Marijuana and Cannabis Questions we need to ask

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Marijuana, it seems, is everywhere. Nearly a dozen states have approved cannabis for recreational use and more than two-thirds have signed off on medical marijuana.[1] Marijuana's active chemical components are becoming more widespread, too. Cannabidiol (CBD), which is derived from cannabis, has popped up seemingly overnight in products from skin cream to candy to dog treats. Hemp, another marijuana analog, already appears in thousands of commercial products. The number is likely to increase thanks to a recent loosening of restrictions on hemp cultivation.[2] With so much going on around marijuana, it makes sense to review what we know and what it might mean for workers' compensation.

Nearly a dozen states have approved cannabis for recreational use and more than two-thirds have signed off on medical marijuana.[1]

It's no secret that the growing popularity of various forms of cannabis increases the likelihood that their use will become a bigger consideration within workers' comp in the coming years, but before we dive into the implications, let's define what we're talking about. In workers' comp, we often use the terms "marijuana" and "cannabis" interchangeably. That's understandable given marijuana is perhaps the more commonly used term.

While marijuana is more of a slang term encompassing the plant and associated products, the term cannabis originates from the plant genus name and is what we most often find in scientific literature. Cannabis generally refers to a preparation of the cannabis plant. Cannabis is comprised of a variety of chemical components, including cannabinoids. Cannabinoids are the active chemical constituents. It's this chemical profile — the percentage of cannabinoids in cannabis — that determines a product's potency and effects. Therefore, the makeup of the cannabis is what matters more than the various strain names or plant species type.[3]

How it works

The simple question of how cannabis works gives way to an intriguing answer. The focus is often on plant-derived cannabinoids. Yet, interestingly, humans have their own cannabinoid systems. Our bodies produce what are called endocannabinoids, or endogenous cannabinoids. Humans possess two cannabinoids receptors: CB1 and CB2. These receptors, found throughout the body, are where various cannabinoids can exert their effects. Depending on where in the body a receptor exists, its task varies. Regardless, in each case, the goal is balance, or homeostasis.

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As an example, let's consider the brain. CB1 receptors are located in the brain and nervous system, organs, glands, and connective tissues. These receptors are responsible primarily for regulation of cognition, memory, motor function, pain, appetite, and sedation. CB2 receptors are present on immune cells, blood-forming cells, and organs and they generally play a role in immune function.

Plant-derived cannabinoids, sometimes referred to as phytocannabinoids, affect these same systems when they are introduced to the body. It's for this reason that medical cannabis is often used to treat pain. A snapshot of patients taking medical cannabis in Colorado and Oregon in 2016 found more than nine in 10 were attempting to alleviate severe pain.[4] About a quarter of patients, who were allowed to identify more than one treatment goal, said they were attempting to combat muscle spasms and symptoms of multiple sclerosis. Fending off nausea was another reason for taking medical cannabis. Fewer patients said they were hoping to find relief from post-traumatic stress disorder, cancer, and seizures and epilepsy, among others.

It's little surprise that patients would identify varying goals when taking cannabis. Proponents point to numerous potential physiological effects that cannabis can produce. These include:

- Improving sleep
- Inhibiting seizures
- Offering neuroprotection
- Reducing anxiety
- Improving psychotropic symptoms
- Preventing nausea
- Stimulating appetite
- Reducing intraocular pressure
- Acting as a bronchodilator
- Relieving pain
- Countering inflammation
- Serving as an anti-proliferative
- Fighting viruses
- Relaxing muscles and reducing muscle spasms

Among the cannabinoids with therapeutic interest, tetrahydrocannabinol (THC) has a number of well-known characteristics such as its psychoactive, analgesic, and anti-nausea properties. Less often known is that THC is also regarded as being neuro-protective and anti-inflammatory.

CBD, by comparison, does not possess psychoactive properties because it shows little affinity for interacting with the CB1 or CB2 receptors, the body's main cannabinoid receptors. Instead, CBD tends to bind to the TRPV1 receptor. This tendency is similar to capsaicin, the chili pepper extract that is sometimes used as a pain reliever. Because CBD alone doesn't produce a high, it's the subject of a good deal of research and numerous orphan drug status designation applications.

When combined with THC's CBD tends to blunt some of unwelcome side effects such as anxiety, dysphoria, panic reactions, and paranoia. At the same time, introducing CBD along with THC can improve some of the therapeutic activity of THC.[5]

Recreation vs. medication

It is important to note there is not a distinct difference between recreational and medical marijuana. Most of what is used recreationally contains THC; that's what causes the high. Cannabis used for medicinal purposes may or may not contain THC. If the product is higher in CBD or purports to be "CBD-only," the user might not experience euphoric effects. Yet there is much variability to consider. For example, cannabinoid products that are marketed as "CBD" products are intended to have a low psychoactive response and little to no THC. If, however, the patient is obtaining cannabis from a dispensary, which would most often be the case, the amount of THC depends on the blend or the plant strain and the chemical profile. Several dispensaries list the chemical makeup — that is, the amount of THC vs. CBD, for example — on the labeling, but there is no regulation to determine accuracy.

There are a number of ways users can obtain the effects of cannabis. It can, of course, be inhaled by smoking or vaporization. It can be eaten in food or delivered through lozenges or lollipops. It can pass through skin as a topical or rectal formulation. Naturally, how the drug is taken helps determine its effects, duration, and possible side effects. For example, smoking or vaping marijuana brings an immediate reaction. By comparison, eating foods that contain marijuana slows the initial reaction through the digestion process though it lengthens the duration.

Side effects can vary

Just as the ingredients and methods of taking cannabis vary, so too do the potential adverse side effects. These can include a rapid heart rate, an irregular heart rate, and hypertension. The drug can also interfere with breathing by causing lung irritation, coughing, wheezing, and production of sputum. Gastrointestinal challenges, such as nausea, vomiting, and dry mouth, can also arise. The potential neurological fallout reads like the boilerplate of a pharmaceutical commercial: Side effects can include lethargy, sedation, drowsiness, slowed reaction time, impaired motor coordination, dizziness, loss of balance, and loss of muscle control.

Also possible are decreased focus, impaired judgment, disorientation, confusion, impaired short-term memory and memory formation, recollection, red eyes, and dilated pupils. Perhaps most famously, the psychoactive side effects can include euphoria, hallucinations, anxiety, and even addiction. A rare but particularly concerning effect is referred to as cannabinoid hyperemesis syndrome in which the cannabis user experiences ongoing cyclic vomiting.

Cannabis can present further risks when combined with other drugs. It can interact with central nervous system depressants, the blood thinner warfarin, tricyclic antidepressants, antiepileptic drugs, hydrocortisone, and antibiotics, for example. Research on some of these drug interactions is lacking because cannabis remains a Schedule I Controlled Substance. This designation means it is defined as having "no currently accepted medical use and a high potential for abuse." It is illegal at the federal level and is therefore difficult to study in the U.S. through controlled trials.

Medical providers should talk with patients to understand their histories and perhaps identify some of the potential effects that might occur. In general, for example, cannabis can exacerbate the effects of other drugs that make patients lethargic.

There are other factors to take into account. Does the patient have a history of psychosis? What about cardiovascular disease or respiratory disease? Is she pregnant? Is there a history of a substance-use disorder?

Cannabis should be considered with the same rigor as other medications in terms of potential side effects, drug interactions, and dosing levels. As with other drugs, some patients merit particular caution. These include those who are under age 25, have active mood disorders, have risk factors for cardiovascular disease, or who use high levels of alcohol or benzodiazepines.

There are other safety considerations that aren't always in play with fully legal medications. Some of these worries are over inconsistency of the product, packaging and labeling, and quality and purity. Beyond that, improper testing can fail to account for undisclosed contents or to identify contaminants.

Variations in the percentages of a product's composition mean one product could be very different from another that contains the same ingredients but at different levels. In fact, every dispensary's product is different. Manufacturers might have similar dosages of THC and CBD, but the varying inactive ingredients could potentially alter absorption, distribution, and metabolism.

Few studies have been done to better understand the efficacy, safety concerns such as drug-drug interactions and side effects, proper dosing ranges, or limitations of use related to inhaled or ingested medical cannabis.

What we know

Despite its widespread availability, we don't have reams of research about the effects of cannabis. Advocates point to a multitude of medicinal benefits ranging from the relief of chronic pain to reducing stress levels to fighting cancer. Yet few studies have been done to better understand the efficacy, safety concerns such as drug-drug interactions and side effects, proper dosing ranges, or limitations of use related to inhaled or ingested medical cannabis.

Many clinicians believe cannabis has a different effect than synthesized cannabinoids. The plant form of cannabis has many distinctive cannabinoid and non-cannabinoid constituents that might work "synergistically." This is the so-called entourage effect. Cannabis products might also be less expensive than pharmaceutical cannabinoids. But the more expensive prescription preparations possess excellent quality control, especially if they're approved by the U.S. Food & Drug Administration (FDA). Plus, pharmaceutical cannabinoids involve precise dosing. Regardless of whether a patient is using cannabis, or its pharmaceutical counterparts, clinicians and consumers should consider the start-low-and-go-slow approach when it comes to dosing.

What might work and what doesn't

While more research is needed, we do have a gathering of evidence that cannabis can bring benefits for some conditions.[6] Here are a few:

- Neuropathic pain: Moderate-quality evidence to support use
- Chronic pain: Conclusive or substantial evidence to support use
- Cancer pain: Cannabis can be a useful adjunct
- Nausea and vomiting: Conclusive or substantial evidence suggesting improvements
- Spasticity (multiple sclerosis (MS) or paraplegia): Moderate-quality conclusive or substantial evidence to support use

A review of the research suggests there are areas where cannabis might offer only limited evidence supporting use. These include Tourette syndrome, HIV/AIDS (appetite/weight loss), anxiety, post-traumatic stress disorder (PTSD), and traumatic brain injury.

There are other conditions where evidence doesn't support use of cannabis or oral cannabinoids . These include acute pain, multiple sclerosis-related tremors, Huntington's disease, glaucoma, schizophrenia, dementia, and depression.

The FDA has allowed some products derived from cannabis. In June 2018, the agency approved Epidiolex®, a liquid extract form of CBD. It's administered as an oral solution for the treatment of seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients aged two and above.

Other formulations have been around longer. In the 1980s, the FDA approved two other pharmaceutical-grade products derived from cannabis. They remain available by prescription. These are dronabinol (or Marinol® or Syndros®) and nabilone (or Cesamet®) and are similar to THC or are synthetic versions of this cannabinoid. Both are indicated for the treatment of chemotherapy-induced nausea/vomiting and appetite enhancement for anorexia due to AIDS or cancer. The FDA's product labeling includes a warning that these products can, like other cannabinoids, affect the central nervous system. The warning also notes the formulations carry the potential for misuse and to produce psychological dependence: The "effects on the mental state are similar to those of cannabis," the agency noted.

What about hemp-derived CBD?

The Agriculture Improvement Act, also known as the Farm Bill, was signed into law in December 2018. With it came the deregulation of hemp-derived cannabis products, namely CBD derived from plants containing no more than 0.3% THC by dry weight. This legislation effectively removed these specific types of products from the definition of cannabis in the Controlled Substances Act. That meant they were no longer classified as illegal at the federal level, thus allowing for less restricted use. However, the Farm Bill explicitly preserved the FDA's authority to regulate hemp-derived CBD products under the Food, Drug & Cosmetic Act (FDCA) and section 351 of the Public Health Service Act. This means that such goods are still subject to the same laws and requirements as any FDA-regulated product that contains any other substance.

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Even though it retains oversight, challenges remain as the FDA works to keep pace with the booming CBD industry. In general, in order for a company to market a product as a drug — defined by the FDCA as any product intended to have a therapeutic or medical use — that product must receive pre-market approval through the FDA's formal drug approval process including human clinical trials or through Over-the Counter (OTC) Drug Review. Unapproved new drugs cannot be distributed or sold, and the FDA has issued more than 90 warning letters over the past 10 years to CBD companies related to fraudulent product and health claims made on websites, social media, and in stores. The FDA also asserts that it has tested the chemical contents of many of these CBD products, and a number of the results have shown inconsistent or inaccurate components. This can be of particular concern for injured workers as several of the "CBD-only" products have been found to contain THC, the component that would show up on a urine drug test.

Further, products containing CBD cannot be marketed as a food or dietary supplement because this is the same ingredient found in an FDA-approved drug product (i.e., Epidiolex). Therefore, CBD is considered a drug. The agency has concerns about the number of products claiming to contain CBD that are marketed for therapeutic or medical uses that have not been approved by the FDA. The FDA regards this as a patient-safety issue. Overall, the FDA's message to the consumer is buyer beware. The FDA continues to gather research data and safety and public health input to develop an applicable regulatory framework, especially when it comes to non-drug uses of cannabis.

Cannabis and treatment guidelines

Many widely used treatment protocols discourage use of cannabis. The Official Disability Guidelines (ODG) don't recommend using cannabinoids to combat pain. Likewise, the American Society of Addiction Medicine (ASAM) states physicians should not recommend that their patients use marijuana for medical purposes.

A task force formed by the American College of Occupational and Environmental Medicine (ACOEM) and the American Association of Occupational Health Nurses (AAOHN) recommended that employers develop policies concerning marijuana use in the workplace and consider the following points:[4]

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- If workers are covered by federal drug-testing regulations (for example, Department of Transportation drivers or others under a federal contract), cannabis use on or off the job is prohibited. Employers could use urine drug screening to ensure compliance.
- If workers are in safety-sensitive positions, they must not be impaired by any substance. Employers could consider banning on-the-job cannabis use even for those workers not covered by federal drug-testing regulations. Employers should also consider their policies in light of state statutes. For employers weighing whether to allow cannabis use, it also is logical to consult with a qualified health professional.
- If cannabis use is allowed, employers should establish a clear policy — with legal advice —and educate employees on the policy and how to evaluate impairment. Communication aimed at educating employees is critical. This should start when a worker is hired and occur regularly.
- If employers choose to prohibit employees from working if impaired by cannabis, there should be clear policies and procedures for supervisors to follow in identifying potential impairment. This would include a process for referring an employee suspected of impairment for an occupational medical evaluation and the resulting actions by human resources departments. Supervisors and workers should be educated about how to recognize signs that an employee might be impaired. This could result from medical cannabis, prescription medications, illicit drugs, alcohol, OTC medications, fatigue, or a combination of these factors.
- If employers are in or near states that allow use of recreational marijuana, they should consider establishing a policy around off-work use of cannabis. In many states, the employer may choose to prohibit employees from working while using or under the influence of cannabis or may choose to prohibit marijuana use both on and off the job.

While national guidelines do not recommend cannabis, this could relate to a lack of large quality-controlled trials. The drug's designation as a Schedule I Controlled Substance has limited the ability to conduct research.

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In those states that do allow use of medical cannabis (along with Washington D.C., Guam, and Puerto Rico), comprehensive programs often include provisions that provide protection from criminal penalties for using cannabis for a medical purpose, according to an analysis by the National Conference of State Legislatures. The rules also often allow people to access cannabis by growing it at home or by obtaining it through dispensaries or some other setup. The provisions also tend to allow for a variety of strains, including those more potent than "low THC." Other rules permit smoking or vaporization of some kind of cannabis product, plant material, or extract.

Final thoughts

What's most clear is that the environment around cannabis is changing. This makes it imperative for those involved in the treatment of injured workers to try to keep up with the shifting rules and to consider the questions that arise in the workplace around cannabis. And employers need to consider their role, too. As use of cannabis and related products such as CBD and hemp increase, there will be more questions about what is permissible in the workplace and how to regulate it. This is a topic that will require recurring and sustained attention.

About Nikki Wilson

Nikki is a Pharm.D. who graduated with her Doctor of Pharmacy and Master of Business Administration (MBA) from Creighton University. As a licensed Pharmacist, Nikki has over nine years of comprehensive industry experience through leadership roles overseeing prescription home delivery programs, clinical pharmacy operations and benefit management, and product development. Today, she is responsible for developing pharmacy product strategy and program capabilities at Coventry with a focus on enhancing patient safety and returning people to work, to play, and to life.

About Coventry

Coventry offers workers' compensation care-management and cost-containment solutions for employers, insurance carriers, and third-party administrators. With roots in both clinical and network services, Coventry leverages more than 35 years of industry experience, knowledge, and data analytics. As a part of the specialty division of Aetna our mission is returning people to work, to play, and to life. And our care-management and cost-containment solutions do just that. Our networks, clinical solutions, specialty programs, and business tools will help you focus on total outcomes.

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