Medical Marijuana

My name is John CM Brust. I am a Professor of Neurology at Columbia University College of Physicians & Surgeons in New York, and I thank the chairs of the Health and Judiciary Committees for the opportunity to discuss Pennsylvania Senate Bill 3 providing for the medical use of Cannabis. The Pennsylvania Neurological Society, whose board voted to oppose this bill, invited me to testify because, as a member of the Guideline Development Subcommittee of the American Academy of Neurology, I co-authored a "Systematic Review of the Efficacy and Safety of Medical Marijuana in Selected Neurologic Disorders." Our literature search yielded 1729 abstracts from scientific journals, of which only 34 full-text articles met inclusion criteria. On the basis of this review, our committee concluded that certain chemical compounds present in Cannabis plants are probably effective in relieving certain symptoms in multiple sclerosis, namely subjective spasticity, painful spasms, central pain, and urinary frequency. Cannabinoid medications are ineffective in treating tremor in multiple sclerosis or abnormal movements in Parkinson disease. Data are insufficient to support or refute benefit in treating Huntington disease, Tourette syndrome, cervical dystonia, or epilepsy.

A problem in putting these data into practice is that the only cannabinoid agents that qualify for Level A recommendation---in other words, established as effective---are marketed as oral Cannabis extracts containing combinations of the cannabinoid compounds tetrahydrocannabinol (THC) and cannabidiol (CBD). Oral sprays containing THC and CBD, oral THC, and a THC analogue nabilone qualify only for Level B recommendation. Oral extracts and oral spray combinations are not available in the United States. THC and nabilone are available but are FDA-approved only for wasting in AIDS and chemotherapy-induced nausea.

Senate Bill 3 includes as "qualified medical conditions": epilepsy and seizures, amyotrophic lateral sclerosis, Parkinson disease, traumatic brain injury, post-concussion syndrome, spinocerebellar ataxia, post-traumatic stress disorder, and severe fibromyalgia. There is no scientific evidence that cannabinoid compounds, alone or in combination, are of benefit in any of these disorders.

Senate Bill 3 is long on bureaucratic structure and short on pharmacology. "Medical cannabis" is to include "extracted oils, edible products, ointments, and tinctures." Who among the 65 authorized processors will determine the proportion of THC, CBD, or other cannabinoid compounds in treating each of the Bill's "qualified medical conditions" for which there is no evidence of benefit? Cannabis contains over 60 cannabinoid compounds as well as several hundred non-cannabinoid compounds. Which will be present in the "extracted oils, edible products, ointments, and tinctures?"

What about side-effects? The bill fails to mention that not only the efficacy but also the safety of Cannabis therapy is unknown, yet it exempts from liability members of the State Board that will supervise the bureaucracy. In fact, acute intoxication from Cannabis can last more than24 hours, resulting in a state of continuous cognitive impairment in daily users. Chronic Cannabis use can cause lasting cognitive impairment and altered brain structure, documented in both animal and human studies. Cannabinoid compounds are addictive---chronic use induces craving.

There is a reason the United States has a Food and Drug Administration charged with verifying the safety and efficacy of pharmaceutical products. The FDA was created to protect the public from purveyors of snake oil. Senate Bill 3 is an attempt to make an end-run around that protection, relying on anecdotal testimonials and political pressure rather than scientific evidence.

Finally, I also participated in drafting for the American Academy of Neurology, which has 27,000 members, a "Legislative Position Statement on the Use of Medical Marijuana in Neurological Disorders." Approved by the AAN Board of Directors, the Statement declared, "The AAN does not advocate for the legalization of marijuana-based products for use in neurologic disorders at this time, as further research is needed to determine the benefits and safety of such products."

Thank you for your attention. I am happy to answer questions.

Position Statement: Use of Medical Marijuana for Neurologic Disorders

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Background Information

The American Academy of Neurology (AAN) is a professional organization of over 28,000 practicing neurologists and neuroscientists with a deep and abiding interest in assuring the best possible care of patients with all types of neurologic disorders. With officials at state and federal levels adopting policies regarding the use of medical marijuana, it is important for the AAN to have an official position on the issue that can assist policymakers.

Description of the Issue

In this position statement, the term "marijuana-based products" refers both to marijuana and to products derived from it. The current medical marijuana legislation being passed by policymakers across the country, which promotes marijuana-based products as treatment options for various neurologic disorders, is not supported by high-level medical research. In addition, there is concern regarding the safety of marijuana-based products, especially for long term use in patients with disorders of the nervous system. The interaction of these compounds with prescription medications is also unknown. Therefore, further research is urgently needed to determine the safety and medical benefit of various forms of marijuana in neurologic disorders, especially those where anecdotal evidence is available. Anecdotal evidence may engender public support for the use of these products but such evidence must be substantiated by rigorous research, which will in turn inform legislative policy.

The AAN's Position

The AAN supports all efforts to conduct rigorous research to evaluate the long-term safety and effectiveness of marijuana-based products. The AAN, for research purposes, requests the reclassification of marijuana-based products from their current Schedule 1 status so as to improve access for study of marijuana or cannabinoids under IRB-approved research protocols. The AAN does not advocate for the legalization of marijuana-based products for use in neurologic disorders at this time, as further research is needed to determine the benefits and safety of such products. This is of paramount importance when marijuana-based products are used in patients with underlying neurologic disorders, or in children whose developing brains may be more vulnerable to the toxic effects of marijuana.

The AAN recognizes that there may be potential use for these agents in the treatment of some neurologic disorders.[1] However, there is not sufficient evidence to make any definitive conclusions regarding the effectiveness of marijuana-based products for many neurologic conditions.[2] Many of the cannabis preparations used in studies are not available in the United States. It is not appropriate to extrapolate the results of trials of standardized preparations to other, non-standardized, non-regulated cannabis products

which may be commercially available in states with laws supporting the use of medical marijuana. Effectiveness of a non-standardized product is not equal to that of standardized products that are studied in clinical trials. Additionally, most currently available marijuana-based products are not regulated by any agency and may not contain the products mentioned by labeling. Quality control is therefore impossible, raising further safety questions. Each product and formulation of cannabis should demonstrate safety and effectiveness via scientific study similar to the process required by the Food and Drug Administration (FDA).

Rationale

Currently, the federal government classifies marijuana products as a Schedule I drug, defined as having no currently accepted medical use and a high potential for abuse. Therefore, state law does not protect an individual who prescribes such products from federal prosecution unless the individual obtains a Schedule I license from the Drug Enforcement Agency (DEA). Some states have enacted bills allowing medical providers to prescribe marijuana-based products, but only if they contain non-psychoactive ingredients. Reclassification by the DEA will expedite future research on marijuana-based products as it will reduce barriers to study participation by investigators who do not possess a schedule I license.

History and Basic Science

Use of marijuana-based products to treat neurologic disorders dates back to the 1800s.[2] Marijuana is derived from the plant Cannabis sativa, which contains over 60 different pharmacologically active compounds referred to as cannabinoids.[3] Delta-9-tetrahydrocannabinol (THC) is the major psychoactive compound which causes the euphoric effect. Other cannabinoid compounds such as cannabinol and cannabidiol (CBD) are not known to have psychoactive properties. Cannabinoid compounds have the potential for therapeutic benefit in a number of neurologic diseases. However, the psychoactive effects can acutely alter a patient's cognition and inhibit normal functioning. Long-term effects on learning and memory may occur. Thus, from a safety perspective, the use of products with a high THC component is controversial. Research is necessary to develop marijuana-based compounds that have minimal psychoactive properties while retaining other desirable, therapeutic pharmacologic effects.

Laws and Regulations

Several agencies and organizations have provided position statements calling for more research on marijuana-based products.[4-6] As of this writing, Minnesota and Colorado have funded studies to assess the efficacy of marijuana-based products. Several states also have passed legislation supporting decriminalization of marijuana based products when used for medical purposes. The legislation typically requires patients to possess a valid registration, based on letters from a physician stating that they have a debilitating medical condition. The legislation also provides for registration of centers to cultivate and sell marijuana products for medical use. The legislation does not usually specify what symptoms of the condition are expected to be improved by medical marijuana. Therefore, patients with one of the medical conditions listed may request letters from their physicians supporting their medical use of marijuana without clear information regarding what exactly is being treated. The legislation does not differentiate between different forms of marijuana, such as oral, smoked, or other marijuana-

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based products, which may have different effectiveness and safety profiles.

Available Studies

Case reports and limited studies have addressed the efficacy of marijuana-based products in treating various neurologic disorders.[7-10] A recent evidence-based guideline by the AAN provided support for the use of specific oral and oromucosal forms of cannabis to improve some symptoms in patients with multiple sclerosis.[1] A subsequent AAN systematic review of medical marijuana for neurologic disorders concluded that oral cannabis extracts are probably ineffective for treating levodopa-induced abnormal involuntary movements in Parkinson's disease, but it did not find evidence for or against the use of oral cannabinoids for several other conditions.[2] These and other reviews emphasize the need for further research. Importantly, there is no evidence to support the use of smoked cannabis.

In clinical studies, side effects of cannabis have included nausea, dizziness, mood changes, hallucinations or suicidal ideation, feeling of intoxication, and increased weakness.[2] Seizures have been reported rarely.[1] The safety of long-term use remains uncertain. Addiction to recreationally used marijuana is controversial, but there is some evidence of tolerance and dependence related to long term heavy use.[11-13] Evidence also suggests that chronic recreational use of marijuana may cause impairment in memory, concentration, and executive functioning. It is unclear how long these effects persist after stopping marijuana use or whether there may be permanent nervous system toxicity.[14-17] One study[18] found that cannabis extracts were associated with memory and verbal learning deficits. The psychopathological and cognitive side effects of marijuana-based products are of concern in patients who may be more vulnerable because of their underlying neurologic disorders. Safety concerns are even greater when considered for use in children.

Position Statement History

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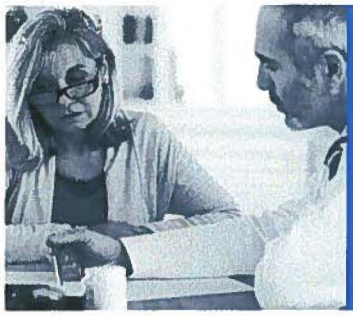

AMERICAN ACADEMY OF NEUROLOGY

Summary of Systematic Review for **PATIENTS** and their **FAMILIES**

MEDICAL MARIJUANA IN CERTAIN NEUROLOGICAL DISORDERS

This fact sheet presents the current research on medical marijuana (cannabis) for treating certain neurological disorders.

The American Academy of Neurology (AAN) is the world's largest association of neurologists and neuroscience professionals. The AAN is dedicated to promoting the highest quality patient-centered care for people with diseases of the brain and nervous system. Experts from the AAN carefully reviewed the available scientific studies on the safety and effectiveness of cannabis use in certain neurological disorders. The following information is based on evidence from those studies.*

To read the full systematic review, visit *AAN.com/guidelines.*

What is medical marijuana?

Marijuana is an herb that grows naturally in the United States. It is also known as cannabis. Medical marijuana is cannabis used as medicine. When used as a drug, marijuana can produce both mental and physical effects. These result from two main types of chemicals in the plant: cannabidiol (CBD) and tetrahydrocannabinol (THC). CBD and THC are taken from the cannabis plant for use in medicine. They also can be created (synthesized) in a lab. THC has a stronger intoxicating effect than CBD.

Is medical marijuana legal to use? Is it regulated?

Cannabis is a federally controlled substance. Until recently, it has been illegal to sell, possess/carry, or use. At this time, doctors can prescribe medical marijuana legally in 21 US states and Washington, DC.

The US Food and Drug Administration (FDA) has approved only two forms of marijuana for medical use: dronabinol (Marinol) and nabilone (Cesamet), both available in pill form. Dronabinol and nabilone are synthetic forms of key ingredients in marijuana. The FDA approved both drugs for treating nausea and vomiting associated with cancer chemotherapy that do not respond to standard treatment. Dronabinol also is approved for loss of appetite associated with weight loss in patients with AIDS. At this time, the drugs are not approved for other uses. In general, clinicians prescribe medical marijuana only when standard treatment has not helped.

The studies examined here looked at four forms of medical marijuana:

- Oral cannabis extract (OCE), a pill made of either pure CBD or a combination of CBD and THC
- Synthetic THC, a human-made form of THC available as a pill
- Nabiximols (Sativex), a mixture of THC and CBD available in oral spray form
- Smoked marijuana in cigarettes of standard drug strength

Which disorders were studied? What do the studies show about medical marijuana for treating these disorders?

This review examined only those studies that met AAN quality standards. Studies with the best design produce the highest quality evidence.

The available studies examined evidence for the safety and effectiveness of medical marijuana for these conditions:

- Various symptoms of multiple sclerosis (MS)
- Temporary, uncontrolled movements as a drug side effect in Parkinson disease (PD)
- Motor (movement) symptoms in Huntington disease (HD)
- Tics in Tourette syndrome
- Cervical dystonia (abnormal neck movements)
- Seizures in epilepsy

Of the studies examined here, only two looked at use of smoked marijuana. One study focused on smoked marijuana for treating pain related to spasticity in MS. The other looked at safety for use in MS. The studies did not provide enough evidence* to show if smoked marijuana is safe or effective.

The evidence from the studies is described below and in the table that follows.

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Symptoms of MS

The studies showed that medical marijuana in pill or oral spray form can help treat certain MS symptoms.

Spasticity and Related Symptoms

Spasticity is chronic muscle tightness. It causes the muscles to become stiff and hard to the touch. Spasticity also can cause pain and painful muscle spasms. These occur when the muscle contracts (tightens) uncontrollably.

Evidence Supporting Use

- There is strong evidence* that OCE pills made from pure CBD:
  - Can help lessen patients' reported spasticity symptoms short-term
- Moderate evidence* shows that THC pills and oral spray:
  - Probably help lessen patients' reported symptoms of spasticity short-term
  - Probably help lessen cramp-like pain or painful spasms
- There is weak evidence* that OCE pills and THC pills:
  - Might help lessen patients' reported spasticity symptoms if treatment is continued for at least one year
  - Might lead to improvement on tests for spasticity a doctor performs, but only if treatment is continued for at least one year

Evidence Against Use

- There is moderate evidence* that OCE pills, THC pills, and oral spray:
  - Probably do *not* lead to improvement short-term on tests for spasticity a doctor performs

Other MS Symptoms

Evidence Supporting Use

- Strong evidence* shows OCE pills:
  - Can help lessen central pain (feelings of painful burning, "pins and needles," and numbness)
- Moderate evidence* also shows the oral spray:
  - Probably helps lessen frequent urination

Evidence Against Use

- Moderate evidence* shows that OCE pills and THC pills:
  - Probably do *not* help lessen frequent urination and bladder control problems
  - Probably do *not* help lessen tremor (shaking) in MS
- Weak evidence* shows the oral spray:
  - Might *not* help lessen tremor in MS

There is not enough evidence to show if the oral spray helps lessen overall bladder symptoms.

Other Neurological Conditions

Temporary, Uncontrolled Movements in PD

For people with PD, common symptoms are shaking, stiffness, and slowness of movement. Clinicians typically treat these symptoms with the drug levodopa. However, in the late stages of the disease, the drug itself can cause temporary, abnormal movements to develop. Moderate evidence* shows that OCE pills likely do *not* help relieve abnormal movements caused by levodopa.

HD, Tourette Syndrome, Cervical Dystonia, Epilepsy

There is not enough evidence* to show whether medical marijuana in pill or oral spray form:

- Reduces motor symptoms in HD
- Relieves tic severity in Tourette syndrome
- Lessens abnormal neck movements in cervical dystonia
- Reduces how often seizures occur in epilepsy

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Important Concerns About Cannabis

There are safety concerns about the use of cannabis. All cannabis products have side effects, and some can be serious. Side effects include:

- Difficulty with attention or concentration
- Dizziness or fainting symptoms
- Drowsiness or tiredness
- Dry mouth
- Feelings of intoxication
- Hallucinations (seeing or hearing things that are not there)
- Impaired judgment or coordination
- Increased spasticity
- Increased weakness
- Loss of balance and falls
- Nausea, vomiting, and constipation
- Psychological problems such as depression or psychosis
- Thinking (cognition) and memory problems

The long-term safety of cannabis is unknown. Most of the studies were short in duration. More research is needed on complications from long-term use. These include serious psychological problems such as depression, suicidal thoughts, and psychosis. About one in every 100 people (or 1 percent of the population) will be affected. More research also is needed on the risk of lung cancer from long-term use of smoked cannabis.

Table: Evidence for Safety and Effectiveness of Medical Marijuana

Findings, by Disorder and Drug Formulation	Strength of Evidence
MS: Spasticity and Related Symptoms	
OCE • Can reduce patients' reported symptoms of spasticity	Strong
OCE • Probably does **not** lead to improvement short-term (12–15 weeks) on tests for spasticity a doctor performs Synthetic THC • Can probably reduce patients' reported symptoms of spasticity • Can probably lessen cramp-like pain or painful spasms • Probably does **not** lead to improvement short-term (15 weeks) on tests for spasticity a doctor performs Oral Spray (Nabiximols) • Can probably lessen patients' reported symptoms of spasticity short-term (6 weeks) • Probably does **not** lead to improvement short-term (6 weeks) on tests for spasticity a doctor performs • Can probably lessen cramp-like pain or painful spasms	Moderate
OCE and Synthetic THC • Might lessen patients' reported symptoms of spasticity if continued for at least one year • Might lead to improvement on tests for spasticity a doctor performs, if treatment continued for at least one year	Weak
Smoked Cannabis • Not enough evidence to show if safe or helpful for pain related to spasticity	Unknown
MS: Central Pain	
OCE • Can help lessen central pain (feelings of painful burning, "pins and needles," and numbness)	Strong
MS: Bladder Problems	
OCE and Synthetic THC • Probably do **not** help lessen frequent urination and bladder control problems Oral Spray (Nabiximols) • Probably helps lessen frequent urination (at 10 weeks)	Moderate
Oral Spray (Nabiximols) • Not enough evidence to show if helps lessen bladder problems overall	Unknown
MS: Tremor	
OCE and Synthetic THC • Probably do **not** help lessen tremor in MS	Moderate
Oral Spray (Nabiximols) • Might **not** help lessen tremor in MS	Weak
PD: Temporary, Uncontrolled Movements	
OCE • Probably does **not** help lessen abnormal movements caused by levodopa	Moderate

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HD: Motor Symptoms	
Synthetic THC • Not enough evidence to show if helps lessen motor symptoms	Unknown
Tourette Syndrome: Tic Severity	
Synthetic THC • Not enough evidence to show if helps lessen tic severity	Unknown
Cervical Dystonia (Abnormal Neck Movements)	
Synthetic THC • Not enough evidence to show if helps lessen abnormal neck movements	Unknown
Epilepsy: Seizure Frequency	
Any Form of Cannabis • Not enough evidence to show if helps lessen how often seizures occur	Unknown

Note: For spasticity in MS, more improvements were seen from patients' reports of symptom relief than from doctors' tests of spasticity. For seizure frequency in epilepsy, there were no studies of high enough quality to review.

This systematic review was endorsed by the American Autonomic Society, the American Epilepsy Society, the Consortium of Multiple Sclerosis Centers, the International Organization of Multiple Sclerosis Nurses, and the International Rett Syndrome Foundation.

This statement is provided as an educational service of the American Academy of Neurology. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved.

*After the experts review all of the published research studies, they describe the strength of the evidence supporting each conclusion:
Strong evidence = more than one high-quality scientific study
Moderate evidence = at least one high-quality scientific study or two or more studies of a lesser quality
Weak evidence = the studies, while supportive, are weak in design or strength of the findings
Not enough evidence = either different studies have come to conflicting results or there are no studies of reasonable quality

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Summary of Systematic Review for **CLINICIANS**

AMERICAN ACADEMY OF NEUROLOGY

EFFICACY AND SAFETY OF THE THERAPEUTIC USE OF MEDICAL MARIJUANA (CANNABIS) IN SELECTED NEUROLOGIC DISORDERS

This is a summary of the American Academy of Neurology (AAN) systematic review regarding the use of medical marijuana (cannabis) for treating selected neurologic disorders.

Please refer to the full systematic review at *AAN.com/guidelines* for more information, including a definition of the classification of evidence.

Forms of Cannabis

A variety of formulations were used in the studies examined, with differing amounts of tetrahydrocannabinol (THC) and cannabidiol (CBD): Some were pills, one was a mucosal spray, and some were vaporized or smoked. See Table 1 in the published systematic review for specific formulations.

Do cannabinoids relieve spasticity in patients with multiple sclerosis (MS)?

Strong evidence	Oral cannabis extract (OCE) is established as effective for reducing patient-reported scores (**2 Class I studies**).
Moderate evidence	OCE is probably ineffective for reducing objective measures at 12 to 15 weeks (**1 Class I study**).
	THC is probably effective for reducing patient-reported scores (**1 Class I study**).
	THC is probably ineffective for reducing objective measures at 15 weeks (**1 Class I study**).
	Nabiximols is probably effective for reducing patient-reported symptoms at 6 weeks (**1 Class I study**) and probably ineffective for reducing objective measures at 6 weeks (**1 Class I study**).
Weak evidence	OCE is possibly effective for reducing objective measures at 1 year (**1 Class II study**).
	THC is possibly effective for reducing objective measures at 1 year (**1 Class II study**).
Insufficient evidence	Smoked marijuana is of uncertain efficacy (**insufficient evidence**).

Overall, 1,619 patients were treated with cannabinoids for less than 6 months. Meta-analysis of simple proportions yielded 6.9% (95% confidence interval [CI] 5.7%–8.2%) who stopped the medication because of adverse effects (AEs). Of the 1,118 who received placebo, 2.2% (95% CI 1.6%–3.5%) stopped because of AEs. Data on the symptoms that caused medication withdrawal were often incomplete.

Clinical Context

Standard medical therapy was continued in these studies, so no comment can be made as to comparative effectiveness.

Multiple methods of measuring spasticity exist. A recent study used correlations with changes on a standard Patient Global Impression of Change scale to determine that a ~ 30% change in spasticity, as measured by the patient-reported numeric rating score, best represented a clinically important difference. More improvements were seen in subjective measures than objective measures, possibly explained in part by the overall improvements in "feelings" or well-being provided by marijuana, or by pain relief allowing improved mobility.

What is the efficacy of using cannabinoids to treat central pain or painful spasms in MS?

Strong evidence	For patients with MS with central pain or painful spasms, OCE is effective for reduction of central pain (**2 Class I studies**).
Moderate evidence	THC or nabiximols (**1 Class I study each**) is probably effective for treating MS-related pain or painful spasms.
Insufficient evidence	Smoked marijuana is of unclear efficacy for reducing pain (**2 Class III studies that examined different issues**).

Do cannabinoids help treat bladder dysfunction in MS?

Moderate evidence	Nabiximols is probably effective for reducing the number of bladder voids per day at 10 weeks (**1 Class I study**).
	THC and OCE are probably ineffective for reducing bladder complaints (**1 Class I study**).
Insufficient evidence	Nabiximols is of unknown efficacy in reducing overall bladder symptoms (**contradictory Class I studies**).

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Do cannabinoids help treat tremor in MS?

Moderate evidence	THC and OCE are probably ineffective for treating MS-related tremor (**1 Class I study**).
Weak evidence	Nabiximols is possibly ineffective (**1 Class II study**).

Do cannabinoids reduce symptoms in involuntary movement disorders?

Motor Symptoms in Huntington Disease

Insufficient evidence	Whereas the 2 studies identified suggest lack of benefit, both were underpowered to detect differences, and thus no reliable conclusions can be drawn (**1 Class I study, 1 Class III study**).

Levodopa-induced Dyskinesias in Parkinson Disease

Moderate evidence	OCE is probably ineffective for treating levodopa-induced dyskinesias in patients with Parkinson disease (**1 Class I study**).

Tic Severity in Tourette Syndrome

Insufficient evidence	For patients with Tourette syndrome, data are insufficient to support or refute efficacy of THC for reducing tic severity (**1 Class II study, 1 Class III study**).

Cervical dystonia

Insufficient evidence	For patients with cervical dystonia, data are insufficient to support or refute the efficacy of dronabinol (**1 Class III study**).

Do cannabinoids decrease seizure frequency in epilepsy?

Insufficient evidence	For patients with epilepsy, data are insufficient to support or refute the efficacy of cannabinoids for reducing seizure frequency (**no Class I–III studies**).

Clinical Context

Neither the present review, nor a Cochrane review which includes abstracts, non–peer-reviewed literature, and anecdotal reports of smoked cannabis use by patients with seizure disorders, concluded there is sufficient evidence to prescribe CBDs or recommend self-treatment with smoked marijuana.

Adverse Effects

Clinical Context

Adverse effects (AEs) are a significant concern with marijuana use. Outside the setting of treatment trials, cognitive impairment is more likely to be of concern. One study of patients with MS who smoked cannabis at least once a month showed an increase in cognitive impairment. Another article showed that patients with MS who used cannabis were twice as likely to be classified as globally cognitively impaired as those who did not use cannabis. Some patients who have neurologic conditions may have preexisting cognitive dysfunction, which may increase their susceptibility to cannabinoids' toxicities. Moreover, it is especially concerning that a medication that may have an AE of suicide may be prescribed in a population such as patients with MS who already are at increased suicide risk.

The table below shows the evidence at a glance.

Table: Evidence for Use of Cannabis to Treat Symptoms of Selected Neurologic Disorders

Evidence, by Disorder and Formulation	OCE Pill	THC Pill	Oral Spray	Smoked Cannabis
MS Symptoms				
Strong Evidence				
Established as effective for reducing patient-reported spasticity scores	X			
Effective for reduction of central pain in patients with MS with central pain or painful spasms	X			

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Evidence, by Disorder and Formulation	OCE Pill	THC Pill	Oral Spray	Smoked Cannabis
MS Symptoms				
Moderate Evidence				
Probably effective for reducing patient-reported spasticity scores		X		
Probably effective for reducing patient-reported spasticity symptoms at 6 weeks			X	
Probably effective for treating MS-related pain or painful spasms		X	X	
Probably ineffective for reducing objective spasticity measures at 15 weeks		X		
Probably ineffective for reducing objective spasticity measures at 12–15 weeks	X			
Probably ineffective for reducing objective spasticity measures at 6 weeks			X	
Probably effective for reducing the number of bladder voids per day at 10 weeks			X	
Probably ineffective for reducing bladder complaints	X	X		
Probably ineffective for treating MS-related tremor	X	X		
Weak Evidence				
Possibly effective for reducing objective spasticity measures at 1 year	X	X		
Possibly ineffective for treating MS-related tremor			X	
Insufficient Evidence				
Efficacy uncertain for reducing spasticity and pain in MS				X
Efficacy unknown for reducing overall bladder symptoms			X	
PD Symptoms				
Moderate Evidence				
Probably ineffective for treating levodopa-induced dyskinesias in patients with Parkinson disease	X			
HD Symptoms				
Insufficient Evidence				
No reliable conclusions can be drawn with regard to motor symptoms in HD		X		
Tourette Syndrome				
Insufficient Evidence				
Data insufficient to support or refute efficacy for reducing tic severity		X		
Cervical Dystonia				
Insufficient Evidence				
Data insufficient to support or refute the efficacy of dronabinol		X		

OCE = oral cannabis extract (contains Δ-9-tetrahydrocannabinol and cannabidiols in varying ratio); THC = Δ-9-tetrahydrocannabinol, the main psychologically active ingredient in cannabis.

Note: Synthetic forms of OCE and THC were used in the studies. Data for seizure frequency in epilepsy not shown because no studies above Class IV available to assess.

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This systematic review was endorsed by the American Autonomic Society, the American Epilepsy Society, the Consortium of Multiple Sclerosis Centers, the International Organization of Multiple Sclerosis Nurses, and the International Rett Syndrome Foundation.

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