Parkinson's Foundation 
Consensus Statement on the Use of Medical Cannabis for Parkinson's Disease 

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Parkinson’s Foundation Consensus Statement on the Use of Medical Cannabis for Parkinson’s Disease

With the growing availability of medical marijuana and other medical cannabis products in the United States, there has been a marked increase in its use for various medical conditions. Currently, medical cannabis is legal in 33 states and the District of Columbia, as well as the U.S. territories Guam, Puerto Rico, the Northern Mariana Islands and the U.S. Virgin Islands. Of these, 17 states list Parkinson’s disease (PD) as a qualifying condition: CA, CT, FL, GA, IL, IA, MA, MO, NH, NM, NY, OH, OK, PA, SC, VT and WV. Cannabidiol (CBD) and hemp products (defined as having less than 0.3% tetrahydrocannabinol - THC) are legally available in all 50 states.

With an array of non-motor and motor symptoms, many people with Parkinson’s disease have looked to medical cannabis to provide some relief. However, little is known about the effects of medical cannabis for Parkinson’s symptoms or the potential side effects and safety issues. To address this, the Parkinson’s Foundation convened a group of experts on March 6-7, 2019 in Denver, CO, to discuss available evidence for the use of cannabis for PD, and gaps in knowledge. This group of more than 40 individuals included physicians, basic scientists, a pharmacist, a PD nurse, industry members, non-profit organizations, the PD community and Foundation staff.

The primary goal of this statement is to provide guidance to both people with Parkinson’s and their physicians for the safe use of medical cannabis for PD. A secondary goal is to uncover gaps in knowledge that should be addressed through rigorous research studies. Regardless of whether a medical cannabis product is approved for Parkinson’s in the future, this will help to inform its use for PD so that it is used in the safest, most effective way possible.
About Cannabis and Available Products

Cannabis contains more than 400 different compounds, of which 100 compounds called cannabinoids have been isolated. The best-known cannabinoids are delta-9-tetrahydrocannabinol (THC), which is responsible for cannabis’ more prominent effects on a person’s mental state (e.g. getting high), and cannabidiol (CBD), which has less of an effect on mental status.

Cannabinoids interact with receptors in the brain called CB1 and CB2. CB1 is concentrated in the central nervous system and CB2 is associated with modifying inflammatory responses and the immune system.

Top Takeaways on the Use of Medical Cannabis for PD

With increased availability of medical cannabis in the US, and increased interest in the PD community, the Parkinson’s Foundation wanted to provide a document to guide our community in making informed decisions about using cannabis for PD.

1. Our experts urge caution: there are adverse effects, toxicity issues, and drug to drug interactions, and we don’t fully know what this means for people with PD who are taking PD medications.

2. Given the lack of any clear data supporting the use of cannabis in PD, the Foundation does not endorse their use for PD symptoms or to modify disease progression. However, because we realize that people with PD are interested in trying cannabis products, we are providing guidance for both general safety as well as working with dispensaries.

3. Some studies have suggested cannabis may be beneficial for non-motor symptoms such as sleep disturbances, pain, anxiety, and gastrointestinal issues. However, these studies are generally small, uncontrolled (meaning there is no placebo comparison, which increases the risk of false positive results), and are open label (meaning both the health providers and patients are aware of the drug or treatment being given, which could influence the results). More rigorous research is needed to determine if there is any medical benefit.
There are many different varieties of cannabis products. These include:

- **Marijuana**, a dried mixture of cannabis and flowers. It is the most widely used cannabis product recreationally and medically and can be smoked, vaporized, or ingested orally.
- **HU-210** is a synthetic street cannabinoid also referred to as “spice” or “K2” that is used recreationally. HU-210 is 100-800 times more potent than THC from cannabis. It is associated with increased toxicity that can be severe and even life-threatening.
- **Hemp** is any part of the cannabis plant that contains less than 0.3% THC on a dry weight basis and is used for its fibrous material or oil for a number of manufacturing and food products. Hemp contains low levels of CBD, but the flowering portions of hemp can be used to extract CBD.
  - CBD oil is considered a “nutraceutical,” a combination of “nutrition” and “pharmaceutical,” and therefore is not regulated by the U.S. Food and Drug Administration (FDA).

- **Epidiolex®,** a plant-based CBD pharmaceutical product, approved in 2018 by the FDA as a Schedule V drug for the treatment of two juvenile forms of epilepsy, Lennox-Gastaut syndrome and Dravet syndrome. Schedule V drugs are considered by the Drug Enforcement Administration (DEA) to have a currently accepted medical use in treatment, but may lead to limited physical or psychological dependence.
- **Dronabinol** and nabilone are older cannabis medications, which are synthetic THC drugs used for the treatment of cancer-induced nausea/vomiting, AIDS, appetite stimulation, etc.
- **Sativex®,** is a combination, THC and CBD, pharmaceutical product approved in Europe. Sativex® is a mouth spray intended to alleviate nerve pain, spasticity, overactive bladder, and other symptoms of...
multiple sclerosis. Currently in the U.S., Sativex® is being evaluated in Phase III clinical trials to relieve persistent chronic pain to patients with advanced cancer.

Available Evidence for Using Medical Cannabis for Parkinson's

Managing PD symptoms is complex. Treating the motor symptoms of the disease must be balanced against potential motor complications of treatments (such as involuntary movement, known as dyskinesia) and motor fluctuations—changes in movement associated generally with taking levodopa), while also taking into account the impact of non-motor symptoms (such as sleepiness, cognitive impairment and low blood pressure) that can also result from therapies.

Drawbacks of Previous Study Findings

Despite the remarkable popularity of marijuana and the surrounding publicity about its potential medical benefits, there have been only four randomized trials of cannabinoids in patients with PD. In a randomized trial participants are divided by chance into separate groups that compare different treatments or other interventions.

These trials have uniformly failed to find evidence of benefit. However, the of lack consistency in the ways the studies were conducted, the ways in which cannabis was given, and the way outcomes were measured, make these studies inconclusive at best. The studies are further limited by small sample sizes (7 to 24 patients) and ill-defined placebos, the inert substances used in comparison with the treatment. There have been no published randomized controlled trials of the effects of smoked cannabis compared to placebo in the PD population.

In 2014 the American Academy of Neurology (AAN) Guideline Development Subcommittee concluded that oral cannabis extract is “probably ineffective” for treating PD patients with dyskinesia (Koppel et al, 2014).
Possible Benefits of Cannabis
In surveys, some PD patients have reported benefits from cannabis products for tremors, and slow and involuntary movement. These benefits were demonstrated in an open-label study of 22 cannabis users and single use of smoked cannabis (Lotan et al 2014). Many of the subjects in this study also noted improvements in ratings of pain and sleep. Although some reports have suggested improvement in pain, anxiety, sleep problems (such as insomnia), weight loss, and nausea, no randomized trials have been performed examining these factors in PD.

We thus do not know whether these reported effects are truly related to cannabis use or may represent placebo effects or other biases in the study. We also do not know the optimal dose or types of cannabinoids to use for PD symptoms.

Potential Side Effects and Safety Issues
Cannabis has shown promise for alleviating some PD symptoms in animal models and in some non-rigorous studies of cannabis in people that did not compare cannabis with a placebo or other treatment. However, there are important side effects and safety issues to consider.

Lung effects
Different forms of cannabis (such as smoking, edibles and topical forms) have different effects on the body. Smoking or vaporizing cannabis creates smoke or vapor that when inhaled can cause issues with breathing. Chronic, heavy use may cause damage to the lungs, increasing risks of lung cancer and emphysema.

Toxicity
When cannabis is taken orally, the effects usually appear much more slowly and last longer than with smoking (after around 60 minutes, and the effects can last 4-8 hours). Oral cannabis products (edibles) have an increased risk of toxicity because it can take a long time for them to have an effect; their effect lasts a long time; and absorption in the body varies for each person. As a result, people may ingest more and more of the product while waiting for the anticipated effects to occur. With many of the oral products, there is a substantial variability in how much THC and CBD they contain.

Drug interactions
Cannabis also has several interactions with other drugs. The different liver enzymes that break down cannabis are also the same enzymes that are responsible for the breakdown of other medications. This in turn creates potential
drug interactions with cannabis if taken at the same time as interacting medications. Drug interactions can potentiate the adverse effects of cannabis (such as sleepiness and anxiety) or they can interact by making certain medications more or less effective. Caution is thus advised and persons on medications should discuss cannabis use with their doctor or pharmacist.

Dependency and addiction
There is a concern about cannabis dependency and addiction. Its use can also result in decreased motivation, which may become a barrier to promoting and maintaining a healthy lifestyle, especially as apathy may already present a significant problem in PD. In a systematic review conducted by the American Academy of Neurology, 6.9% of participants stopped using cannabinoid products due to adverse effects (Koppel, Neurology, 2014). Controversy surrounds the risk of abuse and the idea of cannabis as a “gateway drug.” Some studies have estimated that up to 10% of cannabis users may become addicted and experience withdrawal symptoms after they stop using it. While it is generally believed that people cannot overdose on cannabis, life-threatening complications have been associated with synthetic cannabinoids.

Other adverse effects
There are several different adverse effects associated with cannabis including short-term memory loss, dizziness, fatigue, behavioral and mood changes, and hallucinations. Cannabis is also associated with an increased risk of anxiety and depression. The presence of these complications in people with PD is not well established. However, in PD, these adverse effects may have more serious consequences. Notable side effects have been documented in clinical trials including low blood pressure, imbalance and fatigue.

Lack of regulation
There are no federal standards or regulations to ensure correct amounts of cannabis in compounds, accurate labeling of CBD amounts, or product purity. Studies of compounds obtained through dispensaries found that labels frequently were inaccurate with products.
both containing more or less of key cannabinoids (e.g. THC) than indicated on the label.

We Need More Rigorous Research

“Will marijuana help my PD?” is one of the most frequently asked questions by patients, but the answer is not easy (Robledo and Jankovic, 2017). Despite enormous information in the lay press and social media about the potential benefits of marijuana or various marijuana products there is a remarkable lack of scientific, evidence-based data on the effectiveness and safety of medical cannabis in PD (Kluger et al. 2015).

There is a huge unmet need to develop well-designed studies that will address the question of whether cannabis-based medicines offer therapeutic benefit in the treatment of motor and non-motor symptoms of PD, levodopa-induced dyskinesia, or even as a treatment to treat the underlying disease (Peres et al. 2018).

The number of unanswered questions about the use of cannabinoids in PD far outweighs what we know. Complicating factors include the unusual degree of anecdotal reports (accounts of a person’s experience without scientific evidence), firmly held beliefs despite the absence of rigorous scientific evidence, and widespread access to a variety of poorly regulated compounds. In addition, people with Parkinson’s are frustrated that many of their symptoms are inadequately controlled by traditional therapies, while compounds that have been used for medicinal purposes for thousands of years are inadequately studied and not easily accessible by prescription, and have no guidelines on use and side effects. While the frustration (often shared by health care providers) is understandable, we must study cannabis as rigorously as we do other treatments.

Areas of Interest for Future Researchers

Future research must address several questions the Parkinson’s community finds pressing. These include:

• **How might cannabis be useful in the treatment of PD?**
  There is little evidence so far that cannabinoids are helpful for levodopa-induced dyskinesias. However, there is some evidence that they may help to reduce tremor. It would be helpful to determine if cannabis might treat distressing non-motor symptoms of PD, including sleep disturbances, pain, anxiety and possibly even stomach problems.
• **Are cannabinoids safe for people with Parkinsons?**
Although some people report that cannabis helps them with some non-motor symptoms commonly associated with PD, there are also concerns that they could cause or worsen other problems, such as cognitive impairment, decision-making capacity, imbalance, low blood pressure, apathy and possibly even psychosis and impulse control disorders. Data are needed on potential interactions between cannabinoids and medications used to treat PD or its complications. Researchers also should determine what other factors contribute to individual variations in response to cannabis. For example, women respond differently from men with respect to changes in pain perception.

• **How should cannabis be used?**
There is some evidence that CBD may be more beneficial if it contains small quantities of THC. The way a person uses cannabis can have a profound impact on response. Edibles, while widely thought to be safer than other forms of cannabis, in fact are often associated with toxic effects. Because it takes much longer for edibles to have an effect compared to other forms of cannabis, people are more likely to overdose themselves as they think they haven’t taken enough. This is further complicated by lack of information about the concentration, purity, and potential contaminants in commercially available preparations of CBD. Neither the most beneficial compounds of marijuana nor the most effective doses are known at this time.

• **Could cannabinoids be used to treat the underlying disease?**
Perhaps. Drugs acting on CB2 receptors in the brain, which are associated with modifying inflammatory responses and the immune system, may potentially protect the nervous system in Parkinson’s and other diseases that affect the nervous system. However, the role of modulating inflammation in Parkinson’s is not yet established and there are no data yet in humans supporting the use of cannabinoids for this purpose.

• **What about clinical trials?**
A few clinical trials are already underway but there is much more
work to be done. The most promising avenue for now seems to be the use of CBD for the symptomatic relief of non-motor symptoms associated with PD (anxiety, sleep disturbances, and pain). Preliminary studies need to combine assessment of the most effective way to take cannabis, the most effective dose, and a careful assessment of potential side effects.

Guidance for Using Cannabis for Parkinson’s
In the absence of any clear data supporting the use of cannabinoid products in PD, the Parkinson’s Foundation does not endorse their use in PD. However, we recognize that people may decide to try cannabinoid products for certain symptoms. If you decide to try cannabinoid products we suggest:

- Keep your healthcare providers informed of any use of cannabinoid products, because they may interact with other medications and may cause side effects that could influence your PD care.

- Treat cannabis products as you would any new medication. Always start at a low dose and go up slowly. CBD-only products may also be less likely to cause side effects and could be considered before trying products also containing THC.

- For pain in one specific area, consider creams or patches to reduce general side effects. Be cautious when ingesting edible products, as they can have delayed side effects and increased toxicity.

- Consider working with a single dispensary. As these products are not regulated, do not assume the “dose” on a label obtained from one dispensary will have the same effects as one obtained from a different dispensary.

- Be aware of potential side effects, particularly dizziness, problems with balance, worsening motivation, dry mouth and impaired thinking and memory.
Obtaining Medical Cannabis Through a Dispensary

A dispensary is a location one visits to purchase medical cannabis. They are regulated and taxed according to the state they are located. Dispensaries are not the same as pharmacies in that you will not get a prescription from your doctor for a specific product or dose. You should work with the person at the dispensary to find products that may fit your symptoms. Some dispensaries have staff who are interested in medical uses of cannabinoids, but not all have staff who are equally knowledgeable or helpful. As cannabis products are not tightly regulated, we recommend that you work with the same dispensary, as products that appear similar based on their labels could have very different concentrations of cannabinoids and effects in different dispensaries. You may want to talk to people at your support group or shop around to find a dispensary with knowledgeable staff.

Obtaining A Medical Marijuana License

Depending on your state, some dispensaries require a medical marijuana license. While the process to acquire a medical marijuana may vary, it can typically include the below steps:

- First you may need to visit a physician to complete paperwork for you to get a license. If your primary care physician is not comfortable filling out this paperwork, there are doctors who are licensed to prescribe marijuana for medical use. These doctors may be associated with dispensaries and often work for a cash fee.

- Once the physician paperwork is completed, the physician will typically submit it online or by mail and then you will be required to apply for a license through your state. This typically involves proof of state residency and a small fee.

- Once you get your license you can go to a medical dispensary and purchase the products.

If you live in a state that has both recreational and medical marijuana dispensaries you have the option of getting a license or purchasing cannabinoid products from the recreational dispensary, which does not require a license. People will sometimes decide to not get a license if they want to sample these products without going through a doctor or if they have concerns about being on a state registry. In
general, the products on the recreational side are typically similar to what is available with a license.

Advantages to getting a license may include paying a lower price for products (in Colorado for example you avoid paying a 40% tax by having a license) and the potential of working with staff at dispensaries that may have greater experience in working with older adults and persons with medical issues.

Learn more about Parkinson’s Foundation research at Parkinson.org/Research.

Learn more about Parkinson’s disease and medical marijuana at Parkinson.org/Marijuana.