Physician Guide to Cannabis-Assisted Opioid Reduction

Prepared by Adrianne Wilson-Poe, Ph.D. Distributed by Congressman Earl Blumenauer

Cannabis reduces opioid overdose mortality.

- In states with medicinal cannabis laws, opioid overdoses drop by an average of 25%. This effect gets bigger the longer the law has been in place. For instance, there is a 33% drop in mortality in California, where compassionate use has been in place since 1996 (1).
- This finding was replicated by Columbia's school of public health, using a completely different analysis strategy (2).

Cannabis reduces opioid consumption.

- Cannabis is opioid-sparing in chronic pain patients. When patients are given access to cannabis, they drop their opioid use by roughly 50%. This finding has been replicated several times from Ann Arbor to Jerusalem (3, 4).
- This opioid sparing effect is accompanied by an enhancement of cognitive function once patients begin cannabis therapy: this effect is most likely due to the fact that patients reduce their opioid use (5).
- Cannabis use is associated with a reduction in not only opioid consumption, but also many other drugs including benzodiazepines, which also have a high incidence of fatal overdose. In states with medicinal cannabis laws, the number of prescriptions for analgesic and anxiolytic drugs (among others) are substantially reduced (6). Medicare and Medicaid prescription costs are substantially lower in states with cannabis laws (7).

Cannabis can prevent dose escalation and the development of opioid tolerance.

- Cannabinoids and opioids have acute analgesic synergy. When opioids and cannabinoids are coadministered, they produce greater than additive analgesia (8). This suggests that analgesic dose of opioids is substantially lower for patients using cannabis therapy.
- In chronic pain patients on opioid therapy, cannabis does not affect pharmacokinetics of opioids, yet it still enhances analgesia. This finding further supports a synergistic mechanism of action (9).
- Pre-clinical models indicate that cannabinoids attenuate the development of opioid tolerance (10, 11).

Cannabis, alone or in combination with opioids, could be a viable first-line analgesic.

- The CDC has updated its recommendations in the spring of 2016, stating that most cases of chronicpain should be treated with non-opioids (12).
- The National Academies of Science and Medicine recently conducted an exhaustive review of 10,000+ human studies published since 1999, definitively concluding that cannabis itself (not a specific cannabinoid or cannabis-derived molecule) is safe and effective for the treatment of chronic pain (13).
- When 3,000 chronic pain patients were surveyed, they overwhelmingly preferred cannabis as an opioid alternative (14).
 - o 97% "strongly agreed/agreed" that they could decrease their opioid use when using cannabis
 - o 92% "strongly agreed/agreed" that they prefer cannabis to treat their medical condition
 - o 81% "strongly agreed/ agreed that cannabis by itself was more effective than taking opioids

Cannabis may be a viable tool in medication-assisted relapse prevention

- CBD is non-intoxicating, and is the 2nd most abundant cannabinoid found in cannabis. CBD alleviates the anxiety that leads to drug craving. In human pilot studies, CBD administration is sufficient to prevent heroin craving for at least 7 days (15).
- Cannabis users are more likely to adhere to naltrexone maintenance for opioid dependence (16).

Bibliography and References Cited

- 1. Bachhuber MA, Saloner B, Cunningham CO, Barry CL. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. JAMA Intern Med. 2014;174(10):1668-73. doi: 10.1001/jamainternmed.2014.4005. PubMed PMID: 25154332; PMCID: 4392651.
- 2. Kim JH, Santaella-Tenorio J, Mauro C, Wrobel J, Cerda M, Keyes KM, Hasin D, Martins SS, Li G. State Medical Marijuana Laws and the Prevalence of Opioids Detected Among Fatally Injured Drivers. Am J Public Health. 2016;106(11):2032-7. doi: 10.2105/AJPH.2016.303426. PubMed PMID: 27631755; PMCID: PMC5055785.
- 3. Boehnke KF, Litinas E, Clauw DJ. Medical Cannabis Use Is Associated With Decreased Opiate Medication Use in a Retrospective Cross-Sectional Survey of Patients With Chronic Pain. J Pain. 2016;17(6):739-44. doi: 10.1016/j.jpain.2016.03.002. PubMed PMID: 27001005.
- 4. Haroutounian S, Ratz Y, Ginosar Y, Furmanov K, Saifi F, Meidan R, Davidson E. The Effect of Medicinal Cannabis on Pain and Quality-of-Life Outcomes in Chronic Pain: A Prospective Open-label Study. Clin J Pain. 2016;32(12):1036-43. doi: 10.1097/AJP.0000000000000364. PubMed PMID: 26889611.
- Gruber SA, Sagar KA, Dahlgren MK, Racine MT, Smith RT, Lukas SE. Splendor in the Grass? A Pilot Study Assessing the Impact of Medical Marijuana on Executive Function. Front Pharmacol. 2016;7:355. doi:10.3389/fphar.2016.00355. PubMed PMID: 27790138; PMCID: PMC5062916.
- 6. Bradford AC, Bradford WD. Medical Marijuana Laws Reduce Prescription Medication Use In Medicare Part D. Health Aff (Millwood). 2016;35(7):1230-6. doi: 10.1377/hlthaff.2015.1661. PubMed PMID: 27385238.
- 7. Bradford AC, Bradford WD. Medical Marijuana Laws May Be Associated With A Decline In The Number Of Prescriptions For Medicaid Enrollees. Health Aff (Millwood). 2017;36(5):945-51. doi: 10.1377/hlthaff.2016.1135. PubMed PMID: 28424215.
- 8. Roberts JD, Gennings C, Shih M. Synergistic affective analgesic interaction between delta-9-tetrahydrocannabinol and morphine. European journal of pharmacology. 2006;530(1-2):54-8. Epub 2005/12/27. doi: 10.1016/j.ejphar.2005.11.036. PubMed PMID: 16375890.
- 9. Abrams DI, Couey P, Shade SB, Kelly ME, Benowitz NL. Cannabinoid-opioid interaction in chronic pain. Clinical pharmacology and therapeutics. 2011;90(6):844-51. Epub 2011/11/04. doi: 10.1038/clpt.2011.188. PubMed PMID: 22048225.
- Wilson AR, Maher L, Morgan MM. Repeated cannabinoid injections into the rat periaqueductal gray enhance subsequent morphine antinociception. Neuropharmacology. 2008;55(7):1219-25. doi: 10.1016/j.neuropharm.2008.07.038. PubMed PMID: 18723035; PMCID: 2743428.
- 11. Smith PA, Selley DE, Sim-Selley LJ, Welch SP. Low dose combination of morphine and delta9- tetrahydrocannabinol circumvents antinociceptive tolerance and apparent desensitization of receptors. European journal of pharmacology. 2007;571(2-3):129-37. Epub 2007/07/03. doi: 10.1016/j.ejphar.2007.06.001. PubMed PMID: 17603035; PMCID: 2040345.
- 12. Dowell D, Haegerich TM, Chou R. CDC Guideline for Prescribing Opioids for Chronic Pain United States, 2016. MMWR Recomm Rep. 2016;65(1):1-49. doi: 10.15585/mmwr.rr6501e1. PubMed PMID: 26987082.
- 13. NASEM. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington (DC) 2017.
- 14. Reiman A, Welty M, Solomon P. Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self Report. Cannabis Cannabinoid Res. 2017;2(1):160-6. doi: 10.1089/can.2017.0012. PubMed PMID: 28861516; PMCID: PMC5569620.
- 15. Hurd YL, Yoon M, Manini AF, Hernandez S, Olmedo R, Ostman M, Jutras-Aswad D. Early Phase in the Development of Cannabidiol as a Treatment for Addiction: Opioid Relapse Takes Initial Center Stage. Neurotherapeutics. 2015;12(4):807-15. doi: 10.1007/s13311-015-0373-7. PubMed PMID: 26269227; PMCID: PMC4604178.
- 16. Raby WN, Carpenter KM, Rothenberg J, Brooks AC, Jiang H, Sullivan M, Bisaga A, Comer S, Nunes EV. Intermittent marijuana use is associated with improved retention in naltrexone treatment for opiate-dependence. Am J Addict. 2009;18(4):301-8. doi: 10.1080/10550490902927785. PubMed PMID: 19444734; PMCID: PMC2753886.