variable	State-level Outcome Variable: Natural Log of Hospitalization Rates per 1000 Discharges Point Estimate (95% CI)					
	Marijuana Dependence or Abuse		Opioid Dependence or Abuse		Opioid Pain Reliever Overdose	
Medical Marijuana Policy Marijuana Decriminalization Policy Prescription Drug Monitoring Program Pain Clinic Regulation	0.16 0.13 0.088 0.046	(-0.076, 0.41) (-0.10, 0.36) (-0.21, 0.042) (-0.17, 0.078)	- 0.23 0.094 0.020 0.052	(-0.41, -0.068) ^{**} (-0.15, 0.33) (-0.088, 0.12) (-0.12, 0.23)	- 0.13 0.049 0.027 -0.070	(-0.25, -0.018)* (-0.22, 0.32) (-0.080, 0.13) (-0.16, 0.025)
Number of State-Year Observations Number of Discharges R ²	382 2,237,916 0.90		382 2,176,326 0.96		382 376,680 0.97	

Note: The linear regressions also controlled for state and year fixed effects and state-level time-varying covariates including natural log of population size, unemployment rate, natural log of median household income in constant 2014 dollars, natural log of beer tax per gallon in constant 2014 dollars, and health uninsured rate. Bold value highlighted statistics with p value smaller than .05.

* p < 0.05.

p < 0.01.

Substitution for Prescriptions



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Healer.com © 2016

Lucas & Walsh, 2017

Substitution for Prescriptions





n = 1,513 New Enlgand

Piper et al., 2017



Cannabis for Addiction?

Cannabis Improves Naltrexone Treatment Retention



- Days in treatment (mean):

 Intermittent cannabis use = 113 days
 Consistent cannabis use = 68 days
 Abstinent = 47 days
- Intensive behavioral therapy helped the consistent cannabis group but not the abstinent group.

(Raby et al., 2009)

Cannabis Treats Symptoms Of Opioid Withdrawal

- Nausea, vomiting, diarrhea, cramping
- Muscle spasm
- Anxiety, agitation, restlessness
- Insomnia
- Runny nose, sweating

THC Reduces Withdrawal & Cannabis Use Improves Naltrexone Treatment Retention

- n=60, 8 weeks, long-acting naltrexone injection at 1 & 4 weeks
- Dronabinol (THC) 30mg/day vs placebo for 6 weeks.
- 100% of cannabis users received second injection
- 46% of non-cannabis users received second injection



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Fig. 2. Observed severity scores of self-reported opioid withdrawal during the inpatient detoxification phase of treatment (means with standard error bars). Significantly different between groups (p = 0.005).

(Bisaga et al., 2015)

Effects Of Cannabis Use On Opioid Injection Frequency



- 2007 2012, 357 opioid injectors recruited through street outreach in Denver, >18 years old
- Opioid injection in the previous 30 days as verified by visual signs of recent venipuncture
- Not in methadone treatment at the time of study entry
- Baseline, six-, and 12-month interviews

Corsi et al., 2015

Effects Of Cannabis Use On Opioid Injection Frequency



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Corsi et al., 2015

A Choice?







How To Use Cannabis to Reduce & Replace Opioid Drugs

- 1. Take a small oral or oromucosal dose of cannabis with every dose of opioids
 - Can be as little as 1mg THC, below psychoactive threshold.
 - Use inner inventory and Healer.com programs to find the minimal effective dose.
- 2. Use inhaled cannabis for breakthrough symptoms management and to reduce cravings.

How To Use Cannabis to Reduce (& Replace Opioid Drugs

- 3. Use cannabis to enhance other health-promoting activities, such as exercise, meditation, prayer, journaling/reflecting, psychotherapy.
- 4. Use cannabis to promote regular sleep patterns sedating strains only in the evening.

How To Use Cannabis to Reduce & Replace Opioid Drugs

- Select combination CBD+THC if available to enhance benefits and decrease side effects.
- 1:1 ratio is broadly effective and welltolerated.

How To Use Cannabis to Reduce (& Replace Opioid Drugs

- Cannabis-naïve patients are encouraged to take advantage of 2 week window of opportunity after starting cannabis.
- Most patients reduce opioid dose by 50-80%.

How To Use Cannabis to Reduce & Replace Opioid Drugs



Experienced cannabis users:

- Complete Healer.com 6-day cannabis sensitization program before starting opioid taper, and stay at optimal dose to avoid building cannabis tolerance.
- If currently using inhalation only, try "switching from inhalation to tincture" program to become familiar with oromucosal dosing.

How To Use Cannabis to Reduce & Replace Opioid Drugs

- If low-dose cannabis is not effective, consider high-dose oral cannabis concentrate.
- Begin with 10-20mg active cannabinoids 3x daily, gradually increase to 100-500mg 3x daily.





Patient Narratives

I am 38 years old and I struggled with opiate and alcohol addiction for about 15 years. Long hours as a chef and a couple of minor surgeries where I was prescribed opiates, led me to become dependent on them to get through my day. Pretty soon I was fully consumed by addiction.

Even after going to 2 detoxes and a 28 day rehab in 2010, I still struggled to stay clean for the next 2 years. The 12 step meetings that I was going to several times a week discouraged cannabis use, so I tried to do it their way and didn't use any. That didn't work and led to several relapses. In 2012, I decided to start using a little bit of cannabis before bed to help me get a good nights sleep, and when I was getting stressed, angry, etc. It was very effective in keeping me centered and on the path to recovery, although I didn't feel comfortable (and still don't) sharing this with fellow addicts at meetings.

I had been a cannabis smoker on and off since I was 18, and always enjoyed the effects. In the throes of my opiate addiction however, I got out of the routine of regular cannabis using. I believe that this is because cannabis use tends to magnify my own problems and shortcomings in my mind when I use it, and no drug addict wants to take such an honest look at themselves.

As of right now I have been free of active addiction since January 2012. I have also been a patient of Integr8 Health since 2012. Cannabis is the only thing that I am currently prescribed, and the only substance that I use for pain, stress, etc. I don't know if I would be here today, and sober, if it wasn't for cannabis. I use cannabis throughout the day and before bed, and live a happy, healthy, productive life with my wife and 2 daughters.



I took opiates for 15 years, along with various forms of Benzo's. I had legitimate pain, I fractured my back in 3 places when I was about 19. I healed from the initial injury, but the pain got worse over the next few years, to the point where I was drinking to get by. I had an uncanny knack for being able to walk into a doctors office and get almost anything I asked for due to my injury. Anyway, I took opiates to the tune of 2 Oxycontin 80's & 12 mg Dilaudids for a PRN.



At some point it wasn't just about the pain anymore, it had become more about the addiction. In retrospect, the opiates were only working on the emotional pain, not the physical pain. So to make the long story short, I've been to detox 27 times since I was 27, I've been in three 30-day rehabs, from here to Ohio. I tried half way houses, suboxone treatment etc. It's been 21 months since my first visit to your office, and I literally have not used an opiate since. Thank You.

p.s. I truly believe that medical marijuana has saved my life.

Summary

- The opioid problem is a public health crisis.
- Rx is a bigger problem than heroin.
- Cannabis can replace and reduce opioid use.
- Adding cannabis makes opioids safer by widening the therapeutic window.
- Cannabis prevents opioid-tolerance and the need for dose escalation.
- Cannabis can treat the symptoms of opioid withdrawal.
- Cannabis is safer than other harm reduction options.
- Cannabis is a holistic treatment that addresses many symptoms with minimal adverse effects.





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Opioid Prescriptions Dispensed By Year

Pezalla et al., 2017



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Questions?

Thank you!

Dustin Sulak D.O.

