Policy Ahead of the Science: Medical Cannabis Laws vs. Scientific Evidence

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Key Points

- Three-quarters (37) of US states, the District of Columbia, and 3 territories have legalized medical cannabis
- 42 different conditions in various jurisdictions qualify patients to receive medical cannabis
- The number of qualifying conditions per jurisdiction varies from 5-29
- 50% of qualifying conditions have no or insufficient evidence of benefit from medical cannabis
- 9% of qualifying conditions have limited evidence of harm from medical cannabis
- The mean number of qualifying conditions per jurisdiction and the proportion of qualifying conditions with and without evidence of benefit has not varied meaningfully since 1996.

Synopsis

Forty-one US jurisdictions (37 states) have legalized comprehensive medical cannabis programs since 1996. The number of qualifying conditions per jurisdiction varies from 5-29. Five (12%) of 42 qualifying conditions have conclusive or substantial evidence of efficacy and are listed in more than half of all jurisdictions. Half (50%) of qualifying conditions have no or insufficient scientific evidence of benefit from medical cannabis; 9% of qualifying conditions have limited evidence of harm from medical cannabis. The mean number of qualifying conditions per jurisdiction and the proportion of conditions with and without evidence of benefit have not changed meaningfully since 1996.

Introduction

Legalization of medical cannabis in the United States has expanded substantially since 1996, when California became the first state to legalize medical cannabis. As of March 2022, 37 states, the District of Columbia (DC), and three US territories, Guam, Puerto Rico, and the Virgin Islands, have enacted comprehensive medical cannabis laws. In all but two jurisdictions, these laws list a variety of conditions for which a physician can recommend or certify a patient for medical cannabis. In two jurisdictions, discretion is left entirely to physicians as to which medical conditions would benefit from medical cannabis therapy, i.e., no specific qualifying conditions are listed. In addition, ten states have legalized medical cannabis only for products with low delta-9-tetrahydrocannabinol (THC)/high cannabidiol (CBD) content. All these state laws conflict with federal law. The cannabis plant and all cannabinoids derived from the plant (with the exception of hemp; see below) are classified in Schedule I of the Controlled Substances Act (CSA) of 1970. This classification legally defines them as having no accepted medical use in the United States, lack of accepted safety for use under medical supervision, and high potential for abuse. Cannabinoids derived from hemp are legal under the 2018 Farm Bill, which defines hemp as a cannabis plant with less than 0.3% delta-9-tetrahyrdocannbinol[1]. Hemp is the source of cannabinoids such as CBD and delta-8-THC that are currently sold legally in the US[1].

The legalization of medical cannabis by a political process, passage by state legislature or voter referendum, contrasts with the evidence-based process used by federal regulatory agencies such as the US Food and Drug Administration (FDA) to approve new medications for specific clinical indications. Traditionally, the FDA requires two adequately powered, phase III, randomized,

controlled clinical trials to provide evidence of efficacy and safety. Three cannabinoid-based products have been approved in the US through this process: synthetic THC (dronabinol), a synthetic THC analogue (nabilone), and a plant extract containing only CBD (Table 1). A plant extract containing a nearly 1:1 ratio of THC: CBD (nabiximols), is approved in Canada, Australia and several European countries[2]. (Table 1).

The scientific literature provides a range of systematic reviews on the evidence surrounding the efficacy of cannabis for a range of clinical conditions[3–7]. However, we are not aware of any study that explicitly compares the qualifying conditions listed in US medical cannabis laws with the strength of scientific evidence supporting cannabis therapy for that condition. This article provides a descriptive statistical analysis of the qualifying conditions listed in medical cannabis legislation and the strength of the scientific evidence for the aforementioned conditions; analyzes the distribution and overlap of various qualifying conditions across jurisdictions; examines the association between the number of qualifying conditions in a jurisdiction and the strength of scientific evidence for the listed conditions; and evaluates any changes in the aforementioned variables over time since the first medical cannabis law was enacted in 1996.

Methods

We obtained the year of enactment and the list of conditions qualifying for medical cannabis from the National Conference of State Legislatures (NCSL)[8], which keeps up-to-date information with direct access to the legislative texts on its website. Qualifying conditions were categorized as medical or psychiatric. Similar conditions described with different wording in state laws were combined for clarity in reporting. Phytocannabinoids were defined as products from the whole

plant or extracts enriched in one or more specific cannabinoids. Synthetic cannabinoids were nabilone and dronabinol (synthetic THC).

The scientific evidence for the use of medical cannabis for each qualifying condition was obtained from recent systematic reviews[3–5,7,9–15]. The strength of scientific evidence was evaluated utilizing the framework provided by the National Academies of Science, Engineering and Medicine (NASEM)[5]: conclusive, substantial, moderate, limited, or no evidence in relation to benefits and harms (Table 2). Conditions for which a cannabis product was approved for treatment by the FDA or similar national regulatory authority were graded as having conclusive evidence of benefit. We used the most favorable grade of evidence for any diagnosis within the qualifying condition, regardless of the type or formulation of cannabis product which produced the effect and regardless of whether the beneficial effect was only on secondary symptoms (e.g., pain, sleep, agitation, anxiety) rather than on the disease process itself. For purposes of evaluating changes over time, jurisdictions were grouped into 3 time periods based on first enactment of comprehensive medical cannabis legislation: 1996-2007, 2008-2015, and 2016-2021. These intervals were chosen to have roughly equivalent numbers of jurisdictions in each interval. The 10 jurisdictions with medical cannabis legislation allowing for only low THC/CBD-based products were excluded from the analysis. Formal statistical testing was not done due to the small sample sizes and limited heterogeneity across qualifying conditions, jurisdictions and time.

Results

Prevalence of US Medical Cannabis Programs

As of March, 2022, 37 states, the District of Columbia, Puerto Rico, Guam and the US Virgin Islands have enacted comprehensive medical cannabis legislation (see Appendices 1 and 2)[8]. These programs were enacted at a rate of 4-8 jurisdictions every five years from 1996-2015. The rate of enactment increased to 14 new jurisdictions during the period from 2016-2020. Three new programs were enacted in 2021. In addition, 10 jurisdictions (all states) have medical cannabis legislation allowing only for low THC/CBD-based products. Thus, only 3 states (Idaho, Kansas, Nebraska) and 2 US territories (American Samoa, Northern Mariana Islands) currently have no form of medical cannabis program.

Qualifying Conditions for Medical Cannabis

Qualifying Medical Conditions

Among the 41 jurisdictions with comprehensive medical cannabis programs, 42 different conditions are designated as qualifying: 35 (83%) medical (Appendix 1) and 7 (17%) psychiatric (Appendix 2). These qualifying conditions are not necessarily specific diagnoses but can be symptoms (e.g., pain, nausea/vomiting) or medical status (e.g., “terminal illness”). Two jurisdictions (Oklahoma, Virginia) do not specify any qualifying conditions, leaving the decision to the physician on how best to utilize medical cannabis therapy. Additionally, eighteen (44%) jurisdictions allow physicians or state health authorities to recommend medical cannabis for any condition for which it is believed the benefits of cannabis outweigh the harms. The median number of qualifying conditions per jurisdiction is 13, with a range of 5 conditions (South Dakota) to 29

conditions (Illinois) (Table 3). There was no meaningful change in the mean number of qualifying conditions per jurisdiction between the 1996-2007 period and the 2016-2021 period

The type and number of qualifying medical conditions vary substantially across jurisdictions (Table 3). Nine medical conditions have been adopted by more than 50% of jurisdictions: multiple sclerosis/muscle spasms (98%), cancer (90%), HIV/AIDS (90%), epilepsy/seizures (88%), glaucoma (83%), intractable/chronic pain (83%), cachexia/wasting syndrome (73%), Crohn's disease/inflammatory bowel disease (IBD) (68%), severe nausea/vomiting (60%), and amyotrophic lateral sclerosis (ALS) (58%). All but Crohn's and ALS were included in the original medical cannabis legislation passed in 1996. Crohn's was adopted in 2004 and ALS was adopted in 2008. Eight conditions have been adopted by 25-50 % of jurisdictions: Parkinson's disease (43%), Alzheimer's disease (40%), hepatitis C (38%), autism spectrum disorder (38%), terminal illness (38%), and neurological pathology/trauma (35%) These conditions were adopted between 1998 and 2007, except autism spectrum disorder, which was first adopted in 2016. Six conditions have been adopted by 10-24% of jurisdictions: arthritis (23%), peripheral neuropathy (15%), Huntington's disease (15%), fibromyalgia (15%), sickle cell anemia (15%), and migraine headache (15%). which were adopted between 2004 and 2012, expect for arthritis, which was designated a qualifying condition in 1996. The remaining 11 conditions have been adopted by less than 10% of jurisdictions, all occurring between 2010 and 2014. (Table 4)

Qualifying Psychiatric Conditions

The inclusion of qualifying psychiatric conditions is a more recent and less common phenomenon than medical qualifying conditions (Appendix 2). The earliest qualifying psychiatric condition was

post-traumatic stress disorder (PTSD), first adopted in 2011. It is the only psychiatric condition adopted by more than 25% of jurisdictions. (Table 5)

Strength of Scientific Evidence for Medical Cannabis

The strength of scientific evidence for each qualifying condition is listed in Table 6. The number of qualifying conditions with each level of evidence is listed in Table 7. Evidence is summarized separately for phytocannabinoids (i.e., plant-derived) and two synthetic cannabinoids (nabilone, dronabinol).

Among the 35 qualifying medical conditions, 5 (14%) qualifying conditions have conclusive or substantial evidence of benefit, 5 (14%) qualifying conditions have moderate evidence of benefit, 4 (11%) qualifying conditions have limited evidence of benefit, 21 (60%) qualifying conditions have no or insufficient evidence of benefit; and 2 (6%) qualifying conditions have limited evidence of harm.

Among the seven qualifying psychiatric conditions, one (14%) has moderate evidence of benefit, two (28%) have limited evidence of benefit from medical cannabis, two (28%) have no or insufficient evidence of benefit, one (14%) condition has limited evidence of harm, and one psychiatric condition (PTSD) has limited evidence for harm with phytocannabinoids and limited evidence of benefit with synthetic cannabinoids. Below we provide additional detail about the evidence relating to each qualifying psychiatric condition.

Anxiety is graded as having moderate evidence of efficacy, based on 31 published studies (including 17 randomized controlled trials)[7,9,11]. Efficacy was shown for anxiety accompanying

other conditions (cannabis plant, THC, THC: CBD combinations) and for social anxiety (oral cannabidiol in two one-day studies). No study evaluated other specific anxiety disorders such as panic disorder.

Autism spectrum disorder is graded as having limited evidence of efficacy based on 4 open-label observational studies using CBD-enriched cannabis plant extracts[15]. All studies showed improvement in secondary symptoms such as anxiety, sleep, and agitation. One study also showed improvement in core autism symptom domains such as communication, social interaction, and cognition.

Depression is graded as having limited evidence of harm based on 40 published studies (including 22 randomized controlled trials[7,9,11]. All studies evaluated patients with depressed mood associated with other conditions; none evaluated primary depressive disorder. No study showed a beneficial effect of a cannabis product. Some studies with THC-predominant products found worse mood at higher doses.

Obsessive compulsive disorder is graded as having no or insufficient evidence of efficacy based on one small randomized, placebo-controlled clinical trial that found no benefit from smoked cannabis[9].

Opioid use disorder is graded as having limited evidence of efficacy based on three small randomized clinical trials (two placebo-controlled) using oral dronabinol (synthetic THC) or CBD[9]. All 3 studies showed significant reduction in opioid craving and withdrawal symptoms. No study evaluated opioid use.

Panic disorder (listed independently from anxiety by a few states) is graded as having no or insufficient evidence of efficacy. We are not aware of any published studies evaluating medical cannabis as treatment for panic attacks or panic disorder[7,9,11].

Post-traumatic stress disorder (PTSD) (listed independently from anxiety in several states) is graded as having moderate evidence of efficacy, based on 12 published studies (including one randomized clinical trial)[7,9,11,14]. The randomized placebo-controlled clinical trial found that nabilone (synthetic THC analogue) significantly improved overall well-being and reduced disturbed dreaming but did not alter other core PTSD symptoms such as enhanced startle response, irritability, and impaired concentration. Some small, open-label studies found improvement in several core PTSD symptoms (cannabis plant, CBD). In two studies, a small proportion of patients experienced worsening symptoms.

Association of Frequency of Listing with Strength of Evidence

The 6 most commonly listed (at least 80% of jurisdictions) qualifying conditions have more favorable strength of evidence of benefit than do the 18 least commonly listed (less than 20% of jurisdictions) qualifying conditions (Table 8). Two of the most commonly listed conditions have conclusive or substantial evidence of efficacy, while only three of the least commonly listed conditions have moderate evidence of efficacy. The 5 qualifying conditions with conclusive or substantial evidence of efficacy are more commonly listed (greater than 50% of jurisdictions) than are the 3 qualifying conditions with limited evidence of harm (2 in less than 10% of jurisdictions) (Table 7).

The mean (SD) proportion of qualifying conditions per jurisdiction with at least moderate evidence of efficacy is 39% (11%), with a range of 22% (District of Columbia) to 71% (West Virginia) (Table 5). Conversely, the mean (SD) proportion of qualifying conditions per jurisdiction with no or insufficient evidence of efficacy is 35% (8%). with a range of 14% (West Virginia) to 56% (DC) (Table 5) These proportions do not appear to have changed meaningfully since 1996 (Table 4), nor does there appear to be any association between the number of qualifying conditions adopted by a jurisdiction and the proportion with at least moderate evidence of efficacy (Table 3).

Discussion

We reviewed the 42 different qualifying conditions for which patients may be certified for medical cannabis use in the 37 states, the District of Columbia, and 3 territories that have enacted medical cannabis laws. The number of conditions in each jurisdiction varies widely from as few as 5 qualifying conditions to as many as 29 qualifying conditions; two jurisdictions do not require any specific qualifying condition for medical cannabis therapy. The level of scientific evidence supporting each of these qualifying conditions varies widely as well. Many of the qualifying conditions have little evidence supporting their use. 50% of qualifying conditions have no or insufficient evidence of benefit from medical cannabis; another 9% have limited evidence of harm.

US medical cannabis laws are in conflict with federal law and often with science as well. The stipulation of medical conditions with little evidence supporting the efficacy of medical cannabis is a byproduct of a political process whereby citizens lobby elected officials for the inclusion of conditions often based on anecdotal evidence of benefit. Not only does such use incur the

possibility of adverse effects from cannabis with little prospect of benefit, but there are instances where a discrepancy between policy and science may lead to adverse outcomes. For example, eschewing the effective FDA-approved medications for opioid use disorder in favor of medical cannabis is not evidence-based and may have adverse consequences for the patient[16].

Our analysis revealed other patterns as well. Among the most commonly listed and earliest-adopted conditions are those for which there is the strongest evidence for cannabinoid (including the FDA-approved cannabinoids) pharmacotherapy, including cachexia/weight loss, muscle spasticity associated with multiple sclerosis, nausea and vomiting, chronic pain, and seizures. However, some conditions with evidence demonstrating that medical cannabis pharmacotherapy can be harmful were still listed by many jurisdictions, including glaucoma, which is listed as a qualifying condition in 80% of jurisdictions with medical cannabis laws. In contrast, some psychiatric conditions for which there is limited evidence of benefit from medical cannabis are not listed as qualifying conditions in any jurisdiction, e.g. schizophrenia and tobacco use disorder.[7,9,11] Although there have been US jurisdictions with medical cannabis laws since 1996, little has changed regarding qualifying conditions. The median number of qualifying conditions per jurisdiction and the proportion of conditions supported by evidence has not changed meaningfully since 1996.

Limitations

Our analysis has some limitations. We did not conduct our own systematic review of strength of evidence, but relied on published reviews which may have overlooked some studies. We did not assess the relationship between the year each law was enacted and the year evidence was published.

The level of evidence may have changed in the years following passage of a given medical cannabis law. This may have led to overestimation of the concordance between qualifying conditions and the strength of the evidence supporting the use of medical cannabis for that condition. We were generous in applying the evidence relevant to any condition. Benefit in improving secondary symptoms was given the same weight as improving the disease process itself. For some diseases there is evidence only for secondary symptom improvement, e.g., cancer and neurodegenerative disorders. If one particular cannabinoid formulation or dose had evidence for a specific diagnosis, we gave that grade of evidence to the qualifying condition that included that diagnosis. For example, CBD has conclusive evidence, including FDA approval, as treatment for several syndromes of childhood seizures. Therefore, we gave a grade of "conclusive or substantial" evidence of benefit for epilepsy/seizures as a qualifying condition. Given that jurisdictions allow any potency and formulation of cannabis product to be recommended, this may tend to overestimate the concordance between condition and strength of evidence.

Conclusion

Millions of Americans use cannabis and cannabinoids to treat a host of medical and psychiatric conditions[16]. Many of these conditions are specified in medical cannabis laws as conditions for which patients can be recommended or certified for medical cannabis use. In many jurisdictions, the law allows physicians to certify medical cannabis use for broad and undefined conditions (e.g., terminal or debilitating illness) or for any condition they choose. Because there is limited or no scientific evidence for the efficacy of medical cannabis for the majority of conditions (and evidence of harm for a few), the state-level legal status of medical cannabis runs far ahead of the science in these instances.

This conflict between local law and the strength of evidence for efficacy puts patients and physicians in a difficult position. Cannabis and cannabinoids like CBD remain popular, so patients are either interested in using them to treat their maladies, or are already doing so. Patients may opt for medical cannabis pharmacotherapy for a given medical condition when it is listed in a state law but not evidence-based. In such instances, patients may suffer adverse outcomes and/or fail to receive any therapeutic benefit from medications FDA-approved for their disease condition. Furthermore, physicians often must explain that use of medical cannabis, despite being allowable under local law, may not be in their patient's best interest.

There is a dire need for rigorous research to adequately evaluate the benefits and harms of medical cannabis for a broad range of conditions. This requires both increased resources for clinical research (including adequately designed and powered phase II and phase III controlled clinical trials) and altering federal laws and regulations that hinder the ability to conduct clinical studies with cannabis and cannabinoids. Many stakeholders who profit from cannabinoid sales, including jurisdictions with legalized medical cannabis and companies which sell medical cannabis products, have largely failed to contribute to the evidence base. The rate and scope of cannabinoid research must keep pace with cannabis policy if we are going to maximize the potential benefits and minimize the potential harms of medical cannabis.

Summary

In the context of changing cannabis policies in the United States, 37 states, the District of Columbia, and 3 territories have enacted medical cannabis laws as of March 2022. The number of qualifying conditions stipulated by each state and the strength of scientific evidence supporting the use of medical cannabis for each of these conditions vary widely. The evidence supporting the use of medical cannabis for many of these conditions is weak: 50% of qualifying conditions have no or insufficient evidence of benefit from medical cannabis; 9% of qualifying conditions have limited evidence that medical cannabis may cause harm if used for that condition. Despite intense interest in medical cannabis, the implementation of medical cannabis laws and proportion of qualifying conditions with evidence supporting them has not changed meaningfully since the first medical cannabis law was passed in 1996. As a result, patients and physicians are in difficult positions as they try to utilize medical cannabis safely and effectively for appropriate medical conditions.

Clinical Care Points

- Physicians should be knowledgeable about the current evidence of the benefits and harms of medical cannabis so they can have informed discussions with their patients.
- Physicians should be cautious about recommending medical cannabis in the absence of at least moderate evidence of benefit.
- When recommending medical cannabis, physicians should follow the same clinical approach as when prescribing conventional medication—careful diagnosis, evaluation for comorbidity, and balancing benefits and harms, including potential drug-drug interactions

Tables

Table 1: Cannabis- Based Products with FDA Approval				
Name (brand name)		**Route of Administration**	**CSA Schedule**	**Approved Indications**
Synthetic Cannabinoids				
Dronabinol (Marinol,® Syndros®)	Synthetic THC	Oral	III	Severe Nausea/vomiting Cachexia/weight loss
Nabilone (Cesamet®)	Synthetic THC analog	Oral	II	Severe Nausea/Vomiting
Phytocannabinoids				
Cannabidiol (Epidiolex®)	Cannabidiol extract	Sublingual	not scheduled	Seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, tuberous sclerosis complex in patients >1 year of age
Nabiximols (Sativex®)	1:1 THC/CBD extract	Oral	NDA pending	Muscle spasms/ Multiple Sclerosis, neuropathic cancer pain

CBD- cannabidiol, CSA- Controlled Substances Act, FDA- Food and Drug Administration, NDA- new drug application, THC- delta-9-tetrahydrocannabinol

Table 2: Grading Strength of Scientific Evidence for Therapeutic Efficacy of Medical Cannabis	
Evidence Grade	**Description**
CONCLUSIVE EVIDENCE	Strong evidence from randomized controlled trials to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment. There are many supportive findings from good-quality studies with no credible opposing findings. A firm conclusion can be made, and the limitations to the evidence, including chance, bias, and confounding factors, can be ruled out with reasonable confidence
SUBSTANTIAL EVIDENCE	Strong evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest. For this level of evidence, there are several supportive findings from good quality studies with very few or no credible opposing findings. A firm conclusion can be made, but minor limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.
MODERATE EVIDENCE	Some evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest. For this level of evidence, there are several supportive findings from good- to fair-quality studies with very few or no credible opposing findings. A general conclusion can be made, but limitations, including chance, bias, and confounding factors, cannot be ruled out with reasonable confidence.
LIMITED EVIDENCE	Weak evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest. For this level of evidence, there are supportive findings from fair-quality studies or mixed findings with most favoring one conclusion. A conclusion can be made, but there is significant uncertainty due to chance, bias, and confounding factors.
NO OR INSUFFICIENT EVIDENCE	No or insufficient evidence to support the conclusion that cannabis or cannabinoids are an effective or ineffective treatment for the health endpoint of interest. For this level of evidence, there are mixed findings, a single poor study, or health endpoint has not been studied at all. No conclusion can be made because of substantial uncertainty due to chance, bias, and confounding factors.
Source: [5]	

Table 3: Number and Strength of Evidence for Medical Cannabis Qualifying Conditions by US Jurisdiction				
Year Law Enacted	**Jurisdiction**	**Number of Conditions**	**% of Conditions with at least Moderate Evidence**	**% of Conditions with No or Insufficient Evidence**
1996	California	10	30%	40%
1998	Oregon	8	38%	25%
1998	Washington	13	38%	38%
1999	Alaska	8	38%	38%
1999	Maine	10	40%	40%
2000	Hawaii	13	38%	46%
2001	Colorado	10	30%	30%
2001	Nevada	9	44%	33%
2004	Montana	13	38%	31%
2004	Vermont	8	38%	38%
2006	Rhode Island	11	45%	36%
2007	New Mexico	16	31%	44%
2008	Michigan	19	37%	37%
2010	Arizona	13	46%	38%
2010	District of Columbia	9	22%	56%
2010	New Jersey	15	40%	33%
2011	Delaware	15	40%	33%
2012	Connecticut	19	32%	42%
2013	Massachusetts	8	25%	38%
2013	New Hampshire	19	32%	42%
2014	Illinois	29	31%	45%
2014	Maryland	6	67%	33%
2014	Minnesota	13	46%	23%
2014	New York	17	29%	41%
2016	Arkansas	15	47%	40%
2016	Louisiana	12	33%	33%
2016	North Dakota	15	47%	33%
2016	Ohio	15	47%	27%
2016	Pennsylvania	18	33%	33%
2017	Florida	11	36%	27%
2017	Puerto Rico	21	38%	29%
2018	Missouri	18	33%	39%
2018	Oklahoma*	0	-	-
2018	Utah	11	45%	27%
2018	Guam	8	38%	25%
2019	West Virginia	7	71%	14%
2019	US Virgin Islands	20	20%	25%
2020	Virginia*	0	-	-
2021	Alabama	17	35%	35%
2021	Mississippi	16	25%	38%
2021	South Dakota	5	60%	40%

*Physician is able to recommend medical cannabis for any medical condition

Table 4: Prevalence and Strength of Evidence for Qualifying Medical Conditions					
Year Law Enacted	**Medical Condition**	**# of jurisdictions with approval**	**% of jurisdictions with approval**	**Evidence Grade Phytocannabinoids**	**Evidence Grade Synthetic Cannabinoids**
1996	*Multiple Sclerosis/ Muscle Spasms*	39	95%	2	1
1996	*HIV/AIDS*	36	88%	0.5	0
1996	*Cancer*	36	88%	0	0
1996	*Epilepsy/Seizures*	35	85%	0	0
1996	*Intractable / Chronic Pain*	33	80%	2	0
1996	*Glaucoma*	33	80%	-0.5	0
1996	*Cachexia / Wasting Syndrome*	29	71%	0	0
2004	*Crohn's Disease / IBD*	27	66%	1	0
1996	*Severe Nausea / Vomiting*	24	59%	2	0
2008	*ALS*	23	56%	0	0
2007	*Parkinson's Disease*	17	41%	0.5	0
1999	*Alzheimer's Disease*	16	39%	1	0.5
1999	*Hepatitis C*	15	37%	0	0
2004	*Terminal Illness*	15	37%	0	0
2013	*Neurological Malformation / Trauma*	14	34%	0.5	0
2013	*Tourette's Syndrome*	9	22%	0.5	1
1996	*Arthritis (severe)*	9	22%	0	0
2010	*Muscular Dystrophy*	7	17%	0	0
2012	*Fibromyalgia*	6	15%	1	1
2004	*Peripheral Neuropathy*	6	15%	0	0
2007	*Huntington's Disease*	6	15%	0	0.5
2012	*Sickle Cell Anemia*	6	15%	0	0
2011	*Migraine*	5	12%	1	0
2013	*Systemic Lupus Erythematosus*	3	7%	0	0
2011	*Cirrhosis*	2	5%	0	0
2013	*Polycystic Kidney Disease*	2	5%	0	0
2013	*Ehlers-Danlos Syndrome*	2	5%	0	0
2014	*Obstructive Sleep Apnea*	1	2%	1	1
2010	*Dysmenorrhea*	1	2%	0	0
2012	*Cystic Fibrosis*	1	2%	0	0
2013	*Fibrous Dysplasia*	1	2%	0	0
2013	*Interstitial Cystitis*	1	2%	0	0
2013	*Sjogren's Syndrome*	1	2%	0	0
2014	*Macular Degeneration*	1	2%	0	0
2013	*Chronic Pancreatitis*	1	2%	-0.5	0

Legend	
Score	Interpretation
-2	*conclusive or substantial evidence of harm*
-1	*moderate evidence of harm*
-0.5	*limited evidence of harm*
0	*no or insufficient evidence to support or refute benefit or harm*
0.5	*limited evidence of benefit*
1	*moderate evidence of benefit*
2	*conclusive or substantial evidence of benefit*

AIDS-acquired immunodeficiency syndrome, ALS-amyotrophic lateral sclerosis, HIV-human immunodeficiency virus, IBD-inflammatory bowel disease

Table 5: Prevalence and Strength of Evidence of Qualifying Psychiatric Conditions					
Year Law Enacted	**Psychiatric Condition**	**# of jurisdictions listing**	**% of jurisdictions listing**	**Evidence Grade Cannabinoids**	**Evidence Grade Synthetic Cannabinoids**
2011	*PTSD*	31	76%	-0.5	0.5
2016	*Autism Spectrum Disorder*	15	37%	0.5	0
2018	*Opioid Use Disorder*	7	17%	0	0.5
2015	*Anxiety*	5	12%	1	1
2015	*Depression*	2	5%	0	-0.5
2019	*Obsessive Compulsive Disorder*	1	2%	0	0
2021	*Panic Disorder*	1	2%	0	0

Legend	
Score	Interpretation
-2	*conclusive or substantial evidence of harm*
-1	*moderate evidence of harm*
-0.5	*limited evidence of harm*
0	*No or insufficient evidence to support or refute benefit or harm*
0.5	*limited evidence of benefit*
1	*moderate evidence of benefit*
2	*conclusive or substantial evidence of benefit*

PTSD-post-traumatic stress disorder

Table 6: Medical Cannabis Qualifying Conditions by Strength of Evidence
Conclusive or Substantial Evidence of Benefit
Cachexia/Wasting Syndrome, Epilepsy/Seizures, Multiple Sclerosis/Muscle Spasms, Severe Nausea/Vomiting, Intractable / Chronic Pain
Moderate Evidence of Benefit
Alzheimer's Disease, Anxiety, Crohn's Disease / Inflammatory Bowel Disease, Fibromyalgia, Migraine, Obstructive Sleep Apnea, Post-Traumatic Stress Disorder (Synthetic), Tourette's Syndrome
Limited Evidence of Benefit
Autism Spectrum Disorder, Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome, Neurological Malformation / Trauma, Opioid Use Disorder, Parkinson's Disease
No or Insufficient Evidence to support or refute Benefit or Harm
Amyotrophic Lateral Sclerosis, Arthritis, Cancer, Cachexia / Wasting Syndrome, Cirrhosis, Cystic Fibrosis, Dysmenorrhea, Ehlers-Danlos Syndrome, Fibrous Dysplasia, Hepatitis C, Huntington's Disease, Interstitial Cystitis, Macular Degeneration, Muscular Dystrophy, Obsessive Compulsive Disorder, Panic Disorder, Peripheral Neuropathy, Polycystic Kidney Disease, Sickle Cell Anemia, Sjogren's Syndrome, Systemic Lupus Erythematosus, Terminal Illness
Limited Evidence of Harm
Depression, Glaucoma, Chronic Pancreatitis, Post Traumatic Stress Disorder (Phyto),
Moderate Evidence of Harm
none
Substantial Evidence of Harm
none

Table 7: Strength of Evidence Associated with Medical Cannabis Treatment		
Phytocannabinoids	**Number of Qualifying Conditions**	**% of Qualifying Conditions**
conclusive or substantial evidence of benefit	3	7%
moderate evidence of benefit	6	14%
limited evidence of benefit	4	10%
no or insufficient evidence to support or refute benefit or harm	25	60%
limited evidence of harm	4	10%
moderate evidence of harm	0	0%
substantial evidence of harm	0	0%
Synthetic Cannabinoids (dronabinol/nabilone)	**Number of Qualifying Conditions**	**% of Qualifying Conditions**
conclusive or substantial evidence of benefit	2	5%
moderate evidence of benefit	5	12%
limited evidence of benefit	4	10%
no or insufficient evidence to support or refute benefit or harm	32	76%
limited evidence of harm	1	2%
moderate evidence of harm	0	0%
substantial evidence of harm	0	0%

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Appendix I: Medical Cannabis Qualifying Medical Conditions by Jurisdiction

Medical Cannabis Qualifying Medical Conditions by Jurisdiction										
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**							
			ALS	*Alzheimer's Disease*	*Arthritis*	*Cancer*	*Cachexia / Wasting Syndrome*	*Crohn's Disease / IBD*	*Cirrhosis*	*Cystic Fibrosis*
1996	1996	California			*	*	*			
1998	1999	Alaska				*	*			
1998	2010	District of Columbia	*	*		*	*		*	
1998	1998	Oregon				*	*			
1998	1998	Washington				*	*	*		
1999	1999	Maine	*	*		*		*		
2000	2001	Colorado				*	*			
2000	2000	Hawaii	*		*	*	*	*		
2000	2001	Nevada				*	*			
2004	2004	Montana				*	*	*		
2004	2004	Vermont				*	*			
2006	2006	Rhode Island		*		*	*	*		
2007	2007	New Mexico	*			*	*	*		
2008	2008	Michigan	*	*	*	*	*	*		
2010	2010	Arizona	*	*		*	*	*		
2010	2010	New Jersey	*			*		*		
2011	2011	Delaware	*	*		*	*		*	
2012	2012	Connecticut	*		*	*	*	*		*
2012	2013	Massachusetts	*			*		*		
2013	2014	Illinois	*	*	*	*	*	*		
2013	2013	New Hampshire	*	*		*	*	*		
2014	2017	Maryland					*			
2014	2014	Minnesota				*		*		
2014	2021	New York	*	*	*	*		*		
2014	2015	Guam				*				
2015	2017	Puerto Rico	*	*	*	*		*		
2016	2016	Arkansas	*	*	*	*	*	*		
2016	2017	Florida	*			*		*		
2016	2016	Louisiana				*	*	*		

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)										
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**							
			ALS	*Alzheimer's Disease*	*Arthritis (severe)*	*Cancer*	*Cachexia / Wasting Syndrome*	*Crohn's Disease / IBD*	*Cirrhosis*	*Cystic Fibrosis*
2016	2016	North Dakota	*	*		*	*	*		
2016	2016	Ohio	*	*		*		*		
2016	2016	Pennsylvania	*			*		*		
2017	2019	West Virginia					*			
2018	2018	Missouri	*	*		*	*	*		
2018	2018	Oklahoma								
2018	2018	Utah	*	*		*	*	*		
2019	2019	US Virgin Islands	*	*	*	*	*	*		
2020	2022	Mississippi				*	*	*		
2020	2022	South Dakota					*			
2021	2022	Alabama	*			*	*	*		
2021	2022	Virginia								

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Passed	**Year Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			Dysmenorrhea	*Ehlers-Danlos Syndrome*	*Epilepsy/Seizures*	*Fibromyalgia*	*Fibrous Dysplasia*	*Glaucoma*	*Hepatitis C*
1996	1996	California			*			*	
1998	1999	Alaska			*			*	
1998	2010	District of Columbia			*			*	
1998	1998	Oregon						*	
1998	1998	Washington			*			*	*
1999	1999	Maine			*			*	*
2000	2001	Colorado			*			*	
2000	2000	Hawaii			*			*	
2000	2001	Nevada			*			*	
2004	2004	Montana			*			*	
2004	2004	Vermont			*			*	-
2006	2006	Rhode Island			*			*	*
2007	2007	New Mexico			*			*	*
2008	2008	Michigan			*			*	*
2010	2010	Arizona			*			*	*
2010	2010	New Jersey	*		*			*	
2011	2011	Delaware			*			*	
2012	2012	Connecticut			*	*		*	
2012	2013	Massachusetts						*	*
2013	2014	Illinois		*	*	*	*	*	*
2013	2013	New Hampshire		*	*			*	*
2014	2017	Maryland			*				
2014	2014	Minnesota			*			*	
2014	2021	New York			*				
2014	2015	Guam			*			*	
2015	2017	Puerto Rico			*	*		*	*
2016	2016	Arkansas			*	*		*	
2016	2017	Florida			*			*	
2016	2016	Louisiana			*			*	

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			Dysmenorrhea	*Ehlers-Danlos Syndrome*	*Epilepsy/Seizures*	*Fibromyalgia*	*Fibrous Dysplasia*	*Glaucoma*	*Hepatitis C*
2016	2016	North Dakota			*	*		*	*
2016	2016	Ohio				*		*	*
2016	2016	Pennsylvania			*			*	
2017	2019	West Virginia							
2018	2018	Missouri			*			*	*
2018	2018	Oklahoma							
2018	2018	Utah							
2019	2019	US Virgin Islands			*			*	*
2020	2022	Mississippi			*			*	
2020	2022	South Dakota			*				
2021	2022	Alabama			*				
2021	2022	Virginia							

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			HIV/AIDS	*Huntington's Disease*	*Interstitial Cystitis*	*Systemic Lupus Erythematosus*	*Macular Degeneration*	*Migraine*	*Multiple Sclerosis/ Muscle Spasms*
1996	1996	California	*						*
1998	1999	Alaska	*						*
1998	2010	District of Columbia	*						*
1998	1998	Oregon	*						*
1998	1998	Washington	*						*
1999	1999	Maine	*						*
2000	2001	Colorado	*						*
2000	2000	Hawaii	*			*			*
2000	2001	Nevada	*						*
2004	2004	Montana	*						*
2004	2004	Vermont	*						*
2006	2006	Rhode Island	*						*
2007	2007	New Mexico	*	*					*
2008	2008	Michigan	*						*
2010	2010	Arizona	*						*
2010	2010	New Jersey	*						*
2011	2011	Delaware	*					*	*
2012	2012	Connecticut	*					*	*
2012	2013	Massachusetts	*						*
2013	2014	Illinois	*		*	*		*	*
2013	2013	New Hampshire	*			*			*
2014	2017	Maryland							*
2014	2014	Minnesota	*				*		*
2014	2021	New York	*	*					*
2014	2015	Guam	*						*
2015	2017	Puerto Rico	*					*	*
2016	2016	Arkansas	*						*
2016	2017	Florida	*						*
2016	2016	Louisiana	*						*

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			HIV/AIDS	*Huntington's Disease*	*Interstitial Cystitis*	*Systemic Lupus Erythematosus*	*Macular Degeneration*	*Migraine*	*Multiple Sclerosis/ Muscle Spasms*
2016	2016	North Dakota	*						*
2016	2016	Ohio	*						*
2016	2016	Pennsylvania	*	*					*
2017	2019	West Virginia							*
2018	2018	Missouri	*	*				*	*
2018	2018	Oklahoma							
2018	2018	Utah	*						*
2019	2019	US Virgin Islands	*	*					*
2020	2022	Mississippi	*	*					*
2020	2022	South Dakota							*
2021	2022	Alabama	*						*
2021	2022	Virginia							

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			Muscular Dystrophy	*Severe Nausea/Vomiting*	*Neurological Malformation / Trauma*	*Obstructive Sleep Apnea*	*Intractable / Chronic Pain*	*Chronic Pancreatitis*	*Parkinson's Disease*
1996	1996	California		*			*		
1998	1999	Alaska		*			*		
1998	2010	District of Columbia							
1998	1998	Oregon		*	*		*		
1998	1998	Washington		*^	*		*		
1999	1999	Maine		*					
2000	2001	Colorado					*		
2000	2000	Hawaii		*			*		
2000	2001	Nevada		*			*		
2004	2004	Montana		*	*		*		-
2004	2004	Vermont		*			*		
2006	2006	Rhode Island		*			*		
2007	2007	New Mexico		*			*		*
2008	2008	Michigan		*	*		*		*
2010	2010	Arizona		*			*		
2010	2010	New Jersey	*				*		
2011	2011	Delaware		*			*		
2012	2012	Connecticut	*		*		*		*
2012	2013	Massachusetts							*
2013	2014	Illinois	*	*^	*		*		*
2013	2013	New Hampshire	*	*	*		*	*	*
2014	2017	Maryland		*^			*		
2014	2014	Minnesota				*	*		
2014	2021	New York	*		*		*		*
2014	2015	Guam			*				
2015	2017	Puerto Rico			*		*		*
2016	2016	Arkansas		*			*		
2016	2017	Florida					*		*
2016	2016	Louisiana	*				*		*

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Conditions**						
			Muscular Dystrophy	*Severe Nausea/Vomiting*	*Neurological Malformation / Trauma*	*Obstructive Sleep Apnea*	*Intractable / Chronic Pain*	*Chronic Pancreatitis*	*Parkinson's Disease*
2016	2016	North Dakota		*	*		*		
2016	2016	Ohio			*		*		*
2016	2016	Pennsylvania					*		*
2017	2019	West Virginia		*			*		
2018	2018	Missouri							*
2018	2018	Oklahoma							
2018	2018	Utah		*					
2019	2019	US Virgin Islands		*	*		*		*
2020	2022	Mississippi	*		*		*		*
2020	2022	South Dakota		*			*		
2021	2022	Alabama		*			*		*
2021	2022	Virginia							

Medical Cannabis Qualifying Medical Conditions by Jurisdiction (cont.)									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			Peripheral Neuropathy	*Polycystic Kidney Disease*	*Sickle Cell Anemia*	*Sjogren's Syndrome*	*Terminal Illness*	*Tourette's Syndrome*	*Any condition approved by MD/SHA*
1996	1996	California							*
1998	1999	Alaska							*
1998	2010	District of Columbia							*
1998	1998	Oregon							*
1998	1998	Washington		*'					
1999	1999	Maine							
2000	2001	Colorado							*
2000	2000	Hawaii							
2000	2001	Nevada							*
2004	2004	Montana	*				*		
2004	2004	Vermont							
2006	2006	Rhode Island							*
2007	2007	New Mexico	*				*		
2008	2008	Michigan						*	
2010	2010	Arizona							
2010	2010	New Jersey					*	*	
2011	2011	Delaware					*		
2012	2012	Connecticut			*		*		
2012	2013	Massachusetts							*
2013	2014	Illinois		*		*	*	*	
2013	2013	New Hampshire							*
2014	2014	Maryland							*
2014	2014	Minnesota					*	*	
2014	2021	New York	*						*
2014	2015	Guam							*
2015	2017	Puerto Rico	*				*		
2016	2016	Arkansas	*					*	*
2016	2017	Florida					*		
2016	2016	Louisiana							

Medical Cannabis Qualifying Medical Conditions by Jurisdiction									
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Medical Condition**						
			Peripheral Neuropathy	*Polycystic Kidney Disease*	*Sickle Cell Anemia*	*Sjogren's Syndrome*	*Terminal Illness*	*Tourette's Syndrome*	*Any condition approved by MD/SHA*
2016	2016	North Dakota							*
2016	2016	Ohio			*			*	
2016	2016	Pennsylvania	*		*		*	*	
2017	2019	West Virginia					*		
2018	2018	Missouri			*		*	*	*
2018	2018	Oklahoma							*
2018	2018	Utah					*		
2019	2019	US Virgin Islands					*		
2020	2022	Mississippi			*				
2020	2022	South Dakota							*
2021	2022	Alabama			*		*	*	
2021	2022	Virginia							*

AIDS-acquired immunodeficiency syndrome, ALS-amyotrophic lateral sclerosis, HIV-human immunodeficiency virus, IBD-inflammatory bowel disease, MD-physician, SHA-state health authority

Source: [8]

Appendix II: Medical Cannabis Qualifying Psychiatric Conditions by Jurisdiction

Medical Cannabis Qualifying Psychiatric Conditions By Jurisdiction										
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Psychiatric Condition**							
			Anxiety	*Autism Spectrum Disorder*	*Depression*	*Obsessive Compulsive Disorder*	*Opioid Use Disorder*	*Panic Disorder*	*PTSD*	*Any condition approved by MD/SHA*
1996	1996	California								*
1998	1999	Alaska								*
1998	2010	District of Columbia								*
1998	1998	Oregon								*
1998	1998	Washington							*	
1999	1999	Maine								
2000	2001	Colorado		*			*		*	*
2000	2000	Hawaii							*	
2000	2001	Nevada							*	*
2004	2004	Montana							*	
2004	2004	Vermont								
2006	2006	Rhode Island								*
2007	2007	New Mexico							*	
2008	2008	Michigan		*		*			*	
2010	2010	Arizona							*	
2010	2010	New Jersey	*				*		*	
2011	2011	Delaware		*					*	
2012	2012	Connecticut							*	
2012	2013	Massachusetts							-	*
2013	2014	Illinois		*			*		*	
2013	2013	New Hampshire							*	*
2014	2017	Maryland							*	*
2014	2014	Minnesota		*					*	
2014	2021	New York		*			*		*	*
2014	2015	Guam	*						*	*
2015	2017	Puerto Rico	*	*	*				*	
2016	2016	Arkansas							-	*
2016	2017	Florida							*	
2016	2016	Louisiana		*					*	

Medical Cannabis Qualifying Psychiatric Conditions By Jurisdiction (cont.)										
Year Law Passed	**Year Law Effective**	**Jurisdiction**	**Qualifying Psychiatric Condition**							
			Anxiety	*Autism Spectrum Disorder*	*Depression*	*Obsessive Compulsive Disorder*	*Opioid Use Disorder*	*Panic Disorder*	*PTSD*	*Any condition approved by MD/SHA*
2016	2016	North Dakota							*	*
2016	2016	Ohio							*	
2016	2016	Pennsylvania	*	*			*		*	
2017	2019	West Virginia	*						*	
2018	2018	Missouri		*					*	*
2018	2018	Oklahoma								*
2018	2018	Utah		*					*	
2019	2019	US Virgin Islands		*			*		*	
2020	2022	Mississippi		*			*		*	*
2020	2022	South Dakota								*
2021	2022	Alabama		*	*			*	*	
2021	2022	Virginia								*

MD-physician, PTSD-post-traumatic stress disorder, SHA-state health authority

Source: [8]