



**Reefer Madness Revisited:  
Taking the Insanity Out of Medical Cannabinoids**

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**Disclosure**

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- Consultant/Independent Contractor, Speakers Bureau: kaléo
- Dr. Schatman has no other conflicts of interest, although he is a veteran of 33 Grateful Dead/Dead and Company concerts



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**Learning Objectives**

- Describe the political issues surrounding the legalization of medical marijuana
- Recognize the obstacles to conducting high-quality medical cannabinoid research in the United States
- Discuss how to modify your medical marijuana authorization patterns based on legal realities and empirical data



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### What the Heck is “Medical Marijuana”?!?!

- Lots of questions to be asked...
  - Lengthy history in the US
    - California became the first state to legalize MM in 1996
  - Currently there are MM laws in 33 states plus DC
- National Conference of State Legislatures. State medical marijuana laws, 2/11/2019. Available at: <http://www.ncsl.org/research/health/state-medical-marijuana-laws.aspx>.
- Individual states’ medical marijuana laws are incredibly heterogeneous – varying widely in terms of process of obtaining, limits on possession, rules regulating dispensaries, allowable medical conditions, and every other parameter




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### What is Medical Marijuana?

- In the eyes of the pro-marijuana zealots, ALL marijuana is “medical”
  - In the eyes of the FDA, NO marijuana is “medical”
  - Perhaps the truth falls somewhere in between...
  - CSA (1970) made cannabis a Schedule I drug – “drugs with no currently accepted medical use and a high potential for abuse”
- US Drug Enforcement Administration. Drug Scheduling. Available at: <http://www.justice.gov/ea/druginfo/drugs.shtml>.
- Remains federally “illegal”




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### What is Medical Marijuana? (cont’d)

- Is it legal or illegal?
- Should it be legal?
- Is it safe?
- Is there an evidence basis for efficacy?
- If it’s sold in a dispensary, should it therefore be considered “medical”?
- If it’s “medical,” can it be abused?




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### So Let's Complicate Things Even More...

- What constitutes "recreational marijuana"?
  - Washington
  - Colorado
- Again, to the FDA, legal recreational marijuana doesn't exist
  - Alaska
  - Oregon
  - California
  - Nevada
  - DC
  - Massachusetts
  - Maine
  - Vermont
  - Michigan
- However, tell this to the good citizens of:




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### The Future of Recreational Pot?

- Predictions for legalization in 2019:
  - Connecticut
  - Illinois
  - Minnesota
  - New Hampshire
  - New Jersey
  - New Mexico
  - New York
  - Rhode Island
  - Vermont



Angel T. Forbes, December 26, 2018. Available at: <https://www.forbes.com/sites/angelforbes/2018/12/26/marijuana-the-most-likely-to-legalize-marijuana-in-2019/#d11a065ad1>




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### Politics

- 2014: Congress passes the Rohrabacher–Blumenauer amendment, defunding the DOJ from enforcement of federal law in MM states
  - Lopez G. Vox, May 30, 2014.
- Must be renewed every fiscal year to stay in effect
  - McCoy JJ, New Frontier Data, March 17, 2018. Available at: <https://newfrontierdata.com/marijuana-insights/rohrabacher-blumenauer-what-are-the-stakes-revisited/>.
- Has been successfully renewed each year – attached to the federal budget bill
- Every time a budget agreement can't be reached, federal protection of states' laws is threatened
- And the DOJ can theoretically run wild...




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## Cannabinoids

- Marijuana contains over 100 cannabinoids
- National Institute on Drug Abuse. Drug Facts: Is Marijuana Medicine? Revised April, 2014.
- $\Delta 9$ -tetrahydrocannabinol (THC) – the principle psychoactive constituent of cannabis
  - Gets all of the press – good and bad
  - Recreational marijuana – goal is to maximize THC
  - Seems to be the goal of “medical marijuana” as well...
  - Higher THC fetches a higher price in dispensaries

**Pain**week

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## THC:CBD Ratio

- What kinds of ratios do we see in medical and nonmedical cannabis?
  - Recent study of THC & CBD (medical and recreational) 2008-2017
- Chandra S, et al. Eur Arch Psychiatry Clin Neurosci. 2019; 269(1):5-15.
- THC levels doubled (8.9% in 2008, 17.1% in 2017)
  - CBD levels decreased from 0.37% in 2008 to 0.14% in 2017
  - THC:CBD ratio increase from 23:1 in 2008 to 104:1 in 2017
  - Importance of the ratio: “CBD is nonintoxicating and has been found to offset several, harmful effects of  $\Delta 9$ -THC, including memory impairment and psychotic-like symptoms”

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## THC:CBD Ratio (cont'd)

- Authors conclude, “These trends in the last decade suggest that cannabis is becoming an increasingly harmful product”
  - The THC:CBD ratio is not examined in most studies
    - Most current data come from toxicology following seizures
- Vindenes V, Morland J. Increasing plant concentrations of THC and implications on health related disorders. In: Handbook of Cannabis and Related Pathologies: Biology, Pharmacology, Diagnosis, and Treatment. Academic Press, 2017. pp. 24-32.
- Ability to understand the THC:CBD ratio and the impact of breeding the CBD out of cannabis is essential to understanding its health risks

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### Synthetic THC

- Available as a Schedule III drug (dronabinol/Marinol) since 1985
- Nabilone/Cesamet (Schedule II) – a synthetic THC analogue – also FDA-approved in 1985
- Common side effects include drowsiness, unsteady gait, dizziness, inability to focus thoughts, confusion, mood changes, delusions, and hallucinations

WebMD. Drugs and medications: Marinol oral. <http://www.webmd.com/drugs/2/drug-9308-Marinol-Oral-asox?drugid=9308&drugname=Marinol-Oral&oc=numbers>

- Tolerability is dubious
- Consequently, so is clinical utility for pain

Issa MA, et al. Clin J Pain 2014;30:472-478.




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### Safety Issues Associated with Marijuana

- The myriad safety concerns identified are thought to be due primarily to THC; more THC means more risks

Fischer B, et al. Am J Public Health. 2017;107(6):e1-e12.

- Can we assume that as the THC levels continue to rise, that safety risks will do the same?

- Smoking remains the most common route of administration

Russell C, et al. Int J Drug Policy. 2018;52:87-96.

- Recent review: pulmonary effects are even worse than we'd thought – "Marijuana Lung"

Leib JS, et al. Chronic Obstr Pulm Dis. 2018;5:81-83.

- Tars from smoked marijuana contain more carcinogens than do those from tobacco

Wu TC, et al. N Engl J Med. 1989;318:347-351.




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### Physical Safety Issues

- 2018 review: Concludes that vaporization is safer than smoking from a pulmonary perspective

MacCallum CA, Russo EB. Eur J Intern Med. 2018;49:12-19.

- Cardiovascular - Dysregulation of the endogenous lipid mediator endocannabinoids has been implicated in a variety of cardiovascular pathologies

Pacher P, et al. Nat Rev Cardiol. 2018;15(3):151-166.

- Increases rates of acute myocardial infarction and cardiovascular mortality – doubles rate of MI

Franz CA, Frishman WH. Cardiol Rev. 2016;24:158-162.

- Predicts heart failure and CVA – whether recreational or medical

Kalla A, et al. J Cardiovasc Med (Hagerstown). 2018;19:480-484.




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### Physical Safety Issues (cont'd)

- Increased duration of marijuana use is associated with increased risk of death from hypertension

Yankey BA, et al. Eur J Prev Cardiol. 2017;24(17):1833-1840.

- Associated with higher rates of acute ischemic stroke

Jung JS, et al. Investig Magn Reson Imaging. 2018;22(3):168-171.

- Immunosuppressive – reduces T-cell activation

Henriquez JE, et al. J Pharmacol Exp Ther. 2018;367(1):49-58.

- Implications for cancer, HIV, among others




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### Physical Safety Issues (cont'd)

- Cannabinoid hyperemesis syndrome

- Characterized by a syndrome of cyclic vomiting, abdominal pain, and compulsive showering in some habitual users

- Symptoms improve with cessation utilization

- Prevalence of cannabinoid hyperemesis syndrome seen in EDs quickly doubled following the liberalization of MJ laws in Colorado

Kim HS, et al. Acad Emerg Med. 2015;22:694-699.

- Can masquerade as an eating disorder

Brewerton TD, Anderson O. Int J Eat Disord. 2016;49:828-829.

- Estimated 2.75 million cases in the US annually

Habboushe J, et al. Basic Clin Pharmacol Toxicol. 2018;122:660-662.

- Fatal cases now being reported

Nourbakhsh M, et al. J Forensic Sci. 2019;64(1):270-274.




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### Physical Safety Issues (cont'd)

- Cannabis use is associated with higher rates of occupational injuries, injury severity, and prolonged lost workdays among construction workers

Khashaba E, et al. Toxicol Ind Health. 2018;34:83-90.

- Drugged driving – 96% of cases involve cannabis

Bonar EE, et al. Addict Behav. 2018;78:80-84.

- Drugged driving continues to increase, with increases associated with more traffic fatalities

Robertson RD, et al. Accid Anal Prev. 2017;99(Pt A):236-241.




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### Physical Safety Issues (cont'd)

- French study: 1 in 2 drivers in fatal accidents under the influence of ETOH were also under the influence of cannabis  
Martin JL, et al. PLoS One 2017;12(11):e0187320.
- High-risk drinking behavior recently found to be related to medical cannabis utilization  
Davis AK, et al. Addict Behav. 2018;77:166-171.
- Older adults – cannabis use associated with greater physical injury risk and ED visits  
Choi NG, et al. Am J Drug Alcohol Abuse. 2018;44:215-223.




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### Physical Safety Issues (cont'd)

- Perhaps the issue is that users of MJ have been found to have greater perceived safety than those who don't  
Sattor CE, et al. Addict Behav. 2017;86:114-117.
- Pregnancy: Use of marijuana among pregnant women increased by 69% between 2009 and 2016  
Young-Wolff KC, et al. JAMA 2017;318(24):2490-2491.
- Currently at 22%  
Oga EA, et al. Matern Child Health J. 2019;23(2):250-257.
- Cannabis use associated with preterm birth  
Prunet C, et al. J Gynecol Obstet Hum Reprod. 2017;46(1):19-28.
- Likelihood of stillbirth or miscarriage 12 times higher among women using MJ during pregnancy  
Coleman-Cowger VH, et al. Neurotoxicol Teratol. 2018;68:84-90.




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### Physical Safety Issues (cont'd)

- Addiction
  - Not as severe as opioid or benzo addiction
  - Abrupt cessation results in irritability, insomnia, anorexia  
Haney M, et al. Neuropsychopharmacology 2013;38:1557-1565.
- Perceived barrier to quitting MJ – fear of severe withdrawal symptoms  
Zvolensky MJ, et al. Addict Behav. 2018;76:45-51.
- When used hs, withdrawal's impact on sleep is particularly problematic  
Crantford JA, et al. Drug Alcohol Depend. 2017;180:227-233.
- Reduced MJ use associate with improved sleep quality  
Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.




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### Cognitive Safety Issues

- We've known about chronic MJ use and its impact on diminution of grey matter in the brain for years  
Block RI, et al. Neuroreport 2000;11:491-496.
- Of particular concern in the developing brain
- Executive functioning deficits associated with MJ use  
Clark DB, et al. Front Behav Neurosci. 2017;11:223.
- Myriad studies and reviews indicate that chronic MJ use results in cognitive deficits
  - Long-term and short-term




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### Cognitive Safety Issues (cont'd)

- Long-term deficits ("residual cannabis effect") include (from a meta-analysis):
  - Learning
  - Forgetting/retrieval
  - Abstraction/executive functioning
  - Attention
  - Motor skills
  - Verbal/language

Schreiner AM, Dunn ME. Exp Clin Psychopharmacol. 2012;20(5):420-429.




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### Mental Health Risks

- Most studied issue has been early-onset psychosis and recovery from it in marijuana users
- MJ-psychosis association recognized back to the 1950s  
Ames F. J Ment Sci. 1958;104(437):972-999.
- High THC cannabis increases the risk of psychosis 3-fold compared to nonusers, and 5-fold among daily users  
Di Forti M, et al. Lancet Psychiatry 2015;2(3):233-238.
  - Particularly problematic in patients using ultra-high-THC wax dabs  
Pierre JM, et al. Schizophr Res. 2016;172(1-3):211-212.




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### Mental Health Risks – Psychosis

- Cannabis use in first episode psychosis is associated with failure of anti-psychotic medications

Patel R, et al. BMJ Open. 2016;6(3):e009888.

– As well as adherence to anti-psychotic medications

Schoeler T, et al. Lancet Psychiatry 2017;4(8):627-633.

- Extended abstinence from MJ doesn't seem to reverse symptoms in cannabis-dependent schizophrenics

Rabin RA, et al. Schizophr Res. 2018;194:55-61.

- A risk factor for violent behavior in early phase psychosis

Moulin V, et al. Front Psychiatry. 2018;9:294.




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### Mental Health Risks – Anxiety

- The acute induction of anxiety associated with THC cannot be ignored

- Early studies found an anxiolytic effect of MJ

Sethi BB, et al. Biol Psychiatry 1986;21:3-10.

- 2017 meta-analysis concludes that THC's impact on anxiety is not necessarily impressive

Turna J, et al. Depress Anxiety. 2017;34:1006-1017.

– However, that may have much to do with Indica vs. Sativa strain

- Recent study found that longitudinally, reduction of MJ use was associated with decreased anxiety

Hser YI, et al. J Subst Abuse Treat. 2017;81:53-58.




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### Mental Health Risks – Anxiety (cont'd)

- PTSD: once thought to be "treatable" with cannabis
- However chronic MJ use has been found to impair fear extinction

Papini S, et al. J Abnorm Psychol. 2017;126:117-124.

- MJ use in PTSD patients strongly predicts dropout from therapeutic treatment

Bedard-Gilligan M, et al. Psychol Addict Behav. 2018;32(3):277-288.

- Indicas may be helpful, activating sativas likely to exacerbate

- Good news: dispensary employees found to be more likely to recommend an indica or a hybrid for PTSD than a sativa

Haug NA, et al. Cannabis Cannabinoid Res. 2016;1:244-251.




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## Cannabidiol (CBD)

- Contrary to popular belief, THC is not the most relevant cannabinoid for medical application  
Campos AC, et al. Philos Trans R Soc Lond B Biol Sci. 2012;367:3364-3378.
- CBD was first isolated in 1934  
Robson P. Br J Psychiatry 2001;178:107-115.
- First synthesized in 1967, first easily useable form in 1985  
Baek SH, et al. Tetrahedron Lett. 1985;26:1083-1086.
- Ignored for many years
- Seen as something limiting the amount of THC marijuana could potentially contain




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## CBD

- Of no interest to recreational users... and tragically, for many medical users
- Initially described as "nonpsychotropic"
- However, produces anxiolysis through increasing serotonergic transmission... and reverses allodynia  
De Gregorio D, et al. Pain 2019;160(1):136-150.
- Appears to have a mild antidepressant effect for those with low levels of serotonin  
Sales AJ, et al. Prog Neuropsychopharmacol Biol Psychiatry. 2018;86:255-261.
- More appropriately called "noneuphoriant"  
Russo EB. Ther Clin Risk Manag. 2008;4:245-259.




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## CBD Safety Profile

- Safety has been well-established  
Cunha JM, et al. Pharmacol. 1980;21:175-185.  
Consroe P, et al. Pharmacol Biochem Behav. 1991;40:701-708.  
Zuardi AW, et al. J Psychopharmacol. 2006;20:683-686.  
Zuardi AW, et al. J Psychopharmacol. 2009;23:979-983.  
Zuardi AW, et al. J Psychopharmacol. 2010;24:135-137.  
Bergamaschi MM, et al. Curr Drug Saf. 2011;6:237-239.  
Devinsky O, et al. Lancet Neurol. 2016;15:270-278.  
McGuire P, et al. Am J Psychiatry 2018;175:225-231.
- Attenuates the "high" caused by THC at 8:1 CBD:THC ratio  
Kim PS, Fishman M. Curr Pain Headache Rep. 2017;21(4):19.
- The Director of NIDA wrote, "CBD appears to be a safe drug"  
Volkow N. Huffington Post July 23, 2015.




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### CBD Availability

- Despite its safety profile and the impossibility of abusing it, CBD from whole plant MJ is still considered a Schedule I drug
- Other than recently FDA-approved Epidiolex
- Has been available in all medical marijuana states
- 13 states had the wisdom to legalize it without MM legalization
- New changes in the law allow for CBD from the hemp plant

Traynor K. Am J Health Syst Pharm. 2018;75:1088-1089.  
 McGarrell SL, Maguire TC. National Law Rev. December 20, 2018.  
 Available at: <https://www.natlawreview.com/article/2018-farm-bill-signed-law-includes-major-changes-involving-hemp>.




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### CBD Legal Status

- Hemp plant is in the same genus as MJ, but contains, by definition and law, <0.3% THC content
- THC will not show up in standard UDT immunoassays
- Now most commonly used for pain, anxiety, depression, and sleep disorders
- Due to lack of regulation, CBD products online are often mislabeled regarding constituents

Shannon S, et al. Perm J. 2019;23:18-041.  
 Corroon J, Phillips JA. Cannabis Cannabinoid Res. 2018;3:152-161.  
 Freedman DA, Patel AD. Pediatr Neurol Briefs. 2018;32:3.




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### CBD and Pain

- Much of the existing supportive data is preclinical
- CBD is anti-inflammatory
- Attenuation of early phase inflammation by cannabidiol prevents pain and nerve damage in osteoarthritis
- Found to be anti-inflammatory in human cell lines

Thappa D, et al. FASEB J. 2017;31(Suppl 1):Abstract 811.7.  
 Philpott HT, et al. Pain 2017; 158:2442-2451.  
 Petrosino S, et al. J Pharmacol Exp Ther. 2018;365:652-663.




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### Rat Cheating on a Forced-Swim Test



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### CBD and Pain

- Relevance for back pain: CBD has anti-inflammatory effects on rat nucleus pulposus cells

Chen J, et al. Mol Med Rep. 2016;14:2321-2327.

- Reduces chemotherapy-related peripheral neuropathy, and does so to an even greater degree when combined with low-dose morphine

Harris HM, et al. Med Cannabis Cannabinoids 2018;1:54-59.

- In humans, CBD decreased anxiety and improved sleep scores

Shannon S, et al. Perm J. 2019;23:18-041.

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### More CBD Research

- Safety established when co-administered with fentanyl

Mamini AF, et al. J Addict Med. 2015;9:204-210.

- Enhances fracture healing

Apostu D, et al. Drug Metab Rev. 2019 [Epub ahead of print].

- Animal model: protective effects on lesion-induced intervertebral disc degeneration

Silveira JW, et al. PLoS One 2014;9:e113161.

- Animal model: synergistic with morphine

Neelakantan H, et al. Behav Pharmacol. 2015;26:304-314.

- Human research: effective for reducing chronic pain in kidney transplant patients (small study)

Cufetti L, et al. Transplant Proc. 2018;50:461-464.

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### Marijuana and Pain Research

- Extremely difficult to do in the US
- All federally-funded MM research currently had to use low-grade MJ grown at the U of Mississippi for NIDA
- 3 dose strengths available
  - Low potency (1.29% THC)
  - Moderate potency (3.53%)
  - High potency (7%)
- Why is this a problem?

Wilsey B, et al. J Pain 2013;14:136-148.




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### Marijuana and Pain Research (cont'd)

- Oil or wax dabs available at some dispensaries have THC contents greater than 90%!!!!
  - Now being used regularly by 21.1% of cannabis users
- Medical marijuana sold in dispensaries is higher in THC than that sold on the streets
- Recent breakthrough – NIDA has approved a 13.4% THC MJ for research

Sagar KA, et al. Drug Alcohol Depend. 2018;190:133-142.

Sevigny EL, et al. Int J Drug Pol. 2014;29:308-319.




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### Edibles

- THC dosing in edibles has been described as “insane” by toxicologists
- Edibles are infused with almost pure THC
- They typically take 30-90 minutes to take effect, reach their peak in 1.5-3 hours, and can last for 6-8 hours
- Thus, they don't allow for titration due to a lack of immediate effect
- Labeling of constituents' contents is generally inaccurate

Gussow L. Emerg Med News 2014;36:24.

Vandrey R, et al. J Anal Toxicol. 2017;41(2):83-99.

Tsutaoka B, et al. Clin Pediatr (Phila). 2018;57(2):227-230.




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### Edibles (cont'd)

- This inability to titrate effectively has led to increases in ER visits due to THC intoxication

Kim HS, Monte AA. Ann Emerg Med. 2016;69:71-75.  
 Vo KT, et al. Ann Emerg Med. 2018;71:309-313.

- Myocardial infarction

Saunders A, Stevenson RS. Can J Cardiol. 2019 ;35(2):229.e1-229.e3.

- And multiple deaths

Calandrillo SP, Fulton KJ. University of Washington School of Law Research Paper No. 2018-07, 2018. Available at: [https://papers.ssrn.com/sol3/cases.cfm?abstract\\_id=3163720](https://papers.ssrn.com/sol3/cases.cfm?abstract_id=3163720)




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### Science vs “Religion”

- Medical marijuana advocates tend not to let the data get in the way of their opinions
- Try discussing potential harms of MM on Twitter....
- “There is none so blind as those who will not see...”




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### MM and Pain Research: What DO We Know?

- Is it effective for chronic pain?
- Depends on the properties of the marijuana being used and one’s definition of “effective”
- It also depends upon goals of treatment
  - Is analgesia sufficient, even if it incapacitates the patient?
- It also depends on the medical indication, eg, opioids are effective for many types of pain, but not for neuropathic pain




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### MM and Pain Research

- Neuropathic pain: a number of studies demonstrate analgesia, but requires higher dosages, which result in cognitive deficits

Wilsey B, et al. J Pain 2008;9:506-521.  
 Ellis RJ, et al. Neuropsychopharmacology 2009;34:672-680.  
 Ware MA, et al. CMAJ 2010;182:E694-701.  
 Wallace MS, et al. J Pain 2015;16:616-627.  
 Wilsey B, et al. J Pain 2016;17:982-1000.

- 2013 study using low-dose (1.29% THC) MJ: efficacy for neuropathic pain, without significant cognitive effects

Wilsey B, et al. J Pain 2013;14:136-148.




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### MM and Pain Research (cont'd)

- Conclusions of MJ for neuropathic pain:
  - Weak evidence as effective in terms of analgesia at higher doses
  - Cognitive side effects are dose-related
  - Never studied head-to-head against gabapentinoids
  - Gabapentinoids also have dose-related cognitive side effects
  - Research needed on MM with significant CBD content as well
  - Research needed on the types of MJ actually carried in dispensaries (25%+ THC)
- Recommendation: consider as a last option for neuropathic pain
- Recent Australian review suggests that CBD may be better

Casey SL, Vaughan CW. Medicines (Basel). 2018;5(3), pii: E67.




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### MM and Pain Research (cont'd)

- Musculoskeletal pain and arthritis – “Evidence is needed”
- Rheumatic conditions – no evidence for efficacy
- Fibromyalgia – Israeli study hopeful, but inconclusive
- Headache – very limited evidence for efficacy
- Cancer pain – “prospective clinical trials are needed to provide the robust data required to establish the proper role of cannabinoid and cannabis-based therapy”

Loehle BC, et al. Cannabis Cannabinoid Res. 2017;2:61-71.  
 Steele G, et al. Curr Oncol Rep. 2019;21(1):10.




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## MM and Opioids

- The most compelling evidence basis for MJ in treating chronic pain was for its opioid-sparing effect

Boehnke KF, et al. J Pain 2016;17:739-744.

Vigil JM, et al. PLoS One. 2017;12:e0187795.

- Medical cannabis laws were associated with lower opioid overdose mortality rates

Bachhuber MA, et al. JAMA Intern Med. 2014;174:1668-1673.

- Current data dispel this...

- Recent data indicate that recreational legalization does not influence compliance with opioid therapy

Lo S-Y, et al. Am J Med. 2019;132(3):347-353.




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## MM and Opioids (cont'd)

- Synergistic with opioids? Likely urban myth...
- Not associated with lower prescription rates and dosages of Schedule II opioids

Liang D, et al. Addiction. 2018;113(11):2060-2070.

“Cannabis use appears to increase rather than decrease the risk of developing nonmedical prescription opioid use and opioid use disorder”

Olsson M, et al. Am J Psychiatry. 2018;175(1):47-53.

- “Multivariable analyses indicated that medical cannabis use was significantly associated with risk of prescription opioid misuse”

Nugent SM, et al. Gen Hosp Psychiatry. 2018;50:104-110.




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## MM and Opioids (cont'd)

- Perioperative opioid use is significantly higher in MJ-users despite lower subjective pain scores

Bauer FL, et al. Perm J. 2018 Jul 19:22.

- MJ use recently found to be predictive of opioid dependence

Buteiman ER, et al. Front Psychiatry. 2018;9:283.

- Predictive of a 2.5 fold increase in the rate of opioid aberrancy

DiBenedetto DJ, Schatman ME, et al. Pain Med. 2018;19:1997-2008.

- Medical marijuana users more likely to use prescription drugs – including opioids – nonmedically

Caputi TL, Humphreys K. J Addict Med. 2018;12(4):295-299.




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### “Watcha Smoking, Dude?”

- To talk about “medical marijuana” as a single entity is ridiculous
- We need to be discussing “medical marijuanas”
- Indica or sativa?
  - 2 separate species, usually in a hybrid form
- Indicas empirically established as preferable for pain management, but cause more sedation than sativas

Cohen NL, et al. J Stud Alcohol Drugs. 2016;77(3):515-520.




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### Indica vs Sativa – Street Reputations

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| <ul style="list-style-type: none"> <li>▪ Indicas           <ul style="list-style-type: none"> <li>–Relaxing and calming</li> <li>–Body buzz or ‘couch lock’</li> <li>–Best suited for night use</li> </ul> </li> </ul> | <ul style="list-style-type: none"> <li>▪ Sativas           <ul style="list-style-type: none"> <li>–Uplifting and energetic</li> <li>–Cerebral, spacey, or hallucinogenic</li> <li>–Best suited for day use</li> </ul> </li> </ul> |
|--|---|

• Leaf Science, 2014. Indica vs. Sativa: Understanding The Differences. Available at: <http://www.leafscience.com/2014/06/19/indica-vs-sativa-understanding-differences/>




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### Treatment Recommendation

- “The Medicinal Cannabis Treatment Agreement: Providing Information to Chronic Pain Patients via a Written Document”
  - B Wisey, et al. Clin J Pain 2015;31:1087-1096.
  - Absolutely brilliant!!!!
  - “Medical marijuana” is heavily abused
    - Wen H, et al. J Health Econ. 2015;42:84-80.
- “...physicians would seem to have an obligation to understand and inform their patients on key issues of the evidence base on cannabinoid therapeutics”




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### Medical Cannabis Agreement

- Covers reduction of diversion, particularly to vulnerable children and adolescents
- Addresses inappropriate utilization by the authorized patient
  - We must not lose sight of the data indicating that marijuana is indeed addictive
- Discusses the risks of marijuana generally and to specific populations
- Recommends vaporization over smoking




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### Medical Cannabis Agreement (cont'd)

- Warns against driving a car or operating machinery
- Emphasizes "start low, go slow" when dosing – particularly with new strains
- Covers potential benefits of FDA-approved cannabinoids over smoked marijuana
  - Based on empirical evidence...and clinical experience, I disagree
- Recommends withdrawing slowly if a patient wants to stop
- Addresses the need to evaluate the efficacy and appropriateness of therapy on an ongoing basis
- Covers not using MM in public places




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### Medical Cannabis Agreement (cont'd)

- Warns that medical authorization will NOT protect a patient's job
  - Gives the physician the right to discontinue MM treatment
  - Respect for patient autonomy is contingent upon the doctrine of informed consent
- Dalla-Vorgia P, et al. J Med Ethics 2001;27:59-61.
- This is exactly what these agreements are providing
  - Thus, they constitute ethical pain medicine practice
  - And perhaps even protect the physician as well as the patient




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**Closing Thoughts**

- The future of medical cannabinoids in the US is uncertain
- To assume that marijuana is safe because it's "natural" is neuromysticism
- As is assuming that anecdotal evidence of efficacy provides us with "the truth"
- Improving the quality and quantity of MM research is imperative if MJ is ever to become "medicine"
- CBD, not THC, promises to be the most medically-relevant cannabinoid




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**Closing Thoughts (cont'd)**

- If you're going to use MM in your practice, educate yourself and your patient – and do it right
- Take marijuana as a drug seriously – irrespective of what you smoked as a youth
- If you use an opioid agreement, consider using a medical cannabis agreement
- Practicing cannabinoid medicine is challenging when we know so little
- Better data are hopefully just around the corner




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▪ THANK YOU




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