



February 15, 2021

RE: Medical Marijuana Benefits

In 2013, neurosurgeon Dr. Sanjay Gupta made national headlines with a public apology for previously opposing medical marijuana:

I apologize because I didn't look hard enough, until now. I didn't look far enough. I didn't review papers from smaller labs in other countries doing some remarkable research, and I was too dismissive of the loud chorus of legitimate patients whose symptoms improved on cannabis.¹

Gupta continued, speaking to common misconceptions concerning marijuana's federal prohibition:

I mistakenly believed the Drug Enforcement Agency listed marijuana as a Schedule I substance because of sound scientific proof. Surely, they must have quality reasoning as to why marijuana is in the category of the most dangerous drugs that have "no accepted medicinal use and a high potential for abuse."

They didn't have the science to support that claim, and I now know that when it comes to marijuana neither of those things are true. It doesn't have a high potential for abuse, and there are very legitimate medical applications. In fact, sometimes marijuana is the only thing that works.

Despite increased acceptance from the medical community (former U.S. Surgeon General Joycelyn Elders claims "the unjust prohibition of marijuana has done more damage to public health than has marijuana itself"),² cannabis still carries a social stigma that has been hard to shake. While just the tip of the iceberg, the following studies highlight a wealth of research supporting Elders, Gupta, and the countless medical professionals calling for a change in the public's perception and understanding of medical marijuana.

Study Excerpts

ALS

Peer-reviewed journal *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders* states:

¹ Gupta, S. (2013, August 8). Why I changed my mind on weed. *CNN Health*.

² Nathan, D.L., Clark, H.W., & Elders, J. (2017). The physicians' case for marijuana legalization. *American Journal of Public Health, 107*(11): 1746-7.



Our research indicates that select marijuana compounds, including THC, significantly slow the disease process and extend the life of mice with ALS.³

As lead study author Dr. Mary Abood explains:

The only FDA-approved drug for ALS, riluzole, extends life on average by about two months. Evidence from our study suggests that a marijuana-based therapy could create a much greater effect, perhaps extending life by three years or more.⁴

Follow-up studies support Abood's claim, with a number of publications – including the *Federation of American Societies for Experimental Biology Journal* – reporting similar findings:

These results show that cannabinoids have significant neuroprotective effects in this model of ALS.⁵

ANXIETY & PTSD

A 2016 *Frontiers in Pharmacology* study found that marijuana cannabinoid, CBD, may help post-traumatic stress disorder (PTSD) patients by reducing learned fear – a condition that triggers the fight or flight response at inappropriate times. Researchers write:

A growing body of literature provides compelling evidence that CBD has anxiolytic effects and recent studies have established a role for CBD in regulating learned fear by dampening its expression, disrupting its reconsolidation, and facilitating its extinction.⁶

Marijuana's efficacy in addressing more generalized anxiety symptoms is perhaps best illustrated by a 2019 study finding that after six months of medical marijuana treatment, 45.2% of study participants discontinued benzodiazepine use (e.g., Xanax, Valium, Ativan).⁷

³ Raman, C., McAllister, S.D., Rizvi, G., Patel, S.G., Moore, D.H., & Abood, M.E. (2004). Amyotrophic lateral sclerosis: Delayed disease progression in mice by treatment with a cannabinoid. *Amyotrophic Lateral Sclerosis and Other Motor Neuron Disorders*, 5(1):33-9.

⁴ Society For Neuroscience. (2004, October 27). Marijuana-like compounds may aid array of debilitating conditions ranging from Parkinson's disease to pain. *ScienceDaily*.

⁵ Bilsland, L.G., Dick, J.R., Pryce, G., Petrosino, S., Di Marzo, V., Baker, D., & Greensmith, L. (2006). Increasing cannabinoid levels by pharmacological and genetic manipulation delay disease progression in SOD1 mice. *FASEB Journal*, 20(7): 1003-5.

⁶ Jurkus, R., Day, H. L., Guimarães, F. S., Lee, J. L., Bertoglio, L. J., & Stevenson, C. W. (2016). Cannabidiol regulation of learned fear: Implications for treating anxiety-related disorders. *Frontiers in Pharmacology*, 7: 454.

⁷ Purcell, C., Dava, A., Moolman, N., & Taylor, S.M. (2019). Reduction of benzodiazepine use in patients prescribed medical cannabis. *Cannabis and Cannabinoid Research*, 4(3): 214-18.



CANCER

Research suggests cannabis may exert anti-cancer effects by causing cell death, modulating cell-signaling pathways⁸, and inhibiting tumor invasion.⁹ For instance, a 2011 study found that CBD kills breast cancer cells by inducing endoplasmic reticulum stress and inhibiting cell-signaling.¹⁰ Likewise, colon cancer studies show that CBD has a cancer-protective effect and reduces cell proliferation.¹¹

Perhaps most exciting, the National Cancer Institute notes that:

Cannabinoids appear to kill tumor cells but do not affect their non-transformed counterparts and may even protect them from cell death.¹²

CROHN'S DISEASE

In 2011, the *Israel Medical Association Journal* detailed findings from the first-ever study on cannabis use in Crohn's disease. Conducting retrospective interviews, researchers noted:

The results indicate that cannabis may have a positive effect on disease activity, as reflected by reduction in disease activity index and in the need for other drugs and surgery.¹³

Perhaps of most interest, the study authors add:

The central effect of cannabinoids may induce a sensation of general well-being, which could contribute to the feeling that cannabis use is beneficial. However, this general effect wears off with time as tolerance develops, while the positive effect of cannabis on disease activity in our patients was maintained for an average period of 3.1 years.

⁸ Guzmán M. (2003). Cannabinoids: Potential anticancer agents. *Nature Reviews Cancer*, 3(10), 745-55.

⁹ Vaccani, A., Massi, P., Colombo, A., Rubino, T., & Parolaro, D. (2005). Cannabidiol inhibits human glioma cell migration through a cannabinoid receptor-independent mechanism. *British Journal of Pharmacology*, 144(8), 1032-36.

¹⁰ Shrivastava, A., Kuzontkoski, P.M., Groopman, J.E., & Prasad, A. (2011). Cannabidiol induces programmed cell death in breast cancer cells by coordinating the cross-talk between apoptosis and autophagy. *Molecular Cancer Therapeutics*, 10(7), 1161-72.

¹¹ Aviello, G., Romano, B., Borrelli, F., Capasso, R., Gallo, L., Piscitelli, F., Di Marzo, V., & Izzo, A. A. (2012). Chemopreventive effect of the non-psychoactive phytocannabinoid cannabidiol on experimental colon cancer. *Journal of Molecular Medicine*, 90(8), 925-34.

¹² PDQ Integrative, Alternative, and Complementary Therapies Editorial Board. PDQ Cannabis and Cannabinoids. Bethesda, MD: National Cancer Institute. Updated 11/06/2020. PMID: 26389198.

¹³ Naftali, T., Lev, L.B., Yablecovitch, D., Half, E., & Konikoff, F.M. (2011). Treatment of Crohn's disease with cannabis: An observational study. *The Israel Medical Association Journal*: 13(8), 455-8.



DIABETES

Cannabis users demonstrate a lower risk for diabetes, with a recent study concluding:

In a robust multivariate model controlling for socio-demographic factors, laboratory values and comorbidity, the lower odds of diabetes mellitus among marijuana users was significant [...] Marijuana use was independently associated with a lower prevalence of diabetes mellitus.¹⁴

Speaking of his own separate research, Harvard Medical School professor Dr. Murray Mittleman writes:

The most important finding is that current users of marijuana appeared to have better carbohydrate metabolism than non-users. Their fasting insulin levels were lower, and they appeared to be less resistant to the insulin produced by their body to maintain a normal blood-sugar level.¹⁵¹⁶

EPILEPSY

In a randomized double-blind placebo-controlled trial performed at 30 clinic centers, researchers found that the addition of CBD to traditional seizure medication significantly decreased the rate of drop (or atonic) seizures.¹⁷

Another cannabinoid, CBDV, has recently gained attention with a 2012 study concluding:

The significant anticonvulsant effects and favorable motor side effect profile demonstrated in this study identify CBDV as a potential standalone anti-epileptic drug or as a clinically useful adjunctive treatment alongside other anti-epileptic drugs.¹⁸

GLAUCOMA

¹⁴ Rajavashisth, T.B., Shaheen, M., Norris, K.C., Pan, D., Sinha, S.K., Ortega, J., & Friedman, T.C. (2012). Decreased prevalence of diabetes in marijuana users: Cross-sectional data from the National Health and Nutrition Examination Survey (NHANES) III. *British Medical Journal Open*, 2(1): e000494.

¹⁵ Penner, E.A., Buettner, H., & Mittleman, M. A. (2013). The impact of marijuana use on glucose, insulin, and insulin resistance among US adults. *The American Journal of Medicine*, 126(7), 583-9.

¹⁶ Szalavitz, M. (2013, May 21). Marijuana: The next diabetes drug? *Time*.

¹⁷ Devinsky, O., Patel, A. D., Cross, J.H., Villanueva, V., Wirrell, E.C., Privitera, M., Greenwood, S.M., Roberts, C., Checketts, D., VanLandingham, K.E., Zuberi, S.M., & GWPCARE3 Study Group. (2018). Effect of cannabidiol on drop seizures in the Lennox-Gastaut Syndrome. *The New England Journal of Medicine*, 378(20): 1888-97.

¹⁸ Hill, A.J., Mercier, M.S., Hill, T.D., Glyn, S.E., Jones, N.A., Yamasaki, Y., Futamura, T., Duncan, M., Stott, C.G., Stephens, G.J., Williams, C.M., & Whalley, B.J. (2012). Cannabidivarin is anticonvulsant in mouse and rat. *British Journal of Pharmacology*, 167(8), 1629-42.



A position statement from the American Glaucoma Society acknowledges:

It has been definitively demonstrated, and widely appreciated, that smoking marijuana lowers IOP [intraocular pressure] in both normal individuals and in those with glaucoma, and therefore might be a treatment for glaucoma.¹⁹

While this lowering effect is not without its fair share of controversy, a review published by the *Journal of Clinical Medicine* highlights additional benefits:

Another interesting aspect of cannabinoid usage in glaucoma is connected with the neuroprotective capabilities of these molecules.²⁰

HIV/AIDS

Cannabis has long been recognized as an effective treatment for HIV/AIDS symptoms and medication side effects. According to a 2004 study published by the *Journal of Acquired Immune Deficiency Syndrome*:

A substantial percentage of cannabis users viewed it as beneficial for relief of symptoms commonly associated with HIV/AIDS. Relief from anxiety and depression were among the most frequently reported reasons for smoking cannabis, followed by appetite stimulation and relief of nausea.²¹

As researchers note:

This finding is particularly relevant to issues of antiretroviral medication adherence (ART). Nausea and anorexia are frequently cited as reasons for delayed or missed doses and discontinuation of ART.

MIGRAINES

In 2016, *Pharmacotherapy* published results of a retrospective chart review analyzing medical marijuana use in 121 migraine patients. The study showed marijuana successfully prevented migraines; patients who

¹⁹ Jampel, H. (2009, August 10). Position statement on marijuana and the treatment of glaucoma. *American Glaucoma Society*.

²⁰ Passani, A., Posarelli, C., Sframeli, A.T, Perciballi, L., Pellegrini, M., Guidi, G., & Figus, M. (2020). Cannabinoids in glaucoma patients: The never-ending story. *Journal of Clinical Medicine*, 9(12):3978.

²¹ Prentiss, D., Power, R., Balmas, G., Tzuang, G., & Israelski, D. M. (2004). Patterns of marijuana use among patients with HIV/AIDS followed in a public health care setting. *Journal of Acquired Immune Deficiency Syndrome*, 35(1), 38-45.



used marijuana experienced 5.8 less migraine days a month. Moreover, patients also reported that marijuana stopped migraines in-progress.²²

These findings support a separate study presented at the Third Congress of the European Academy of Neurology which concluded:

We were able to demonstrate that cannabinoids are an alternative to established treatments in migraine prevention.²³

MULTIPLE SCLEROSIS

A five-week double-blind placebo-controlled study found that multiple sclerosis patients who used whole-plant cannabis-based medication (including cannabinoids THC and CBD) experienced reduced pain intensity.²⁴

The same 2005 study also found that cannabis-based medication decreased sleep disturbances, leading researchers to conclude:

Cannabis-based medicine is effective in reducing pain and sleep disturbance in patients with multiple sclerosis related central neuropathic pain and is mostly well tolerated.

OBESITY

In 2011, the *American Journal of Epidemiology* reviewed two population-based nationally representative studies exploring the relationship between marijuana use and obesity. After analyzing results from over 50,000 respondents, researchers concluded:

The prevalence of obesity was significantly lower in cannabis users than in non-users [...] The proportion of obese participants decreased with the frequency of cannabis use.²⁵

Addressing widely held stereotypes, the authors add:

²² Rhyne, D.N., Anderson, S.L., Gedde, M., & Borgelt, L.M. (2016). Effects of medical marijuana on migraine headache frequency in an adult population. *Pharmacotherapy*, 36(5), 505-10.

²³ EMJ Neurology. (2017). Review of the 3rd European Academy of Neurology Congress 2017. *European Medical Journal*, 5(1):12-29.

²⁴ Rog, D. J., Nurmikko, T.J., Friede, T., & Young, C.A. (2005). Randomized, controlled trial of cannabis-based medicine in central pain in multiple sclerosis. *Neurology*, 65(6), 812-19.

²⁵ Le Strat, Y., & Le Foll, B. (2011). Obesity and cannabis use: results from 2 representative national surveys. *American Journal of Epidemiology*, 174(8), 929-33.



This cross-sectional analysis indicated that despite the evidence that cannabis use stimulates appetite in clinical trials and laboratory studies, cannabis users are actually less likely to be obese than non-users in the general population.

Likewise, a study from 2006 found that even though marijuana use may be correlated with increased caloric intake, it is not associated with higher body mass index (BMI) or glucose levels.²⁶

PAIN

After administering standardized doses of smoked marijuana using a uniform puff and breath-hold procedure, researchers found that:

...a linear analgesic [pain relief] dose response for... cannabis substantiated previous empirical reports of pain relief.²⁷

The study authors concluded that marijuana reduced pain intensity and unpleasantness equally, meaning that (like opioids) cannabis does not rely on a relaxing or tranquilizing effect, but rather “reduces both the core component of nociception and the emotional aspect of the pain experience to an equal degree.”

PARKINSON’S DISEASE

In 2014, *Clinical Neuropharmacology* reported that marijuana improves Parkinson’s motor symptoms including tremors, rigidity, and bradykinesia, as well as non-motor symptoms such as pain and sleep disorders.²⁸ Follow-up studies appear to support these results, with a 2015 survey finding:

Cannabis was rated as the most effective therapy for sleep and mood improvement amongst all complementary and alternative medications.²⁹

Likewise, the *Journal of Psychopharmacology* reports:

²⁶ Rodondi, N., Pletcher, M.J., Liu, K., Hulley, S.B., Sidney, S., & Coronary Artery Risk Development in Young Adults (CARDIA) Study (2006). Marijuana use, diet, body mass index, and cardiovascular risk factors (from the CARDIA study). *The American Journal of Cardiology*, 98(4), 478-84.

²⁷ Wilsey, B., Marcotte, T., Tsodikov, A., Millman, J., Bentley, H., Gouaux, B., & Fishman, S. (2008). A randomized, placebo-controlled, crossover trial of cannabis cigarettes in neuropathic pain. *The Journal of Pain*, 9(6), 506-21.

²⁸ Lotan, I., Treves, T. A., Roditi, Y., & Djaldetti, R. (2014). Cannabis (medical marijuana) treatment for motor and non-motor symptoms of Parkinson disease: An open-label observational study. *Clinical Neuropharmacology*, 37(2), 41-44.

²⁹ Finseth, T.A., Hedeman, J.L., Brown, R.P., Johnson, K.I., Binder, M.S., & Kluger, B.M. (2015). Self-reported efficacy of cannabis and other complementary medicine modalities by Parkinson's disease patients in Colorado. *Evidence-based Complementary and Alternative Medicine*, 2015: 874849.



We found significant improvements in measures of functioning and well-being of Parkinson's disease patients treated with CBD compared to a group that received placebo.³⁰

Respiratory Health: Risks Rebuttal

Any claim of substantial evidence of a statistical association between long-term cannabis smoking and worsening respiratory symptoms and more frequent chronic bronchitis episodes stands in contrast to what is considered the largest and longest study ever to consider the issue of marijuana and impaired lung function.

According to a twenty-year study published by the *Journal of the American Medical Association*, researchers found that:

Occasional and low cumulative marijuana use was not associated with adverse effects on pulmonary function.³¹

Interestingly, results also suggest that low and moderate levels of marijuana use may even improve lung function, as measured by two lung capacity tests: FEV1 and FVC. As associate professor of epidemiology and biostatistics at the University of California and lead study author Dr. Mark Pletcher explains:

FEV1 and FVC both actually increased with moderate and occasional use of marijuana [...] It's a weird effect to see and we couldn't make it go away.

A systematic review by Health Canada drew similar conclusions:

The association between chronic heavy cannabis smoking (without tobacco) and chronic obstructive pulmonary disease, is unclear, but if there is one, is possibly small.³²

As *Respiratory Care* warns:

³⁰ Chagas, M.H., Zuardi, A.W., Tumas, V., Pena-Pereira, M.A., Sobreira, E.T., Bergamaschi, M.M., dos Santos, A.C., Teixeira, A.L., Hallak, J.E., & Crippa, J.A. (2014). Effects of cannabidiol in the treatment of patients with Parkinson's disease: An exploratory double-blind trial. *Journal of Psychopharmacology*, 28(11): 1088-98.

³¹ Pletcher, M.J., Vittinghoff, E., Kalhan, R., Richman, J., Safford, M., Sidney, S., Lin, F., & Kertesz, S. (2012). Association between marijuana exposure and pulmonary function over 20 years. *Journal of the American Medical Association*, 307(2):173-81.

³² Health Canada. (2018). Information for health care professionals: Cannabis (marihuana, marijuana) and the cannabinoids.



Although much is known about tobacco smoke, less is known about marijuana smoke, and inferences cannot be made about one based on the other.³³

Importantly, in a retrospective cohort study of 64,855 participants, researchers found:

Marijuana use was not associated with tobacco-related cancers or with cancer of the following sites: colorectal, lung, melanoma, breast.³⁴

Likewise, a population-based case-control study of 611 lung cancer patients revealed that chronic low cannabis exposure was not associated with an increased risk of lung cancer or other upper aerodigestive tract cancers.³⁵ Furthermore, the same study found no positive associations with any cancer type (oral, pharyngeal, laryngeal, lung, or esophagus) when adjusting for several confounders, including cigarette smoking.

These results led researchers to conclude:

[Our study] suggests that the association of these cancers with marijuana, even long-term or heavy use, is not strong and may be below practically detectable limits.

In 2006, another set of researchers conducted a systematic review assessing 19 studies that evaluated premalignant or malignant lung lesions in persons 18 years or older who inhaled marijuana. As summarized by the study authors:

[These] observational studies failed to demonstrate statistically significant associations between cannabis inhalation and lung cancer after adjusting for tobacco use.³⁶

Supporting this conclusion, Health Canada notes:

At present, no conclusive positive associations can be drawn between cannabis smoking and incidence of lung or upper airway cancer.³⁷

³³ Martinasek, M.P., McGrogan, J.B., & Maysonet, A. (2016). A systematic review of the respiratory effects of inhalational marijuana. *Respiratory Care*, 61(111): 1543-51.

³⁴ Sidney, S., Quesenberry, C.P., Friedman, G.D., & Tekawa, I.S. (1997). Marijuana use and cancer incidence (California, United States). *Cancer Causes Control*, 8(5): 722-8.

³⁵ Hashibe, M., Morgenstern, H., Cui, Y., Tashkin, D.P., Zhang, Z.F., Cozen, W., Mack, T.M., & Greenland, S. (2006). Marijuana use and the risk of lung and upper aerodigestive tract cancers: Results of a population-based case-control study. *Cancer Epidemiology, Biomarkers & Prevention*, 15(10): 1829-34.

³⁶ Mehra, R., Moore, B.A., Crothers, K., Tetrault, J., & Fiellin, D.A. (2006). The association between marijuana smoking and lung cancer: A systematic review. *Archives of Internal Medicine*, 166(13): 1359-67.

³⁷ Health Canada. (2018). Information for health care professionals: Cannabis (marihuana, marijuana) and the cannabinoids.



Summary

In addition to the stated health benefits, medical marijuana has also been shown to decrease opioid dependence, cocaine addiction, and alcohol use. According to the *British Medical Journal*:

An increase from one available [marijuana] dispensary in a county to two is associated with a 17% reduction in opioid-related overdose deaths; an increase from two to three is associated with a further 8.5% reduction.³⁸

Likewise, *Pharmacology, Biochemistry, and Behavior* found:

CBD treatment dose-dependently diminished cocaine self-administration and moved the dose-response curve downward.³⁹

Lastly, the *International Journal of Drug Policy* reports:

Following medical cannabis initiation, 44% of participants reported decreases in alcohol use frequency over 30 days, and 34% decreased the number of standard drinks they had per week.⁴⁰

Again, while just a small sampling of the research supporting medical marijuana's efficacy and rightful place in modern medicine, the studies above provide apt rationale for the passion exhibited by medical cannabis advocates, physicians, and patients – a passion we can only hope will be increasingly reflected in public dialogue and future legislative policies.

A handwritten signature in black ink, appearing to read "Jessica Walters", with a long horizontal flourish extending to the right.

Jessica Walters
Chief Medical Researcher
E: jessica@cannamd.com

³⁸ Hsu, G. & Kovács, B. (2021) Association between county level cannabis dispensary counts and opioid related mortality rates in the United States: Panel data study. *British Medical Journal*, 372: m4957.

³⁹ Rodrigues, L.A., Caroba, M., Taba, F.K., Filev, R., & Gallassi, A.D. (2020). Evaluation of the potential use of cannabidiol in the treatment of cocaine use disorder: A systematic review. *Pharmacology, Biochemistry, and Behavior*, 196: 172982.

⁴⁰ Lucas, P., Boyd, S., Milloy, M-J., & Walsh, Z. (2020). Reductions in alcohol use following medical cannabis initiation: Results from a large cross-sectional survey of medical cannabis patients in Canada. *International Journal of Drug Policy*, 86: 102963.