CBD Condition Guide

Here are the conditions/ailments that will be covered in the following pages:

**Aches and Pains**: No CBD only human studies - preclinical, animal, and THC+CBD studies show promise.

**Anxiety**: Generalized anxiety and Extinction of fear memory studies on humans - could find additional studies if desired, but not many

**Arthritis**: No human studies

**Autism**: Included a review that summarized that CBD may help with Autism symptoms and that it did help with epilepsy, which is common in those with Autism. Could link additional studies, mainly on autism with epilepsy

**Depression**: No human studies - animal studies show antidepressant qualities

**Digestion**: No human clinical studies - animal studies show beneficial properties in regards to digestion - one study on human biopsies found anti-inflammatory benefit for those with Ulcerative Colitis, an inflammatory condition that impacts digestion

**Epilepsy**: CBD approved for those with epilepsy in numerous states - currently Epidiolex, a cannabis-derived CBD oil, is undergoing clinical trials - numerous human studies have found CBD to correlate with reduced epileptic seizure frequency in adults and children.

(Fibromyalgia - could add)

**Headaches/Migraines**: No CBD only human studies - endocannabinoid deficiency hypothesis in migraines briefly outlined. Preclinical, animal, and THC+CBD studies show promise.

**Immune system**: Few human studies, however 1 phase II study found that CBD may help prevent Graft-versus-host disease in patients receiving bone marrow transplants.

**Inflammation**: Few human studies exist, however studies on human skin cultures and biopsies from patients with Ulcerative Colitis found CBD to act as an anti-inflammatory. Many preclinical and animal models have found the same - more research on human subjects is needed.

(MS - could add)

**Parkinson’s Disease - General**: One human study found benefits for PD patients with CBD supplementation
Parkinson’s Disease - Psychosis and Bipolar disorder in Parkinson’s disease patients: One preliminary human study demonstrated benefits of CBD in those with psychosis and bipolar disorder in PD patients

Pets: Largely due to legal concerns, there has been very little research regarding CBD oil or any other cannabinoid product in household pets

PTSD: Very limited human studies - 1 study showed benefits for a young girl with PTSD and CBD supplementation

Schizophrenia: Multiple human studies have found benefits of CBD supplementation in schizophrenia patients.

Sleep: Limited human studies, conflicting results in animal studies. Very small human studies found CBD may help those with PTSD and Parkinson’s related sleep disorders.
Aches and Pains

Human studies into CBD by itself for aches and pains are lacking. There exist many animal and preclinical studies that demonstrate promise, as well as THC+CBD combinations, however until there are human studies conclusions cannot be drawn.

Note: See Parkinson’s as in one human study (only 21 patients and not placebo controlled). CBD supplementation was found to be correlated with increased quality of life scores, one of which was bodily discomfort, which shows promise of CBD helping those with discomfort.

Animal Study 1: CBD Effective at Reducing Neuropathic and Inflammatory Pain in a Rat Model

Cannabidiol, the major psycho-inactive component of cannabis, has substantial anti-inflammatory and immunomodulatory effects. This study investigated its therapeutic potential on neuropathic (sciatic nerve chronic constriction) and inflammatory pain (complete Freund’s adjuvant intraplantar injection) in rats. In both models, daily oral treatment with cannabidiol (2.5-20 mg/kg to neuropathic and 20 mg/kg to adjuvant-injected rats) from day 7 to day 14 after the injury, or intraplantar injection, reduced hyperalgesia to thermal and mechanical stimuli. In the neuropathic animals, the anti-hyperalgesic effect of cannabidiol (20 mg/kg) was prevented by the vanilloid antagonist capsazepine (10 mg/kg, i.p.), but not by cannabinoid receptor antagonists. Cannabidiol's activity was associated with a reduction in the content of several mediators, such as prostaglandin E(2) (PGE(2)), lipid peroxide and nitric oxide (NO), and in the over-activity of glutathione-related enzymes. Cannabidiol only reduced the over-expression of constitutive endothelial NO synthase (NOS), without significantly affecting the inducible form (iNOS) in inflamed paw tissues. Cannabidiol had no effect on neuronal and iNOS isoforms in injured sciatic nerve. The compound's efficacy on neuropathic pain was not accompanied by any reduction in nuclear factor-kappaB (NF-kappaB) activation and tumor necrosis factor alpha (TNFalpha) content. The results indicate a potential for therapeutic use of cannabidiol in chronic painful states.
Animal Study 2: CBD Prevented Later Development of Pain and Nerve Damage in Rats with Osteoarthritis

Osteoarthritis (OA) is a multifactorial joint disease, which includes joint degeneration, intermittent inflammation, and peripheral neuropathy. Cannabidiol (CBD) is a noneuphoria producing constituent of cannabis that has the potential to relieve pain. The aim of this study was to determine whether CBD is anti-nociceptive in OA, and whether inhibition of inflammation by CBD could prevent the development of OA pain and joint neuropathy. Osteoarthritis was induced in male Wistar rats (150-175 g) by intra-articular injection of sodium monoiodoacetate (MIA; 3 mg). On day 14 (end-stage OA), joint afferent mechanosensitivity was assessed using in vivo electrophysiology, whereas pain behaviour was measured by von Frey hair algesiometry and dynamic incapacitance. To investigate acute joint inflammation, blood flow and leukocyte trafficking were measured on day 1 after MIA. Joint nerve myelination was calculated by G-ratio analysis. The therapeutic and prophylactic effects of peripheral CBD (100-300 μg) were assessed. In end-stage OA, CBD dose-dependently decreased joint afferent firing rate, and increased withdrawal threshold and weight bearing ($P < 0.0001; n = 8$). Acute, transient joint inflammation was reduced by local CBD treatment ($P < 0.0001; n = 6$). Prophylactic administration of CBD prevented the development of MIA-induced joint pain at later time points ($P < 0.0001; n = 8$), and was also found to be neuroprotective ($P < 0.05; n = 6-8$). The data presented here indicate that local administration of CBD blocked OA pain. Prophylactic CBD treatment prevented the later development of pain and nerve damage in these OA joints. These findings suggest that CBD may be a safe, useful therapeutic for treating OA joint neuropathic pain.
1. **Generalized Anxiety - Human Study Shows CBD at 300 mg to Reduce Public Speaking Induced Anxiety**

Main Study Conclusion Quote: “The results confirmed that the acute administration of CBD induced anxiolytic effects with a dose-dependent inverted U-shaped curve in healthy subjects, since the subjective anxiety measures were reduced with CBD 300 mg, but not with CBD 100 and 900 mg, in the post-speech phase.” (What this means is that at high and low amounts anxiety was not reduced, but it was at the middle dose of 300 mg CBD)

Published in *Frontiers in Pharmacology*, 60 healthy subjects were assigned to one of five groups: placebo, clonazepam (1 mg), and CBD (100, 300, and 900 mg). Next these subjects underwent a real situation public speaking test.

The participants completed the sedation and anxiety portion of the Visual Analog and Mood Scale and also had their heart rate and blood pressure recorded. It was concluded that CBD at 300 mg, but not at 100 or 900 mg, resulted in reduced subjective anxiety measures post-speech.⁸


2. **Inhaled CBD Enhanced Extinction of Fear Memories in Healthy Adults at 32 mg CBD**

Main Study Conclusion Quote: “These findings provide the first evidence that CBD can enhance consolidation of extinction learning in humans and suggest that CBD may have potential as an adjunct to extinction-based therapies for anxiety disorders.”
A 2013 study published in Psychopharmacology (Berl) took 48 healthy participants and subjected them to a Pavlovian fear-conditioning paradigm in order to research the effects of CBD on extinction and consolidation of fear memories.\(^\text{13}\)

In this double-blind, placebo-controlled study, researchers concluded that 32 mg of inhaled CBD prior to or after extinction training of fear memories led to a significant reduction in expectancy of shock during reinstatement.


**Arthritis**

Human studies into CBD by itself for arthritis are lacking. There exist many animal and preclinical studies that demonstrate promise, as well as THC+CBD combinations, however until there are human studies conclusions cannot be drawn.
Autism

Those with ASD are often plagued with anxiety, behavioral and motor difficulties, and seizures. Recently interest in the use of CBD and other cannabinoids for those with ASD has been growing in the general public, however as of yet studies specifically revolving around ASD and CBD are extremely limited.

Studies on CBD for other conditions, particularly for those suffering from epilepsy, have found relief for many similar symptoms that may be applicable to ASD as well. While these studies provide a basis for hope that CBD oil may help those with ASD, further studies on autism specifically are needed before definitive conclusions can be drawn.

In a 2017 review published in the *Journal of Pediatric Neurology*, researchers sought to examine the current evidence surrounding the efficacy of CBD in treating pediatric epilepsy.²

What the researchers concluded from the existing studies was that CBD was effective in treating seizures, as well as exhibiting a positive effect on measures of behavior similar to those suffered by ASD (autism spectrum disorder) patients.

*Also see epilepsy, as 20-30% of those with autism spectrum disorder also have epilepsy, and CBD has been found in human studies to be correlated with reduced epileptic seizure frequency.*


https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5473390/
**Depression**

**Human studies into CBD by itself for depression are lacking.** There exist many animal and preclinical studies that demonstrate promise, however until there are human studies conclusions cannot be drawn.

2014 Study Summarizing Animal Study Findings:

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.


Digestion

*Summary of research:*

Digestive discomfort is a common complaint, with most everyone suffering from bloating, pain, nausea, or vomiting at one time or another.

Human studies into CBD by itself for digestion are lacking. There exist many animal and preclinical studies that demonstrate promise, as well as THC+CBD combinations, however until there are human studies on CBD alone conclusions cannot be drawn.

In a 2011 review published by Sharkey, it was stated that researchers have found a link between the endocannabinoid system and vomiting and nausea.²

Furthermore, chronic conditions, including irritable bowel syndrome (IBS), ulcerative colitis, and Crohn’s disease are on the rise. These conditions are often linked with inflammation in the digestive tract, and CBD in preclinical and animal studies have found anti-inflammatory effects of CBD.

*Study:* Ulcerative Colitis: CBD Found to Reduce Intestinal Inflammation in Mice with UC and Human Patient Biopsies ²

*Study Name:* Cannabidiol reduces intestinal inflammation through the control of neuroimmune axis

*Study Date:* 2011

*Published In:* *PLoS One*

*Details:* Experiments were conducted on mice and biopsies from human patients with ulcerative colitis (UC)
**Conclusion Quote:** "CBD targets enteric reactive gliosis, counteracts the inflammatory environment induced by LPS in mice and in human colonic cultures derived from UC patients. These actions lead to a reduction of intestinal damage mediated by PPARgamma receptor pathway. Our results therefore indicate that CBD indeed unravels a new therapeutic strategy to treat inflammatory bowel diseases."

Epilepsy

In numerous states, *Cannabis sativa* or its compounds, such as cannabidiol (CBD), have been approved for the treatment of epilepsy.

Currently clinical trials are underway for Epidiolex, a Cannabis derived CBD oil, in the treatment of epilepsy.

The results of these Phase 3 clinical trials were such that the FDA granted Epidiolex with Fast Track and Orphan Drug Designations for DS, LGS, and TSC.

*Cannabidiol Helps Reduce Seizures in Patients with Treatment Resistant Epilepsy (TRE)*

**Conclusion Quote** Our findings suggest that cannabidiol might reduce seizure frequency and might have an adequate safety profile in children and young adults with highly treatment-resistant epilepsy. Randomised controlled trials are warranted to characterise the safety profile and true efficacy of this compound.

**Study Details:**
In a 2016 study published in *The Lancet Neurology*, 162 patients between 1 and 30 years of age who had childhood onset, severe, intractable, treatment-resistant epilepsy were treated with oral CBD (in addition to their antiepileptic drugs) daily for 12 weeks.\(^2\)

CBD dosage started at 2-5 mg/kg body weight/day and was slowly increased up to an intolerance or a maximum of 25 mg/kg/day or 50 mg/kg/day, depending on the study site.

The researchers found a 36.5% average reduction in monthly motor seizures following the 12 weeks of CBD treatment. They concluded that cannabidiol may reduce the frequency of seizures for young adults and children with TRE. CBD side effects were reported to be adequate, with mostly mild side effects observed.
Of these side effects, one of the most common had to do with the interaction of CBD with the antiepileptic drug (AED) Clobazam. In the study, 85 participants were taking Clobazam, with 51% of these patients experiencing fatigue or somnolence, in comparison to 21% of the patients who were treated with a different AED.

This study was not a placebo-controlled study, thus further studies need to be conducted to rule out any placebo effect.

O’Connell B, Gloss D, Devinsky O. Cannabinoids in treatment-resistant epilepsy: A review. Epilepsy & Behavior. 2017; 70(B):341-348


Headaches/Migraines

Human studies into CBD by itself for headaches and migraine headaches are lacking. There exist many animal and preclinical studies that demonstrate promise, as well as THC+CBD combinations, however until there are human studies conclusions cannot be drawn.

Study Title: Clinical endocannabinoid deficiency (CECD): can this concept explain therapeutic benefits of cannabis in migraine, fibromyalgia, irritable bowel syndrome and other treatment-resistant conditions?

One study examined the idea that “clinical endocannabinoid deficiency (CECD), and the prospect that it could underlie the pathophysiology of migraine, fibromyalgia, irritable bowel syndrome, and other functional conditions alleviated by clinical cannabis.”

The scientific evidence out there led the researchers to this conclusion:

Study Conclusion Quote:

“Migraine, fibromyalgia, IBS and related conditions display common clinical, biochemical and pathophysiological patterns that suggest an underlying clinical endocannabinoid deficiency that may be suitably treated with cannabinoid medicines.”


[http://doi.org/10.1089/can.2016.0009](http://doi.org/10.1089/can.2016.0009)
Immune System

There are few human studies surrounding CBD and the immune system, leaving much more research needed before conclusions can be drawn. One phase II study did find that CBD may help to reduce the incidence of acute Graft-versus-host-disease in those undergoing bone marrow transplants:

Study Abstract:
Graft-versus-host-disease (GVHD) is a major obstacle to successful allogeneic hematopoietic cell transplantation (alloHCT). Cannabidiol (CBD), a nonpsychotropic ingredient of Cannabis sativa, possesses potent anti-inflammatory and immunosuppressive properties. We hypothesized that CBD may decrease GVHD incidence and severity after alloHCT. We conducted a phase II study. GVHD prophylaxis consisted of cyclosporine and a short course of methotrexate. Patients transplanted from an unrelated donor were given low-dose anti-T cell globulin. CBD 300 mg/day was given orally starting 7 days before transplantation until day 30. Forty-eight consecutive adult patients undergoing alloHCT were enrolled. Thirty-eight patients (79%) had acute leukemia or myelodysplastic syndrome and 35 patients (73%) were given myeloablative conditioning. The donor was either an HLA-identical sibling (n = 28), a 10/10 matched unrelated donor (n = 16), or a 1-antigen-mismatched unrelated donor (n = 4). The median follow-up was 16 months (range, 7 to 23). No grades 3 to 4 toxicities were attributed to CBD. None of the patients developed acute GVHD while consuming CBD. In an intention-to-treat analysis, we found that the cumulative incidence rates of grades II to IV and grades III to IV acute GVHD by day 100 were 12.1% and 5%, respectively. Compared with 101 historical control subjects given standard GVHD prophylaxis, the hazard ratio of developing grades II to IV acute GVHD among subjects treated with CBD plus standard GVHD prophylaxis was .3 (P = .0002). Rates of nonrelapse mortality at 100 days and at 1 year after transplantation were 8.6% and 13.4%, respectively. Among patients surviving more than 100 days, the cumulative incidences of moderate-to-severe chronic GVHD at 12 and 18 months were 20% and 33%, respectively. The combination of CBD with standard GVHD prophylaxis is a safe and promising strategy to reduce the incidence of acute GVHD. A randomized double-blind controlled study is warranted. (clinicaltrials.gov: NCT01385124).

Inflammation

Overview:

Chronic inflammation has been tied to a variety of chronic conditions, including arthritis, acne, depression, metabolic syndrome, cancer, autoimmune disorders, cardiovascular disease, and central nervous system disorders, among others.

The endocannabinoid system is involved in the inflammatory response, leading to the hypothesis that CBD, through its influence on the endocannabinoid system, may help.

Numerous animal studies have found an anti-inflammatory effect of CBD. Further studies need to be conducted on humans before conclusions can be made.

While the FDA has approved testing of CBD in exploratory trials for various orphan diseases, the research is in its infancy. It will take time before these trials have been conducted, written, and published.¹

Study 1: CBD Exerts Anti-Inflammatory Actions on Human Skin Cultures

Study Name: Cannabidiol exerts sebostatic and antiinflammatory effects on human sebocytes
Study Date: 2014
Published In: Journal of Clinical Investigation

Details: Researchers took human sebocytes and human skin organ cultures to test the impact of CBD on human sebaceous gland function.

Conclusion Quote: “Collectively, our findings suggest that, due to the combined lipostatic, antiproliferative, and antiinflammatory effects, CBD has potential as a promising therapeutic agent for the treatment of acne vulgaris.”
**You can also refer the study in digestion where CBD was found to reduce intestinal inflammation in ulcerative colitis patient biopsies.**
Parkinson’s Disease

“In a study with a total of 21 Parkinson's patients (without comorbid psychiatric conditions or dementia) who were treated with either placebo, 75 mg/day CBD or 300 mg/day CBD in an exploratory double-blind trial for 6 weeks, the higher CBD dose showed significant improvement of quality of life, as measured with PDQ-39. This rating instrument comprised the following factors: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. For the factor, “activities of daily living,” a possible dose-dependent relationship could exist between the low and high CBD group—the two CBD groups scored significantly different here. Side effects were evaluated with the UKU (Udvalg for Kliniske Undersøgelser). This assessment instrument analyzes adverse medication effects, including psychic, neurologic, autonomic, and other manifestations. Using the UKU and verbal reports, no significant side effects were recognized in any of the CBD groups.”


Psychosis and Bipolar Disorder in Parkinson’s Patients

One preliminary study on human subjects showed promise of CBD for those with Parkinson’s disease related psychosis and bipolar disorder.

Study: Cannabidiol for the treatment of psychosis in Parkinson’s disease  
Year: 2009  
Journal: Journal of Psychopharmacology

Study details: **Only 6 patients with PD and psychotic symptoms** - 4 weeks of CBD supplementation

Abstract:

The management of psychosis in Parkinson’s disease (PD) has been considered a great challenge for clinicians and there is a need for new pharmacological intervention. Previously an antipsychotic and neuroprotective effect of Cannabidiol (CBD) has been suggested. Therefore, the aim of the present study was to directly evaluate for the first time, the efficacy, tolerability and safety of CBD on PD patients with psychotic symptoms. This was an open-label pilot study. Six consecutive outpatients (four men and two women) with the diagnosis of PD and who had psychosis for at least 3 months were selected for the study. All patients received CBD in flexible dose (started with an oral dose of 150 mg/day) for 4 weeks, in addition to their usual therapy. The psychotic symptoms evaluated by the Brief Psychiatric Rating Scale and the Parkinson Psychosis Questionnaire showed a significant decrease under CBD treatment. CBD did not worsen the motor function and decreased the total scores of the Unified Parkinson’s Disease Rating Scale. No adverse effect was observed during the treatment. These preliminary data suggest that CBD may be effective, safe and well tolerated for the treatment of the psychosis in PD.

**Pets**

Largely due to legal concerns, there has been very little research regarding CBD oil or any other cannabinoid product in household pets.
Post-Traumatic Stress Disorder (PTSD)

Human studies into CBD for PTSD are lacking. There exist many animal and preclinical studies that demonstrate promise, however until there are human studies conclusions cannot be drawn. There does exist one study on CBD supplementation by a singular young girl suffering from PTSD

1. Sleep Improvements found in 1 Young Girl with PTSD

Abstract:

**INTRODUCTION:** Anxiety and sleep disorders are often the result of posttraumatic stress disorder and can contribute to an impaired ability to focus and to demonstration of oppositional behaviors.

**CASE PRESENTATION:**
These symptoms were present in our patient, a ten-year-old girl who was sexually abused and had minimal parental supervision as a young child under the age of five. Pharmaceutical medications provided partial relief, but results were not long-lasting, and there were major side effects. A trial of cannabidiol oil resulted in a maintained decrease in anxiety and a steady improvement in the quality and quantity of the patient's sleep.

**DISCUSSION:**
Cannabidiol oil, an increasingly popular treatment of anxiety and sleep issues, has been documented as being an effective alternative to pharmaceutical medications. This case study provides clinical data that support the use of cannabidiol oil as a safe treatment for reducing anxiety and improving sleep in a young girl with posttraumatic stress disorder.

Schizophrenia

Multiple human studies have found benefit of CBD in schizophrenia patients.

A double-blind, randomized clinical trial of CBD versus amisulpride, a potent antipsychotic in acute schizophrenia, was performed on a total of 42 subjects, who were treated for 28 days starting with 200 mg CBD per day each. The dose was increased stepwise by 200 mg per day to 4×200 mg CBD daily (total 800 mg per day) within the first week. The respective treatment was maintained for three additional weeks. A reduction of each treatment to 600 mg per day was allowed for clinical reasons, such as unwanted side effects after week 2. This was the case for three patients in the CBD group and five patients in the amisulpride group. While both treatments were effective (no significant difference in PANSS total score), CBD showed the better side effect profile. Amisulpride, working as a dopamine D2/D3-receptor antagonist, is one of the most effective treatment options for schizophrenia. CBD treatment was accompanied by a substantial increase in serum anandamide levels, which was significantly associated with clinical improvement, suggesting inhibition of anandamide deactivation via reduced FAAH activity.

In addition, the FAAH substrates palmitoylethanolamide and linoleoyl-ethanolamide (both lipid mediators) were also elevated in the CBD group. CBD showed less serum prolactin increase (predictor of galactorrhoea and sexual dysfunction), fewer extrapyramidal symptoms measured with the Extrapyramidal Symptom Scale, and less weight gain. Moreover, electrocardiograms as well as routine blood parameters were other parameters whose effects were measured but not reported in the study. CBD better safety profile might improve acute compliance and long-term treatment adherence.

A press release by GW Pharmaceuticals of September 15th, 2015, described 88 patients with treatment-resistant schizophrenic psychosis, treated either with CBD (in addition to their regular medication) or placebo. Important clinical parameters improved in the CBD group and the number of mild side effects was comparable to the placebo group.

Sleep

Scientific studies on CBD and sleep have found contradictory results, with most of these results in animal studies. Based on these animal studies, CBD may promote wakefulness in health individuals and help those with sleep problems caused by anxiety to sleep. Much more research on humans is needed, however there are some human studies showing that CBD may help promote sleep in those individuals with trouble sleeping due to different conditions, including PTSD and Parkinson's disease.

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2. Cannabidiol Helps Improve Complex Sleep-Related Behaviors for Parkinson's Disease Patients
Abstract:
What is known and objective: Cannabidiol (CBD) is the main non-psychotropic component of the Cannabis sativa plant. REM sleep behaviour disorder (RBD) is a parasomnia characterized by the loss of muscle atonia during REM sleep associated with nightmares and active behaviour during dreaming. We have described the effects of CBD in RBD symptoms in patients with Parkinson’s disease.

Cases summary: Four patients treated with CBD had prompt and substantial reduction in the frequency of RBD-related events without side effects.

What is new and conclusion: This case series indicates that CBD is able to control the symptoms of RBD.

