10-28-2019

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Recommended Citation

Wendelboe AM, Mathew R, Chongsuwat T, Rainwater E, Wendelboe MA, Wickersham E, Chou AF. Is there less opioid abuse in states where marijuana has been decriminalized, either for medicinal or recreational use? A Clin-IQ. J Patient Cent Res Rev. 2019;6:267-73. doi: [10.17294/2330-0698.1704](https://doi.org/10.17294/2330-0698.1704)

Published quarterly by Midwest-based health system Advocate Aurora Health and indexed in PubMed Central, the Journal of Patient-Centered Research and Reviews (JPCRR) is an open access, peer-reviewed medical journal focused on disseminating scholarly works devoted to improving patient-centered care practices, health outcomes, and the patient experience.

Is There Less Opioid Abuse in States Where Marijuana Has Been Decriminalized, Either for Medicinal or Recreational Use? A Clin-IQ

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Abstract

Opioid use, abuse, and associated mortality have reached an epidemic level. In some states, cannabis is being used to treat chronic pain. To examine the hypothesis that medical marijuana legislation may reduce adverse opioid-related outcomes if patients substitute cannabis for opioids for pain management, we conducted a clinical inquiry (Clin-IQ). We searched Ovid MEDLINE, Ovid MEDLINE In-Process, and Embase for studies using the search terms marijuana, cannabis, legal, marijuana smoking, medical marijuana, opioid-related disorders, cannabis use, medical cannabis, legal aspect, and opiate addiction. We included population-based articles published from January 1, 2012, through December 5, 2018, that assessed the relationship between marijuana use and decriminalization and the aforementioned opioid-related outcomes. Ten peer-reviewed studies met the inclusion criteria; 3 cross-sectional studies, 6 ecologic studies (ie, using aggregate data), and 1 retrospective cohort study. Eight studies reported associations between policies decriminalizing marijuana and reduced prescription opioid use, 1 study was inconclusive, and the retrospective cohort study reported an increase in adverse opioid-related outcomes. These results should be interpreted with caution given limitations associated with the studies' design. Results demonstrating association between marijuana decriminalization and opioid-related outcomes are mixed. Longitudinal studies are needed, and further analysis of this policy should continue to be tracked. (*J Patient Cent Res Rev*. 2019;6:267-273.)

Keywords

medical marijuana; cannabis; analgesic; opioid; epidemiology; ecologic analysis; decriminalization

Clinical Question

Is there less opioid abuse in states where marijuana use has been decriminalized, either for medicinal or recreational use?

Brief Answer

Yes. However, the evidence is mixed. While most reviewed studies showed reductions in rates of opioid overdose and opioid-related hospitalizations, among other outcomes, in states with medical marijuana

laws, a patient-level report and National Institute on Drug Abuse data indicated an increase in opioid use among cannabis users and higher rates of opioid-related deaths in these states. Given these mixed results, robust prospective studies are needed to determine the impact of marijuana legislation on opioid use and abuse.

Level of Evidence: B

Literature Search

Databases: Ovid MEDLINE, Ovid MEDLINE In-Process, PubMed, Embase.

Date range of literature search: January 1, 2012, through December 5, 2018.

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Exclusion criteria: Animal studies, injectable drugs, cannabidiol, non-English language.

Inclusion criteria: Date range within 2012–2018.

Search terms: Marijuana, cannabis, legal, marijuana smoking, medical marijuana, opioid-related disorders, cannabis use, medical cannabis, legal aspect, opiate addiction.

Background

An estimated 25 million adults in the United States suffer from daily pain, and another 23 million have severe, recurrent pain. Persistent pain causes disability, loss of productivity, lower quality of life, and overall poor health.¹ There has been a steady increase in the number of opioid prescriptions in the past few decades to manage pain. It is now estimated that the number of annual prescriptions for opioids is approximately equal to the number of adults in the country.^{2,3} Rates of adverse effects of opiate medications, the primary concerns being addiction and overdose,⁴ have concomitantly increased with prescription opioid use. As a result, an average of 115 individuals die daily in the United States from opioid overdose.⁵

Patients who abuse or are dependent on prescription opioids are 40 times more likely to use or abuse heroin compared to those who take opioids as prescribed and have no dependency issues. It is estimated that 4% of prescription opioid users are expected to become heroin users.⁶ While the hypothesis that marijuana may substitute for opioids exists, there is a concurrent hypothesis that opioid and marijuana use are not mutually exclusive and may be co-occurring. For example, an increase in opioid use/abuse may be associated with an increase in marijuana use. One study reported co-occurring marijuana use to be 13.2% among nonopioid users, 18.3% among prescription opioid users, 40.1% among prescription opioid misusers, 39.9% among those with prescription opioid use disorder, and 58% among heroin users.⁷

In response to the opioid crisis, the U.S. Food and Drug Administration (FDA), among other medical and public health organizations, has attempted to identify strategies to curb this epidemic. Marijuana is reported to be an effective method to relieve pain,^{8,9} and authors of a systematic review of the literature concluded that there

are data, though limited, suggesting an association between medical cannabis and a reduction in mortality associated with prescription opioid use.¹⁰ As of 2015 (the cutoff year for data used in the analyses of this study), there were 23 states that had legalized medical marijuana. As of 2016, 31 states had legalized medical marijuana; among these 31, 8 states plus Washington, DC, also had legalized recreational marijuana.¹¹

Almost two decades after the initiation of individual state-led legalization of medical marijuana, there is mixed evidence regarding the impact of marijuana on opioid-related mortality rates. To that end, the objective of this clinical inquiry (Clin-IQ) project is to explore if a state's decriminalization of marijuana, whether medical or recreational, can attenuate the opioid crisis.

Methods

We searched Ovid MEDLINE, Ovid MEDLINE In-Process, PubMed, and Embase using the search terms marijuana, cannabis, legal, marijuana smoking, medical marijuana, opioid-related disorders, cannabis use, medical cannabis, legal aspect, and opiate addiction. Studies of animals, injectable drugs, and cannabidiol (commonly referred to as CBD) were excluded. We included articles published from January 1, 2012, through December 5, 2018; however, we limited marijuana-related data to 2015 or prior and opioid-related data to 2016 or prior to allow a minimum of 1 year to elapse between marijuana decriminalization and subsequent measures of opioid use. Surveillance data for opioid use were not complete for years 2017 and beyond at the time this study was conducted.

Summary of Evidence

Table 1 summarizes the reviewed literature, which included 1 retrospective cohort study, 3 cross-sectional studies, and 6 ecologic studies using aggregate data.

The retrospective cohort study accessed data from the National Epidemiological Survey on Alcohol and Related Conditions, which assessed associations between cannabis use and 1) prevalent opioid use, 2) incident opioid use, and 3) prescription opioid use disorder.¹² This data set included a measure of patients' chronic pain. Investigators reported that cannabis use was associated with greater opioid use as defined by these outcomes.¹²

Table 1. Summary of Studies Describing the Impact of Medical Marijuana Legislation on Opioid Abuse

Authors (Year)	Objective	Study Design	Population, Data Collected	Results, Conclusions
Bachuber et al (2014) ²¹	Determine association between presence of state medical cannabis laws and opioid-analgesic-overdose mortality	Ecologic	Annual state-level death certificate data from 1999 to 2010 comparing overdose-related mortality with time of marijuana legalization	<ul style="list-style-type: none"> Medical marijuana legalization associated with a 24.8% decrease in state-level opioid-overdose mortality rates compared to states without marijuana policies
Bradford and Bradford (2016) ¹⁶	Investigate how implementation of state-level marijuana laws changes prescribing patterns	Ecologic	All drugs covered under Medicare Part D from 2010 to 2013	<ul style="list-style-type: none"> Average 1826 fewer daily doses of prescriptions for pain among states where medical marijuana is decriminalized compared to states where marijuana is illegal ($P < 0.01$)
Bradford and Bradford (2017) ¹⁷	Investigate association between state-level marijuana laws and prescription drug spending	Ecologic	Average number of opioid prescriptions filled by Medicaid beneficiaries during 2007–2014	<ul style="list-style-type: none"> Approximately \$1.01 billion savings in 2014 if every state had medical marijuana legislation
Corroon et al (2017) ¹⁴	Survey marijuana users to determine intentional substitution of cannabis for prescription drugs	Cross-sectional	2774 self-selected marijuana users largely from U.S., Canada, Europe	<ul style="list-style-type: none"> Cannabis as substitute for prescription drugs, including opioids No influence by state marijuana legislation
Liang et al (2018) ¹⁸	Examine if statewide policies were associated with a reduction in opioids received by Medicaid enrollees	Ecologic	Prescription medication data for patients enrolled in fee-for-service Medicaid programs	<ul style="list-style-type: none"> Schedule II opioids (eg, hydrocodone, oxycodone [95% of all prescription opioids]) were not associated, but Schedule III opioids (eg, codeine) were associated with medical cannabis legalization
Olfson et al (2018) ¹²	Determine association between cannabis use and change in risk of incident nonmedical prescription opioid use	Retrospective cohort	34,653 participants in waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions	<ul style="list-style-type: none"> Increase odds (odds ratio: 2.8) of incident nonmedical opioid among cannabis users Similar results when controlling for self-reported pain
Piper et al (2017) ¹⁵	Study the potential substitution effect of medical marijuana for opioids	Cross-sectional	Online survey ($n=1513$) of members of dispensaries from Maine, Vermont, Rhode Island	<ul style="list-style-type: none"> Identified that 76.7% of opioid users substituted marijuana for opioids to treat chronic pain Not designed to estimate impact of state marijuana legislation
Powell et al (2018) ¹⁹	Assess impact of timing of medical marijuana legislation on opioid-related mortality rates	Ecologic	State-reported opioid-related mortality rates stratified by timing of enacting medical marijuana legislation: <2010, ≥2010, or never	<ul style="list-style-type: none"> States enacting medical marijuana legislation reported deaths per 100,000 as: ≥2010: 3.27; never: 4.05; <2010: 4.55
Shi (2017) ²⁰	Examine associations between state medical marijuana policies and hospitalizations related to marijuana and opioids	Ecologic	Annual state-level hospitalization data from 1997 to 2014 in 27 states	<ul style="list-style-type: none"> Medical marijuana legalization was associated with 9.4%–23.0% state-level decrease in opioid-related hospitalizations compared to states without marijuana policies
Wen et al (2015) ¹³	Examine effect of medical marijuana legislation on substance use outcomes in 10 states	Cross-sectional	Data from NSDUH during 2004–2012; questions collect self-reported use of marijuana, alcohol, prescription pain killers	<ul style="list-style-type: none"> No statistically significant association was observed between marijuana use and prescription pain killer use

NSDUH, National Survey on Drug Use and Health.

The highest quality of the cross-sectional studies used data collected from the National Survey on Drug Use and Health, which is sponsored by the U.S. Substance Abuse and Mental Health Services Administration.¹³ Self-reported marijuana use was compared to self-reported use of prescription pain killers, from 2004 to 2012 in 10 states. No significant association was observed in either adolescents (age 12–20 years) or adults (age 21+ years).¹³

The other two cross-sectional studies were based on convenience samples and investigated cannabis use as a substitution for opioids. Corroon et al surveyed marijuana users (n=2774) residing in the United States, Canada, Europe, and “other” via Facebook.¹⁴ About 60% of those surveyed self-identified as medical marijuana users. Among the 1248 who responded affirmatively to the question, “Have you ever used cannabis as a substitute for prescription drugs?” substitutions of marijuana were most commonly made for narcotic opioids (35.8%), anxiolytics/benzodiazepines (13.6%), and antidepressants (12.7%). This study found a positive, though not statistically significant, association between substituting marijuana use for opioid use. The study design limited the ability to determine either causation or association.¹⁴ The study by Piper et al involved medical marijuana users (n=1513) in Maine, Vermont, and Rhode Island.¹⁵ Of respondents who reported regular use of opioid pain medications (n=215), more than three-quarters (76.7%) reported a reduction in opioid use after starting medical marijuana, supporting marijuana use as a substitution for pain medication. This study was conducted only in states where marijuana had been decriminalized; therefore, the impact of legal marijuana use cannot be assessed in the absence of a control group. In addition, multiple authors of this study had previous or hold current employment in cannabis dispensaries, presenting potential conflicts of interest.¹⁵ Both of these studies had limitations related to selection bias, convenience sampling, and survey design.

A 2016 study by Bradford and Bradford used 2010–2013 data of all prescription drugs covered under Medicare Part D to investigate the effects of medical marijuana laws on opioid-prescribing patterns.¹⁶ Data included 9 medical conditions, including pain, that were mentioned in at least 4 states’ medical marijuana laws and have at least 1 FDA-approved drug for off-label use. A bivariate analysis comparing “prescriptions filled in a state” and year of marijuana legalization resulted in

1826 fewer daily doses for pain medication filled per physician per year ($P<0.01$). To evaluate unobserved characteristics of general differences in prescribing behaviors between physicians in states with and those without marijuana laws, these results were compared with other drug categories for which marijuana has no clinical benefit (blood thinners, antibiotics, etc), and no difference was found. Primary weaknesses of this study included the ecologic study design and sample population consisting of only those ≥ 65 years of age and enrolled in Medicare Part D.¹⁶ Bradford and Bradford conducted a subsequent study of similar design using Medicaid data and reported similar findings.¹⁷

Another study used state-level Medicaid data to assess changes in prescription opioid use over time.¹⁸ Prescription opioids were stratified into Schedule II (eg, hydrocodone and oxycodone) and Schedule III opioids (eg, codeine). Variables indicating the presence and time of enactment of statewide medical cannabis laws were included in the statistical analysis. The authors reported no association with decreased use of Schedule II opioids but a significant reduction in the use of Schedule III opioids in states that had decriminalized medical marijuana. It should be noted that Schedule II opioids account for approximately 95% of all prescription opioids; therefore, the overall impact of these reported associations is limited.¹⁸

Powell et al employed a study design similar to that of Bradford and Bradford but which stratified states into categories based on the timing of adopting medical marijuana laws.¹⁹ Using 2010 as a cutoff, states enacting medical marijuana legislation before 2010 were considered early adopters and those in 2010 or after were late adopters. States that did not have medical marijuana laws were never adopters. Primary results were mixed; late adopters were found to have the lowest opioid-related mortality rates, followed by never adopters. Early adopter states were found to have the highest opioid-related mortality rates.¹⁹

In a 2017 ecologic study, Shi applied linear time-series regression analysis using State Inpatient Databases that included information from 27 states that met the inclusion criteria.²⁰ This study tested associations between the implementation of medical marijuana policies and rates of hospitalizations from 1997 to 2014 for opioid abuse/dependence, marijuana abuse/dependence, and opioid-

related overdose. Results showed an increase in marijuana and opioid-related hospitalizations in all 27 states by 300%, on average, during this time period. However, implementing medical marijuana policies was associated with reduction in hospitalization rates by 23% for opioid dependence or abuse ($P=0.008$) and 13% for opioid pain reliever overdose ($P<0.05$). Additional analyses with lagged effects were conducted, and when assuming a 1-year lag post-medical marijuana policy implementation, there was a 9.4% reduction in hospitalization rates for opioid dependence or abuse ($P<0.05$). However, no difference was observed for marijuana-related hospitalizations. Inconsistencies in data collection and coding practices were limitations of this study.²⁰

A 2014 ecologic study by Bachuber et al investigated the association of medical marijuana and opioid-overdose mortality in the United States using vital records.²¹ Applying time-series analysis, the authors compared opioid-overdose mortality rates between all 13 states

that had medical marijuana laws effective prior to and during 1999–2010 and those that did not have medical marijuana policies. Results showed a 24.8% lower mean annual opioid-overdose mortality rate (95% CI: -37.5% to -9.5%; $P=0.003$) in states with the uptake of marijuana laws compared to states without marijuana laws. This association strengthened over time. The primary weakness of this study is its ecologic/aggregate study design precluding information about medical use among fatal overdose decedents.²¹

To supplement the published literature, we accessed data on the prevalence of opioid prescriptions per 100 population and opioid-related overdose mortality rates per 100,000 population for 2016 from the National Institutes of Health/National Institute on Drug Abuse.^{22,23} Tables 2 and 3 summarize these results for states where medical marijuana had and had not been decriminalized by 2015, respectively. The crude average prevalence of opioid prescriptions is approximately 20 people per 100

Table 2. Among States Where Medical Marijuana Was Decriminalized by 2015, the State-Specific Years When Marijuana Was Decriminalized for Medical and Recreational Use, Prevalence of Opioid Prescriptions in 2016, and Opioid-Related Death Rate in 2016

State	Year Medical	Year Recreational	Opioid Prescriptions per 100 Population ²²	Opioid Death Rate (per 100,000 Population) ²³
Alaska	1998	2014	58.9	12.5
Arizona	2010	NA	70.2	11.4
California	1996	2016	44.8	4.9
Colorado	2000	2012	59.8	9.5
Connecticut	2012	NA	55.9	24.5
Delaware	2011	NA	79.2	16.9
Hawaii	2000	NA	41.9	5.2
Illinois	2013	NA	56.8	15.3
Maine	1999	2016	66.9	25.2
Maryland	2003	NA	58.7	30
Massachusetts	2012	2016	47.1	29.7
Michigan	2008	NA	84.9	18.5
Minnesota	2014	NA	46.9	7.4
Montana	2004	NA	69.8	4.2
Nevada	2000	2016	80.7	13.3
New Hampshire	2013	NA	64.3	35.8
New Jersey	2009	NA	52.6	16
New Mexico	2007	NA	65.1	17.5
New York	2014	NA	42.7	15.1
Oregon	1998	2014	76.3	7.6
Rhode Island	2007	NA	60.3	26.7
Vermont	2004	NA	58.6	18.4
Washington	1998	2012	64.9	30

Table 3. Among States Where Medical Marijuana Was Illegal Through 2015, Prevalence of Opioid Prescriptions and Opioid-Related Death Rate in 2016

State	Opioid Prescriptions per 100 Population ²²	Opioid Death Rate (per 100,000 Population) ²³
Alabama	121.0	7.5
Arkansas	114.6	5.9
Florida	66.6	14.4
Georgia	77.8	8.8
Idaho	77.6	7.4
Indiana	83.9	12.6
Iowa	64.0	6.2
Kansas	76.9	5.1
Kentucky	97.2	23.6
Louisiana	98.1	7.7
Mississippi	105.6	6.2
Missouri	80.4	15.9
Nebraska	62.8	2.4
North Carolina	82.5	15.4
North Dakota	47.8	7.6
Ohio	75.3	32.9
Oklahoma	97.9	11.6
Pennsylvania	69.5	18.5
South Carolina	89.4	13.1
South Dakota	54.8	5.0
Tennessee	107.5	18.1
Texas	57.6	4.9
Utah	70.4	16.4
Virginia	63.4	13.5
West Virginia	96.0	43.4
Wisconsin	62.2	15.8
Wyoming	71.1	8.7

higher among states where medical marijuana is illegal (mean: 81.1 of 100; range: 47.8–121.0) than states where medical marijuana has been decriminalized (mean: 61.2 of 100; range: 41.9–84.9).²² No adjustment was made for time between policy change and measurement of opioid prescription prevalence or opioid-related overdose mortality rate. In contrast, the average death rate of opioid-related overdoses is 3.79 people per 100,000 higher among states where medical marijuana has been decriminalized (mean: 17.2 of 100,000; range: 4.2–35.8) compared to states where marijuana was illegal through 2015 (mean: 13.4 of 100,000; range: 2.4–43.4).²³ These findings stem from a crude analysis using ecologic/aggregate study design; therefore, overall impact and interpretation is limited.

Given that state-level data are ecologic and the person-level data are drawn from convenience samples, these data serve to generate hypotheses rather than establishing causal relationships. This field is rapidly changing because of policy implications. For example, clinical practice may have changed as a result of the U.S. Centers for Disease Control and Prevention guidance on the prescribing practices of opioids.²⁴ Using the Strength of Recommendation Taxonomy (SORT) criteria by Ebell et al, the level of evidence to support the hypothesis that opioid use decreases among states where marijuana use has been decriminalized is level B (“recommendation based on inconsistent or limited-quality patient-oriented evidence”).²⁵ Additional epidemiologic studies at the patient level (especially cohort studies) are needed to better understand the impact decriminalizing marijuana use has on opioid abuse.

Conclusions

With the ongoing opioid epidemic, it is critical to scrutinize medical marijuana as a substitute for pain medications in terms of its analgesic properties and potential harm. Based on this literature review, there is mixed evidence regarding the impact of marijuana legislation and prescription opioid-related outcomes. Eight studies provided evidence of reductions in the rate of opioid overdose, opioid-related hospitalizations, number of narcotic pain prescriptions written, and patient-reported substitution of marijuana for opiates, in states with medical marijuana laws. However, the one patient-level study reported an actual increase in opioid use among cannabis users. Data from the National Institute on Drug Abuse also indicated states with medical marijuana laws had higher rates of opioid-related overdose deaths. In addition, the variability across study design, measures of opioid abuse, and measures of marijuana use in the reviewed studies contributes to the challenges in identifying a consistent pattern in the results.

Given these mixed results, more robust studies in which patients are followed prospectively to measure the association between cannabis use and opioid-related outcomes are sorely needed to determine the impact of marijuana legislation on opioid use and abuse.

Patient-Friendly Recap

- The opioid addiction epidemic has pushed health care providers to seek out new means of managing chronic pain.
- In states where legal to do so, marijuana is likely to be increasingly prescribed in lieu of opioids when attempting to treat patients with chronic pain.
- After reviewing the available literature to date, the authors concluded there is less overall opioid abuse in states that have legalized marijuana; however, some contradictory data indicating opioid-related deaths may increase in these same states suggests further research is necessary.

Author Contributions

Study design: A. Wendelboe, Mathew, Chongsuwat, Rainwater, Wickersham, Chou. Data acquisition or analysis: A. Wendelboe, Mathew, Chongsuwat, M. Wendelboe, Chou. Manuscript drafting: A. Wendelboe, Mathew, Chongsuwat, M. Wendelboe, Chou. Critical revision: A. Wendelboe, Rainwater, Wickersham, Chou.

Conflicts of Interest

None.

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