

# Minnesota Medical Cannabis Program Petition to Add a Qualifying Medical Condition

## Making Your Petition

Any person may petition the Minnesota Department of Health (“the department” or “MDH”) to add a qualifying medical condition to those listed in subdivision 14 of Minnesota Statutes section 152.22.

Petitions will be accepted only between June 1, 2020, and July 31, 2020. Petitions received outside of these dates will not be reviewed.

**Petitions must be sent by certified U.S. mail to:**

Minnesota Department of Health  
Office of Medical Cannabis  
P.O. Box 64882  
St. Paul, MN 55164-0882

**Or by email to:**

Health.Cannabis.AddMedicalCondition@state.mn.us

## Instructions

- Complete each section of this petition and attach all supporting documents. Clearly indicate which section of the petition an attachment is for.
- This is a fillable PDF. Save the PDF to your computer before typing in the form fields. Otherwise, print the form and complete it by hand.
- Each petition is limited to one proposed qualifying medical condition. If your petition includes more than one medical condition, it will be dismissed.
- If you are petitioning for the addition of a medical condition that was considered but not approved in a prior year’s petition process, you must include new scientific evidence or research to support your petition or describe substantially different symptoms. The MDH website has the petitions and review material for each petitioned medical condition reviewed in prior years. See [Adding New Medical Conditions - Medical Cannabis Program \(http://www.health.state.mn.us/people/cannabis/rulemaking/addconditions.html\)](http://www.health.state.mn.us/people/cannabis/rulemaking/addconditions.html). Petitions that do not include new scientific evidence or research to support your petition or describe substantially different symptoms will not be considered.
- If the petition is accepted for consideration, MDH will send the petition documents to the Medical Cannabis Review Panel (“Review Panel”). MDH staff will also provide information to the Review Panel about the proposed qualifying condition, its prevalence, and the effectiveness of current treatments.

MINNESOTA MEDICAL CANNABIS PROGRAM PETITION TO ADD  
A QUALIFYING MEDICAL CONDITION

- You may withdraw your petition any time before the Review Panel's first public meeting of the year by submitting a written statement to MDH stating that you want to withdraw it.

## **Petition Review Process**

- An appointed citizens Review Panel will meet to review all eligible petitions and supporting documentation.
- MDH will post notice of the public meetings of the Review Panel on its medical cannabis website.
- After the public meeting and by Nov. 2, 2020, the Review Panel will provide the Commissioner of Health a written report of findings.
- The Commissioner will approve or deny the petition by Dec. 1, 2020.

***Petition starts on next page.***

Minnesota Department of Health  
Office of Medical Cannabis  
PO Box 64882  
St. Paul, MN 55164-0882  
[health.cannabis@state.mn.us](mailto:health.cannabis@state.mn.us)  
[www.health.state.mn.us](http://www.health.state.mn.us)

05/04/20

*To obtain this information in a different format, call: 651-201-5598.*

MINNESOTA MEDICAL CANNABIS PROGRAM PETITION TO ADD  
A QUALIFYING MEDICAL CONDITION

**Section A: Petitioner's Information**

Name (First, Middle, Last) [REDACTED]		
Home Address (including Apartment or Street Number) [REDACTED]		
City [REDACTED]	State MN	ZIP Code [REDACTED]
Telephone Number [REDACTED]	Email Address [REDACTED]	

**Section B: Medical Condition You Are Requesting Be Added**

Please specify the name and provide a brief description of the proposed qualifying medical condition. Be as precise as possible in identifying the condition. Optional: Include diagnostic code(s), citing the associated ICD-9 or ICD- 10 code(s), if you know them. ***Attach additional pages as needed.***

Anxiety (ICD 10: F40-F42)

\* See attached \*

### Section C: Symptoms of the Proposed Medical Condition and/or Its Treatment

Describe the extent to which the proposed qualifying medical condition or the treatments cause suffering and impair a person's daily life. ***Attach additional pages if needed.***

\* See attached \*

### Section D: Availability of Conventional Medical Therapies

Describe conventional medical therapies available and the degree to which they ease the suffering caused by the proposed qualifying medical condition or its treatment. ***Attach additional pages if needed.***

\* See attached \*

### Section E: Anticipated Benefits from Medical Cannabis

Describe the anticipated benefits from the medical use of cannabis specific to the proposed qualifying medical condition. **Attach additional pages if needed.**

\* See attached \*

### Section F (optional): Scientific Evidence of Support for Medical Cannabis Treatment

Strengthen your petition by including evidence generally accepted by the medical community and other experts supporting the use of medical cannabis to alleviate suffering caused by the proposed medical disease or its treatment. This includes but is not limited to full text, peer-reviewed published journals, or other completed medical studies. Please attach complete copies of any article or reference, not abstracts.

I have attached relevant articles. *(check box if you have attached scientific articles or studies)*

### Section G (optional): Letters in Support of Adding the Medical Condition

Attach letters of support for the use of medical cannabis from persons knowledgeable about the proposed qualifying medical condition, such as a licensed health care professional.

I have attached letters of support. *(check box if you have attached letters of support)*

MINNESOTA MEDICAL CANNABIS PROGRAM PETITION TO ADD  
A QUALIFYING MEDICAL CONDITION

**Section H: Acknowledgement and Signature**

*Please note: Any individually identifiable health information relating to any past, present, or future health condition or health care contained in this petition is classified as a health record under Minnesota Statutes §144.291, and is not subject to public disclosure.*

**I certify that the information provided in this petition is true and accurate to the best of my knowledge.**



07/31/2020

SIGNATURE	DATE (mm/dd/yyyy)
-----------	-------------------

## Section A: Petitioner's Information

Gunnar Aas o/b/o Sensible Minnesota  
Board President, Sensible Minnesota  
[REDACTED]

### Co-Petitioners:

Maren Schroeder  
Policy Director, Sensible Change Minnesota  
[REDACTED]

Sarah Overby, LPN  
Director of Medical Education, Minnesota Medical Solutions, A Vireo Health Company  
[REDACTED]

Stephen Dahmer, MD  
Chief Medical Officer, Minnesota Medical Solutions, A Vireo Health Company  
[REDACTED]

Grace Liu  
Student, University of Minnesota - Twin Cities  
[REDACTED]

## Section B: Medical Condition You Are Requesting to be Added

### Anxiety (ICD-10: F40-F42)

A group of mental disorders characterized by significant feelings of anxiety and fear. There are several anxiety disorders, including generalized anxiety disorder, specific phobia, social anxiety disorder, separation anxiety disorder, agoraphobia, panic disorder, and selective mutism. People often have more than one anxiety disorder.

## Section C: Symptoms of Proposed Medical Condition and/or It's Treatment

Patients with anxiety disorders frequently have intense, excessive, and persistent worry and fear about everyday situations. Often, anxiety disorders involve repeated episodes of sudden feelings of intense anxiety and fear or terror that reach a peak within minutes (i.e. panic attacks). Common signs and symptoms of anxiety include feeling nervous, restless, or tense; having a sense of impending danger, panic, or doom; having an increased heart rate; breathing rapidly (hyperventilation); sweating; trembling; feeling weak or tired; trouble concentrating or

thinking about anything other than the present worry; having trouble sleeping; experiencing gastrointestinal (GI) problems such as indigestion, stomach cramps, diarrhea, constipation, etc.; having difficulty controlling worry; and having the urge to avoid things that trigger anxiety. These feelings or anxiety and panic, along with the comprehensive symptoms, are difficult to control, are out of proportion to the actual danger, often interfere with daily activities, and can last a long time; they may cause a person to be severely impaired in activities of daily life, such as work, socializing, shopping, family activities, relationships, etc.

#### **Section D: Availability of Conventional Medical Therapies**

Treatments available for anxiety include: anti-anxiety medications (i.e. benzodiazepines and non-benzodiazepine medication buspirone), antidepressants, beta-blockers, and cognitive behavioral therapy (CBT).

Benzodiazepines (i.e. Xanax, Valium, Ativan, etc.): Benzodiazepines are commonly used for anxiety caused by anxiety disorders, panic disorder, and a variety of other conditions. They act on gamma-aminobutyric-acid-A (GABA-A) receptors in the brain, making the nerves in the brain less sensitive to stimulation, creating a calming effect. Benzodiazepines often cause drowsiness, sleepiness, and/or dizziness. Other commonly reported side effects include amnesia (forgetfulness), confusion, constipation, nausea, sexual dysfunction, unsteadiness when walking or standing, unusually slow and shallow breathing, and/or vision problems (blurred or double vision). Some patients may develop a paradoxical reaction to benzodiazepines, in which they become agitated or very anxious, develop hallucinations, have difficulty sleeping or exhibit bizarre behavior (such as taking off their clothes in public or taking unnecessary risks). Tolerance on benzodiazepines develops quickly, and withdrawal symptoms may occur with abrupt discontinuation. Symptoms of withdrawal may include convulsions, cramps, insomnia, sweating, tremors, and vomiting. Benzodiazepines have rather quick onset of action (30-60 minutes), so they may be used as needed.

Buspirone is a serotonin receptor agonist, increasing action at serotonin receptors in the brain, helping alleviate anxiety. It is used to treat symptoms of anxiety such as fear, tension, irritability, dizziness, pounding heartbeat, and other physical symptoms. Buspirone often causes headaches, dizziness, drowsiness, sleep problems (insomnia), nausea, upset stomach, and/or feeling nervous or excited. Additionally, it may cause serious side effects such as chest pains, shortness of breath, and/or lightheadedness. Buspirone has serious interactions with many other medications, and dosing must be maintained meticulously.

Antidepressants are most commonly used to treat depression, but are often very helpful in the treatment of anxiety, whether from anxiety disorders or other disorders such as



obsessive-compulsive disorder (OCD), panic disorder, and post-traumatic stress disorder. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) are the most effective antidepressants used in the treatment of anxiety. These medications increase the amount of serotonin and/or norepinephrine available in the brain, which may help improve symptoms of anxiety. Common SSRIs prescribed for anxiety include fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), escitalopram (Lexapro), and citalopram (Celexa). Common SNRIs prescribed for anxiety include venlafaxine (Effexor), and duloxetine (Cymbalta). Common side effects of these medications include fatigue, nausea, agitation, drowsiness, weight gain, diarrhea, insomnia, sexual dysfunction, nervousness, headaches, dry mouth, and/or increased sweating. SSRIs and SNRIs take up to four to six weeks to begin relieving anxiety symptoms, so they are used for chronic anxiety. These medications may also result in withdrawal, so discontinuation must be tapered by a professional. If not, antidepressant withdrawal can trigger symptoms such as extreme depression and fatigue, irritability, anxiety, flu-like symptoms, and insomnia. Antidepressant withdrawal can also lead to an increased risk of suicide.

Beta blockers - including drugs such as propranolol (Inderal) and atenolol (Tenormin) - are used in the treatment of high blood pressure and heart problems. These medications work by blocking the effects of norepinephrine, which helps control the physical symptoms of anxiety such as rapid heart rate, a trembling voice, sweating, dizziness, and shaky hands, thus they are prescribed off-label for anxiety. Because beta blockers do not lessen the emotional symptoms or anxiety, they are most helpful for phobias such as social phobia and performance anxiety. Common side effects of beta blockers include dizziness, sleepiness, weakness, fatigue, nausea, headache, constipation, and diarrhea.

Cognitive Behavioral Therapy (CBT) teaches individuals different ways of thinking, behaving, and reacting to anxiety-producing and fearful objects and situations. CBT can also help people learn and practice social skills, which is vital for treating social anxiety disorder.

## Section E: Anticipated Benefits from Medical Cannabis

### 1.) Reduction of benzodiazepine use (see PDF attachment)

Chad Purcell et al. 2019 - Reduction of Benzodiazepine Use in Patients Prescribed Medical Cannabis

### 2.) Improved QOL (see PDF attachment)

Nicolas J. Schlienz et al. 2020 - A Cross-Sectional and Prospective Comparison of Medicinal Cannabis Users and Controls on Self-Reported Health

<https://www.openaccessgovernment.org/cannabis-treating-anxiety/77936/> (#3-6 below)

### 3.) Relieving the symptoms of anxiety

Using CBD products can reduce rapid heart rate, panic, trembling and twitching muscles and overall body tension. These are some of the prevalent anxiety symptoms. By alleviating these symptoms, CBD can reduce the overall anxiety one experiences. Cannabis can also treat nausea, palpitations and insomnia that accompany anxiety disorders.

### 4.) Improving brain health and function

If your anxiety stems from mental health issues, cannabis products like CBD can offer relief. There is adequate information supporting the mental health benefits of cannabis. It can reduce stress, depression, PTSD and mood swings. Cannabis can also reduce headaches and migraines or even help in fighting brain tumours.

### 5.) Regulating homeostasis

Homeostasis or balance is responsible for reducing hormonal imbalances during stressful conditions. The endocannabinoid system is responsible for regulating homeostasis. As such, experts believe the action of cannabis on receptors within this system can result in benefits for anxiety patients. This is particularly helpful for those who experience social anxiety.

### 6.) Reducing inhibitions

The psychoactive effects of THC-rich cannabis can help to reduce inhibitions and mental noise in social events. For instance, using cannabis in a party can promote social interactions just like

a glass of wine does. CBD can relax brain functions allowing you to have a good time. However, results vary among users, so this area requires precaution and emphasis on small doses.

## Section F: Scientific Evidence for Support of Medical Cannabis Treatment

**Bruce D, Foster E, Shattell M. Perceived Efficacy of Medical Cannabis in the Treatment of Co-Occurring Health-Related Quality of Life Symptoms [published online ahead of print, 2019 Nov 6]. *Behav Med.* 2019;1-5. doi:10.1080/08964289.2019.1683712**

Here's a report on a Nov. 2019 survey on the perceived efficacy of medical cannabis for people enrolled in Illinois' medical cannabis program. The abstract notes, "Pain was the most frequently reported HRQoL treated by MC, followed by anxiety, insomnia, and depression.

**Likar R, Köstenberger M, Nahler G. Cannabidiol bei Tumorerkrankungen [Cannabidiol in cancer treatment]. *Schmerz.* 2020;34(2):117-122. doi:10.1007/s00482-019-00438-9**

A 2020 review concluded that "preclinical studies, particularly recent ones, including numerous animal models of tumors, unanimously suggest the therapeutic efficacy of CBD" and that "CBD may potentially play a role in the palliative care of patients, especially concerning symptoms such as pain, insomnia, anxiety, and depression."

**Weiss, M. C., Hibbs, J., Mchugh, T. W., Buckley, M., Larson, S., Green, N., . . . Martinez, D. (2020). A survey of breast cancer patients' use of cannabis before, during, and after treatment. *Journal of Clinical Oncology*, 38(15\_suppl). doi:10.1200/jco.2020.38.15\_suppl.e19210**

12/16/2019 - 1/19/2020: Of the 612 breast cancer participants that completed the cannabis survey, 42% used medical cannabis products to relieve symptoms, **including insomnia (70%), pain (59%), anxiety (57%), stress (51%), and nausea/vomiting (46%)**

**Turna J, Simpson W, Patterson B, Lucas P, Van Ameringen M. Cannabis use behaviors and prevalence of anxiety and depressive symptoms in a cohort of Canadian medicinal cannabis users . *Journal of Psychiatric Research*. 2019;111:134-139.**

**doi:10.1016/j.jpsychires.2019.01.024**

Overall, 2032 completed responses with a verified user number were collected. Of the total sample, 888 (43.7%) reported CMP authorization to treat anxiety symptoms and completed all psychometric screening instruments. Rates of probable disorders were high (Generalized Anxiety Disorder: 45.6%, Social Anxiety Disorder: 42.4%, Major Depressive Disorder: 25.7%, Panic Disorder/Agoraphobia: 25.7%); 63.4% met screening criteria for  $\geq 1$  disorder. Most (92%) reported that cannabis improved their symptoms, despite continuing to endorse moderate-level severity. Nearly half (49%) reported replacing a non-psychiatric (53.7%) or psychiatric medication (46.3%) prescribed to them by their physician with CMP.

**Yang K, Moore A, Nguyen K, Nafsu R, Kaufmann C. Cannabis use for anxiety among older adults. *The American Journal of Geriatric Psychiatry*. 2020;28(4):S81-S82.**

**doi:10.1016/j.jagp.2020.01.108**

568 geriatric patients self-administered survey over a period of 12 weeks. N=82 reported cannabis use within the past 3 years. Among recent use, 24.4% (n=20) reported using cannabis to treat anxiety. Of those, 70% (n=14) perceived cannabis to be extremely or somewhat helpful for anxiety whereas 15% (n=3) reported cannabis to be minimally helpful or not helpful at all for anxiety and 15% (n=3) did not respond to the question.

**Ferber SG, Namdar D, Hen-Shoval D, et al. The "Entourage Effect": Terpenes Coupled with Cannabinoids for the Treatment of Mood Disorders and Anxiety Disorders. *CN*.**

**2020;18(2):87-96. doi:10.2174/1570159X17666190903103923**

Literature review on the effects of cannabinoids and the possibility of enhancing cannabinoid activity on psychiatric symptoms by the addition of terpenes and terpenoids. Possible underlying mechanisms for the antidepressant and anxiolytic effects are reviewed.

Sarris J, Sinclair J, Karamacoska D, Davidson M, Firth J. Medicinal cannabis for psychiatric disorders: a clinically-focused systematic review. *BMC Psychiatry*. 2020;20(1):24.  
doi:10.1186/s12888-019-2409-8

**Methods:** The first clinically-focused systematic review on the emerging medical application of cannabis across all major psychiatric disorders was conducted. Current evidence regarding whole plant formulations and plant-derived cannabinoid isolates in mood, anxiety, sleep, psychotic disorders and attention deficit/hyperactivity disorder (ADHD) is discussed; while also detailing clinical prescription considerations (including pharmacogenomics), occupational and public health elements, and future research recommendations. The systematic review of the literature was conducted during 2019, assessing the data from all case studies and clinical trials involving medicinal cannabis or plant-derived isolates for all major psychiatric disorders (neurological conditions and pain were omitted). **Results:** The present evidence in the emerging field of cannabinoid therapeutics in psychiatry is nascent, and thereby it is currently premature to recommend cannabinoid-based interventions. Isolated positive studies have, however, revealed tentative support for cannabinoids (namely cannabidiol; CBD) for reducing social anxiety; with mixed (mainly positive) evidence for adjunctive use in schizophrenia. Case studies suggest that medicinal cannabis may be beneficial for improving sleep and post-traumatic stress disorder, however evidence is currently weak. Preliminary research findings indicate no benefit for depression from high delta-9 tetrahydrocannabinol (THC) therapeutics, or for CBD in mania. One isolated study indicates some potential efficacy for an oral cannabinoid/ terpene combination in ADHD. Clinical prescriptive consideration involves caution in the use of high-THC formulations (avoidance in youth, and in people with anxiety or psychotic disorders), gradual titration, regular assessment, and caution in cardiovascular and respiratory disorders, pregnancy and breast-feeding. **Conclusions:** There is currently encouraging, albeit embryonic, evidence for medicinal cannabis in the treatment of a range of psychiatric disorders. Supportive findings are emerging for some key isolates, however, clinicians need to be mindful of a range of prescriptive and occupational safety considerations, especially if initiating higher dose THC formulas

**Bergamaschi MM, Queiroz RH, Chagas MH, de Oliveira DC, De Martinis BS, Kapczinski F, et al. Cannabidiol reduces the anxiety induced by simulated public speaking in treatment-naïve social phobia patients. *Neuropsychopharmacology*. 2011;36:1219–26. <https://doi-org.eresources.mssm.edu/10.1038/npp.2011.6>.**

This preliminary study aimed to compare the effects of a simulation public speaking test (SPST) on healthy control (HC) patients and treatment-naïve SAD patients who received a single dose of CBD or placebo. A total of 24 never-treated patients with SAD were allocated to receive either CBD (600 mg;  $n=12$ ) or placebo (placebo;  $n=12$ ) in a double-blind randomized design 1 h and a half before the test. The same number of HC ( $n=12$ ) performed the SPST without receiving any medication. Each volunteer participated in only one experimental session in a double-blind procedure. Subjective ratings on the Visual Analogue Mood Scale (VAMS) and Negative Self-Statement scale (SSPS-N) and physiological measures (blood pressure, heart rate, and skin conductance) were measured at six different time points during the SPST. The results were submitted to a repeated-measures analysis of variance. Pretreatment with CBD significantly reduced anxiety, cognitive impairment and discomfort in their speech performance, and significantly decreased alert in their anticipatory speech. The placebo group presented higher anxiety, cognitive impairment, discomfort, and alert levels when compared with the control group as assessed with the VAMS. The SSPS-N scores evidenced significant increases during the testing of the placebo group that was almost abolished in the CBD group. No significant differences were observed between CBD and HC in SSPS-N scores or in the cognitive impairment, discomfort, and alert factors of VAMS. The increase in anxiety induced by the SPST on subjects with SAD was reduced with the use of CBD, resulting in a similar response as the HC.

**Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a Potential Treatment for Anxiety Disorders. *Neurotherapeutics*. 2015;12(4):825-836. [doi:10.1007/s13311-015-0387-1](https://doi.org/10.1007/s13311-015-0387-1)**

“We found that existing preclinical evidence strongly supports CBD as a treatment for generalized anxiety disorder, panic disorder, social anxiety disorder, obsessive–compulsive disorder, and post-traumatic stress disorder when administered acutely; however, few studies have investigated chronic CBD dosing. Likewise, evidence from human studies supports an anxiolytic role of CBD, but is currently limited to acute dosing, also with few studies in clinical populations. Overall, current evidence indicates CBD has considerable potential as a treatment for multiple anxiety disorders, with need for further study of chronic and therapeutic effects in relevant clinical populations.”

**Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. Pills to Pot: Observational Analyses of Cannabis Substitution Among Medical Cannabis Users With Chronic Pain. *The Journal of Pain*. 2019;20(7):830-841. doi:10.1016/j.jpain.2019.01.010**

There were 1,321 participants (59% female, 54% ≥50 years old) who completed the survey. Consistent with other observational studies, approximately 80% reported substituting cannabis for traditional pain medications (53% for opioids, 22% for benzodiazepines), citing fewer side effects and better symptom management as their rationale for doing so.

**Childs E, Lutz JA, de Wit H. Dose-related effects of delta-9-THC on emotional responses to acute psychosocial stress. *Drug Alcohol Depend*. 2017;177:136-144. doi:10.1016/j.drugalcdep.2017.03.030**

**Methods:** Healthy volunteers (N=42) participated in two experimental sessions, one with psychosocial stress (Trier Social Stress Test, TSST) and another with a non-stressful task, after receiving 0 (N=13), 7.5mg (N=14) or 12.5mg (N=15) oral THC. Capsules were administered under randomized, double blind conditions, 2.5h before the tasks began. We measured subjective mood and drug effects, vital signs and salivary cortisol before and at repeated times after the capsule and tasks. Subjects also appraised the tasks, before and after completion. **Results:** In comparison to placebo, 7.5mg THC significantly reduced self-reported subjective distress after the TSST and attenuated post-task appraisals of the TSST as threatening and challenging. By contrast, 12.5mg THC increased negative mood overall i.e., both before and throughout the tasks, and pre-task ratings of the TSST as threatening and challenging. It also impaired TSST performance and attenuated blood pressure reactivity to the stressor. **Conclusions:** Our findings suggest that a low dose of THC produces subjective stress-relieving effects in line with those commonly reported among cannabis users, but that higher doses may non-specifically increase negative mood.

**Kosiba JD, Maisto SA, Ditre JW. Patient-reported use of medical cannabis for pain, anxiety, and depression symptoms: Systematic review and meta-analysis. *Social Science & Medicine*. 2019;233:181-192. doi:10.1016/j.socscimed.2019.06.005**

Meta-analytic results indicated that pain (64%), anxiety (50%), and depression/mood (34%) were common reasons for medical cannabis use. No evidence for publication bias was detected, despite heterogeneity in prevalence rates. A comprehensive assessment of study quality identified a number of specific methodological limitations of the existing research, including challenges in patient recruitment, use of restrictive sampling frames, and a lack of randomized recruitment methods and validated assessment measures.

**Poli P, Crestani F, Salvadori C, et al. Medical cannabis in patients with chronic pain: effect on pain relief, pain disability, and psychological aspects: a prospective non randomized single arm clinical trial. *Clin Ter* 2018; 169:e102–107.**

This trial found long-term cannabis to be effective for alleviating chronic pain. It also supported its anxiolytic effects through assessing anxiety as a secondary psychological outcome. Evidence for cannabis in anxiety can also be drawn from studies where it has been assessed as a secondary outcome, including two clinical trials investigating the efficacy of long-term use of cannabis or related compounds for other health conditions. A prospective open-label study assessed the effect of a cannabis herbal tea on pain-related symptoms, anxiety, and depression in patients (N = 338) with chronic pain for 12 months. At the 3-month assessment point, patients reported significant improvements in anxiety as shown by a 3-point decrease in the Hospital Anxiety and Depression Scale, which were maintained at endpoint.

**Szkudlarek HJ, Desai SJ, Renard J, et al. D-9-Tetrahydrocannabinol and Cannabidiol produce dissociable effects on prefrontal cortical executive function and regulation of affective behaviors. *Neuropsychopharmacology* 2019; 4:817–825.**

The authors compared the effects of THC and CBD in the prefrontal cortex, finding that they had differential effects on anxiety. Findings supported the notion that the therapeutic benefits of CBD may only be prevalent in the presence of THC during stressful states within the PFC, which is of clinical importance.



**Van Ameringen M, Zhang J, Patterson B, Turna J. The role of cannabis in treating anxiety: an update. *Current Opinion in Psychiatry*. 2020;33(1):1-7. doi:10.1097/YCO.0000000000000566**

Summary: The literature evaluating the efficacy of cannabis in anxiety disorders is in its infancy. The survey data is generally positive. Although, while some animal studies posit cannabis constituents to have anxiolytic effects, others suggest the opposite or null results. Few new clinical trials have been conducted recently, and the extant trials have significant flaws in methodology. Although anecdotal evidence from survey studies, and a small signal found in animal studies and single-dose clinical trials provide early support that cannabis may be effective for alleviating anxiety, ultimately, the current evidence is equivocal. More high-quality clinical trials must be published before sound conclusions regarding the efficacy of cannabis for treating anxiety can be drawn

**Linares IM, Zuardi AW, Pereira LC, et al. Cannabidiol presents an inverted U-shaped dose-response curve in a simulated public speaking test. *Rev Bras Psiquiatr* 2019; 41:9–14.**

Recent RCT in social anxiety disorder, in which 57 healthy males received a single-dose of oral CBD (150, 300, or 600 mg) or placebo. Following CBD administration, individuals completed a simulated public speaking test during which anxiety levels were assessed using a Subjective Visual Analogue Mood Scale. Compared to placebo, those who received 300 mg CBD 90 min prior to the public speaking task had significantly lower ratings of social anxiety ( $P = 0.042$ ); whereas 150 and 600 mg CBD did not produce any detectable benefits. This study was the first to confirm the U-shaped dose–response curve to CBD in humans, which has only been observed in animals previously. It highlights the importance of understanding dosage-specific effects of CBD in anxiety.

Purcell C, Davis A, Moolman N, Taylor SM. Reduction of Benzodiazepine Use in Patients Prescribed Medical Cannabis. *Cannabis and Cannabinoid Research*. 2019;4(3):214-218. doi:10.1089/can.2018.0020

Methods: A retrospective analysis was performed on a cohort of 146 medical cannabis patients (average age 47 years, 61% female, 54% reporting prior use of cannabis) who reported benzodiazepine use at initiation of cannabis therapy. These data are a part of a database gathered by a medical cannabis clinic (Canabo Medical). Descriptive statistics were used to quantify associations of the proportion of benzodiazepine use with time on medical cannabis therapy. Results: After completing an average 2-month prescription course of medical cannabis, 30.1% of patients had discontinued benzodiazepines. At a follow-up after two prescriptions, 65 total patients (44.5%) had discontinued benzodiazepines. At the final follow-up period after three medical cannabis prescription courses, 66 total patients (45.2%) had discontinued benzodiazepine use, showing a stable cessation rate over an average of 6 months. Conclusion: Within a cohort of 146 patients initiated on medical cannabis therapy, 45.2% patients successfully discontinued their pre-existing benzodiazepine therapy. This observation merits further investigation into the risks and benefits of the therapeutic use of medical cannabis and its role relating to benzodiazepine use.

#### **ONGOING STUDIES:**

Currently, two trials listed on ClinicalTrials.Gov directly investigate the relationship between cannabis use and anxiety. The first is a prospective study of changes in anxiety, negative affect, and inflammation following self-directed use of smoked cannabis flower and edibles [29]. Particularly, the study aims to understand differences between the anxiolytic effects of THC-based strains versus CBD-based strains versus strains that contain different ratios of THC and CBD (1 : 0, 1 : 1, or 0 : 1). The second trial assesses the efficacy of CBD oil for the treatment of several anxiety disorders, including Generalized Anxiety Disorder, Social Anxiety Disorder, Panic Disorder, and agoraphobia. Participants will be randomized to receive CBD oil or placebo for an 8-week period and assessed based on the Hamilton Anxiety Rating Scale (HAM-A) [30].