The Problems with Today's High-Potency THC

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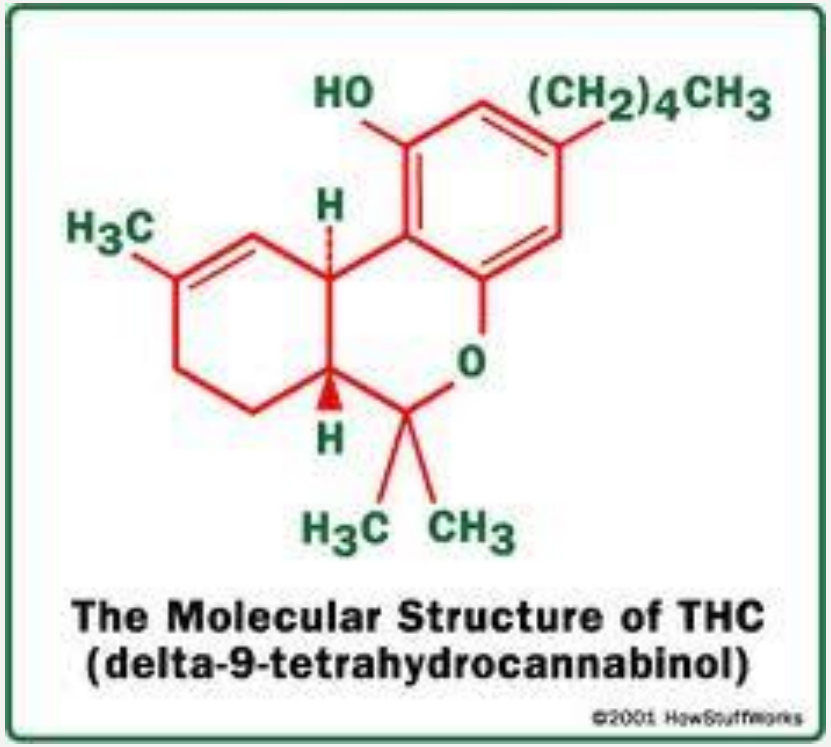
February 9, 2021

MARIJUANA AND THE ADOLESCENT BRAIN

VIRTUAL PRESENTATION FOR SUBLETTE PREVENTION COALITION, WYOMING

CANNABIS

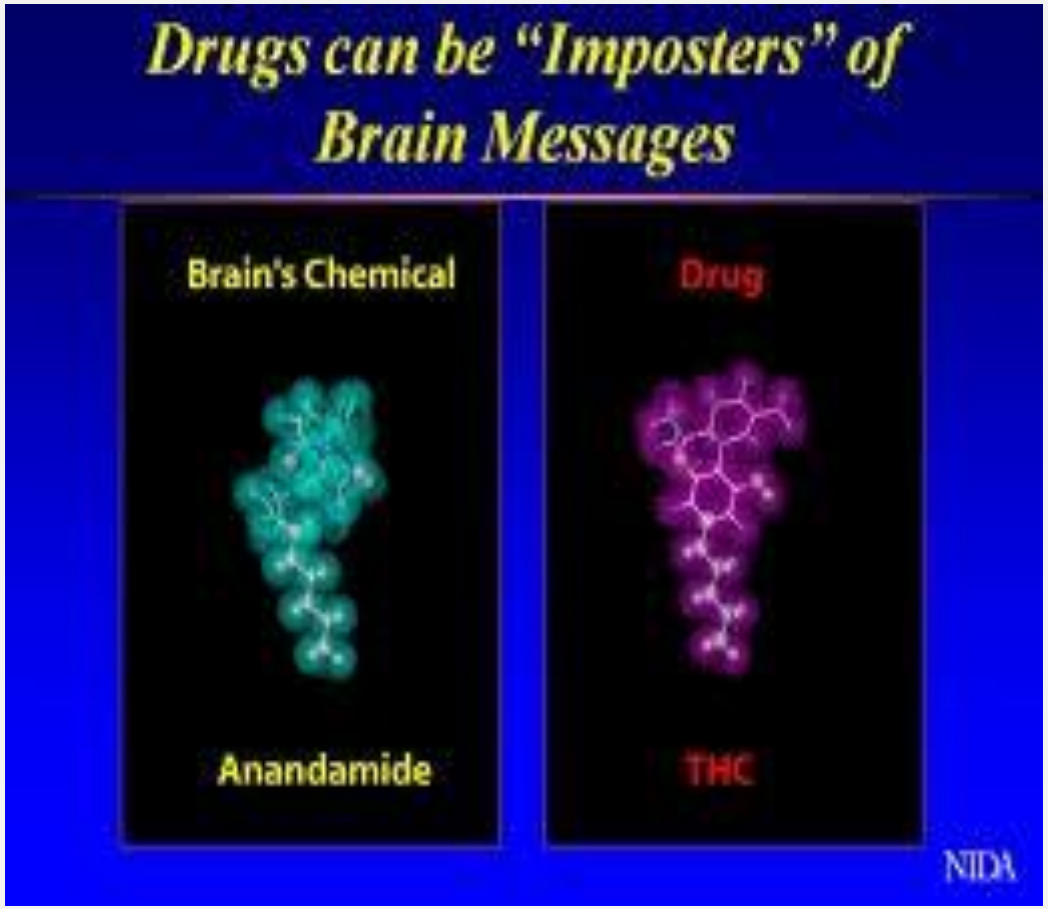
- Complex alkaloid mixture of more than 400 compounds
- At least 60 different compounds described with activity on the cannabinergic system in the body
- Most abundant cannabinoids are
  - Delta-9 tetrahydrocannabinol (most psychoactive) - THC
  - Cannabidiol - CBD
  - Cannabinol
- Effect first discovered in 1963 by Raphael Mechoulam in Israel – he injected THC into aggressive rhesus monkeys – they became calm and sedated



CANNABINERGIC SYSTEM

Two main cannabis receptors:

- CB1–present throughout CNS
  - Hippocampus
  - Cortex
  - Olfactory areas
  - Basal ganglia
  - Cerebellum
  - Spinal cord
- CB2 – located peripherally, linked with immune system
  - Spleen
  - Macrophages



Anandamides discovered in 1992 – Sanskrit word for "supreme joy

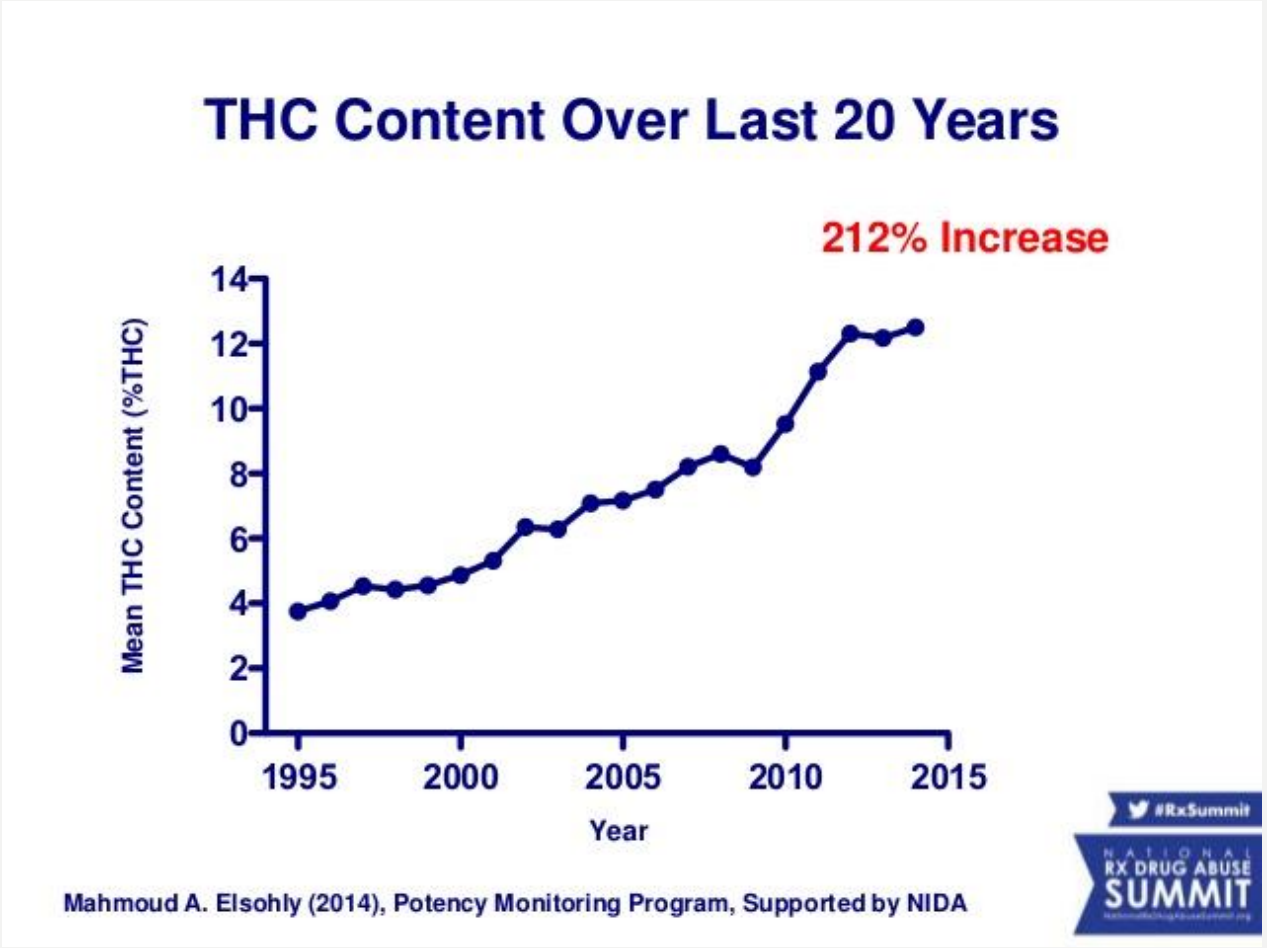
ENDOCANNABINOID RECEPTORS

- This is our mood regulatory system – CB1 receptors are for anandamides - "supreme joy"
- CB1 receptors regulate the balance between excitatory and inhibitory neuronal activity
- Exposure to cannabis during adolescence disrupts glutamate which plays an important role in synaptic pruning in PFC – disrupting normal brain development

Lubman et al. Cannabis and adolescent brain development. Pharmacology and Therapeutics 2015;148:1-16

BUT MARIJUANA TODAY IS NOT WHAT IT WAS IN THE PAST

Without any regulation, our state government has allowed the cannabis industry to increase the potency in marijuana and call it "medical" so that children and adults believe it is safe and good for them.



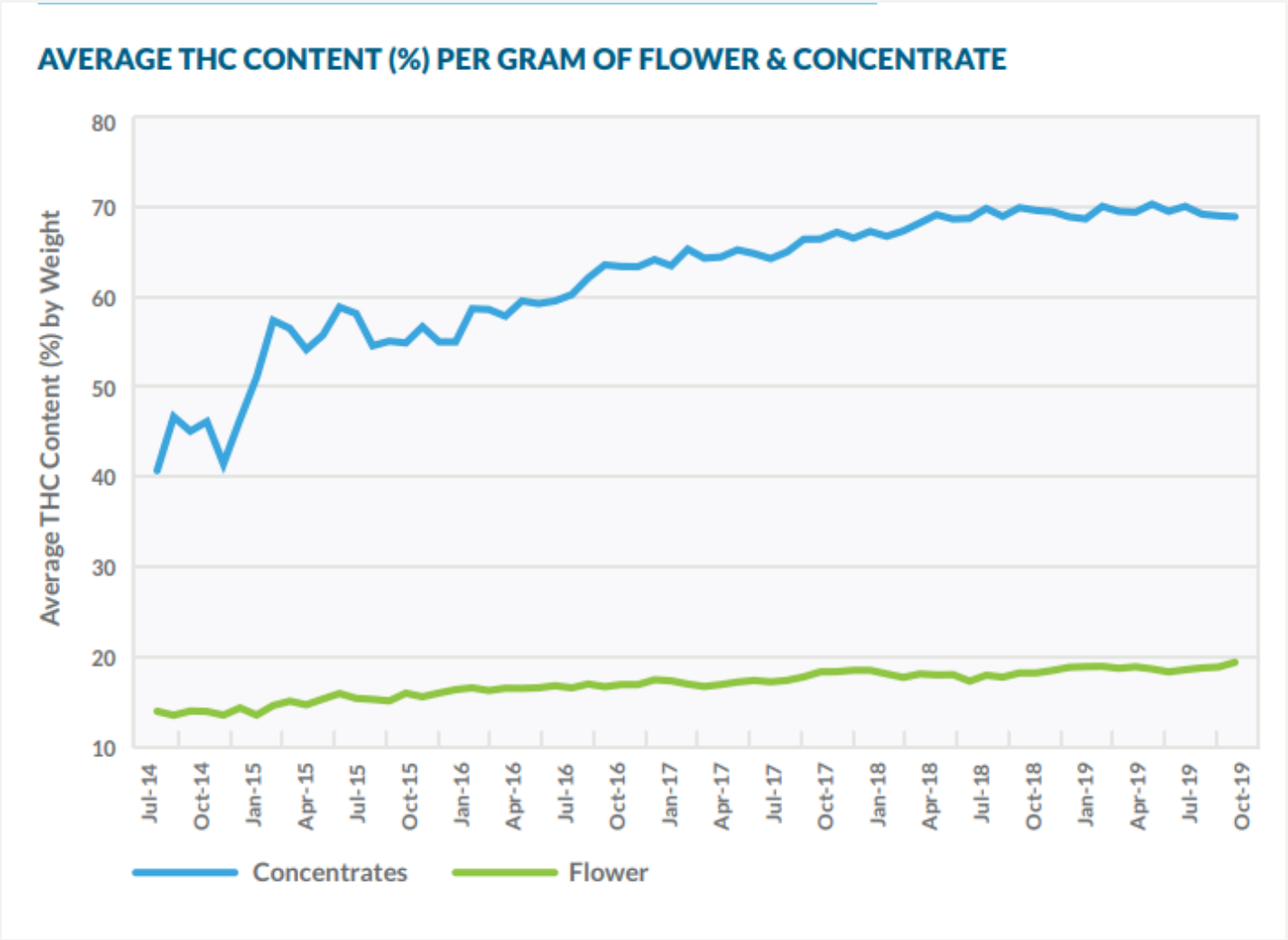
MASSIVE INCREASE IN THC POTENCY SINCE THE 1980'S

Up to the 1980's THC content was less than 2%

2000 – when Colorado legalized medical marijuana – THC not higher than 5% and there were no concentrates

2010 – concentrates began to appear in medical dispensaries

Average potency of marijuana flowers/buds in Colorado is now **18.8% THC** while the average potency for concentrates is **69.4%**. Potency rates of up to **95%** have been recorded.



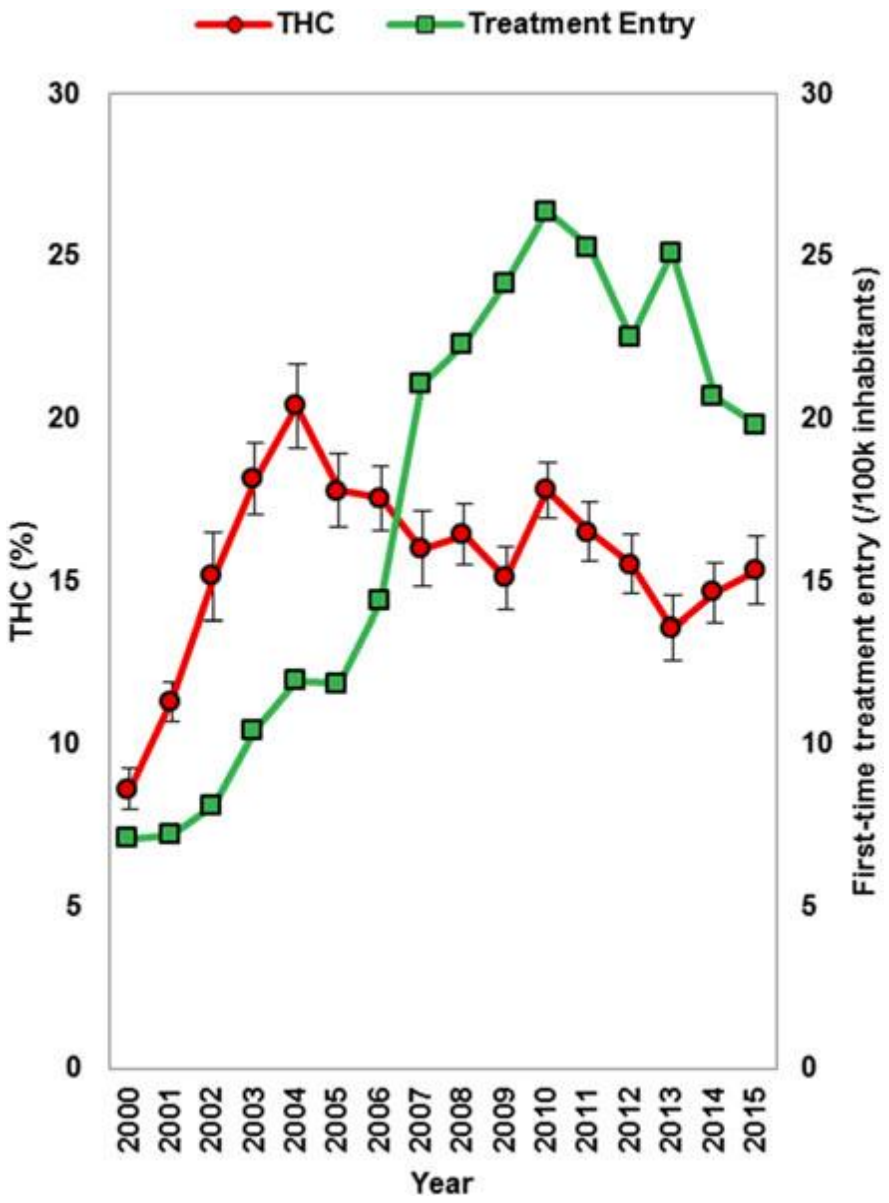
2019 Regulated Marijuana Market Update, Colorado Department of Revenue, Marijuana Enforcement Division

RESEARCH SUPPORTING THE USE OF SMOKED CANNABIS FOR MEDICAL CONDITIONS DONE WITH <10% THC WHEN COLORADO LEGALIZED MEDICAL MARIJUANA THE THC WAS 5%

- Studies using smoked cannabis - all lower than 10% THC - Whiting PF, Wolff RF, Deshpande S et al. Cannabinoids for medical use a systematic review and meta-analysis. JAMA 2015;313:2456-2473
- A study in healthy volunteers on the effects of cannabis on capsaicin-induced pain found that there is a window of modest analgesia for smoked cannabis
  - 2% THC providing no benefit
  - 4% THC providing significant decrease in pain
  - 8% THC resulting in an increase in pain or hyperalgesia.
  - Wallace M et al. Anesthesiology 2007;107:785-796

THE HIGHER THE POTENCY OF THE DRUG THE MORE POTENTIAL FOR ADDICTION

- Nicotine – FDA now talking about reducing nicotine concentration in tobacco
- Alcohol – 3.2 beer versus Vodka
- Cocaine – coca leaf versus crack cocaine
- Opioids – codeine versus Oxycontin
- Cannabis – marijuana of the 60s-80s when THC was <2% versus current high potency THC 17-28% in the flower, 85-90% in the concentrates



Changes in cannabis potency and first-time admissions to drug treatment: A 16-year study in the Netherlands

Fig. 1. Mean (95% CI) concentrations of δ-9-tetrahydrocannabinol (THC) in domestic herbal cannabis and first-time cannabis admissions to specialist drug treatment (per 100 000 inhabitants) from 2000 to 2015.

Laar MV et al. Limitations to the Dutch cannabis toleration policy, assumptions underlying the reclassification of cannabis above 15% THC. In J Drug Policy 2016;34:58-64.

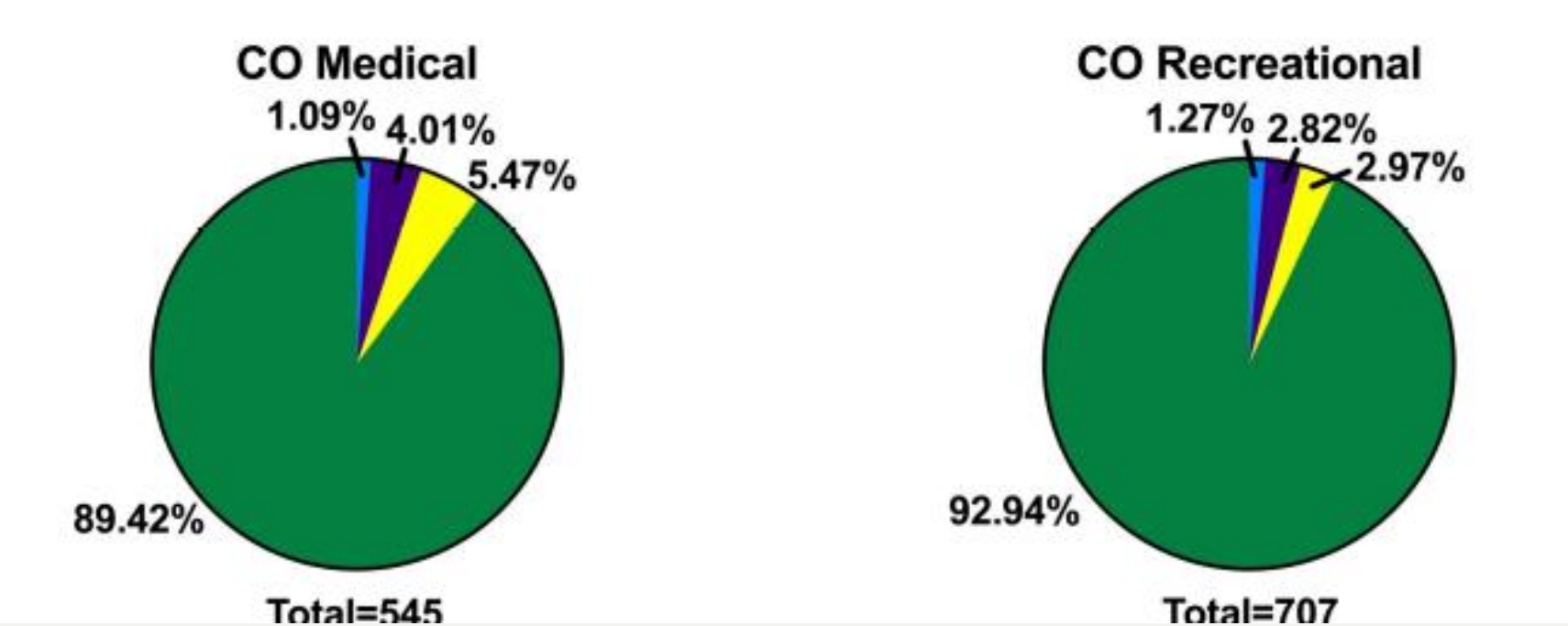
THC POTENCIES ABOVE 15% SHOULD BE CONSIDERED A HARD DRUG

After the Dutch observed negative impacts from rising THC potencies, a team of health experts concluded that **THC potencies above 15% should be considered a hard drug, like cocaine**

MARIJUANA WITHDRAWAL SYNDROME

- Increased anger
- Irritability
- Depression
- Restlessness
- Headache
- Loss of appetite
- Insomnia
- Severe cravings for marijuana

MOST PRODUCTS AVAILABLE IN COLORADO MEDICAL AND RECREATIONAL DISPENSARIES CONTAIN GREATER THAN 15% THC



ABSOLUTELY NO RESEARCH supports high-potency THC concentrates like dab, shatter, wax, or hash oil as safe or effective to treat any medically diagnosed condition

Cash MC, Cunnane K, Fan C, Romero-Sandoval EA. Mapping cannabis potency in medical and recreational programs in the United States. PLOS ONE 2020

FORMULATIONS – CAN BE UP TO 95% THC

Joint

Bong

Oil

Dabbing

Shatter

There has been a significant increase in dabbing and use of edibles among adolescents in Colorado between 2015 and 2017. JAMA Pediatrics 2019;173:988-989

The use of electronic cigarettes (e-cigarettes) and vape devices by youth has also rapidly increased, driven in large part by marketing and advertising by e-cigarette companies J Am Acad Pediatrics.2019;143(6):e20182741

Among adolescents reporting use of electronic vapor products in Colorado, 50.1% reported using marijuana in the past 30 days versus 7.6% of those not using vape products. NEJM 2019;380:689-690.

EXAMPLE OF WHAT IS AVAILABLE AS "MEDICINE"

Available in both **medical** and recreational dispensaries

IN THE INDUSTRY'S OWN WORDS
Disclaimer on package

"There may be long term physical or mental health risks from use of marijuana including additional risks for women who are or may become pregnant or are breastfeeding. Use of marijuana may impair your ability to drive a car or operate machinery. **This product was produced without regulatory oversight for health, safety or efficacy.** This product complies with testing requirements. This packaging is child resistant. This product is intended to be inhaled."

KIDS ARE INCREASINGLY USING CONCENTRATES

- 2019 Healthy Kids Colorado Survey - Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020. Data Sources: Healthy Kids Colorado Survey (HKCS) 2019.
- 10.2% of high school students report using dab
- those who admit to using marijuana, 52% report dabbing - a nearly 70% increase in only 2 years
- Where are they getting it?
- One source is kids 18-20 with a medical marijuana card
- The CDPHE medical marijuana registry indicates there has been a significant increase in medical marijuana cards for this age group over the last three years
- 3,322 in December 2017 to 3,900 in November 2020, with the primary indication being "severe pain" (kids ages 0-10=131 valid cards, kids 11-17 = 140 valid cards in November 2020)

COLORADO YOUNG ADULTS 18-25 YEAR OLDS ARE AT HIGHEST RISK

- Highest marijuana-consuming population in the state
- Almost double national rate for daily marijuana use (among young adults who were in middle and high school when legalization occurred)
- Most likely to be unsafe while high
- 1 in 3 are consuming marijuana
- 1 in 7 are consuming marijuana DAILY
- 1 in 20 are driving after using

Behavioral Risk Factor Surveillance System (BRFSS) data, 2019
Colorado Department of Health and Environment

In the medical market:

- twice as much can be bought daily – 2 ounces versus 1 ounce in recreational
- taxes significantly lower
- no marijuana recommendation specifications or monitoring or control for "looping"

70% of the communities in Colorado opted-out of having dispensaries so the prevalence of dispensaries is even higher in some communities

Table 1

U.S. States with Medical or Recreational Cannabis Laws (May 2016)

State	Has MCL	MCL duration (years)	Has RCL	Permit home cultivation	Permit dispensary	# de jure operating dispensaries	U.S. Census Population (2015)	Dispensary per 100,000 people
AK	Yes	18	Yes	Yes	No	0	738,432	0.00
AZ	Yes	6	No	Yes	Yes	93	6,828,065	1.36
CA	Yes	20	No	Yes	Yes	1000–2000 *	39,144,818	2.55–5.11
CO	Yes	16	Yes	Yes	Yes	949	5,456,574	17.39
CT	Yes	4	No	No	Yes	6	3,590,886	0.17
DC	Yes	6	Yes	Yes	Yes	5	945,934	0.53
DE	Yes	5	No	No	Yes	1	672,228	0.15
HI	Yes	16	No	Yes	Yes	0	1,431,603	0.00
IL	Yes	3	No	No	Yes	36	12,859,995	0.28
ME	Yes	17	No	Yes	Yes	8	1,329,328	0.60
MD	Yes	2	No	No	Yes	0	6,006,401	0.00
MA	Yes	4	No	Yes	Yes	6	6,794,422	0.09
MI	Yes	8	No	Yes	No	0	9,922,576	0.00
MN	Yes	2	No	No	Yes	3	5,489,594	0.05
MT	Yes	12	No	Yes	No	0	1,032,949	0.00
NV	Yes	16	No	Yes	Yes	26	2,890,845	0.90
NH	Yes	3	No	No	Yes	0	1,330,608	0.00
NJ	Yes	6	No	No	Yes	6	8,958,013	0.07
NM	Yes	9	No	Yes	Yes	23	2,085,109	1.10
NY	Yes	2	No	No	Yes	17	19,795,791	0.09
OR	Yes	18	Yes	Yes	Yes	423	4,028,977	10.50
PA	Yes	0.1	No	No	Yes	0	12,802,503	0.00
RI	Yes	10	No	Yes	Yes	3	1,056,298	0.28
VT	Yes	12	No	Yes	Yes	4	626,042	0.64
WA	Yes	18	Yes	Yes	Yes	237	7,170,351	3.31

Borodovsky JT et al. Drug Alcohol Depend 2017 177:299-306

EXAMINING ASSOCIATIONS BETWEEN LICENSED AND UNLICENSED OUTLET DENSITY AND CANNABIS OUTCOMES FROM PREOPENING TO POSTOPENING OF RECREATIONAL CANNABIS OUTLETS

PEDERSON ER ET AL. AM J ADDICTIONS 2020 DOI: 10.1111/AJAD.13132

- 1097 young adults aged 21 and older living in Los Angeles County were surveyed before licensed recreational cannabis outlets opened (Time 1: July to December 2017) and after (Time 2: July 2018 to June 2019)
- Higher density of both licensed and unlicensed cannabis outlets near young adults' homes was associated with greater likelihood of use, heavier use, stronger intentions to use, and more problematic use, during a period after the opening of recreational cannabis outlets
- A higher number of licensed cannabis outlets within 4 miles of home was significantly associated with a greater likelihood of past-month cannabis use after controlling for any use the prior year

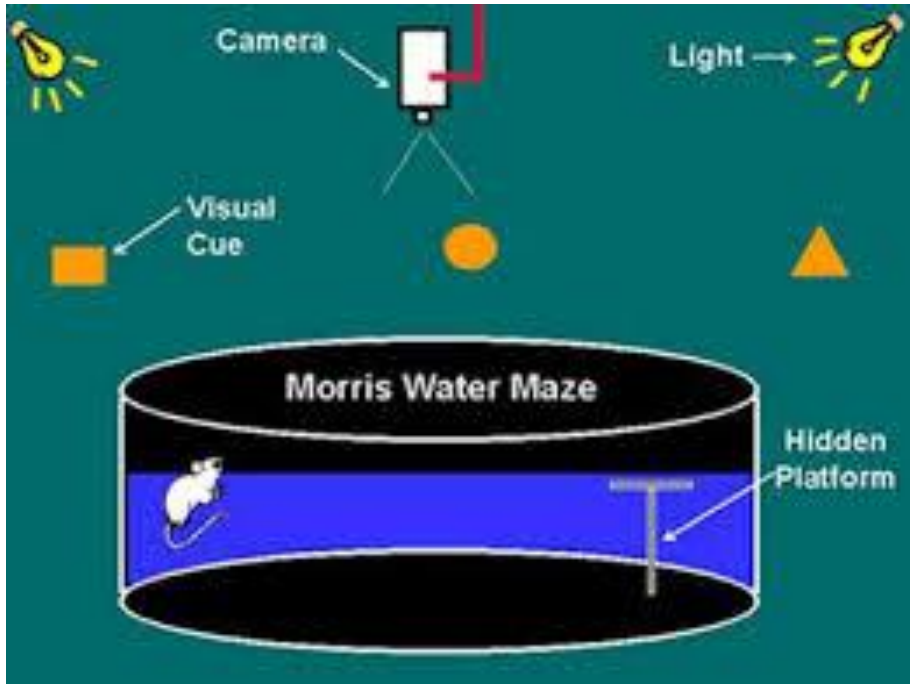
THE BELIEF THAT THESE PRODUCTS ARE SAFE AND MEDICALLY LEGITIMATE HAS NEGATIVELY AFFECTED THE MOST VULNERABLE IN OUR SOCIETY

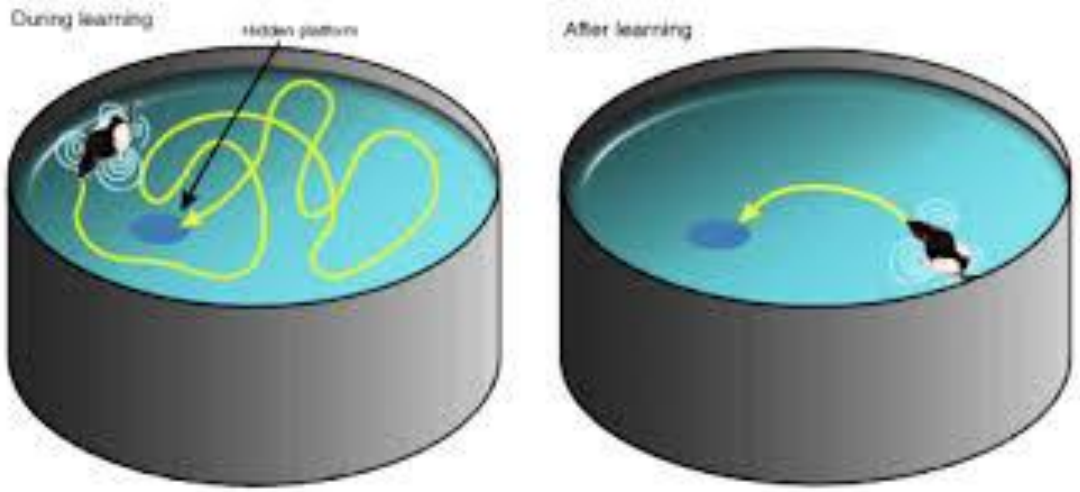
- Children, Adolescents, Young Adults, and those with mental health and/or addiction problems have seen increases in :
- Addiction
- Greater Adolescent Use
- Negative mental health outcomes
- Greater medical costs
- Diminished potential for legions of teenagers

EFFECTS ON LEARNING

HIPPOCAMPUS AND NEUROGENESIS

ALL DRUGS OF ABUSE NEGATIVELY EFFECT THE HIPPOCAMPUS, DECREASE NEUROGENESIS AND IMPAIR THE ABILITY TO LEARN NEW THINGS, THIS IS TRUE FOR ALCOHOL, COCAINE, METHAMPHETAMINES, HEROIN, NICOTINE, THC



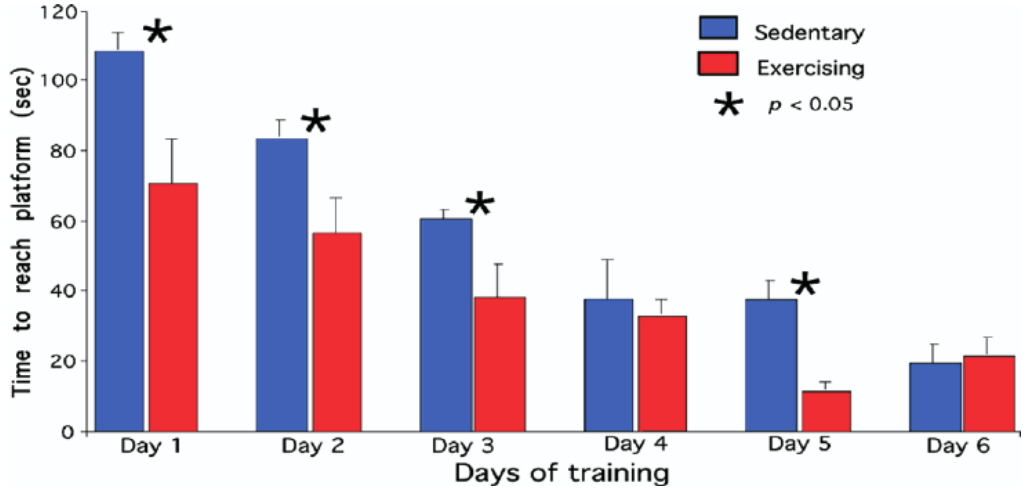


LEARNING TESTS

DRUGS AND LEARNING

After drug use, 1st, 2nd, every time, they can't find the platform

STOPPING DRUGS AND EXERCISING IMPROVES ABILITY TO LEARN NEW THINGS

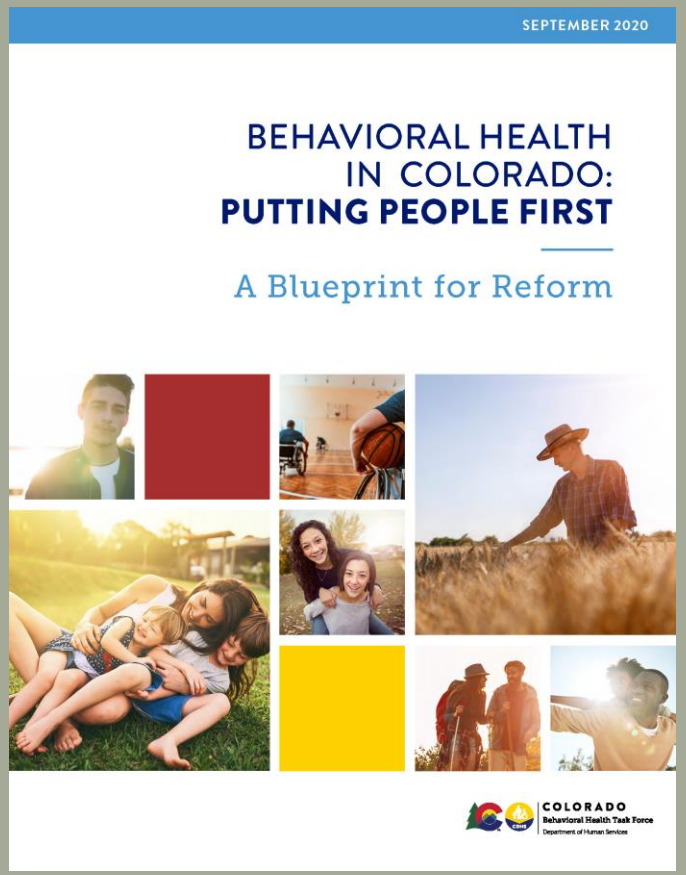


THE IMPACT

COLORADO IS IN THE MIDST OF A BEHAVIORAL HEALTH CRISIS

According to the CDC, Colorado has the 7th HIGHEST suicide rate in the nation

- In September, the Governor released a blueprint for reforming behavioral health
- No mention of cannabis, yet high-potency THC is playing a significant role in this crisis
- **we need to follow the SCIENCE**
- It's time to acknowledge the harms of high-potency THC on behavioral health, **and do something about it**



HIGH POTENCY CANNABIS ASSOCIATED WITH A TRIPLED RISK FOR PSYCHOSIS

- DiForti et al. Lancet Psychiatry, 2015
- London – analyzed 780 people ages 18-65, 410 with first episode psychosis and 370 healthy controls
- High potency – THC > 15% - 3X increased risk of psychosis
- Daily use – 5X increased risk
- Psychosis not associated with Hash < 5% THC

MULTICENTER CASE-CONTROL STUDY ACROSS TEN EUROPEAN AND ONE BRAZILIAN SITE REPLICATES THE STRONG EFFECT OF DAILY USE OF HIGH-POTENCY CANNABIS ON THE ODDS FOR PSYCHOTIC DISORDER

Between 2010 and 2015, 901 patients with first-episode psychosis, 11 sites and 1,237 population controls from those same sites

Those using high potency THC greater than **10%** - 3 times more likely to develop psychosis.
If they were using daily – nearly 5 times more likely.

If high-potency cannabis were no longer available, 12.2% of cases of first-episode psychosis could be prevented across the 11 sites, rising to 30.3% in London and 50.3% in Amsterdam.

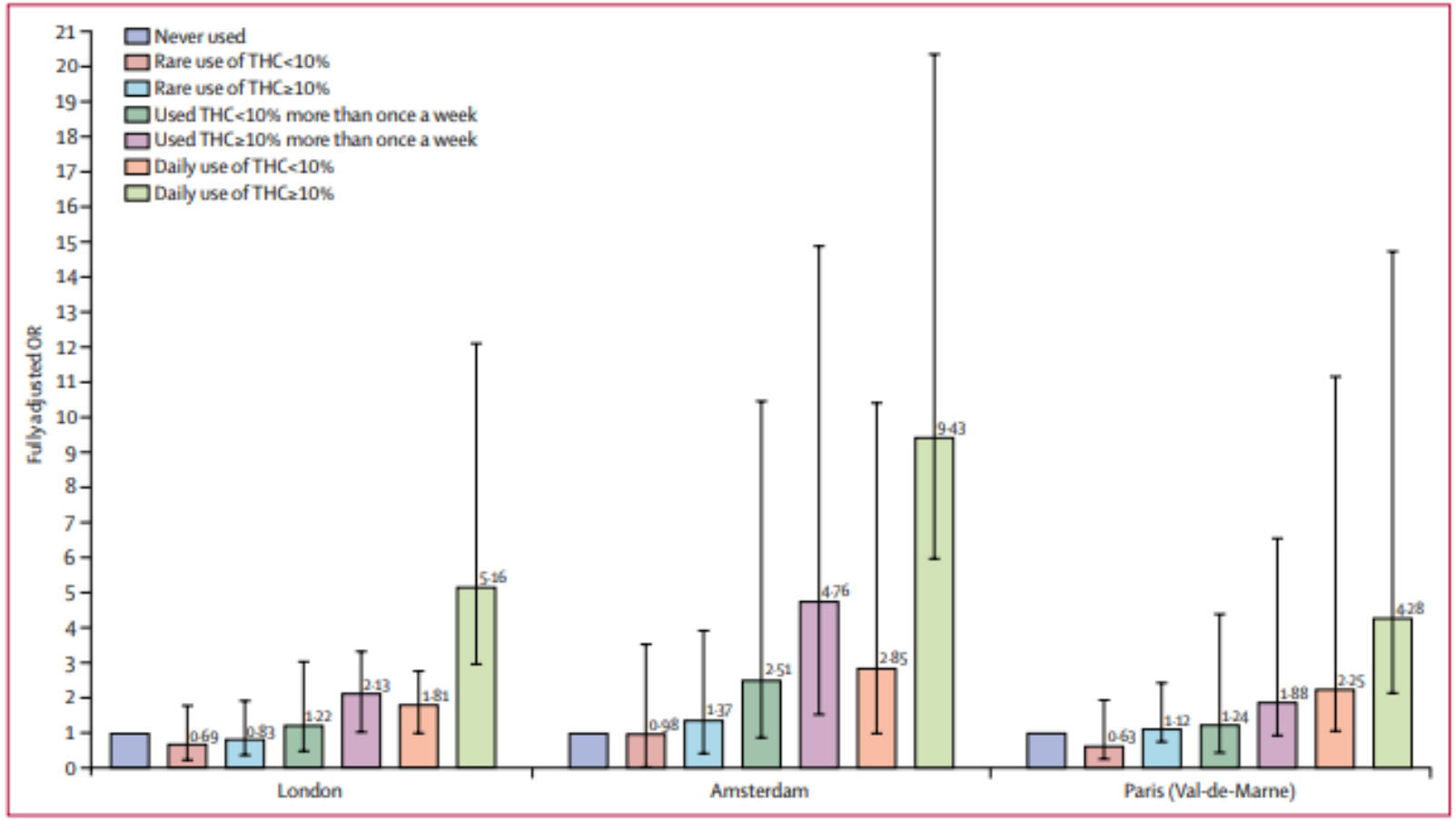
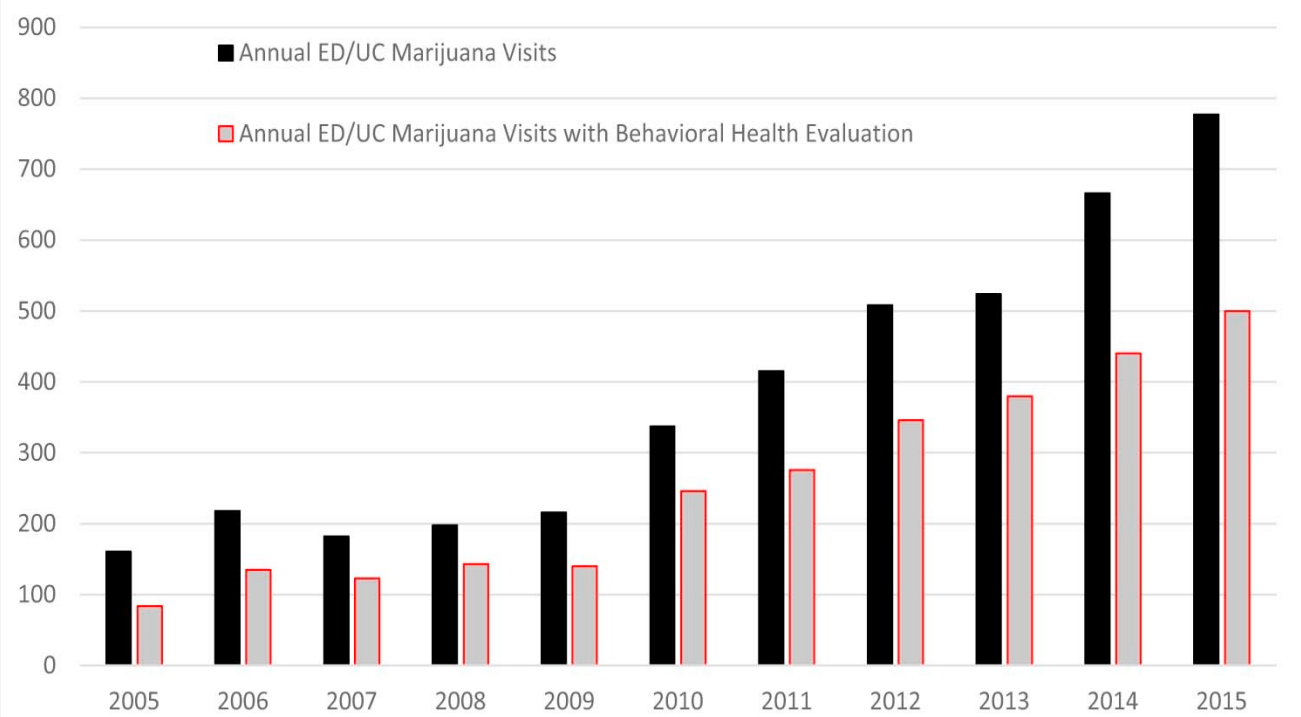


Figure 2: **Fully adjusted ORs of psychotic disorders for the combined measure of frequency plus type of cannabis use in three sites**
Data are shown for the three sites with the greatest consumption of cannabis: London (201 cases, 230 controls), Amsterdam (96 cases, 101 controls), and Paris (54 cases, 100 controls). Error bars represent 95% CIs. OR=odds ratio.

DiForti M et al. Lancet Psychiatry 2019

MAJORITY OF VISITS WITH CANNABIS GET A BEHAVIORAL HEALTH EVALUATION



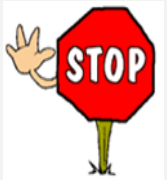
Number ED/UC visits with cannabis associated ICD codes or positive urine drug screens by adolescents aged ≥13 and < 21 by year to a tertiary care children's hospital system in Colorado by year

Wang GS, Davies SD, Halmo LS, Sass A, Mistry RD. Impact of marijuana legalization in Colorado on adolescent emergency and urgent care visits. Journal of Adolescent Health 2018 Available online 30 March 2018.

NORMAL BRAIN DEVELOPMENT DURING ADOLESCENCE - NEUROTRANSMITTER DEVELOPMENT

- Lots of Dopamine and Glutamate - stimulatory neurotransmitters – "stepping on the gas" – go,go,go – learn, explore, do

- Decreased Serotonin and GABA – suppressive neurotransmitters – "stepping on the brake" located in the prefrontal motor cortex – the last part of the brain to fully develop



Schepis et al. Neurobiological Processes in Adolescent Addictive Disorders. Am J Addictions. 2008;17:6-23

BEHAVIORAL FACTORS RELATING TO SUBSTANCE ABUSE IN ADOLESCENTS

- ↑ neurobiological based tendencies for risk-taking with decreased suppressive and regulatory control
- lots of Go, go, go

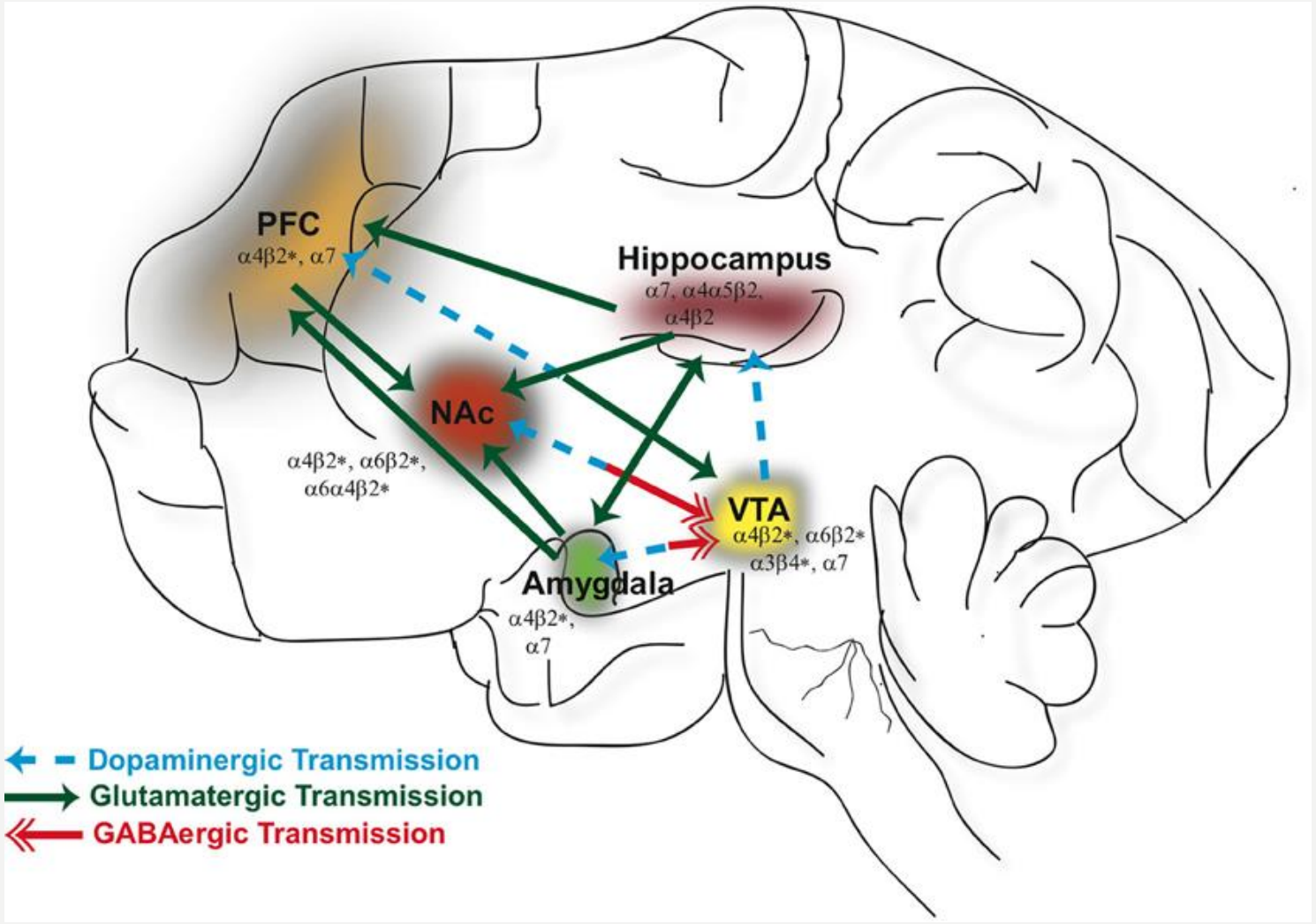
- very little ability to put on the brakes

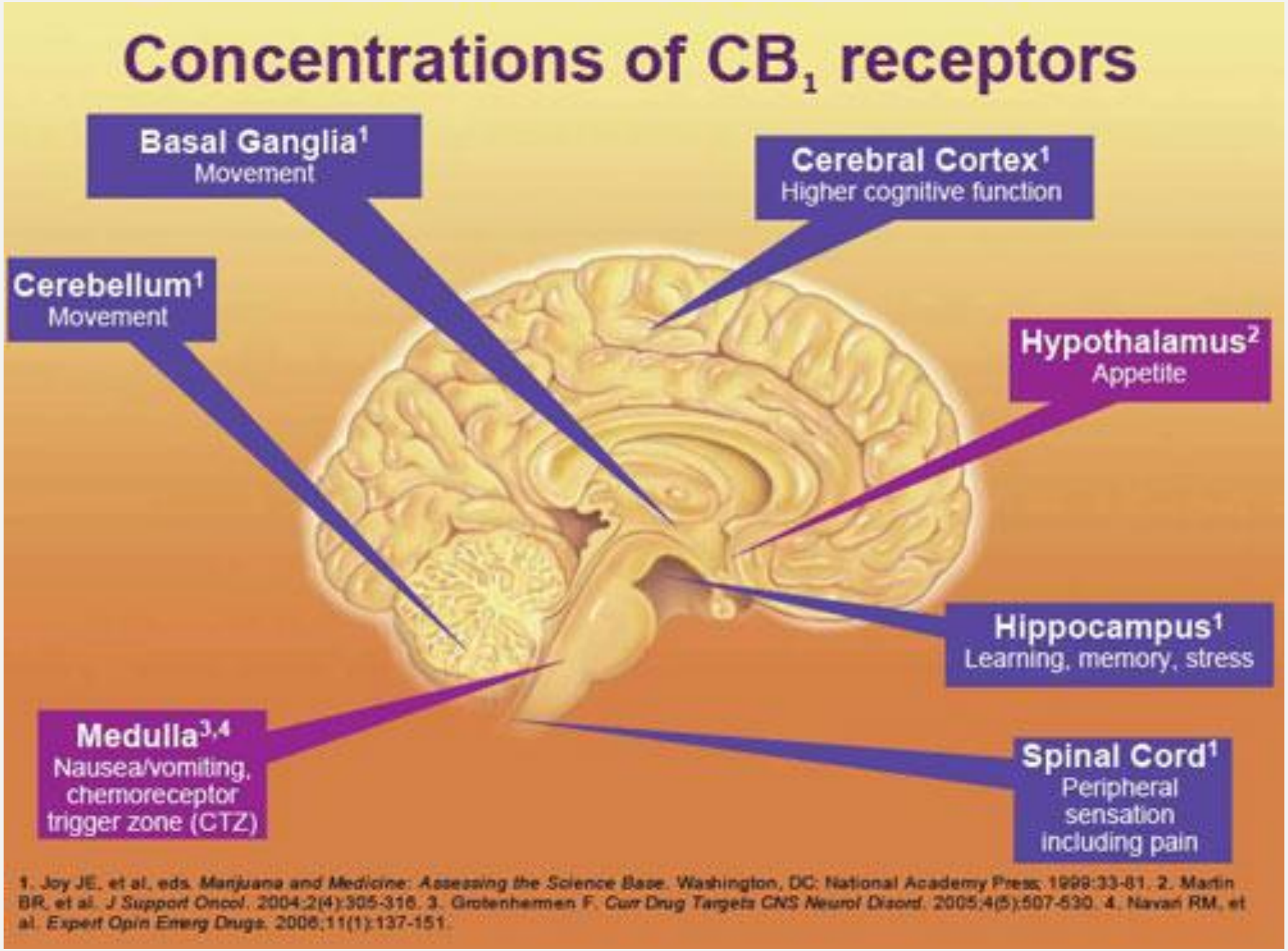
- ↓ in parental monitoring
- ↑ in peer affiliation

ACETYLCHOLINE - ACH

- Another important brain neurotransmitter – helps us focus and concentrate
- ACH innervation of the PFC reaches mature levels during adolescence – receptors = nACHRs
- Involved in promoting or preventing neuronal cell death – depending on developmental stage
- Nicotine works on these receptors and can mess up the fine tuning of the brain during adolescence

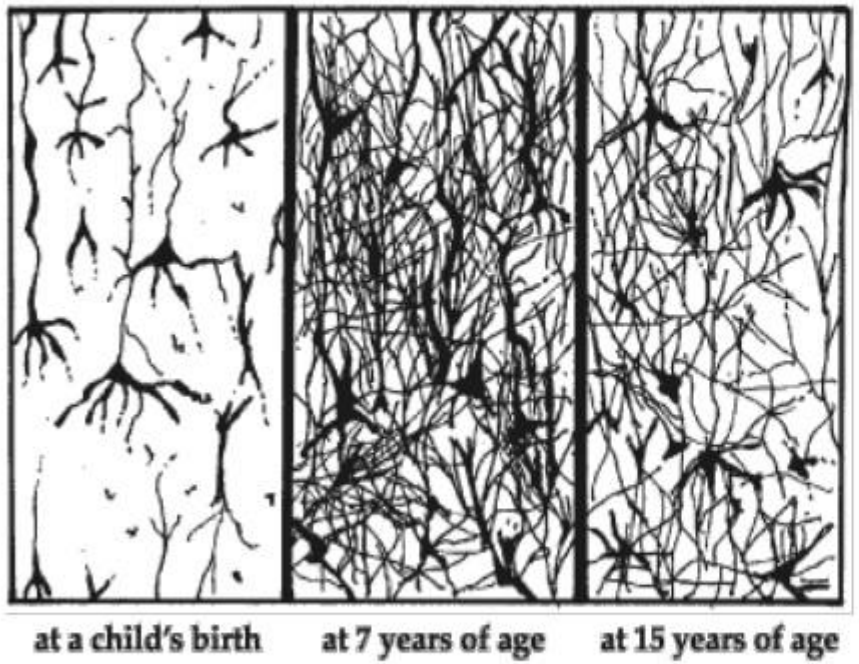
NICOTINIC CHOLINERGIC NEURONS




Concentrations of CB1 receptors
Basal Ganglia[1]
Movement
Cerebral Cortex[1]
Higher cognitive function
Cerebellum[1]
Movement
Hypothalamus[2]
Appetite
Hippocampus[1]
Learning, memory, stress
Medulla[3,4]
Nausea/vomiting, chemoreceptor trigger zone (CTZ)
Spinal Cord[1]
Peripheral sensation including pain
1. Joy JE, et al, eds. Marijuana and Medicine: Assessing the Science Base. Washington, DC: National Academy Press; 1999:33-81. 2. Martin BR, et al. J Support Oncol. 2004;2(4):305-316. 3. Grotenhermen F. Curr Drug Targets CNS Neurol Disord. 2005;4(5):507-530. 4. Navari RM, et al. Expert Opin Emerg Drugs. 2006;11(1):137-151.

Both the Nicotinic Cholinergic and the Cannabinoid CB1 receptors play a significant role in pruning during brain development in adolescence

Synaptic Pruning



The next change after this synaptic growth spurt is a selective pruning which takes place.

In adolescence, most of this pruning is taking place in the frontal lobes.

The adolescent loses approximately 3 percent of the gray matter in the frontal lobes.

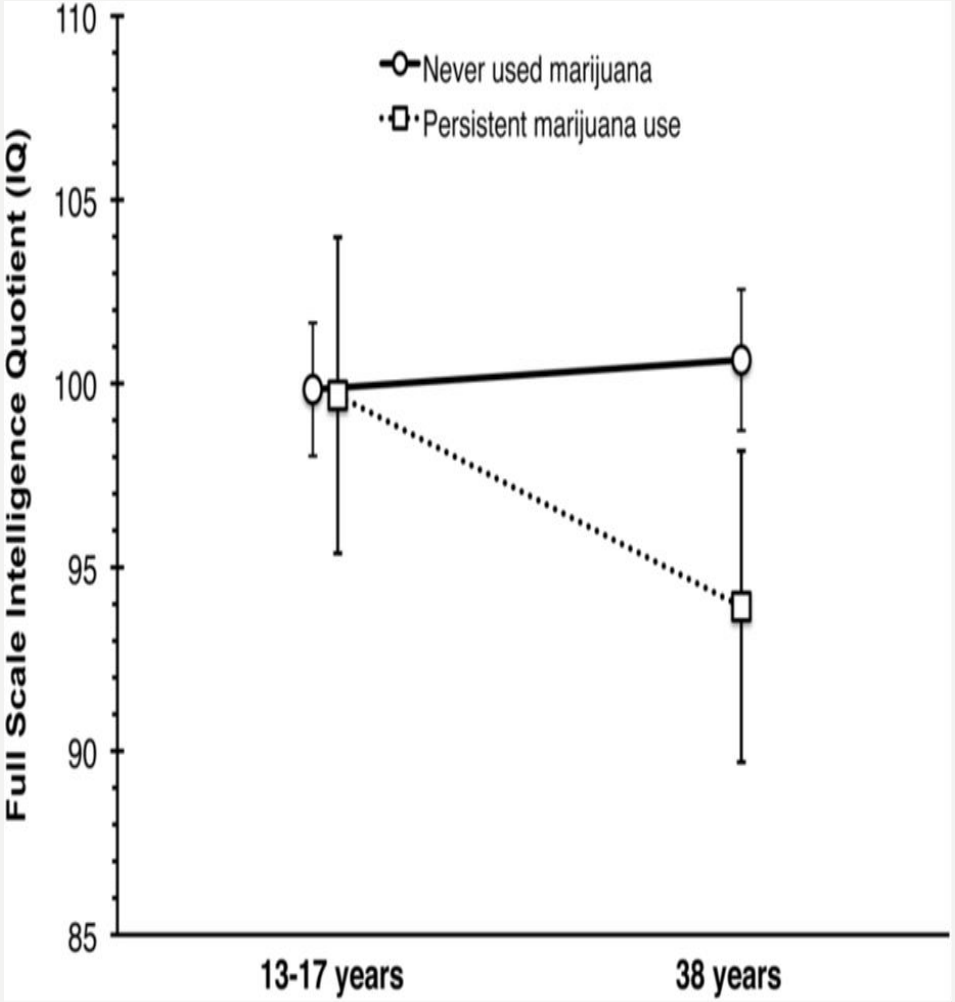
GREY MATTER VOLUME DIFFERENCES ASSOCIATED WITH EXTREMELY LOW LEVELS OF CANNABIS USE IN ADOLESCENCE

ORR C ET AL. JOURNAL OF NEUROSCIENCE 2019; 39:1817-1827

- 46 boys and girls with just one or two incidences of cannabis use versus controls with no exposure to cannabis – matched on alcohol, nicotine use – high school students in 4 European Countries
- Also studied controls who went on to use cannabis 2 years later versus those who didn't
- Significantly greater GMV in those who used cannabis in bilateral hippocampus, amygdala, striatum, extending into the left prefrontal cortex
- There was no GMV differences in THC naïve 14-year-olds who later used cannabis at 16, so differences did not precede use and were not explained by group differences in demographic, personality, psychopathology, or other substance use factors
- **The endocannabinoid system (ECS) mediates maturation-related neural reorganization which may place adolescents at heightened vulnerability to structural brain effects of cannabis exposure as adolescence is a time of rapid neural maturation**

IQ AND BRAIN DEVELOPMENT STUDIES

- Prospective study New Zealand – 1,037 individuals followed for 20 years
- Neuropsych testing at 13 before initiation of cannabis and again at age 38
- IQ decrease by 8 points with early persistent teen use of cannabis
- Meier et al. Proc Natl Acad Sci, 2012



IQ AND BRAIN DEVELOPMENT STUDIES

- Prospective study of 648 children and exposure to cannabis in-utero
- Women interviewed about the amount and frequency of marijuana use at 4 and 7 months of pregnancy and delivery
- Children assessed with IQ test at age 6
- Examiners blinded to exposure
- In Utero exposure (light to moderate marijuana users, approx. 3x/week) has a significant negative effect on school-age intellectual development
- Goldschmidt L et al. J Am Acad Child Adolesc Psychiatry, 2008.

ASSOCIATIONS BETWEEN PRENATAL CANNABIS EXPOSURE AND CHILDHOOD OUTCOMES

RESULTS FROM THE ABCD STUDY PAUL SE ET AL. JAMA PSYCHIATRY 2020

- cross-sectional analysis of 11,489 children (655 exposed to cannabis prenatally)
- prenatal cannabis exposure after maternal knowledge of pregnancy was associated with greater psychopathology during middle childhood, even after accounting for potentially confounding variables.
- Prenatal cannabis exposure may increase risk for psychopathology
- consistent with recent recommendations by the Surgeon General of the United States, these data suggest that cannabis use during pregnancy should be discouraged by clinicians and dispensaries.

MATERNAL CANNABIS USE IN PREGNANCY AND CHILD NEURODEVELOPMENTAL OUTCOMES CORSI DJ ET AL. NATURE MEDICINE 2020

- retrospective analysis of all live births in Ontario, Canada, between 1 April 2007 and 31 March 2012.
- Association between maternal cannabis use in pregnancy and the incidence of autism spectrum disorder in the offspring.
- The incidence of autism spectrum disorder diagnosis was
  - 4.00 per 1,000 person-years among children with exposure
  - 2.42 per 1,000 among unexposed children
- The incidence of intellectual disability and learning disorders was higher among offspring of mothers who use cannabis in pregnancy, although less statistically robust

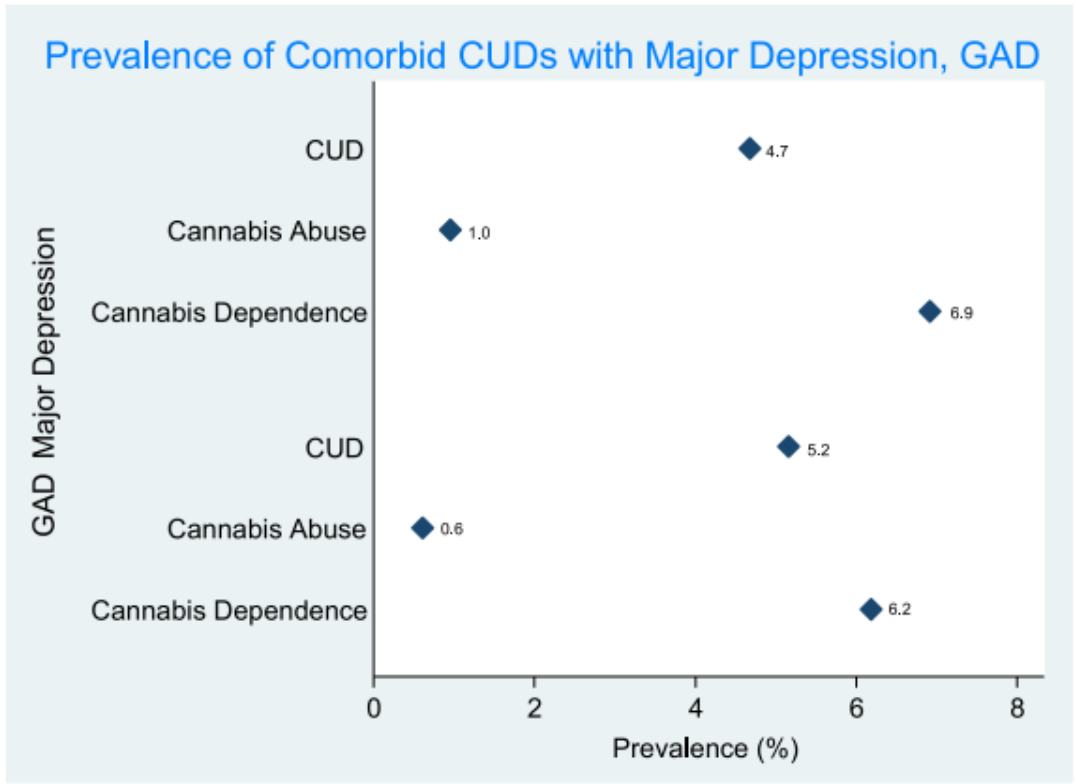
RECOMMENDATIONS FROM CANNABIS DISPENSARIES ABOUT FIRST-TRIMESTER CANNABIS USE

- Phone script - caller stated she was 8 weeks pregnant and experiencing morning sickness - "Are there any products that are recommended for morning sickness?"
- 400 dispensaries contacted in Colorado
- Nearly 70% of Colorado cannabis dispensaries contacted recommended cannabis products to treat nausea in the first trimester.
- Few dispensaries encouraged discussion with a health care provider without prompting.
- Example: "Technically, with you being pregnant, I do not think you are supposed to be consuming that, but if I were to suggest something, I suggest something high in THC."
- Bud Tenders Practicing Medicine without a License
- Dickson B et al. Obstet Gynecol 2018;131:1031–8)

MARIJUANA AND MENTAL ILLNESS

- 3,239 Australian young adults were followed from birth to the age of 21
- Potential confounding factors were prospectively measured when the child was born and at 14 years.
- After controlling for confounding factors, those who started using cannabis before age 15 years and used it frequently at 21 years were more likely to report symptoms of anxiety and depression in early adulthood than those who did not use cannabis. (odds ratio 3.4; 95% CI 1.9-6.1).
- Independent of individual and family background or other drug use
- Hayatbakhsh MR et al. Cannabis and anxiety and depression in young adults: a large prospective study. J Am Acad Child Adolesc Psychiatry 2007 Mar;46(3):408-17.

THREE-FOLD COMORBID ASSOCIATION BETWEEN CANNABIS USE DISORDER AND BOTH MAJOR DEPRESSION AND GENERALIZED ANXIETY DISORDER



CUD, Cannabis use disorders; GAD, Generalized Anxiety Disorder

Fig. 2. Prevalence of comorbid substance use disorders with major depression CUD, Cannabis use disorders; GAD, Generalized Anxiety Disorder.

Comorbid Cannabis Use Disorder with Major Depression and Generalized Anxiety Disorder: A Systematic Review with Meta-analysis of Nationally Representative Epidemiological Surveys
Onaemo VN, Fawehinmi TO, D'Arcy C
J Affective Disorders 2021:281:467-475

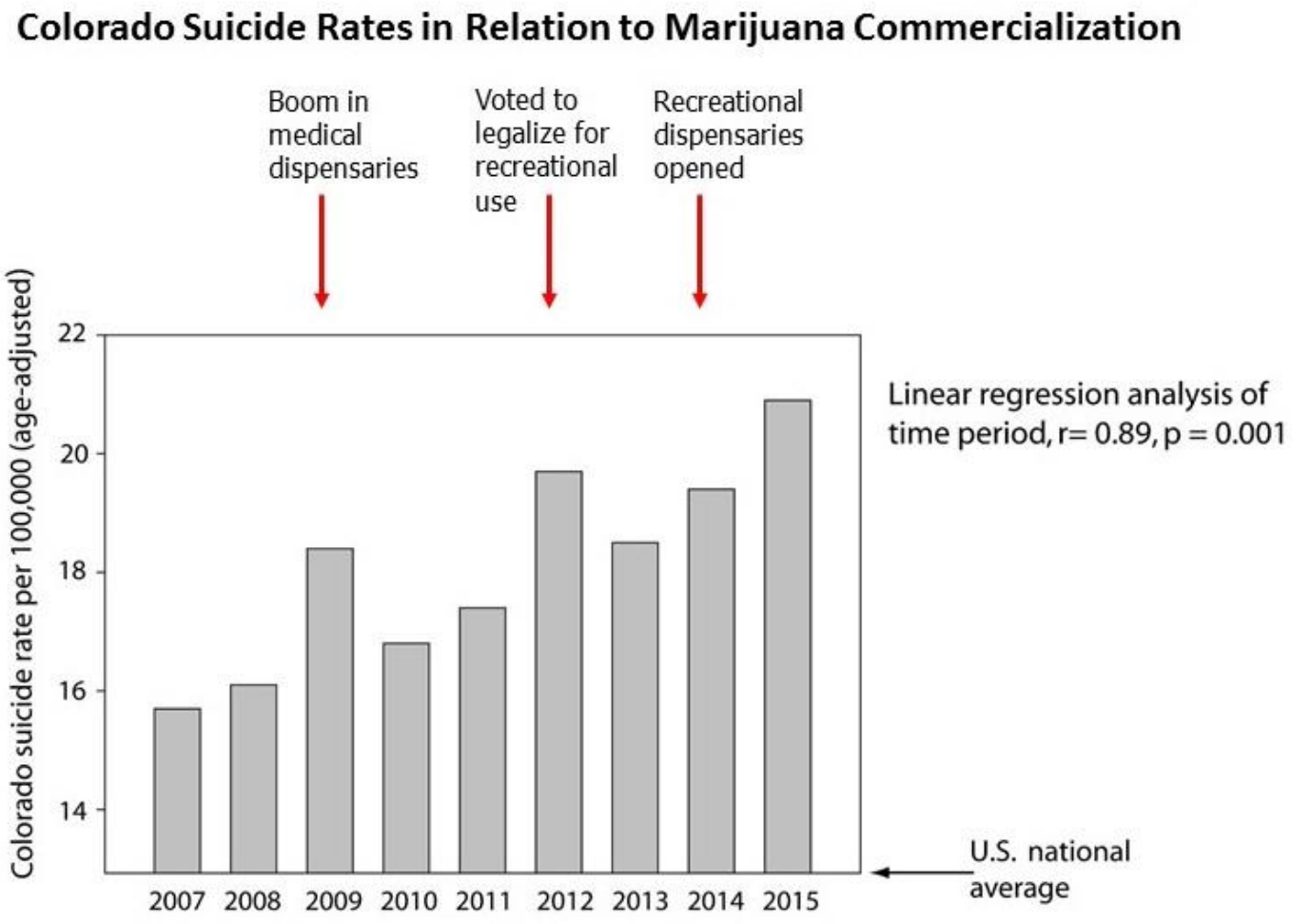
Base on large national surveys from the US and Australia. Sample sizes ranged from 5,877 to 43,093 with a total sample size of 176,976 for all 6 surveys included in the analysis

ATTEMPTS TO ADD PTSD

- A growing number of states have identified PTSD as an approved condition for medical marijuana
- Observational study of 2276 Veterans treated in VA PTSD treatment programs
  - Never used marijuana – significantly lower symptom severity 4 months later
  - "Starters" – highest levels of violent behavior and PTSD symptoms 4 months after treatment
  - "Stoppers" – lowest level of PTSD symptoms at 4 months after treatment
- Wilkinson et al. J Clin Psychology 2015

WHY MARIJUANA (THC) IS NOT THE ANSWER FOR PTSD

- Similar as to why benzodiazepines are not the answer
- Temporary relief – numbing, disconnecting from the traumatic emotions
- Cognitive impairment, a-motivational syndrome, potential for psychosis or worsening psychosis from PTSD
- Addiction potential and vicious cycle
- False memories



CORRELATION OF MARIJUANA AND SUICIDE

In fact, veteran suicides have not decreased. Instead, they are up 32% since 2001, compared to a national increase of 23% during the same period – Congressional Hearing **4/27/17**

2020 National Veteran Suicide Prevention Report from the Department of Veterans Affairs – Colorado's rate significantly higher that then national rate. 217 Veteran suicide deaths in Colorado last year – all time high and 25% increase over 2018

Christine Miller, PhD

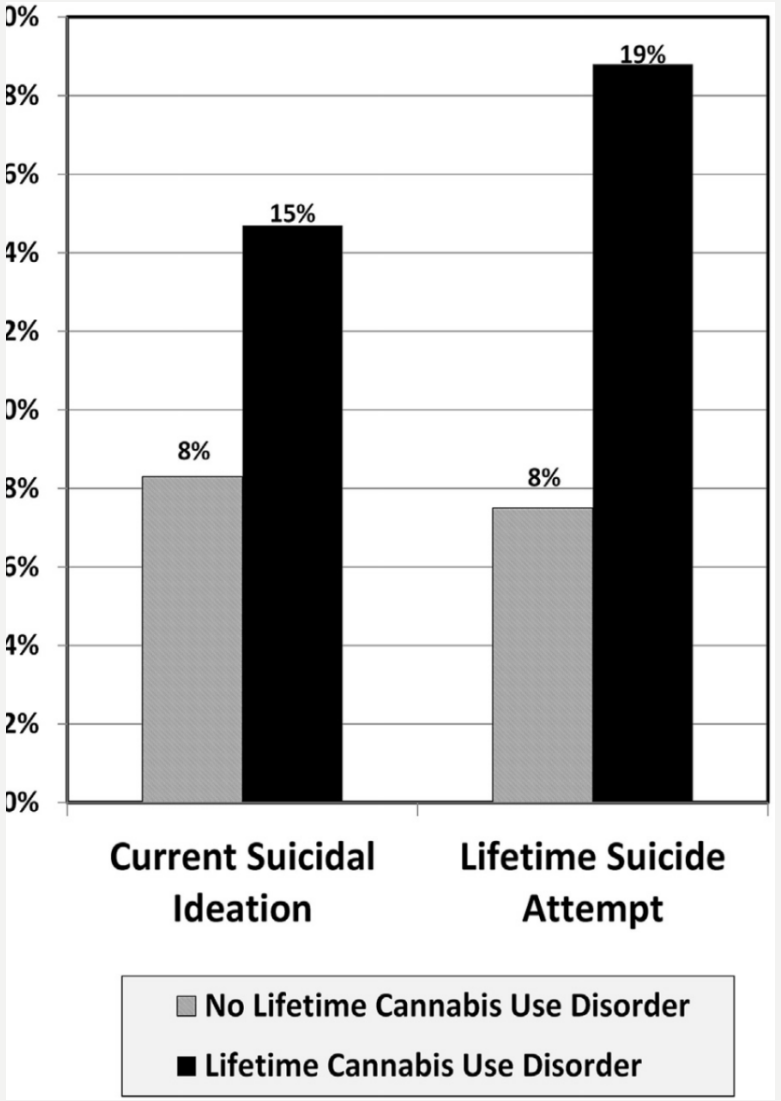
CANNABIS USE DISORDER AND SUICIDE ATTEMPTS IN IRAQ/AFGHANISTAN-ERA VETERANS

Kimbrel NA et al. J Psychiatric Research 2017:89;1-5

3233 veterans in cross-sectional, multi-site study by VA

Cannabis use disorder was significantly associated with both current suicidal ideation ($p<.0001$) and lifetime history of suicide attempts ($p<.0001$) compared to veterans with no lifetime history of cannabis use disorder

The significance difference continued even after adjusting for sex, PTSD, depression, alcohol use disorder, non-cannabis drug use disorder, history of childhood sexual abuse and combat exposure.

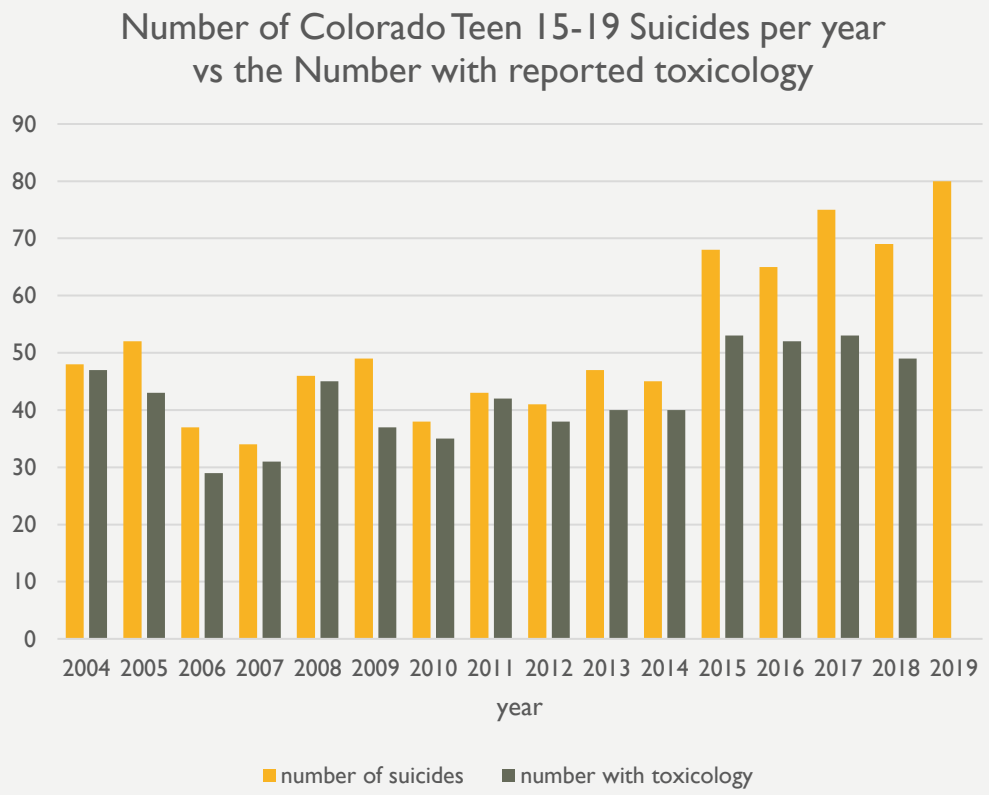


SUICIDE AND ADOLESCENT CANNABIS USE

- Systematic review and meta-analysis
- Eleven studies, N=23,317 adolescents
- Risk of depression OR = 1.4
- Suicidal Ideation OR = 1.5
- Suicide attempt OR = 3.5
- Significantly higher in adolescent cannabis users than in non-users

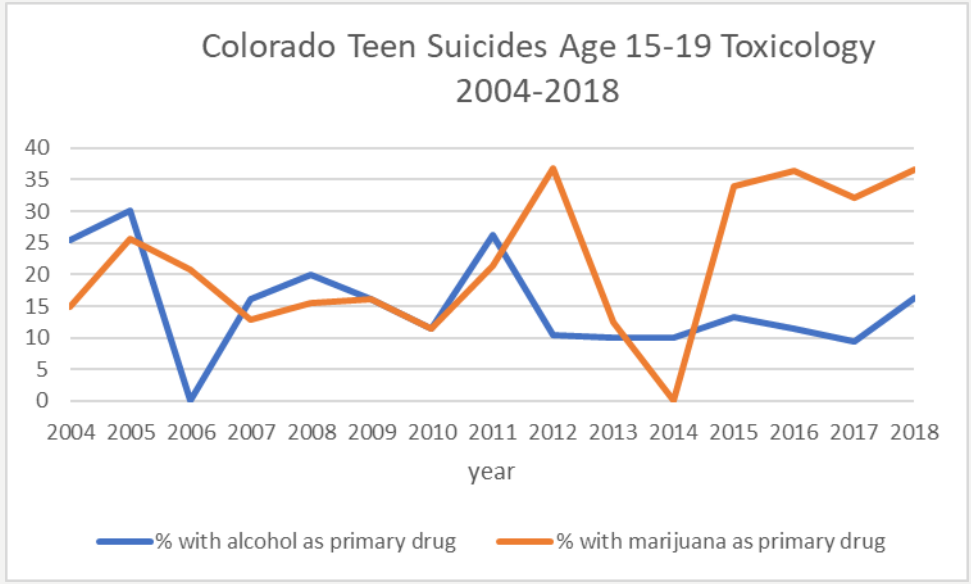
Gobbi G et al. Associations of cannabis use in adolescence and risk of depression , anxiety, and suicidality in young adulthood: a systematic review and meta-analysis. JAMA Psychiatry. 2019;76:426-434.

THC IS THE NUMBER ONE DRUG FOUND IN TEENS AGE 15-19 WHO DIED BY SUICIDE IN COLORADO



Colorado Violent Death Reporting System

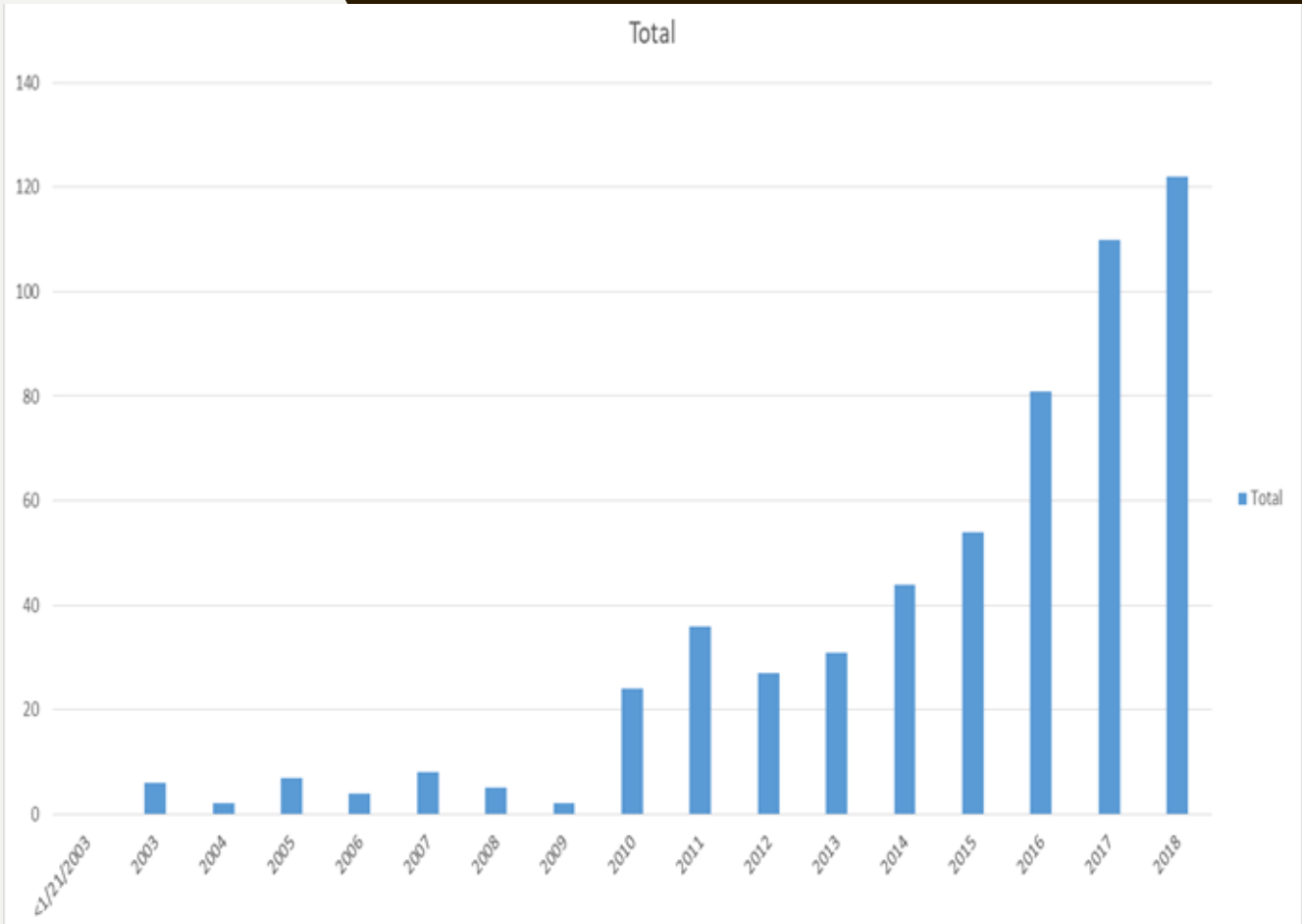
There has clearly been a significant increase in the number of teen suicides in Colorado in last five years– and there has been a significant increase in the percent of teen suicides with marijuana in their system - it is the number one drug found when toxicology is reported. It seems to correlate with the increased THC potency and availability/use of concentrates – we need data to confirm that.



CANNABINOID HYPEREMESIS SYNDROME

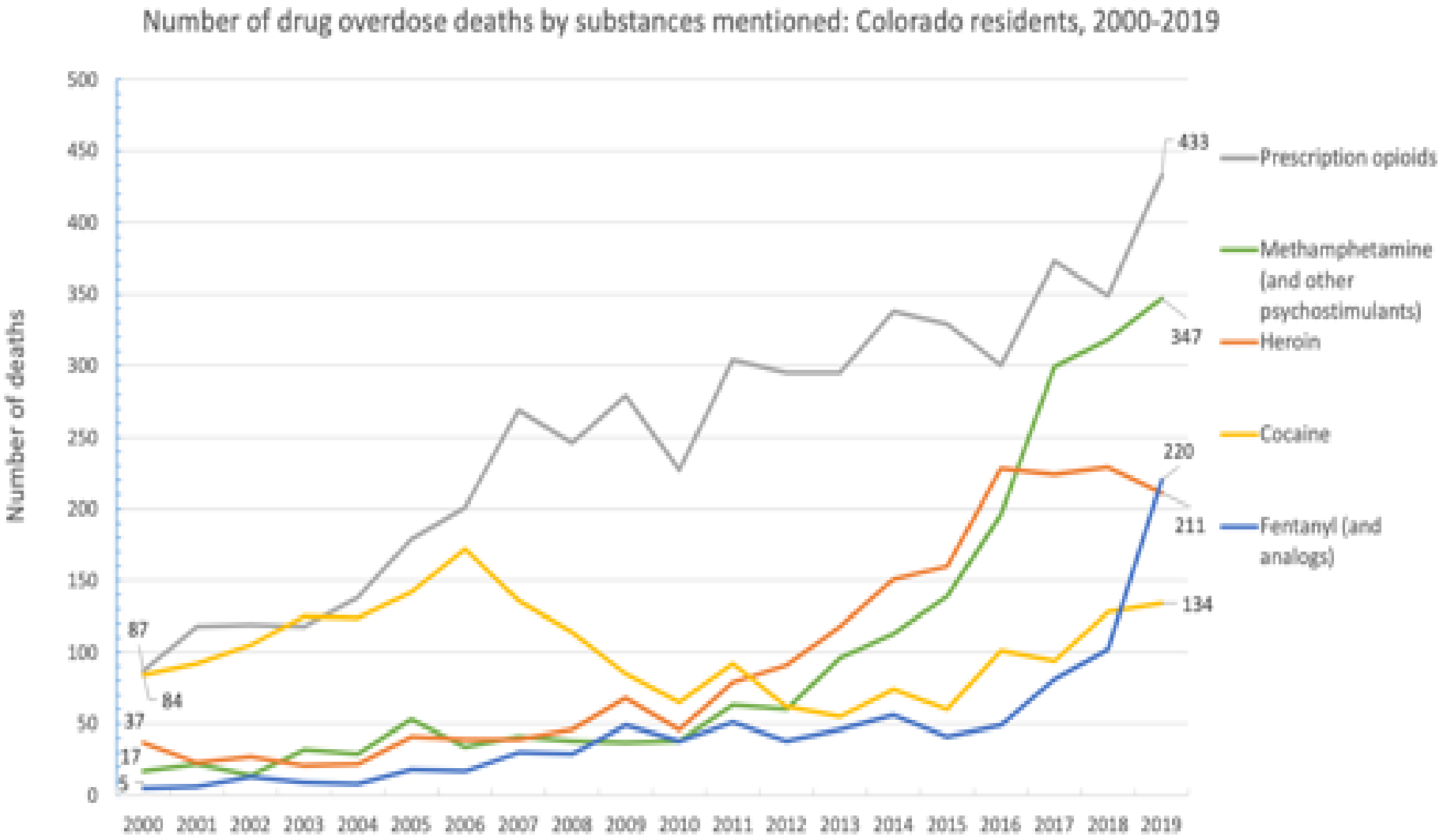
- Once extremely rare, but now flooding Emergency Rooms in Colorado
- Uncontrolled cyclic vomiting that often requires emergency treatment to stop vomiting and rehydrate
- Severe abdominal pain
- Medications don't control the symptoms
- Causing people to receive full medical work-ups costing hundreds of thousands of dollars
- Higher THC potency is causing people to be addicted and use more often, increasing risk of CHS
- Only solution is quit using cannabis

CHS INCREASING EVERY YEAR



Data collected by Brad Roberts, MD, ER physician in Parkview, Pueblo, CO

MARIJUANA HAS NOT DECREASED OPIOID OVERDOSE DEATHS IN COLORADO



Marijuana commercialized

2019 data shows a **24% increase in prescription overdose deaths** and 115% increase in fentanyl deaths since 2000

First use of marijuana before the age of 18 has the highest contribution to opiate use disorders (OUD)- a much higher contribution compared to early initiation of alcohol.

Wadeker AS, Understanding opiate use disorders (OUD) using a tree-based classifiers. Drug and Alcohol Dependence 2020

SOLUTIONS/RECOMMENDATIONS

- Educate, educate, educate, increase prevention efforts
- **Improve data collection to monitor and respond to impacts of high potency THC (particularly for high risk and vulnerable populations)**
- **Treat medical marijuana more like a medicine by requiring that marijuana recommendations specify THC and/or CBD potency, frequency and method of use, and are limited in duration. Require that medical marijuana purchases be monitored like PDMP system. Require that youth ages 18-20 meet the same marijuana recommendation requirements as those ages 0-18.**
- Cap THC concentrations and eliminate the concentrates
- Increase funding and availability of treatment
- Increase research on CBD and lower doses of THC
- Strong ban on any advertising that appears to be directed toward youth – for all drugs including marijuana, tobacco and alcohol