

A PETITION TO
ADD ‘DEBILITATING ANXIETY’
AS A QUALIFYING CONDITION FOR
MEDICAL CANNABIS IN DELAWARE

Submitted TO
Office of Medical Marijuana
417 Federal Street - Suite 130 - Dover, Delaware 19901

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DECLARATION OF INTENT

I am petitioning the state of Delaware to add "Debilitating Anxiety" to the list of Qualifying Conditions for medical cannabis in the state of Delaware.

A legal precedent was established on November 29th, 2016 in DE Title 16, Section 4909A, which states **anxiety and depression** are already qualifying conditions for patients younger than 18 years of age if related to a Terminal Illness.

PETITION FOR CHANGE

1. EXISTING LEGAL PRECEDENT FROM DE TITLE 16 SECTION 4909A

The terms anxiety and depression are already qualifying conditions for patients younger than 18 years of age if related to a Terminal Illness.

78 Del. Laws, c. 23, § 1; 70 Del. Laws, c. 186, § 1; 80 Del. Laws, c. 39, § 2.;

§ 4909A Issuance of registry identification cards [Effective Nov. 29, 2016]

(b) The Department shall not issue a registry identification card to a qualifying patient who is younger than 18 years of age, except as follows:

(1) The qualifying patient has any of the following related to a terminal illness:

a. Pain;

b. Anxiety;

c. Depression;

(2) The qualifying patient has intractable epilepsy or seizure disorder; or

(3) The qualifying patient has a chronic or debilitating disease or medical condition where the patient has failed treatment involving 1 or more of the following symptoms: cachexia or wasting syndrome; intractable nausea; severe, painful and persistent muscle spasms.

(4) A qualifying patient who is younger than 18 years of age may only receive marijuana oil.

2. PROPOSED LANGUAGE FOR ANXIETY AND MENTAL HEALTH CONDITIONS

I would like to petition the State of Delaware to add language to the definitions of Debilitating medical conditions to include anxiety or other mental health conditions.

§ 4902A Definitions [Effective Nov. 29, 2016]

(3) "Debilitating medical condition" means 1 or more of the following:

*a. Terminal illness, cancer, positive status for human immunodeficiency virus, acquired immune deficiency syndrome, decompensated cirrhosis, amyotrophic lateral sclerosis, agitation of Alzheimer's disease, post-traumatic stress disorder, **debilitating anxiety**, intractable epilepsy, seizure disorder, or the treatment of these conditions;*

*b. A chronic or debilitating disease or medical condition or **mental health condition** or its treatment that produces 1 or more of the following: cachexia or wasting syndrome; severe, debilitating pain, **debilitating anxiety** that has not responded to previously prescribed medication or surgical measures for more than 3 months or for which other treatment options produced serious side effects; intractable nausea; seizures; severe and*

persistent muscle spasms, including but not limited to those characteristic of multiple sclerosis;

3. MY FATHER'S BATTLE WITH ANXIETY AND WITHDRAWAL

Bob's Bill (DE House Bill 400, 2016) was dedicated in memory of my father, Robert "Bob" Jester was diagnosed with Stage 3 Lung Cancer and despite having a qualifying condition he was denied access to medical cannabis.

In August 2015, my Dad began palliative care at home with Delaware Hospice. After a few months of palliative care, my father's oncologist (who previously denied my father access to medical cannabis) decided that my Dad no longer needed the prescription medication, Ativan (Generic- Lorazepam) that he had been taking to treat his anxiety for the past 30+ years. The doctor did not renew my Dad's prescription and my father began withdrawal within 2-3 days of being taken off the Lorazepam. As the withdrawal symptoms worsened, his behavior became unpredictable regularly becoming irate, loud, difficult, and defiant. The hospice staff continued to plead with the doctor to renew the Lorazepam, but the doctor refused. His primary care provider was in the State of Maryland. Since Bob's primary care provider was an out of state doctor, Delaware Hospice still could not renew the prescription. The doctor discouraged the Hospice Doctors and Nurse Practitioners at Delaware Hospice from renewing the Lorazepam prescription. Dad was bedridden by this time and could not leave the house, so finding a new primary care provider in Delaware was not an option.

Dad's withdrawal symptoms continued to get worse; his behavior became increasingly disturbed ultimately pushing him to fall into a deep depression with bouts of extreme paranoia. A few days before Thanksgiving, his withdrawal hit rock bottom my elderly Aunt had to wrestle a gun away from my father. Only after the suicide attempt, we finally appealed successfully to another doctor at the same oncology practice as his main the doctor to finally renew Dad's prescription for Lorazepam.

Within 24 hours of restarting the Lorazepam, Bob's withdrawal symptoms had completely subsided. Dad continued a steady decline for the remainder of 2015 and found peace on January 7th, 2016.

EXTENT TO WHICH THE CONDITION IS GENERALLY ACCEPTED AS A DEBILITATING MEDICAL CONDITION (6.3.1)

Anxiety disorders are common in people of all ages. They can range in severity from mild to debilitating. When a person has an anxiety disorder, they may feel fearful or uncertain almost all the time. According to the National Institute of Mental Health, the fear and anxiety that occur due to an anxiety disorder are markedly different than the brief episodes of these feelings that are commonly related to normal events, such as speaking at a public event or meeting a blind date. In most cases, if a person has an anxiety disorder, their anxiety disorder symptoms will persist for more than six months.

More than 40 million people in the United States over the age of 18 suffer from some form of anxiety disorder. Collectively, these conditions are the most common mental illness in the country. Consider the fact that more people suffer anxiety disorders than arthritis, the leading cause of physical disability that affects more than 30 million people.

Whether Generalized Anxiety Disorder, Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder, Social Anxiety Disorder, or Panic Disorder, millions are plagued each day by stress and anxiety that leads to dozens of other stress-related ailments and physical conditions, including agoraphobia, high blood pressure, and cardiovascular conditions.

Those who suffer from anxiety-related disorders experience a variety of symptoms, from irritability, feelings of dread, and nausea to insomnia, fatigue, chest pain and heart palpitations, shortness of breath, and panic attacks. For many, severe anxiety, along with the fear and hopelessness that often accompany it, becomes a debilitating condition that results in damaged careers, wrecked social lives, and tarnished family relations. Often, those who suffer severe anxiety also succumb to depression and self-medicate with alcohol or opiate.

1. GENERALIZED ANXIETY DISORDER (GAD)

Generalized Anxiety Disorder is an anxiety disorder in which an individual experiences uncontrollable, persistent worry about a variety of everyday problems. This anxiety and worry is exaggerated and inconsistent with the degree of anxiety that the situation warrants. This anxiety and worry may impair the individual's sleep, appetite, and ability to concentrate. The individual may experience physiological symptoms including headache, stomach upset, hot flashes, muscle tension, and fatigue as well as irritability and an inability to relax. This anxiety can become so intense that it impairs the individual's ability to carry out activities of daily living.

If you have generalized anxiety disorder, you may feel constantly worried even if there is no real reason to worry about anything. In most cases, this type of anxiety disorder starts when you are in your teens, and its symptoms get worse as you progress through adulthood.

2. PANIC DISORDER (CHARACTERIZED BY ANXIETY OR PANIC ATTACKS)

Panic Disorder is an anxiety disorder that is characterized by repeated, sudden, discrete periods of intense anxiety accompanied by physiological symptoms such as tachycardia (racing heart), sweating, weakness, stomach upset, shortness of breath, dizziness, nausea, and/or chest pain, among other symptoms. Panic attacks are frequently accompanied by a fear of impending doom, fear of “going crazy,” fear that one is having a heart attack, and/or fear of “losing control.” Individuals who experience panic attacks typically experience anticipatory anxiety regarding future panic attacks and can become disabled by their fear, unable to carry out daily activities

If you suffer from panic attacks, you may have a panic disorder. This condition, which is often marked by extreme anxiety, may cause you to feel panicked about small things, and these feelings may escalate during times of stress. Sadly, many people with panic disorders may struggle with embarrassment. They may feel embarrassed that simple tasks, such as driving a car or shopping for groceries, are difficult and sometimes impossible to do.

3. OBSESSIVE-COMPULSIVE DISORDER (OCD)

Many people think they have obsessive-compulsive disorder if they clean their house obsessively or consistently check their car door after locking it. However, a person with OCD struggles with ending their compulsive desire to repeat the same actions over and over again. In most cases, anxiety disorder symptoms associated with OCD appear during childhood.

4. PHOBIAS

A phobia is the persistent, irrational fear of – and wish to avoid – an object, activity or situation that causes severe anxiety in someone. If you or someone you love has intense and irrational fears of things that are really not that dangerous, a phobia may be in play. People who suffer from phobias fear all kinds of things.

There are specific phobias (fear of heights, spiders etc.), that are easy for people to handle but there are other phobias - like agoraphobia (fear of open spaces) or social phobias - that are much less manageable. These can have a dramatic effect on the quality of life of sufferers who often severely limit their activities to avoid situations that make them anxious.

If you have a phobia, you may experience any of the following anxiety disorder symptoms when you are facing something you fear: Feelings of panic, Elevated heart rate, Inability to catch your breath or shortness of breath, and unexplained shaking.

5. SOCIAL ANXIETY DISORDER

People who fear what other people think of them and as a result avoid social situations are considered to have a social phobia. Symptoms include blushing, hand tremor, nausea with the possibility of it progressing to panic attacks. Social phobias are associated with a fear of criticism and low self-esteem. According to the Anxiety and Depression Association of America, you may have a social anxiety disorder if you feel afraid of being judged by others. In some cases, your symptoms may be so devastating that they may disrupt your relationships or your daily life. Typically, the onset of this

disorder happens at age 13, and over one-third of the people who suffer from this disorder suffer from it for 10 or more years before seeking help.

EXTENT TO WHICH CONVENTIONAL TREATMENTS ARE CAUSING OR ADDING TO A PATIENT'S SUFFERING (6.3.2)

Synthetic drugs and medication can relieve some of the symptoms of anxiety, but it doesn't cure the underlying problem and it's usually not a long-term solution. Anxiety medications also come with side effects and safety concerns, such as the risk of addiction. The medications used to treat this wide variety of anxiety disorders are quite common and include Xanax (alprazolam), Ativan (lorazepam), and Valium (diazepam).

Also frequently prescribed are Prozac (fluoxetine), Zoloft (sertraline), and Wellbutrin (bupropion). Despite their commonality, many of these drugs deliver agonizing side effects that are often worse than the conditions they are prescribed to treat. Insomnia, depression, hallucinations, and even suicidal thoughts (especially in teens) are all-too-common with these drugs.

1. COMMON SIDE-EFFECTS OF BENZODIAZEPINES OR TRANQUILIZERS

Anti-anxiety drugs like benzodiazepines work by reducing brain activity. While this temporarily relieves anxiety, it can also lead to unwanted side effects. The higher the dose, the more pronounced these side effects typically become. However, some people feel sleepy, foggy, and uncoordinated even on low doses of benzodiazepines, which can cause problems with work, school, or everyday activities such as driving. Some even feel a medication hangover the next day. Other well-documented side effects include”

- Drowsiness, lack of energy
- Clumsiness, slow reflexes
- Slurred speech
- Confusion and disorientation
- Depression
- Dizziness, lightheadedness
- Impaired thinking and judgment
- Memory loss, forgetfulness
- Nausea, stomach upset
- Blurred or double vision

Because benzodiazepines are metabolized slowly, the medication can build up in the body when used over longer periods of time. The result is over sedation. People who are over sedated may look like they're drunk.

2. PARADOXICAL EFFECTS OF ANTI-ANXIETY DRUGS

Despite their sedating properties, some people who take anti-anxiety medication experience paradoxical excitement. The most common paradoxical reactions are increased anxiety, irritability, and

agitation. However, more severe effects can also occur, including mania, hostility, rage, aggression, impulsive behavior, and hallucinations. Benzodiazepines are also associated with depression. Beyond the common side effects, medication for anxiety comes with additional risks. While the tranquilizing anti-anxiety drugs are relatively safe when taken only occasionally and in small doses, they can lead to severe problems when combined with other substances or taken over long periods of time. Furthermore, some people will have adverse reactions to any amount of anti-anxiety medication. They are not safe for everyone, even when used responsibly.

3. DRUG INTERACTIONS AND OVERDOSE

Used alone, anti-anxiety medications such as Xanax or Valium rarely cause fatal overdose, even when taken in large doses. But when combined with other central nervous system depressants, the toxic effects of these anxiety medications increase.

Taking anti-anxiety medication with alcohol, prescription painkillers, or sleeping pills can be deadly. Dangerous drug interactions can also occur when anti-anxiety drugs are taken with antihistamines, which are found in many over-the-counter cold and allergy medicines and sleep aids. Antidepressants such as Prozac and Zoloft can also heighten their toxicity. Always talk to your doctor or pharmacist before combining medications.

4. ANTI-ANXIETY DRUG RISK FACTORS

Anyone who takes anti-anxiety medication can experience unpleasant or dangerous side effects. But certain individuals are at a higher risk:

PEOPLE OVER 65.

Older adults are more sensitive to the sedating effects of anti-anxiety medication. Even small doses can cause confusion, amnesia, loss of balance, and cognitive impairment that looks like dementia. Anti-anxiety drug use in the elderly is associated with an increased risk of falls, broken hips and legs, and car accidents.

PREGNANT WOMEN.

Expectant mothers should avoid anti-anxiety drugs. Since these anxiety medications cross the placenta, their use during pregnancy can lead to dependence in the baby. Following birth, the baby will then go through withdrawal, with symptoms such as muscle weakness, irritability, sleep and breathing problems, and trembling. These anxiety drugs are excreted in breast milk, so they should be avoided while breastfeeding, too.

PEOPLE WITH A HISTORY OF SUBSTANCE ABUSE.

Anyone with a current or former problem with alcohol or drugs should avoid anti-anxiety drugs or use them only with extreme caution. The greatest benefit of benzodiazepines is that they work quickly, but this also makes them addictive. This can quickly lead to their abuse, often in dangerous combination with alcohol or other illicit drugs.

Anti-anxiety medication causes drowsiness and poor coordination, which contributes to accidents at home, at work, and on the road. Studies show that taking anti-anxiety medication increases your risk of having a serious traffic accident.

5. ANTI-ANXIETY DRUG DEPENDENCE AND WITHDRAWAL

Anti-anxiety medications including popular benzodiazepines such as Xanax, Klonopin, Valium, and Ativan are meant for short-term use. However, many people take anti-anxiety drugs for long periods of time. This is risky because, when taken regularly, benzodiazepines quickly lead to physical dependence. Drug tolerance is also common, with increasingly larger doses needed to get the same anxiety relief as before. According to the American Academy of Family Physicians, benzodiazepines lose their therapeutic anti-anxiety effect after 4 to 6 months of regular use.

Most people become addicted to their anti-anxiety drug within a couple of months, but problems may arise sooner. For some, drug dependency develops after a few short weeks. Once you're physically dependent on an anxiety medication, it's difficult to stop taking it. The body is used to the medication, so withdrawal symptoms occur if the dose is decreased or discontinued.

Psychological dependence can be an issue, too. If you've been relying on an anti-anxiety drug to keep your anxiety in check, you may lose confidence in your own abilities to deal with life's difficulties and start to think you "need" the medication to survive.

6. OTHER TYPES OF MEDICATIONS FOR ANXIETY

Because of the many safety concerns linked to anti-anxiety drugs, other medications for treating anxiety have gained in popularity. The alternatives to the anti-anxiety tranquilizers include antidepressants, buspirone, and beta blockers.

Many medications originally approved for the treatment of depression have been found to relieve symptoms of anxiety. These include certain selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and the newer atypical antidepressants.

All antidepressants are required by the FDA to carry a warning about the risk of suicidal thoughts, hostility, and agitation. There is also the risk that antidepressants will cause an increase, rather than a decrease, in depression and anxiety. The antidepressants most widely prescribed for anxiety are SSRIs such as Prozac, Zoloft, Paxil, Lexapro, and Celexa. These work by regulating serotonin levels in the brain to elevate mood and have been used to treat panic disorder, obsessive-compulsive disorder (OCD), and generalized anxiety disorder (GAD). Common side effects include: Nausea, Nervousness, Headaches, Sleepiness, Sexual dysfunction, Dizziness, Stomach upset, and Weight gain. Although physical dependence is not as quick to develop with antidepressants, withdrawal can still be an issue. Long-term benzodiazepine users are often depressed, and higher doses are believed to increase the risk of both depressive symptoms and suicidal thoughts and feelings. Furthermore, benzodiazepines can cause emotional blunting or numbness. The medication relieves the anxiety, but it also blocks feelings of pleasure or pain and if discontinued too quickly, antidepressant withdrawal can trigger

symptoms such as extreme depression and fatigue, irritability, anxiety, flu-like symptoms, and insomnia.

7. RISKS ASSOCIATED WITH LONG-TERM BENZODIAZEPINE USE

<http://www.aafp.org/afp/2013/0815/p224.html>

In summary, it is unclear where long-term benzodiazepine use fits into current medical practice. Many patients underestimate the degree of impairment caused by benzodiazepines. Benzodiazepines increase the risk of addiction, withdrawal, cognitive decline, motor vehicle crashes, and hip fracture. The risk of overdose is particularly great when combined with sedative drugs such as opioids or alcohol. For these reasons, if used, benzodiazepines generally should not be prescribed continuously for more than one month. There are effective alternatives. Psychotherapy and antidepressants are the treatments of choice for anxiety disorders. Short-term medications that can be used for anxiety without risk of addiction include propranolol, anticonvulsants, or major tranquilizers. Finally, insomnia can be treated with trazodone, doxepin, or ramelteon (Rozerem) without risk of rebound insomnia.

8. BENZODIAZEPINE USE MAY RAISE RISK OF ALZHEIMER'S DISEASE

<https://www.health.harvard.edu/blog/benzodiazepine-use-may-raise-risk-alzheimers-disease-201409107397>

People who had taken a benzodiazepine for three months or less had about the same dementia risk as those who had never taken one. Taking the drug for three to six months raised the risk of developing Alzheimer's by 32%, and taking it for more than six months boosted the risk by 84%.

9. THE DANGERS OF BENZO WITHDRAWALS

<https://www.pbainstitute.com/dangers-benzo-withdrawals-right/>

Although many substance abusers consider the effects of benzodiazepines to be much less pronounced than more preferable, powerful substances like heroin and painkillers, benzodiazepines are still incredibly dangerous for a few important reasons. First, being that their effects are less pronounced than most other substances, people who abuse benzodiazepines are prone to overdosing

by taking too many of them in an attempt to amplify their effects. Additionally, substance abusers frequently take benzodiazepines with other substances, especially opiates, because layering the drugs amplifies the effects of both; again, this significantly increases one's **potential for overdosing**. There are some combinations involving benzodiazepines that can very easily be lethal, including the mixing of benzodiazepines with methadone or other opioids.

However, one of the most unexpected dangers of benzodiazepines is when a person stops taking the drug. When an addict wants to overcome his or her addiction, the first step is to cease consumption and complete a detox. For a benzodiazepine addict, detoxing is one of the most dangerous phases of its abuse. Benzodiazepines were put to medicinal use due to their being so effective for altering one's brain chemistry, but this efficacy is also what makes them dangerous. In effect, when a medication is significantly altering one's neurochemical levels, he or she can't simply just stop taking the drug due to its intense physiological effects on the brain and the body becoming intensely dependent on the drug's effects. This makes benzodiazepines quite similar to alcohol in the sense that both substances can harm addicts who cease consumption too abruptly. Without the proper precautions, there have been a number of instances of benzodiazepine withdrawal **becoming fatal**.

10. LONG-TERM USE OF BENZODIAZEPINE DRUGS FOR ANXIETY AND SLEEP DISORDERS LINKED TO INCREASED ALZHEIMER'S RISK

<https://alzheimersnewstoday.com/2014/09/12/long-term-use-of-benzodiazepine-drugs-for-anxiety-and-sleep-disorders-linked-to-increased-alzheimers-risk/>

However, with their study finding risk of Alzheimer's disease increased by 43-51% among those who had used benzodiazepines in the past, the researchers say it reinforces suspicion of an increased risk of Alzheimer type dementia among benzodiazepine users, particularly long term users, and provides arguments for carefully evaluating the indications for use of this drug class — especially considering the prevalence and chronicity of benzodiazepine use in older people. They contend that with no preventive or curative treatment having been shown to be satisfactorily effective for Alzheimer's disease, identification of putative alterable risk factors should be prioritized, and with increasing incidence of dementia in developed countries, greater likelihood of Alzheimer's development in 43-51% of benzodiazepine users would generate a huge number of excess cases.

11. CONCLUSIONS

Antidepressants are often preferred over the traditional anti-anxiety drugs because the risk for dependency and abuse is smaller. However, antidepressants take up to 4 to 6 weeks to begin relieving anxiety symptoms, so they can't be taken "as needed." For example, antidepressants wouldn't help at all if you waited until you were having a panic attack to take them. Their use is limited to chronic anxiety problems that require ongoing treatment.

With such negative (and highly ironic) side effects from these pharmaceutical treatments, it's no wonder that millions of Americans have opted to self-medicate with alcohol, opiates, or medical cannabis. Unlike cannabis, many pharmaceutical treatments result in physical addiction, including withdrawal when abruptly discontinued. In addition, most of these drugs can lead to overdose, something that's impossible with marijuana (even with concentrates like kief, hash oil, and wax).

In 2014, a school teacher in California reported collapsing on her kitchen floor and being unconscious for more than an hour. Upon waking, she suffered tremors and hallucinations. "I felt these horrible jolts running through my head and body; I couldn't stop jerking. Then I began seeing stuff that wasn't there, creepy-crawly things. I didn't know what was happening, but I worried I might be dying."

Unfortunately, these were simply the withdrawal symptoms of Xanax, a drug she consumed for more than eight years to battle insomnia, which her doctor believed to be caused by anxiety. At the time she discontinued use and suffered these withdrawal symptoms, she was being prescribed 6 mg of the drug, an unusually high dosage.

Harris Stratyner, co-chairman of the National Council on Alcoholism and Drug Dependence, emphasized that many such cases result from patients using these dangerous drugs as prescribed, with no signs of abuse. He said:

"Dependence on benzodiazepines like Xanax is a serious problem, especially among young women. Frequently, it's not because they've been abusing the drugs; it can be caused by following the prescription their doctor gave them."

EXTENT TO ANXIETY SEVERELY IMPAIR THE PATIENT'S ABILITY TO CARRY ON ACTIVITIES OF DAILY LIVING (6.3.3)

1. MENTAL HEALTH & ANXIETY

UNIVERSITY OF MICHIGAN HEALTH SYSTEM, DEPARTMENT OF PSYCHIATRY
http://www.psych.med.umich.edu/mental_health/anxiety.asp

Approximately 40 million American adults are affected by an anxiety disorder each year causing them to experience persistent distress which has a significant impact upon their daily functioning. feeling worried or nervous is a normal part of everyday life. Everyone frets or feels anxious from time to time. Mild to moderate anxiety can help you focus your attention, energy, and motivation. If anxiety is severe, you may have feelings of helplessness, confusion, and extreme worry that are out of proportion with the actual seriousness or likelihood of the feared event. Overwhelming anxiety that interferes with daily life is not normal. This type of anxiety may be a symptom of another problem, such as depression.

Anxiety can cause physical and emotional symptoms. A specific situation or fear can cause some or all of these symptoms for a short time. When the situation passes, the symptoms usually go away.

Physical symptoms of anxiety include:

- Trembling, twitching, or shaking.
- Feeling of fullness in the throat or chest.
- Breathlessness or rapid heartbeat.
- Lightheadedness or dizziness.
- Sweating or cold, clammy hands.
- Feeling jumpy.
- Muscle tension, aches, or soreness (myalgia).
- Extreme tiredness.
- Sleep problems, such as the inability to fall asleep or stay asleep, early waking, or restlessness (not feeling rested when you wake up).

Anxiety affects the part of the brain that helps control how you communicate. This makes it more difficult to express yourself creatively or function effectively in relationships. Emotional symptoms of anxiety include:

- Restlessness, irritability, or feeling on edge or keyed up.
- Worrying too much.
- Fearing that something bad is going to happen; feeling doomed.
- Inability to concentrate; feeling like your mind goes blank.

Anxiety disorders occur when people have both physical and emotional symptoms. Anxiety disorders interfere with how a person gets along with others and affect daily activities. Women are twice as

likely as men to have problems with anxiety disorders. Examples of anxiety disorders include panic attacks, phobias, obsessive-compulsive disorder, and post-traumatic stress disorder (PTSD).

Often the cause of anxiety disorders is not known. Many people with an anxiety disorder say they have felt nervous and anxious all their lives. This problem can occur at any age. Children who have at least one parent with the diagnosis of depression are more than twice as likely to have an anxiety disorder as other children.

Anxiety disorders often occur with other problems, such as:

- Mental health problems, such as depression or substance abuse.
- A physical problem, such as heart or lung disease. A complete medical examination may be needed before an anxiety disorder can be diagnosed.

Anxiety disorders come in many different forms, all of which involve excessive worrying, uneasiness, apprehension and fear. Social anxiety, phobias, obsessive-compulsive disorder(OCD) and post-traumatic stress disorder (PTSD) all fall under the category of anxiety disorders.

While anxiety is a natural occurrence for all people, those who suffer from anxiety disorders experience severe impairment from their worries. It is estimated that approximately 18% of Americans and 14% of Europeans suffer from some form of anxiety disorder.

2. THE ECONOMIC BURDEN OF ANXIETY DISORDERS IN THE 1990S (1999)

JOURNAL OF CLINICAL PSYCHIATRY. 1999 JUL;60(7):427-35.

<http://www.ncbi.nlm.nih.gov/pubmed/10453795>

According to a 1999 study published in **The Journal of Clinical Psychiatry**, anxiety disorders cost the United States more than \$40 billion — about one-third of the nation’s \$150 billion mental health bill at the time.

“We estimated the annual cost of anxiety disorders to be approximately \$42.3 billion in 1990 in the United States, or \$1542 per sufferer. This comprises \$23.0 billion (or 54% of the total cost) in non-psychiatric medical treatment costs, \$13.3 billion (31%) in psychiatric treatment costs, \$4.1 billion (10%) in indirect workplace costs, \$1.2 billion (3%) in mortality costs, and \$0.8 billion (2%) in prescription pharmaceutical costs. Of the \$256 in workplace costs per anxious worker, 88% is attributable to lost productivity while at work as opposed to absenteeism. Posttraumatic stress disorder and panic disorder are the anxiety disorders found to have the highest rates of service use. Other than simple phobia, all anxiety disorders analyzed are associated with impairment in workplace performance.”

3. GENERALIZED ANXIETY DISORDER: PREVALENCE, BURDEN, AND COST TO SOCIETY (2002)

HANS-ULRICH WITTCHEN PH.D. JOURNAL OF DEPRESSION AND ANXIETY

<http://onlinelibrary.wiley.com/doi/10.1002/da.10065/abstract>

Generalized anxiety disorder (GAD) is a prevalent and disabling disorder characterized by persistent worrying, anxiety symptoms, and tension. It is the most frequent anxiety disorder in primary care, being present in 22% of primary care patients who complain of anxiety problems. The high prevalence rate of GAD in primary care (8%) compared to that reported in the general population (12-month prevalence 1.9–5.1%) suggests that GAD patients are high users of primary care resources. GAD affects women more frequently than men and prevalence rates are high in midlife (prevalence in females over age 35: 10%) and older subjects but relatively low in adolescents. The natural course of GAD can be characterized as chronic with few complete remissions, a waxing and waning course of GAD symptoms, and the occurrence of substantial comorbidity particularly with depression.

Patients with GAD demonstrate a considerable degree of impairment and disability, even in its pure form, uncomplicated by depression or other mental disorders. The degree of impairment is similar to that of cases with major depression. GAD comorbid with depression usually reveals considerably higher numbers of disability days in the past month than either condition in its pure form. As a result, GAD is associated with a significant economic burden owing to decreased work productivity and increased use of health care services, particularly primary health care. The appropriate use of psychological treatments and antidepressants may improve both anxiety and depression symptoms and may also play a role in preventing comorbid major depression in GAD thus reducing the burden on both the individual and society.

EXTENT TO WHICH CONVENTIONAL TREATMENTS MAY ALLEVIATE SUFFERING (6.3.4)

The medications used to treat this wide variety of anxiety disorders are quite common and include Xanax (alprazolam), Ativan (lorazepam), and Valium (diazepam). Also frequently prescribed are Prozac (fluoxetine), Zoloft (sertraline), and Wellbutrin (bupropion). Despite their commonality, many of these drugs deliver agonizing side effects that are often worse than the conditions they are prescribed to treat. Insomnia, depression, hallucinations, and even suicidal thoughts (especially in teens) are all-too-common with these drugs.

1. RISKS OF ANTI-ANXIETY DRUGS

Anti-anxiety drugs like benzodiazepines work by reducing brain activity. While this temporarily relieves anxiety, it can also lead to unwanted side effects. The higher the dose, the more pronounced these side effects typically become. However, some people feel sleepy, foggy, and uncoordinated even on low doses of benzodiazepines, which can cause problems with work, school, or everyday activities such as driving. Some even feel a medication hangover the next day. Because benzodiazepines are metabolized slowly, the medication can build up in the body when used over longer periods of time. The result is over sedation. People who are over sedated may look like they're drunk.

Because of the many safety concerns linked to anti-anxiety drugs, other medications for treating anxiety have gained in popularity. The alternatives to the anti-anxiety tranquilizers include antidepressants, buspirone, and beta blockers. Many medications originally approved for the treatment of depression have been found to relieve symptoms of anxiety. These include certain selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), and the newer atypical antidepressants.

2. RISKS OF ANTI-DEPRESSANTS

All antidepressants are required by the FDA to carry a warning about the risk of suicidal thoughts, hostility, and agitation. There is also the risk that antidepressants will cause an increase, rather than a decrease, in depression and anxiety. The antidepressants most widely prescribed for anxiety are SSRIs such as Prozac, Zoloft, Paxil, Lexapro, and Celexa. These work by regulating serotonin levels in the brain to elevate mood and have been used to treat panic disorder, obsessive-compulsive disorder (OCD), and generalized anxiety disorder (GAD).

Common side effects include: Nausea, Nervousness, Headaches, Sleepiness, Sexual dysfunction, Dizziness, Stomach upset, and Weight gain. Although physical dependence is not as quick to develop with antidepressants, withdrawal can still be an issue.

3. RISKS OF LONG-TERM BENODIAZEPINE USE

Long-term benzodiazepine users are often depressed, and higher doses are believed to increase the risk of both depressive symptoms and suicidal thoughts and feelings. Furthermore, benzodiazepines can cause emotional blunting or numbness. The medication relieves the anxiety, but it also blocks feelings of pleasure or pain and if discontinued too quickly, antidepressant withdrawal can trigger symptoms such as extreme depression and fatigue, irritability, anxiety, flu-like symptoms, and insomnia.

Medication can relieve some of the symptoms of anxiety, but it doesn't cure the underlying problem and it's usually not a long-term solution. Anxiety medications also come with side effects and safety concerns, such as the risk of addiction.

THE EXTENT TO WHICH EVIDENCE THAT IS GENERALLY ACCEPTED AMONG THE MEDICAL COMMUNITY AND OTHER EXPERTS SUPPORTS A FINDING THAT THE USE OF MARIJUANA ALLEVIATES SUFFERING CAUSED BY THE CONDITION OR TREATMENT (6.3.5)

Cannabis has long had a reputation as a substance that helps users “chill out” and relax. Indica strains are infamous for delivering so much relaxation. Scientists now understand that a cannabinoid molecule known as cannabidiol, or CBD, is responsible for many of the anxiety-relieving effects of marijuana. CBD, like the more well-known cannabinoid THC, is one of over 100 such molecules found in the marijuana plant. CBD has been shown to act on natural receptors that are found in our nervous system known as CB1 receptors. CBD, a Cannabis sativa constituent, is a pharmacologically broad-spectrum drug that in recent years has drawn increasing interest as a treatment for a range of neuropsychiatric disorders. When properly dosed and recommended by a physician (something only possible in legal states with dispensary networks), cannabis — especially strains low in THC and high in CBD — may be an effective and significantly safer alternative to the slew of pharmaceutical drugs commonly prescribed for many forms of anxiety.

Marijuana can reduce anxiety because of its effect on the cannabinoid receptors compensating for the reduction in the production of natural endocannabinoids, specifically in the amygdala which is the part of the brain that is involved in regulating anxiety and the fight-or-flight response.

1. EFFECTS OF CANNABIDIOL (CBD) ON REGIONAL CEREBRAL BLOOD FLOW (2004).

DEPARTMENT OF NEUROPSYCHIATRY AND MEDICAL PSYCHOLOGY, FACULTY OF MEDICINE OF RIBEIRÃO PRETO, UNIVERSITY OF SÃO PAULO, BRAZIL.

1. <https://www.ncbi.nlm.nih.gov/pubmed/14583744>

CBD significantly decreased subjective anxiety and increased mental sedation, while placebo did not induce significant changes. Assessment of brain regions where anxiolytic effects of CBD were predicted a priori revealed two voxel clusters of significantly decreased ECD uptake in the CBD relative to the placebo condition ($p < 0.001$, uncorrected for multiple comparisons). These included a medial temporal cluster encompassing the left amygdala-hippocampal complex, extending into the hypothalamus, and a second cluster in the left posterior cingulate gyrus. There was also a cluster of greater activity with CBD than placebo in the left parahippocampal gyrus ($p < 0.001$). These results suggest that CBD has anxiolytic properties, and that these effects are mediated by an action on limbic and paralimbic brain areas.

2. MEDICINAL USE OF CANNABIS IN THE UNITED STATES: HISTORICAL PERSPECTIVES, CURRENT TRENDS, AND FUTURE DIRECTIONS (2009)

UNIVERSITY OF WASHINGTON, SEATTLE, WA, USA.

<https://www.ncbi.nlm.nih.gov/pubmed/19662925>

Cannabis (marijuana) has been used for medicinal purposes for millennia, said to be first noted by the Chinese in c. 2737 BCE. Medicinal cannabis arrived in the United States much later, burdened with a remarkably checkered, yet colorful, history. Despite early robust use, after the advent of opioids and aspirin, medicinal cannabis use faded. The past few decades have seen renewed interest in medicinal cannabis, with the National Institutes of Health, the Institute of Medicine, and the American College of Physicians, all issuing statements of support for further research and development.

The recently discovered endocannabinoid system has greatly increased our understanding of the actions of exogenous cannabis. Endocannabinoids appear to control pain, muscle tone, mood state, appetite, and inflammation, among other effects. Cannabis contains more than 100 different cannabinoids and has the capacity for analgesia through neuromodulation in ascending and descending pain pathways, neuroprotection, and anti-inflammatory mechanisms.

3. NEURAL BASIS OF ANXIOLYTIC EFFECTS OF CANNABIDIOL (CBD) IN GENERALIZED SOCIAL ANXIETY DISORDER: A PRELIMINARY REPORT (2011).

DEPARTMENT OF NEUROSCIENCES AND BEHAVIOR, DIVISION OF PSYCHIATRY, UNIVERSITY OF SÃO PAULO, RIBEIRÃO PRETO, SÃO PAULO, BRAZIL.

- <http://www.ncbi.nlm.nih.gov/pubmed/20829306>

Animal and human studies indicate that cannabidiol (CBD), a major constituent of cannabis, has anxiolytic properties. However, no study to date has investigated the effects of this compound on human pathological anxiety and its underlying brain mechanisms... Relative to placebo, CBD was associated with significantly decreased subjective anxiety ($p < 0.001$), reduced ECD uptake in the left parahippocampal gyrus, hippocampus, and inferior temporal gyrus ($p < 0.001$, uncorrected), and increased ECD uptake in the right posterior cingulate gyrus ($p < 0.001$, uncorrected). These results suggest that CBD reduces anxiety in SAD and that this is related to its effects on activity in limbic and paralimbic brain areas.

4. CANNABIDIOL REDUCES THE ANXIETY INDUCED BY SIMULATED PUBLIC SPEAKING IN TREATMENT-NAÏVE SOCIAL PHOBIA PATIENTS (2011)

DEPARTMENT OF NEUROSCIENCE AND BEHAVIOR, SCHOOL OF MEDICINE OF RIBEIRÃO PRETO, UNIVERSITY OF SÃO PAULO, SP, BRAZIL.

<https://www.ncbi.nlm.nih.gov/pubmed/21307846>

Generalized Social Anxiety Disorder (SAD) is one of the most common anxiety conditions with impairment in social life. Cannabidiol (CBD), one major non-psychotomimetic compound of the cannabis sativa plant, has shown anxiolytic effects both in humans and in animals.

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 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.

5. THE ANXIOLYTIC EFFECT OF CANNABIDIOL ON CHRONICALLY STRESSED MICE DEPENDS ON HIPPOCAMPAL NEUROGENESIS: INVOLVEMENT OF THE ENDOCANNABINOID SYSTEM (2013).

DEPARTMENT OF PHARMACOLOGY, SCHOOL OF MEDICINE OF RIBEIRÃO PRETO, CENTRE FOR INTERDISCIPLINARY RESEARCH ON APPLIED NEUROSCIENCES (NAPNA), UNIVERSITY OF SAO PAULO, BRAZIL.

<http://www.ncbi.nlm.nih.gov/pubmed/23298518>

*Cannabidiol (CBD), the main non-psychotomimetic component of the plant Cannabis sativa, exerts therapeutically promising effects on human mental health such as inhibition of psychosis, anxiety and depression... **These findings support that the anxiolytic effect of chronic CBD administration in stressed mice depends on its proneurogenic action in the adult hippocampus by facilitating endocannabinoid-mediated signaling.***

6. THE ENDOCANNABINOID SYSTEM AND THE BRAIN (2013)

INSTITUTE FOR DRUG RESEARCH, HEBREW UNIVERSITY, JERUSALEM, ISRAEL.

<http://www.ncbi.nlm.nih.gov/pubmed/22804774?dopt=Abstract>

The historical use of cannabis to treat anxiety disorders goes back possibly thousands of years. The use of cannabis in the treatment of anxiety disorders was first described by ancient Indian medical literature, which said that cannabis helped its user to be “delivered from all worries and care”

In 1563, Garcia de Orta, a Portuguese physician, herbalist, and naturalist, published Colóquios dos simples e drogas da Índia, the earliest book on the medicinal plants of India. The publication claimed that cannabis helped patients suffering from anxiety to be “delivered from all worries and care.”

In 1621, nearly half a millennium ago, English clergyman Robert Burton suggested cannabis for the treatment of depression, one of the most common symptoms of anxiety disorders. In 1860, the Ohio State Medical Committee on Cannabis concluded:

“As a calmative and hypnotic, in all forms of nervous inquietude and cerebral excitement, [cannabis] will be found an invaluable agent, as it produces none of those functional derangements or sequences that render many of the more customary remedies objectionable.”

The Ohio State Medical Committee report also noted that Indica strains were best for treating anxiety, although it wasn’t known at the time that it was because they typically contain more CBD, which is believed to be more effective than THC for the condition.

In 1982, a study published in the journal **Psychopharmacology** revealed that CBD, the non-psychoactive cannabinoid that is commonly used to treat childhood epilepsy and put cancer into remission, decreased the anxiety experienced by high quantities of THC.

In 2011, researchers at the University of Sao Paulo in Brazil gave 400 mg doses of CBD to patients suffering from generalized Social Anxiety Disorder (SAD), a condition that afflicts roughly 12 percent of Americans at some point in their lives. It found that cerebral blood flow after CBD treatment indicates an anxiolytic (anti-anxiety) effect in the regions of the brain that control emotion.

7. CANNABIDIOL, A CANNABIS SATIVA CONSTITUENT, AS AN ANXIOLYTIC DRUG (2012).

LABORATORY OF PANIC AND RESPIRATION, INSTITUTE OF PSYCHIATRY, UNIVERSIDADE FEDERAL DO RIO DE JANEIRO, BRAZIL.

<http://www.ncbi.nlm.nih.gov/pubmed/22729452>

RESULTS:

Studies using animal models of anxiety and involving healthy volunteers clearly suggest an anxiolytic-like effect of CBD. Moreover, CBD was shown to reduce anxiety in patients with social anxiety disorder.

CONCLUSION:

Future clinical trials involving patients with different anxiety disorders are warranted, especially of panic disorder, obsessive-compulsive disorder, social anxiety disorder, and post-traumatic stress disorders. The adequate therapeutic window of CBD and the precise mechanisms involved in its anxiolytic action remain to be determined.

8. ANXIOGENIC-LIKE EFFECTS OF CHRONIC CANNABIDIOL ADMINISTRATION IN RATS (2012).

SCHOOL OF BIOMEDICAL SCIENCES, UNIVERSITY OF NOTTINGHAM MEDICAL SCHOOL, QUEEN'S MEDICAL CENTRE, NOTTINGHAM, UK.

<http://www.ncbi.nlm.nih.gov/pubmed/22083592>

Chronic administration of CBD produced an anxiogenic-like effect in clear opposition to the acute anxiolytic profile previously reported. In addition, CBD decreased the expression of proteins that have been shown to be enhanced by chronic treatment with antidepressant/anxiolytic drugs.

9. CANNABIDIOL REDUCES THE ANXIETY INDUCED BY SIMULATED PUBLIC SPEAKING IN TREATMENT-NAÏVE SOCIAL PHOBIA PATIENTS (2011).

DEPARTMENT OF NEUROSCIENCE AND BEHAVIOR, SCHOOL OF MEDICINE OF RIBEIRÃO PRETO, UNIVERSITY OF SÃO PAULO, SP, BRAZIL.

<http://www.ncbi.nlm.nih.gov/pubmed/21307846>

Social Anxiety Disorder (SAD) is one of the most common anxiety conditions with impairment in social life. Cannabidiol (CBD), one major non-psychotomimetic compound of the cannabis sativa plant, has shown anxiolytic effects both in humans and in animals. 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.

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 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."

10. PLANT-BASED MEDICINES FOR ANXIETY DISORDERS, PART 2: A REVIEW OF CLINICAL STUDIES WITH SUPPORTING PRECLINICAL EVIDENCE (2013).

DEPARTMENT OF PSYCHIATRY AND THE MELBOURNE CLINIC, FACULTY OF MEDICINE, UNIVERSITY OF MELBOURNE, 2 SALISBURY STREET, RICHMOND, VIC 3121, AUSTRALIA.

<https://www.ncbi.nlm.nih.gov/pubmed/23653088>

Research in the area of herbal psychopharmacology has revealed a variety of promising medicines that may provide benefit in the treatment of general anxiety and specific anxiety disorders. However, a comprehensive review of plant-based anxiolytics has been absent to date. Thus, our aim was to provide a comprehensive narrative review of plant-based medicines that have clinical and/or preclinical evidence of anxiolytic activity. We present the article in two parts. In part one, we reviewed herbal medicines for which only preclinical investigations for anxiolytic activity have been performed. In this current article (part two), we review herbal medicines for which there have been both preclinical and clinical investigations of anxiolytic activity.

A search of MEDLINE (PubMed), CINAHL, Scopus and the Cochrane Library databases was conducted (up to 28 October 2012) for English language papers using the search terms 'anxiety' OR 'anxiety disorder' OR 'generalized anxiety disorder' OR 'social phobia' OR 'post-traumatic stress disorder' OR 'panic disorder' OR 'agoraphobia' OR 'obsessive compulsive disorder' in combination with the search terms 'Herb*' OR 'Medicinal Plants' OR 'Botanical Medicine' OR 'Chinese herb*', in addition to individual herbal medicines. This search of the literature revealed 1,525 papers, of which 53 plants were included in the review (having at least one study using the whole plant extract). Of these plants, 21 had human clinical trial evidence (reviewed here in part two), with the other 32 having solely preclinical evidence (reviewed in part one).

*Support for efficacy was found for chronic use (i.e. greater than one day) of the following herbs in treating a range of anxiety disorders in human clinical trials: Piper methysticum, Matricaria recutita, Ginkgo biloba, Scutellaria lateriflora, Silybum marianum, Passiflora incarnata, Withania somniferum, Galphimia glauca, Centella asiatica, Rhodiola rosea, Echinacea spp., Melissa officinalis and Echinum amoenum. For several of the plants studied, conclusions need to be tempered due to methodological issues such as small sample sizes, brief intervention durations and non-replication. Current evidence does not support Hypericum perforatum or Valeriana spp. for any anxiety disorder. Acute anxiolytic activity was found for Centella asiatica, Salvia spp., Melissa officinalis, Passiflora incarnata and Citrus aurantium. Bacopa monnieri has shown anxiolytic effects in people with cognitive decline. **The therapeutic application of psychotropic plant-based treatments for anxiety disorders is also discussed, specifically Psychotria viridis and Banisteriopsis caarti (ayahuasca), Psilocybe spp. and cannabidiol-enriched (low tetrahydrocannabinol (Δ 9)-THC) Cannabis.***

11. THERAPEUTIC BENEFITS OF CANNABIS: A PATIENT SURVEY (2014).

KEAUHOU URGENT CARE CENTER, KAILUA KONA, HI 96740

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3998228/>

Other reported therapeutic benefits included relief from stress/anxiety (50% of respondents), relief of insomnia (45%), improved appetite (12%), decreased nausea (10%), increased focus/concentration (9%), and relief from depression (7%). Several patients wrote notes (see below) relating that cannabis helped them to decrease or discontinue medications for pain, anxiety, and insomnia. Other reported benefits did not extend to 5% or more of respondents.

Six patients (6%) wrote brief notes relating how cannabis helped them to decrease or to discontinue other medications.

Comments included the following: "Medical cannabis replaced my need for oxycodone. Now I don't need them at all." "I do not need Xanax anymore." "In the last two years I have been able to drop meds for anxiety, sleep, and depression." "I've cut back 18 pills on my morphine dosage."

CONCLUSIONS:

More research needs to be pursued to discover degrees of efficacy in other areas of promise such as in treating anxiety, depression, bipolar disorder, autism, nausea, vomiting, muscle spasms, seizures, and many neurologic disorders. Patients deserve to have cannabis released from its current federal prohibition so that scientific research can proceed and so that physicians can prescribe cannabis with the same freedom accorded any other safe and effective medications.

12. ANTIDEPRESSANT-LIKE AND ANXIOLYTIC-LIKE EFFECTS OF CANNABIDIOL: A CHEMICAL COMPOUND OF CANNABIS SATIVA. (2014)

INSTITUTE OF PSYCHIATRY - FEDERAL UNIVERSITY OF RIO DE JANEIRO. LABORATORY OF PANIC AND RESPIRATION.

<https://www.ncbi.nlm.nih.gov/pubmed/24923339>

Anxiety and depression are pathologies that affect human beings in many aspects of life, including social life, productivity and health.

Cannabidiol (CBD) is a constituent non-psychotomimetic of Cannabis sativa with great psychiatric potential, including uses as an antidepressant-like and anxiolytic-like compound. The aim of this study is to review studies of animal models using CBD as an anxiolytic-like and antidepressant-like compound. Studies involving animal models, performing a variety of experiments on the above-mentioned disorders, such as the forced swimming test (FST), elevated plus maze (EPM) and Vogel conflict test (VCT), suggest that CBD exhibited an anti-anxiety and antidepressant effects in animal models discussed. Experiments with CBD demonstrated non-activation of neuroreceptors CB1 and CB2. Most of the studies demonstrated a good interaction between CBD and the 5-HT1A neuro-receptor.

13. CANNABIDIOL AS A POTENTIAL TREATMENT FOR ANXIETY DISORDERS (2015).

NEW YORK UNIVERSITY SCHOOL OF MEDICINE, INSTITUTO DE NEUROCIENCIAS DE ALICANTE, NEW YORK, NY, USA.

UNIVERSIDAD MIGUEL HERNÁNDEZ AND CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS, ALICANTE, SPAIN.

<http://www.ncbi.nlm.nih.gov/pubmed/26341731>

The purpose of the current review is to determine CBD's potential as a treatment for anxiety-related disorders, by assessing evidence from preclinical, human experimental, clinical, and epidemiological studies.

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.

14. CANNABIDIOL REGULATION OF LEARNED FEAR: IMPLICATIONS FOR TREATING ANXIETY RELATED DISORDERS (2016)

UNIVERSITY OF NOTTINGHAM UK.

- School of Mathematical Sciences, University of Nottingham University Park, Nottingham, UK.
- School of Biosciences, University of Nottingham Loughborough, UK.
- Department of Pharmacology, University of São Paulo São Paulo, Brazil.
- School of Psychology, University of Birmingham Birmingham, UK.
- Department of Pharmacology, Federal University of Santa Catarina Florianopolis, Brazil.

<https://www.ncbi.nlm.nih.gov/pubmed/27932983>

The effects of psychological treatments such as exposure therapy are often only temporary and medications can be ineffective and have adverse side effects. Growing evidence from human and animal studies indicates that cannabidiol, the main non-psychotomimetic phytocannabinoid present in *Cannabis sativa*, alleviates anxiety in paradigms assessing innate fear. More recently, the effects of cannabidiol on learned fear have been investigated in preclinical studies with translational relevance for phobias and PTSD.

The evidence indicates that cannabidiol reduces learned fear in different ways: (1) cannabidiol decreases fear expression acutely, (2) cannabidiol disrupts memory reconsolidation, leading to sustained fear attenuation upon memory retrieval, and (3) cannabidiol enhances extinction, the psychological process by which exposure therapy inhibits learned fear. We also present novel data on cannabidiol regulation of learned fear related to explicit cues, which indicates that auditory fear expression is also reduced acutely by cannabidiol. We conclude by outlining future directions for research to elucidate the neural circuit, psychological, cellular, and molecular mechanisms underlying the regulation of fear memory processing by cannabidiol. This line of investigation may lead to the development of cannabidiol as a novel therapeutic approach for treating anxiety and trauma-related disorders such as phobias and PTSD in the future.

15. CANNABINOIDS AND POST-TRAUMATIC STRESS DISORDER: CLINICAL AND PRECLINICAL EVIDENCE FOR TREATMENT AND PREVENTION (2016)

DEPARTMENT OF PSYCHOLOGY, UNIVERSITY OF HAIFA, HAIFA, ISRAEL.

<https://www.ncbi.nlm.nih.gov/pubmed/27551883>

There is substantial evidence from studies in humans and animal models for a role of the endocannabinoid system in the control of emotional states.

Preliminary studies in humans also suggest that treatment with cannabinoids may decrease PTSD symptoms including sleep quality, frequency of nightmares, and hyperarousal. Studies in animal models have shown that cannabinoids can prevent the effects of stress on emotional function and memory processes, facilitate fear extinction, and have an anti-anxiety-like effect in a variety of tasks. Moreover, cannabinoids administered shortly after exposure to a traumatic event were found to prevent the development of PTSD-like phenotype. In this article, we review the existing literature on the use of cannabinoids for treating and preventing PTSD in humans and animal models.

16. COULD CANNABIDIOL BE USED AS AN ALTERNATIVE TO ANTIPSYCHOTICS? (2016)

DEPARTMENT OF NEUROSCIENCES, FACULTY OF MEDICINE, UNIVERSITÉ DE MONTRÉAL,
MONTREAL, QUEBEC H3C 3J7, CANADA.

<https://www.ncbi.nlm.nih.gov/pubmed/27157263>

Schizophrenia is a mental disorder that affects close to 1% of the population. Individuals with this disorder often present signs such as hallucination, anxiety, reduced attention, and social withdrawal. Although antipsychotic drugs remain the cornerstone of schizophrenia treatment, they are associated with severe side effects.

Recently, the endocannabinoid system (ECS) has emerged as a potential therapeutic target for pharmacotherapy that is involved in a wide range of disorders, including schizophrenia. Since its discovery, a lot of effort has been devoted to the study of compounds that can modulate its activity for therapeutic purposes. Among them, cannabidiol (CBD), a non-psychoactive component of cannabis, shows great promise for the treatment of psychosis, and is associated with fewer extrapyramidal side effects than conventional antipsychotic drugs.

17. EVIDENCES FOR THE ANTI-PANIC ACTIONS OF CANNABIDIOL (2016)

DEPARTMENT OF PHARMACOLOGY SCHOOL OF MEDICINE OF RIBEIRÃO PRETO UNIVERSITY OF SÃO PAULO RIBEIRÃO PRETO-SP, BRAZIL.

<https://www.ncbi.nlm.nih.gov/pubmed/27157263>

Panic disorder (PD) is a disabling psychiatry condition that affects approximately 5% of the worldwide population. Currently, long-term selective serotonin reuptake inhibitors (SSRIs) are the first-line treatment for PD; however, the common side-effect profiles and drug interactions may provoke patients to abandon the treatment, leading to PD symptoms relapse.

Cannabidiol (CBD) is the major non-psychotomimetic constituent of the Cannabis sativa plant with anti-anxiety properties that has been suggested as an alternative for treating anxiety disorders. In the present chapter, we included both experimental laboratory animal and human studies that have investigated the putative anti-panic properties of CBD. Taken together, the studies assessed in the present chapter clearly suggest an anxiolytic-like effect of CBD in both animal models and healthy volunteers.

18. HARVARD: MARIJUANA DOESN'T CAUSE SCHIZOPRENIA

<https://psychcentral.com/news/2013/12/10/harvard-marijuana-doesnt-cause-schizophrenia/63148.html>

“The results of the current study suggest that having an increased familial morbid risk for schizophrenia may be the underlying basis for schizophrenia in cannabis users and not cannabis use by itself,” note the researchers... “While cannabis may have an effect on the age of onset of schizophrenia it is unlikely to be the cause of illness,” said the researchers, who were led by Ashley C. Proal from Harvard Medical School.

In general, we found a tendency for depression and bipolar disorder to be increased in the relatives of cannabis users in both the patient and control samples. This might suggest that cannabis users are more prone to affective disorders than their non-using samples or vice versa.” Future research is needed to understand this relationship.

19. TIME: MARIJUANA APPEARS TO BENEFIT MENTAL HEALTH

<http://time.com/4573129/marijuana-cannabis-mental-health/>

In their report, published in the journal Clinical Psychology Review, researchers found evidence that cannabis can likely benefit people dealing with depression, social anxiety and PTSD, though it may not be ideal for people with bipolar disorder, for instance, for which there appears to be more negative side effects than positive ones. “This is a substance that has potential use for mental health,” says Zach Walsh, an associate professor of psychology at the University of British Columbia. “We should be looking at it in the same way [as other drugs] and be holding it up to the same standard.”

20. ROLLING STONE: CAN MARIJUANA IMPROVE YOUR EMOTIONAL STATE?

<http://www.rollingstone.com/politics/news/can-marijuana-improve-your-emotional-state-20130821>

The researchers concluded that the way the human brain reacts to THC could have significant implications for mental health treatment. “These findings,” they wrote, “add to existing evidence that implicate the endocannabinoid system in modulation of emotional reactions, and support a previously suggested role for the endocannabinoid system in abnormal emotional processing associated with various psychiatric disorders.”

LETTERS OF SUPPORT FROM MEDICAL PROFESSIONALS (6.3.6)



Canna Care Docs
A Division of MedEval, Corp.
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To: Delaware department of Health

Re: PTSD and anxiety/depression in medical marijuana

As an experienced physician in the field of medical cannabis therapy, I have been asked to comment on the problems with PTSD and anxiety/depression in practice.

PTSD

Currently there are 9 job vacancies for every practicing psychiatrist. This creates a logjam in any approval system where psychiatric endorsement is required. The use of other qualified health professionals such as clinical psychologists would somewhat ameliorate this situation. Given a clinical psychologist's approval, the evaluation system for these patients would be expedited when signed off by the MD or DO. Currently, most patients seem to come from the armed forces separation system where PTSD is documented, but the criteria are uncertain and the qualifications of the responsible physicians unknown. Nevertheless, we have to accept their documentation since it is part of their medical pension rating and is the one that is most available.

Anxiety/Depression

Patients who have poor response to conventional therapy and have suitable medical follow-up, and those who cannot use standard therapy for medical reasons (ie inflammatory bowel syndrome, etc.) may be good candidates for cannabis therapy. Use of non-hallucinogenic cannabidiol preparations commonly results in better situational adjustment with decreased bipolarity. Use of vaporized or sublingual administration routes opens up an enhanced patient group for therapy when they cannot use routine oral administration.

A handwritten signature in blue ink, appearing to read "James S. Warson MD FACS".

James S Warson MD FACS
Medical Director, Canna Care Docs Mid-Atlantic Region