



Is Marijuana Medical?

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Disclosures

- Heron Therapeutics-Advisory Board for new product development

Disclaimer

- This presentation does not represent the views or beliefs of Prisma Health System.



Objectives

1. Define terms related to “medical marijuana”.
2. Review Senate bill S. 366.
3. Discuss economic impact of legalization of marijuana.
4. Review the literature related to use of marijuana as a medicine.
5. Discuss the issues related to legalized marijuana.



Definitions

✓ **Prescription:** order for medication which is dispensed to or for and ultimate user:
Requirements?

- Date of issue
- Patient's name
- Practitioner's name, address, and identifiers
- Drug name
- Drug strength
- Dosage form
- Quantity prescribed
- Directions for use
- Number of refill (if any)
- Signature

Veterinary Patient Canine Feline Exotic

For _____ Date _____

R_x Address _____

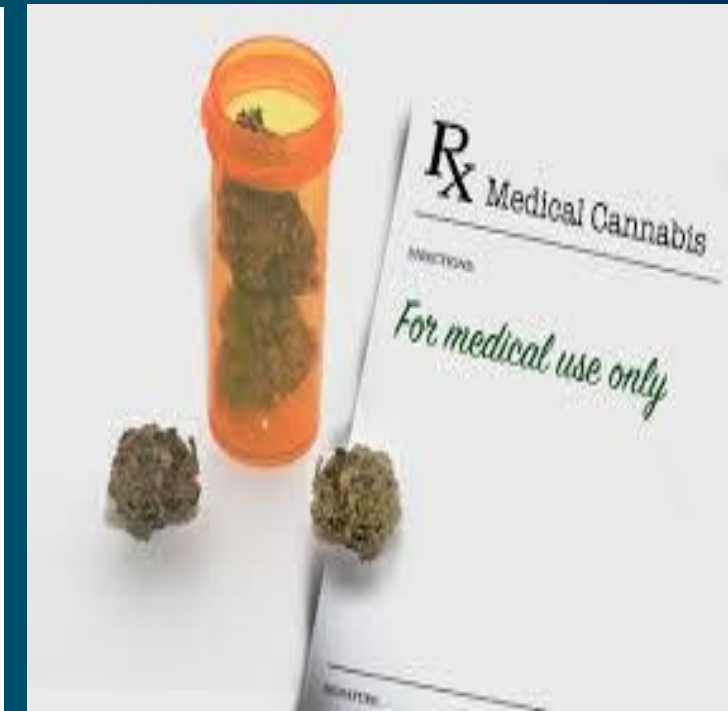
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Rept	ut	Dicum		
1	2	3	4	5 times
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PPN	Non Regt.			

Dr. _____ Dt. _____

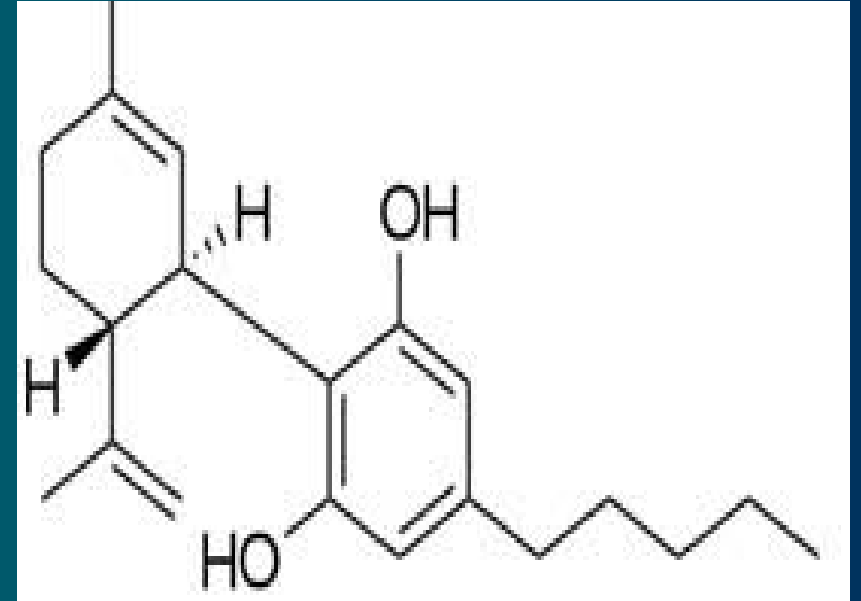
Substitution Permitted Dispense as Written

DEA No. _____



CBD

- Cannabidiol: is primarily derived from Hemp
 - Hemp must contain < 0.3% of THC
 - Non psychotropic
 - Comes as liquid, capsules, ointments, edibles
 - Not regulated on concentration (but is legal?)



CBD claims...

BENEFITS OF CANNABIDIOL

THAT HAVE BEEN CLINICALLY VALIDATED



- ✓ **REDUCES** NAUSEA AND VOMITING
- ✓ **SUPPRESSES** SEIZURE ACTIVITY
- ✓ **COMBATS** PSYCHOSIS DISORDERS
- ✓ **COMBATS** INFLAMMATORY DISORDERS
- ✓ **COMBATS** NEURODEGENERATIVE DISORDERS
- ✓ **COMBATS** TUMOR AND CANCER CELLS
- ✓ **COMBATS** ANXIETY AND DEPRESSION DISORDERS



CBD Oil

May Help With The Following:



100%
Natural & Organic
Purest CBD Hemp
Products

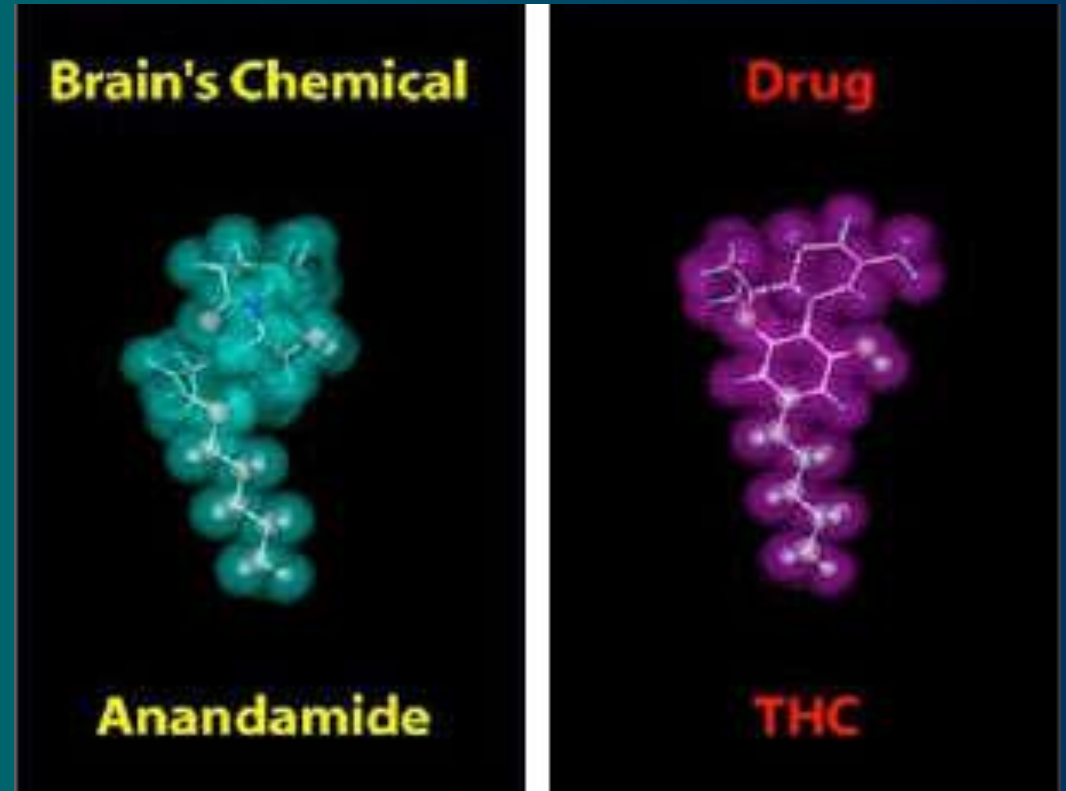
- ✓ Kills or slows bacteria growth (Anti-Bacterial)
- ✓ Reduces Blood Sugar Levels (Anti-Diabetic)
- ✓ Reduces Inflammation (Anti-Inflammatory)
- ✓ Reduces Risk of Artery Blockage (Anti-Ischemic)
- ✓ Reduces Seizures and Convulsions (Anti-Epileptic)
- ✓ Inhibits Tumor/Cancer Cell Growth (Anti-Proliferative)
- ✓ Treats Psoriasis (Anti-Psoriatic)
- ✓ Suppresses Muscle Spasms (Anti-Spasmodic)
- ✓ Promotes Bone Growth (Bone Stimulant)
- ✓ Tranquilizing, used to treat Psychosis (Anti-Psychotic)
- ✓ Relieves Anxiety (Anxiolytic)
- ✓ Relieves Pain (Analgesic)
- ✓ Protects Nervous System Degeneration (Neuroprotective)
- ✓ Reduces Contractions in the small Intestine (Intestinal Anti-Prokinetic)

Made in USA, no heat processing, non gmo, CO2 extracted using only Organic Ingredients. Combination of both the CBD Isolate along with the Full Spectrum Whole Plant Hemp Oil.



THC

- Δ -9 tetrahydrocannabinol: psychoactive compound within marijuana
 - Does contain CBD
 - Similar to Anandamide- naturally occurring brain chemical
 - Can induce psychosis-through glutamate and dopamine alterations (counterbalance)





South Carolina Compassionate Care Act



SC
GOOD PEOPLE
GOOD MEDICINE
CA
GOOD REASON



South Carolina Compassionate Care Act

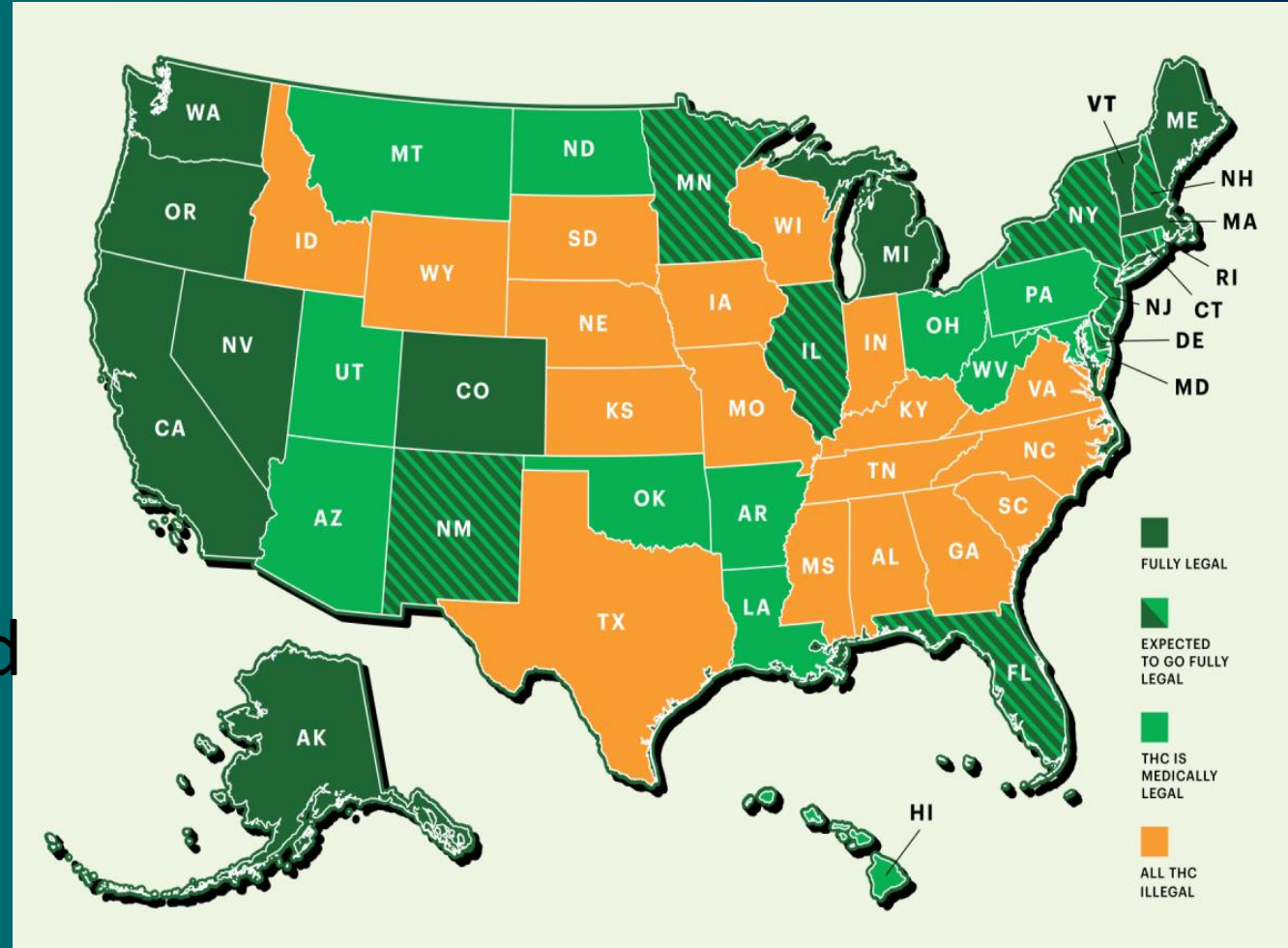
- This topic has been debated for years now
- Bills have been introduced and revised for at least 5 years now
- Most recent bill S. 366 was introduced in 2019 redline amendments passed subcommittee and “waiting” on the Senate Medical Affairs committee
- Currently House bill H. 3660 continues “carried the bill over”



S. 366 (most momentum)

- Most recent April 2019
- It is currently **53** pages
- 33 states and DC have removed criminal penalty
- 11 state have recreational usage

Now 36 states for medical and
15 for recreational



Highlights of S. 366

“Medical Marijuana for?”

1. Debilitating medical conditions...



Debilitating Medical Conditions

1. Cancer
2. Multiple Sclerosis
3. Neurologic disease or disorder (including epilepsy)
4. Glaucoma
5. PTSD
6. Crohn's disease
7. Sickle cell
8. Ulcerative Colitis
9. Cachexia
10. Autism
11. Severe Nausea (not from pregnancy)
12. Chronic medical conditions causing muscle spasms
13. Chronic or debilitating disease or medical condition for which an opioid is currently prescribed



“Medical Marijuana for?”

1. Debilitating medical conditions...
2. Terminal illness with life expectancy <1 year
3. Serious medical condition may be added by Medical Cannabis Advisory Board



Medical Cannabis Advisory Board

1. Meet 2x year
2. Review petitions, consult with experts (?), review research every 180 days
3. 4-year term
4. Members are not entitled to compensation by may be entitled to some benefits????



Highlights of S. 366

- Cannabis will not be legalized for any other purpose other than medical
 - But 15 states now have recreational usage?
- “Allowable amount of medical cannabis” means: up to 2 ounces of cannabis or equivalent for 14 days?
 - What does that mean????



2 ounces, Is this a lot?

- Based on 1 ounces
 - 1 ounce of marijuana yields approximately **84** joints
 - 1 joint, at minimum, results in 4 hours of intoxication
 - 84 joints x 4 hours of intoxication each = 336 hours high per ounce of marijuana
 - 336 hours = 14 days of continual high per ounce
 - That's 1 ounce so **double** it...
 - Who is going to monitor the distribution?



Highlights of S. 366

- Cannabis will not be legalized for any other purpose other than medical
- “Allowable amount of medical cannabis”: up to 2 ounces of cannabis or equivalent for 14 days
- Must be < 50% THC by weight?
“Not your mother’s marijuana” Dr. Jerome Adams

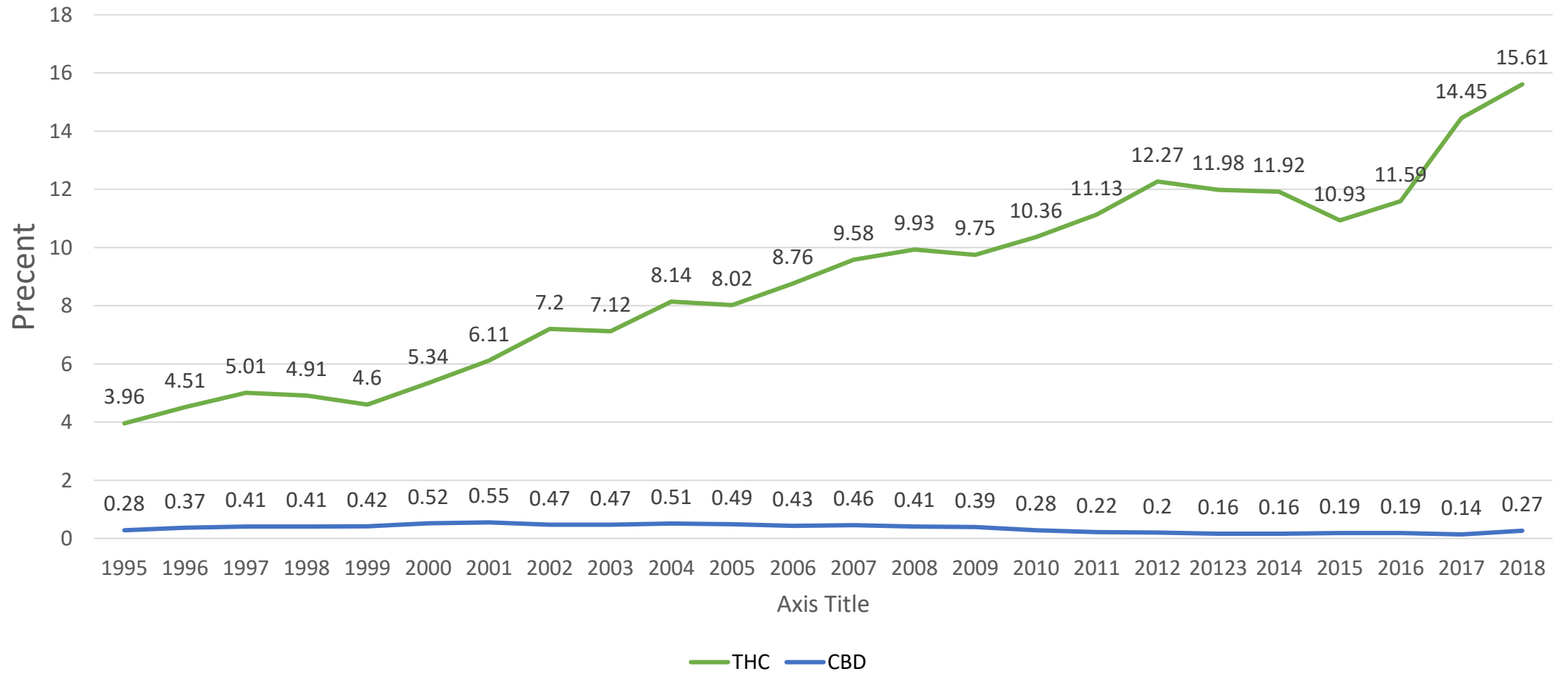


THC changes over time

- The University of Mississippi Potency Monitoring Project began monitoring marijuana THC levels in the mid-1970s and has found that marijuana potency has been steadily rising over the years.
 - In the mid-1970s, average THC levels of seized marijuana were less than 1%.
 - By 1985: 3.5 %
 - By 2006: 8.8 %
 - By 2009: 10.1%



Marijuana Potency



<https://www.drugabuse.gov/drug-topics/marijuana/marijuana-potency>

Highlights of S. 366

- Cannabis will not be legalized for any other purpose other than medical
- “Allowable amount of medical cannabis”: up to 2 ounces of cannabis or equivalent for 14 days
- Must be < 50% THC by weight?
- Must have a physician patient relationship
- Physicians must have a “certification” to recommend?



Certification requirements

1. Must complete 3 hours of training on medical cannabis
2. File a form
 - This must be completed: within one year of first certificate issued
 - Before issuing 16 certificates
3. *X-waiver requires 8 hours in person training???*



Highlights of S 366

- Cannabis will not be legalized for any other purpose other than medical
- “Allowable amount of medical cannabis” means: up to 2 ounces of cannabis or equivalent for 14 days
- Must be < 50% THC by weight?
- Must have a physician patient relationship
- Physicians must have a “certification” to recommend?
- Unlawful to “smoke” cannabis.
 - Vaping???



Vaping THC



- Many published reports of adolescent use and severe vaping illness.



Highlights of S. 366

- Development of “independent” testing laboratories
 - “seed to sale” tracking system
- A lot of questions here???



Highlights of S. 366

- Development of “independent” testing laboratories
 - “seed to sale” tracking system
- Not within 1000 feet of a school
 - But allowable exception?
- Dispensary must “contract” with at least one pharmacist, PA/NP
 - For education in person or telehealth
 - Who supervises?



**When it hurts
to move on,**

**just remember
the pain you felt
hanging on.**



Claims

- Economic benefit
- Medical improvements
- Decrease overdoses
- Solution for “Opioid Epidemic”
- Decrease ER/ED utilizations
- Reduction in:
 - Traffic accidents
 - Traffic violations
 - Drug trafficking
- Just to name a few



Off the top of my head!

Economics

- Estimate of greater than \$8 billion from taxation, licensing and industry¹
- Each state will vary significantly¹
 - Oregon \$500 million
 - Colorado \$47-100 million
- For every dollar (\$1) “gained in tax revenue” must spend \$4.50 to mitigate²
- Cost for “independent testing Labs”
- Tobacco and Alcohol taxation...sound similar?



1. D. Evans, The Economic Impacts of Marijuana Legalization, The Journal of Global Drug Policy and Practice, (2013).
2. J. Hunt, Economic and Social Costs of Legalized Marijuana, Centennial Institute, 2018.

Economic

- As of FY 2016 the tax revenue of Colorado
 - **0.8% of annual budget**
- As of June 2017 Colorado has 392 Starbucks and 208 McDonalds
 - **491** Retail Marijuana stores
- Diversion of “Colorado” marijuana via mail increased by
 - **1042%**; 52 parcels (2009-12) to 594 parcels (2013-17)
 - These investigations cost someone some \$\$\$’s



Medical Improvements

- CBD has shown some benefits
 - Dravet Syndrome: (approx. 1 year of age)
 - Severe myoclonic epilepsy
 - Mutation in α -1 subunit of voltage gated Na⁺ channel gene (*SCN1A*)
 - “drug resistant” may require multiple drugs
 - Cannabidiol (CBD) did show significant reduction in seizures, include is serious adverse events in CBD group (somnolence, loss of appetite, diarrhea)
 - Lennox-Gastaut Syndrome: (before 8 years of age)
 - Less consistently define, multiple seizure types
 - Multiple causes
 - Cannabidiol (CBD) did show a reduction in seizure frequency but did have higher adverse events



Lead to...

- Epidiolex®
 - Prescribable
 - Dosagable
 - Dispensable
 - Start 2.5mg/kg BID, one week can increase to max 10mg/kg BID (max 20mg/kg/day)



FDA NEWS RELEASE



FDA Approves First Drug Comprised of an Active Ingredient Derived from Marijuana to Treat Rare, Severe Forms of Epilepsy



World of “Pain”

Systematic Reviews and Meta-Analyses

PAIN

©  

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

Emily Stockings^{a,*}, Gabrielle Campbell^a, Wayne D. Hall^{b,c}, Suzanne Nielsen^a, Dino Zagic^a, Rakin Rahman^a, Bridin Murnion^{d,e}, Michael Farrell^a, Megan Weier^a, Louisa Degenhardt^a

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- 91/104 studies
- “There is no significant impacts on physical or emotional functioning, and low-quality evidence of improved sleep and patient global impression of change.”
- “It seems unlikely that cannabinoids are highly effective medicine for CNCP.”



Stockings, Emily, Campbell, Gabrielle; et al, 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: October 2018 - Volume 159 - Issue 10 - p 1932-1954

World of "Pain"

Narang et al. (United States) ⁴⁷	Total N: 30	CNCP	Analgesic	(1) Dronabinol (oral)† 10 mg	1 d (very short-term study)	10 mg	50%: not assessed	Moderate/low risk
	Age: 43.76 (11.8) Male %: 46.7	(Neuropathic pain [n = 7]; nociceptive pain [n = 7]; mixed neuropathic and nociceptive [n = 11]; and uncategorised pain [n = 6])	Adjuvant Cointerventions: opioids	(2) Dronabinol (oral)† 20 mg	1 d (very short-term study)	20 mg	30%: not assessed Pain intensity: significant, positive effect (incomplete data reported)	LOCF
Wallace et al. (United States) ⁸⁹	Total N: 16	Neuropathic pain	Analgesic	<i>C. sativa</i> (vaporised)†	1 d (very short-term study)	(1) 1%	50%: not assessed	Moderate/unclear risk
	Age: 56.9 (8.2)	(Diabetes-related)	Adjuvant			(2) 4% (3) 7%	30%: no benefit (cross-over data not presented in usable format)	NR
	Male %: 56		Cointerventions: other diabetes medication; opioids; and NSAIDs				Pain intensity: significant, positive effect (cross-over data not presented in usable format)	
Ware et al. (Canada) ⁹⁰	Total N: 31 Age: 49.5 (11.2)	Fibromyalgia	Sleep; analgesic; mood; quality of life; and global satisfaction	Nabilone (oral)†	2 wk (very short-term study)	NR (0.5-1 mg)	50%: not assessed 30%: not assessed	Moderate/low risk NR
	Male %: 16		Adjuvant Cointerventions: NR				Pain intensity: no benefit*	



Stockings, Emily,*; Campbell, Gabrielle; et al, 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: October 2018 - Volume 159 - Issue 10 - p 1932-1954

World of “Pain”

- 4-year study
- Over 1500 patients
- Had greater pain and lower self-efficacy
- No evidence of reduction in pain intensity

Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study

Gabrielle Campbell, Wayne D Hall, Amy Peacock, Nicholas Lintzeris, Raimondo Bruno, Briony Larance, Suzanne Nielsen, Milton Cohen, Gary Chan, Richard P Mattick, Fiona Blyth, Marian Shanahan, Timothy Dobbins, Michael Farrell, Louisa Degenhardt



Gabrielle Campbell, Wayne D Hall, Amy Peacock, et al, Effect of cannabis use in people with chronic non-cancer pain prescribed opioids: findings from a 4-year prospective cohort study, *The Lancet Public Health*, Volume 3, Issue 7, 2018, Pages e341-e350.

From surgery...

The grass is not always greener:
a multi-institutional pilot study of
marijuana use and acute pain
management following traumatic injury



Kristin Salottolo^{1,2,3,4}, Laura Peck⁵, Allen Tanner II⁶, Matthew M. Carrick⁷, Robert Madayag⁸, Emmett McGuire⁵
and David Bar-Or^{1,2,3,4*}

- Determined “drug” usage by self report and UDS’s
- Reviewed Illicit (cocaine, meth, PCP), Benzo’s, Barbiturates, and opiates
- Results...



Outcome, stratified	Marijuana user (n = 54)	No marijuana use (n = 207)	p value
No other drug use ^a	(n = 40)	(n = 198)	
Mean opioid consumption	8.53 (0.33)	5.86 (0.18)	< 0.001
LSM ^b opioid consumption	7.57 (0.36)	5.65 (0.18)	< 0.001
Mean pain NRS score	5.17 (0.15)	4.17 (0.07)	< 0.001
LSM ^b mean pain NRS score	4.92 (0.16)	4.19 (0.11)	< 0.001
Other drug use ^a	(n = 14)	(n = 9)	
Mean opioid consumption	8.81 (0.82)	10.58 (0.97)	0.29
LSM ^b opioid consumption	5.59 (0.81)	6.10 (1.17)	0.71
Mean pain NRS score	5.02 (0.24)	5.54 (0.25)	0.15
LSM ^b mean pain NRS score	5.28 (0.34)	6.00 (0.48)	0.07

Analyzed with a repeated measures linear mixed model

LSM least square mean

^aDrug use: amphetamines, barbiturates, benzodiazepines, cocaine, methamphetamine, and opiates

^bAdjusted for ISS, age, and cause of motor vehicle crash injury

P < 0.05 in italic is clinically significant

- Marijuana use lead to increased the consumption of opioids
- Greater report pain scores



Opioid Use Disorder (OUD)

Cannabis Use and Risk of Prescription Opioid Use Disorder in the United States

Mark Olfson, M.D., M.P.H., Melanie M. Wall, Ph.D., Shang-Min Liu, M.S., Carlos Blanco, M.D., Ph.D.

- Increase risk of developing nonmedical prescription opioid use and opioid use disorder.



Overdose (Opioid) reduction

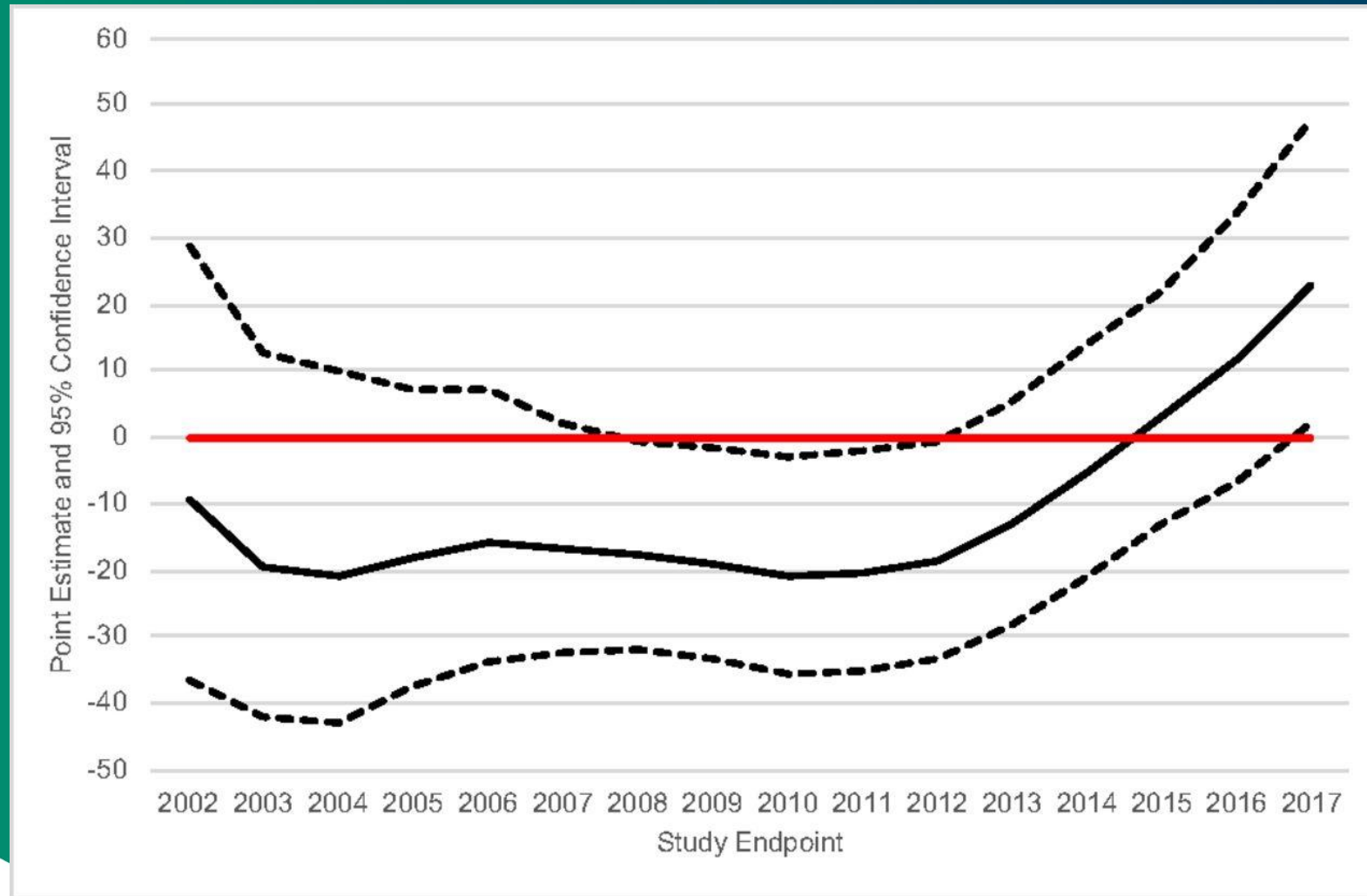
- Report of decrease overdoses (1999-2010) did not hold up overtime
- Opioid overdose mortality reversed direction
- “Enacting medical cannabis laws will reduce opioid overdose death should be met with skepticism.”

Association Between Medical Cannabis Laws and Opioid Overdose Mortality Has Reversed Over Time

Chelsea L Shover ¹, Corey S Davis ², Sanford C Gordon ³, Keith Humphreys ^{4 5}



Changes in point estimate and 95% CI of association between medical cannabis law and age-adjusted opioid overdose death rate by the last year included in the analysis since 1999.

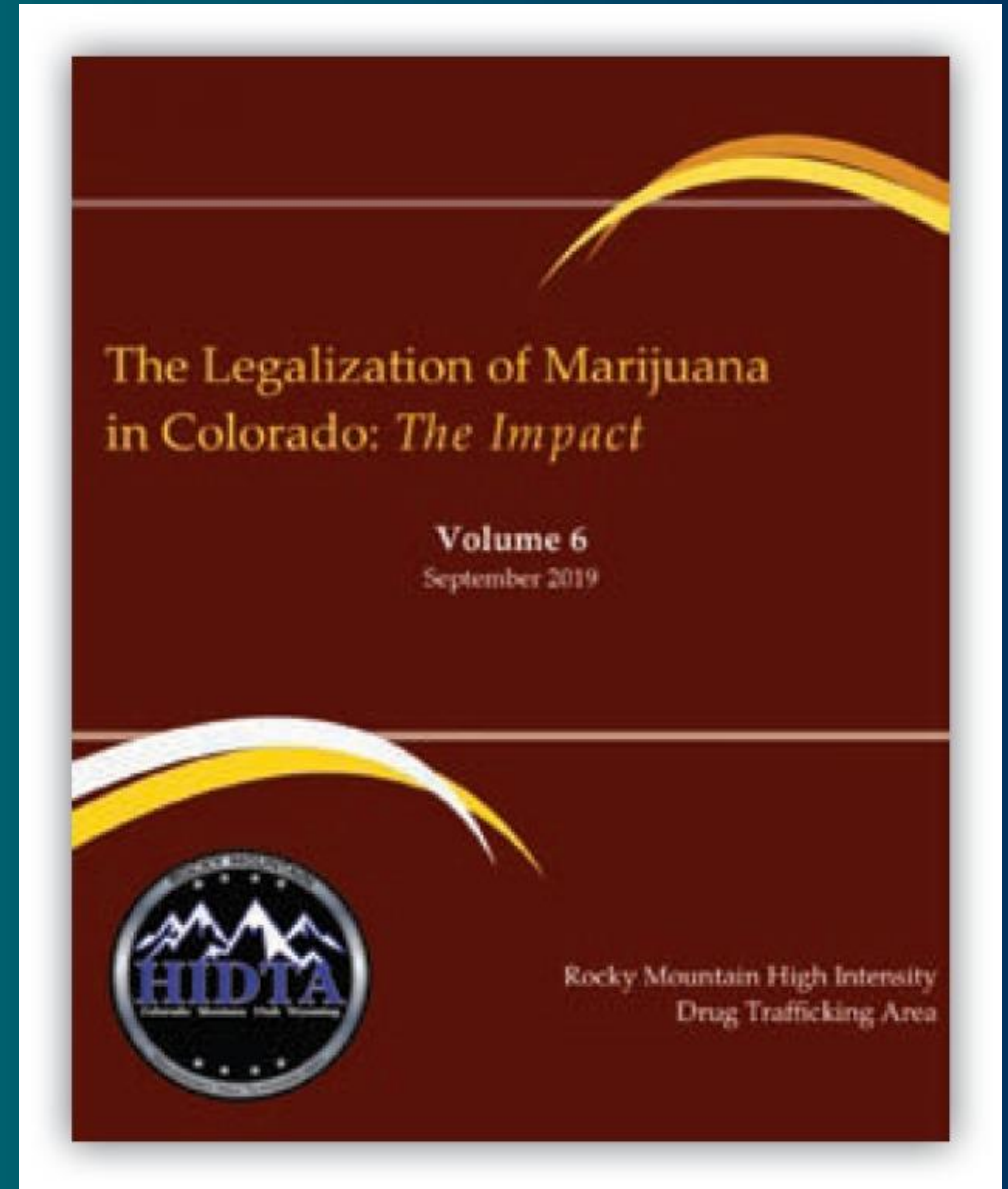


Chelsea L. Shover et al. PNAS 2019;116:26:12624-12626



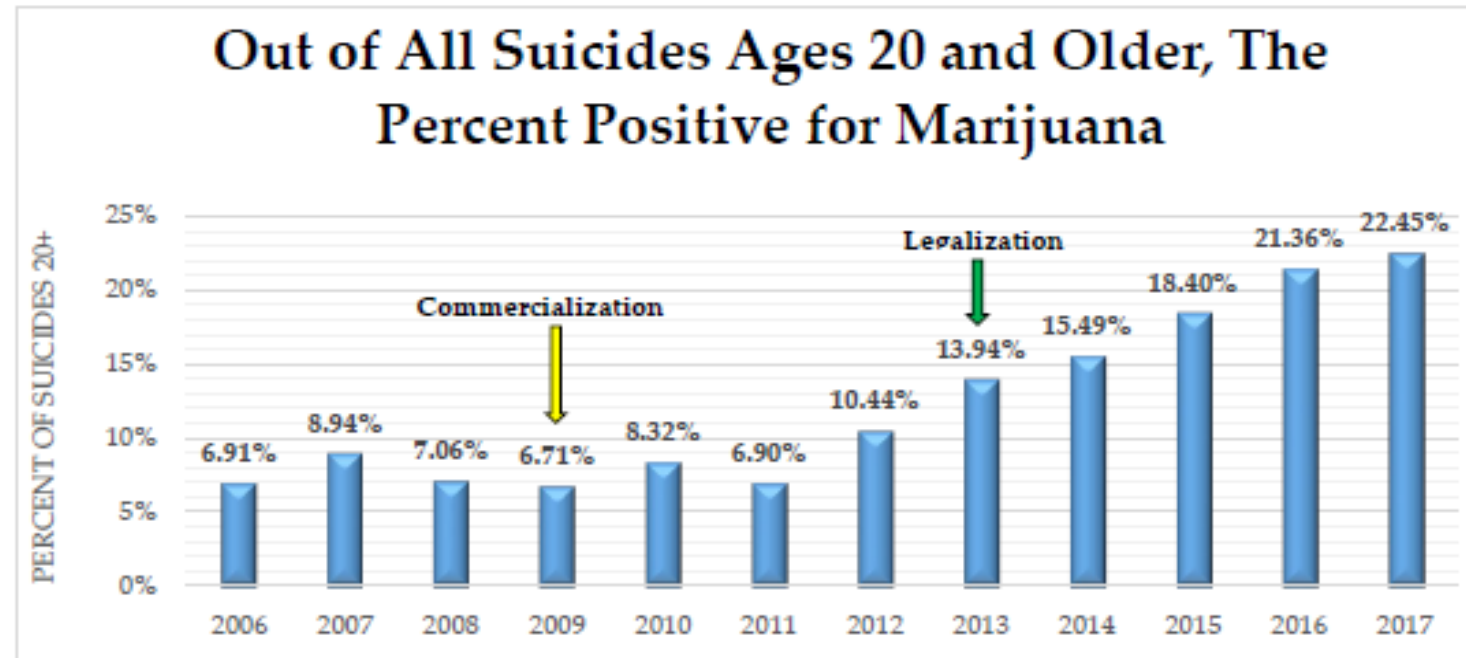
Lessons from my father...

- Drivers testing + THC increased 109%
- Traffic deaths involving + THC more than doubled (1 person killed every 3 days)
- 12 ≥ yo usage increased 58%
- Emergency room visits related to THC increased 54%
- THC related hospitalization increased 101%
- Seizure of Colorado marijuana increased: 1042%; 52 parcels (2009-12) to 594 parcels (2013-17)
- **64** local jurisdictions in Colorado banned medical and recreational marijuana businesses



Toxicology

- Increase of 23% of suicide victims + THC



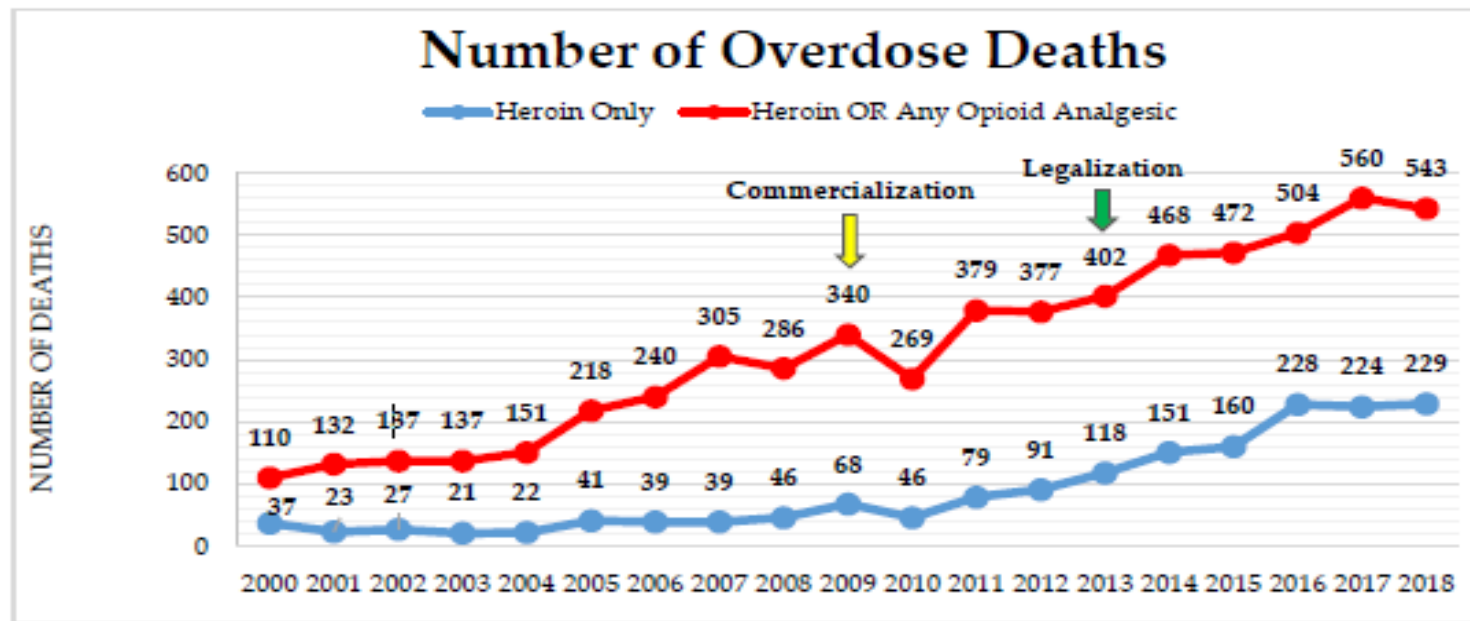
SOURCE: Colorado Department of Public Health and Environment (CDPHE), Colorado Violent Death Reporting System



Overdoses

Colorado Opioid Overdose Deaths

- ❖ This data is included in response to reports of declining opioid overdose deaths post marijuana legalization.



Source: Colorado Department of Public Health & Environment, Vital Statistics Program



Does route matter?

- Review of ED visits from marijuana related illnesses
- Compared edibles versus inhaled
- Inhaled visits more frequent (approx. 90%)
- Reasons for visits: (in order of frequency)
 1. Hyperemesis syndrome
 2. Intoxication
 3. Psychiatric symptoms (new acute, acute worsening, worsening of chronic)
- Edibles caused more psychiatric and cardiovascular visits



Hyperemesis Syndrome

- Recongized before 2009...
- Reported numerous system issues...



Table 1 Harmful effects of cannabinoids on body systems^[1,6,7]

Cognitive and mental health

- Impaired memory
- Impaired attention, organization and integration of complex information
- Association with schizophrenia
- Increased risk for depression

Pulmonary

- Carcinogenic effect
- Obstructive lung disease
- Increased propensity toward infections
- Acute and chronic bronchitis

Behavioural

- Weapon possession and physical fighting
- Unwanted and unprotected sexual encounters
- Unwanted pregnancies
- School dropout
- Amotivational syndrome
- Impairment of driving skill and coordination

Endocrine

- Decreased testosterone, sperm motility and production, disruption of ovulatory cycle

Pregnancy

- Low birth weight
- Problems with attention, memory and higher cognitive function

Cardiovascular

- Stroke
- Dose-dependent increase in HR
- Orthostasis
- Decreased exercise tolerance
- Precipitation of angina or myocardial infarction

Hyperemesis Syndrome

- Type of cyclic vomiting syndrome but with frequent marijuana use
- “hot bathing” improves symptoms
- Treatments: supportive care but cessation of marijuana is “best” treatment



Symptoms of Cannabinoid Hyperemesis Syndrome

Nausea



Tendency to use extremely hot baths/showers for relief



Stomach pain



Difficulty eating or keeping food down



Weight loss



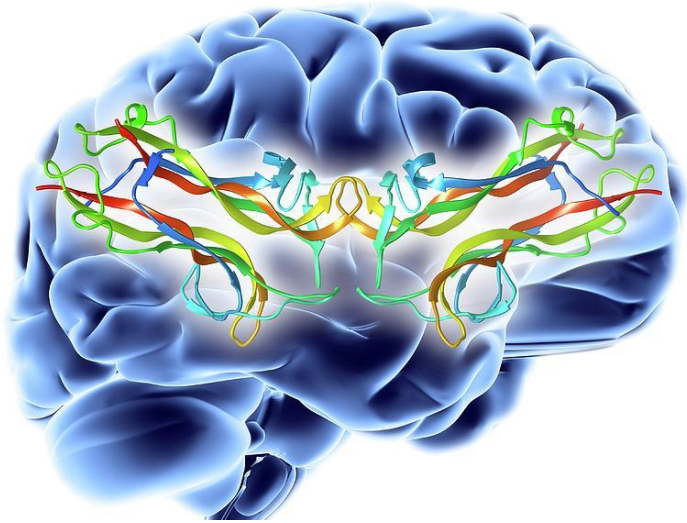
Severe vomiting and/or diarrhea, sometimes for days or weeks



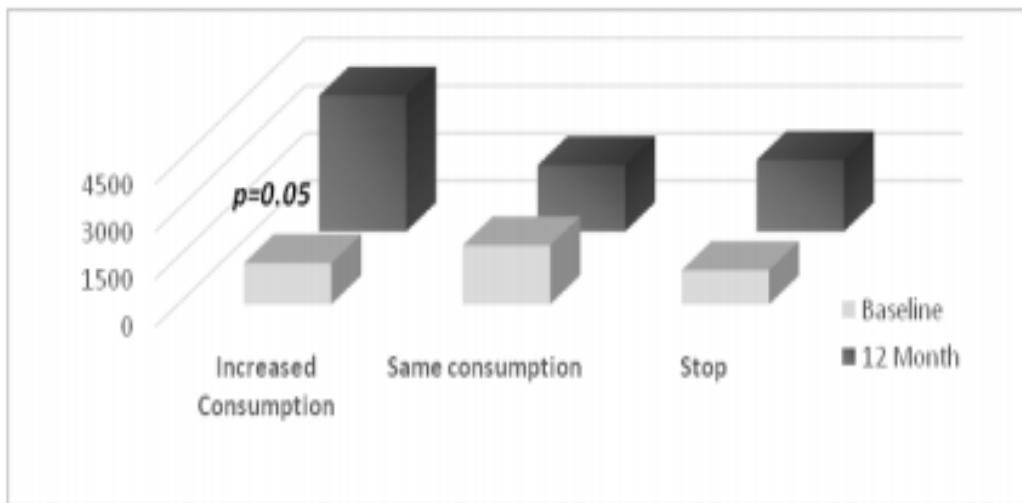
Source: Annals of Internal Medicine, March 2019; Base & Clinical Pharmacology & Toxicology, January 2018; BMJ Journals Gut, October 2004

BUSINESS INSIDER

Brain development-Brain Derived Neurotropic Factor (BDNF)



- Plays a “critical role” in brain development and plasticity
- Longitudinal study for uniformity
- Many animal studies demonstrate alterations
- Dose and time dependent
- Provide plausible explanation to cravings
- High concentration in the Hippocampus
- Increases odd for hyperexcitability
- Confirmed by volumetric reduction of hippocampus



In South Carolina

- Approximately 11%, 12+ have used marijuana in last year
- 6.7% last month
- 33.3% high school age have “tried” marijuana
- 50% of discharged patient from DAODAS treatment facilities were for Marijuana use disorder
- Marijuana use is widespread throughout SC and places “individuals at higher odds of other substance use and adverse behaviors”.



it's a big
DEAL



In Summary:

- THC and CBD are very different compounds
- The economic benefit is questionable
- Most claims of benefit are unfounded
- Marijuana is an addictive substance
- This is a pathway to reactionary usage/legalization
- Let's not have an "Opioids 2.0"



My ask...

- Please do your due diligence
- Let's not assume anything
- Safety for our patients is paramount





- Kevin B. Walker, M.D., FASA

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