Pragmatic use of cannabis products for chronic pain

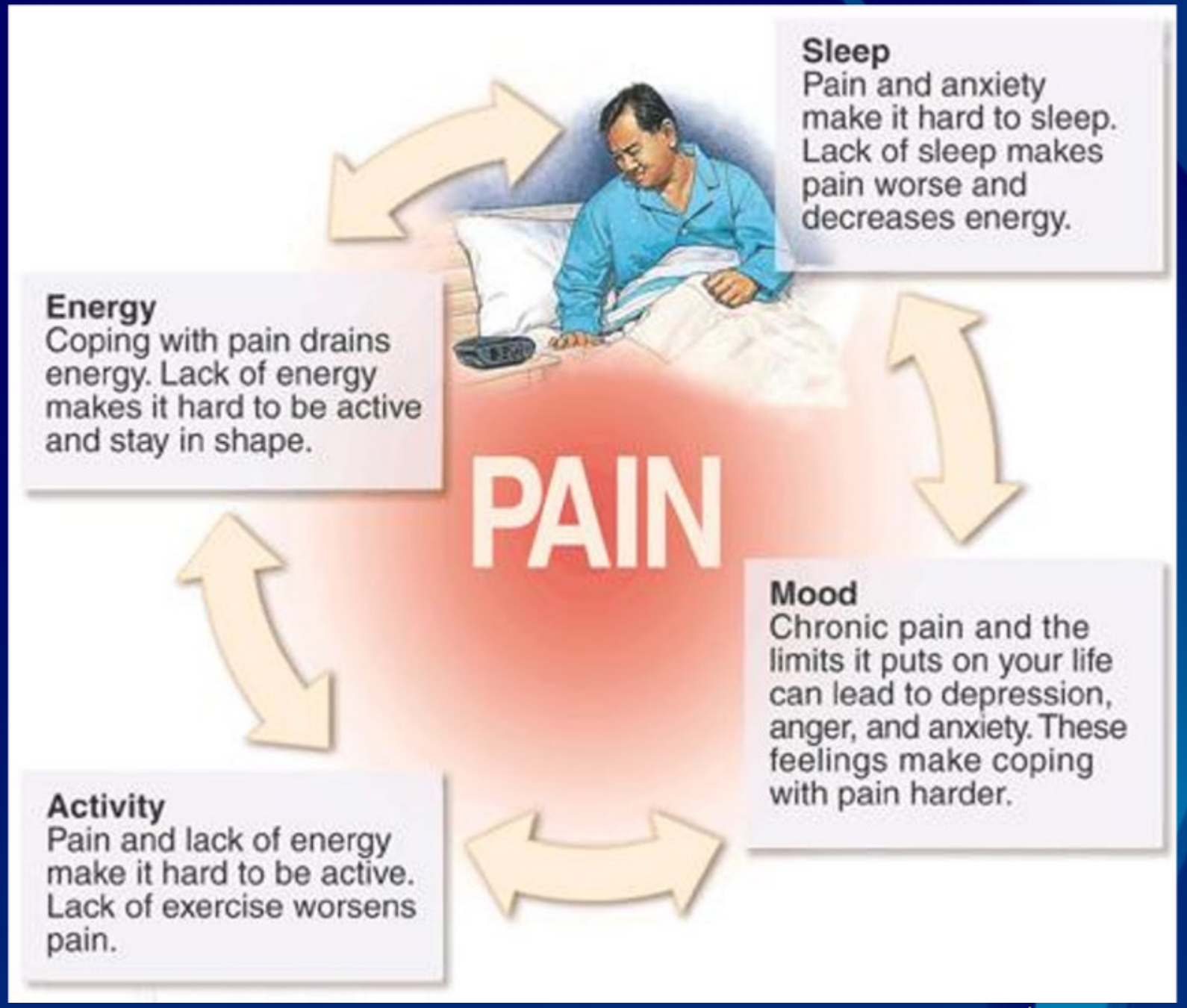
Understanding risks and benefits from clinical trials and naturalistic trends of cannabis use

Kevin F. Boehnke, PhD

Research Assistant Professor
Anesthesiology Department,
Chronic Pain and Fatigue Research Center
University of Michigan

Disclosures

Sponsor Name	*Honoraria/ Expenses*	*Consulting/ Advisory Board*	*Funded Research*	*Royalties/ Patent*	*Stock Options*	*Ownership/ Equity Position*	*Employee*	*Other (please specify)*
Vireo Health								Data Safety and monitoring committee (unpaid)
Tryp Therapeutics			X					Protocol development funding
National Institutes of Health			X					R01AT010381 (NCCIH), K01DA049219 (NIDA) , and R34AR078435 (NIAMS)
State of Michigan			X					State of Michigan Veteran's Marijuana Research Program



http://poc.select.kramesstaywell.com/Content/healthsheets-v1/the-cycle-of-chronic-pain

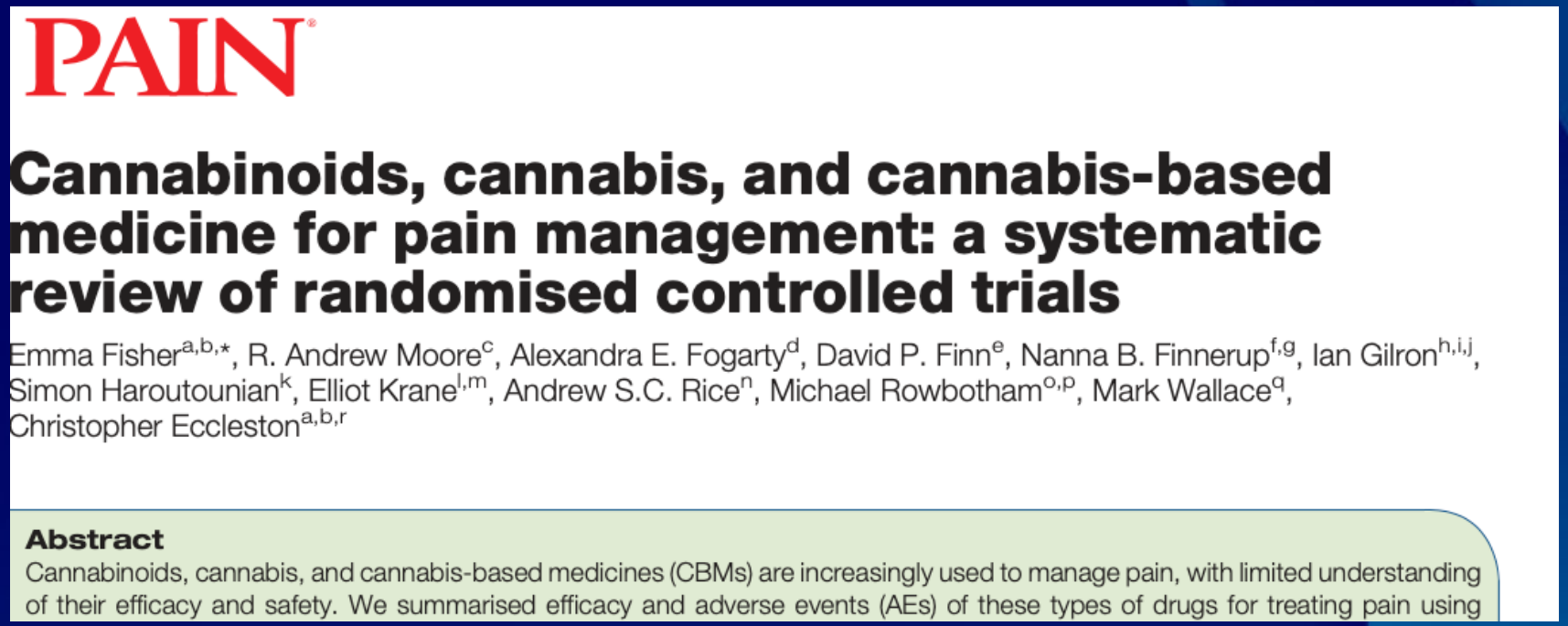
Mechanistic Characterization of Pain

Variable degrees of any mechanism can contribute in any disease

	Nociceptive	Neuropathic	Centralized
Cause	Inflammation or damage	Nerve damage or entrapment	CNS or systemic problem
Clinical features	Pain is well localized, consistent effect of activity on pain	Follows distribution of peripheral nerves (i.e. dermatome or stocking/glove), episodic, lancinating, numbness, tingling	Pain is widespread and accompanied by fatigue, sleep, memory and/or mood difficulties as well as history of previous pain elsewhere in body
Screening tools		PainDETECT	Body map or FM Survey
Treatment	NSAIDs, injections, surgery, ? opioids	Local treatments aimed at nerve (surgery, injections, topical) or CNS-acting drugs	CNS-acting drugs, non-pharmacological therapies
Classic examples	Osteoarthritis Autoimmune disorders Cancer pain	Diabetic painful neuropathy Post-herpetic neuralgia Sciatica, carpal tunnel syndrome	Fibromyalgia Functional GI disorders Temporomandibular disorder Tension headache Interstitial cystitis, bladder pain syndrome

Mixed Pain States

Cannabis clinical trials for chronic pain



PAIN

Cannabinoids, cannabis, and cannabis-based medicine for pain management: a systematic review of randomised controlled trials

Emma Fisher[a,b,*], R. Andrew Moore[c], Alexandra E. Fogarty[d], David P. Finn[e], Nanna B. Finnerup[f,g], Ian Gilron[h,i,j], Simon Haroutounian[k], Elliot Krane[l,m], Andrew S.C. Rice[n], Michael Rowbotham[o,p], Mark Wallace[q], Christopher Eccleston[a,b,r]

Abstract

Cannabinoids, cannabis, and cannabis-based medicines (CBMs) are increasingly used to manage pain, with limited understanding of their efficacy and safety. We summarised efficacy and adverse events (AEs) of these types of drugs for treating pain using

- Limited: short length, small sample size, generalizability
  - Many used THC alone or THC + CBD
- Most support in neuropathic pain (THC+CBD) – poor evidence for other pain mechanisms
- Increased risk of short-term AEs (mostly minor)

1. Fisher, Emma, et al. "Cannabinoids, cannabis, and cannabis-based medicine for pain management: a systematic review of randomised controlled trials." *Pain* 162 (2021): S45-S66.

Study drugs used in clinical trials

Medical cannabis and CBD products

https://images.pexels.com/photos/3465383/pexels-photo-3465383.jpeg?auto=compress&cs=tinysrgb&fit=crop&h=627&w=1200

American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY ELSEVIER
The Journal of Pain, Vol 20, No 11 (November), 2019: pp 1362–1372
Available online at www.jpain.org and www.sciencedirect.com

Cannabis Use Preferences and Decision-making Among a Cross-sectional Cohort of Medical Cannabis Patients with Chronic Pain

Kevin F. Boehnke,* J. Ryan Scott,* Evangelos Litinas,† Suzanne Sisley,‡ Daniel J. Clauw,* Jenna Goesling,* and David A. Williams*

Table 3. Type and Number of Cannabis Administration Routes Employed Across Groups

	Total (N = 1,276)	Male (N = 524)	Female (N = 752)	X2 (df)	P-value	MED (N = 686)	MEDREC (N = 590)	X2 (df)	P-value	Novice (N = 471)	Experienced (N = 805)	X2 (df)	P-value
Administration route (any ranking)													

Table 2. Preferred Cannabinoid Ratios Among Study Population, Males versus Females, MED versus MEDREC Users, and Novice versus Experienced Users

	Total (N = 925)	Male (N = 376)	Female (N = 549)	X2 (df)	P-value	MED (N = 507)	MEDREC (N = 418)	X2 (df)	P-value	Novice (N = 335)	Experienced (N = 590)	X2 (df)	P-value
High THC: low CBD	157 (17.0%)	74 (19.7%)	83 (15.1%)	32.9 (6)	<.0001	68 (13.4%)	89 (21.3%)	40.6 (6)	<.0001	67 (20.0%)	90 (15.3%)	13.4 (6)	.037
High THC: high CBD	342 (37.0%)	164 (43.6%)	178 (32.4%)			165 (32.5%)	177 (42.3%)			99 (29.6%)	243 (41.2%)		
Low THC: high CBD	312 (33.7%)	88 (23.4%)	224 (40.8%)			208 (41.0%)	104 (24.9%)			123 (36.7%)	189 (32.0%)		
Low THC: low CBD	34 (3.7%)	14 (3.7%)	20 (3.6%)			17 (3.4%)	17 (4.1%)			15 (4.5%)	19 (3.2%)		
Only THC	13 (1.4%)	8 (2.1%)	5 (0.9%)			7 (1.4%)	6 (1.4%)			5 (1.5%)	8 (1.4%)		
Only CBD	21 (2.3%)	8 (2.1%)	13 (2.4%)			18 (3.6%)	3 (0.7%)			9 (2.7%)	12 (2.0%)		
Other	46 (5.0%)	20 (5.3%)	26 (4.7%)			24 (4.7%)	22 (5.3%)			17 (5.1%)	29 (4.9%)		

There were significant differences in cannabinoid preferences between groups. Females, MED, and novice users preferred low THC: high CBD ratios significant more than their counterparts, who tended to prefer high quantities of THC.

Subgroups	n (%)	Example quote
Non-inhalation	204 (18.8%)	"2 drops of 1000mg CBD oil, 2x day." "I take both THC & CBD tinctures in the AM, and usually a salve, then I put some Hash tincture in the water I have throughout the day. At night it can vary - sometimes just salve, sometimes nothing, sometimes an edible."
Inhalation	393 (36.1%)	"I vape a sativa dominant hybrid in the morning and sometimes late afternoon. I smoke indica before bed." "I smoke high THC out of a pipe every hour or two throughout the day."
Non-inhalation+inhalation	490 (45.1%)	"I medicate with 5mg 2:1 CBD:THC gummy. I immediately vape 3 drags from a 2:1 cartridge. I then micro-dose the same at 2.5 mg every 2 hours with 2 hits off the 2:1 vape pen. When I get home after work, I take a 2mg THC blueberry and water-vape a very small mt of an indica. Then, before bed I water vape slightly more indica and take a 5mg dose of a THC/indica gummy." "7 drops CBD twice daily, 2 drops 1:1 ratio before bed, vaporize higher THC as needed (esp. for neuropathic pain relief)."

Boehnke et al, *Journal of cannabis research* 4.1 (2022): 1-11.

Substitution of Cannabis for Medications

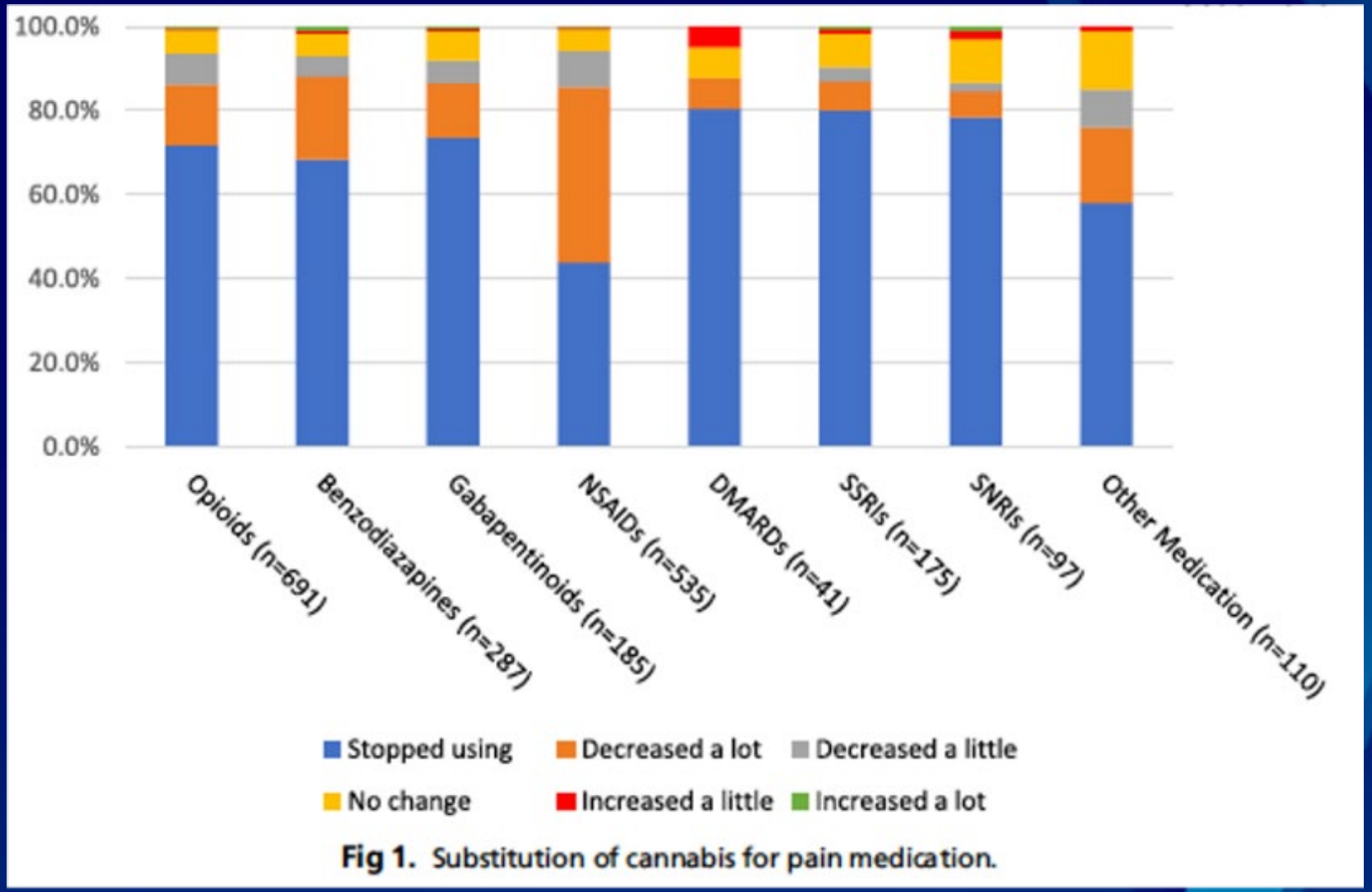
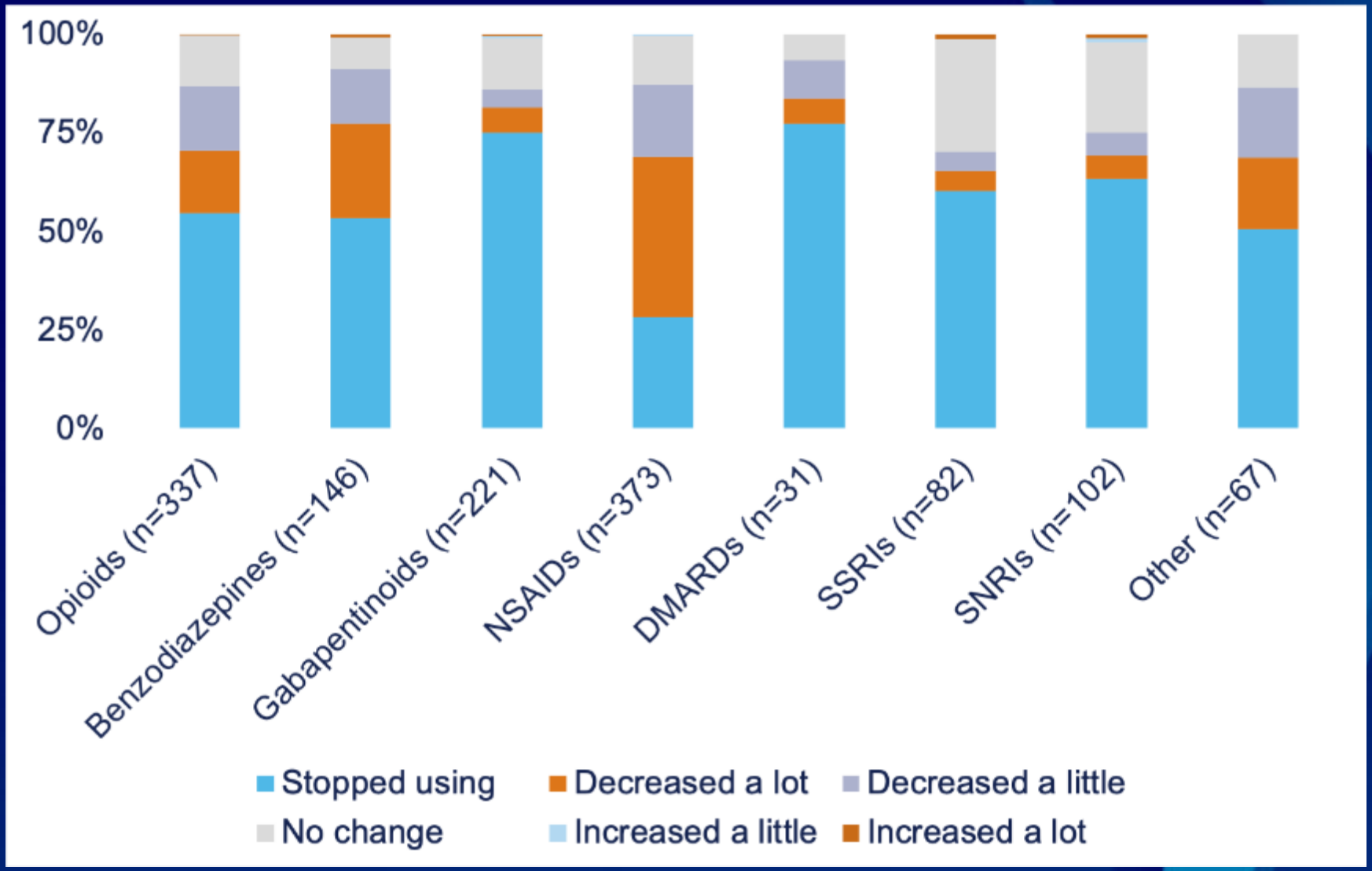


Fig 1. Substitution of cannabis for pain medication.

Figure 1 from: Boehnke, Kevin F., et al. *The Journal of Pain* 20.7 (2019): 830-841.

Substitution of CBD products for pain medications



From Boehnke et al, *Journal of Pain* 22.11 (2021): 1418-1428.

- 1. Lucas P, Walsh Z, Crosby K, et al. Substituting cannabis for prescription drugs, alcohol and other substances among medical cannabis patients: The impact of contextual factors. *Drug Alcohol Rev.* 2016;35(3):326-333.
- 2. Lucas P, Walsh Z. Medical cannabis access, use, and substitution for prescription opioids and other substances: A survey of authorized medical cannabis patients. *Int J Drug Policy.* 2017;42:30-35.
- 3. Baron EP, Lucas P, Eades J, Hogue O. Patterns of medicinal cannabis use, strain analysis, and substitution effect among patients with migraine, headache, arthritis, and chronic pain in a medicinal cannabis cohort. *J Headache Pain.* 2018;19(1):37.
- 4. Lucas P, Baron EP, Jikomes N. Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients. *Harm Reduct J.* 2019;16(1):9.
- 5. 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):739-744.
- 6. Boehnke KF, Scott JR, Litinas E, Sisley S, Williams DA, Clauw DJ. Pills to Pot: Observational Analyses of Cannabis Substitution Among Medical Cannabis Users With Chronic Pain. *J Pain.* 2019;20(7):830-841.
- 7. Reiman A, Welty M, Solomon P. Cannabis as a Substitute for Opioid-Based Pain Medication: Patient Self-Report. *Cannabis Cannabinoid Res.* 2017;2(1):160-166.
- 8. Corroon JM, Jr., Mischley LK, Sexton M. Cannabis as a substitute for prescription drugs - a cross-sectional study. *J Pain Res.* 2017;10:989-998.
- 9. Piper BJ, DeKeuster RM, Beals ML, et al. Substitution of medical cannabis for pharmaceutical agents for pain, anxiety, and sleep. *J Psychopharmacol.* 2017;31(5):569-575.
- 10. Abuhasira R, Schleider LB, Mechoulam R, Novack V. Epidemiological characteristics, safety and efficacy of medical cannabis in the elderly. *Eur J Intern Med.* 2018;49:44-50.
- 11. Sagy I, Bar-Lev Schleider L, Abu-Shakra M, Novack V. Safety and Efficacy of Medical Cannabis in Fibromyalgia. *J Clin Med.* 2019;8(6).
- 12. Bar-Lev Schleider L, Mechoulam R, Lederman V, et al. Prospective analysis of safety and efficacy of medical cannabis in large unselected population of patients with cancer. *Eur J Intern Med.* 2018;49:37-43.
- 13. Naftali T, Bar-Lev Schleider L, Sklerovsky Benjaminov F, Lish I, Konikoff FM, Ringel Y. Medical cannabis for inflammatory bowel disease: real-life experience of mode of consumption and assessment of side-effects. *Eur J Gastroenterol Hepatol.* 2019;31(11):1376-1381.
- 14. Haroutounian S, Ratz Y, Ginosar Y, et al. 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):1036-1043.
- 15. Ishida JH, Wong PO, Cohen BE, Vali M, Steigerwald S, Keyhani S. Substitution of marijuana for opioids in a national survey of US adults. *PLoS One.* 2019;14(10):e0222577.

Summary

- Clinical trials suggest that cannabis may be helpful for some people, but these studies are limited
- Cannabis-related risks are real but comparatively lower than many other pain medications (e.g., opioids)
- The clinical trial literature does not adequately represent trends in real-world use