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An Integrated Review of Cannabis and Cannabinoids in Adult Oncologic Pain Management

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ABSTRACT

Objective: The objective of this paper is to review the available literature regarding the use of cannabis and cannabinoids in adult oncologic pain management.
Design and Data Sources: A integrative review was conducted on March 1, 2018 using PubMed, MEDLINE, CINAHL, Embase, and Scopus. A snowball method was used to extract studies included in systematic reviews that were not included in the primary literature search.
Review Method: Articles reviewed address the use of cannabinoids or cannabis for pain management in oncology patients, either as stand- alone or adjuvant therapy.
Results: The final number of articles included is nine articles. Of the nine studies reviewed, eight reviewed the effect of the cannabinoid THC on cancer pain, and one study reviewed the use of medicinally available whole plant cannabis. The following study types were included: multiple multi-center, randomized, placebo- controlled trials and two prospective observational survey studies.
Results and Conclusions: Of the eight studies that reviewed the effect of the cannabinoid THC, five found THC to be more effective than placebo, one found THC to be more effective than placebo in American patients but ineffective in patients from other countries, and two found THC to be no more effective than placebo. The study that reviewed the effect of the whole plant cannabis found that there was a significant decrease in pain among those patients smoking cannabis.
Nursing Practice Implications: The lack of evidence in this field of research suggests a need to change policy surrounding cannabis research.

Background and Significance

Over the past 10 years there have been significant changes to laws governing the medical use of cannabis in the United States and internationally. The U.S. Drug Enforcement Agency currently classifies cannabis, commonly referred to as marijuana or pot, as a "Schedule I controlled substance with no currently accepted medical use and a high potential for abuse" under the Comprehensive Drug Abuse Prevention and Control Act of 1970 (United States Drug Enforcement Administration, n.d.). However, the U.S. Food and Drug Administration has considered how it might evaluate the scientific rigor of medicinal cannabis claims, and the review of public data regarding safety and abuse potential is ongoing (United States Food and Drug Administration, 2017). Notably, as of March 2018, 30 states and the District of Columbia have passed laws that broadly legalize medical cannabis. Eight states and the District of Columbia legalized cannabis for recreational use, and some states have decriminalized the possession of small amounts of cannabis (State Marijuana Laws in 2018 Map, 2018).

Moreover, a 2017 World Health Organization report found that several countries have modified their national controls to accommodate cannabidiol as a medicinal product (Expert Committee on Drug Dependence, 2017). In addition to these national and global changes, there has been increasing interest in the role that cannabis and cannabinoids play in the care of adult patients with cancer among researchers. A 2016 guideline summary on the management of chronic pain in survivors of adult cancers states that "clinicians may follow specific state regulations that allow access to medical

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cannabis or cannabinoids for patients with chronic pain after a consideration of the potential benefits and risks of the available formulations" (Paice et al., 2016, p. 3326).

According to a 2015 National Survey on Drug Use and Health, cannabis is the most popular illicit drug in the United States, based on past-month users (Center for Behavioral Health Statistics and Quality, 2016). In addition, a 2014 survey found that 89.5% of current adult cannabis users used cannabis for recreational reasons and 46.6% of adults used cannabis in part or entirely for medicinal purposes, with 10.5% of adults solely using cannabis for medicinal purposes (Schauer, King, Bunnell, Promoff, & McAfee, 2016).

Patients and providers alike are hopeful that cannabis will provide an additional treatment option for those who have symptoms uncontrolled by conventional medications. One particular symptom of interest is pain management. Cancer pain results from inflammation, mechanical invasion of bone or other pain-sensitive structure, or nerve injury. It is severe, persistent, and often resistant to treatment with opioids (Abrams & Guzman, 2015). Researchers have found that certain cannabinoid-1 receptors in the central nervous system are found in high concentrations in areas of the brain that modulate nociceptive processing, with a similar distribution to opioid receptors (Fine & Rosenfeld, 2013).

Despite evolving state policies, the increasing prevalence of cannabis use, and its implications for potential medical symptom management, the federal government's restrictive policies and regulations regarding research into the harms and benefits of cannabis products have limited research in the United States. Efforts to determine the value of cannabis or cannabinoids for treating medical conditions require researchers to obtain a number of approvals from the National Institute on Drug Abuse, the U.S. Food and Drug Administration, the U.S. Drug Enforcement Administration, institutional review boards, offices or departments in state government, state boards of medical examiners, and other local agencies (National Academies of Sciences, Engineering, and Medicine; Health and Medicine Division; Board on Population Health and Public Health Practice; Committee on the Health Effects of Marijuana, 2017). This has created a gap in the evidence available for providers and patients to consult while making decisions regarding the use of cannabis and cannabinoids. Stringent federal and local regulations result in the lack of evidence-based information on the potential pain management applications of cannabis and cannabinoids.

The purpose of this paper is to examine clinical studies conducted from 1975-2018 on medical cannabis and cannabinoid use for pain management in adult oncology patients. The research question is as follows: In adult patients with oncologic diseases (population) is cannabinoid or cannabis usage (intervention) a beneficial palliative care intervention for pain management (outcome)?

Methods

A literature search was performed on March 1, 2018 using the following electronic databases: PubMed, MEDLINE, CINAHL, Embase, and Scopus. The search used a combination of key terms. Additionally, within the PubMed and MEDLINE database, MeSH terms were used. For Embase, MeSH terms identified in PubMed and MEDLINE were used as key terms without the MeSH headings. By using MeSH terms where appropriate, the potential exclusion of studies as a result of differing terminology was reduced.

The following search was conducted across the PubMed and MEDLINE databases: (marijuana OR "Cannabis"[Mesh] OR "Medical Marijuana"[Mesh]) AND ("palliative care" OR "palliative medicine" OR "end of life" OR "pain") AND ("oncology" OR "cancer" OR "oncological pain")

The following search was conducted across the Web of Science, Embase, Scopus, and CINAHL databases: (marijuana OR "Cannabis" OR "Medical Marijuana") AND ("palliative care" OR "palliative medicine" OR "end of life" OR "pain") AND ("oncology" OR "cancer" OR "oncological pain")

To be included, studies had to address the use of cannabinoids or cannabis for pain management in oncology patients, either as standalone or adjuvant therapy. In addition, the studies' settings included any country, not only the United States, because of the more liberal legal policies surrounding cannabinoid usage internationally. Studies had to include patients who were 18 years old or older because of the legal and ethical implications of cannabis usage. Studies had to have the full text available through university library means. Studies involving pediatric patients were excluded. Articles not written in English were excluded. Studies that focused solely on patients with human immunodeficiency virus and multiple sclerosis were excluded. Articles that were case studies, expert opinions, and qualitative studies were excluded based on low level of evidence. Articles that could not be accessed via the university libraries were excluded.

Within the five databases (PubMed, MEDLINE, CINAHL, Embase, and Scopus), preference was given to articles less than 5 years old, but because of limitations in the quantity and quality of the literature published within the last 5 years, the search was broadened to include older studies (since 1975), provided the study evaluated the effect of cannabinoids or cannabis on controlling cancer pain.

A total of 123 records were initially identified. Duplicates were removed using deduplicating tools built into RefWorks, leading to 108 studies. Record screening was conducted based on title and abstract, leading to the exclusion of 22 articles (based on exclusion criteria described previously), and 86 full-text articles were assessed for eligibility. Full-text articles were excluded based on low level of evidence ($n = 23$), participant population ($n = 10$), differing outcome criteria ($n = 33$), systematic reviews ($n = 7$), and not being written in English ($n = 4$).

The researchers used a snowball method to extract studies included in systematic reviews that were not included in the primary literature search ($n = 5$) and then added these to the existing articles from the initial search that met inclusion criteria ($n = 4$). The final number of articles included in the table of evidence is nine articles (Table 1). The following study types were included: multiple multicenter, randomized, placebo-controlled trials, and two prospective observational survey studies. The studies were graded by consensus of the researchers using the Oxford Center for Evidence-Based Medicine levels of evidence (2009) (Table 2). The methodology flowsheet of the integrative review is demonstrated in Figure 1.

Results

The studies reviewed analyzed the effect of cannabinoids and cannabis on oncology pain. To assess pain, five studies used the Numeric Rating Scale for Pain Intensity (NRS-PI), three studies used a four-descriptor Verbal Rating Scale of Pain Intensity, and one used the Brief Pain Inventory (BPI) Short Form. The lack of standardized pain measurement tools decreased the ability to compare results across studies. These three pain measurements scales have been found to be valid and to have sensitivity to changes in pain in adult oncology patients (Jensen, 2003). The NRS-PI, however, has been found to be more sensitive than the Verbal Rating Scale (VRS) of Pain Intensity (Breivik, Björnsson, & Skovlund, 2000).

Furthermore, a computerized simulation study found that the NRS-PI had almost identical values in the same patient at various times after surgery, whereas the four-point VRS seemed to underestimate the most intense pain compared with the NRS-PI (Breivik et al., 2000). Moreover, Breivik et al. (2000) found that after randomly sampling 10,000 times repeatedly from simultaneous observations of NRS and VRS, the power to detect a difference in

Table 1
Table of Evidence

Citation	Purpose	Design/Method	Setting	Major Findings	Level of Evidence	Limitations
1. Noyes, Brunck, Baram, & Canter, 1975.	Determine if oral THC provides an analgesic effect in patients suffering from cancer pain. Understand the dose range where THC provides pain relief without toxic side effects.	Double-blind, randomized controlled trial. Patients received one oral dose of either placebo or THC in varying amounts (5, 10, 15, 20 mg) at 8:30 a.m. Patients reported pain and pain relief hourly. RNs completed subjective side effect observations.	University of Iowa Clinical Research Center	Significant trend toward lesser pain with increasing THC doses. Pain relief from 15 and 20 mg THC was significantly higher than placebo. Pain relief from THC developed slowly and was prolonged. Patients receiving 20 mg THC were heavily sedated, and 15 mg produced drowsiness. Heart rate and blood pressure decreased with 15- and 20-mg doses of THC.	2b: Low- quality RCT	Small sample size limits power of study. Patients only received one dose of each medication, limiting understanding of chronic response to medications.
2. Noyes, Brunk, Avery, & Canter, 1975.	Estimate the relative potency of the analgesic effects of THC and codeine.	Double-blind randomized controlled trial. Patients were admitted to a research facility and given a test drug daily at 8:30 a.m. Pain assessments and side effect surveys were administered hourly. RNs completed subjective side effect observations.	University of Iowa Hospital Clinical Research Center	The analgesic effect of THC developed slowly and was prolonged. The pain reduction experienced with 10 mg THC was roughly equivalent to 120 mg codeine and well tolerated. Side effects for 10 mg THC were mild and brief. Side effects for 20 mg THC were more significant, with patients voicing concern. 10 mg THC can be used for relief of mild pain.	2b: Low- quality RCT	Small sample size limits power of study. Patients only received one dose of each medication, limiting understanding of chronic response to medications. Patients reported altered pain response in THC (the same pain "bothered them less"), limiting the understanding of THC's impact on pain. Comparison to codeine is antiquated—doesn't provide comparison to more commonly used pain medications.
3. Jochimsen, Lawton, VerSteeg, & Noyes, 1978.	Assess the effect of benzopyranoperidine (a delta-9-tetrahydrocannabinol) on cancer pain and to compare it with codeine and a placebo.	Double-blind study. Over the course of the study, all 35 patients received each of the following on 1 day out of the 5-day evaluation period: 2 mg benzopyranoperidine, 4 mg benzopyranoperidine, 60 mg codeine sulfate, 120 mg codeine sulfate, and 1 placebo dose. A nurse observed all 35 patients and recorded each patient's degree of pain relief every 6 hours after the medication was given. The nurse assessed pain intensity when the medication was administered and every hour after (for 6 hours). Every hour, patients rated their pain and answered an 11-item questionnaire.	Clinical Research Center at the University of Iowa	The 120-mg dose of codeine was the only dose found to provide pain relief that was clinically significant. No difference in pain relief was identified among placebo, 60 mg codeine, 2 mg benzopyranoperidine, and 4 mg benzopyranoperidine. The two doses of benzopyranoperidine (2 mg, 4 mg) were not as effective at controlling pain as either dose of codeine (120 mg or 60 mg). The two tested doses of benzopyranoperidine were no more effective at controlling pain than the placebo dose. Compared with the placebo dose, both doses of benzopyranoperidine appeared to enhance the participant's pain perception.	2b: Low-quality RCT	Majority of participants were women (29/35) with breast or gynecologic malignancies, which make us question whether these results are transferrable to other types of cancer malignancies. Concludes by saying the doses of benzopyranoperidine examined are not effective at serving as an analgesic but does not suggest potential for future studies to build off of this (e.g., does not suggest the potential for testing increased doses of benzopyranoperidines).
4. Staquet, Gantt, & Machin, 1978.	Determine the effects of a synthetic nitrogen analog of tetrahydrocannabinol (NIB) on cancer pain.	Two randomized, double-blind trials. The first trial compared 4 mg NIB, 50 mg codeine, and a placebo. There were 30 patients included in this trial, and each patient received one of three medications over 3 consecutive	Data and patients from hospitals in Brussels, Belgium, and Chicago, Illinois	NIB should not be used in practice because phase I studies have reported frequent side effects. However, findings suggest that nontoxic derivatives of tetrahydrocannabinols may be effective in reducing cancer pain. In the first trial, NIB's effects on	2b: Low- quality RCT	Sample sizes were small (30 patients in first trial; 15 patients in second trial). Patients were only followed for 6 hours per medication (would have been more effective if they followed patients using these medications over a longer period).

(*continued on next page*)

Table 1 (*continued*)

Citation	Purpose	Design/Method	Setting	Major Findings	Level of Evidence	Limitations
		days (received a different medication each day). The second trial compared 50 mg secobarbital, 4 mg NIB, and a placebo. There were 15 patients included in this trial, and each patient received one of the three medications within 3 consecutive days (after the 3 days each participant had received each medication over 1 day). Each day, the patient's pain was monitored subjectively every hour for 6 hours. Pain intensity differences (PIDs) were calculated by identifying how many hours (out of 6) a patient's pain fell below his or her premedicated pain level.		cancer pain was similar to codeine and more effective than the placebo In the second trial, NIB's effect on cancer pain was superior to the placebo and secobarbital.		Pain was measured subjectively (provider perception) vs. objectively (asking patients their pain level).
5. Portenoy et al., 2012.	Evaluate a novel cannabinoid formulation, nabiximols, "using a study design intended to obtain information about its dose response for analgesia and safety in a population with advanced cancer and opioid-refractory pain," (446).	Randomized, double-blind, placebo-controlled, graded-dose study. Participants were randomly assigned to receive placebo or nabiximols at a low dose (1-4 sprays/day), medium dose (6-10 sprays/day), or high dose (11-16 sprays/day).	Patients screened in 84 study centers across North America, Europe, Latin America, and South Africa	"There were no significant differences in pain response among different dose groups that were randomized to placebo" (442). No analgesic effect was found in high-dose group, and high dose was not well tolerated (high withdrawal rate because of side effects) Low-dose nabiximols provided a 26% improvement in pain compared with baseline. Nabiximols have analgesic efficacy when given as an add-on therapy for patients with poor response to opioids.	2b: Low- quality RCT	The forced dose titration design potentially decreased understanding of analgesic efficacy and side effects. Study did not titrate opioid dosing based on pain response from nabiximols, preventing evaluation of the opioid-sparing effect of nabiximols.
6. Johnson, Lossignol, Burnell-Nugent, & Fallon, 2013.	Determine the long-term safety and tolerability of THC/CBD spray and THC spray in relieving advanced cancer pain.	"In total, 43 patients with cancer-related pain experiencing inadequate analgesia despite chronic opioid dosing, who had participated in a previous three-arm (THC/CBD spray, THC spray, or placebo), two-week parent randomized controlled trial, entered this open-label, multicenter, follow-up study" (207). "Patients self-titrated THC/CBD spray (n = 39) or THC spray (n = 4) to symptom relief or maximum dose and were regularly reviewed for safety, tolerability, and evidence of clinical benefit" (207).	22 study sites, including 21 centers in the U.K. and 1 in Belgium	"The efficacy end point of change from baseline in mean Brief Pain Inventory-Short Form scores for 'pain severity' and 'worst pain' domains showed a decrease (i.e., improvement) at each visit in the THC/CBD spray patients. Similarly, the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30 scores showed a decrease (i.e., improvement) from baseline in the domains of insomnia, pain, and fatigue" (207-208).	2b: Cohort study	A total of 23 patients (59%) receiving THC/CBD spray and 1 patient (25%) taking THC spray withdrew because of adverse effects

7. Bar-Sela et al., 2013.	Evaluate the advantages and side effects of using cannabis by cancer patients with medicinal cannabis licenses.	Prospective observational study included two interviews based on questionnaires regarding symptoms and side effects, the first held on the day the license was issued and the second 6-8 weeks later. "Cancer symptoms and cannabis side effects were documented on scales from 0 to 4 following the CTCAE. The distress thermometer was used also" (1). "The data collected included information on the cannabis use, such as regular use or interrupted" (2).	Rambam Health Care Campus, Haifa, Israel	"Twenty-five (12%) patients stopped treatment after less than a week, mainly because of the side effects that influenced their quality of life or the absence of any clinical improvement" (3). Of those with continuous cannabis use, "All cancer or anti-cancer treatment-related symptoms, including nausea, vomiting, mood disorders, fatigue, weight loss, anorexia, constipation, sexual function, sleep disorders, itching, and pain had significant improvement ($p <$ .001)" (3). Seventy patients used pain medication at the beginning, of whom 2 (1.7%) had dose elevation and 31 (43%) dose reduction.	2b: Cohort study	Nature of the study leads to attrition—24% of the study population died before the second follow-up interview, and 10% did not use cannabis despite having the license. There was "lack of an appropriate control group for comparison, since the overall improvement in perceived health quality might be attributed simply to time or other factors unrelated to treatment" (7); also, "cannabis effects are only reported when self-report-based methodologies are used may imply that the 'real' effect may be one of psychological order, rather than specific effects on the body physiology" (7).
8. Lynch, Cesar-Rittenberg, & Hohmann, 2014.	Study nabiximols (oral mucosal spray containing cannabinoids) for the treatment of chemotherapy-induced neuropathic pain.	Randomized, placebo-controlled crossover pilot study. "Study drug was nabiximols, an oromucosal whole cannabis-based spray combining tetrahydrocannabinol with cannabidiol, minor cannabinoids and terpenoids, plus ethanol and propylene glycol excipients, and peppermint flavoring" (167). Patients received drug for 4 weeks with pain assessments on week 2 and 4	Participants recruited through posters in oncology clinics at University Teaching Hospital (Capital District Health Authority, Halifax, Nova Scotia, Canada) and advertisements in newspaper	"No statistically significant difference [was found] between the treatment and the placebo groups on the NRS-PI" (166). "A responder analysis demonstrated that there were five participants who reported a two-point or greater reduction in pain that trended toward statistical significance and the number needed to treat was five" (166).	2b: Low- quality RCT	183 participants would have been required for statistical significance.
9. Fallon et al., 2017.	Assess the analgesic efficacy of adjunctive Sativex (Δ9-tetrahydrocannabinol (27 mg/mL): cannabidiol (25 mg/mL) in advanced cancer patients with chronic pain unalleviated by optimized opioid therapy	Both trials described were phase 3, double-blind, multicenter, randomized, placebo-controlled trials. Study 1 was a classic RCT design. Study 2 had a two-part randomized withdrawal design.	Study 1 was conducted at 101 centers in Belgium, Bulgaria, Czech Republic, Estonia, Germany, Hungary, Latvia, Lithuania, Poland, Romania, the United Kingdom, and the United States. Study 2 was conducted in 65 centers in Australia, Bulgaria, Germany, Hungary, India, Israel, Italy, Lithuania, Poland, Romania, Spain, Taiwan, and the United Kingdom.	The primary efficacy endpoints (percent improvement, study 1, and mean change in average daily pain NRS scores, study 2) were not met in either study. Post hoc analyses of the primary endpoints identified statistically favorable treatment effect for Sativex in U.S. patients <65 years (median treatment difference: 8.8; 95% CI: 0.00-17.95; $p = .040$) that was not found in patients <65 years from the rest of the world (median treatment difference: 0.2; 95% CI: −5.00 to 7.74; $p = .794$). Treatment effect in favor of Sativex was found on quality-of-life questionnaires, despite the fact that similar effects were not found on NRS score. The safety profile of Sativex was consistent with earlier studies, and no evidence of abuse or misuse was identified.	2b: Low- quality RCT	In both trials a significant number of participants withdrew from the study (32% and 20.6% in study 1 and 24.3% and 14.6% in study 2 in the therapy and placebo arms, respectively). Moreover, the relatively high mortality rates reported in both studies (10% and 12.6%, and 22.3% and 9%) further increased the number of lost patients. Missing data are a well-known factor that negatively affects study outcomes. The nature of the primary endpoints may have affected outcomes. Self-reported NRS scores can be associated with day-to-day variations in mood, a phenomenon expected to have a significant impact in a fragile population of patients with advanced cancer.

THC = Δ9-tetrahydrocannabinol; RN = registered nurse; CBD = cannabidiol; CTCAE = Common Terminology Criteria for Adverse Events; NRS = Numeric Rating Scale; CI = confidence interval.

Table 2
Oxford Center Levels of Evidence for Therapy

Level	Description
1a	SR (with homogeneity) of RCTs
1b	Individual RCT (with narrow confidence interval)
1c	All or none
2a	Systematic review with homogeneity of cohort studies
2b	Individual cohort study; low-quality RCT (e.g., <80% follow-up)
2c	Outcome research; ecological studies
3a	Systematic review with homogeneity of case-control studies
3b	Individual case-control studies
4	Case series; poor quality cohort or case-control studies
5	Expert opinion omitting explicit critical appraisal (includes opinion based upon physiology, bench research, or first principles)

SR = systematic review; RCT = randomized controlled trial.

pain intensity was higher with the NRS compared with the VRS data. Thus the NRS has higher sensitivity than the VRS. Researchers have found that the BPI Short Form is valid and reliable for patients with medical and surgical cancer pain, with Cronbach α coefficients of $r = 0.95$ and $r = 0.97$, respectively (Tan et al., 2004; Tittle, McMillan, & Hagan, 2003). It is notable that the studies analyzed by this paper used numerous pain measurement tools, limiting the ability to compare results across studies.

Of the nine studies reviewed, eight studies (Table 1, studies 1-6, 8, and 9) reviewed the effect of the cannabinoid Δ9-tetrahydrocannabinol (THC, the principal psychoactive component of cannabis) on cancer pain. The study designs had a level of evidence of 2b (seven low-quality RCTs and two cohort studies) when analyzed using the Oxford Center for Evidence-Based Medicine therapy rating tool. THC was administered through oral sprays and tablets. Of these eight studies, five found THC to be more effective than placebo (studies 1, 2, and 4-6), one found THC to be more effective than placebo in American patients but ineffective in patients from other countries (study 9), and two found THC to be no more effective than placebo (studies 3 and 8). Of the five studies that found THC to be more effective than placebo, four noted that high-dose THC administration resulted in a high-rate of negative side effects among patients (studies 1, 2, 5, and 9). Ten-milligram tablets of THC were generally well tolerated, resulting in mild pain relief. The studies reviewed suggest that the administration of low-dose THC may provide a novel intervention for patients who have cancer pain refractory to opioids and conventional pain management techniques. In addition, Bar-Sela et al. (2013) reviewed the use of medicinally available whole plant cannabis (study 7). This study found that there was a significant decrease in pain among those patients smoking cannabis; however, the study has a lower level of evidence (IV) because it was a prospective observational study.

Studies included men and women suffering from a broad spectrum of oncologic conditions, such as breast cancer, lymphoma, cervical cancer, and other advanced cancers. Study participants were patients from North America, South America, Europe, Asia, Australia, and Africa.

Conclusions and Limitations

Because of the limited number of studies available on the efficacy of cannabis and cannabinoids in alleviating adult cancer pain, it is

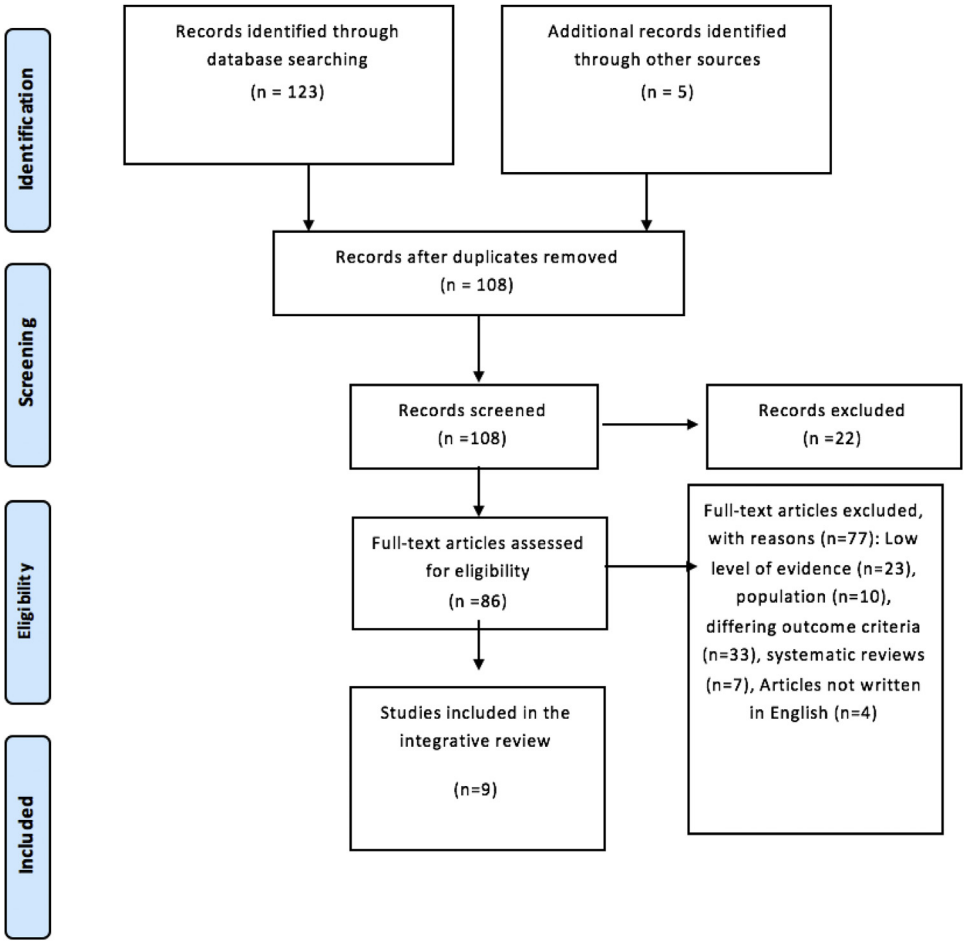

Figure 1. Flowsheet of integrative review.

challenging to make a definitive recommendation for practice. Although the current evidence is sparse, there is sufficient evidence to support further research into the use of low-dose THC in cancer pain. The lack of evidence in this field of research suggests a need to change policy surrounding cannabis and cannabinoid research. Cannabis is a schedule I drug, indicating there is no accepted medical use. Thus researchers must navigate a complex bureaucracy to receive permission to study its effects. To promote further research, nurses and other health care professionals should lobby to remove cannabis from the schedule I drug list, supporting the potential medical uses.

There are several noteworthy limitations to the studies reviewed by this paper. Primarily, there is a limited amount of high-quality evidence surrounding the use of cannabinoids and cannabis in oncology patients, likely because of the legal issues surrounding cannabis. Many studies reviewed took place in foreign countries, potentially limiting their application to the United States. Only three of the nine studies analyzed had a sample size larger than 50 patients, limiting the power of the results. Additionally, many studies had high withdrawal rates, particularly in the study group. Several studies noted that individuals randomly assigned to cannabinoids were more likely to withdraw from the trial because of negative side effects, potentially limiting the understanding of the negative side effects associated with cannabinoids. In addition, the classic side effects associated with cannabis and cannabinoids (such as feeling “high”) often informed patients that they were receiving the study drug. This potentially influenced patient reporting of drug efficacy and side effects. Furthermore, the primary research teams involved in the various studies often overlapped, potentially introducing a researcher bias. Moreover, because many of the studies used different measures of pain (NRS, BPI, and VRS), it may be difficult to interpret findings across studies. However, in future studies, using the NRS and BPI pain measure tools is recommended because of the greater validity and reliability of these tools compared with the VRS. Finally, three studies only administered one dose of the THC medication, which may not provide an appropriate understanding of how cannabinoids can affect long-term oncologic pain management.

Although the studies reviewed had small sample sizes, the patients included represented a wide demographic. Men and women with a broad spectrum of oncologic conditions were included. Study participants were patients from North America, South America, Europe, Asia, Australia, and Africa. This diversity in study participants provided a broad demographic cohort of patients.

Implications for Nursing

As the interest in cannabis and cannabinoid usage for oncologic pain management grows, nurses have the opportunity to advocate for further research and policy change. Nurses are able to directly support, educate, and monitor patients' oncology palliation process, of which cannabis may play a role in the future. The pertinent implications for nursing practice include the need to increase knowledge concerning the benefits and limitations of cannabis use, guiding patients' use of cannabis for palliative care, and empowering patients to make choices regarding cannabis use for cancer treatment and palliation based on growing evidence.

Cannabis and cannabinoids are still widely known to be an illicit substance, and nurses may need to overcome stigmas and fears surrounding its use. Nurses have the opportunity to empower patients through the dissemination of the latest evidence. Through candid and evidence-based discussions about cannabis usage with patients, nurses can help to move the health care system beyond cannabis prohibition stigmas and toward increased research on cannabis and cannabinoids for use in oncology pain.

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