Medical Marijuana Research

Key medical references addressing marijuana's ability to alleviate select conditions are below, with related symptoms or conditions grouped together. Much of this research was compiled by the research team at the Marijuana Policy Project, although some was sourced from other directories, including the National Academy Press (NAP) and the National Institute of Health (NIH). For the full *Medical Conditions Handout*, visit the MPP's website here.

Severe, Debilitating Pain

Studies have shown that marijuana is effective in treating pain, including neuropathic pain, which is commonly seen in multiple sclerosis, HIV/AIDS, and other ailments, and notoriously resistant to treatment with conventional pain drugs. Research also suggests that marijuana use may allow reduced opioid doses when given in combination.

(1) Wilsey, Barth, et al., "Low Dose Vaporized Cannabis Significantly Improves Neuropathic Pain," The Journal of Pain: Official Journal of the American Pain Society 14.2 (2013): 136–148.

This double-blind, placebo-controlled study on 30 human subjects found that even low doses of vaporized marijuana were effective at alleviating treatment-resistant neuropathic pain. "Psychoactive effects were minimal and well tolerated, and neuropsychological effects were of limited duration and readily reversible within 1 to 2 hours."

(2) Donald Abrams, et al., "Cannabinoid-opioid interaction in chronic pain," Clinical Pharmacology & Therapeutics (2011): 844-851.

This clinical trial involved 21 individuals with severe pain who were taking sustained-release morphine or oxycodone. It found that vaporized marijuana augmented the analgesic effects of opioids. The authors reported that the adding vaporized marijuana "may allow for opioid treatment at lower doses with fewer side effects."

(3) Mark Ware, et al., "Smoked cannabis for chronic neuropathic pain: a randomized controlled trial," Canadian Medical Association Journal (2010): 694-701.

This trial found that "a single inhalation of 25 mg of 9.4% tetrahydrocannabinol herbal cannabis three times daily for five days reduced the intensity of pain, improved sleep and was well tolerated."

(4) Donald Abrams, et al., "Cannabis in Painful HIV-Associated Sensory Neuropathy: A Randomized Placebo-Controlled Trial," Neurology 68, no. 7 (2007): 515-21.

This clinical trial involved HIV/AIDS patients suffering from HIV-associated sensory neuropathy, a painful condition estimated to eventually afflict up to one third of HIVinfected persons. There are presently no FDA-approved treatments for this indication.
Donald Abrams and his colleagues tested the efficacy of smoked marijuana on both HIV neuropathy and a type of laboratory-induced pain. Smoked marijuana produced an average 34% reduction in pain and was well tolerated.

(5) R.J. Ellis, et al., "Smoked Medicinal Cannabis For Neuropathic Pain in HIV: a Randomized, Crossover Clinical Trial," Neuropsychopharmacology 34, no. 3 (2009): 672-80.

This trial focused on patients with HIV-associated neuropathy refractory to at least two previous analgesic classes. Ellis and colleagues reported, "In the present experiment, cannabis reduced pain intensity and unpleasantness equally. Thus, as with opioids, cannabis does not rely on a relaxing or tranquilizing effect, (e.g. anxiolysis) but rather reduces both the core component of nociception and the emotional aspect of the pain experience to an equal degree. ... In general, side effects and changes in mood were inconsequential."

(6) B. Wilsey, et al., "A Randomized, Placebo-Controlled, Crossover Trial of Cannabis Cigarettes in Neuropathic Pain," Journal of Pain 9, no. 6 (2008): 506-21.

This study investigated the efficacy of smoked marijuana in patients suffering from neuropathic pain related to a variety of conditions, including multiple sclerosis, spinal cord injury, diabetes, and complex regional pain syndrome. Wilsey and colleagues concluded, "This study adds to a growing body of evidence that cannabis may be effective at ameliorating neuropathic pain, and may be an alternative for patients who do not respond to, or cannot tolerate, other drugs."

(7) David Baker, et al., "The Therapeutic Potential of Cannabis," The Lancet Neurology 2, no. 5 (2003): 291 -8.
This review, written prior to publication of the clinical trials described above, discussed in detail the biochemical basis for marijuana's analgesic effects. It also discussed the drawbacks of oral dosing (taking a pill with cannabinoids), explaining that "oral administration is probably the least satisfactory route for cannabis owing to sequestration of cannabinoids into fat from which there is slow and variable release into plasma. In addition, significant first-pass metabolism in the liver, which degrades THC, contributes to the variability of circulating concentrations of orally administered cannabinoids, which makes dose titration more difficult and therefore increases the

potential for adverse psychoactive effects. Smoking has been the route of choice for many cannabis users because it delivers a more rapid 'hit' and allows more accurate dose-titration."

(8) M.E. Lynch, J. Young, A.J. Clark, "A Case Series of Patients Using Medicinal Marihuana for Management of Chronic Pain Under the Canadian Marihuana Medical Access Regulations," Journal of Pain and Symptom Management 32, no. 5 (2006): 497-501.

This case series is based on 30 patients qualified to use medical marijuana under Canadian regulations, seen at a pain management center in Nova Scotia. All suffered from chronic, severe pain that had not responded to conventional approaches. On an 11 -point scale, 93% reported pain relief equal to six or greater, and many reported relief of other symptoms such as spasticity, poor sleep, nausea, and vomiting. 70% reported being "able to decrease use of other medications that had been causing side effects (e.g., NSAIDs, opioids, and antidepressants)."

(9) Johnson, Jeremy R., Burnell-Nugent, Mary, Lossignol, Dominique, GanaeMotan, Elena Doina, Potts, Richard & Fallon, Marie T. (2010). "Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC extract in Patients with Intractable Cancer-Related Pain," Journal of Pain and Symptom Management 39(2): 167-179.

This study compared the efficacy of a THC:CBD extract, a strictly THC extract, and a placebo for pain relief in patients suffering from intractable cancer-related pain. On the numerical rating scale for pain, the THC:CBD extract showed a statistically significant reduction in pain from the placebo, while the THC extract did not. A statistically significant odds ratio of 2:1 was shown between patients using the THC:CBD extract versus placebo for patients who experienced a reduction in pain of greater than 30%.

(1 0) Webb, Charles W. & Webb, Sandra M. (2014). "Therapeutic Benefits of Cannabis: A Patient Survey," Hawai'i Journal of Medicine & Public Health 73(4): 109-111 .

Researchers handed out surveys to 100 patients returning for annual medical marijuana recertification in the state of Hawaii. Of the 94% of patients that responded, 97% used medical marijuana for pain relief with an average pain improvement from 7.8 to 2.8 on a ten-point scale. Additionally, 50% of the patients reported relief from anxiety, 45% reported relief from insomnia, and 71% reported no adverse side effects at all. The study concluded that medical cannabis has the potential to treat numerous medical conditions.

Glaucoma

Glaucoma is a leading cause of blindness, damaging the optic nerve, which is responsible for carrying images from the eye to the brain. High pressure within the eye is one of the main risk factors for this optic nerve damage. There currently is no cure for

glaucoma. Marijuana helps relieve the pressure within the eye, thus preventing damage.
Although other drugs are considered first-line glaucoma treatments, some patients and physicians have found marijuana useful when conventional drugs fail. One of the three patients who still receive medical marijuana from the federal government – Elvy Musikka – is a glaucoma patient, who also successfully argued in a Florida court case that marijuana was medically necessary to maintaining her vision.

(1) J.E. Joy, S.J. Watson, and J.A. Benson, Marijuana and Medicine: Assessing the Science Base (National Academy Press, 1999).

"In a number of studies of healthy adults and glaucoma pressure, IOP (intra-ocular pressure) was reduced by an average of 25% after smoking a marijuana cigarette that contained approximately 2% THC — a reduction as good as that observed with most other medications available today."

(2) An excerpt from "Marijuana As Medicine?: The Science Beyond the Controversy" pg. 126. (National Academy Press, 2000)

"Several clinical studies have found that cannabinoids or marijuana reduce intraocular pressure (IOP) as well as do most conventional glaucoma medications.1 This is true whether the cannabinoids are administered orally, intravenously, or by inhalation but not when they are applied directly to the eye. Smoked or eaten marijuana, THC and synthetic cannabinoids in pill form, and intravenous injections of several natural cannabinoids have all been shown to reduce IOP significantly in both glaucoma patients and healthy adults with normal IOP. In most trials a single dose of marijuana or cannabinoid maintained this effect for three to four hours."

Amyotrophic Lateral Sclerosis (ALS)

Amyotrophic Lateral Sclerosis (ALS), also known as Lou Gehrig's disease, is a progressive neurodegenerative disease that affects nerve cells in the brain and the spinal cord, progressively reducing the ability of the brain to initiate and control muscle movement. Some research has shown that cannabinoids can delay the progression of ALS. Some ALS patients have indicated that medical marijuana has helped alleviate their symptoms, such as pain, appetite loss, depression, and drooling.

(1) Gregory T. Carter and Bill S. Rosen, "Marijuana in the Management of Amyotrophic Lateral Sclerosis," American Journal of Hospice and Palliative Care 18, no. 4 (2001): 264-69.

This review article, co-authored by a leading ALS and palliative medicine researcher from the University of Washington, concluded that marijuana may help with many symptoms of ALS, including pain, spasticity, drooling, dysautonomia, and wasting. The authors also discussed how marijuana's antioxidative and neuroprotective effects

may prolong neuronal cell survival, and concluded, "In areas where it is legal to do so, marijuana should be considered in the pharmacological management of ALS."

(2) E. de Lago, J. Fernández-Ruiz, "Cannabinoids and Neuroprotection in Motor Related Disorders," CNS and Neurological Disorders — Drug Targets 6, no. 6 (2007): 377-87.

This review explored in detail the mechanisms of cannabinoid neuroprotection related to a variety of disorders, including ALS.

(3) Dagmar Amtmann, et al., "Survey of Cannabis Use in Patients With Amyotrophic Lateral Sclerosis," American Journal of Hospice and Palliative Medicine, March-April 2004.

This anonymous survey of 131 people with ALS found that 10 percent had reported using marijuana in the past year, reporting relief of multiple symptoms. The authors concluded, "...results indicate that cannabis may be moderately effective at reducing symptoms of appetite loss, depression, pain, spasticity, and drooling."

Crohn's Disease and Irritable Bowel Syndrome (IBS)

Crohn's disease is marked by inflammation of the digestive tract, most commonly the lower part of the small intestine. It can cause severe abdominal pain, nausea, and weight loss – all symptoms that marijuana can help mitigate, as noted in other sections of this document. Preclinical research has demonstrated the role of the endocannabinoid system, the body's natural, marijuana-like chemicals, in protecting the GI tract, providing support for anecdotal reports of relief.

IBS is a functional gastrointestinal disorder, with many similar symptoms to Crohn's Disease. It is constituted as a group of symptoms—including abdominal pain and changes in the pattern of bowel movements without any evidence of underlying damage. These symptoms occur over a long time, often years. It has been classified into four main types depending on if diarrhea is common, constipation is common, both are common, or neither occurs very often (IBS-D, IBS-C, IBS-M, or IBS-U respectively). IBS negatively affects quality of life and may result in missed school or work. Disorders such as anxiety, major depression, and chronic fatigue syndrome, are common among people with IBS.

(1) J.E. Joy, S.J. Watson, and J.A. Benson, Marijuana and Medicine: Assessing the Science Base (National Academy Press, 1999).
"For patients ... who suffer simultaneously from severe pain, nausea, and appetite loss, cannabinoid drugs might offer broad-spectrum relief not found in any other single medication."

(2) F. Massa, M. Storr, and B. Lutz, "The Endocannabinoid System in the

Physiology and Pathophysiology of the Gastrointestinal Tract," Journal of Molecular Medicine 83, no. 12 (2005): 944-54.

This review article noted, "Under pathophysiological conditions induced experimentally in rodents, the endocannabinoid system conveys protection to the GI tract (e.g. from inflammation and abnormally high gastric and enteric secretions). Such protective activities are largely in agreement with anecdotal reports from folk medicine on the use of Cannabis sativa extracts by subjects suffering from various GI disorders."

(3) Timna Naftali, et al., "Cannabis induces a clinical response in patients with Crohn's disease: A prospective placebo-controlled study," Clinical Gastroenterology and Hepatology (2013).
This placebo-controlled clinical trial found that complete remission was achieved in five out of 11 subjects who were administered cannabis, compared to one of the 10 who received a placebo. "A clinical response was observed in 10 of 11 subjects in the cannabis group and four of 10 in the placebo group. Three patients in the cannabis group were weaned from steroid dependency. Subjects receiving cannabis reported improved appetite and sleep, with no significant side effects." (technical parentheticals within the quote deleted)

(4) Adi Lahate, et al., "Impact of Cannabis Treatment on the Quality of Life, Weight, and Clinical Disease Activity in Inflammatory Bowel Disease Patients: A Pilot Prospective Study," Digestion (2012).

This study found that inhaled cannabis improve s quality of life in patients with Crohn's disease and ulcerative colitis. After three months of treatment, patients had a statistically significant increase in weight and improvement in clinical disease activity index. The data showed "a statistically significant improvement in almost all aspects of patients' daily life." This included "a statistically significant physical pain reduction during treatment, as well as improvement in mental distress …" In addition, none of the patients "complained of any side effect that disturbed their working ability. In fact, as was shown in the results, there was a statistically significant improvement in patients' ability to work after treatment."

(5) Timna Naftali, et al., "Treatment of Crohn's Disease with Cannabis: An Observational Study," Israel Medical Association Journal (2011).

This study of 30 patients found that 21 had significant improvement with cannabis treatment. "The mean number of bowel movements decreased from eight to five a day and the need for other drugs was significantly reduced … the number of patients requiring steroid treatment was reduced from 26 to 4. Fifteen of the patients had 19 surgeries during an average period of 9 years before cannabis use, but only 2 required surgery during an average period of 3 years of cannabis use." The authors noted the effects could be due to cannabis' anti-inflammatory properties. In addition, "Cannabinoids influence gastrointestinal motility and, in particular, have an anti-diarrheal effect …"

Parkinson's Disease

Cannabidiol (CBD) is the main non-psychotropic component of the *Cannabis sativa* plant. REM sleep behavior disorder (RBD) is a parasomnia characterized by the loss of muscle atonia during REM sleep associated with nightmares and active behavior during dreaming. We have described the effects of CBD in RBD symptoms in patients with Parkinson's disease.

(1) M. H. N. Chagas, MD PhD, et al. "Cannabidiol can improve complex sleep-related behaviours associated with rapid eye movement sleep behaviour disorder in Parkinson's disease patients: a case series." Journal of Clinical Pharmacy and Therapeutics Volume 39, Issue 5, pages 564–566, October 2014

"Four patients treated with CBD had prompt and substantial reduction in the frequency of RBD-related events without side effects. This case series indicates that CBD is able to control the symptoms of RBD."

(2) Lotan I, et al. "Medical marijuana (cannabis) treatment for motor and non-motor symptoms in Parkinson's disease. An open-label observational study" MDS 2013.

Excerpt from presentation on the study's findings at the *International Congress on Parkinson's Disease and Movement Disorders.* Dr. Ruth Djaldetti, MD, of Tel Aviv University Israel.

"Overall, patients' scores on the standard Unified Parkinson's Disease Rating Scale (UPDRS) averaged 33 before they smoked cannabis in the laboratory and averaged 24 after 30 minutes (P<0.01), Ruth Djaldetti, MD, of Tel Aviv University Israel, reported at her poster presentation at the International Congress on Parkinson's Disease and Movement Disorders. "We not only saw improvement in tremor in these patients, but also in rigidity and in bradykinesia," Djaldetti told MedPage Today. "

Post Traumatic Stress Disorder

Post-traumatic stress disorder involves a person developing characteristic symptoms — such as flashbacks, numbing, and avoidance — after personally experiencing an extremely traumatic stressor. Available treatments are often not effective. Unfortunately, there has been limited research on whole plant marijuana and PTSD, including due to the U.S. federal government refusing to provide marijuana to an FDA-approved and institutional review board-approved study. However, there are clinical trials are ongoing in Israel, where an open pilot study found marijuana effective at alleviating symptoms of combat veterans. In addition, other human and animal evidence supports the therapeutic potential of cannabis and cannabinoids in treating

PTSD symptoms.

(1) Torsten Passie, et al., "Mitigation of post-traumatic stress symptom by Cannabis resin: A review of the clinical and neurobiological evidence," Drug Testing and Analysis (201 2): 649-659

This is a case report of a 19-year-old patient who had severe PTSD, including panic attacks and self-mutilation. He discovered that his major symptoms were dramatically reduced by smoking cannabis resin. As the abstract explains, "The major part of this review is concerned with the clinical and preclinical neurobiological evidence in order to offer a potential explanation of these effects on symptom reduction in PTSD." It noted, "Evidence is increasingly accumulating that cannabinoids might play a role in fear extinction and anti-depressive effects."

(2) George Fraser, "The Use of a Synthetic Cannabinoid in the Management of Treatment-Resistant Nightmares in Posttraumatic Stress Disorder (PTSD)," CNS Neuroscience & Therapeutics 15, no 1. (2009): 84-88.

This study involved administering a naboline — a prescription drug made of a synthetic cannabinoid (component of marijuana) to patients with treatment-resistant nightmares who had PTSD. They reported, "The majority of patients (72%) receiving nabilone experienced either cessation of nightmares or a significant reduction in nightmare intensity. Subjective improvement in sleep time, the quality of sleep, and the reduction of day-time flashbacks and night sweats were also noted by some patients."

(3) Eti Ganon-Elaza and Irit Akirav, "Cannabinoids Prevent the Development of Behavioral and Endocrine Alterations in a Rat Model of Intense Stress," Neuropsychopharmacology (2012): 456–466.

In this study, synthetic marijuana was given to rats after a traumatic event. It was able to block symptoms of PTSD after the rodents were exposed to extreme stress. All of the rats experienced anxiety, but symptoms of PTSD disappeared in the group given marijuana within the two or 24-hour time frame. The findings concluded that, "cannabinoids could serve as a pharmacological treatment of stress- and trauma-related disorder."

(4) George R. Greer M.D., Charles S. Grob M.D. & Adam L. Halberstadt Ph.D. (2014). "PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program," Journal of Psychoactive Drugs 46(1): 73-77.

In 2011, 34% of patients participating in New Mexico's medical cannabis program were diagnosed with PTSD. Authors evaluated patients based on the ClinicianAdministered PTSD Score (CAPS). The results showed a statistically significant decline in the CAPS scores for patients using cannabis across all major categories in the CAPS evaluation. Based on these conclusions, the authors showed that cannabis is associated with a reduction in PTSD symptoms for some patients and supported a placebo-controlled study for further research.

(5) Papini, Santiago, Sullivan, Gregory M., Hein, Denise A., Shvil, Erel & Neria, Yuval. (2015). "Toward a translational approach to targeting the endocannabinoid system in posttraumatic stress disorder: A critical review of preclinical research," Biological Psychology 104: 8-18.

This study trained mice to develop fear-based responses to certain stimuli and then examined the effects of cannabinoids on the treatment of PTSD developed through previous conditioning. The study confirmed previous research that disruption of CB1 receptors impairs fear extinction (the ability of an organism to stop reacting negatively to stimuli after the negative consequences of that stimuli cease). The study also found some success in treating rats with CB1 agonists during extinction therapy and found similar results for humans. The study concluded that using CB1 agonists could be used to improve the effectiveness of extinction therapy for those with PTSD or for those at risk for developing PTSD.

(6) Roitman, Pablo, Mechoulam, Raphael, Cooper-Kazas, Rena & Shalev, Arieh. (2014). "Preliminary, Open-Label, Pilot Study PTSD," Clinical Drug Investigation 34: 587-591.

This study examined the effects of orally ingested THC for 10 subjects with posttraumatic stress disorder. Patients experienced only mild side effects like dry mouth or dizziness in some cases, and none of the side effects were severe enough to cause the patients to drop out of the study. The data showed a statistically significant relationship between using THC to treat PTSD and an improvement in overall severity of sleep quality, nightmare frequency, and PTSD hyperarousal symptoms like feelings of tenseness or being easily startled. The authors recommend further research based on the results of the pilot study.