

Caring for Patients Using Medical Marijuana

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Since 1996, 33 U.S. states, the District of Columbia, Guam, Puerto Rico, the U.S. Virgin Islands, and all Canadian provinces have passed legislation legalizing the use of marijuana for medical purposes. Another 13 states allow use of low delta-9 tetrahydrocannabinol/high cannabidiol products for medical reasons in some situations or as a legal defense to its use. Yet cannabis remains a Schedule I Controlled Substance, impacting not only the legality of a healthcare provider's prescription of cannabis outside of a medical marijuana program, but also the accessibility of marijuana available for research. The classification of cannabis as a Schedule I Controlled Substance therefore directly limits the amount of moderate- to high-quality human evidence regarding the effectiveness of cannabis for certain conditions, dosage, adverse effects, or safety. Regardless of the limited evidence, individuals are using medical cannabis products more frequently, and nurses are left without evidence-based, clinical resources when caring for them. To address this lack of resources, the National Council of State Boards of Nursing Board of Directors appointed members to the Medical Marijuana Nursing Guidelines Committee to develop recommendations to guide nurses' care of patients using medical marijuana. This article presents their recommendations, which were published in July 2018, and various updates since that publication.

Objectives

- Explore the regulatory and legislative history of medical marijuana.
- Discuss current legislative and legal approaches to cannabis availability and dispensation.
- Identify principles to guide nurses' care of patients using medical cannabis.
- Gain an understanding of the ethical and safety considerations regarding a patient's treatment with cannabis.

Cannabis use has been documented as far back as 2900 B.C. Its use was well documented as the prime medicine for more than 100 illnesses and diseases in the U.S. pharmacopoeia in the 1800s through early 1900s (Marijuana Policy Project, 2014). Recreational use of cannabis, as well as the use of the name "marihuana," was introduced into American culture after the Mexican Revolution of 1910 (PBS, 1998). During the depression, some research linked the use of cannabis with violence, crime, and other socially deviant behaviors (PBS, 1998). By the 1930s, a fear of cannabis had crept in, and by 1931, 29 states had outlawed cannabis, which eliminated its availability as an over-the-counter drug (PBS, 1998). In 1937, Congress passed the Marihuana Tax Act, effectively criminalizing cannabis by the use of an exorbitant tax for certain authorized medical uses (Marihuana Tax Act of 1937).

The 1960s brought a changing cultural climate and more lenient attitudes toward cannabis. Now government reports found that cannabis did not induce violence (PBS, 1998). The case of

Leary v. United States (1969) challenged the constitutionality of the Marihuana Tax Act of 1937, and the U.S. Supreme Court found that the Act was unconstitutional. Congress quickly responded by enacting the Comprehensive Drug Abuse Prevention and Control Act in 1970, which created the Controlled Substances Act (CSA), a classification system and prescriptive restrictions for various drugs and substances—Schedules I through V (Comprehensive Drug Abuse Prevention and Control Act, 1970).

Substances with a high potential for abuse without any accepted medical use (i.e., heroin, LSD, ecstasy) are included in Schedule I—the most stringent prescriptive restriction, which includes prohibition on most research using those controlled substances except under rigorous government oversight. The list of Schedule I Controlled Substances also includes cannabis, thereby continuing the restriction of cannabis use by prohibiting healthcare practitioners from prescribing cannabis.

Cannabis use remained restricted until the first legalization of medical marijuana was approved in California in 1996; however, the federal government opposed the approval and threatened to revoke the prescription-writing abilities of physicians who recommended or prescribed cannabis. It wasn't until 2000 that a group of physicians challenged the government's policy and prevailed in court with a decision to allow physicians to recommend—but not prescribe—medical marijuana (Marijuana Policy Project, 2014). Since then, 33 U.S. states, the District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands have passed comprehensive medical marijuana programs (MMPs). Another 13 states allow the use of low THC/high CBD products for medical reasons in some situ-

ations or as a legal defense to its use (National Conference of State Legislatures [NCSL], 2019). All provinces/territories of Canada (Government of Canada, 2016) have passed legislation legalizing the use of cannabis for medical purposes.

With this legalization comes an increasing number of patients who use medical marijuana along with a larger population who use cannabis obtained through other means to self-treat various symptoms. Evidence supporting cannabis use to manage medical conditions is limited by legal restrictions on using cannabis for research purposes; thus, nurses are left without evidence-based, clinical resources when caring for patients who use medical marijuana products.

Statutory authorization of cannabis use for certain conditions is influenced by the limited available research, but more so influenced by advocacy groups and anecdotal evidence. Regardless of existing evidence or lack thereof, individuals are using cannabis and nurses will care for these patients more frequently. To address the lack of guidelines for nurses when caring for individuals using cannabis, the National Council of State Boards of Nursing Board of Directors appointed members to the Medical Marijuana Nursing Guidelines Committee to develop guidelines and recommendations to guide nurses' care of patients using medical marijuana, and those guidelines were published in July 2018 (National Council of State Boards of Nursing, 2018).

This article presents principles of safe and knowledgeable practice guidelines when caring for patients using medical marijuana, as recommended by the committee, including (a) a working knowledge of the current state of legalization of medical cannabis use and their jurisdiction's MMP; (b) current approaches to cannabis availability, dispensing cannabis, and qualifying conditions with and without evidence; (c) an understanding of the endocannabinoid system and its pharmacokinetics; and (d) identifying dosage, methods of administration, adverse reactions, and safety and ethical considerations for patient use of medical marijuana. This article uses several terms related to cannabis, medical marijuana, and their official programs. See Table 1 for a list of definitions for the terms used in this article.

Current Legal Approaches to Cannabis Availability and Dispensing

Over the past few decades, the federal government and individual jurisdictions have instituted varying laws, rules, and regulations regarding the availability and dispensing of cannabis for medical purposes.

Federal Legislation

The Comprehensive Drug Abuse Prevention and Control Act (1970), was enacted to protect the public, stating "illegal importation, manufacture, distribution, and possession and improper use of controlled substances have a substantial and detrimental effect on the health and general welfare of the American people."

Specifically, the CSA, Title II of the Comprehensive Drug Abuse Prevention and Control Act of 1970, created the schedules of controlled substances.

Because cannabis is included in Schedule I of the CSA, not only does that imply that cannabis has no accepted medical value and present a high potential for abuse, it also places severe restrictions on cannabis research (Comprehensive Drug Abuse Prevention and Control Act, 1970). Numerous federal bills have been introduced in an effort to amend the CSA by rescheduling cannabis to allow for more research. Various petitions have been filed with the U.S. Drug Enforcement Administration (DEA) to reschedule cannabis, and several lawsuits have challenged the constitutionality of including cannabis in the CSA. No bill, petition, or lawsuit has prevailed in rescheduling cannabis.

Again in 2016, congressional representatives called on the DEA to reschedule cannabis (Bernstein, 2016). Subsequently, the U.S. Food and Drug Administration (FDA) requested a scientific and medical evaluation and scheduling recommendation from the U.S. Department of Health and Human Services (Rosenberg, 2016a). After review, the department concluded that "marijuana has a high potential for abuse, has no accepted medical use in the United States, and lacks an acceptable level of safety for use even under medical supervision" (Denial of Petition to Initiate Proceedings, 2016). Based on this report, the DEA denied the petition to reschedule cannabis as a Schedule II Controlled Substance (Rosenberg, 2016b).

The DEA, however, did recognize the lack of scientific study on cannabis and announced a policy change to expand the number of DEA-registered cannabis manufacturers (Rosenberg, 2016a). This expansion was expected to provide an increased supply of cannabis for FDA-authorized research purposes. Thirty-three entities applied to the DEA to become cannabis manufacturers for research, yet as of July 2019, no applications have been reviewed by the DEA (Scottsdale Research Institute, LLC, 2019). In June 2019, a petition sought to compel the DEA to process the applications, claiming that it has unlawfully failed to act on medical cannabis research applications since 2016 (Scottsdale Research Institute, LLC, 2019). A federal court in July 2019 ordered the DEA to respond within a month (U.S. Court of Appeals, 2019). The DEA responded by publishing a policy statement, "providing notice of pending applications" to register as marijuana manufacturers for researchers and that the "DEA intends to propose new regulations that will govern the marijuana growers program for scientific and medical research" (DEA, 2019).

Current State and Jurisdiction Legislation

Since the first MMP in California (Compassionate Use Act of 1996), the trend among states is legalizing cannabis for medical use (Halperin, 2016). Thirty-four U.S. states, the District of Columbia, Guam, Puerto Rico, and the U.S. Virgin Islands, as well as all Canadian provinces, have passed comprehensive MMPs (NCSL, 2019). Another 13 states allow use of low THC/high CBD

TABLE 1

Definition of Terms

Authorize. Any act of certification, attestation, or other method for a practitioner to affirm that a patient may benefit from medical cannabis.

Cannabidiol (CBD). A major cannabinoid that indirectly antagonizes cannabinoid receptors, which may attenuate the psychoactive effects of tetrahydrocannabinol.

Cannabinoid. Any chemical compound that acts on cannabinoid receptors. These include endogenous and exogenous cannabinoids.

Cannabinol (CBN). A cannabinoid more commonly found in aged cannabis as a metabolite of other cannabinoids.

Cannabis. Any raw preparation of the leaves or flowers from the plant genus *Cannabis*.

Certify. For the purpose of this article, to “certify” is the act of confirming that a patient has a qualifying condition. Many jurisdictions use alternative phrases, such as “attest” or “authorize”; however, 13 of 29 jurisdictions use “certify” language in their statutes.

Clinical research. For the purpose of this article, “clinical research” involves studies that experimentally assign randomized human participants to one or more drug interventions to evaluate the effects on health outcomes. Contrasted with **pre-clinical research or studies**, which experimentally or observationally use animal models, cell cultures, and/or biochemical assays to determine possible biological effects of an intervention. These studies also include observational studies of human participants that do not control interventions.

delta-9 tetrahydrocannabinol (THC). One of many cannabinoids found in cannabis. THC is believed to be responsible for most of

the characteristic psychoactive effects of cannabis (Compton, 2017).

Dronabinol. The generic name for synthetic tetrahydrocannabinol. It is the active ingredient in the Food & Drug Administration (FDA)-approved drug Marinol (FDA, 2017).

Endocannabinoid system. A biological system that consists of endocannabinoids, cannabinoid receptors, and the enzymes responsible for synthesis and degradation of endocannabinoids (Mackie, 2008).

Marijuana. A cultivated cannabis plant, whether for recreational or medical use. The words “marijuana” and “cannabis” are often used interchangeably in various lay and scientific literature. This article will primarily use the word “cannabis” as a shorthand that also includes cannabinoids. When referring to a medical marijuana program, this report will use the word “marijuana,” as it is often used within program references.

Medical marijuana program (MMP). The official jurisdictional resource for the use of cannabis for medical purposes. To locate a specific jurisdiction’s MMP, search the jurisdiction’s website or department of health for “medical cannabis program” or “medical marijuana program” (National Conference of State Legislatures, 2017).

Nabilone. The generic name for a synthetic cannabinoid similar to tetrahydrocannabinol. It is the active ingredient in the FDA-approved drug Cesamet (FDA, 2006a).

Schedule I Controlled Substances. Defined in the federal Controlled Substances Act as those substances that have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and lack accepted safety for use of the substance under medical supervision.

products for medical reasons in some situations or as a legal defense to its use (NCSL, 2019). However, this type of program is not considered an MMP.

Procuring Certification for Medical Marijuana

Since a healthcare provider cannot prescribe cannabis, each MMP includes a list of medical conditions or symptoms, known as qualifying conditions, for which an individual may use medical marijuana (NCSL, 2019). The healthcare provider determines whether the individual has a qualifying condition and completes a certification for the MMP. Generally, MMPs include various provisions regarding the process for procuring a certification for the use of cannabis as well as the amount of cannabis distributed to an individual, and legal protections extend to patients, designated caregivers, and healthcare providers (NCSL, 2019).

Some MMPs require a bona fide healthcare provider–patient relationship to certify a patient as having a qualifying condition. Other MMPs require a preexisting and ongoing relationship with the patient as a treating healthcare provider, and some note the relationship may not be limited to issuing a written certifi-

cation for the patient or a consultation simply for that purpose. Additionally, a few MMPs specify that an advanced practice registered nurse can certify a qualifying condition (NCSL, 2019). Some MMPs require a specific course or training for a provider to participate in certifying an MMP qualifying condition (NCSL, 2019).

Patients with a certification of a qualifying condition must register with their local state MMP. A registered patient can obtain cannabis from a jurisdiction-authorized cannabis dispensary. Procurement and administration of cannabis for medical purposes are limited to the patient and/or the patient’s designated caregiver. The MMP will specify whether designated caregivers are permissible as well as the applicable process for registration as a designated caregiver (NCSL, 2019). In some jurisdictions, the MMP allows an employee of a hospice provider or nursing or medical facility, a visiting nurse, a personal care attendant, or a home health aide to act as a designated caregiver for the administration of medical marijuana (NCSL, 2019).

The laws regarding MMPs are frequently changing. Nurses caring for patients using medical marijuana should review the unique characteristics of a jurisdiction’s MMP that may affect their

TABLE 2

Conditions With Moderate- to High-Quality Cannabis Therapeutic Clinical Evidence

- Cachexia
- Chemotherapy-induced nausea and vomiting
- Pain (resulting from cancer or rheumatoid arthritis)
- Chronic pain (resulting from fibromyalgia)
- Neuropathies (resulting from HIV/AIDS, multiple sclerosis, or diabetes)
- Spasticity (from multiple sclerosis or spinal cord injury)
- Seizure frequency reduction

practice. The relevant statute can be located through the jurisdiction's department of health and MMP. Useful links are provided through the NCSL (2019).

Reconciling State and Federal Laws

Many questions arise regarding the conflict between the current federal prohibition and state MMPs. Although the use of marijuana pursuant to authorized MMPs appears to conflict with federal law and regulations, the 10th Amendment gives the state a certain degree of autonomy where Congress cannot commandeer state processes (Mikos, 2012). The anti-commandeering doctrine limits the supremacy clause by prohibiting the federal government from forcing states to do its bidding. At present, there is no controlling case law holding that Congress intended to pre-empt the field of regulation of cannabis use under its supremacy powers (*Beek v. City of Wyoming*, 2014; Mikos, 2012). Furthermore, the Rohrabacher-Farr amendment (also known as the Rohrabacher-Blumenauer amendment), a federal spending provision, currently prohibits the U.S. Department of Justice (DOJ) from prosecuting state-compliant medical marijuana patients and providers (Consolidated and Further Continuing Appropriations Act, 2014).

The DOJ issues position papers to describe specific prosecutorial policy on various matters. In 2009, the U.S. attorney general took a position that discouraged federal prosecutors from prosecuting people who distribute or use cannabis for medical purposes in compliance under the law of the applicable jurisdiction (DOJ, 2009); similar guidance was given in 2011, 2013, and 2014 (Cole, 2011, 2013a, 2013b; Wilkinson, 2014). In January 2018, the U.S. attorney general rescinded the previous nationwide guidance specific to marijuana enforcement (Sessions, 2018). The 2018 memorandum provides that federal prosecutors must follow the well-established principles in deciding which cases to prosecute—namely, the prosecution is to weigh all relevant considerations, including priorities set by the attorneys general, seriousness of the crime, deterrent effect of criminal prosecution, and cumulative impact of particular crimes on the community. The rescinding of memorandums from the previous attorney general makes the issue less clear, in that it takes away express guidance and is more general. However, since the 2018 memorandum, no lawsuits have

been filed prosecuting those who distribute or use cannabis for medical purposes.

Lack of Evidence on Safety and Efficacy

Cannabis as a therapeutic agent has not been reviewed by the FDA to determine whether it is safe or effective; thus, cannabis products are generally not subject to the quality standards and safety information collection standards applicable to most prescription drugs (with the exception of the synthetic THC products Marinol, Cesamet, Syndros, and CBD plant-derived Epidiolex).

Moderate- to high-quality clinical evidence has emerged that establishes the efficacy of cannabis for certain therapeutic applications (Table 2); however, its safety has not been fully established by large-scale, randomized controlled trials. Some safety information does exist for cannabis (Ware, Wang, Shapiro, & Collet, 2015), but the current research does not fully encompass all available formulations of cannabis or conditions and populations treated with cannabis. Thus, the current evidence for the efficacy and safety of cannabis and cannabinoids has narrow application.

MMPs operate on the best available scientific information, which is limited by the restrictions on cannabis research. Therefore, many qualifying conditions were likely included in MMPs because of promising preclinical research (including research on animals and isolated cellular/tissue samples), anecdotal evidence, or advocacy efforts. For the majority of qualifying conditions typically included in a jurisdiction's MMP, sufficient experimental evidence does not exist to reasonably demonstrate the therapeutic efficacy, especially for long-term use. Without additional large-scale clinical studies, cannabis remains a complementary and alternative medicine. It is the hope of many researchers and medical organizations that future research will be less restricted and therefore will allow more scientific evidence to clarify well-founded dosages, delivery routes, and indications.

Qualifying Conditions by Clinical Evidence

More than 60 qualifying conditions are included across the various MMPs, the most common of which are noted in Table 3. Some of the conditions have some scientifically supportable evidence of cannabis efficacy in addressing symptoms, whereas others have no clinical evidence.

Moderate- to high-quality evidence via multiple studies is available for effective treatment with cannabis for the following conditions:

- Cachexia (Abrams et al., 2003; Andries, Frystyk, Flyvbjerg, & Støvring, 2014; Haney, Rabkin, Gunderson, & Foltin, 2005; Haney et al., 2007; Timpone et al., 1997)
- Chemotherapy-induced nausea and vomiting (Meiri et al., 2007; Söderpalm et al., 2001)
- Pain (resulting from cancer or rheumatoid arthritis) (Blake, Robson, Ho, Jubb, & McCabe, 2006; Johnson et al., 2010)

- Chronic pain (resulting from fibromyalgia) (Skrabek, Galimova, Ethans, & Perry, 2008)
- Neuropathies (resulting from HIV/AIDS, multiple sclerosis, or diabetes) (Langford et al., 2013; Turcotte et al., 2015; Wallace, Marcotte, Umlauf, Gouaux, & Atkinson, 2015)
- Spasticity (from multiple sclerosis or spinal cord injury) (Pooyania, Ethans, Szturm, Casey, & Perry, 2010)
- Seizure frequency reduction (for Dravet syndrome and Lennox-Gastaut syndrome) (Devinsky et al., 2017; Thiele et al., 2018; GW's Epidiolex Clinical Program, 2018)

Two additional conditions show promising research, but the evidence is limited to one moderate- to high-quality study each for posttraumatic stress disorder (PTSD) nightmare reduction (Jetly, Heber, Fraser, & Boisvert, 2015) and tic improvement (for Tourette's syndrome) (Müller-Vahl et al., 2002). These conditions require additional research to verify the studies' findings.

Cannabis may be effective for other conditions; however, available moderate- to high-quality research has not proven additional effectiveness to this date. Improvements in other symptoms might be attributed to the more general effects of cannabis such as sedation, appetite stimulation, and euphoria. Instead of cannabis treating underlying symptoms, these general effects of cannabis may help mask symptoms and increase a subjective sense of well-being, which could improve self-reported quality of life in some patients (Fox, Bain, Glickman, Carroll, & Zajicek, 2004; Greenberg et al., 1994).

Evaluating Evidence

Qualifying conditions included in MMP statutes may be justified with human clinical evidence, preclinical animal or cellular studies, or no study at all (Madras, 2015; Maust, Bonar, Ilgen, Blow, & Kales, 2016). Practitioners must recognize and differentiate between quality human scientific evidence and preclinical animal or cellular studies. For example, neurodegenerative conditions and those relating to brain trauma, which are included in some jurisdictional qualifying conditions, may be included due to animal or cellular research and observational studies (Mechoulam, Panikashvili, & Shohami, 2002).

No human studies have confirmed evidence for neuroprotective, antitumoral, and antibacterial effects of cannabinoids. Although some preclinical animal and cellular studies provide evidence for those effects (Russo, 2011), no generalizations can be made to the human population. Such studies are largely suggestive for future research.

Pharmacokinetics and Administration Guidelines

Endocannabinoid System

It was not until 1964 that scientists first isolated the cannabinoid THC from cannabis. Continuing research over the next 2 decades resulted in the discovery of the body's receptor for THC

TABLE 3

The Most Common Qualifying Conditions Across All U.S. Medical Marijuana Programs^a

- Amyotrophic lateral sclerosis
- Cachexia
- Cancer
- Crohn disease and other irritable bowel syndromes
- Epilepsy/seizures
- Glaucoma
- HIV/AIDS
- Multiple sclerosis
- Nausea
- Pain
- Persistent muscle spasms
- Posttraumatic stress disorder

^aThere are more than 60 qualifying conditions included among the different jurisdictional laws.

and an understanding of the endocannabinoid system (ECS). The ECS consists of endocannabinoids, cannabinoid receptors, and the enzymes responsible for synthesis and degradation of endocannabinoids (Mackie, 2008). These cannabinoid receptors are evident throughout the body embedded in cell membranes, which have important roles in homeostasis, neural development, and plasticity.

Through ECS mapping, we can now see how cannabinoids bind, protect, and act as neurotransmitters. Endocannabinoids are naturally occurring substances within the body (American Cannabis Nurses Association [ACNA], n.d.). Cannabinoid receptor 1 (CB1) is located mainly in the brain and central nervous system, but also in the peripheral nervous system (sympathetic nerve terminals) and in the pituitary gland, immune cells, heart, blood vessels, lungs, small intestine reproductive tissues, urinary bladder, adrenal gland, liver, and adipose tissue (ACNA, n.d.). Cannabinoid receptor 2 (CB2) is found predominately in peripheral immune, microglial, brainstem, skin, and spleen cells. CB2 primarily responds by inhibiting inflammatory mediators. (ACNA, n.d.).

Phytocannabinoids, cannabinoids from plant substances (cannabis), can mimic endocannabinoids and make the cells do all or most of the actions they would normally do in the presence of endocannabinoids. Although there are more than 100 cannabinoids in cannabis, the most well-known of these cannabinoids is THC; however, CBD and cannabinol (CBN) are also gaining attention (Pacher, Bátkai, & Kunos, 2006). THC reacts with both CB1 and CB2 receptors, allowing a range of effects on the body and mind. CBD does not react with either CB1 or CB2 receptors but instead interacts with enzymes of the ECS to delay reuptake of endogenous cannabinoids and modulates several noncannabinoid receptors and ion channels (ACNA, n.d.).

FDA-Approved Synthetic and Plant-Based Cannabis Medications

The FDA approved the synthetic cannabinoid products dronabinol (Marinol and Syndros) and nabilone (Cesamet) in 1985 (FDA,

2006a; FDA, 2006b). These drugs are synthetic cannabinoids primarily interacting on the CB1 receptor, similar to that of THC. Dronabinol is indicated for anorexia associated with weight loss in patients with AIDS and for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments. Nabilone is indicated for nausea and vomiting only.

Sativex, another pharmaceutical marijuana product, contains a 1:1 ratio of THC and CBD and is administered as an oral mucosal spray. Sativex is indicated for adults with moderate to severe spasticity due to multiple sclerosis who have not responded adequately to other anti-spasticity medication (GW Pharmaceuticals, n.d.). Although approved for use in over 25 countries, this product is not approved in the United States.

Epidiolex, an oral CBD plant-derived product recently approved by the FDA, is based on four clinical trials in patients aged 2 years or older with either Lennox-Gastaut syndrome or Dravet syndrome (FDA, 2018). Following Epidiolex's approval by the FDA, the DEA reclassified Epidiolex as a Schedule V drug (low potential for addiction or abuse) (DEA, 2018b).

Cannabis Administration Methods

Synthetic and plant-derived products approved by the FDA have specific administration methods. Non-FDA-approved cannabis products have varying administration methods, including inhalation via smoking, vape or vaporizer, oral mucosal sprays, edibles, concentrates (dabbing or inhaling small quantities of a concentrated and vaporized drug), cannabis oil or resin, cannabis infused butter/oil, ingestible oils, tinctures, and topicals. Smoking and oromucosal sprays are the most studied. Insufficient scientific evidence exists for the effectiveness of vaporized cannabis, edibles, dabbing, and other routes of delivery.

Generally, oral administration has delayed effects (Grotenhermen, 2003). However, delayed effects may have benefits for patients wishing to control symptoms over a longer period than what can be achieved with a comparable dose via inhalation and oromucosal delivery (Grotenhermen, 2003). Sublingual and mucosal sprays directly access the bloodstream and, as a result, oromucosal doses have less dosage variability than smoked cannabis and edibles but are limited by slower absorption and lower rate of THC delivery to the brain (Karschner et al., 2011).

Smoked and vaporized cannabis have the advantage of rapid absorption into the bloodstream (Grotenhermen, 2003). Vaporization creates fewer pyrolytic compounds that irritate respiratory tissue (Hazeekamp, Ruhaak, Zuurman, van Gerven, & Verpoorte, 2006). However, both methods show significant loss of active compounds, with an average 35% of THC directly exhaled (Hazeekamp et al., 2006; Herning, Hooker, & Jones, 1986).

Administration of medical cannabis can only be carried out by the certified patient or the designated caregivers registered to care for the patient according to the MMP. Some jurisdictions' MMP allows certain healthcare professionals to register as a des-

ignated caregiver and may administer medical marijuana (NCSL, 2019).

Storage considerations include keeping cannabis out of the reach of children, minors, and nonregistered individuals; storing all cannabis products in a locked area; keeping cannabis in child-resistant packaging; and storing raw cannabis in a cool, dry place.

Disposal of unused cannabis products should be completed according to the DEA's Disposal Act (DEA, 2018a). Generally, one can locate a collection receptacle via the DEA Registration Call Center (800-882-9539).

Dosage Considerations for Cannabis

The only specific dosing guidelines for cannabis are for those synthetic and plant-derived products approved by the FDA. These products are available through prescription, can be dispensed through a pharmacy, and may be covered by some insurance providers.

Whole plant cannabis and other non-FDA approved cannabis products cannot be prescribed. Requiring a certification of a qualifying condition from a healthcare provider, authorizing practitioners cannot provide the patient with a specific dosage, dosing schedule, or recommended delivery method. Therefore, many healthcare practitioners feel unprepared to educate patients, resulting in practitioners deferring to dispensary staff as the cannabis subject experts (Kondrad & Reid, 2013; Rubin, 2017). The patient decides which licensed dispensary to use, and the dispensary staff will offer specifics concerning administration, formulations, and dosages. However, dispensaries vary widely in their product quality, laboratory testing, proper and accurate product labelling, and employee expertise (Haug et al., 2016; Vandrey et al., 2015). A recent analysis of 31 companies selling CBD products found that only approximately 31% of products were accurately labelled (Bonn-Miller et al., 2017). This same survey found that approximately 21% of products had non-negligible amounts of other cannabinoids, including THC.

Numerous factors may alter the physiologic effects of cannabis in any given patient. Important considerations for usage and amount include the individual's age, health history, prior experience with cannabis, concurrent medications, the product's cannabinoid concentrations, method of administration, and timing of doses.

A patient survey showed that self-titration to the desired effect is the most common strategy for dosing (Hazeekamp, Ware, Muller-Vahl, Abrams, & Grotenhermen, 2013). Kowal, Hazeekamp, and Grotenhermen (2016) noted that because of the large variation in patient responses to cannabis, patients will need to understand that they must titrate their personal dosage and establish the minimum efficacious dose and a stable schedule over 1 to 2 weeks. A dosage diary, maintained by the patient or caregiver, can be helpful to keep track of dosages, administration methods, formulations, and scheduling.

Adverse Effects

Dai and Richter (2019) recently published their study—the first of its kind—on the national estimates of current and daily marijuana use among adults with medical conditions. The findings indicated that:

Compared with those with no medical conditions, adults with medical conditions had a significantly higher prevalence of current and daily marijuana use across all age groups except those aged 65 years or older. Among young adults aged 18 to 24 years with medical conditions, 25.2% reported current use of marijuana and 11.2% used marijuana on a daily basis (Dai & Richter, 2019).

This prevalence decreased with increasing age; for those aged 65 or older with medical conditions, 2.4% reported current use of marijuana and 0.9% used marijuana on a daily basis (Dai & Richter, 2019).

Additionally, the study (Dai & Richter, 2019) reported the prevalence of marijuana use by medical condition and age, as well as medical condition and marijuana administration method. There is large variation of marijuana use among adults with medical conditions across select U.S. states and territories. These results indicate that the prevalence of cannabis use both recreationally and medically is cause for surveillance of marijuana use and open discussions with patients about the benefits and risks associated with marijuana for their comorbid conditions and long-term health (Dai & Richter, 2019).

There are specific groups of patients that may be at risk when using cannabis. The lack of rigorous scientific research on cannabis limits specific safety information, however some preclinical and clinical research does provide correlative evidence for certain patient groups. Other groups may be at risk due to insufficient data to evaluate the effects of marijuana and caution should be applied.

The general adverse effects of THC can include increased heart rate, increased appetite, sleepiness, dizziness, decreased blood pressure, dry mouth/dry eyes, decreased urination, hallucination, paranoia, anxiety, and impaired attention, memory, and psychomotor performance (FDA, 2017).

Cannabinoid receptors are effectively absent in the brainstem cardiorespiratory center (Glass, Faull, & Dragunow, 1997), which is believed to preclude the possibility of a fatal overdose from cannabinoid intake. However, there are references to overdose in cannabis research that relate to situations in which patients have higher than normal blood concentrations of cannabinoids, usually from overconsumption of edible THC products (Cao, Srisuma, Bronstein, & Hoyte, 2016). These increased concentrations cause prolonged and often debilitating psychoses or hyperemesis syndrome. In some cases, these adverse effects can possibly increase the risk of fatalities (Calabria, Degenhardt, Hall, & Lynskey, 2010), though overdose of cannabinoids alone has not been proven to cause fatalities.

In the case of CBD products, only a few studies indicate adverse effects. A moderate- to high-quality study involving adults with schizophrenia and CBD use reported sedative effects (Hallak et al., 2010). In a separate study of adolescents with epilepsy using CBD, diarrhea, vomiting, fatigue, pyrexia, somnolence, and abnormal results on liver function tests were reported (Devinsky et al., 2017). Because no large-scale studies on the adverse effects of CBD have been completed, any description of CBD adverse effects in a specific population cannot be generalized.

Adolescence

Several studies show a correlation between cannabis use and poor grades, high rates of school drop out, lower income, lower percentage of college degree completion, greater need for economic assistance, unemployment, and use of other drugs (Crean, Crane, & Mason, 2011; Madras, 2015). These trends are related to recreational rather than medical cannabis use, but multiple confounding factors that may drive these correlations cannot be ignored in a clinical context, especially when clinicians are authorizing the use of compounds that can be abused (Meier et al., 2012; Schuster, Hoepfner, Evins, & Gilman, 2016; Schoeler, Kambeitz, Behlke, Murray, & Bhattacharyya, 2016; Smith et al., 2015; Yücel et al., 2008).

Fertility

No human studies are available; however, two preclinical studies indicate that interference with endogenous cannabinoids might increase chances of failed embryo implantation (Park, McPartland, & Glass, 2004) and that cannabinoids are capable of deregulating spermatogenesis, leading to reduced fertility or infertility (Di Giacomo, De Domenico, Sette, Geremia, & Grimaldi, 2016). These same cannabinoids may even alter sperm function (du Plessis, Agarwal, & Syriac, 2015).

Pregnancy and Neonates

The meta-analysis conducted by Gunn et al. (2016) indicates that exposure to cannabis in utero is associated with an increased risk of decreased birthweight and higher odds of the newborn being placed in a neonatal intensive care unit. The pooled dataset also showed a greater risk of anemia in mothers who had used cannabis during pregnancy. Only one preclinical study assessed the signaling pathways affected by prenatal THC exposure. This preclinical study shows that early exposure in utero disrupts endocannabinoid signaling and results in noticeable rewiring of mice fetal cortical circuitry (Tortoriello et al., 2014). Presently, there are no reliable data for neurodevelopmental outcomes with early exposure to cannabis in neonatal life, through either breastfeeding or second-hand inhalation (Jaques et al., 2014; Jutras-Aswad, DiNieri, Harkany, & Hurd, 2009; Volkow, Baler, Compton, & Weiss, 2014). THC can be detected in breast milk shortly after use; however, the effects of THC in breast milk on neonatal development and neurologic function is currently unknown (Baker et al., 2018). A number of low-

quality observational studies attempted to elucidate patterns of use and developmental outcomes, but their methods were imprecise or lacked longitudinal evaluation (cited in Gunn et al., 2016)

Immunocompromised Patients

Cannabis and cannabinoid preparations (gels, tinctures, drops, sprays) can pose a serious risk to immunocompromised patients if not prepared in a sterile environment (National Academies, 2017; Thompson et al., 2017). Many jurisdictions require laboratory testing of cannabis for contaminants (Rough, 2017). The local health department or MMP can provide more information on the quality-assurance practices in a specific jurisdiction.

Dyskinesia

It is highly likely that cannabis will exacerbate symptoms of poor balance and posture in patients with dyskinetic disorders (Greenberg et al., 1994).

Altered Cognition

Research regarding cognitive deficits is more abundant in healthy adult participants. Insufficient evidence exists for cognitive effects in individuals with conditions that already may affect cognition (Weier & Hall, 2017). The research that does exist suggests that patients who suffer from diseases with neurologic symptoms may show greater cognitive impairment (reviewed in Walsh et al., 2017). This exacerbation of symptoms may decrease the overall effectiveness of cannabis as a therapeutic in such patients (Koppel et al., 2014). Clinical studies have shown that patients with MS who smoke cannabis at least once per month show an increase in cognitive impairment and are twice as likely to be classified as globally cognitively impaired as those who do not use cannabis (Koppel et al., 2014). Cognitive impairment by cannabis may be dose- and age-dependent (Crean et al., 2011; Solowij & Pesa, 2012). Insufficient clinical data exist on the cognitive impairment of healthy children and adolescents.

Mania and Predisposition to Mania

There is a significant relationship between cannabis use and subsequent exacerbation and onset of bipolar disorder manic symptoms, with a roughly threefold increased risk of new onset of manic symptoms (Gibbs et al., 2015). Individuals with bipolar disorder and a cannabis use disorder also have an increased risk (odds ratio = 1.44) of suicide attempts (Carrà, Bartoli, Crocarno, Brady, & Clerici, 2014). However, these findings are not conclusive for causality. The observed correlation of cannabis use that precedes or coincides with the manic symptoms of bipolar disorder, as well as the association between cannabis use and new-onset manic symptoms and depressive disorders, suggests a tentative causal influence of cannabis on the development of bipolar disorder symptoms (Baethge et al., 2008; Lev-Ran et al., 2014).

Schizophrenia

Although accumulating evidence suggests a link between cannabis exposure and schizophrenia, no research exists that concludes that cannabis use causes schizophrenia (Walsh et al., 2017). Research supports a correlation between cannabis abuse and significantly more and earlier psychotic relapses among schizophrenic patients (Linszen, Dingemans, & Lenior, 1994). The literature on cannabis and schizophrenia is scant and spread across low-quality studies and morphologic studies, but a comprehensive overview of cannabis and psychosis, schizophrenia, and schizophreniform disorder can be found in Wilkinson, Radhakrishnan, and D'Souza (2014).

Pre-existing Conditions

Individuals with asthma, bronchitis, emphysema, or any pulmonary disease should be cautioned about the use of inhaled cannabis (Hall & Solowij, 1998; Tashkin, 2013); patients with heart problems, alcohol and other drug dependence, or illnesses that may be exacerbated by cannabis use should be cautioned about the use of cannabis (FDA, 2004). Anyone with severe diseases of the liver or kidneys should also take special precaution that the metabolic breakdown of cannabinoids does not worsen their conditions (Ishida et al., 2008; Parfieniuk & Flisiak, 2008). In patients who suffer from seizures, high concentrations of THC may promote seizures (Katona, 2015; Rosenberg, Tsien, Whalley, & Devinsky, 2015).

Individuals with a history of suicide attempt or who are at risk for suicide and those with schizophrenia, bipolar disorder, or other psychotic condition should be informed about the risks of cannabis use and be advised to not use cannabis. Individuals with PTSD may experience distinct adverse outcomes if they also develop cannabis use disorder and should be monitored closely (Walsh et al., 2017). The risk of suicide and cannabis use is a contentious area of study. Current findings are contradictory, and more research is needed to confirm any association between cannabis use and suicide risk while controlling for numerous confounding variables (Walsh et al., 2017). Individuals with a greater risk of psychological disturbances and suicidal ideation should take precautions when using cannabis as a therapeutic (Wilkinson, Radhakrishnan, & D'Souza, 2014).

Policy Statements and Warnings

The American Academy of Pediatrics (AAP) is opposed to marijuana use in patients aged 0 to 21 years due to the data supporting the negative health and brain development effects of marijuana. The AAP also opposes the use of marijuana outside the processes of the FDA; however the AAP does recognize that marijuana may be an option for children with life-limiting or severely debilitating conditions or for whom current therapies are inadequate (Committee on Substance Abuse, 2015).

Similarly, the American College of Obstetricians and Gynecologists (ACOG) encourages women who are pregnant or contemplating pregnancy to discontinue marijuana use due to con-

cerns regarding impaired neurodevelopment. Also, marijuana use is discouraged during lactation and breastfeeding due to insufficient data evaluating the effects of marijuana use on breastmilk and infants (Committee on Obstetric Practice, 2017).

Very recently, the U.S. Surgeon General issued an advisory on marijuana use and the developing brain (U.S. Department of Health & Human Services, 2019), stating that no amount of marijuana use during pregnancy or adolescence is known to be safe. Currently, the safest choice for pregnant women and adolescents is not to use marijuana.

In September 2019, the Centers for Disease Control and Prevention (CDC), FDA, state and local health departments, and other clinical and public health partners were investigating a multistate outbreak of lung injury associated with e-cigarette product (devices, liquids, refill pods, and/or cartridges) use (CDC, 2019). The CDC released interim recommendations for healthcare providers, health departments, and the public and stated, “Until we know more, if you are concerned about these specific health risks, CDC recommends that you consider refraining from using e-cigarette or vaping products” (CDC, 2019).

Abuse, Dependence, and Withdrawal

Substance-induced psychosis (SIP) is characterized by hallucinations, paranoia, delusions, confusion, and disorientation (American Psychiatric Association, 2013). SIP most frequently results from the ingestion of large doses of THC, which results in SIP episodes that are typically acute and resolve relatively quickly (Wilkinson et al., 2014).

Cannabis use disorder is defined as a problematic pattern of cannabis use leading to clinically significant impairment or distress; the clinical indications are included in the *Diagnostic and Statistical Manual of Mental Disorders*, 5th edition (American Psychiatric Association, 2013). Long-term cannabis use has the potential to lead to addiction, especially in individuals who are predisposed to addiction; approximately 9% of individuals who try cannabis are at risk for addiction (Lopez-Quintero et al., 2011). This percentage increases to roughly 16% among adult users with a history of adolescent cannabis use and to 25% to 50% among adults who use cannabis daily (Caldeira, Arria, O’Grady, Vincent, & Wish, 2008; Hall & Solowij, 1998).

Cannabinoid hyperemesis syndrome is a clinical diagnosis typically seen in patients younger than 50 years with a long history of marijuana use (Lu & Agito, 2015). The presentation includes severe, cyclic nausea; vomiting; and compulsively taking extremely hot showers or baths. Other associated nonspecific symptoms are diaphoresis, bloating, abdominal discomfort, flushing, and weight loss. These symptoms are relieved with long, hot showers or baths and cessation of marijuana use (Lu & Agito, 2015).

The average amount and duration of cannabis use required to establish dependence and withdrawal symptoms are poorly understood (Freeman & Winstock, 2015; Verweij et al., 2010).

However, mild withdrawal symptoms have been reported in less than 7 days with a regimen of 20 mg of THC taken every 3 to 4 hours (Jones, Benowitz, & Hering, 1981). Withdrawal symptoms for cannabis include irritability, nervousness, sleeping difficulties, dysphoria, decreased appetite, restlessness, depressed mood, physical discomfort, strange and vivid dreams, craving, and anxiety (Hesse & Thylstrup, 2013).

Ethical Considerations

The care of patients by nurses in any capacity is grounded in ethical practice—that is, the moral principles that guide one’s conduct. Beneficence, nonmaleficence, autonomy, fairness, and loyalty are some of the more common moral principles that guide one’s conduct. In addition to personal ethics, nurses are also guided by standards of practice, which are based on professional values and/or a code of ethics. Awareness of one’s own beliefs and attitudes about any therapeutic intervention is vital, as nurses are expected to provide patient care without judgment. Regarding the care of patients using medical marijuana, nurses should approach their patients without judgment regarding their choice of treatment or preferences in managing pain and other distressing symptoms.

Although medical cannabis legislation is evolving and more jurisdictions are adopting MMPs, social acceptance may not be evolving at the same pace. In addition, scientific evidence for cannabis use exists for some but not all conditions. The evolution of legislation, social acceptance, and scientific evidence creates ethically challenging patient care situations. Ethical decision making regarding a patient’s care must include the patient as well as the family, caregivers, and other practitioners involved in the patient’s care.

Necessary considerations regarding a patient’s treatment with cannabis include, but are not limited to:

- Clinical indications, such as diagnosis, history, goals for use of medical marijuana, probability of success, and other options for care
- Patient’s personal preferences based on information of benefits and risks
- Attention to decision making by the patient’s proxy, parent, or guardian (if the patient is incapacitated in decision making or is a minor)
- Quality of life based on the patient’s subjective viewpoint
- Situational context, such as family and other important relationships, economic factors, access to care, and potential harm to others.

Conclusion

Without evidence that is scientifically rigorous, statistically reportable, and based on patient populations, nurses will face increasing challenges concerning medical cannabis. To address these challenges, nurses must have more nuanced knowledge while caring

for patients who use medical cannabis. The principles of essential knowledge regarding legislation and legalization of cannabis, along with an understanding of cannabis pharmacokinetics, administration, safety, and ethical considerations presented in this article, will create a strong foundation for safe and knowledgeable nursing care of patients using medical cannabis.

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Caring for Patients Using Medical Marijuana

Objectives

- Explore the regulatory and legislative history of medical marijuana.
- Discuss current legislative and legal approaches to cannabis availability and dispensation.
- Identify principles to guide nurses' care of patients using medical cannabis.
- Gain an understanding of the ethical and safety considerations regarding a patient's treatment with cannabis.



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Posttest

Please circle the correct answer.

- 1. Which statement is true about historical restrictions of the use of medical marijuana?**
 - a. Cannabis was neither used for illnesses nor sold over the counter until 2000.
 - b. Cannabis remained restricted until legalization by all states in 2017.
 - c. There have never been any restrictions on the use or prescription of cannabis for designated illnesses.
 - d. By 1936, every state had passed a law to restrict possession of cannabis and eliminate its availability as an over-the-counter drug.
- 2. What is the regulatory authority for restricting the use of cannabis by prohibiting healthcare practitioners from prescribing cannabis?**
 - a. The Food and Drug Administration
 - b. The Comprehensive Drug Abuse Prevention and Control Act
 - c. There was no regulatory basis for restricting the use of cannabis for medical purposes.
 - d. NCSBN recommendations
- 3. What is the current legislative status on legalizing the use of cannabis for medical purposes?**
 - a. There are 33 states plus the District of Columbia, Guam, Puerto Rico, and all provinces/territories of Canada that have passed legislation legalizing the use of cannabis for medical purposes.
 - b. There is federal legislation legalizing the use of cannabis for all states and federal jurisdictions.
 - c. The only legalization of medical marijuana was approved in California.
 - d. There is still no legislative authority to use cannabis for medical purposes.
- 4. What are the guidelines for nurses who care for individuals utilizing cannabis?**
 - a. There are plenty of evidence-based, clinical resources for nurses to use when caring for patients who use medical cannabis products.
 - b. All qualifying conditions for cannabis use that are present in statutes have credible evidence of their effect.
 - c. The safety of cannabis in the treatment of certain conditions has been fully established by large-scale, randomized clinical trials.
 - d. The principles suggested by the Medical Marijuana Nursing Guidelines Committee guide nurses' care of patients using medical cannabis.
- 5. Where can nurses find the specifics of each jurisdiction's medical marijuana legislation to stay current with unique characteristics that might affect their practice?**
 - a. The jurisdiction's medical marijuana program (MMP) or department of health
 - b. The Federal Assembly of State Legislatures
 - c. The federal medical marijuana registry
 - d. The jurisdiction's law enforcement agency
- 6. Why is cannabis considered a Schedule I Controlled Substance?**
 - a. To allow opportunities for research
 - b. Because there is low potential for abuse
 - c. Because there is high potential for abuse, no accepted medical use in the United States, and lack of an acceptable level of safety for use even under medical supervision
 - d. For its high medical value
- 7. What is the trend in current medical marijuana state legislation?**
 - a. Medical cannabis laws have not yet been successfully passed by state legislatures.
 - b. Medical cannabis legislation has still not been enacted in the U.S. Virgin Islands or Guam.
 - c. State legislative interest has been impeded by federal prohibitions.
 - d. The trend among states is toward legalizing cannabis for medical use.
- 8. What, if any, provisions are granted for the use and distribution of cannabis?**
 - a. MMPs include various provisions regarding the process for procurement and distribution of cannabis.
 - b. There are only provisions for the amount of cannabis distributed to an individual.
 - c. There are only provisions for legal protections extended to patients, caregivers, or healthcare providers for the use of cannabis.
 - d. There are no authorized provisions for the use and distribution of cannabis.
- 9. What are the qualifications for a patient to use medical cannabis?**
 - a. They must be of sound mind.
 - b. They must have a certified qualifying condition.
 - c. They must register with their local state MMP.
 - d. Both b and c

10. What are the criteria for a qualifying condition?

- a. Clinical evidence of effectiveness for that condition
- b. Based on U.S. Food and Drug Administration standards for safety and efficacy
- c. Included in the list of qualifying conditions within an MMP
- d. Justified by either preclinical animal or cellular studies

11. How should nurses ethically approach patients using medical marijuana?

- a. Suggesting other options and alternatives for managing pain and other symptoms
- b. Without judgment regarding the patient's choice of treatment or preferences in managing pain and other distressing symptoms
- c. Exclusively, with the patient, without any interference from family, caregivers, or other practitioners involved in the patient's care
- d. Using current legislation, social acceptance, and scientific evidence as a guide

12. How can nurses address the increasing challenges concerning medical cannabis?

- a. Examine current evidence, which is scientifically rigorous, statistically reportable, and based on patient populations.
- b. Use personal judgment when providing patient care to patients using medical marijuana.
- c. Create a strong foundation for safe and knowledgeable nursing care of patients using medical cannabis through essential knowledge of legislation and legalization of cannabis.
- d. Disregard standards of practice based on professional values and/or a code of ethics.

Evaluation Form (required)

1. Rate your achievement of each objective from 5 (high/excellent) to 1 (low/poor).

- Explore the regulatory and legislative history of medical marijuana.
1 2 3 4 5
- Discuss current legislative and legal approaches to cannabis availability and dispensation.
1 2 3 4 5
- Identify principles to guide nurses' care of patients using medical cannabis.
1 2 3 4 5
- Gain an understanding of the ethical and safety considerations regarding a patient's treatment with cannabis.
1 2 3 4 5

2. Rate each of the following items from 5 (strongly agree) to 1 (strongly disagree):

- The authors were knowledgeable about the subject.
1 2 3 4 5
- The methods of presentation (text, tables, figures, etc.) were effective.
1 2 3 4 5
- The content was relevant to the objectives.
1 2 3 4 5
- The article was useful to me in my work.
1 2 3 4 5

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