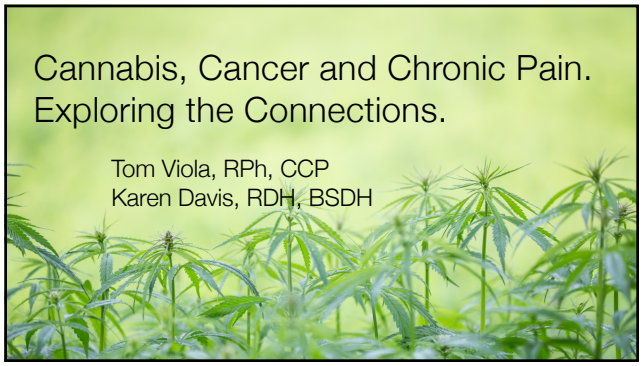
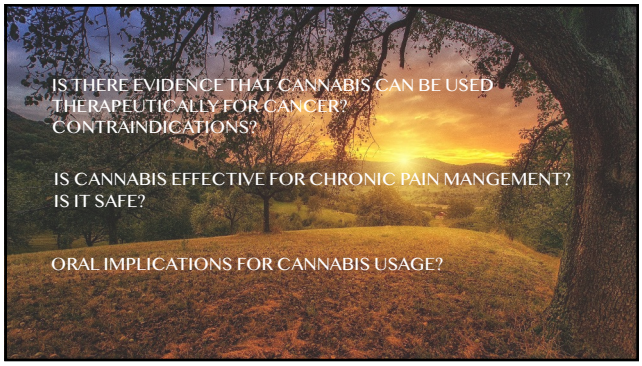

Cannabis, Cancer and Chronic Pain.
Exploring the Connections.
Tom Viola, RPh, CCP
Karen Davis, RDH, BSDH

1


Celebrate LIFE

2


IS THERE EVIDENCE THAT CANNABIS CAN BE USED THERAPEUTICALLY FOR CANCER?
CONTRAINDICATIONS?
IS CANNABIS EFFECTIVE FOR CHRONIC PAIN MANGEMENT?
IS IT SAFE?
ORAL IMPLICATIONS FOR CANNABIS USAGE?

3


Complex
Conflicting
Confusing

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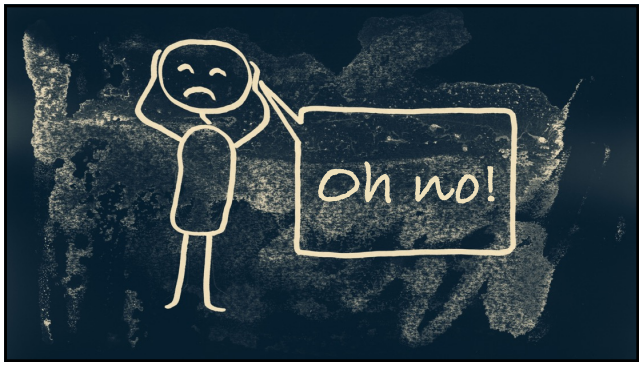
oh no!

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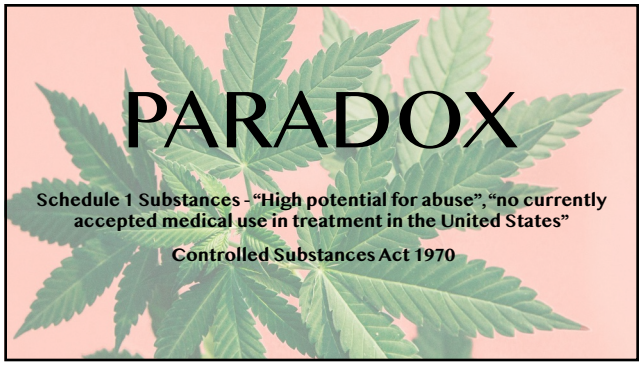
PARADOX
Schedule 1 Substances - "High potential for abuse", "no currently accepted medical use in treatment in the United States"
Controlled Substances Act 1970

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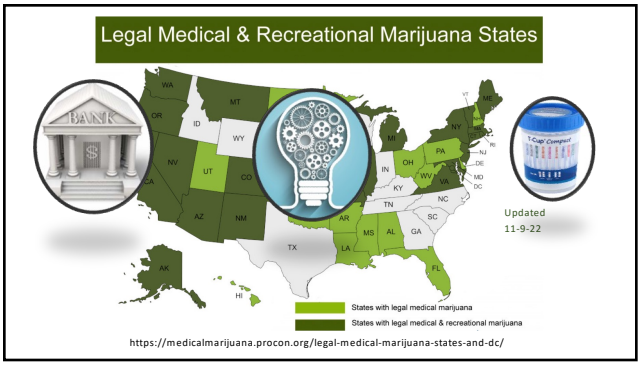
Legal Medical & Recreational Marijuana States
BANK
Updated
11-9-22
States with legal medical marijuana
States with legal medical & recreational marijuana
https://medicalmarijuana.procon.org/legal-medical-marijuana-states-and-dc/

8

9

10

Medical Cannabis Safety

In accordance with other studies evaluating the safety of cannabis treatment over all indications, **cannabis was found to be safe and well tolerated.**

Thirty percent of patients reported at least one side effect at six months, but the side effects were **relatively minor: dizziness, dry mouth, increased appetite, sleepiness and psychoactive effect.**

Lihi Bar-Lev Schleider, Raphael Mechoulam, Violeta Lederman, Mario Hilou, Ori Lencovsky, Oded Betzalel, Liat Shbiro, Victor Novack. Prospective analysis of safety and efficacy of medical cannabis in large unselected population of patients with cancer. European Journal of Internal Medicine. 2018;(4):37-43

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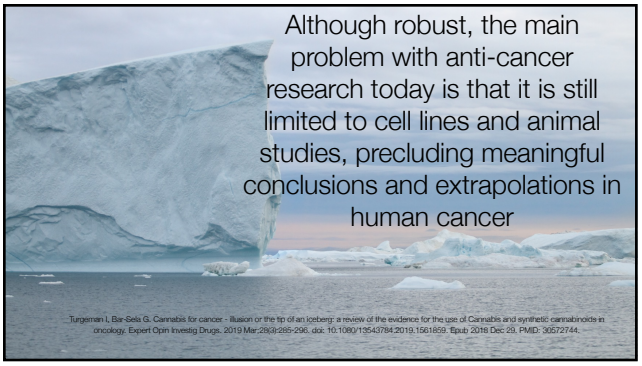

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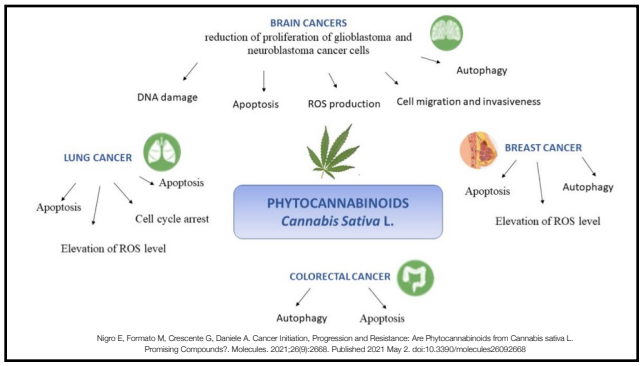

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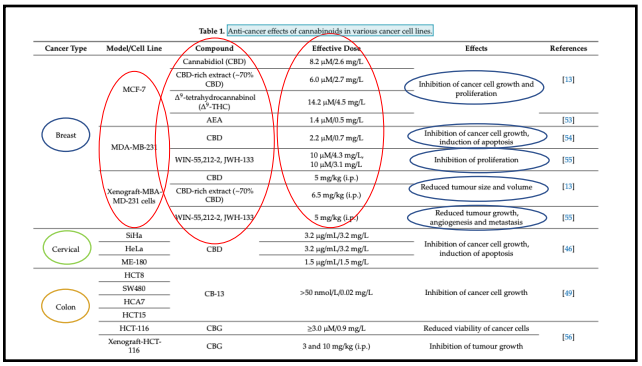

Table 1. Anti-cancer effects of cannabinoids in various cancer cell lines.

Cancer Type	Model/Cell Line	Compound	Effective Dose	Effects	References
Breast	MCF-7	Cannabidiol (CBD)	8.2 μM/2.6 mg/L	Inhibition of cancer cell growth and proliferation	[13]
		CBD-rich extract (~70% CBD)	6.0 μM/2.7 mg/L		
		Δ^9-tetrahydrocannabinol (Δ^9-THC)	14.2 μM/4.5 mg/L		
		AEA	1.4 μM/0.5 mg/L		[53]
	MDA-MB-231	CBD	2.2 μM/0.7 mg/L	Inhibition of cancer cell growth, induction of apoptosis	[54]
		WIN-55,212-2, JWH-133	10 μM/4.3 mg/L, 10 μM/3.1 mg/L	Inhibition of proliferation	[55]
	Xenograft-MBA-MD-231 cells	CBD	5 mg/kg (i.p.)	Reduced tumour size and volume	[13]
		CBD-rich extract (~70% CBD)	6.5 mg/kg (i.p.)		
		WIN-55,212-2, JWH-133	5 mg/kg (i.p.)	Reduced tumour growth, angiogenesis and metastasis	[55]
Cervical	SiHa	CBD	3.2 μg/mL/3.2 mg/L	Inhibition of cancer cell growth, induction of apoptosis	[46]
	HeLa		3.2 μg/mL/3.2 mg/L		
	ME-180		1.5 μg/mL/1.5 mg/L		
Colon	HCT8	CB-13	>50 nmol/L/0.02 mg/L	Inhibition of cancer cell growth	[49]
	SW480				
	HCA7				
	HCT15				
	HCT-116	CBG	≥3.0 μM/0.9 mg/L	Reduced viability of cancer cells	[56]
	Xenograft-HCT-116	CBG	3 and 10 mg/kg (i.p.)	Inhibition of tumour growth	

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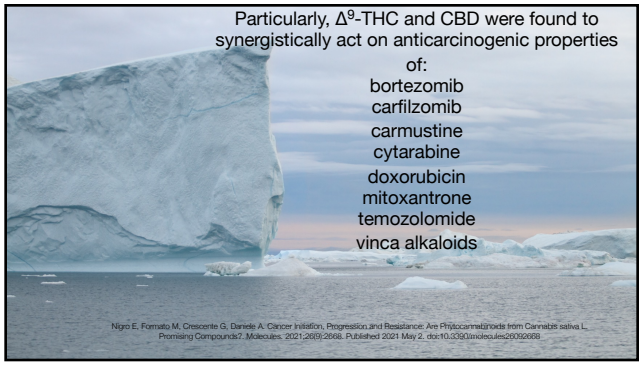
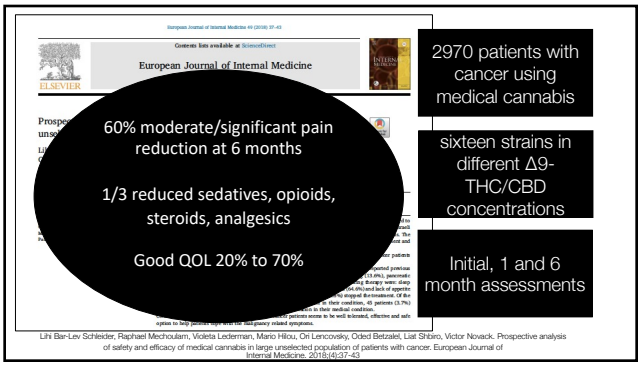


15

Ongoing Clinical Trials

- THC, CBD combinations
- THC, CBD independent or combined with chemotherapies
- THC, CBD independent or combined with radiotherapies
- THC, CBD independent or combined with immunotherapies

16



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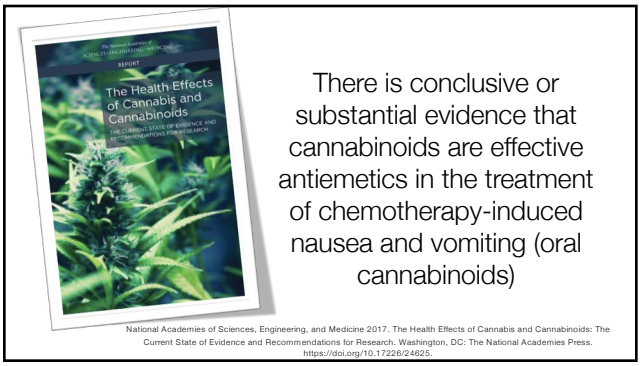

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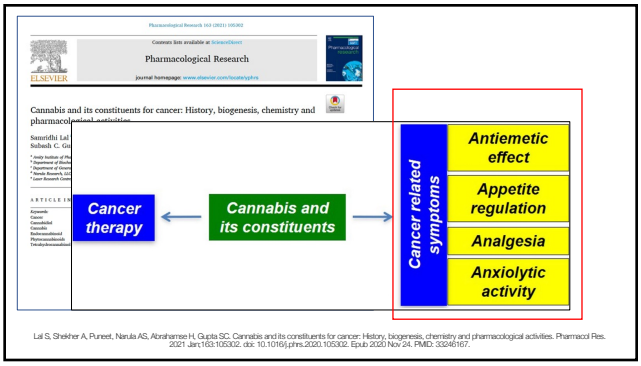

19

"The dose makes the poison..."

Hart et al. demonstrated that while high concentrations of cannabinoids have antiproliferative effects on tumors, treatment of lung, brain and genitourinary carcinoma cell lines with low concentrations results in rapid epidermal growth factor receptor and metalloprotease-dependent cancer cell proliferation

Turgeman I, Bar-Sela G. Cannabis for cancer - illusion or the tip of an iceberg: a review of the evidence for the use of Cannabis and synthetic cannabinoids in oncology. Expert Opin Investig Drugs. 2019 Mar;28(3):285-296. doi: 10.1080/13543784.2019.1561859. Epub 2018 Dec 29. PMID: 30572744.

20

Caution....

In a multi-variant model, the authors found significantly reduced response rate to immunotherapy in a cohort of 140 patients with, and without cannabionoid treatment, after taking into account confounders such as performance status and Cannabis composition.

Turgeman I, Bar-Sela G. Cannabis for cancer - illusion or the tip of an iceberg: a review of the evidence for the use of Cannabis and synthetic cannabinoids in oncology. Expert Opin Investig Drugs. 2019 Mar;28(3):285-296. doi: 10.1080/13543784.2019.1561859. Epub 2018 Dec 29. PMID: 30572744.

21

Cannabis Indications in Oncology

Strong Evidence - green | Weak Evidence - yellow | No significant evidence - red

Chemotherapy induced nausea and vomiting	Cancer associated pain	Anorexia and cachexia syndrome
Insomnia	Depression and anxiety	Cancer treatment

Turgeman I, Bar-Sela G. Cannabis for cancer - illusion or the tip of an iceberg: a review of the evidence for the use of Cannabis and synthetic cannabinoids in oncology. Expert Opin Investig Drugs. 2019 Mar;28(3):285-296. doi: 10.1080/13543784.2019.1561859. Epub 2018 Dec 29. PMID: 30572744.

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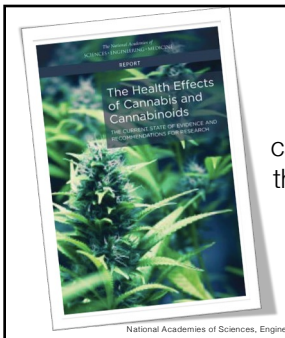

There is conclusive or substantial evidence that cannabinoids are effective for the treatment of chronic pain in adults (cannabis).

National Academies of Sciences, Engineering, and Medicine 2017. The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press. https://doi.org/10.17226/24625.

25

Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies

Evidence for effectiveness of cannabinoids in CNCP is limited

104 studies (9958 participants)

Those experiencing 30% reduction in pain:
29.0% (cannabinoids) vs 25.9% (placebo)

Those experiencing 50% reduction in pain:
18.2% (cannabinoids) vs 14.4% (placebo)

Stockings E, Campbell G, Hall WD, Nielsen S, Zagic D, Rahman R, Murnion B, Farrell M, Weier M, Degenhardt L. Cannabis and cannabinoids for the treatment of people with chronic noncancer pain conditions: a systematic review and meta-analysis of controlled and observational studies. Pain. 2018 Oct;159(10):1932-1954. doi: 10.1097/j.pain.0000000000001293. PMID: 29847469.

26

Medical cannabis - highest use substance for LBP in aged population (65-79) ***Systematic Review 23 articles***

THC binds CB1 and CB2 pain receptors
CBD stimulates release of β-endorphin, suppressing pain, and CBD promotes production of body's own cannabinoids

Some studies reported **high satisfaction** for mgmt. of back pain THC/CBD
Some studies reported **minimal relief** from chronic pain with THC/CBD

Differences in analgesic effects among various administration methods & ratios of THC/CBD are **currently unclear and remain a research priority.**

Senderovich H, Wagman H, Zhang D, Vinoraj D, Waicus S: The Effectiveness of Cannabis and Cannabis Derivatives in Treating Lower Back Pain in the Aged Population: A Systematic Review. Gerontology 2021. doi: 10.1159/000518269

27

Medicinal Cannabis for Inflammatory Bowel Disease: A Survey of Perspectives, Experiences, and Current Use in Australian Patients

Online survey IBD patients / 838 responses
25.3% (n = 212) respondents were current or previous users of MC

Only 3 respondents reported using legally assessed products

92.7% endorsed cannabis as effective in symptom mgmt: abdominal pain, stress, sleep, cramping, anxiety

Melissa J Benson, PhD, Sarah V Abeles, BSc, Susan J Connor, MD, PhD, Crispin J Corte, MD, PhD, Lewis J Martin, PhD, Lucy K Gold, BSc, Anastasia S Suraev, MPsych(Clin), Iain S McGregor, PhD, Medicinal Cannabis for Inflammatory Bowel Disease: A Survey of Perspectives, Experiences, and Current Use in Australian Patients, Crohn's & Colitis 360, Volume 2, Issue 2, April 2020, otaa015, https://doi.org/10.1093/crocol/otaa015

28

Medical Cannabis Reduces Chronic or Neuropathic Pain in Advanced Cancer Patients

Review 1975-2017: 5 Clinical studies evaluating effect of THC or CBD on controlling cancer pain

- THC oil capsules
- THC oromucosal spray
- THC:CBD oromucosal spray

Doses 2.7 – 42.2 mg/day THC and 0-40 mg CBD daily

Higher THC correlated in increased pain relief in most studies
1 study found sig. pain relief in low doses

Blake A, Wan BA, Malek L, DeAngelis C, Diaz P, Lao N, Chow E, O'Hearn S. A selective review of medical cannabis in cancer pain management. Ann Palliat Med 2017;6(Suppl 2):S215-S222. doi: 10.21037/apm.2017.08.05

29

Strains to relieve pain...

•**ACDC:**This is a non-psychoactive strain that makes you feel happy, uplifted, relaxed and focused. HIGH THC/HIGH CBD

•**Blackberry Kush:** High in THC, Blackberry Kush is particularly known for its intense pain-relieving effects. It also makes you feel relaxed, sleepy and euphoric and is best taken at nighttime or on days you don't have much to do

.

•**Harlequin:** HIGH CBD/LOW THC. Due to its CBD and THC content, Harlequin kills your pain while keeping you mentally alert. As such, this is a good option for daytime use.

https://www.marijuanadoctors.com/conditions/cancer/

30

BMJ | Journals

2021 Review of RCT Medical Cannabis for Pain Management

32 trials (5174 adult patients)

Moderate to high certainty evidence shows that non-inhaled medical cannabis or cannabinoids results in a small to very small improvement in pain relief, physical functioning, and sleep quality among patients with chronic pain, along with several transient adverse side effects, compared with placebo.

Wang L, Hong PJ, May C, Rehman Y, et al., Medical cannabis or cannabinoids for chronic non-cancer and cancer related pain: a systematic review and meta-analysis of randomised clinical trials. BMJ. 2021 Sep 8;374:n1034. doi: 10.1136/bmj.n1034. PMID: 34497047.

31

Annals of Internal Medicine®

Reviews | August 2022

Cannabis-Based Products for Chronic Pain

A Systematic Review

Conclusion:

Oral, synthetic cannabis products with high THC-to-CBD ratios and sublingual, extracted cannabis products with comparable THC-to-CBD ratios may be associated with short-term improvements in chronic pain and increased risk for dizziness and sedation. Studies are needed on long-term outcomes and further evaluation of product formulation effects.

Limitation:

Variation in interventions; lack of study details, including unclear availability in the United States; and inadequate evidence for some products.

Marian S. McDonagh, Benjamin J. Morasco, Jesse Wagner, et al. Cannabis-Based Products for Chronic Pain: A Systematic Review. Ann Intern Med.2022;175:1143-1153. [EpUb 7 June 2022]. doi:10.7326/M22-0516

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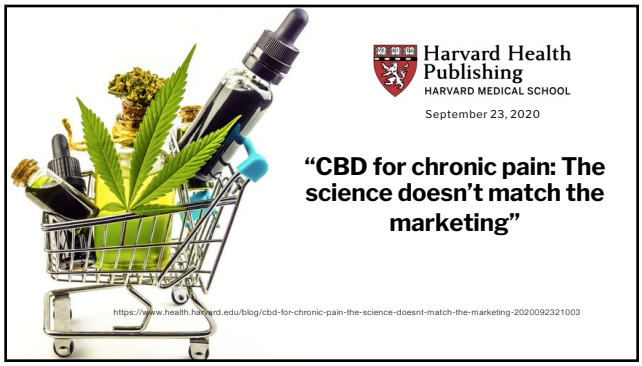
Harvard Health Publishing
HARVARD MEDICAL SCHOOL
September 23, 2020
"CBD for chronic pain: The science doesn't match the marketing"
https://www.health.harvard.edu/blog/cbd-for-chronic-pain-the-science-doesnt-match-the-marketing-202009232100

33


"I'd be wary of simple solutions to complex problems."
Jeb Bush

34


What's on your mind?

35


Oral Health Considerations

36

Smoking most common use with rapid onset (10 minutes) and duration 2-4 hours

Combustion at extremely high temperatures produces toxic byproducts, and chronic use is associated with respiratory symptoms

Turgeman I, Bar-Sela G. Cannabis for cancer - illusion or the tip of an iceberg: a review of the evidence for the use of Cannabis and synthetic cannabinoids in oncology. Expert Opin Investig Drugs. 2019 Mar;28(3):285-296. doi: 10.1080/13543784.2019.1561859. Epub 2018 Dec 29. PMID: 30572744.

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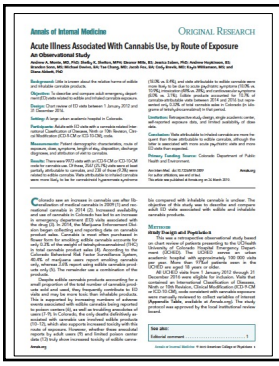


Annals of Internal Medicine — ORIGINAL RESEARCH

Acute Illness Associated With Cannabis Use, by Route of Exposure
An Observational Study

ER visits evaluated between January 1, 2012 and December 31, 2016.

Edible products accounted for 10.7% of cannabis-attributable visits in Colorado

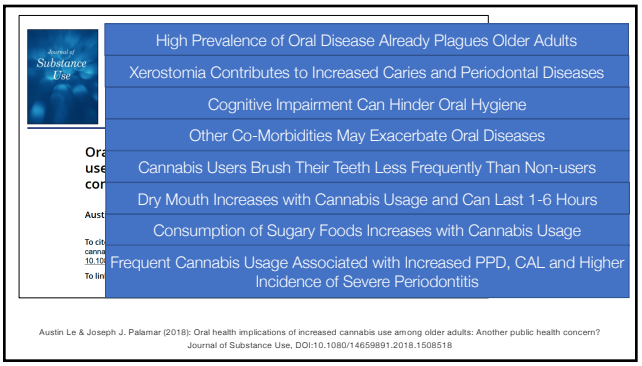
Edibles ER visits:
Acute psychiatric symptoms: 18%
Intoxication 48%
Cardiovascular symptoms 8%

Monte A A, Shelton, SK, et. al. Acute illness associated with cannabis use, by Route of exposure. An Observational Study. Ann Intern Med. doi:10.7326/M18-2809

40


Following alcohol and tobacco cannabis is the third most commonly used controlled substance by older adults
2013 13% aged 65 and older were users. Projected to be 20% by 2030

41


High Prevalence of Oral Disease Already Plagues Older Adults
Xerostomia Contributes to Increased Caries and Periodontal Diseases
Cognitive Impairment Can Hinder Oral Hygiene
Other Co-Morbidities May Exacerbate Oral Diseases
Cannabis Users Brush Their Teeth Less Frequently Than Non-users
Dry Mouth Increases with Cannabis Usage and Can Last 1-6 Hours
Consumption of Sugary Foods Increases with Cannabis Usage
Frequent Cannabis Usage Associated with Increased PPD, CAL and Higher Incidence of Severe Periodontitis
Austin Le & Joseph J. Palamar (2018): Oral health implications of increased cannabis use among older adults: Another public health concern? Journal of Substance Use, DOI:10.1080/14659891.2018.1508518

42


Journal of Substance Use
2013 Published Data Confirms Substance Abuse Disorder is on the Rise
Aging Population at Increased Risk for Several Psychosocial Factors Increasing Risk for Substance Abuse: Bereavement, Loneliness, Depression
Future burden of Oral Diseases Posed by Older Adults Using Cannabis May Be Greater Than Anticipated
Austin Le & Joseph J. Palamar (2018): Oral health implications of increased cannabis use among older adults: Another public health concern? Journal of Substance Use, DOI:10.1080/14659891.2018.1508518

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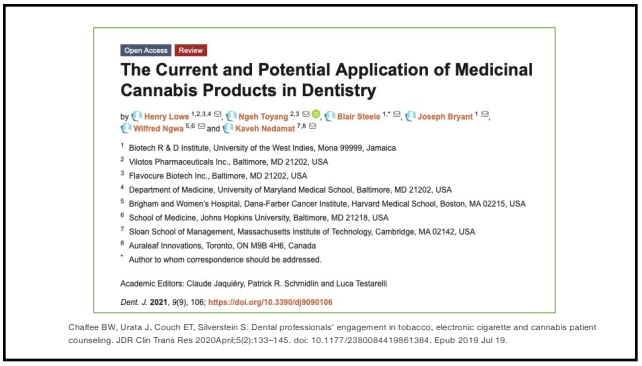
Open Access
Review
The Current and Potential Application of Medicinal Cannabis Products in Dentistry
Chaffee BW, Urata J, Couch ET, Silverstein S. Dental professionals' engagement in tobacco, electronic cigarette and cannabis patient counseling. JDR Clin Trans Res 2020Apr;5(2):133–145. doi: 10.1177/2380084419861384. Epub 2019 Jul 19.

44

	Potential Applications of Secondary Metabolites of *C. sativa* L. in Dentistry	Appropriate Property of Secondary Metabolite	Reference
	Cannabinoids		
1.	General oral hygiene (Cannabidiol, delta9-tetrahydrocannabinol ajulemic acid, Cannabigerol)	Antifungal Antibacterial	[41,84,93,105,117,118,210]
2.	Toothache (Cannabidiol, HU-320)	Analgesic	[41,151,163]
3.	Dental caries/cavities (Cannabidiol, Cannabigerol and Delta9-tetrahydrocannabinol)	Anti-bacterial Analgesic	[41,47,48,84,93,117,118,191,211]
4.	Abscesses (Cannabidiol and delta9-tetrahydrocannabinol)	Anti-bacterial Anti-pruritic	[191]
5.	Prevention of biofilm attachment on teeth (Cannabidiol and delta9-tetrahydrocannabinol)	Anti-bacterial	[84,191]
6.	Burning Mouth Syndrome (Cannabidiol)	Analgesic	[191]
7.	Oral and Salivary Gland Cancers (Cannabidiol)	Anti-cancer Anti-metastatic	[191]

Lowe, H.; Toyang, N.; Steele, B.; Bryant, J.; Ngwa,W.; Nedamat, K. The Current and Potential Application of Medicinal Cannabis Products in Dentistry. Dent. J. 2021, 9, 106. https://doi.org/10.3390/dj9090106

45

Potential Applications of secondary metabolites of *C. sativa* L. in dentistry.

8.	Periodontitis (most severe form of gum disease) (Cannabidiol, HU-320, delta9-tetrahydrocannabinol, AEA)	Anti-bacterial Anti-inflammatory Analgesic	[84,151,188,191,212,213]
9.	Periodontal (Gum) disease (Cannabidiol, delta9-tetrahydrocannabinol, Cannabigerol and HU-320)	Anti-bacterial Anti-inflammatory Analgesic	[84,93,117,118,151,211]
10.	Gingivitis (Cannabidiol, delta9-tetrahydrocannabinol, Cannabigerol, and HU-320)	Anti-bacterial Anti-inflammatory Analgesic	[84,93,117,118,151,211]
11.	Oral Mucositis and other forms of oral cancer (Cannabidiol, delta9-tetrahydrocannabinol, JWH-133m, WIN-55,212-2, Cannabinol, Cannabicyclol)	Anti-bacterial Anti-cancer Anti-metastatic Anti-inflammatory Analgesic Antioxidant	[84,154,191,192,198,214]
12.	Dental Anxiety (Cannabidiol)	Anxiolytic	[191,215]
13.	Sleep issues resulting from dental anxiety (Cannabidiol and delta-9-tetrahydrocannabinol (THC))	Relaxant	[216]

Lowe, H.; Toyang, N.; Steele, B.; Bryant, J.; Ngwa,W.; Nedamat, K. The Current and Potential Application of Medicinal Cannabis Products in Dentistry. Dent. J. 2021, 9, 106. https://doi.org/10.3390/dj9090106

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Promising

Potential

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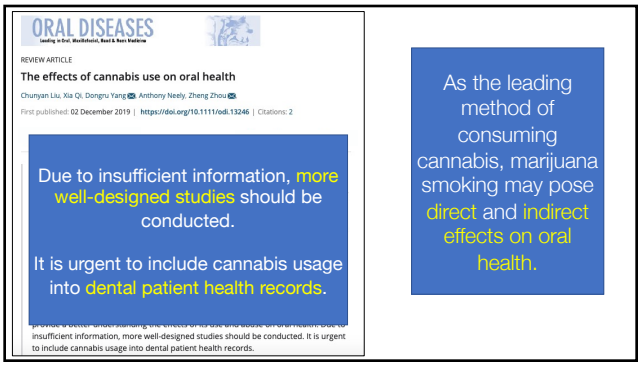

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Oral health

In a statewide survey of California dentists and dental hygienists, only 1 in 4 reported asking patients about cannabis, in contrast to the approximately 60% who asked specifically about tobacco cigarettes.

Chaffee BW, Urata J, Couch ET, Silverstein S. Dental professionals' engagement in tobacco, electronic cigarette and cannabis patient counseling. JDR Clin Trans Res 2020April;5(2):133–145. doi: 10.1177/2380084419861384. Epub 2019 Jul 19.

50

Medical History

Are you currently using any form of Cannabis for medical or recreational purposes?

Chaffee BW, Urata J, Couch ET, Silverstein S. Dental professionals' engagement in tobacco, electronic cigarette and cannabis patient counseling. JDR Clin Trans Res 2020April;5(2):133–145. doi: 10.1177/2380084419861384. Epub 2019 Jul 19.

51

Cannabis: A joint problem for patients and the dental profession

Table 2 The difference between tobacco and cannabis
Cannabis joints are usually smoked for a longer period of time than tobacco.[4]
Cannabis joints are usually smoked to a shorter joint length, which results in a greater number of toxins entering the mouth.[4]
Cannabis has a higher combustion temperature compared to tobacco.[4]
There is greater carboxyhaemoglobin concentration and tar retention in lower airway in cannabis smokers.[4]
Tobacco found in cigarettes is regulated. Whereas, cannabis is a non-regulated substance.

Joshi, S., Ashley, M. Cannabis: A joint problem for patients and the dental profession. *Br Dent J* **220,** 597–601 (2016). https://doi.org/10.1038/sj.bdj.2016.416 [4]Gates P, Jaffe A, Copeland J. Cannabis smoking and respiratory health: Consideration of the literature. *Respirology* 2014; **3:** 655–662.

52

Cannabis: A joint problem for patients and the dental profession

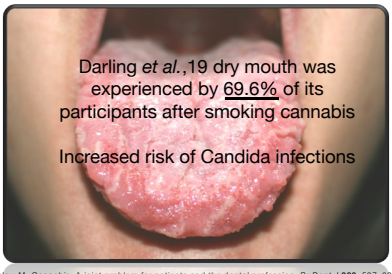
22-year-old patient who smoked six cannabis 'joints' a day for the last 8 years.
Cannabis users surveyed: 63% who experienced increased hunger post use – favored sweets

Various studies show 2.5 – 6 times higher decay rates in cannabis users compare to non-users

Joshi, S., Ashley, M. Cannabis: A joint problem for patients and the dental profession. *Br Dent J* **220,** 597–601 (2016). https://doi.org/10.1038/sj.bdj.2016.416

53

Cannabis: A joint problem for patients and the dental profession



Joshi, S., Ashley, M. Cannabis: A joint problem for patients and the dental profession. *Br Dent J* **220,** 597–601 (2016). https://doi.org/10.1038/sj.bdj.2016.416

54

Cannabis: A joint problem for patients and the dental profession

A sample size of 85 participants were used and divided into two groups. The control group were tobacco smokers only and the test group used cannabis and tobacco

The results obtained showed that cannabis users brushed their teeth less frequently than the control group. In addition, the control group visited their dentist more regularly whereas only 21% in the test group visited their dentist annually.

Joshi, S., Ashley, M. Cannabis: A joint problem for patients and the dental profession. *Br Dent J* **220,** 597–601 (2016). https://doi.org/10.1038/sj.bdj.2016.416

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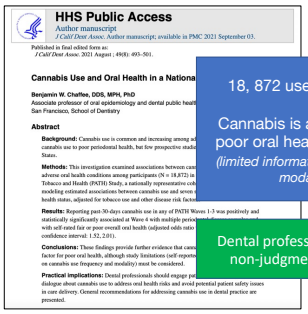

18, 872 users – self reported outcomes

Cannabis is an independent risk factor for poor oral health, although study limitations *(limited information on cannabis use frequency and modality must be considered)*

Dental professionals should engage patients in non-judgmental dialog about cannabis use

Chaffee BW. Cannabis Use and Oral Health in a National Cohort of Adults. *J Calif Dent Assoc*. 2021;49(8):493-501.

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Philipsoralhealthcare.com
IOInternational.com
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Probioralhealth.com

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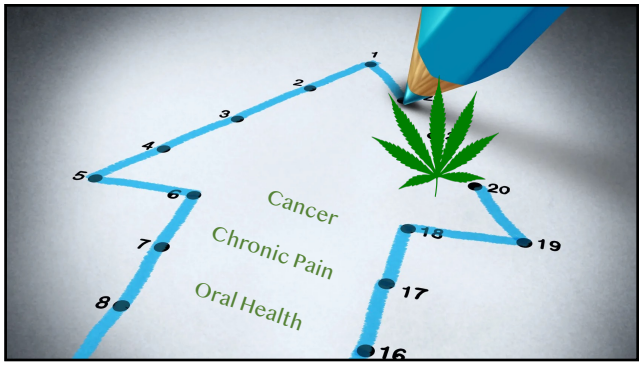
Cancer
Chronic Pain
Oral Health
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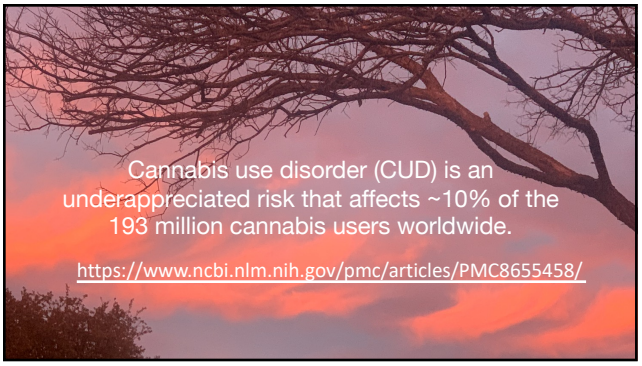
Cannabis use disorder (CUD) is an underappreciated risk that affects ~10% of the 193 million cannabis users worldwide.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8655458/

60


Adolescence and the developing brain
https://pubmed.ncbi.nlm.nih.gov/34021274/
https://pubmed.ncbi.nlm.nih.gov/31619494/

61


YOUR Questions?
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62