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The use of cannabis in response to the opioid crisis: A review of the literature

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ABSTRACT

Background: A staggering number of Americans are dying from overdoses attributed to prescription opioid medications (POMs). In response, states are creating policies related to POM harm reduction strategies, overdose prevention, and alternative therapies for pain management, such as cannabis (medical marijuana). However, little is known about how the use of cannabis for pain management may be associated with POM use.

Purpose: The purpose of this article is to examine state medical cannabis (MC) use laws and policies and their potential association with POM use and related harms.

Methods: A systematic literature review was conducted to explore United States policies related to MC use and the association with POM use and related harms. Medline, PubMed, CINAHL, and Cochrane databases were searched to identify peer-reviewed articles published between 2010 and 2017. Using the search criteria, 11,513 records were identified, with 789 abstracts reviewed, and then 134 full-text articles screened for eligibility.

Findings: Of 134 articles, 10 articles met inclusion criteria. Four articles were cross-sectional online survey studies of MC substitution for POM, six were secondary data analyses exploring state-level POM overdose fatalities, hospitalizations related to MC or POM harms, opioid use disorder admissions, motor vehicle fatalities, and Medicare and Medicaid prescription cost analyses. The literature suggests MC laws could be associated with decreased POM use, fewer POM-related hospitalizations, lower rates of opioid overdose, and reduced national health care expenditures related to POM overdose and misuse. However, available literature on the topic is sparse and has notable limitations.

Conclusions: Review of the current literature suggests states that implement MC policies could reduce POM-associated mortality, improve pain management, and significantly reduce health care costs. However, MC research is constrained by federal policy restrictions, and more research related to MC as a potential alternative to POM for pain management, MC harms, and its impact on POM-related harms and health care costs should be a priority of public health, medical, and nursing research.

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Background and Significance

The United States is currently in the midst of an opioid crisis, with an estimated 3.8 million adults misusing prescription opioid medications (POMs) (Center for Behavioral Health Statistics and Quality, 2016). Reports suggest that POM misuse can progress to heroin use (Jones, 2013; Cicero, Ellis, Suratt, & Kurtz, 2014; Muhuri, Gfroerer, & Davies, 2013; Rudd, Aleshire, Zibbel, & Gladden, 2016) and a 200% increase rate of death from opioid overdose (Rudd et al., 2016). POMs were involved in over 15,000 deaths in 2015, and the most common POMs involved were oxycodone, hydrocodone, and methadone (Centers for Disease Control [CDC], 2016; Rudd et al., 2016). A public health state of emergency has been declared in at least six states within the United States. (Allen, 2017; Schneider, 2016; Turque, 2017). However, despite the national demand for POM harm reduction strategies such as reforming prescribing practices, using the reversal drug naloxone, and finding alternatives to POMs for pain, the opioid epidemic remains a major public health crisis (CDC, 2016; National Institute on Drug Abuse, 2015).

The National Academies of Science (NAS) 2011 report estimated pain affects at least 100 million American adults, costs society up to $635 billion annually, and reduces quality of life (NAS, 2011). Interestingly, when considering the misuse of POMs (e.g., taking not as prescribed, taking more tablets than directed), research shows that the most common motivation is to relieve physical pain (Hughes et al., 2016). Therefore, an integrative approach to pain management, involving safer, nonaddictive, alternatives to POMs, are essential to continue to treat patients in pain.

Cannabis has been studied as an emerging therapy for pain control (Abrams et al., 2007; Andreae et al., 2015; Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015; Ware et al., 2010; Whiting et al., 2015; Wilsey et al., 2013), and patients are using it for pain control, both with and without concurrent POM use (Perron, Bohnert, Perone, Bonn-Miller, & Ilgen, 2015). Cannabis remains a Schedule I controlled substance under federal law; nonetheless, cannabis is currently the most commonly used illicit drug with 22.2 million Americans (12 years and older) self-reported as current users (used in the past 30 days), either for medicinal or recreational purposes (Center for Behavioral Health Statistics and Quality, 2016). The National Academies of Science, Engineering, and Medicine (NASEM) concluded that there is "substantial evidence that cannabis is an effective treatment for chronic pain in adults" (NASEM, 2017, p. 90), while a recent systematic review found limited evidence cannabis improves only some types of chronic pain (Nugent et al., 2017). Medicinal use of cannabis (MC) is not without risks, and more research is needed to formalize dose, route, concentration, and safety information. Research on cannabis remains challenging, however, due to restrictive policies related to its status as a controlled substance under federal law (National Institute on Drug Abuse, 2016a, 2016b; Thomas & Pollard, 2016). Despite this need for further research, cannabis has become legal for medicinal use in 29 states and the District of Columbia (National Council of State Legislators, 2017). There is a critical knowledge gap regarding how MC policies will affect pain management and POM use across the United States. To address this gap, a systematic review of the current literature was conducted to explore the research question: Is there an association between MC laws and POM use and harms?

Methods

Search Strategy

The term "opioid epidemic" encompasses both POM and illicit opioids (such as heroin). This review focuses on POMs and POM-related harms such as overdose, opioid use disorder (OUD), and the associated health care costs—not on harms related only to illicit opioids.

A literature review was conducted by searching the electronic databases Medline, CINAHL, PubMed, Cochrane Review, and Google Scholar. The keyword opioid was used with additional MeSH terms including opioid analgesic, opioid-related disorders, prescription drug misuse, OUD, opioid policy, overdose, and prescription pain medication. Cannabis and medical marijuana were also used as keyword search terms, including MeSH terms of cannabis and pain, cannabis and opioids, alternative therapies, substance use disorder, cannabis use disorder, and cannabis policy. After separate searches of terms related to cannabis and terms related to opioids were completed, the two searches of opioid and cannabis were combined to find articles that utilized both terms. The health sciences librarian replicated the literature search for completeness.

Inclusion search criteria included peer-reviewed articles published in English between 2010 and July 2017 with applicability to the research question, as well as policy overview articles addressing state-level statistics related to costs, overdose, opioid or cannabis use disorders in states with MC laws. The publication timeline was selected to: (a) encompass the period when POM sales peaked and began to decline as a result of national recognition of the public health risk they posed (Staffa, 2017), (b) the publication of the landmark NAS (2011) report identifying pain as a major public health problem requiring treatment; and (c) the date by which (2010) approximately half of the current state medical cannabis (MC) laws had been initiated (National Council of State Legislators, 2017). Articles were excluded if they were not peer reviewed, discussed laws and policies of countries other than the United States, covered topics related either to POM or MC, but not to both, related only to illicit opioids (e.g., heroin), did not include an analysis after the state passed MC laws, or were not relevant to the research question.

Sample

A total of 11,513 possible articles were identified through the initial keyword search. After duplicates were removed, 789 article abstracts were screened for applicability. Of 789, a total of 379 articles were removed for lack of peer review, because they were editorial/opinion articles, or because they did not relate to the research question. Of the 410 articles remaining, abstracts were screened and 276 articles were excluded for being either single subject (opioids or cannabis) or not applying to the research question. The first author completed a full-text review of the remaining articles ($n = 134$) to verify they met eligibility criteria (Figure 1), resulting in 13 articles. When each of the 13 publications were reviewed, 3 were removed for being international studies. As a result, a total of 10 articles fully met inclusion criteria and comprise the sample for this review.

Findings/Results

Table 1 summarizes the 10 studies that met the inclusion criteria. It is important to note that articles use various terms to describe related, but not necessarily identical, concepts, such as opioid misuse vs. opioid abuse. For clarity, the terminology used in the original article is utilized throughout this report.

Of these 10 studies reviewed, two studies specifically addressed the substitution of MC for POM (Corroon, Mischley, & Sexton, 2017; Sexton, Cuttler, Finnell, & Mischley, 2016). Sexton et al. (2016) found that in a survey of MC patients ($n = 1,429$) in Washington, nearly 60% reported substituting cannabis for any prescription drug, and 25% specifically for pain medication, including POMs, many doing so without physician supervision. Corroon et al. (2017) surveyed 2,774 MC patients online and through a Washington state dispensary. Forty-six percentage reported using cannabis as a substitute for prescription drugs, most commonly POMs. When states with MC laws were compared with those without, there were no differences in prescription drug substitutions based on access to MC (Corroon et al., 2017).

In addition to substitution of MC for POMs, two studies reported MC use was associated with decreased POM use (Boehnke, Litinas, & Clauw, 2016; Reiman, Welty, & Solomon, 2017). Boehnke et al. (2016) studied changes in opioid use and quality of life in MC users in Michigan through an online survey and found MC use was associated with a 64% decrease in POM use and 45% improvement in quality of life. Reiman (2017) found that 97% of those MC users surveyed in California reported decreasing use of POMs when concurrently using MC, and 93% reported preferring MC to POMs for pain relief without a specific reason cited.

Powell, Pacula, and Jacobson (2015) studied the impact of MC laws on opioid-related harms by reviewing treatment admissions for POM abuse and state-level POM overdose deaths from 1999 to 2013; they concluded states permitting MC dispensaries had a relative decrease in both POM addictions (as measured by treatment facility admissions) and POM overdose deaths compared with states that did not. Powell et al. (2015) found a decrease in POM overdose and POM addiction only in states with MC dispensaries, suggesting actual availability of MC is the factor that reduces POM overdose and addiction levels, not simply having an MC law that makes it legal to use.

Bachhuber, Saloner, Cunningham, and Barry (2014) analyzed POM overdose deaths from three states that had MC laws prior to 1999 (California, Oregon, and Washington), as well as 10 states that implemented MC laws between 1999 and 2010 and 9 states that did not have MC laws effective until after 2010. The authors reported that the age-adjusted opioid mortality rate was 24.8% lower in states with MC laws ($p = .003$) and concluded MC laws could be associated with lower rates of POM overdose deaths.

The policy literature includes several examples of analyses indicating that access to MC use may result in a decline in POM prescriptions and expenditures. Bradford and Bradford (2017) found Medicaid beneficiaries filled fewer prescriptions, including those for POMs, in states that passed MC laws. They extrapolated their findings nationally and estimated that if all states had MC laws in 2014, there would be a $1.01 billion savings in prescription drug costs. Importantly, this analysis did not differentiate cost savings specifically related to POM, but the authors performed a subanalysis in nine broad clinical diagnosis areas for which cannabis is commonly used (e.g., anxiety, depression, glaucoma, nausea, pain, psychosis, seizure, sleep, spasticity), and there was an 11 percent reduction in drugs used to treat pain ($p < .01$). The same authors also previously evaluated the use of prescription medications by Medicare Part D recipients and found that the use of POMs declined once MC laws were initiated in the state (Bradford & Bradford, 2016).

A recent study by Shi (2017) analyzed the association between state MC policy and hospital admissions related to cannabis and opioids in 27 states. MC legalization was associated with a 23% and 13% reduction in hospitalizations for OUD related to POM and opioid overdose, respectively. There was no evidence that MC policy implementation was associated with subsequent increase in cannabis-related hospitalizations (Shi, 2017). Kim et al. (2016) analyzed drivers in fatal car accidents in 18 states before and after MC laws were initiated; they found a significantly decreased number of opioid positive tests among 21- to 40-year olds in states after MC laws had been passed (odds ratio 0.50, 95% confidence interval 0.67; interaction $p < .001$). However, the authors did not differentiate opioid positivity from POM vs. opioid positivity from illicit opioids, such as heroin.

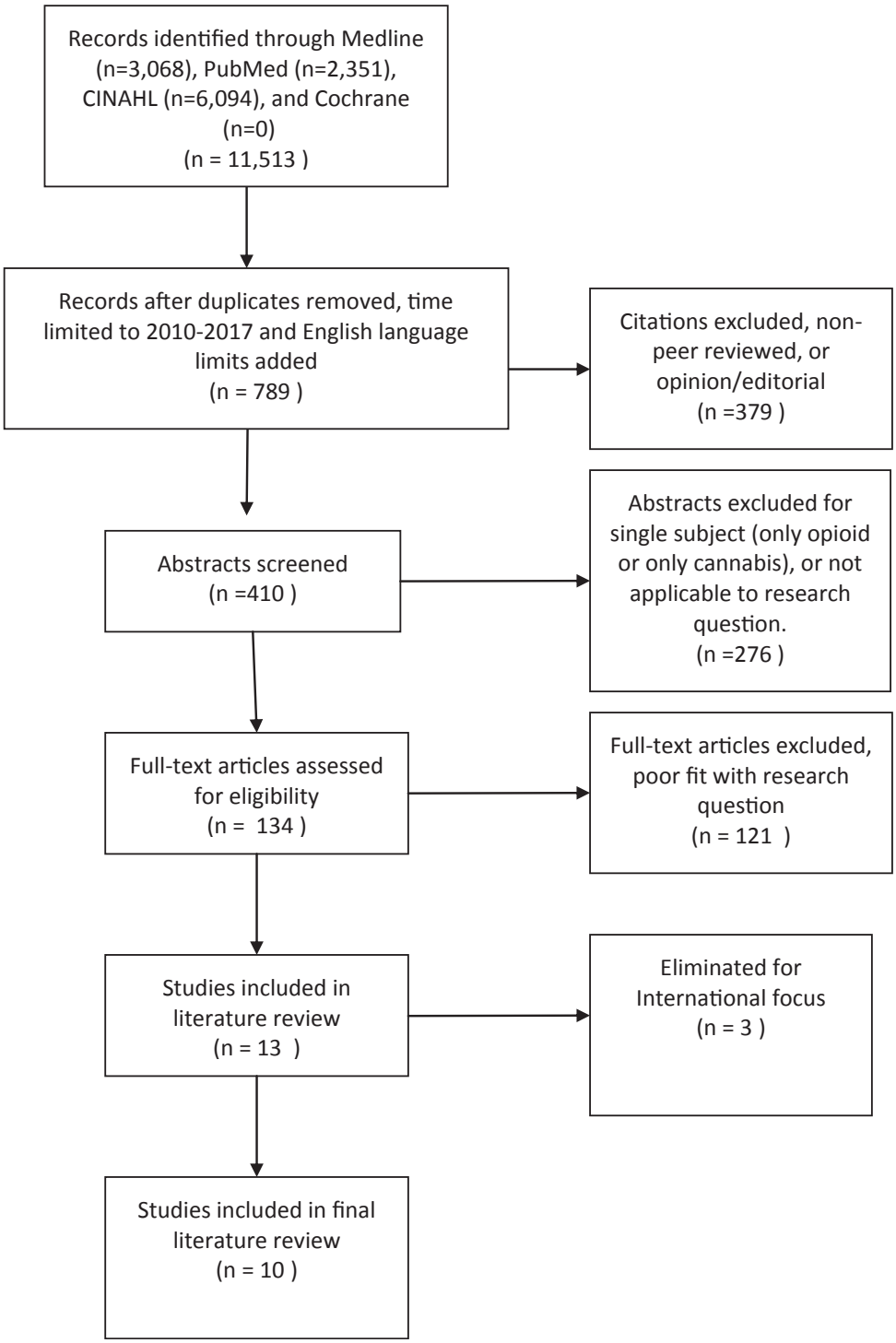

Figure 1 – Literature Search Flow Diagram

Discussion and Recommendations

All 10 studies reviewed indicate a connection between MC and reduced POM harms. The key outcomes measured included opioid-related overdoses, fatalities, POM abuse, hospitalizations, use, and cost. POM abuse was typically operationalized as admission to treatment facilities or hospitalizations for POM-related harms. States with laws allowing MC use were found to have lower POM overdose mortality rates (Bachhuber et al., 2014), especially in states with active, legal MC dispensaries (Powell et al., 2015), a decrease in POM use (Boehnke et al., 2016; Corroon et al., 2017; Reiman et al., 2017; Sexton et al., 2016), cost savings for prescription drugs for which cannabis could serve as an alternative

Table 1 — Literature

Study/Title	Purpose	Study Design	Data Sources	Location	Sample	Outcome Measure	Key Results and Conclusions
Bradford and Bradford (2017) Medical marijuana laws may be associated with ad decline in the number of prescriptions for Medicaid enrollees	Address the association between MC laws and number of prescriptions filled by Medicaid beneficiaries	Primary explanatory bivariate model	Medicaid fee-for-service prescription data, state drug utilization data	24 states	24 states with medical marijuana law, 9 clinical areas of prescription drugs for which MC could be a substitute	State Drug Utilization from CMS Medicaid enrollees in nine condition categories	Medicaid cost savings associated with MC laws = $19.825 million per state = total of $3.89 billion nationally if all states had MC laws. Medicaid beneficiaries in states with MC laws will fill fewer prescriptions.
Corroon et al. (2017) Cannabis as a substitute for prescription drugs—a cross-sectional study	Survey cannabis users for intentional substitutions of cannabis for prescription drugs	Cross-sectional survey	Anonymous questionnaire	WA, CA, OR, CO, recruit via social media and cannabis dispensary in WA	$n = 2,774$	Anonymous online survey, self selected	46% used cannabis as substitute for prescription drug, most commonly POM. No difference between states with MC laws vs. none. Substitutions are happening, state laws may not influence individual decision making.
Reiman et al. (2017) Cannabis as a substitute for opioid-based pain medication: patient self-report	Data gathering about the use of cannabis as a substitute for opioid and nonopioid-based pain medication	Cross-sectional survey	Self-reported data HelloMD database, using modified TOPS instrument	CA	$n = 2,897$	E-mail survey to 67,422 MC patients. Demographics, conditions for use, method of ingestion, substitute for POM, non-POM efficacy	97% reported decreased POM consumed when concurrently using cannabis, 93% prefer cannabis to POM. Clinical outcomes needed for MC as POM substitute; consider MC for treatment of POM dependence.
Shi (2017) Medical marijuana policies and hospitalizations related to marijuana and opioid pain reliever	Associations between state MC policy and hospitalizations related to cannabis and POM	Linear time-series regression	State inpatient databases, state-level annual admin records of discharges 1997–2014	27 states	382 state-year observation	Rates of hospitalization involving marijuana, opioid, abuse, and POM overdose. State, year effects	MC legalization was associated with 23% reduction in hospitalizations for opioid abuse or dependence and 13% reduction in POM overdose. MC policies associated with reduced POM-related hospitalizations.
Boehnke et al. (2016) MC use is associated with decreased opiate medication use	Does MC use for chronic pain changes individual patterns of opioid use	Cross-sectional, retrospective survey	Online questionnaire survey	MI	$n = 244$ MC dispensary patients with chronic pain who use MC	Demographic, change in opioid use, quality-of-life, medication classes used, medication side	MC use associated with 64% decrease in POM use and 45% improvement in quality of life. MC for chronic pain may benefit some patients, may improve quality of life.

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Table 1 – (*Continued*)

Study/Title	Purpose	Study Design	Data Sources	Location	Sample	Outcome Measure	Key Results and Conclusions
in a retrospective cross-sectional survey of patients with chronic pain						effects before and after MC initiation	Confirm with longitudinal studies.
Bradford and Bradford (2016) Medical marijuana laws reduce prescription medication use in Medicare Part D	Does implementing state MC laws change prescribing patterns and expenditures in Medicare Part D	Regression modeling	Medicare Part D enrollees from 2010 to 2013	24 states	24 states with medical marijuana law, 9 clinical areas	Nine clinical condition categories covered by state MC laws, drug data with at least one on-label use	$165.2 million reduction in costs of prescription drugs for which MC could serve as alternative per year in 2013. Availability of MC has significant effect on Medicare Part D expenditures.
Kim et al. (2016) State medical marijuana laws and the prevalence of opioids detected among fatally injured drivers	Association between MC laws and positive opioid test	Multilevel logistic regression	FARS data from 18 states that tested for alcohol and other drugs	18 states	$n = 68,394$	Fatality analysis data from 18 states in 80% of fatal car accidents	Significant reduction in opioid positivity for drivers 21–40 years old. MC laws associated with reductions in opioid positivity among 21- to 40-year old fatally injured drivers and may reduce opioid use and overdose.
Sexton et al. (2016) A cross-sectional survey of MC users: patterns of use and perceived efficacy	Inform practice, research, and policy, identify between medicolegal and patient outcome discrepancy	Cross-sectional survey	Author developed survey, 44 items, including 10 item PROMIS® global health short form	WA state cannabis dispensary	$n = 1,429$	Anonymous online survey, self selected	59.8% substituted for prescriptions 25% substituting for pain meds including opioids. Patient-reported outcomes favor MC use for broad diagnoses, largely unsupported by formal research. Discrepancy between approval of MC and actual use.
Powell et al. (2015) Do medical marijuana laws reduce addictions and deaths related to pain killers?	Impact of MC laws on POM misuse	Differences—in differences, event study, and synthetic control group	POM abuse treatment admissions TEDS, state POM overdose deaths NVSS ARCOS, and NSDUH	24 states with MC laws, 18 with protection against MC dispensary	Multiple database	Opioid treatment admissions, opioid overdose deaths, nonmedical use ARCOS NSDUH	Presence of MC dispensary decreases treatment admissions for POM addiction, reduces deaths due to opioid overdose. Access to MC has potential benefit of reducing POM abuse.
Bachhuber et al. (2014) MC laws and	To determine relationship between state	Time-series analysis Regression	State death certificate and MC laws and	13 states, 1999–2010	3 states with laws prior to study, 10 states with laws	POM overdose deaths	MC laws associated with 24.8% lower state-level POM overdose mortality rates

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Table 1 – (Continued)

Study/Title	Purpose	Study Design	Data Sources	Location	Sample	Outcome Measure	Key Results and Conclusions
opioid analgesic overdose mortality in the United States, 1999–2010	MC laws and POM overdose mortality rate	models for state policies	opioid analgesic overdose mortality		initiated during study period		compared with states without. MC may intersect with policies to prevent POM overdose.

Note. ARCOS, Automation of Reports and Consolidated Orders System, monitors and records controlled substances; FARS, Fatality Analysis Reporting System; MC, medical cannabis; NSDUH, National Survey on Drug Use and Health: state-level data on self-reported nonmedical use of prescription pain relievers; NVSS, National Vital Statistics System; POM, prescription opioid medication; TEDS, Treatment Episode Data Set; TOPS, Tilray Observational Patient Survey.

(Bradford & Bradford, 2016, 2017), a decrease in opioid positivity in fatally injured drivers (Kim et al., 2016), and reduced POM-related hospitalizations (Shi, 2017). This literature review is consistent with international research from Canada (Lucas et al., 2013; Lucas & Walsh, 2017) and Israel (Haroutounian et al., 2016) that concluded patients are substituting MC for POMs as an alternative pain management strategy (Haroutounian et al., 2016; Lucas et al., 2013; Lucas & Walsh, 2017).

One potential explanation for these findings is that there are behavioral, anatomical, and biochemical similarities between the opioid receptor system and the cannabinoid receptor system (Bushlin, Rozenfield, & Devi, 2010). This could have implications not only for the substitution of POMs with MC but also a reduction in POM use when patients use MC. Although the long-term risks of MC legalization are unclear, there have been zero reported deaths directly related to cannabis overdose, whereas there were 33,091 deaths related to all opioids in 2015, over 15,000 of which were attributed to POMs such as hydrocodone, oxycodone, and fentanyl (CDC, 2015; Rudd et al., 2016). However, Colorado, a state with both liberal MC and recreational cannabis laws, has seen an increase in tetrahydrocannabinol (the primary psychoactive component of cannabis) positive drivers in traffic fatalities, (Reed, 2016).

This review underscores the importance of multiple harm reduction strategies, including exploring integrative and alternative therapies for pain management, to reduce the number of deaths associated with POM. To our knowledge, this is the first literature review to examine if there is an association between MC laws and POM use, abuse, cost, and overdose in the United States. More research is needed to strengthen preliminary empirical findings that access to MC is a viable pain management strategy for creating positive risk/benefit profiles for patients with chronic pain while reducing POM-associated harms from therapeutic use.

Limitations

There are important limitations to the 10 studies reviewed. The primary limitation involves study design. Four studies exclusively relied on self-report survey data to evaluate whether MC patients were reducing their POM use and why. Participants providing self-report data through Internet surveys can be subject to both selection bias and recall bias. The self-report data presented in these studies provides little clarity regarding the reasons patients substituted MC for POM; for example, pain level or side effect profiles were not primary reasons discussed in any of the studies, and quality-of-life was an outcome in only one study (Boehnke et al., 2016). Additionally, there is no ability to differentiate outcomes resulting from recreational use, as compared with medical use, of either cannabis or POMs.

These studies were all descriptive and did not empirically test the effectiveness of MC in actually reducing pain, or the impact of potential MC-related harms, which would be important considerations for clinical practice. None of the studies considered the influence of clinical diagnosis (e.g., are results different for participants with myofascial pain vs. pain from the disease of cancer?). Additionally, outcomes measures were conceptualized and operationalized inconsistently across studies, making it difficult to compare findings or draw general conclusions. For example, "opioid abuse" or "problematic opioid use" was determined by admissions to treatment facilities (Powell et al., 2015), opioid-related hospitalizations (Shi, 2017), or a combination of Treatment Episode Data Set and National Vital Statistics System data (Powell et al., 2015). Finally, clear differentiation between licit opioids (such as POMs) and illicit opioids (such as heroin) is lacking in several of the studies.

Most importantly, the literature reviewed compared the medical use of cannabis with POM-related harms. This is problematic for two key reasons. First, there was a lack of equal consideration for MC-related harms in the study designs. Second, POM harms such as overdose, admission to treatment facilities, or hospitalizations are, to an unknown extent, the consequences of *nonmedical* (or recreational) POM misuse vs. legitimate POM use for medical reasons. Therefore, conclusions based on comparing medical vs. nonmedical use and harms of two different substances must be interpreted with significant caution.

Implications for Nursing Practice

Health practitioners need to be a strong voice urging policy makers and research funding entities to support further investigation of MC as an alternative pain management and harm reduction strategy for patients. Recent large-scale NIH funding for MC research is an important first step (NIH, 2017). Nurses should be advocates for patient-centered, integrative pain management approaches, which may include the safe and appropriate prescribing of POMs when needed, and conceivably the use of MC as further information becomes available, which is already being done in some states. However, there is still much unknown regarding the potential harms of MC, and more data are needed to understand potential complications of MC such as respiratory disease, substance abuse, psychiatric disorders, and impaired cognitive function.

The official American Nurses Association (ANA) position statement on MC is that cannabis should be reclassified as a federal Schedule II controlled substance for purposes of facilitating research. The ANA also advocates for the development of prescribing standards with specific dose, route, side effect profile, and indications for cannabis preparations, as well as evidence-based standards for its use (ANA, 2016). It is important for nurses to remember that MC is still illegal under federal law, and tolerance of more liberal state cannabis laws can change at any time given national politics and the interests of the sitting Attorney General. Federal prosecution against practitioners who prescribe or dispense MC is always possible as long as cannabis remains federally classified under Schedule I, and this risk must be taken into consideration prior to making any clinical recommendations.

Conclusions

The opioid epidemic is a public health crisis that is at least partially driven by harms associated with POM use. States are passing laws allowing use of MC and patients are using MC, but currently there is little understanding of how this influences POM use or of MC-related harms. This literature review provides preliminary evidence that states with MC laws have experienced reported decreases in POM use, abuse, overdose, and costs. However, existing evidence is limited by significant methodological shortcomings; so, general conclusions are difficult to draw.

The use of MC as an alternative to POMs for pain management warrants additional empirical attention as a potential harm reduction strategy. NASEM (2017) recommends more clinical trials to elucidate appropriate MC forms, routes of administration, and combination of products for treating pain, but access to MC products to fully evaluate these questions is challenging due to federal regulations. However, the recently funded National Institutes of Health longitudinal study to research the impacts of MC on opioid use is a critical step in the right direction (NIH, 2017; Williams, 2017). MCs potential as an alternative pain treatment modality to help mitigate the major public health opioid crisis, could be a missed opportunity if data on safety, efficacy, and outcomes are not collected and explored. Health care practitioners, particularly nurses who are charged with ensuring patient comfort, have a vested interest in providing viable alternatives to POMs when appropriate, as part of an integrative approach to pain management, and must advocate for more research to better understand the public health implications and risks and benefits of such alternatives.

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