



Investing for tomorrow, delivering today.

Medical Cannabis Program

Cannabis *N*_{ugs} *O*_f *W*_{isdom}

Gary J. French, MD

Medical Director

Elizabeth Bisio, MHP, CHES

Health Educator

Disclaimer

- The opinions shared during this meeting do not necessarily reflect the position of the Medical Cannabis Program.
- The Medical Cannabis Program does not endorse any specific product, producer, or vendor.
- The information presented in this meeting is as of May 18, 2023, and is subject to change as additional data is gathered and research is performed.

Updates

- Electronic applications only
 - No more paper submissions
 - Online Patient Portal is HIPAA compliant
- Senate Bill 242
 - No more annual verifications
 - 2-year card with 2-year requirement
- Digital card only
 - No more plastic cards
 - Annual verification dates removed
- Insomnia approved as a qualifying condition
 - Added to list beginning June 1, 2023

Insomnia

- Experienced by 50 to 70 million U.S. adults.¹
- Generates over 5 million office visits per year in the United States alone.²
- 25 percent of Americans will experience acute insomnia.³
- 10 to 15 percent endorse chronic insomnia.⁴
- Common in older adults and women
- Increasing in unemployed, divorced, widowed, separated, or of lower socioeconomic status

Impact of insomnia

- Decreased quality of life
 - high blood pressure
 - weakened immune performance
 - weight gain
 - lack of libido
 - some cancers
- Decreased cognitive function and performance
 - mood swings
 - paranoia
 - depression
 - dementia

Impact of insomnia

- Cardiovascular risk and mortality
 - higher risk of diabetes
 - stroke
 - cardiovascular disease
- Self-medication leading to substance abuse
- Association with suicide

How much Sleep is needed?^{5,6}

Table showing age groups and recommended amount of daily sleep for each

Age Group	Age	Recommended Hours of Sleep
Infant	4-12 months	12-16 hours per 24 hours (including naps)
Toddler	1-2 years	11-14 hours per 24 hours (including naps)
Pre-School	3-5 years	10-13 hours per 24 hours (including naps)
School Age	6-12 years	9-12 hours per 24 hours
Teen	13-18 years	8-10 hours per 24 hours
Adult	18-60 years	7 or more hours per night

Insomnia Questionnaires

- Sleep Condition Indicator (SCI) - score 16 or less indicates probable insomnia
- Insomnia Severity Index (ISI) - score 15 or more indicates moderate to severe insomnia
- Dysfunctional Beliefs and Attitudes about Sleep (DBAS) Scale
- Daytime Insomnia Symptom Scale (DISS)
- Flinders Fatigue Scale

Treatments for insomnia

- Cognitive behavioral therapy
- Pharmacological therapies
- Alternative therapies
 - Valerian
 - Melatonin
 - Cannabis

Cognitive Behavioral Therapies

- General Sleep Education
- Bedtime Restriction Therapy
- Stimulus Control Therapy
- Relaxation Techniques
- Cognitive Restructuring

Simple Steps to Improve Sleep

- Maintain a regular wake up time, even on weekends, regardless of a poor night sleep
- Resolve concerns or worries before bedtime
- Avoid going to bed until you are drowsy and ready to sleep
- Try not to force sleep
- Avoid daytime naps, especially if they are longer than 20–30 minutes or occur late in the day
- Reserve the bedroom for sleep and intimacy, and adjust the bedroom environment as needed to decrease stimuli (e.g. reduce ambient light, turn off the television or radio)
- Avoid bright light immediately before bed or while in bed including TV and mobile phone use

Simple Steps to Improve Sleep

- Avoid visual access to a clock throughout the night
- Allow sufficient time in bed to gain an adequate amount of sleep
- Avoid caffeinated beverages after lunch
- Avoid alcohol late afternoon and evening
- Avoid large meals immediately before bed
- Avoid smoking or other nicotine intake, particularly during the evening
- Avoid pets sleeping in the bedroom
- Exercise regularly for at least 20 minutes, preferably more than 1-2 hours prior to bedtime
- Do not stay in bed if you do not fall asleep quickly (stimulus control therapy) and encourage relaxing activities before bedtime or during

Pharmacological Therapies

- Prescription sleep aids – trazodone, amitriptyline, and doxepin
- Added to sleep aids – opioids and sedatives
- Benzodiazepines – diazepam and lorazepam
- GABA medications - zolpidem and eszopiclone
- Anti-psychotics – aripiprazole, olanzapine, quetiapine, and risperidone

Cannabis for Insomnia⁷

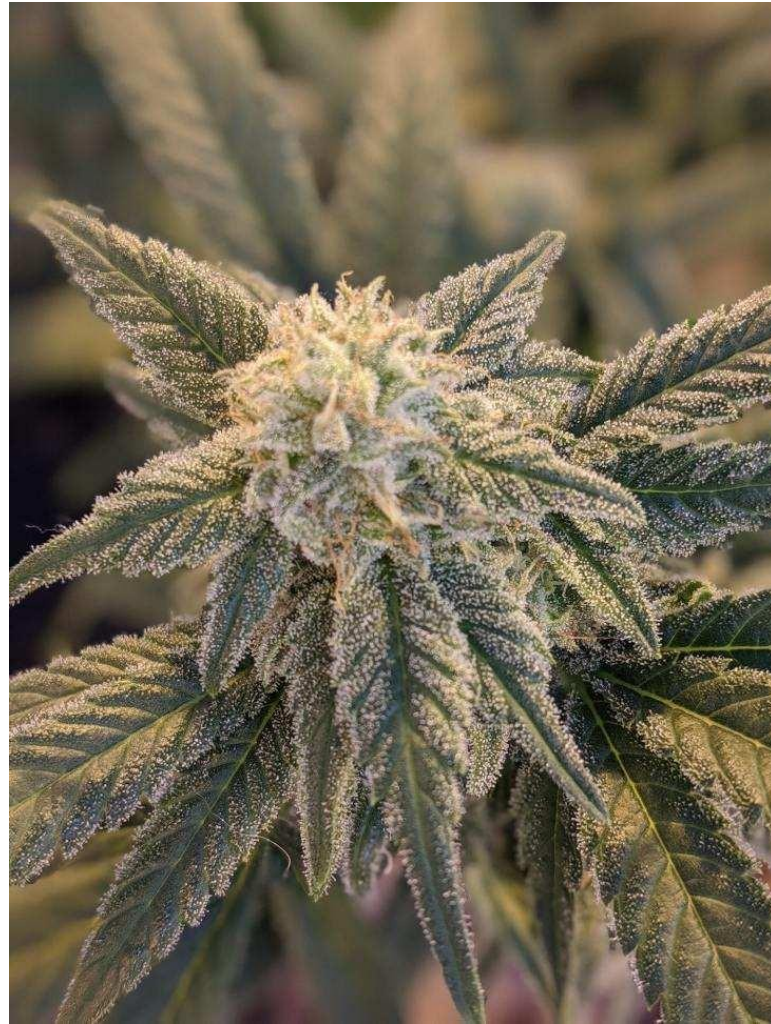
- Sleep-related disorders represent one of the most common uses for cannabis products.
- 71% of patients using cannabis products reported a subjective improvement in their sleep.
- 39% of patients reduced and/or discontinued prescription therapy.
- 21% of patients experienced manageable dose-dependent adverse effects - (did not result in discontinuation of medical cannabis therapy)

Mechanism

- Cannabis, specifically with strains containing small amounts of tetrahydrocannabinol (THC), can have a positive impact on sleep.⁸ At lower doses, THC can reduce sleep onset latency and has been associated with greater ease of falling asleep, increased slow-wave sleep, and increased total sleep time.⁹ At higher doses, THC has demonstrated a reduction in REM sleep.⁷
- Cannabidiol (CBD), can have a stimulating effect at lower doses, but when used in higher doses has been shown to increase total sleep time and decrease the frequency of arousals during the night.⁷

540 distinct chemical compounds

- More than 113 different phytocannabinoids¹⁰
- More than 200 terpenes – (aromatic compounds)¹¹
- More than 20 Flavonoids – (color producers)¹²



Entourage Effect

- The mechanism by which cannabis compounds act synergistically to modulate the overall effects of the plant.
- Estimated to be over 1,000 different strains of cannabis each with its own special ratio of compounds.
- Limitless options for potential treatments, but hard to predict, replicate, or study.

Cannabinoids that affect sleep

- Cannabidiol (CBD)
 - Low doses – stimulating effect¹³
 - Higher doses – sedative effect, increase total sleep time, and decrease frequency of arousals¹³
- Tetrahydrocannabinol (THC)
 - Low doses – reduce sleep latency, increased slow-wave sleep and increased total sleep time.⁹
 - High doses – reduction in total REM and REM density.¹⁴
- Cannabinol (CBN)
 - May increase drowsiness when added.¹⁵

Cannabinoids for insomnia¹⁶

- Higher CBD
- Lower THC
- Addition of CBN

Terpenes that affect sleep¹⁷

- Myrcene – sedative effect¹⁸
- Beta Pinene – reduce anxiety, stress, and pain¹⁹
- Beta-Caryophyllene - reduce pain and inflammation²⁰
- Linalool – reduce anxiety and stress²¹
- Terpinolene – sedative effect and anti-inflammatory²²

Flavonoids that affect sleep

- Apigenin – Chamomile Tea²³
- Linarin – Valerian Root²⁴
- Myricetin – St. John's Wort²⁵

Recommendations – (routes & products)

- Route
 - Edible or tincture
 - Slower uptake, longer lasting
- Product
 - Higher CBD: Lower THC ratio
 - Indica Strains/Indica-dominant hybrids
 - Cannabinol (CBN)
 - THC breaks down to CBN as cannabis ages.
 - Terpenes
 - myrcene, pinene, caryophyllene, linalool, terpinolene
 - Flavonoids
 - apigenin, linarin, myricetin

Best strains

- Northern lights
- Wedding cake
- Hindu Kush
- Kosher Kush
- Bubba Kush
- Granddaddy Purple
- Gelato
- The White
- Mochi

Caution²⁶

- High doses of THC can reduce REM sleep and REM density thereby reducing restorative sleep.
 - Lead to poor concentration and grogginess
 - Decrease the brain's ability to process emotions and create new memories.
- High dose THC and chronic cannabis use may lead to cannabis withdrawal symptoms.
 - Cause sleep disruptions²⁷ – (falling asleep, wake up, wake up early, sleep longer, sleep less)
 - Increased REM may lead to an increase in the frequency and intensity of dreams & nightmares^(PTSD)

Possibly Contraindicated – Children and adolescents²⁸

- Study
 - Analyzed data from 1,882 young adults from the Colorado Twin Registry.
 - Each had completed surveys about their sleep habits, marijuana use and mental health.
 - One-third of subjects who started using marijuana regularly before age 18 had insomnia in adulthood (20% among those who didn't)
 - The same pattern held true for a particularly hazardous form of insomnia known as “short sleep” (sleeping fewer than six hours per night on a regular basis).
 - About one in 10 subjects who used cannabis regularly as teens grew up to be short-sleepers (5% of non-users)

Possibly Contraindicated – Children and adolescents²⁸

- Theory
 - Receptors are being desensitized or disturbed from all the cannabis use at a time that the brain is still developing, and that leads to waking issues later.
 - Cannabis use in adolescence leads to structural changes in the brain.
- Recommendation
 - “We would not recommend that teenagers utilize marijuana to promote their sleep. Anytime you are dealing with a developing brain you need to be cautious.”

Possibly Contraindication – Pregnant individuals²⁹

- Study
 - Data from the Adolescent Brain Cognitive Development Study (ABCD Study®) was used to determine whether maternal reports of prenatal cannabis use were associated with child sleep outcomes.
 - 11,875 children ages 9-10
 - Endorsement of any prenatal cannabis use was associated with symptoms of disorders of initiating and maintaining sleep, disorders of arousal, sleep wake disorders, disorders of excessive somnolence, and a summed sleep disorder score (all $\beta > 0.10$ and $p < 0.03$)
 - while frequency of prenatal daily cannabis use was significantly associated with disorders of excessive somnolence ($\beta=0.29$, $p=0.03$).
 - These associations remain when controlling for a range of covariates including prenatal substance exposure, mother's education, combined household income, parental marital status, race, child sex, child age, tobacco and alcohol use during pregnancy

Possibly Contraindication – Pregnant individuals²⁹

- Theory
 - Neurodevelopmental alterations in response to prenatal THC in the endocannabinoid system.
 - Prenatal exposure to drugs has been linked to environmental factors which could negatively influence sleep in childhood.
- Recommendation
 - "Although causality is not established, the results suggest potential long-term effects of prenatal cannabis exposure on sleep and the prudence of abstinence from cannabis use while pregnant."

Recommendations - (timing & patients)

- Avoid daily use
 - Withdrawal concerns
- Avoid in children and adolescents
 - Consider conditions other than insomnia
- Avoid in pregnancy – (*throughout all three trimesters*)³⁰
 - Consider conditions other than insomnia

Cognitive therapy / Sleep hygiene options must be addressed

References

- 1. Institute of Medicine (US) Committee on Sleep Medicine and Research. Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. Colten HR, Altevogt BM, editors. Washington (DC): National Academies Press (US); 2006. PMID: 20669438.
- 2. Ford ES, Wheaton AG, Cunningham TJ, Giles WH, Chapman DP, Croft JB. Trends in outpatient visits for insomnia, sleep apnea, and prescriptions for sleep medications among US adults: findings from the National Ambulatory Medical Care survey 1999-2010. *Sleep*. 2014 Aug 1;37(8):1283-93. doi: 10.5665/sleep.3914. PMID: 25083008; PMCID: PMC4096197.
- 3. University of Pennsylvania School of Medicine. (2018, June 5). One in four Americans develop insomnia each year: 75 percent of those with insomnia recover. ScienceDaily. Retrieved May 5, 2023, from www.sciencedaily.com/releases/2018/06/180605154114.htm.
- 4. Bhaskar S, Hemavathy D, Prasad S. Prevalence of chronic insomnia in adult patients and its correlation with medical comorbidities. *J Family Med Prim Care*. 2016 OctDec;5(4):780-784. doi: 10.4103/2249-4863.201153. PMID: 28348990; PMCID: PMC5353813.
- 5. Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, et al. Recommended amount of sleep for pediatric populations: a consensus statement of the American Academy of Sleep Medicine. *J Clin Sleep Med* 2016;12(6):785-786. <https://aasm.org/resources/pdf/pediatricsleepdurationconsensus.pdf> [PDF - 221KB]
- 6. Watson NF, Badr MS, Belenky G, Bliwise DL, Buxton OM, Buysse D, et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. *Sleep* 2015;38(6):843-844. <https://aasm.org/resources/pdf/pressroom/adult-sleep-duration-consensus.pdf> [PDF - 250KB]
- 7. Vaillancourt R, Gallagher S, Cameron JD, Dhalla R. Cannabis use in patients with insomnia and sleep disorders: Retrospective chart review. *Can Pharm J (Ott)*. 2022 Apr 15;155(3):175-180. doi: 10.1177/17151635221089617. PMID: 35519083; PMCID: PMC9067069.
- 8. Kim D. Insomnia. *Compendium of Therapeutics for Minor Ailments*. Ottawa, ON: Canadian Pharmacists Association; 2018. Available: https://myrxtx-ca.proxy.lib.uwaterloo.ca/print/new/documents/MA_CHAPTER/en/insomnia_minor
- 9. Babson KA, Sottile J, Morabito D. Cannabis, Cannabinoids, and Sleep: a Review of the Literature. *Curr Psychiatry Rep*. 2017 Apr;19(4):23. doi: 10.1007/s11920-017-0775-9. PMID: 28349316.
- 10. Ng T, Gupta V. Tetrahydrocannabinol (THC). 2022 Sep 26. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan -. PMID: 33085321.

References

- 11. Sommano SR, Chittasupho C, Ruksiriwanich W, Jantrawut P. The Cannabis Terpenes. *Molecules*. 2020 Dec 8;25(24):5792. doi: 10.3390/molecules25245792. PMID: 33302574; PMCID: PMC7763918.
- 12. Bautista JL, Yu S, Tian L. Flavonoids in *Cannabis sativa*: Biosynthesis, Bioactivities, and Biotechnology. *ACS Omega*. 2021 Feb 18;6(8):5119-5123. doi: 10.1021/acsomega.1c00318. PMID: 33681553; PMCID: PMC7931196.
- 13. Kuhathasan, N., Dufort, A., MacKillop, J., Gottschalk, R., Minuzzi, L., & Frey, B. N. (2019). The use of cannabinoids for sleep: A critical review on clinical trials. *Experimental and clinical psychopharmacology*, 27(4), 383.
- 14. Grotenhermen, F. (2003). Pharmacokinetics and pharmacodynamics of cannabinoids. *Clinical pharmacokinetics*, 42, 327-360.
- 15. Karniol IG, et al.. Effects of delta9-tetrahydrocannabinol and cannabiniol in man. *Pharmacology*. 1975;13(6):502-512.
- 16. Babson KA, Sottile J, Morabito D. Cannabis, Cannabinoids, and Sleep: a Review of the Literature. *Curr Psychiatry Rep*. 2017 Apr;19(4):23. doi: 10.1007/s11920-017-0775-9. PMID: 28349316.
- 17. Weston-Green K, Clunas H, Jimenez Naranjo C. A Review of the Potential Use of Pinene and Linalool as Terpene-Based Medicines for Brain Health: Discovering Novel Therapeutics in the Flavours and Fragrances of Cannabis. *Front Psychiatry*. 2021 Aug 26;12:583211. doi: 10.3389/fpsy.2021.583211. PMID: 34512404; PMCID: PMC8426550.
- 18. Lorenzetti BB, Souza GE, Sarti SJ, Santos Filho D, Ferreira SH. Myrcene mimics the peripheral analgesic activity of lemon grass tea. *J Ethnopharmacol*. 1991 Aug;34(1):43-8. doi: 10.1016/0378-8741(91)90187-i. PMID: 1753786.
- 19. Salehi B, Upadhyay S, Erdogan Orhan I, Kumar Jugran A, L D Jayaweera S, A Dias D, Sharopov F, Taheri Y, Martins N, Baghalpour N, Cho WC, Sharifi-Rad J. Therapeutic Potential of α - and β -Pinene: A Miracle Gift of Nature. *Biomolecules*. 2019 Nov 14;9(11):738. doi: 10.3390/biom9110738. PMID: 31739596; PMCID: PMC6920849.
- 20. Gertsch J, Leonti M, Raduner S, Racz I, Chen JZ, Xie XQ, Altmann KH, Karsak M, Zimmer A. Beta-caryophyllene is a dietary cannabinoid. *Proc Natl Acad Sci U S A*. 2008 Jul 1;105(26):9099-104. doi: 10.1073/pnas.0803601105. Epub 2008 Jun 23. PMID: 18574142; PMCID: PMC2449371.

References

- 21. Nascimento SS, Camargo EA, DeSantana JM, Araújo AA, Menezes PP, Lucca-Júnior W, Albuquerque-Júnior RL, Bonjardim LR, Quintans-Júnior LJ. Linalool and linalool complexed in β -cyclodextrin produce anti-hyperalgesic activity and increase Fos protein expression in animal model for fibromyalgia. *Naunyn Schmiedeberg's Arch Pharmacol*. 2014 Oct;387(10):935-42. doi: 10.1007/s00210-014-1007-z. Epub 2014 Jun 24. PMID: 24958161.
- 22. Ito K, Ito M. The sedative effect of inhaled terpinolene in mice and its structure-activity relationships. *J Nat Med*. 2013 Oct;67(4):833-7. doi: 10.1007/s11418-012-0732-1. Epub 2013 Jan 22. PMID: 23339024.
- 23. Salehi B, Venditti A, Sharifi-Rad M, Kregiel D, Sharifi-Rad J, Durazzo A, Lucarini M, Santini A, Souto EB, Novellino E, Antolak H, Azzini E, Setzer WN, Martins N. The Therapeutic Potential of Apigenin. *Int J Mol Sci*. 2019 Mar 15;20(6):1305. doi: 10.3390/ijms20061305. PMID: 30875872; PMCID: PMC6472148.
- 24. Fernández S, Wasowski C, Paladini AC, Marder M. Sedative and sleep-enhancing properties of linarin, a flavonoid-isolated from *Valeriana officinalis*. *Pharmacol Biochem Behav*. 2004 Feb;77(2):399-404. doi: 10.1016/j.pbb.2003.12.003. PMID: 14751470.
- 25. Zhang XH, Ma ZG, Rowlands DK, Gou YL, Fok KL, Wong HY, Yu MK, Tsang LL, Mu L, Chen L, Yung WH, Chung YW, Zhang BL, Zhao H, Chan HC. Flavonoid Myricetin Modulates GABA(A) Receptor Activity through Activation of Ca(2+) Channels and CaMK-II Pathway. *Evid Based Complement Alternat Med*. 2012;2012:758097. doi: 10.1155/2012/758097. Epub 2012 Nov 11. PMID: 23258999; PMCID: PMC3520426.
- 26. Kolla BP, Hayes L, Cox C, Eatwell L, Deyo-Svendsen M, Mansukhani MP. The Effects of Cannabinoids on Sleep. *J Prim Care Community Health*. 2022 Jan-Dec;13:21501319221081277. doi: 10.1177/21501319221081277. PMID: 35459406; PMCID: PMC9036386.
- 27. Levin KH, Copersino ML, Heishman SJ, Liu F, Kelly DL, Boggs DL, Gorelick DA. Cannabis withdrawal symptoms in non-treatment-seeking adult cannabis smokers. *Drug Alcohol Depend*. 2010 Sep 1;111(1-2):120-7. doi: 10.1016/j.drugalcdep.2010.04.010. Epub 2010 May 26. PMID: 20510550; PMCID: PMC2930056.
- 28. Winiger EA, Huggett SB, Hatoum AS, Friedman NP, Drake CL, Wright KP, Hewitt JK. Onset of regular cannabis use and young adult insomnia: an analysis of shared genetic liability. *Sleep*. 2020 May 12;43(5):zsz293. doi: 10.1093/sleep/zsz293. PMID: 31855253; PMCID: PMC7368342.
- 29. Winiger EA, Hewitt JK. Prenatal cannabis exposure and sleep outcomes in children 9-10 years of age in the adolescent brain cognitive development SM study. *Sleep Health*. 2020 Dec;6(6):787-789. doi: 10.1016/j.sleh.2020.05.006. Epub 2020 Jun 28. PMID: 32605891; PMCID: PMC7749837.
- 30. Dodge P, Nadolski K, Kopkau H, Zablocki V, Forrester K and Bailey BA (2023) The impact of timing of in utero marijuana exposure on fetal growth. *Front. Pediatr*. 11:1103749. doi: 10.3389/fped.2023.1103749.

Any questions?



For More Information

- Website: www.nmhealth.org/go/mcp
- Phone: (505) 827-2321
- Email: medical.cannabis@doh.nm.gov

THANK YOU!!