Virtual Colorado MAT Learning Forum

Cannabis

Weighing the evidence behind the risks and benefits

Ryan Jackman, MD

SCL - St. Mary's Integrated Addiction Medicine

January 9, 2020

Monthly Webinars

- ***Virtual CO MAT Learning Forum***

  1st Thursday 12:30pm-1:30pm

  REGISTER

- ***Induction Basics: Tips from the Trenches****

  2nd Tuesday 7:30am-8:30am

  REGISTER

  * *same topic each month*

- ***Denver Health Learning Collaborative***

  3rd Wednesday 12:15pm-1:15pm

  REGISTER

Denver Health Addiction Journal Club

- 2020 Dates
  - *Every fourth Tuesday January-October*
  - *November 10th*
  - *December 8th*
  - Time; noon to 1 pm
- To join; email ITMATTTRs2@UCDENVER.EDU

CANNABIS

Weighing the evidence behind the risks and benefits

Ryan Jackman, MD

SCL - St. Mary's Integrated Addiction Medicine

Disclaimer

What this presentation is:

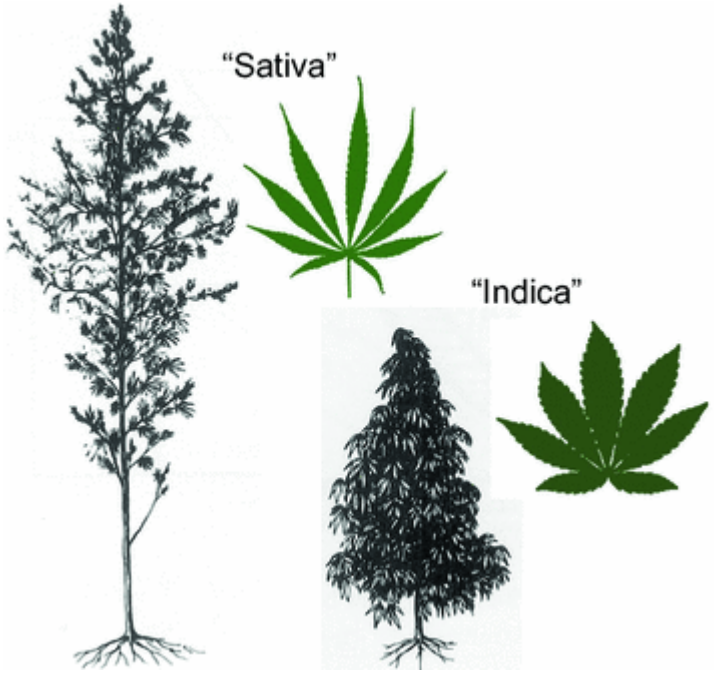
- Review of the history of cannabis, and how it has changed over time
- Discussion of the medical literature regarding evidence for the benefits and harms of cannabis, and where further studies are needed.
- Discussion regarding diagnosing cannabis use disorder in a state where it's use is legal

What this presentation is not:

- A discussion of laws and regulations on medical and recreational cannabis
- An advanced lesson in botany
- 100% unbiased

Cannabis: A brief History

- *Cannabis sativa* is native to Central Asia (China), and was originally cultivated there for its strength as a fiber, ability to be used as a food, and for seeds potential medicinal value.
- *Cannabis indica* is native to the Southern Asia (India) and was originally cultivated for its THC content and psychoactive potential
- *Cannabis ruderalis* is thought to be the ancestor of both strains or a hybrid of that ancestor.



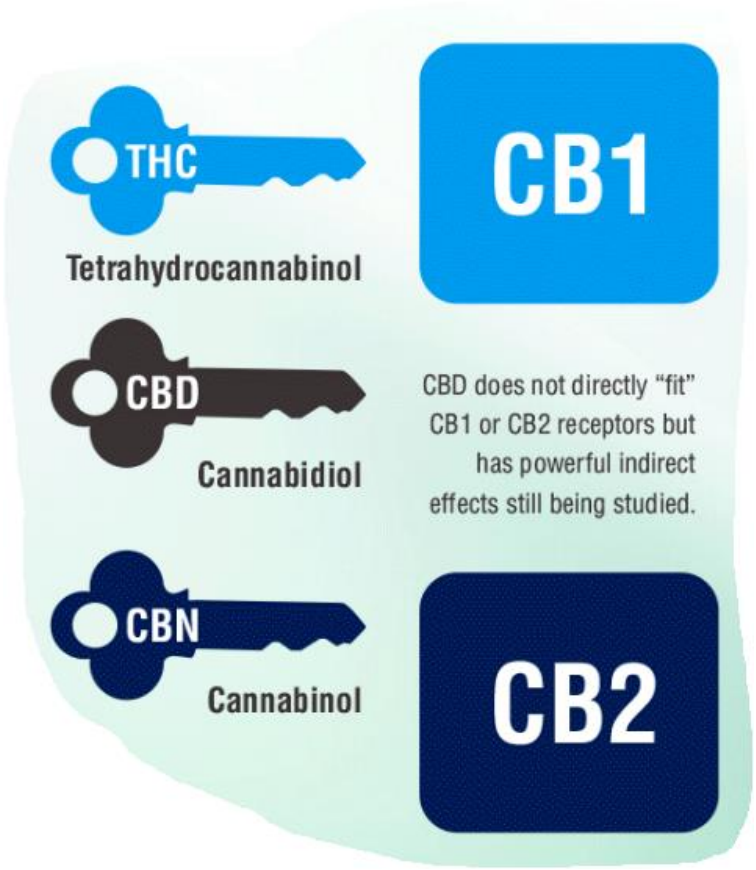
A brief history continued

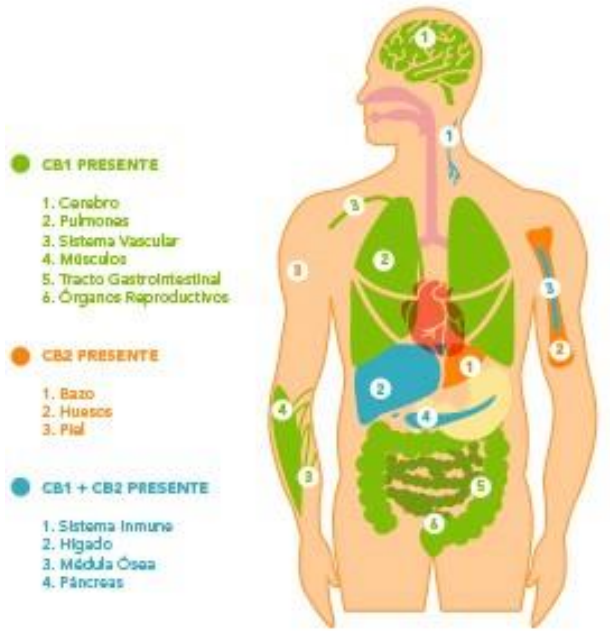
- 2700 BC Pen Ts'ao identifies cannabis for medicinal value (seeds)
- 450 BC: Herodotus, records use of the seeds at a Scythian funeral for their euphoric effect
- 200 BC: Greco-Roman use for toothaches, earaches, labor pains. Used as an anesthetic combined with wine.
- 1600 AD first record of being transported to the New World due to ease with which it grew
- 1839 AD introduced to Western Medicine by William O'Shaughnessy – Cholera
- 1800s-1900s numerous countries criminalize its use: Singapore (1870), Greece (1890), Mexico (1920), South Africa (1922), Canada (1923), Australia (1926), U.K. (1928), U.S. (1937)
- 1960 -1995 THC, Anandamide, 2AG, and the cannabinoid receptors are identified

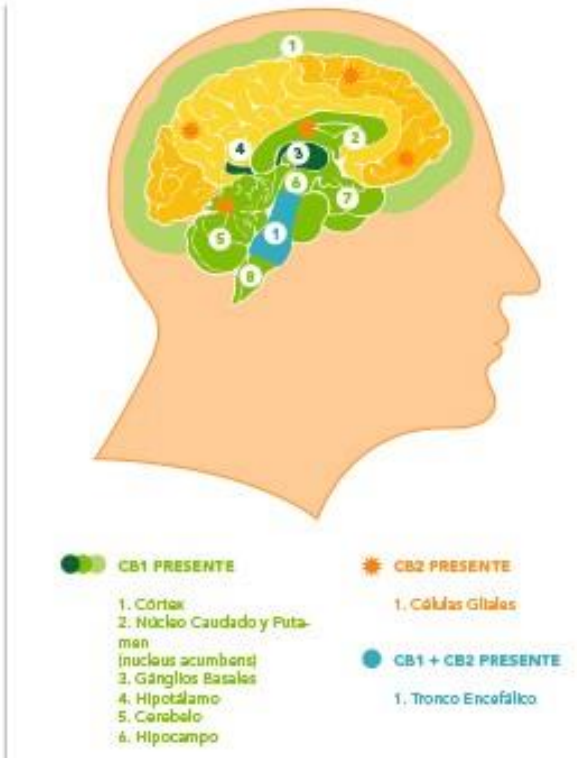
"RECEPTORS ARE MADE FOR COMPOUNDS THAT WE PRODUCE, NOT BECAUSE THERE IS A PLANT OUT THERE"

-Raphael Mechoulam

Cannabis Receptors: Types, Locations, and Ligands

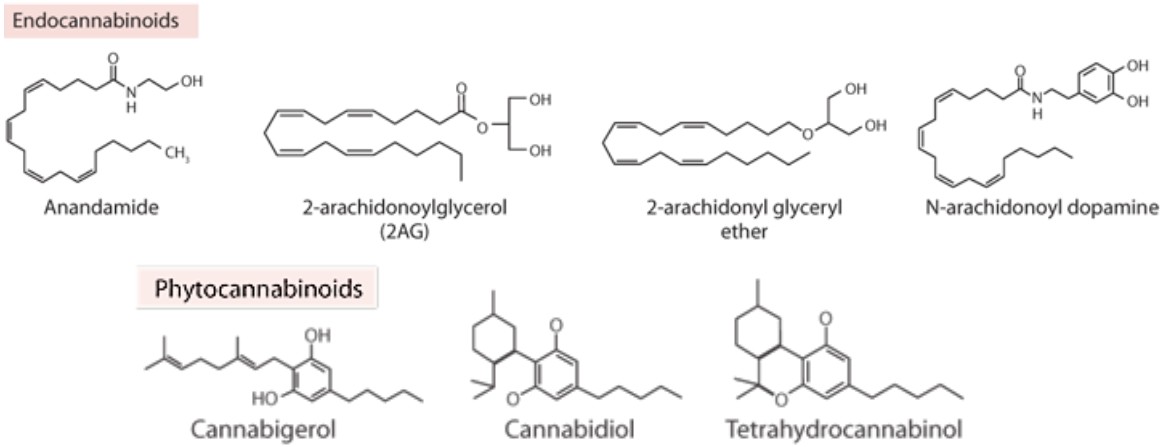


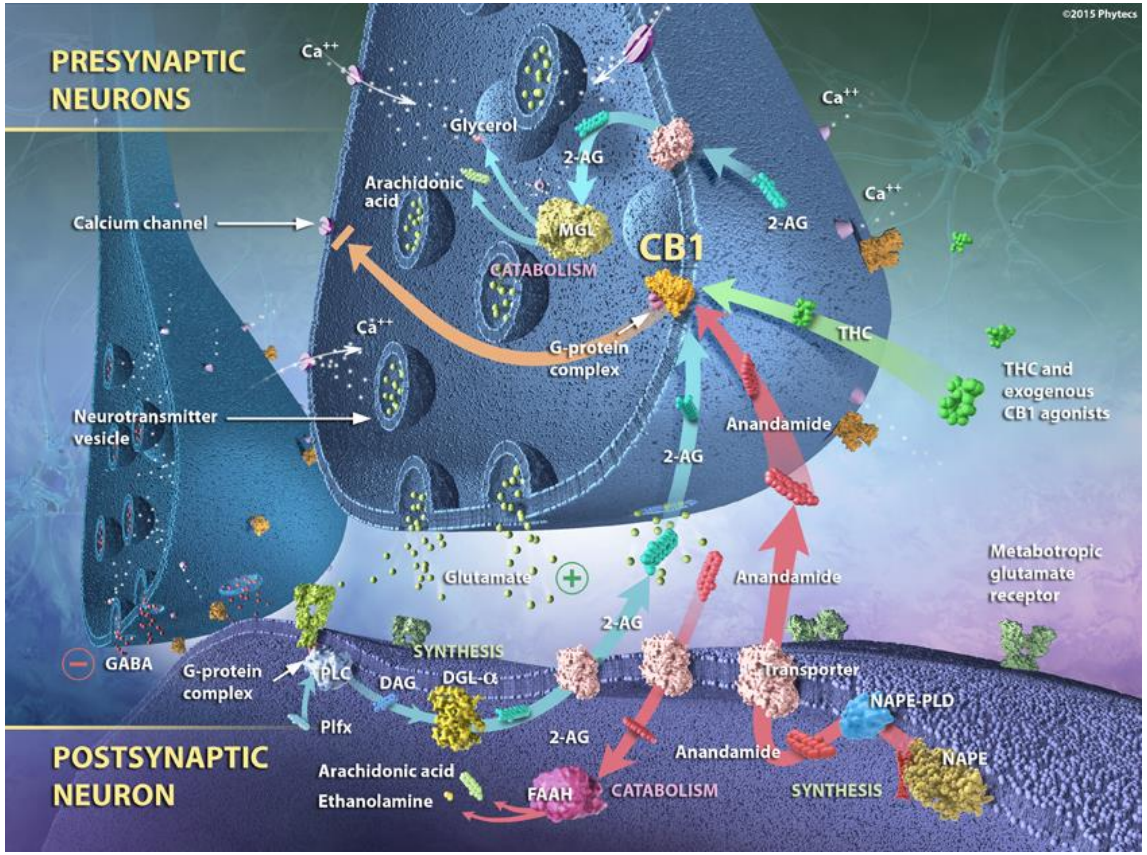




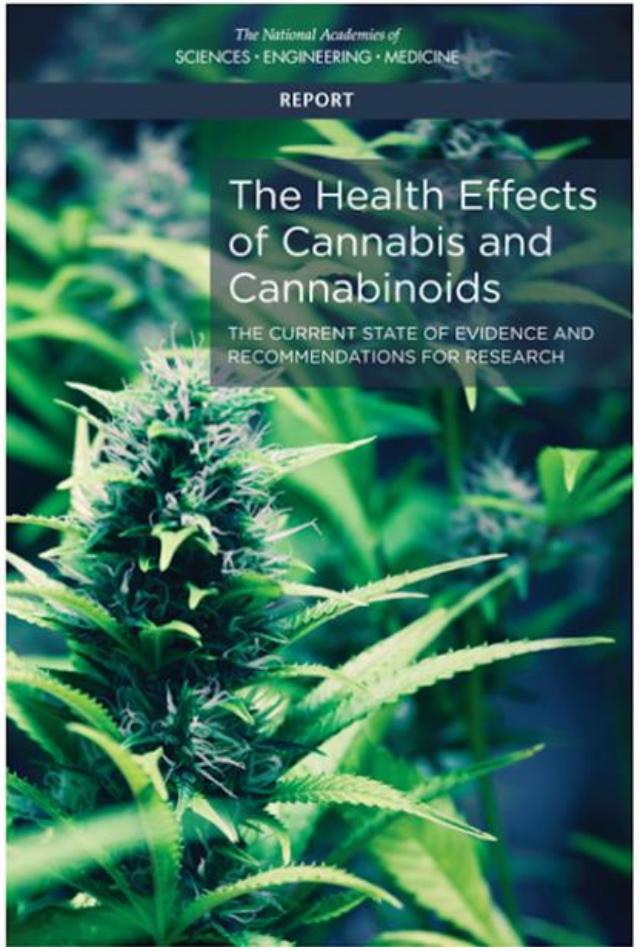
Neurobiology of Cannabis Receptors

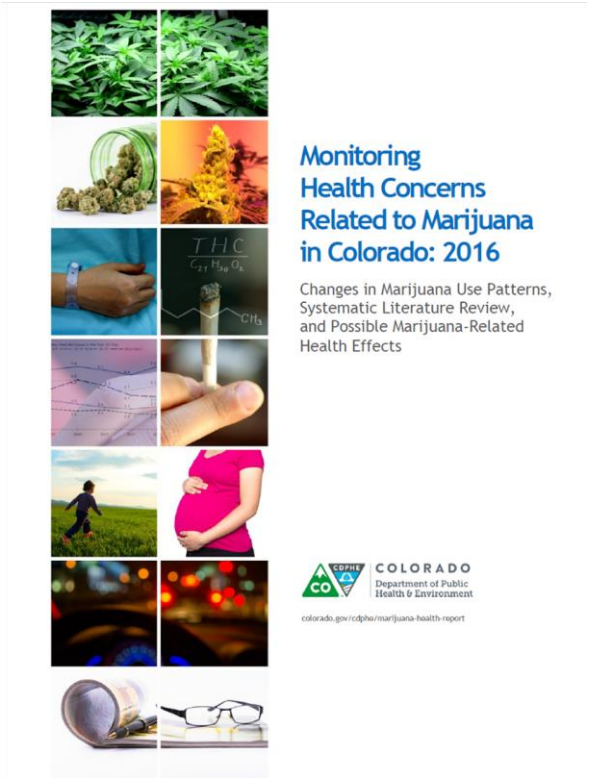
The endocannabinoid system plays a key role in dialing down neurotransmitter release

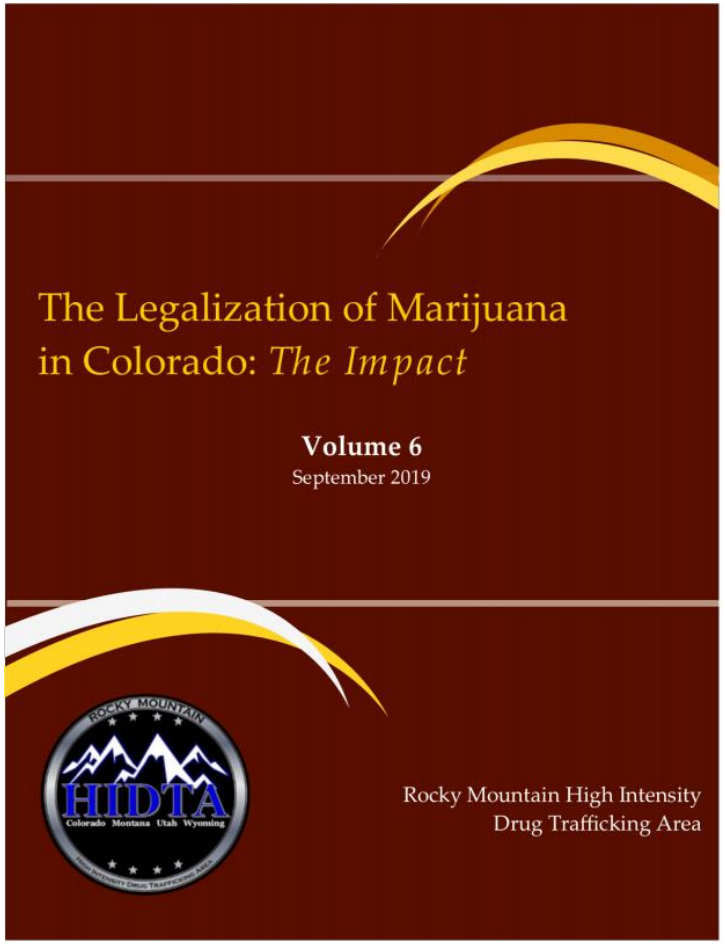




Risks and benefits of exploiting the endocannabinoid system







Cannabis / Cannabinoids: Therapeutic EVIDENCE

CONCLUSIVE or SUBSTANTIAL

- Chronic pain
- Antiemetics for chemo-induced nausea/vomiting
- MS spasticity symptoms

MODERATE

- Improving short-term sleep in obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and MS

LIMITED

- ↑ appetite and ↓ weight loss associated w/ HIV/AIDS
- ↓ symptoms of Tourette syndrome
- ↓ anxiety symptoms in social anxiety disorders
- ↓ PTSD symptoms
- Better outcomes (i.e., mortality, disability) after traumatic brain injury

NO or INSUFFICIENT

- Cancers, including glioma
- Cancer-associated anorexia cachexia syndrome and anorexia nervosa
- Symptoms of irritable bowel syndrome
- Epilepsy
- Spasticity in patients w/ paralysis due to spinal cord injury
- Amyotrophic lateral sclerosis related symptoms
- Chorea and certain neuropsychiatric symptoms associated w/ Huntington's disease
- Motor system symptoms associated w/ Parkinson's disease
- Dystonia
- Achieving abstinence in the use of addictive substances
- Improved mental health outcomes in individuals w/ schizophrenia

Parhami I, Hurley B, American Society of Addiction Medicine, 2018 Annual Conference. (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

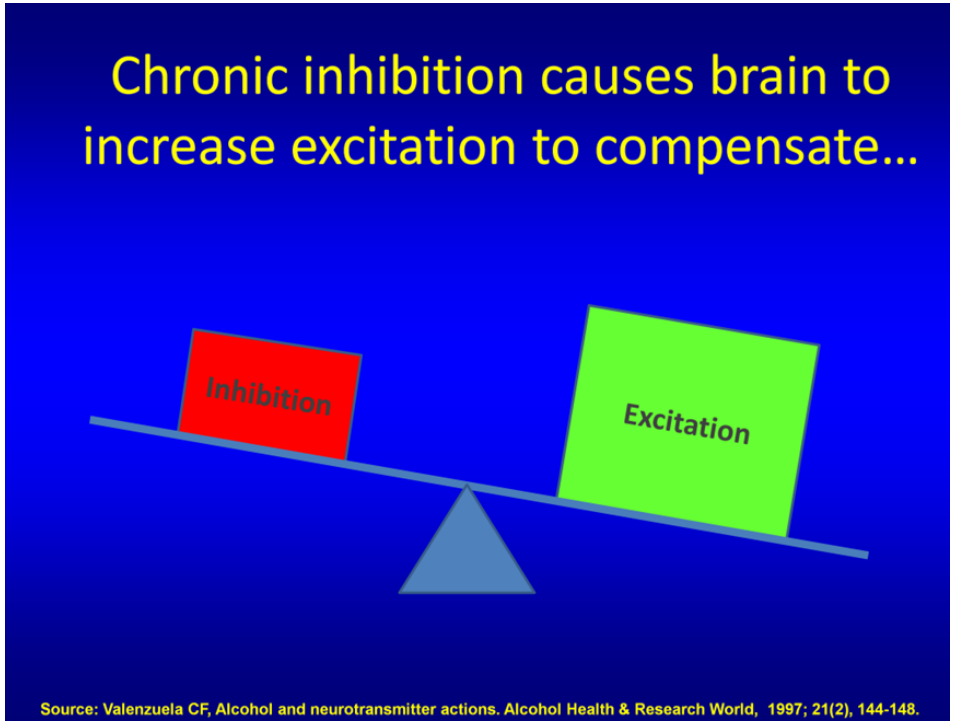
Los Angeles County
DEPARTMENT OF
MENTAL HEALTH

Antiemetic

- 28 RCTs were reviewed comparing cannabis to placebo or other agents like ondansetron (Zofran).
- Only 3 studies in children
- Mainly in Chemo-induced nausea
- Found that cannabis was as effective as other agents, but was preferred over other agents
- Cannabis had more side effects (dizziness, dysphoria, euphoria, sedation)
- Studies over 30 years old and are the reason we have dronabinol (Marinol) and nabilone (Cesamet) that are FDA approved

Cannabis Hyperemesis Syndrome

- Occurs in individuals with regular use (20 days or more per month) of high THC containing products
- In a recent study 32.9% experienced CHS (This would be 2.75 million persons if extrapolated to the general population)



Chronic Pain

- In 2014, 94% of Coloradans with medical marijuana had them for "severe pain"
- Multiple studies in states that have enacted medical marijuana laws demonstrate decreases in their opioid overdose rates, including relative to states that don't have legal marijuana access

Studies that associate marijuana with decrease in opioid use and overdose

- Bachhuber MA, Saloner B, Cunningham CO, et al. Medical cannabis laws and opioid analgesic overdose mortality in the United States, 1999-2010. *JAMA Intern Med* 2014; 174:1668-1673
- Kim JH, Santaella-Tenorio J, Mauro C, et al. State medical marijuana laws and the prevalence of opioids detected among fatally injured drivers. *Am J Public Health* 2016; 106:2032-2037
- 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; 36:945-951

Studies that suggest that this is not the case

- Caputi TL, Humphreys K. Medical marijuana users are more likely to use prescription drugs medically and nonmedically. *J Addict Med* 2018; 12:295-299
- Rogers AH, Bakhshaie J, Buckner JD, et al. Opioid and cannabis co-use among adults with chronic pain. *J Addict Med* 2019; 13:287-294

Chronic pain continued

CONCLUSION:

There is evidence for the use of low-dose medical marijuana in refractory neuropathic pain in conjunction with traditional analgesics. However, trials were limited by short duration, variability in dosing and strength of delta-9-tetrahydrocannabinol, and lack of functional outcomes. Although well tolerated in the short term, the long-term effects of psychoactive and neurocognitive effects of medical marijuana remain unknown. Generalizing the use of medical marijuana to all CNCP conditions does not appear to be supported by existing evidence. Clinicians should exercise caution when prescribing medical marijuana for patients, especially in those with nonneuropathic CNCP.

Deshpande A, Mailis-Gagnon A, Zoheiry N, et al. Efficacy and adverse effects of medical marijuana for chronic noncancer pain: systematic review of randomized controlled trials. *Can Fam Physician* 2015; 61:e372–e381

Results: Medical marijuana users were significantly more likely (RR 1.62, 95% confidence interval [CI] 1.50–1.74) to report medical use of prescription drugs in the past 12 months. Individuals who used medical marijuana were also significantly more likely to report nonmedical use in the past 12 months of any prescription drug (RR 2.12, 95% CI 1.67–2.62), with elevated risks for pain relievers (RR 1.95, 95% CI 1.41–2.62), stimulants (RR 1.86, 95% CI 1.09–3.02), and tranquilizers (RR 2.18, 95% CI 1.45–3.16).

Conclusions: Our findings disconfirm the hypothesis that a population-level negative correlation between medical marijuana use and prescription drug harms occurs because medical marijuana users are less likely to use prescription drugs, either medically or nonmedically. Medical marijuana users should be a target population in efforts to combat nonmedical prescription drug use.

Caputi TL, Humphreys K. Medical marijuana users are more likely to use prescription drugs medically and nonmedically. *J Addict Med* 2018; 12:295–299

Epilepsy

- Cannabis may interact with some current antiepileptic medications
- There is insufficient evidence that cannabis decreases seizure frequency when reviewing epilepsy diagnoses collectively
- There is evidence that when assessing refractory epilepsy - particularly Lennox-Gestaut and Dravet's Syndromes that cannabis may have a role.
- A 2016 study showed that in treating intractable seizures in 74 children with a CBD to THC 20:1 ratio for an average of 6 months that 18 percent of children experienced a 75–100 percent reduction in seizure frequency, 34 percent experienced a 50–75 percent reduction, 12 percent reported a 25–50 percent reduction, 26 percent reported a reduction of less than 25 percent, and 7 percent reported aggravation of seizures.

EVIDENCE | Cannabis / Cannabinoids and Medical/Health Risk

CONCLUSIVE or SUBSTANTIAL

- ↑ respiratory symptoms and chronic bronchitis episodes
- ↑ motor vehicle crashes
- ↑ lower birth weight of offspring

MODERATE

- ↑ overdose injuries, including respiratory distress, among pediatric populations where cannabis is legal
- CESSATION of cannabis use associated w/ improvements in respiratory symptoms
- *NO* association w/ lung, head and neck cancers

LIMITED

- ↑ prediabetes
- ↑ non-seminoma-type testicular germ cell tumors
- ↑ triggering of acute myocardial infarction or stroke
- ↓ metabolic syndrome and diabetes
- ↑ chronic obstructive pulmonary disease
- ↓ production of several inflammatory cytokines
- ↑ pregnancy complications
- ↑ admission of infant to neonatal intensive care unit

NO or INSUFFICIENT

- Incidence of esophageal, bladder, prostate, cervical, penile, and anal cancer; malignant gliomas, non-Hodgkin lymphoma, Kaposi's sarcoma
- ↑ leukemia, rhabdomyosarcoma, astrocytoma, or neuroblastoma in offspring
- Hospital admissions for COPD
- Asthma development or asthma exacerbation
- All-cause mortality
- Occupational accidents or injuries
- Death due to cannabis overdose
- Later outcomes in offspring (e.g., sudden infant death syndrome, cognition/academic achievement, and later substance use)

Parhami I, Hurley B, American Society of Addiction Medicine, 2018 Annual Conference. (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

Los Angeles County
DEPARTMENT OF MENTAL HEALTH

CNN health Food Fitness Wellness Parenting Vital Signs • LIVE TV Edition

Vaping-related lung injuries surpass 2,500 cases nationwide, CDC says

By Jacqueline Howard, CNN

Updated 2:08 PM ET, Thu December 19, 2019

As of December 17th the CDC reports

- 2,506 cases with injuries in all 50 states, District of Columbia, and Puerto Rico
- 54 deaths in 27 states (CO is not currently one of them)
- Median age is 24, range 13-75, median age of deaths is 52 years (17-75)
- 84% used cannabis, 64% used both cannabis and nicotine, 11% used nicotine exclusively
- Vitamin E acetate is currently suspected to be the culprit

MFS 2019 shows that 12th grader cannabis vaping is up to 20.8%

Original Article

Effect of intrauterine marijuana exposure on fetal growth patterns and placental vascular resistance

Bobby K. Brar, Pooja S. Patil, David N. Jackson, Michael O. Gardner, James M. Alexander & Nora M. Doyle

Received 04 Sep 2019, Accepted 18 Oct 2019, Published online: 11 Nov 2019

The Journal of Maternal-Fetal &Neonatal Medicine

Results: In 55 first trimester ultrasounds, there were no differences in crown rump lengths or nuchal translucencies between the groups. Likewise, in 195-second trimester ultrasounds, no differences were noted in biometry. Second trimester umbilical artery systolic to diastolic ratios were higher in marijuana users compared to nonusers (4.02 versus 3.92, $p = .024$). In the third trimester, 26 of 192 marijuana exposed fetuses were growth restricted compared to 6 of 192 controls ($p = .002$), and umbilical artery systolic to diastolic ratios were higher (3.52 versus 3.12, $p = .0001$). Four cases of absent and reversed en diastolic flow were observed in marijuana users, while no cases were observed in controls.

Conclusions: Our data shows that daily marijuana use is associated with impaired fetal growth and increased placental vascular resistance. Marijuana consumption in pregnancy should be avoided until further studies delineate its exact potential for fetotoxicity.

ORIGINAL RESEARCH

Cannabis Use Based on Urine Drug Screens in Pregnancy and Its Association With Infant Birth Weight

Howard, D. Scott MD; Dhanraj, David N. MD, MBA; Devaiah, C. Ganga MS; Lambers, Donna S. MD

Journal of Addiction Medicine: November/December 2019

Results:
The prevalence of cannabis use in pregnancies not complicated by use of other drugs as evidenced by tetrahydrocannabinol in the urine of 2173 patients was 22.6%. Infants born to mothers who tested positive for only tetrahydrocannabinol in urine at both presentation for prenatal care and delivery were of lower median birth weight compared with those who tested negative [2925 g (IQR 2522–3265) vs 3235 g (IQR 2900–3591), *P* = <0.001]. There was no clinically relevant difference in gestational age at birth [39.0 weeks (IQR 37.1–40.0) vs 39.3 weeks (IQR 38.3–40.0), *P* = 0.012] between those positive for tetrahydrocannabinol (THC) and those who tested negative. Concomitant tobacco use during pregnancy was not noted to impact infant birth weight using the analysis of covariance. Higher perinatal mortality was observed among those who used cannabis with an adjusted odds ratio of 4.2 (95% CI, 1.53–11.49).

Conclusions:
Cannabis use is negatively correlated with fetal birth weight (up to 450 g less) in patients who tested positive for THC when compared with those who did not as documented in the urine drug screens. On the basis of these findings, additional patient education and cessation interventions should be explored with regard to cannabis use in pregnancy.

Cardiol Ther. 2018 Jun; 7(1): 45–59.
Published online 2017 Dec 7. doi: 10.1007/s40119-017-0102-x
PMCID: PMC5986667
PMID: 29218644

Cardiovascular Complications of Marijuana and Related Substances: A Review

Amitoj Singh, Sajeev Saluja, Akshat Kumar, Sahil Agrawal, Munveer Thind, Sudip Nanda, and Jamshid Shirani

Cannabis is associated with:

- Activation of the sympathetic nervous system and inhibition of the parasympathetic autonomic nervous system induces tachyarrhythmias and atrial fibrillation
- Cannabinoids reduce myocardial contractility through CBR1 mediated effects
- Induction of hypercoagulable state increases risk for AMI and CVA
- Young men with no pre-existing coronary artery disease at increased risk for events including sudden cardiac death

Circulation. 2001 Jun 12;103(23):2805-9.

Triggering myocardial infarction by marijuana.

Mittleman MA[1], Lewis RA, Maclure M, Sherwood JB, Muller JE.

- Risk of AMI increases nearly fivefold within an hour of exposure to cannabis compared to nonusers

EVIDENCE | Cannabis / Cannabinoids and Mental Health Risks

CONCLUSIVE or SUBSTANTIAL

- ↑ schizophrenia or other psychoses, w/ highest risk among most frequent cannabis users

MODERATE

- ↑ Impairment in learning, memory, and attention
- ↑ mania/hypomania symptoms
- ↑ depressive disorders
- ↑ suicidal ideation/attempts/completion w/ higher incidence among heavier cannabis users
- ↑ social anxiety disorder
- ↑ negative symptoms of schizophrenia (e.g., blunted affect)
- Better cognitive performance among individuals w/ psychotic disorders and a history of cannabis use vs. those without history of cannabis use

LIMITED

- ↑ impairment of academic achievement
- ↑ unemployment/low income rates
- ↑ impairment of social functioning and developmentally appropriate social roles
- Sustained abstinence continues to be associated w/ impairments in cognitive domains of learning, memory, and attention
- ↑ positive symptoms of schizophrenia (e.g., hallucinations)
- ↑ anxiety symptoms
- ↑ PTSD severity
- ↑ development of bipolar disorder and any anxiety disorder, except social anxiety disorder

NO or INSUFFICIENT

- Changes in the course or symptoms of depressive disorders
- Development of PTSD

Parhami I, Hurley B, American Society of Addiction Medicine, 2018 Annual Conference. (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

Los Angeles County
DEPARTMENT OF
MENTAL HEALTH

THE LANCET
Psychiatry

Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis

Nicola Black, PhD; Emily Stockings, PhD; Gabrielle Campbell, PhD; Lucy T Tran, BPsychSci(Hons); Dino Zagic, BPsychSci(Hons); Prof Wayne D Hall, PhD; et al.

Volume 6 Issue 12, P995-1010, December 1, 2019

Findings

83 eligible studies (40 randomised controlled trials, n=3067) were included: 42 for depression (23 randomised controlled trials; n=2551), 31 for anxiety (17 randomised controlled trials; n=605), eight for Tourette syndrome (two randomised controlled trials; n=36), three for ADHD (one randomised controlled trial; n=30), 12 for post-traumatic stress disorder (one randomised controlled trial; n=10), and 11 for psychosis (six randomised controlled trials; n=281). Pharmaceutical THC (with or without CBD) improved anxiety symptoms among individuals with other medical conditions (primarily chronic non-cancer pain and multiple sclerosis; SMD −0·25 [95% CI −0·49 to −0·01]; seven studies; n=252), although the evidence GRADE was very low. Pharmaceutical THC (with or without CBD) worsened negative symptoms of psychosis in a single study (SMD 0·36 [95% CI 0·10 to 0·62]; n=24). Pharmaceutical THC (with or without CBD) did not significantly affect any other primary outcomes for the mental disorders examined but did increase the number of people who had adverse events (OR 1·99 [95% CI 1·20 to 3·29]; ten studies; n=1495) and withdrawals due to adverse events (2·78 [1·59 to 4·86]; 11 studies; n=1621) compared with placebo across all mental disorders examined. Few randomised controlled trials examined the role of pharmaceutical CBD or medicinal cannabis.

Interpretation

There is scarce evidence to suggest that cannabinoids improve depressive disorders and symptoms, anxiety disorders, attention-deficit hyperactivity disorder, Tourette syndrome, post-traumatic stress disorder, or psychosis. There is very low quality evidence that pharmaceutical THC (with or without CBD) leads to a small improvement in symptoms of anxiety among individuals with other medical conditions. There remains insufficient evidence to provide guidance on the use of cannabinoids for treating mental disorders within a regulatory framework. Further high-quality studies directly examining the effect of cannabinoids on treating mental disorders are needed.

Research Report

Rapid increase in the prevalence of cannabis use among people with depression in the United States, 2005–17: the role of differentially changing risk perceptions

Lauren R. Pacek, Andrea H. Weinberger, Jiaqi Zhu, Renee D. Goodwin

Society for the Study of Addiction , First published 4 December 2019

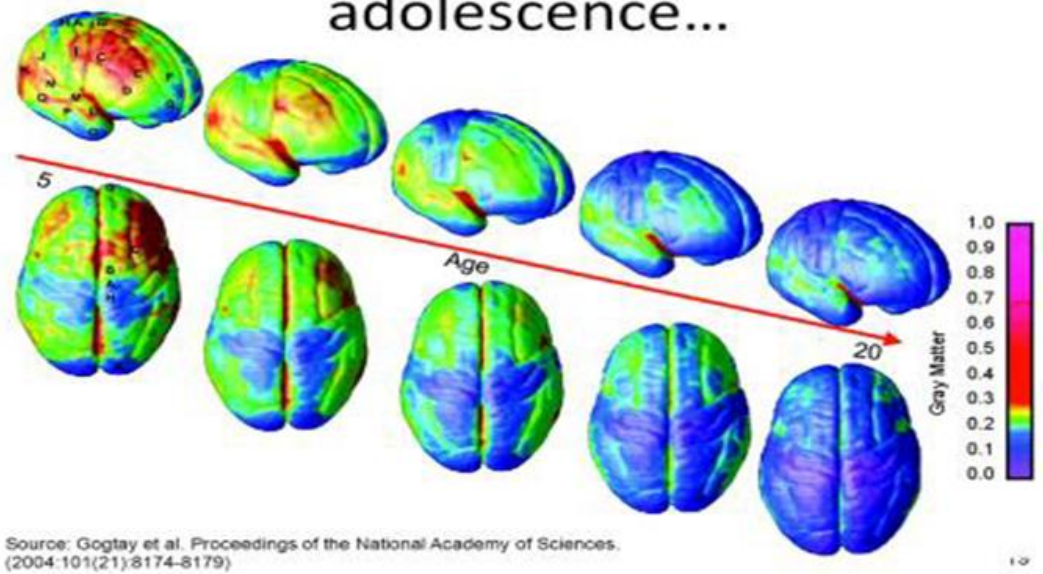
Findings

The prevalence of any, daily and non-daily cannabis use in the past month was higher among those with depression versus those without [e.g. 2017 for any use: 18.94 versus 8.67%; adjusted odds ratio (aOR) = 2.17 (95% confidence interval (CI) = 1.92, 2.45)]. Any, daily and non-daily cannabis use increased among people with and without depression from 2005 to 2017, yet the increase in any (aORs = 1.06 versus 1.05; *P* = 0.008) and daily (aORs = 1.10 versus 1.07; *P* = 0.021) cannabis use adjusted for socio-demographic characteristics was more rapid among those with depression. Perception of great risk associated with regular cannabis use was significantly lower among those with depression (*P* < 0.001) and decreased significantly more rapidly over the study period among people with depression, compared with those without (aORs = 0.89 versus 0.92; *P* < 0.001).

Conclusions

The prevalence of cannabis use in the United States increased from 2005 to 2017 among people with and without depression and was approximately twice as common among those with depression. People with depression experienced a more rapid decrease in perception of risk, which may be related to the more rapid increase in any and daily past-month cannabis use in this group.

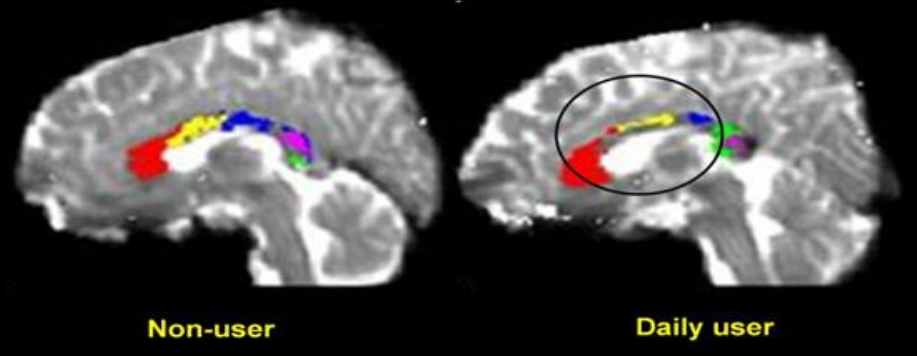
Myelination happens throughout adolescence...



Source: Gogtay et al. Proceedings of the National Academy of Sciences. (2004:101(21):8174-8179)

Slide courtesy of Susan Tapert, PhD.

White matter structure differences between marijuana users and non-users



Source: Arnone D, Barrick TR, Chengappa S et al. Corpus callosum damage in heavy marijuana use: Preliminary evidence from diffusion tensor tractography and tract-based spatial statistics. NeuroImage, 2008; 41:1067-1074

The Philadelphia Inquirer

Cannabis-related psychosis, addiction, ER visits: For young users, marijuana can be a dangerous game

by Rita Giordano, Updated: December 23, 2019

Episodes of acute psychosis seem to go away if the user stays off the drug. But adolescents who use especially high-potency marijuana may be at increased risk for developing a chronic psychotic disorder such as schizophrenia, particularly if they had a genetic predisposition. A recent article in the journal the Lancet said at least 12% of new cases of psychosis could be eliminated if high-potency marijuana wasn't available.

The National Institute on Drug Abuse cites research that suggests between 9% and 30% of people who use marijuana may develop use disorder, and the risk increases the younger someone starts using. Individuals who begin using cannabis before age 18 are four to seven times more likely than adults to develop marijuana use disorder. And the likelihood is that more young people will be impacted; two studies published earlier this month in the Journal of the American Medical Association found that more teenagers are vaping cannabis than ever before.

EVIDENCE | Problem Cannabis Use Associations

CONCLUSIVE or SUBSTANTIAL

Risk Factors for Developing Problem Cannabis Use

- Initiating cannabis use at earlier age
- Increases in cannabis use frequency
- Being male and smoking cigarettes

- Stimulant treatment of ADHD during adolescence is NOT a risk factor for the development of problem cannabis use

MODERATE

- ↑ PTSD severity
- ↑ substance use related disorders

Risk Factors for Developing Problem Cannabis Use

- Exposure to combined use of abused drugs
- Male
- Major depressive disorder
- *In Adolescents*: the frequency of cannabis use, oppositional behaviors, a younger age of first alcohol use, nicotine use, parental substance use, poor school performance, antisocial behaviors, and sexual abuse

NOT Associated w/ Developing Problem Cannabis Use

- Neither alcohol nor nicotine dependence alone
- Anxiety, personality disorders, or bipolar disorders
- Adolescent ADHD

LIMITED

- The initiation of tobacco use
- Changes in the rates and use patterns of other substances
- Childhood anxiety / depression are risk factors for development of problem cannabis use

Parhami I, Hurley B, American Society of Addiction Medicine, 2018 Annual Conference. (Adapted from: National Academies of Sciences, Engineering, and Medicine. 2017. The health effects of cannabis and cannabinoids: Current state of evidence and recommendations for research. Washington, DC: The National Academies Press.)

Los Angeles County
DEPARTMENT OF
MENTAL HEALTH

Treatment of CUD

Published in final edited form as:
J Addict Med. 2016 ; 10(4): 274–279. doi:10.1097/ADM.0000000000000229.

Sativex Associated With Behavioral-Relapse Prevention Strategy as Treatment For Cannabis Dependence: A case series

Jose M. Trigo[1], **Alexandra Soliman**[1], **Gregory Staios**[1], **Lena Quilty**[2], **Benedikt Fischer**[3,6,7,11], **Tony P. George**[4,7], **Jurgen Rehm**[3,5,6,7,8], **Peter Selby**[7,9,10], **Allan J. Barnes**[12], **Marilyn A. Huestis**[12], and **Bernard Le Foll**[1,9]

Conclusions—In summary, this pilot study found that with Sativex in combination with MET/CBT cannabis use decreased and withdrawal did not increase in the four participants completing the study. Further systematic exploration of Sativex as a pharmacological treatment option for cannabis dependence should be performed.

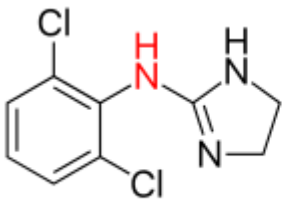
Published in final edited form as:
Drug Alcohol Depend. 2016 February 1; 159: 53–60. doi:10.1016/j.drugalcdep.2015.11.025.

Dronabinol and Lofexidine for Cannabis Use Disorder: A Randomized, Double-Blind, Placebo-Controlled Trial*

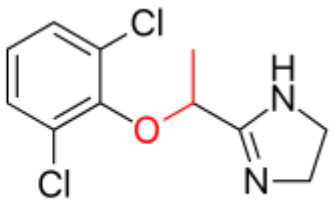
Frances R. Levin[1,2], **John J. Mariani**[1,2], **Martina Pavlicova**[3], **Daniel Brooks**[1], **Andrew Glass**[4], **Amy Mahony**[1], **Edward V. Nunes**[1,2], **Adam Bisaga**[1,2], **Elias Dakwar**[1,2], **Kenneth M. Carpenter**[1,2], **Maria A. Sullivan**[1,2], and **Jean C. Choi**[4]

Methods—One hundred fifty six cannabis-dependent adults were enrolled and following a 1-week placebo lead-in phase 122 were randomized in a double-blind, placebo-controlled, 11-week trial. Participants were randomized to receive dronabinol 20 mg three times a day and lofexidine 0.6 mg three times a day or placebo. Medications were maintained until the end of week eight, were then tapered over two weeks and patients were monitored off medications during the last study week. All participants received weekly motivational enhancement and relapse prevention therapy. Marijuana use was assessed using the timeline follow-back method.

Results—There was no significant difference between treatment groups in the proportion of participants who achieved 3 weeks of abstinence during the maintenance phase of the trial (27.9 % for the medication group and 29.5% for the placebo group), although both groups showed a reduction over time.



clonidine



lofexidine

Published in final edited form as:
Curr Psychiatr. 2018 June ; 17(6): 30–55.

N-acetylcysteine: A potential treatment for substance use disorders

Cessation

An open-label, pilot clinical trial found significant reductions in self-reported marijuana use and craving—but not in biomarkers of use—among 24 adolescents after 4 weeks of NAC, 1,200 mg twice daily.[24] In an 8-week, double-blind randomized controlled trial of 116 adolescents, NAC, 1,200 mg twice daily, plus contingency management doubled the odds of abstinence, but had no effect on self-reported craving or use.[25,26] In a sample of 302 adults, a 12-week trial of NAC, 1,200 mg twice daily, plus contingency management was no more effective than contingency management alone in promoting abstinence.[27]

Appropriate populations

Evidence is stronger for use of NAC among adolescents (age 15 to 21 years) than for individuals older than age 21.[25,27] Further research is needed to explore potential reasons for age-specific effects.

History repeating?

The British Decision

- The Indian Hemp Drugs Commission of 1893
  - Determine whether cannabis was more dangerous than opium because of the number of psychiatric hospitalizations for "cannabis induced insanity"
  - 361 page + 6 volume appendices ruled that the connection between use and insanity were overstated and that its use should not be criminalized just taxed more.
  - 120 page critique by Indian Nationals released pointing out that no distinction had been made between Bhang, Ganja, and Charas
  - The number of psychiatric admissions did not decrease after the report. Diagnosis listed as "Toxic Insanity"

Colorado Today

- Medical Use of Marijuana Act (2000), Legalization of Recreational Use (2012)
- 2018 statistics per The Impact Report 2019
  - 25% tax (10% sales+15% excise tax): Marijuana tax revenue represents 0.9% of CO FY 2018 budget
  - Marijuana use for ages 12+ increased by 58%, adult use increase 94% (both ranked 4th in US)
  - ED visits increase by 54%, hospitalization 101%
  - Marijuana only exposures quadrupled and suicide in which marijuana was present increased by 9%
  - Traffic deaths in which driver was positive increase 109%, overall traffic deaths increased by 31%

As of June 2017, there were 491 retail marijuana stores in the state of Colorado compared to 392 Starbucks and 208 McDonald's




QUESTIONS / DISCUSSION

Webinars

- See our website for previous presentations & resources as well as upcoming topics
  - https://www.practiceinnovationco.org/itmatttrs2/mat-forum/