

Medical Marijuana Study Subcommittee Meeting June 21, 2021

Kenneth Finn, MD

Marijuana and Cannabinoids

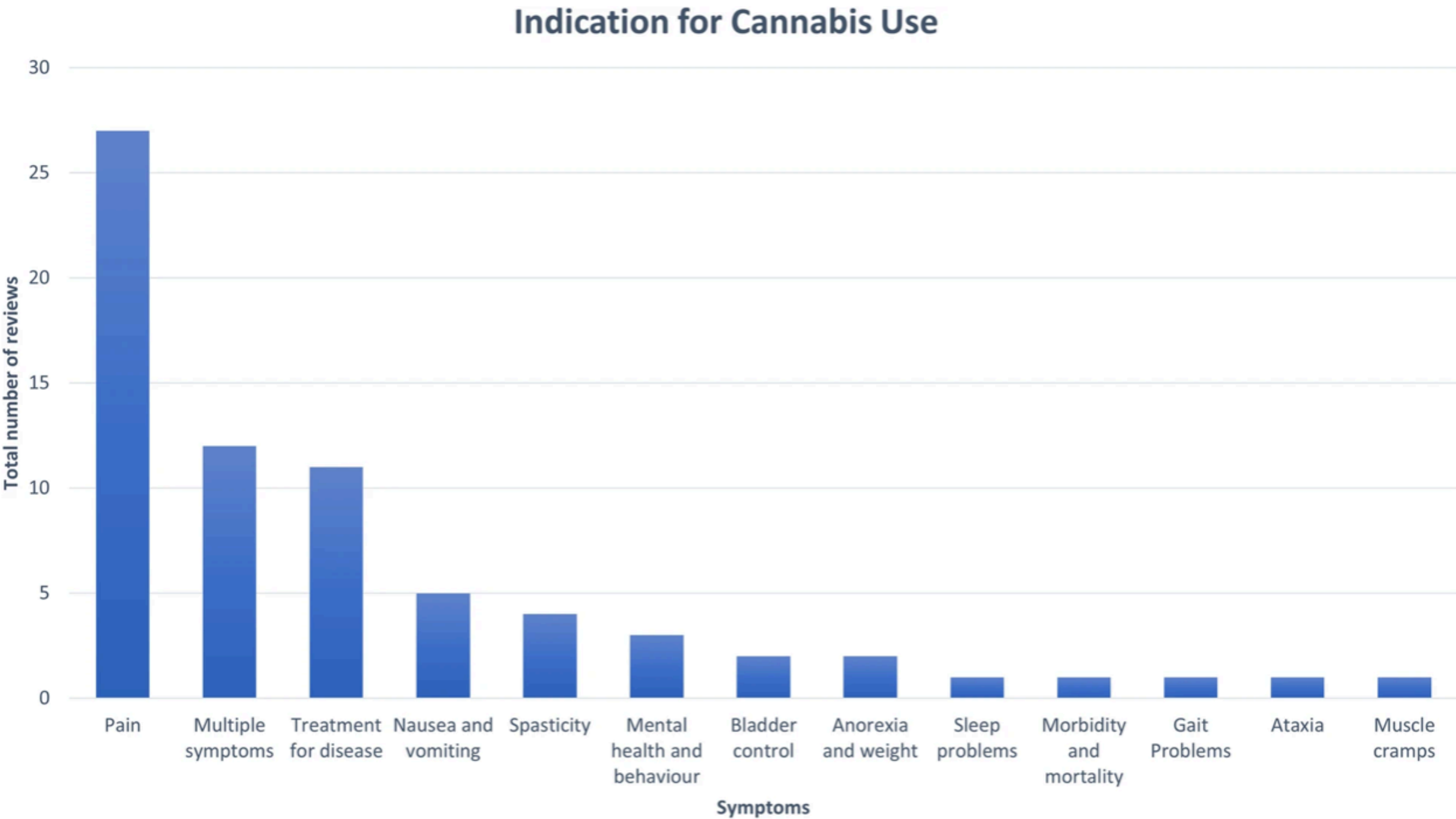
- Marijuana is not a medication. Marijuana is a plant
- Support FDA drug-development process for cannabinoids, including evidence-based dosing guidelines of cannabis-based medications

Terminology

- Cannabis-based medication
 - Registered medicinal cannabis extracts with defined and standardized THC and THC/CBD content should be classified as ‘cannabis-derived’ or ‘cannabis-based’ medicines.
 - Examples: Epidiolex®, Sativex ®(natural); dronabinol (semi-synthetic); nabilone (synthetic)
- Medical cannabis
 - Cannabis plants and plant material, for example flowers, marijuana, hashish, buds, leaves or full plant extracts used for medical reasons.
 - Poorly regulated and poorly tested for contaminants

National Ambulatory Care Survey, 2016

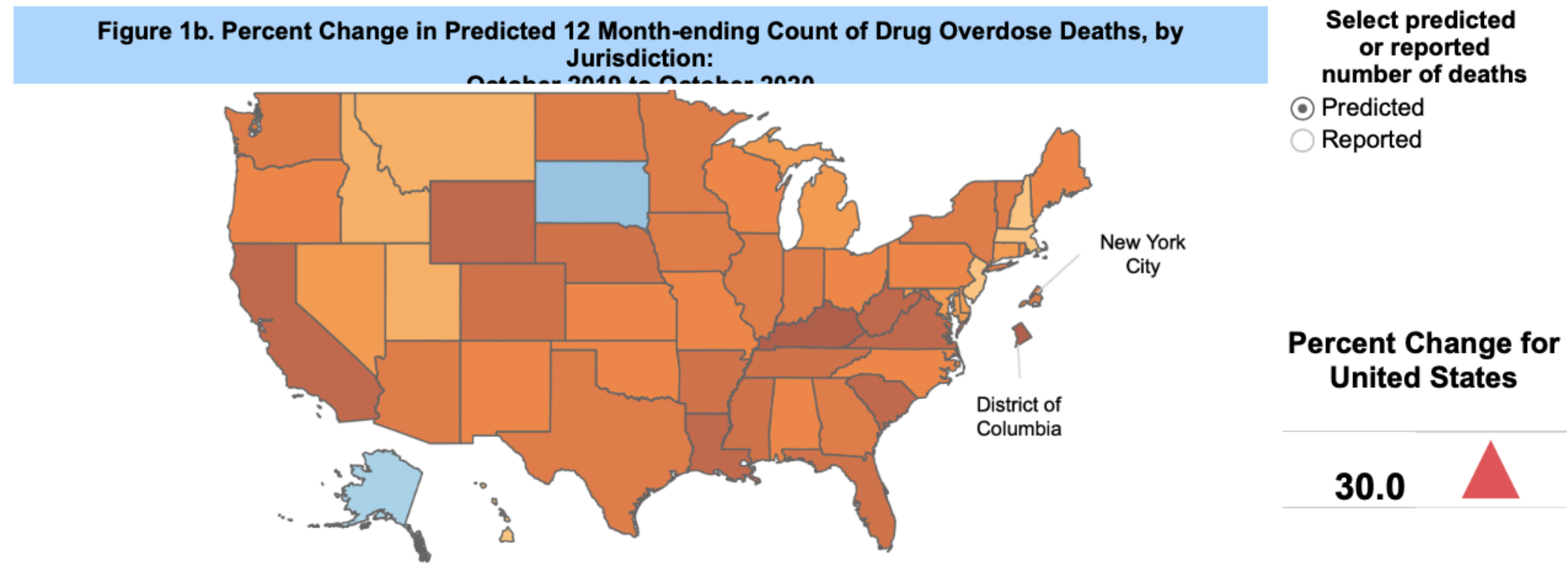
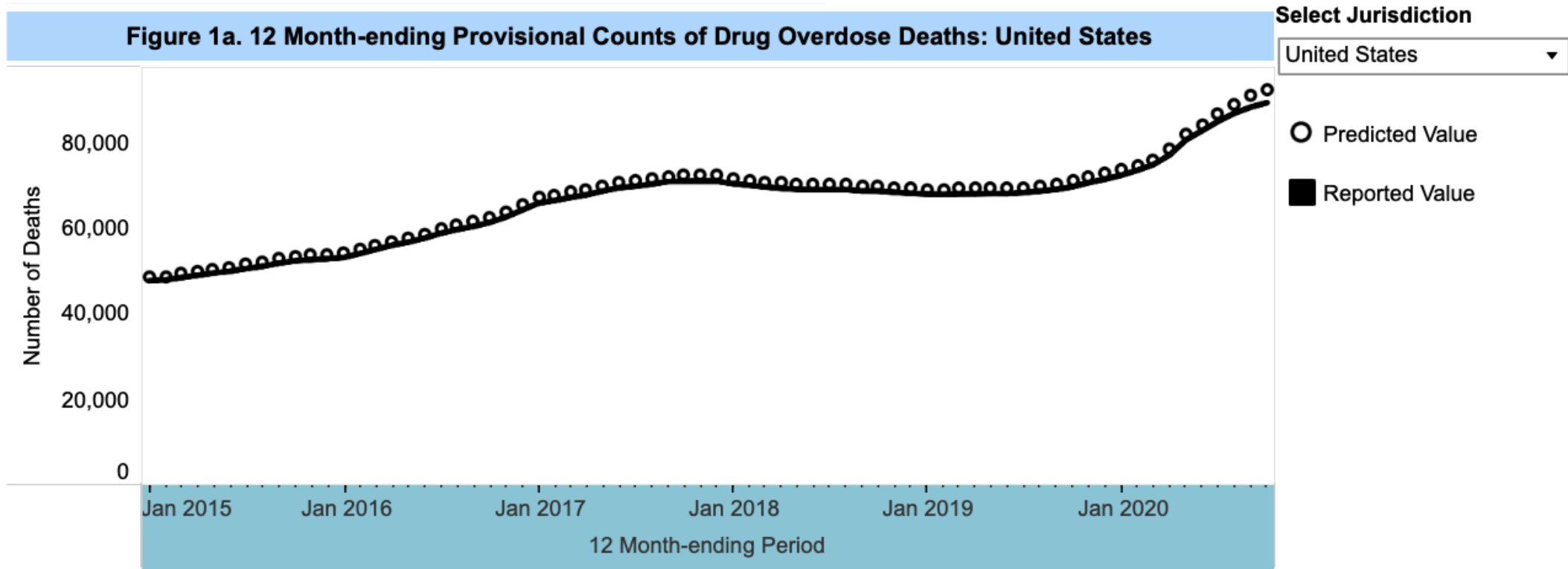
- National Survey
 - Why people see their doctor
 - **Knee pain** the only pain diagnosis in top 20 reasons
 - Others **not** in top 20: Back pain, Shoulder pain, Neck pain, Neuropathy, Headache, Fibromyalgia, Cancer, Seizure, other
-
- https://www.cdc.gov/nchs/data/ahcd/namcs_summary/2016_namcs_web_tables.pdf



Indications for cannabis use across included reviews

12 Month–ending Provisional Number of Drug Overdose Deaths

Based on data available for analysis on: 5/2/2021



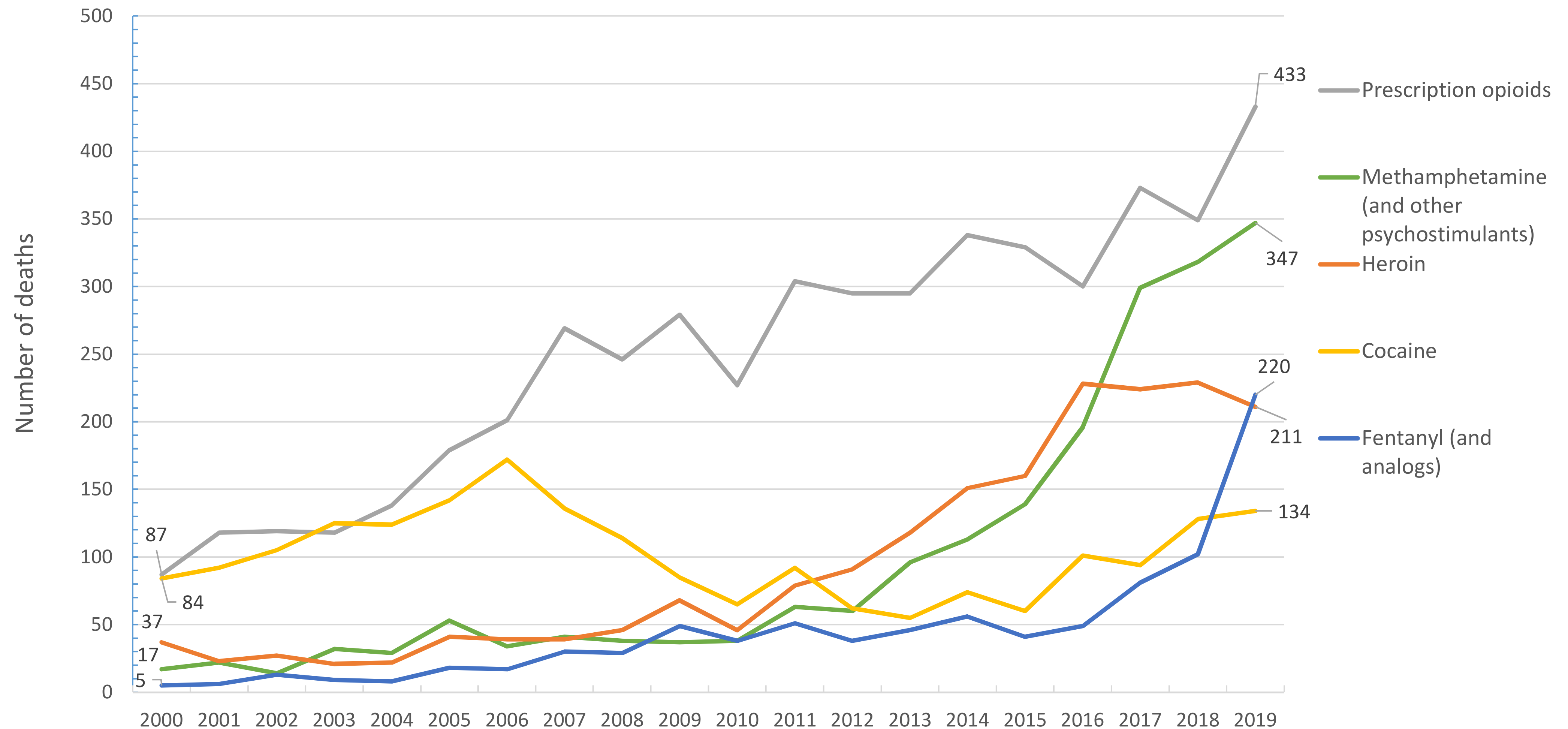
NOTES: *Reported* provisional counts for 12-month ending periods are the number of deaths received and processed for the 12-month period ending in the month indicated. Drug overdose deaths are often initially reported with no cause of death (pending investigation), because they require lengthy investigation, including toxicology testing. Reported provisional counts may not include all deaths that occurred during a given time period. Therefore, they should not be considered comparable with final data and are subject to change. *Predicted* provisional counts represent estimates of the number of deaths adjusted for incomplete reporting (see **Technical notes**).

Deaths are classified by the reporting jurisdiction in which the death occurred. Percent change refers to the relative difference between the reported or predicted provisional numbers of deaths due to drug overdose occurring in the 12-month period ending in the month indicated compared with the 12-month period ending in the same month of the previous year. Drug overdose deaths are identified using ICD–10 underlying cause-of-death codes: X40–X44, X60–X64, X85, and Y10–Y14.

Drug overdose deaths in the United States rose by an estimated 29% between September 2019 and September 2020 to **90,237**

<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard>

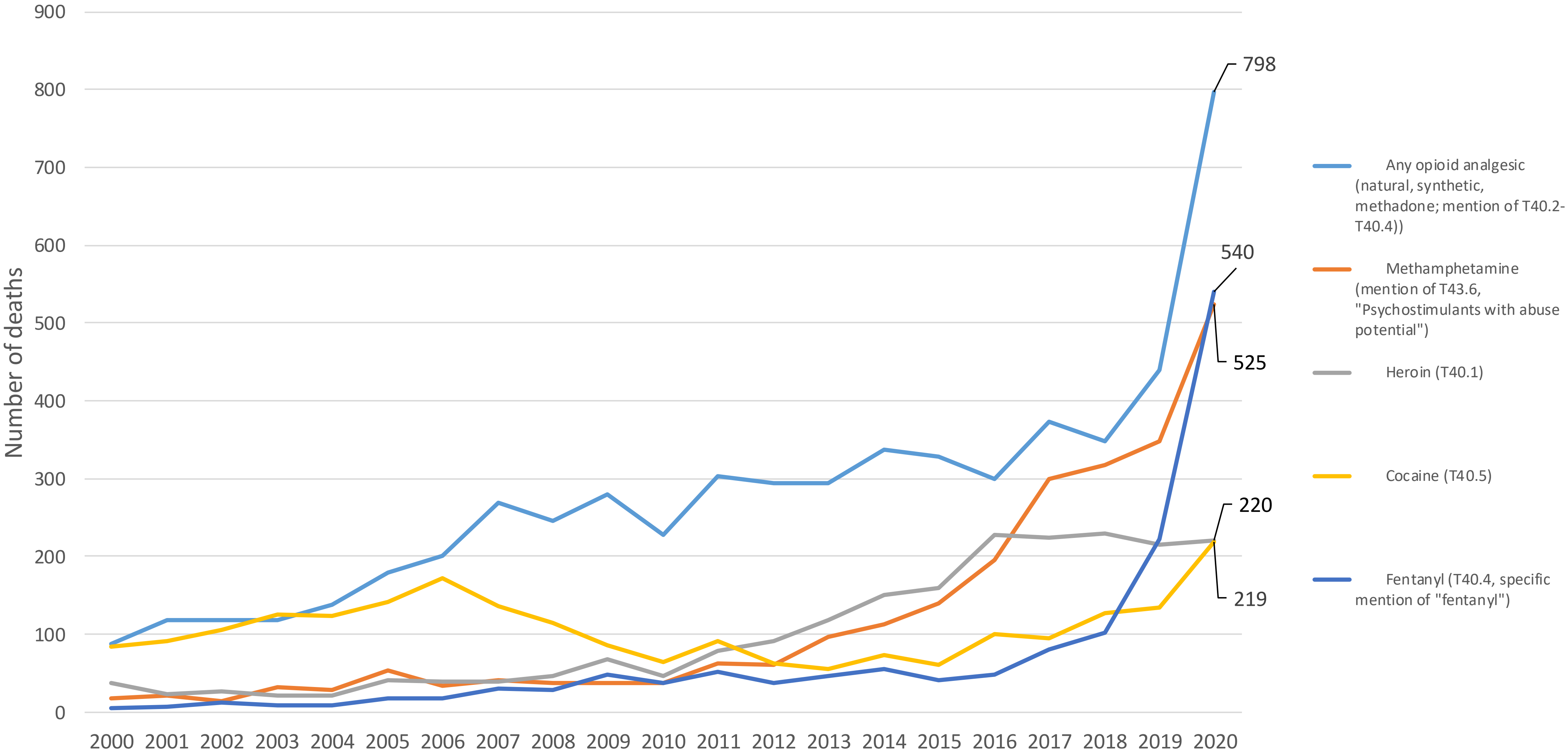
Number of drug overdose deaths by substances mentioned: Colorado residents, 2000-2019



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

2019 data shows a **24% increase** (433 total) in prescription opioid overdose deaths and **115% increase** (220 total) in fentanyl deaths

Number of drug overdose deaths by substances mentioned: Colorado residents, 2000-2020

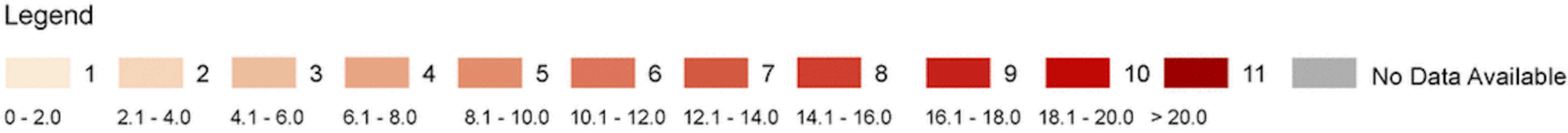
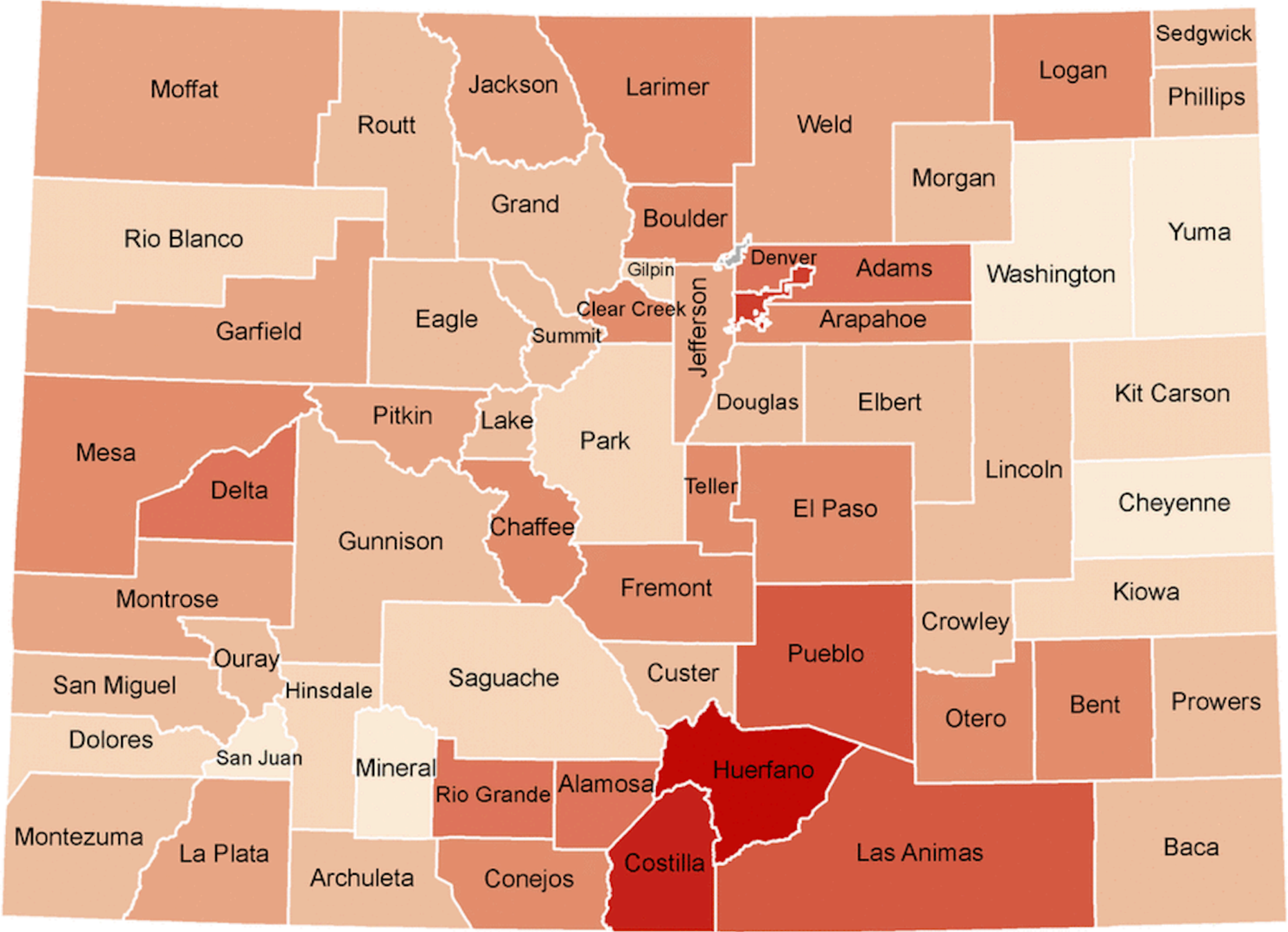


Source: Vital Statistics Program, Colorado Department of Public Health and Environment

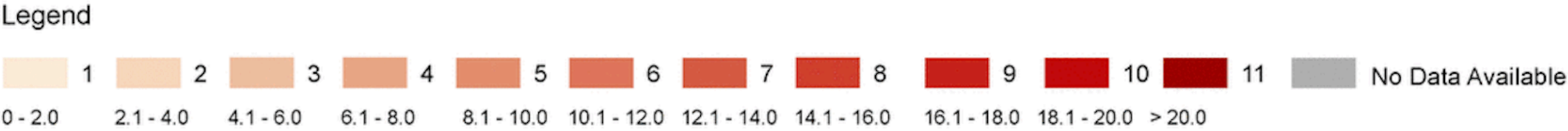
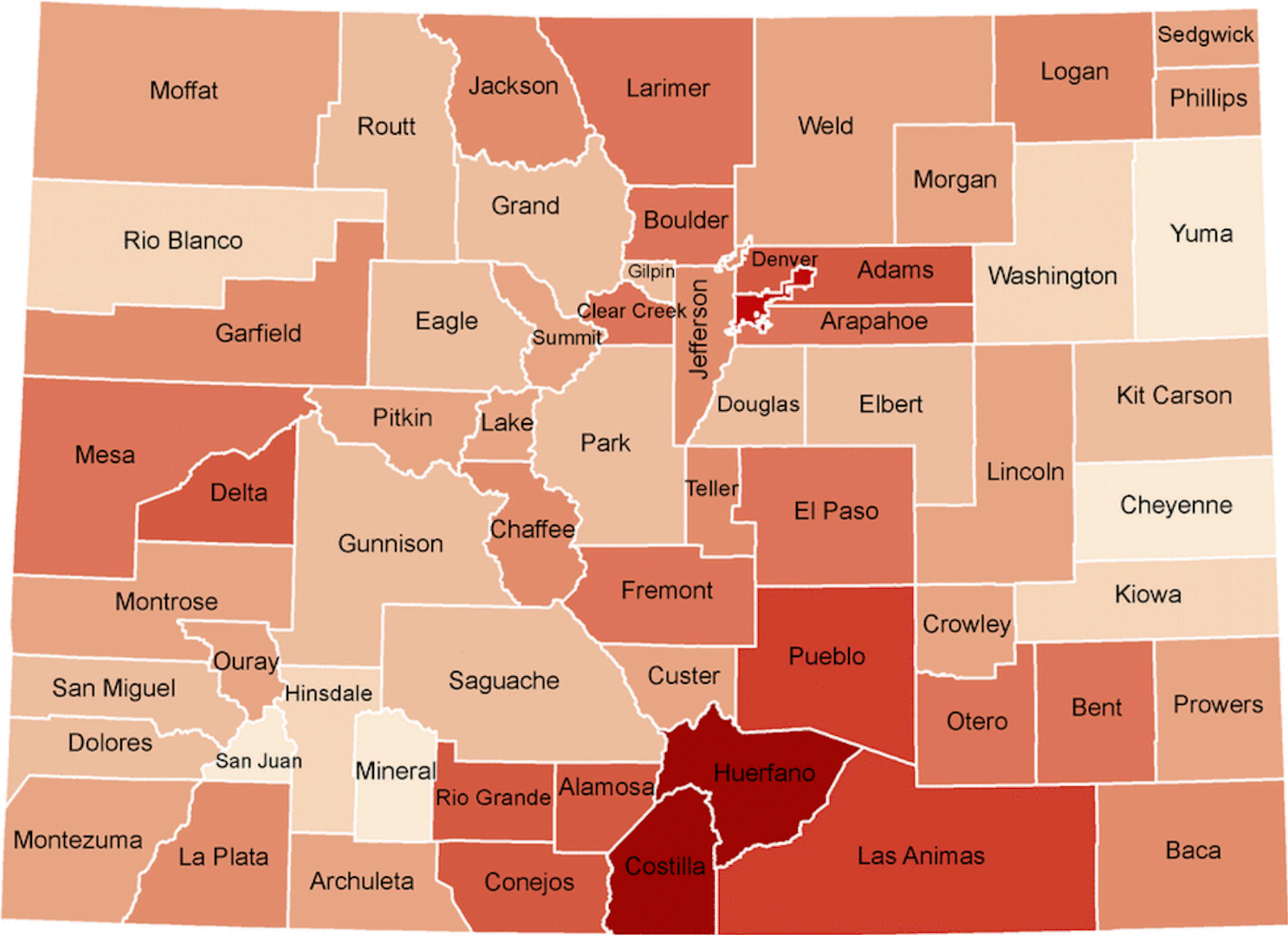
Colorado Health Institute Opioid Overdose Deaths by County 2002-2014

coloradohealthinstitute.org

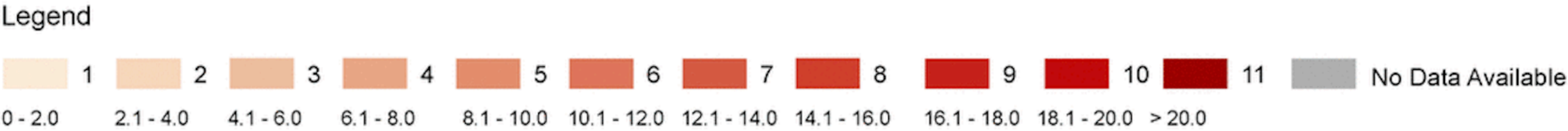
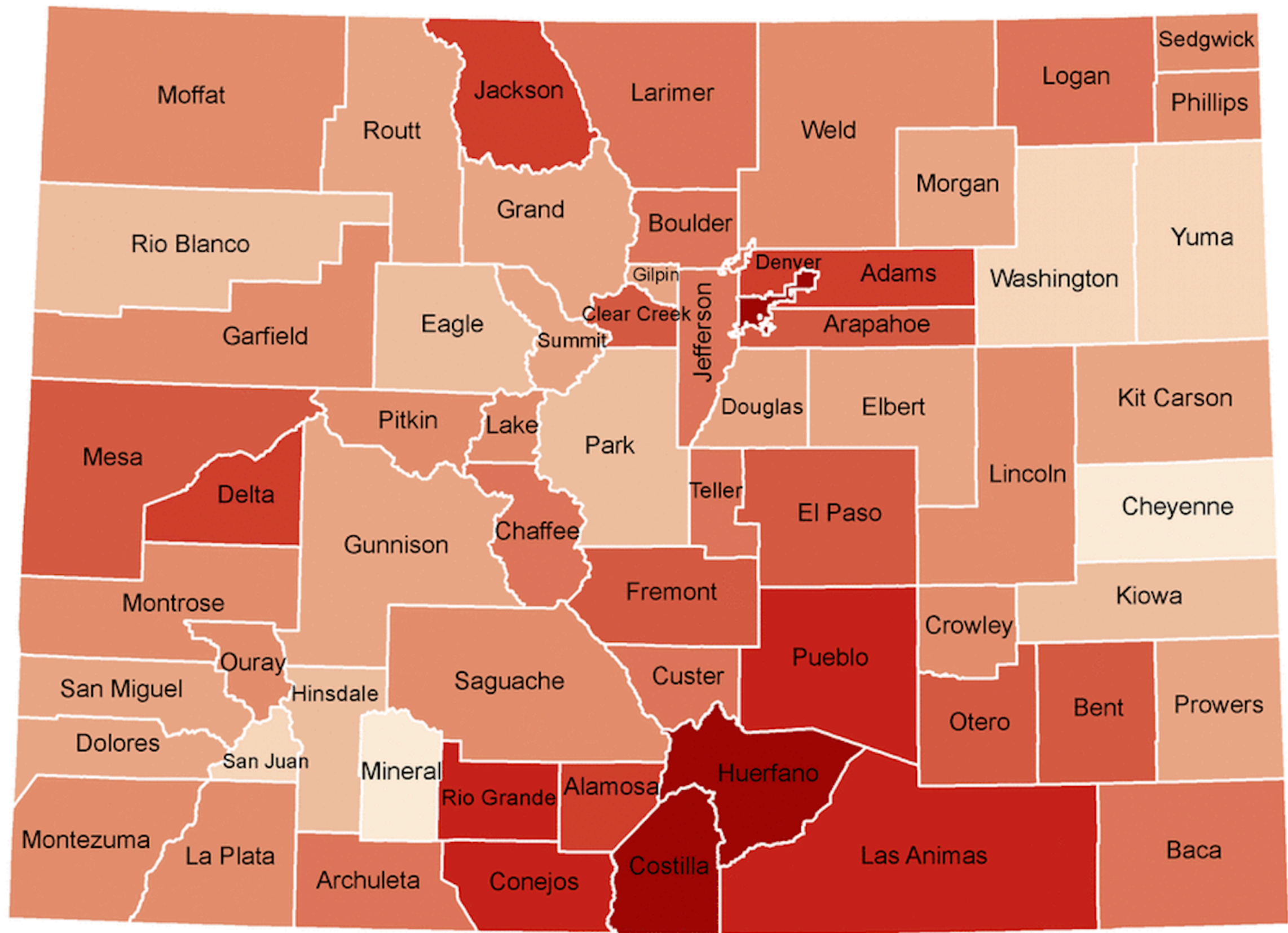
Colorado Drug Overdose Death Rate, 2002



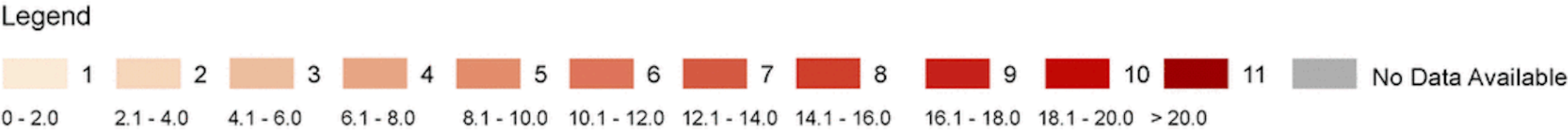
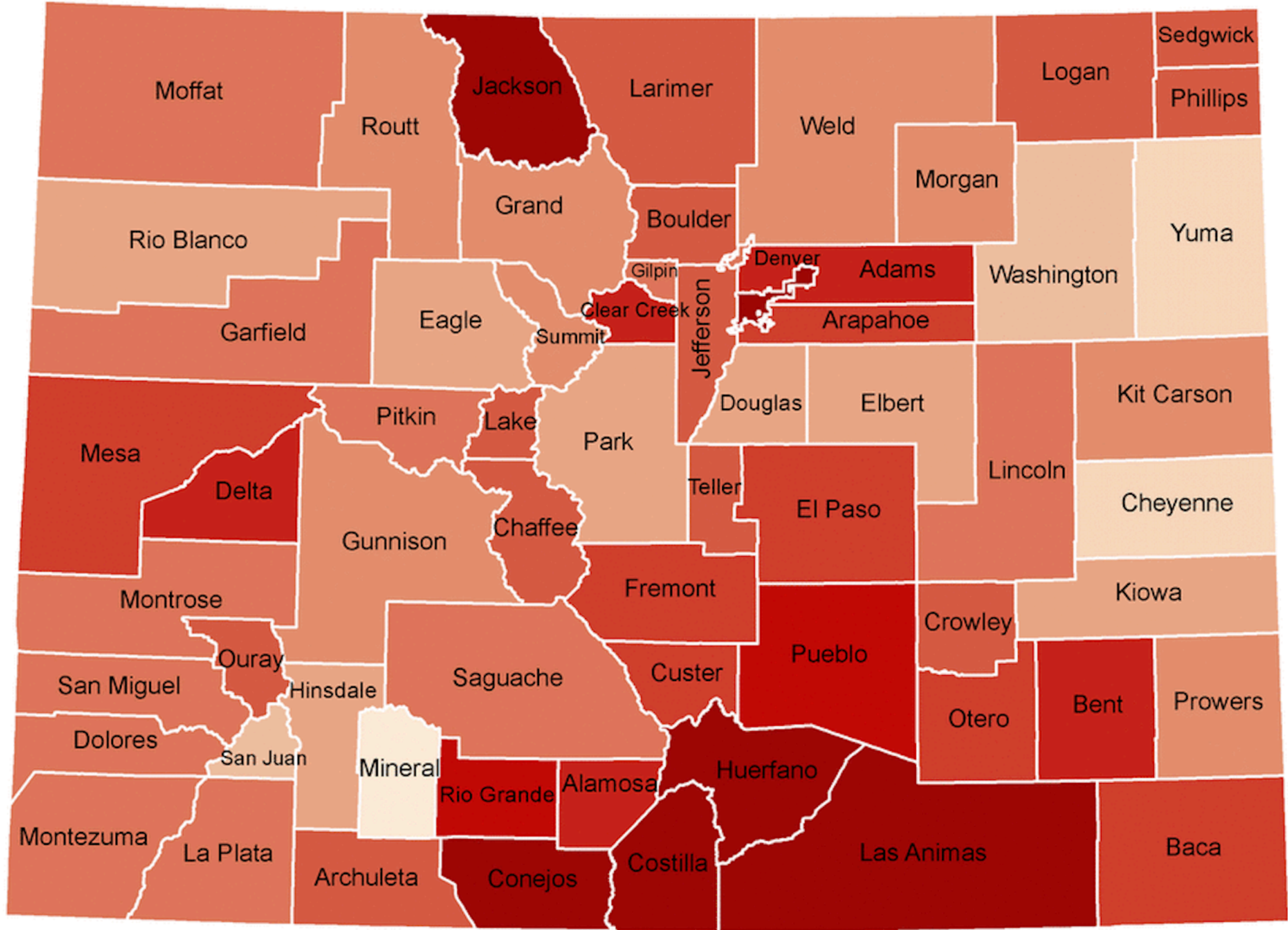
Colorado Drug Overdose Death Rate, 2005



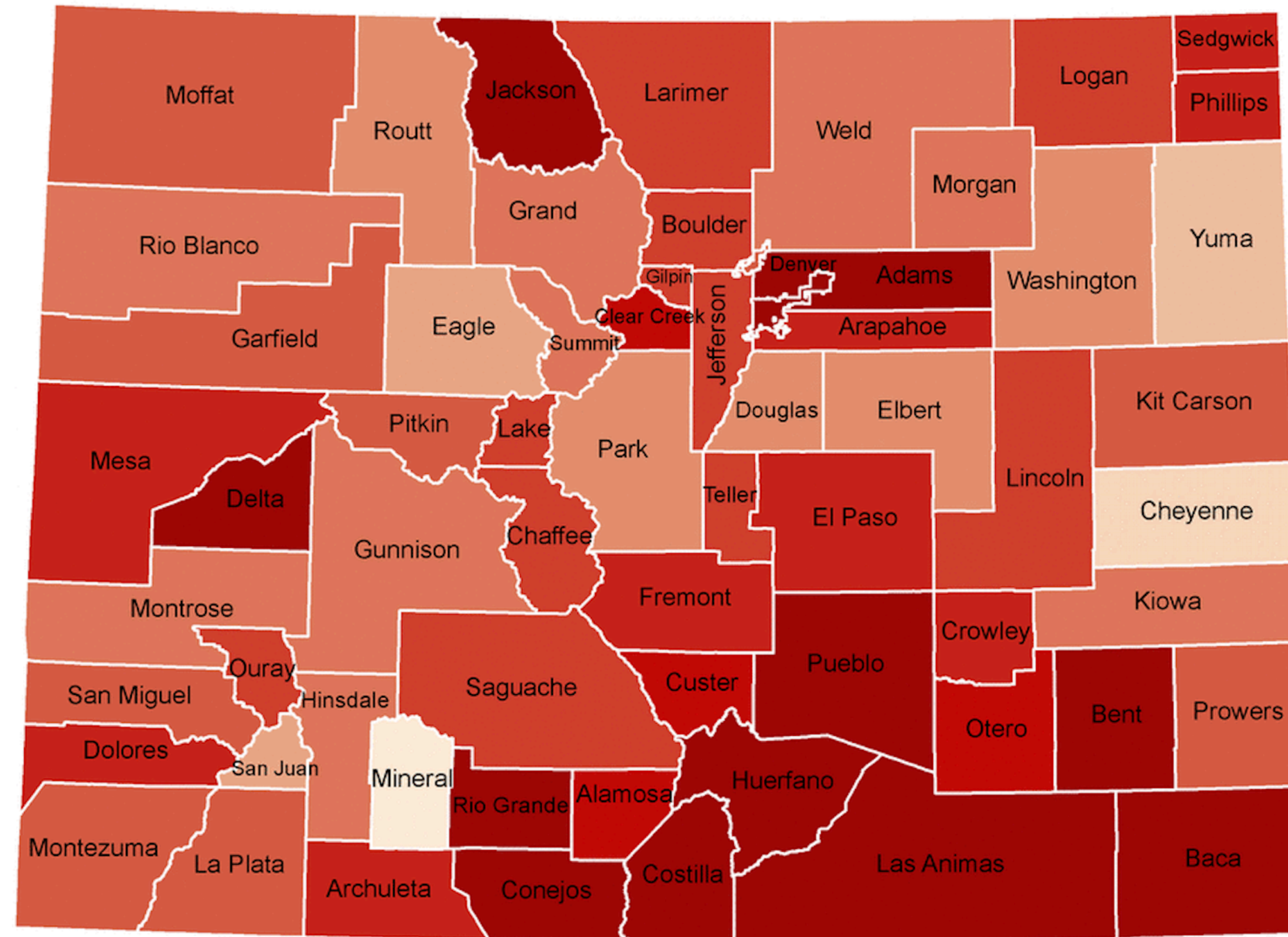
Colorado Drug Overdose Death Rate, 2008



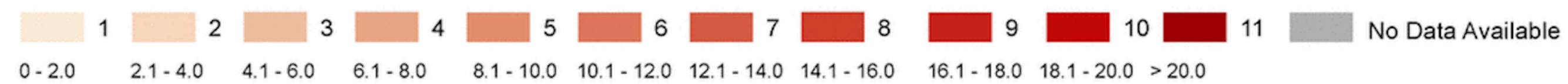
Colorado Drug Overdose Death Rate, 2011



Colorado Drug Overdose Death Rate, 2014



Legend



Evidence

- 2021, International Association for the Study of Pain
 - Due to the **lack of high-quality clinical evidence**, IASP does not currently endorse general use of cannabis and cannabinoids for pain relief.
- 2021, Australian and New Zealand College of Anaesthetists, Faculty of Pain Medicine
 - The evidence available is either **unsupportive** of using cannabinoid products in chronic non-cancer pain (CNCP), or is of **such low quality** that no valid scientific conclusion can be drawn

Opioids

- 2020, Drug and Alcohol Dependence, Wadekar: The dominant predictor of OUD is first use of marijuana before the age of 18 years
- 2020, Youth Risk Behavior Survey; Lifetime marijuana use is the number one risk factor for prescription opioid misuse.
- 2020; Ramadan; Past-year marijuana use was significantly associated with an increase in odds of reporting opioid dependence, and past-year non-medical use opioids

Opioids

- There is **no evidence** supporting the use of **dispensary** cannabis for chronic non-cancer pain
- There is **no evidence** for substituting opioids with **dispensary** cannabis
- Cannabis users are **more likely** to develop opioid use disorder or misuse their opioids and have higher depression and anxiety scores, and other negative psychiatric effects
- States with medical marijuana programs typically have **higher opioid overdose deaths** than non-medical marijuana states
- Any real or perceived benefit **outweighed** by current evidence



- Teen visits to Emergency Departments **increase** post legalization **with 71%** for psychiatric events (Colorado, Wang, 2018)

G.S. Wang et al. / Journal of Adolescent Health 63 (2018) 239–241

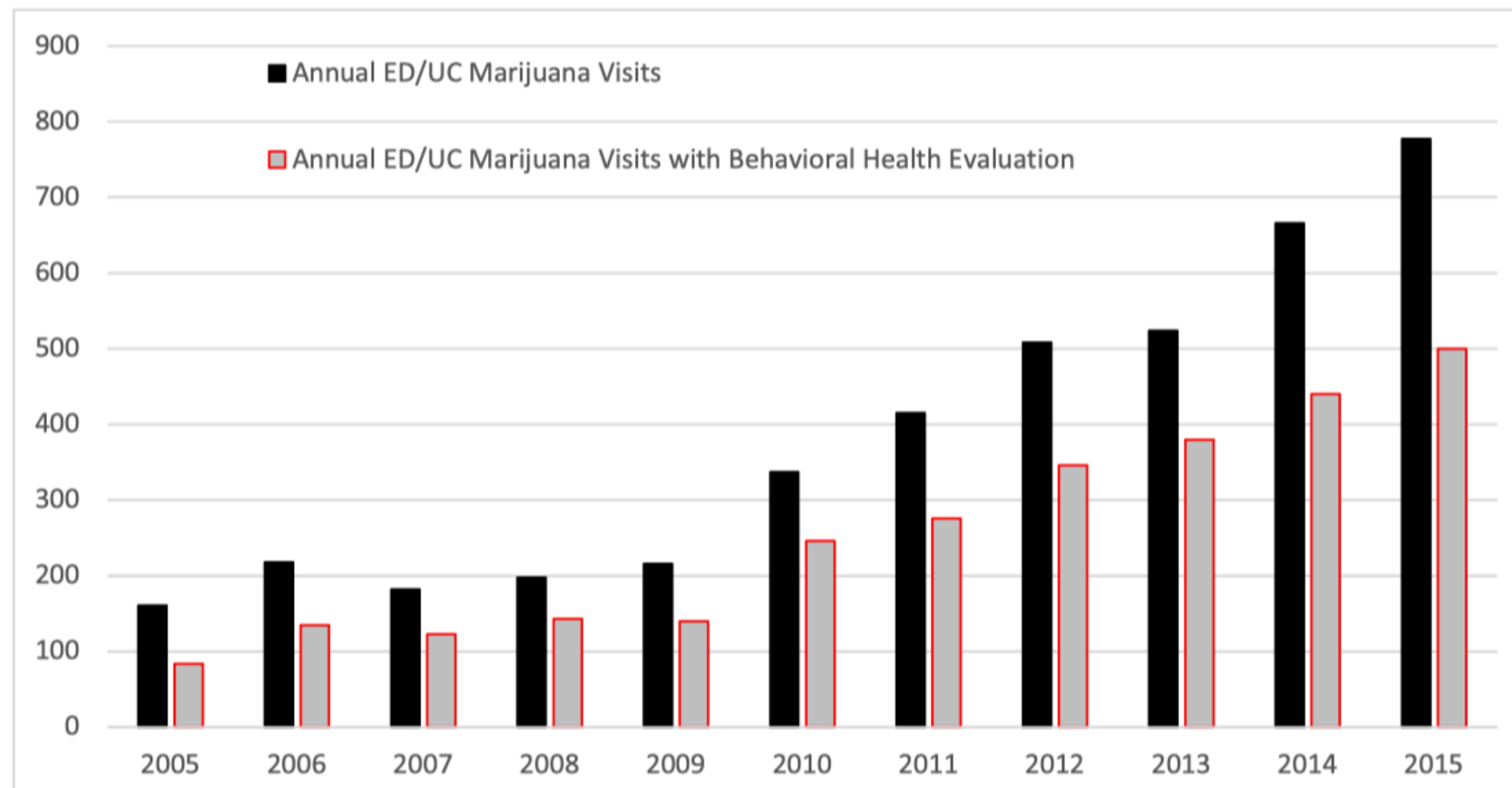
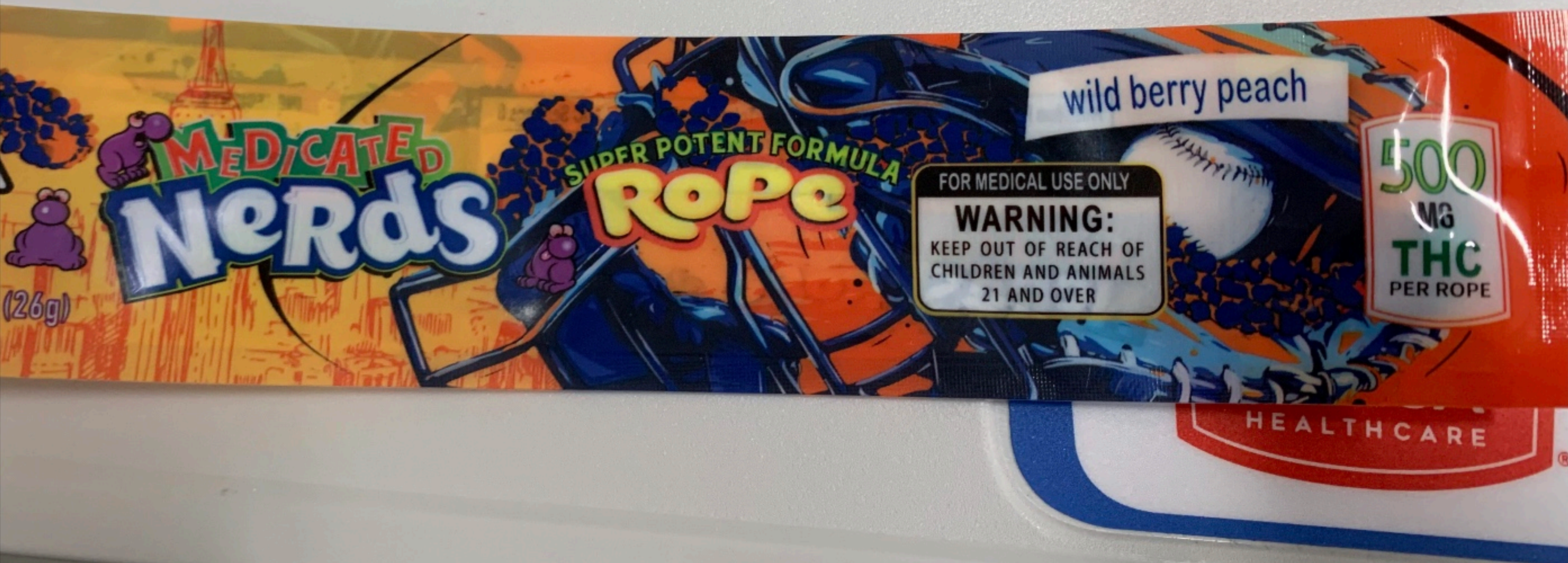


Figure 1. Annual marijuana-related emergency department (ED) and urgent care (UC) visits from a tertiary care children's hospital in Colorado.



wild berry peach

FOR MEDICAL USE ONLY

WARNING:

KEEP OUT OF REACH OF
CHILDREN AND ANIMALS
21 AND OVER

500
MG
THC
PER ROPE

HEALTHCARE

Nutrition Facts / Dosage Facts - Per Serving - Total Dosage 420MG / THC Servings 8

Serving Size: 50MG **Amount Per Serving:** **Calories** 8, **Total Fat** 0 g. **Protein** 0 g. Not a significant source of calories from fat, saturated fat, trans fat, cholesterol, dietary fiber, vitamin A, vitamin C, calcium and iron. Percent Daily Values (DV) are based on a 2,000 calorie diet.

MEDICATED
Nerds

ROPE



SUPER POT

Youth Risk Behavior Survey

August 2020

- Every other drug among young people is going down with the exception of marijuana.
- Lifetime marijuana use is the number one risk factor for prescription opioid misuse.
- 21.7% of high schoolers report marijuana use
- 43.5% of students who reported currently abusing prescription opioids also reported currently using marijuana

Healthy Kids Colorado Survey

August 2020

- **32.4%** of youth **drove a vehicle after using marijuana** in the past month, **up from 9.0%** in 2017
- **More than half** of high school students who use marijuana reported that they **dab marijuana** to get high
 - Dabbing” is a method of inhaling **highly concentrated THC** (commonly referred to as hash oil, wax or shatter) using a **blow torch-heated** delivery system commonly referred to as a dab rig
- Results also show a **69% increase** in students vaping marijuana in two years
- More than 20% of adolescents have **used in the past 30 days** and got their marijuana **from an adult**

Adolescent Cannabis Use and Opioids

- March 29, 2021; JAMA Pediatrics
- “Within a year of first trying marijuana, 10.7% of adolescents (12-17 yo) had become addicted to it....within three years of first trying the drug, 20% of adolescents became addicted to it.”
- Compared to opioids (11.2%, 10.6%)
- At 3 years of first trying marijuana vs. opioids (12-17 yo), marijuana has a higher percentage of addiction

STUDY SUBJECTS (FIRST TIME USERS)	ADDICTION RATE AFTER 1 YEAR	ADDICTION RATE AFTER 3 YEARS
Cannabis (age 12-17)	10.7%	20.1%
Cannabis (18-25)	6.4%	10.9%
Opioid (12-17)	11.2%	10.6%
Opioid (18-25)	6.9%	7.3%
Cocaine (18-25)	5.6%	6.4%
Heroin (18-25)	30.9%	42.5%

Cannabis Use and Depression

- JAMA Psychiatry, August 18, 2020
- Adults 20-50 yo, N=16,216
- Individuals with depression are at increasing risk of cannabis use, with a particularly strong increase in daily or near daily cannabis use
- Individuals with depression had approximately double the odds of using cannabis compared with people without depression

Self-Harm and Mortality Risk

January 2021

- Cannabis use disorder is a common comorbidity and **risk marker** for self-harm, all-cause mortality, and **death** by unintentional overdose and **homicide** among youths with mood disorders
- Cannabis use disorder was significantly associated with nonfatal **self-harm** and all-cause **mortality**

JAMA Pediatrics; January 19, 2021

<https://jamanetwork.com/journals/jamapediatrics/article-abstract/2775255>

Suicidality

- American Academy of Pediatrics, March 2021
- Current **adolescent prescription opioid misuse** is associated with **increases in the risk for suicide-related behaviors**
- Adolescent marijuana use —> opioid misuse —> suicidality

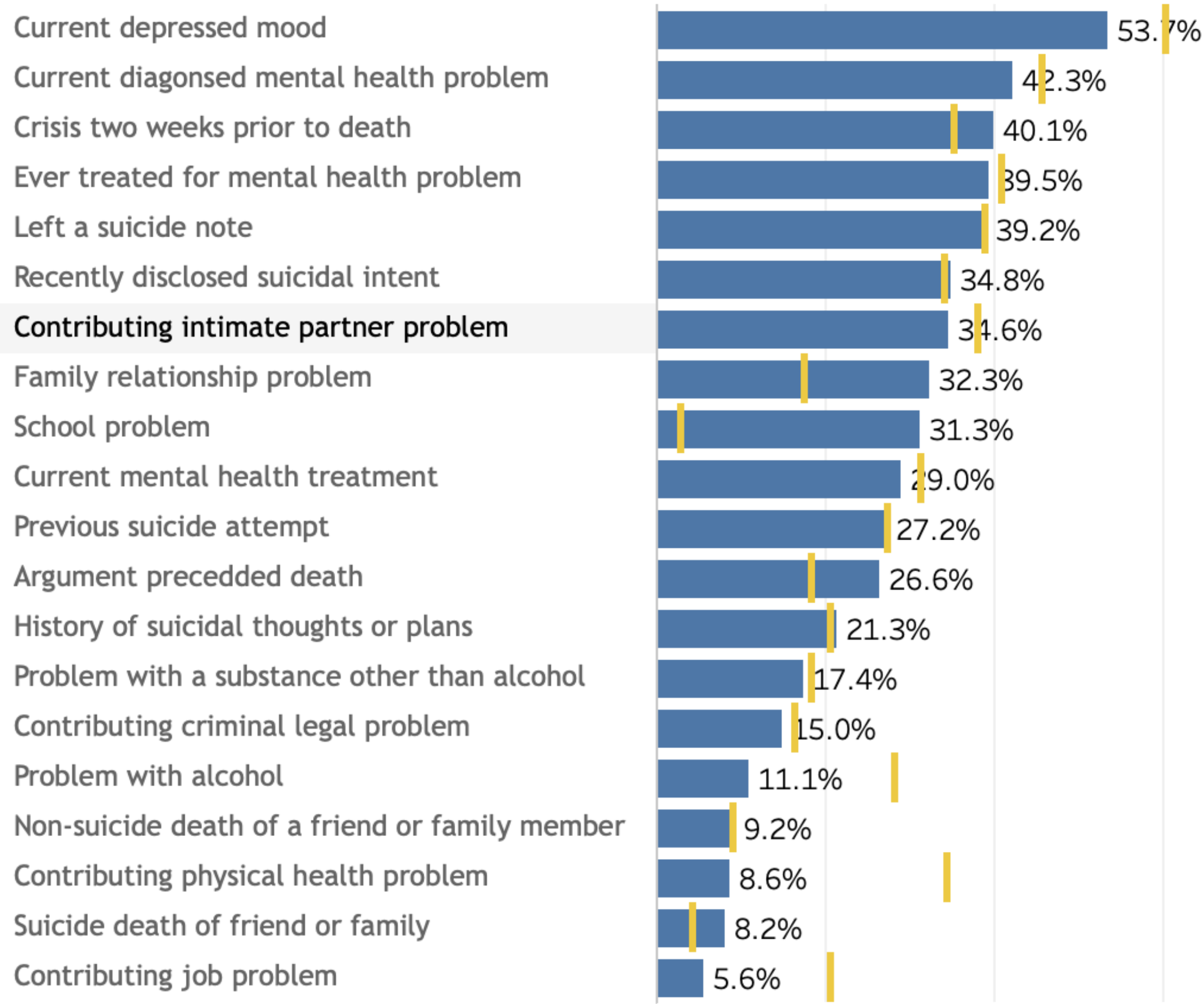
Circumstances

Entire state:

1+ circumstances known	12,254
No circumstances known	733

Selected population:

1+ circumstances known	12,254
No circumstances known	733



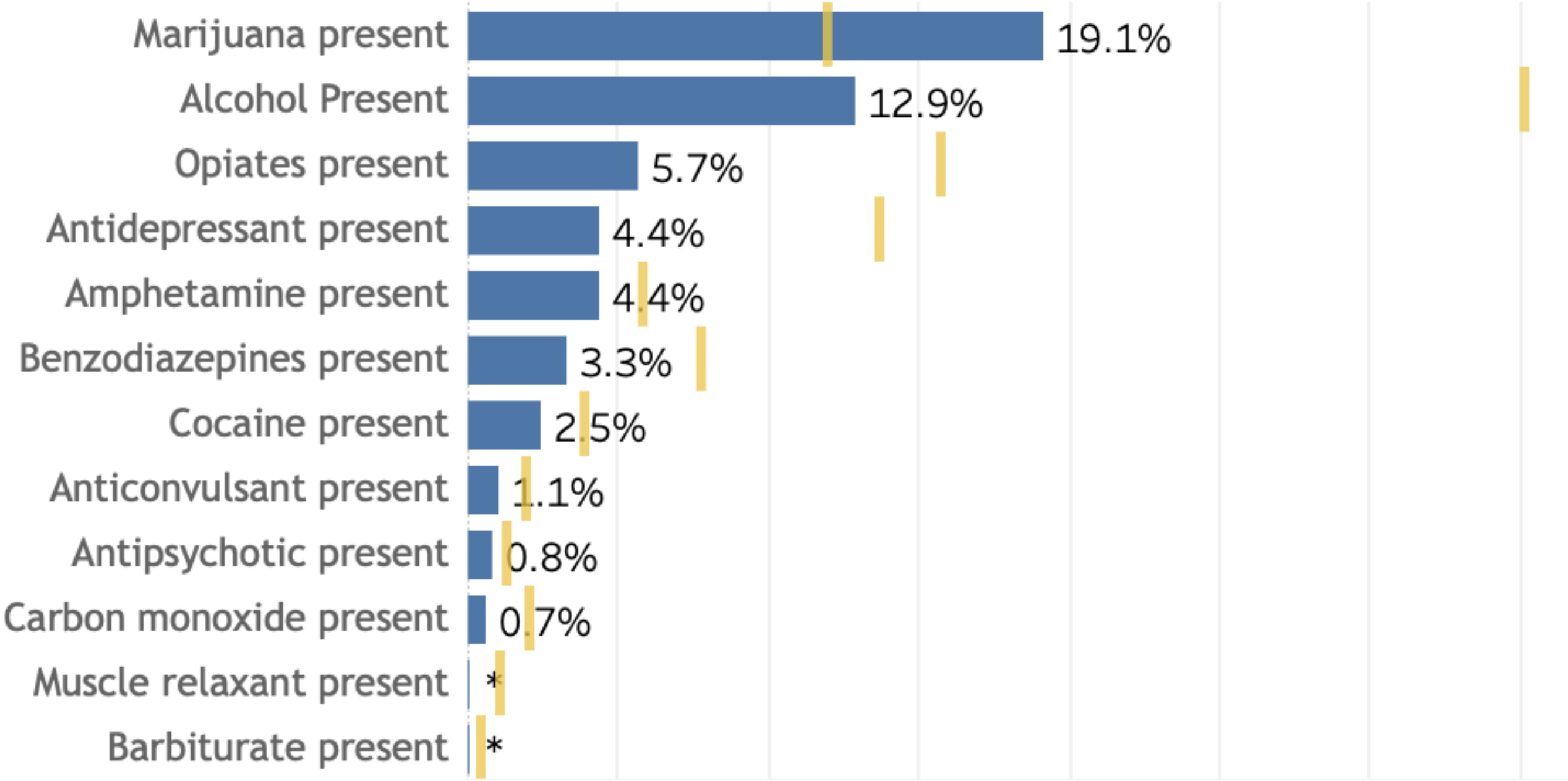
Toxicology

Entire state:

Toxicology info available	10,781
No toxicology info available	2,206

Selected population:

Toxicology info available	10,781
No toxicology info available	2,206



Trend **began 2012** and has **remained #1** since then

https://cohealthviz.dphe.state.co.us/t/HSEBPublic/views/CoVDRS_12_1_17/

Story1?:embed=y&:showAppBanner=false&:showShareOptions=true&:display_count=no&:showVizHome=no#4

Pregnancy/In Utero Exposure



Marijuana Tampons for Menstrual Cramps



<https://tipshire.com/marijuana-tampons-combat-menstrual-cramps/>

Pregnancy/In Utero Exposure

- Prenatal cannabis use and childhood outcomes: **ABCD Study** (*Paul, et. al., JAMA Psychiatry, 2020*), N=11,875, 9-11 years after birth
- Prenatal cannabis exposure is associated with **greater psychopathology**
 - psychotic-like experiences (**PLEs**)
 - attention, thought, and social problems
 - **lower** birth weight and **lower** intracranial volumes

Pregnancy/In Utero Exposure

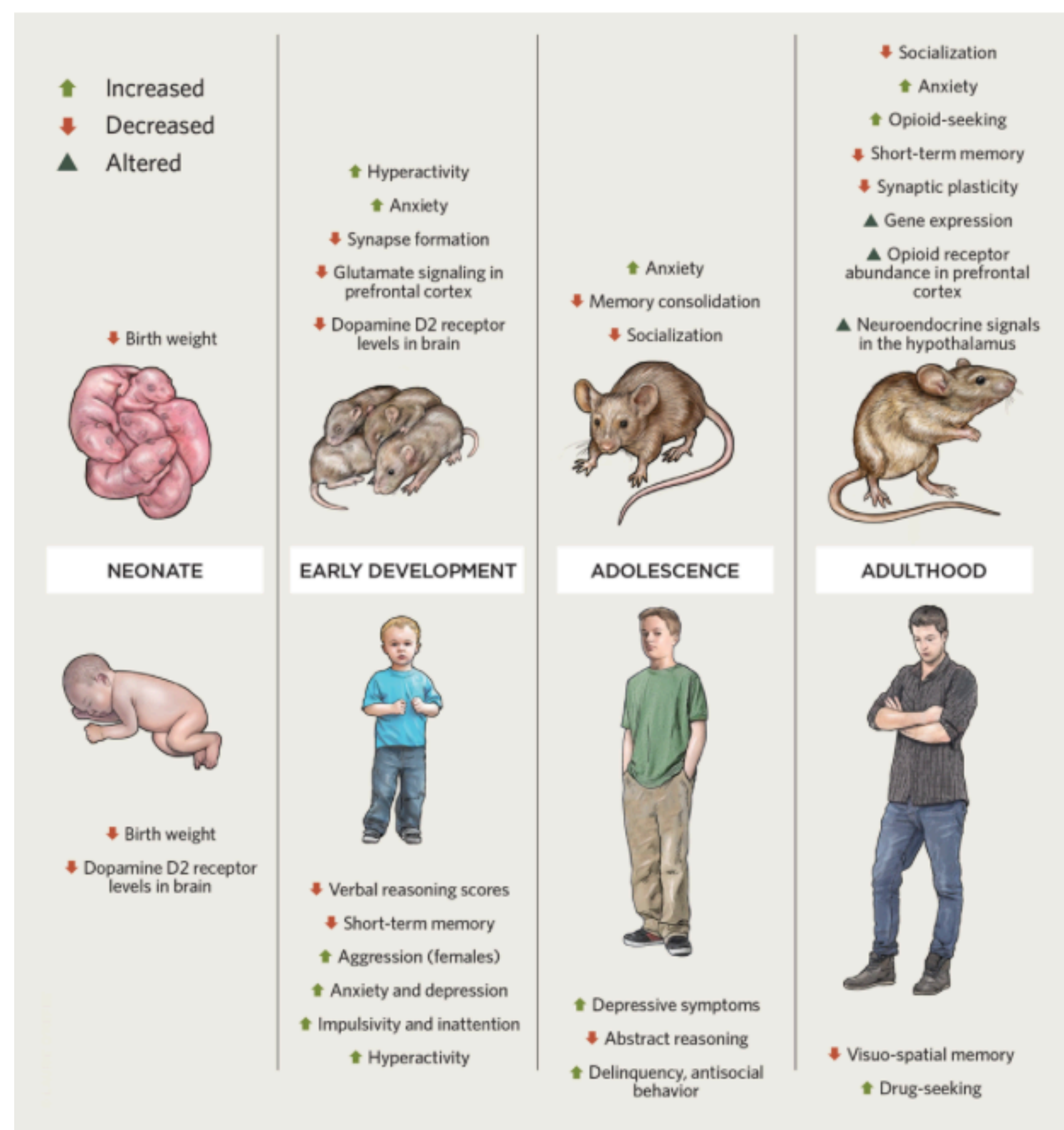
- There are associations ($P < 0.05$) between **prenatal marijuana exposure** and decreased performance on memory, impulse control, problem-solving, quantitative reasoning, verbal development and visual analysis tests; as well as increased performance on attention and global motion perception tests (*Sharapova, 2018*)
- **Neuropsychological decline** in persistent users which continues after cessation and persistent users showing a greater decline (*Meier, PNAS, 2012*)
- Average decline of approximately **2 IQ points** following exposure to cannabis in youth. (*Power, et. al.; Psychological Medicine, January, 2021*)

Pregnancy/In Utero Exposure

- More than 70% of surveyed dispensaries in Colorado **recommended cannabis use during first trimester** pregnancy (*Dickson, et. al., Obst and Gyn, 2018*)
- **THC crosses the placenta** and is found in breast milk and can be detected for up to 6 days after last use (*Bertrand, Pediatrics, 2018*)
- THC may persist in breast milk for **up to 6 weeks** after cessation (*Wymore, et. al., JAMA Pediatrics, Mar 2021*)
- Prenatal marijuana **exposure impacts executive functioning** into young adulthood: An fMRI study (*Smith et. al., Neurotox and Tera, 2016*)

Pregnancy/In Utero Exposure

- Evidence for adverse effects of **paternal THC** administration on neurodevelopment in the offspring (*Slotkin, et. al.; Toxicological Sciences, 174(2), 2020, 210–217*)
 - Impact on behavior, attention, and reward
- A longitudinal study of the impact of marijuana on adult memory function: Prenatal, adolescent, and young adult exposures, (*Neurotoxicology and Teratology (2021)*)
 - **First trimester** marijuana exposure indirectly predicted **young adult memory**.
 - Early onset marijuana use predicted **increased memory deficits** in young adulthood.





Product Integrity

- Cannabinoid Dose and Label Accuracy in Edible Medical Cannabis Products
- San Francisco, Los Angeles, Seattle
- Regarding THC
 - 17% accurately labeled
- Regarding CBD
 - 59% had detectable levels of CBD

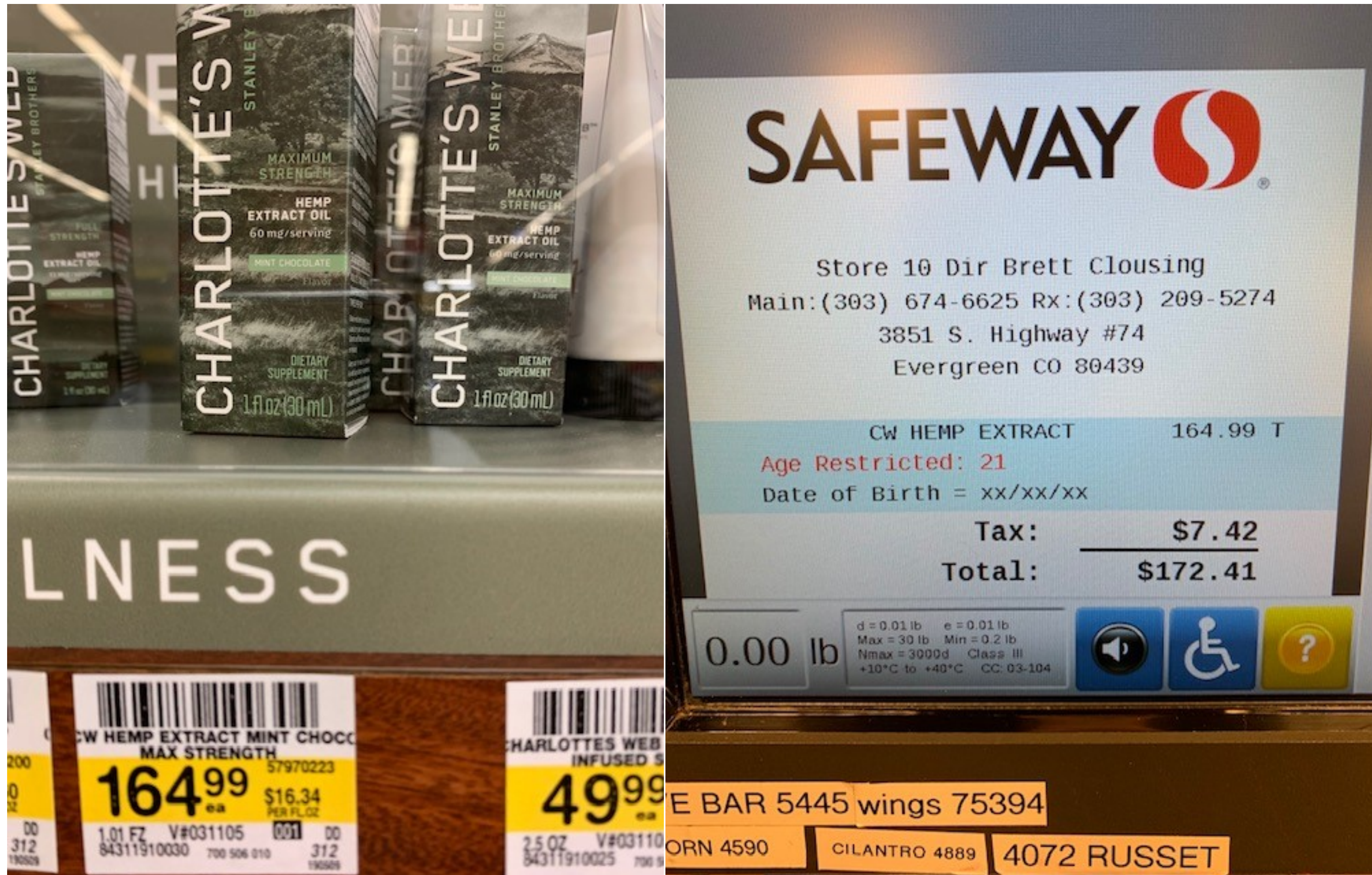
Product Integrity

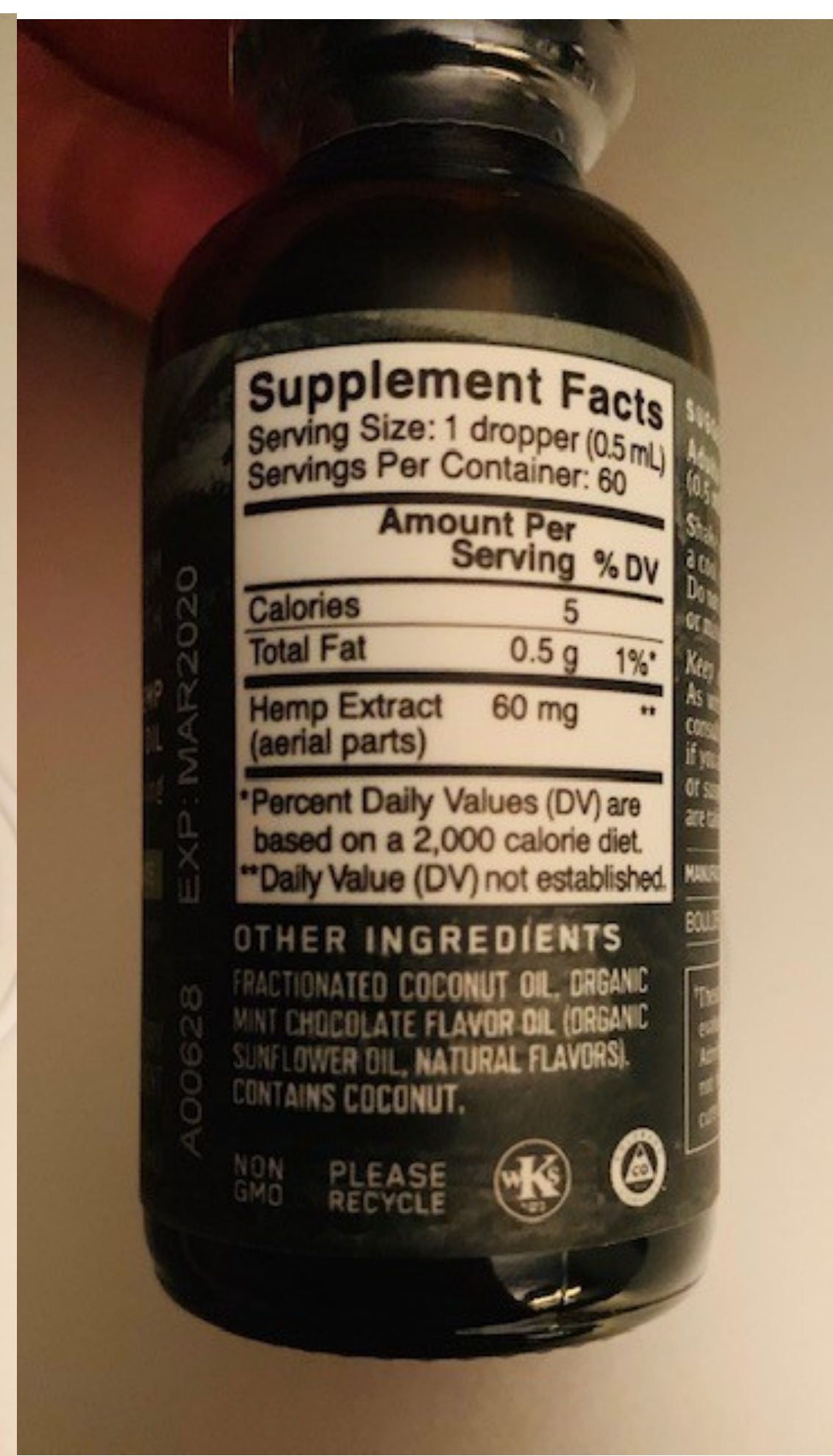
- Labeling Accuracy of Cannabidiol Extracts Sold Online
- Wide range of CBD concentrations
 - 0.10 mg/ml to 655.27 mg/ml
- Regarding CBD
 - 31% were accurately labeled
 - THC was detected in 21.4%

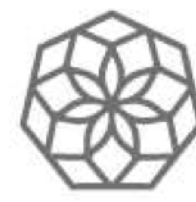
Product Integrity

- Among participants who reported using CBD-dominant or equal CBD-THC products, there was **no detectable CBD** metabolite in 30.3% and 37.0%, respectively
- **THC** was detected in 78.8% from participants reporting use of **CBD-dominant** products
- Among samples from participants reporting THC-dominant or equal CBD-THC products, **no THC metabolites** were present in 10.9% and 35.2%, respectively.

Insidious Products







CHARLOTTE'S WEB™

STANLEY BROTHERS Boulder, CO 80301 • 719-419-8169

CERTIFICATE OF ANALYSIS

Product Name: Charlotte's Web Hemp Extract Oil Maximum Strength Mint Chocolate 30mL

Product Batch: A00700

Product Code: 910.069

Best By: July 2020

Parameter	Result
Cannabinoids	
<i>Testing performed by Eurofins Food Chemistry Testing – Boulder, CO</i>	
THC	2.8 mg/mL
THC-A	0.033 mg/mL
THC-V	None Detected
CBD	64.3 mg/mL
CBD-A	0.44 mg/mL
CBD-V	0.31 mg/mL
CBG	0.32 mg/mL
CBG-A	None Detected
CBN	0.23 mg/mL
CBC	2.3 mg/mL
Total THC per Bottle	84 mg
Total THC per Serving	1.4 mg

Manufactured By: Charlotte's Web Inc.

Manufacture Date: 16JAN19, 18JAN19 - 20JAN19

Batch Size: 297,540 mL

Units Manufactured: 9,773

Industry Failures

- Oregon Secretary of State, 2019: “Oregon’s marijuana testing program **cannot ensure** that test results are reliable, and products are **safe**”. Only **3% of stores** had a compliance inspection. (<https://sos.oregon.gov/audits/Documents/2019-04.pdf>)
- California has an 18% fail rate and “**unacceptable**” levels of pesticides, solvents, and bacteria, including E. coli and Salmonella” (<https://www.breitbart.com/local/2018/09/12/report-california-regulators-fail-18-of-recreational-marijuana-tested/>)
- Colorado **does not test or recall** products on a regular basis

Colorado, October 8, 2020



- CDPHE and DOR safety advisory
- Yeast, mold, and arsenic at unacceptable limits
- “Return” your product
 - Dispensaries (med and rec) do not require customers register for recall notices
 - By the time you get notice, product likely consumed

https://drive.google.com/file/d/1xowig7vPtl-lz_xUAALt3DIxeGua1xY6/view

Colorado, March 31, 2021



- Unsafe levels of **cadmium**
 - Known human carcinogen, teratogen, and can cause renal damage
 - Pulmonary edema, anemia
- Products from November 2020-January 2021

Recall deals blow to California's marijuana industry

December 2018

- Sacramento laboratory was caught **faking** pesticide test results
- The director had been **faking test results** for 22 of the 66 pesticides he was required under California law to analyze.
- Nearly 850 batches — tens of **thousands of pounds** of flower, and an **equal amount** of other products, like oils and vaping material — are under the recall.

Med Man Issues Voluntary Nationwide Recall of Up2 Due to Presence of Undeclared Sildenafil

November 8, 2019

FDA

- Sildenafil is an FDA-approved prescription drug for erectile dysfunction.
- The presence of sildenafil in Up2 products renders them **unapproved drugs** for which safety and efficacy have not been established, therefore subject to recall.
- **Undeclared ingredient** may interact with nitrates found in some prescription drugs, such as nitroglycerin, and may **lower blood pressure** to dangerous levels which can be life threatening

<https://www.fda.gov/safety/recalls-market-withdrawals-safety-alerts/med-man-issues-voluntary-nationwide-recall-up2-due-presence-undeclared-sildenafil>

Florida August 18, 2020

- Florida medical cannabis company told to recall moldy flower
- The state health department's Office of Medical Marijuana Use said the product, Granddaddy Purple Whole Flower, tested **above the acceptable limit** for **aspergillus**
- Surterra Wellness dispensed **17,448,318 ounces** of medical marijuana flower, a little more than **545 tons**, in July

January 2021

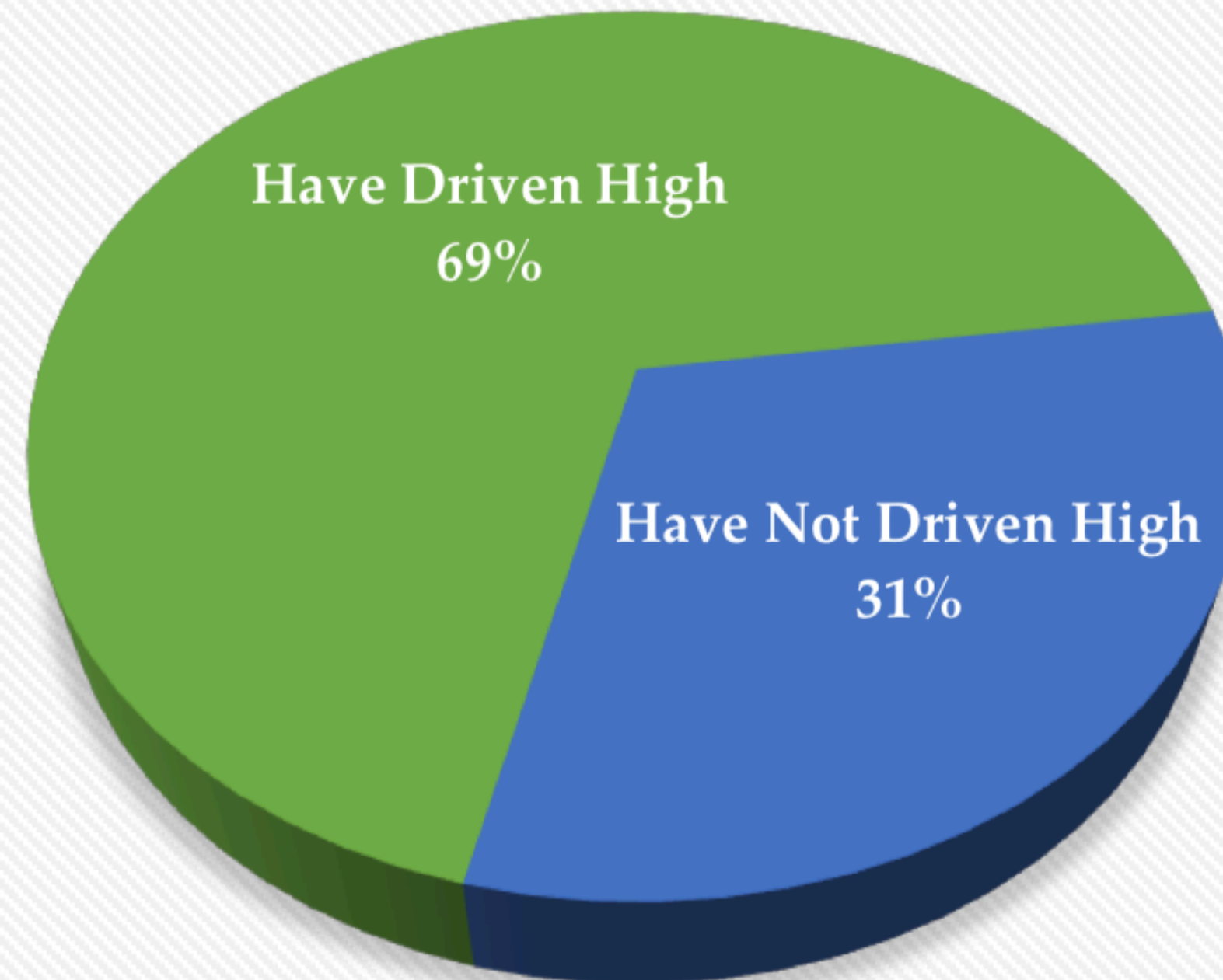
Nevada Lab Faking Data

- **Hiding** the presence of potentially **dangerous contaminants** and also **inflating THC levels** in marijuana
- Routinely passing samples that had previously failed testing for **pesticides, microtoxins, heavy metals and microbials**, all regulated contaminants. Samples, which are supposed to be tested once, were **sometimes tested up to five times** before "passing."
- Routinely **inflating THC levels** up to 5 percent higher than the actual THC levels. THC potency is known to drive **higher retail prices**
- **Failing** to properly dispose of more than 12,000 samples

Driving, Marijuana, and Opioids

- Drivers who test positive for marijuana are significantly more likely to test positive for prescription opioids
- Those testing positive for marijuana were 28% more likely to test positive for prescription opioids (Fatality Analysis Reporting System, N=47,602)
- Those testing positive for marijuana were twice as likely to test positive for prescription opioids (National Roadside Survey, N=7,881)

Percentage of Marijuana Users Who Admit to Driving High within the Last Year



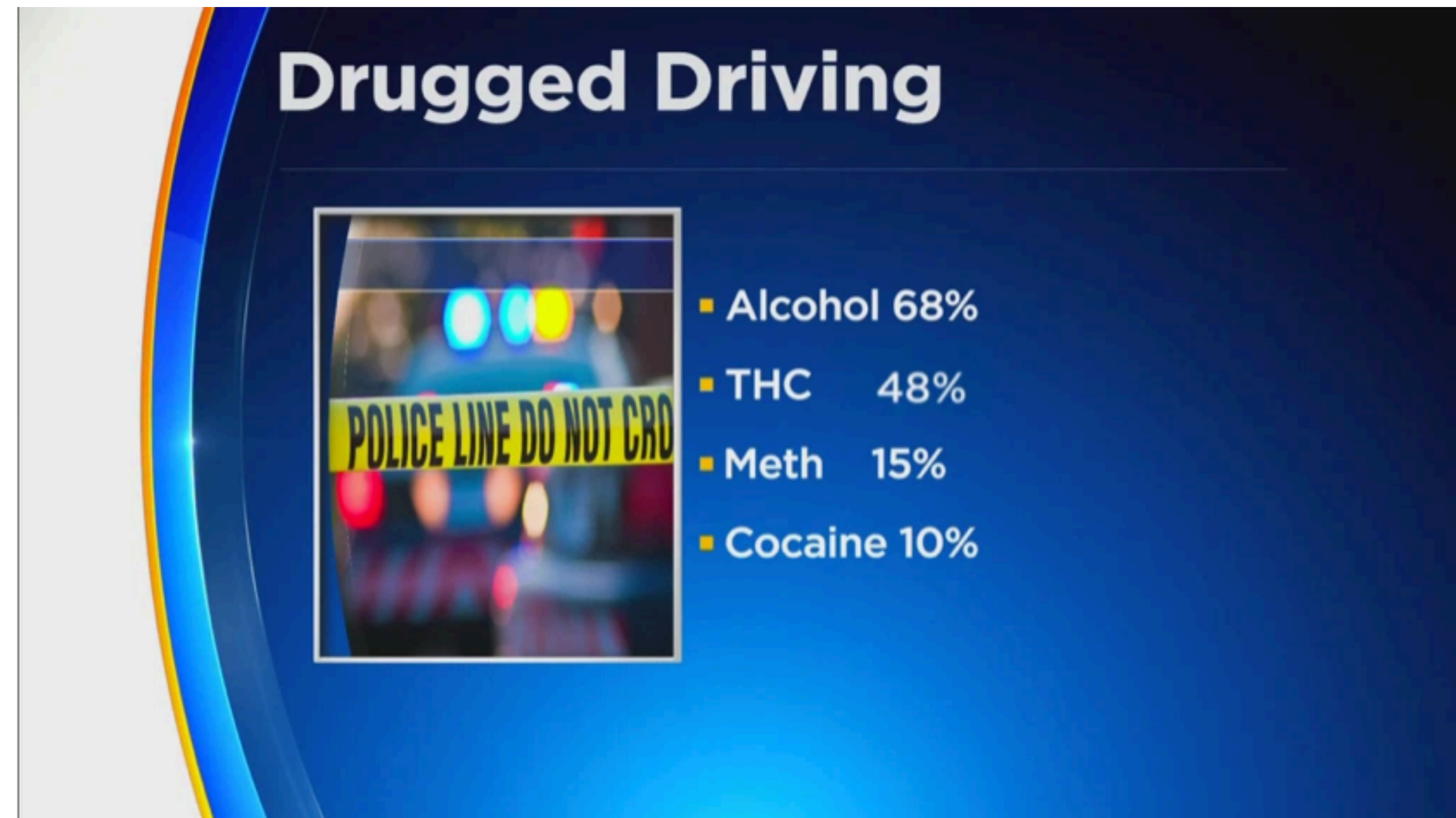
The Colorado Department of Transportation (CDOT) collected survey responses from over 11,000 anonymous marijuana users and non-users.

The above data is part of the preliminary data released by CDOT in April of 2018.

SOURCE: Colorado Department of Transportation, *Cannabis Conversation Survey*

Colorado DUI 2020

- Colorado State Patrol says DUI arrests involving marijuana are up 48% in the last year (2019-2020)
- The number of marijuana impaired drivers involved in deadly crashes has risen every year between 2017 and 2019



Alcohol + Marijuana + Driving

- People who use both alcohol and marijuana are **some of the most dangerous drivers on the road** – they are significantly more likely to speed, text, intentionally run red lights, and drive aggressively than those who don't
- Drivers who use both **marijuana and alcohol** were significantly more prone to driving under the influence of alcohol versus those who only drink alcohol but do not use marijuana

A Few Other Medical Impacts

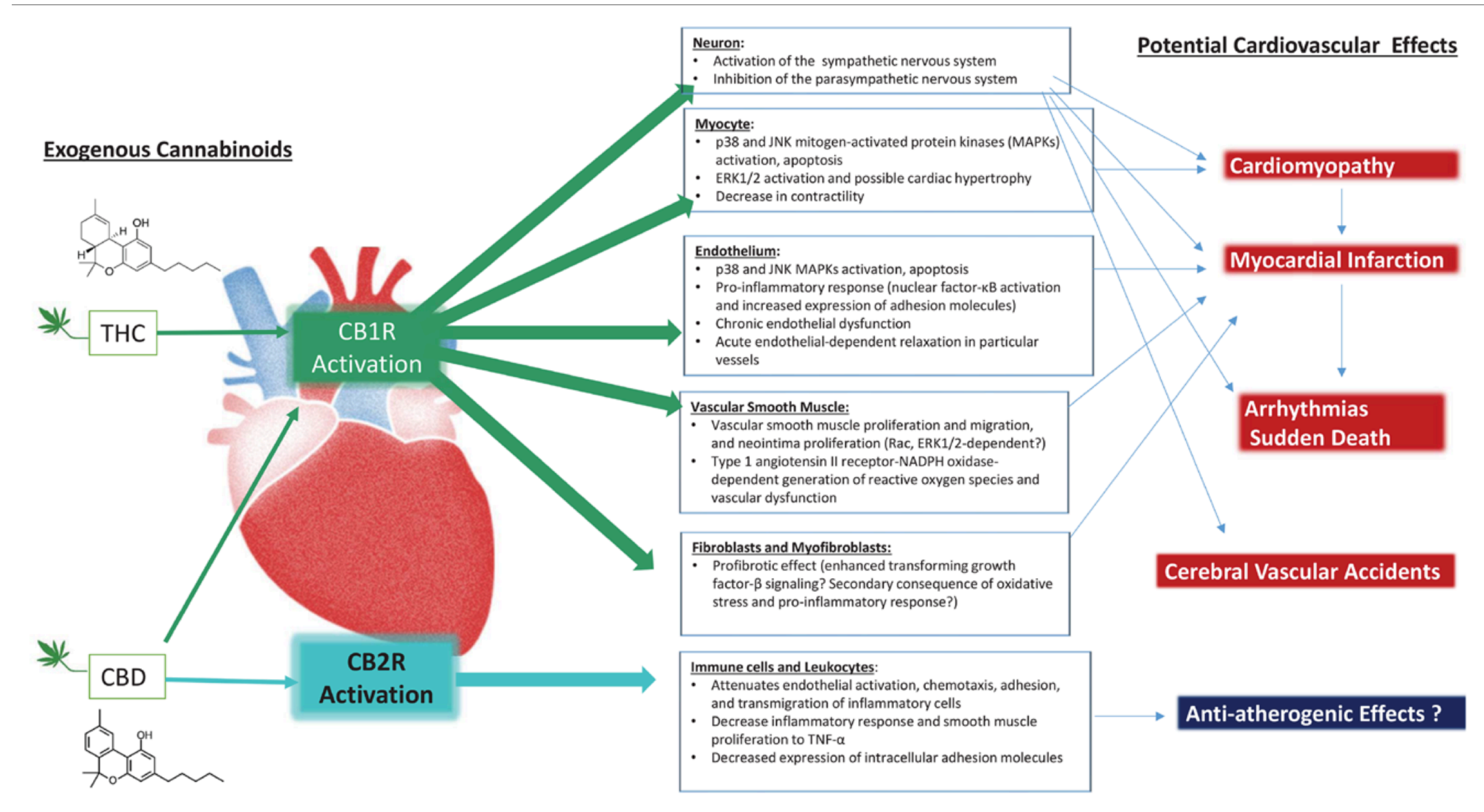
COVID: FOLLOW THE SCIENCE



POT: FOLLOW THE MONEY

American Heart Association

August 5, 2020



Maternal cannabis use in pregnancy and child neurodevelopmental outcomes, August 2020

- Cannabis use in pregnancy was linked to an **increased risk of preterm birth**
- Women who used cannabis during pregnancy **often used other substances** including tobacco, alcohol and opioids.
- Considering those findings, in the current study the researchers specifically looked at 2,200 women who reported using **only cannabis** during pregnancy, and no other substances.
- Babies born to this group **still had an increased risk of autism** compared to those who did not use cannabis.

Associations Between Prenatal Cannabis Exposure and Childhood Outcomes; Results From the ABCD Study

September 2020

- N=11,875, ages 9-11
- Cannabis exposure only, before and after maternal knowledge of pregnancy, were associated with greater offspring psychopathology characteristics
- Exposure after maternal knowledge of pregnancy remained associated with greater psychotic-like experiences, attention, thought, and social problems
- Prenatal cannabis exposure and its correlated factors are associated with greater risk for psychopathology during middle childhood.



Joe Amon, The Denver Post

Marijuana plants are lined up on the driveway outside of a suspected illegal grow operation at a home in Aurora on Wednesday morning, Oct. 10, 2018. Federal and local agents fanned out across the Denver metro area Wednesday morning executing more than two dozen search warrants on suspected illegal marijuana grow houses, authorities say.

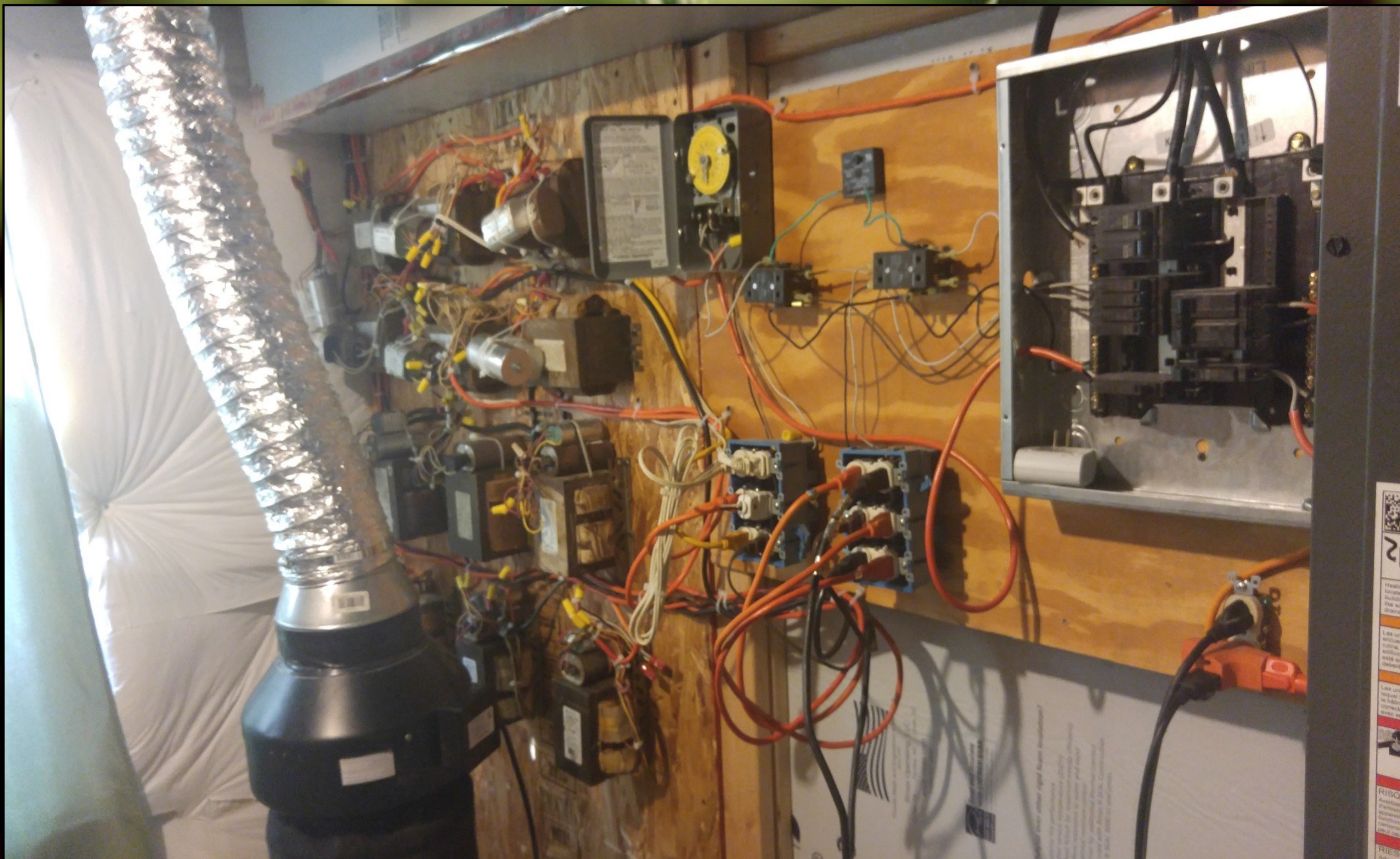


Joe Amon, The Denver Post

A DEA agent carries marijuana plants out of a suspected illegal grow operation at a home in Aurora on Wednesday morning, Oct. 10, 2018. Federal and local agents fanned out across the Denver metro area Wednesday morning executing more than two dozen search warrants on suspected illegal marijuana grow houses, authorities say.



Altered Electrical



Hazards for First Responders



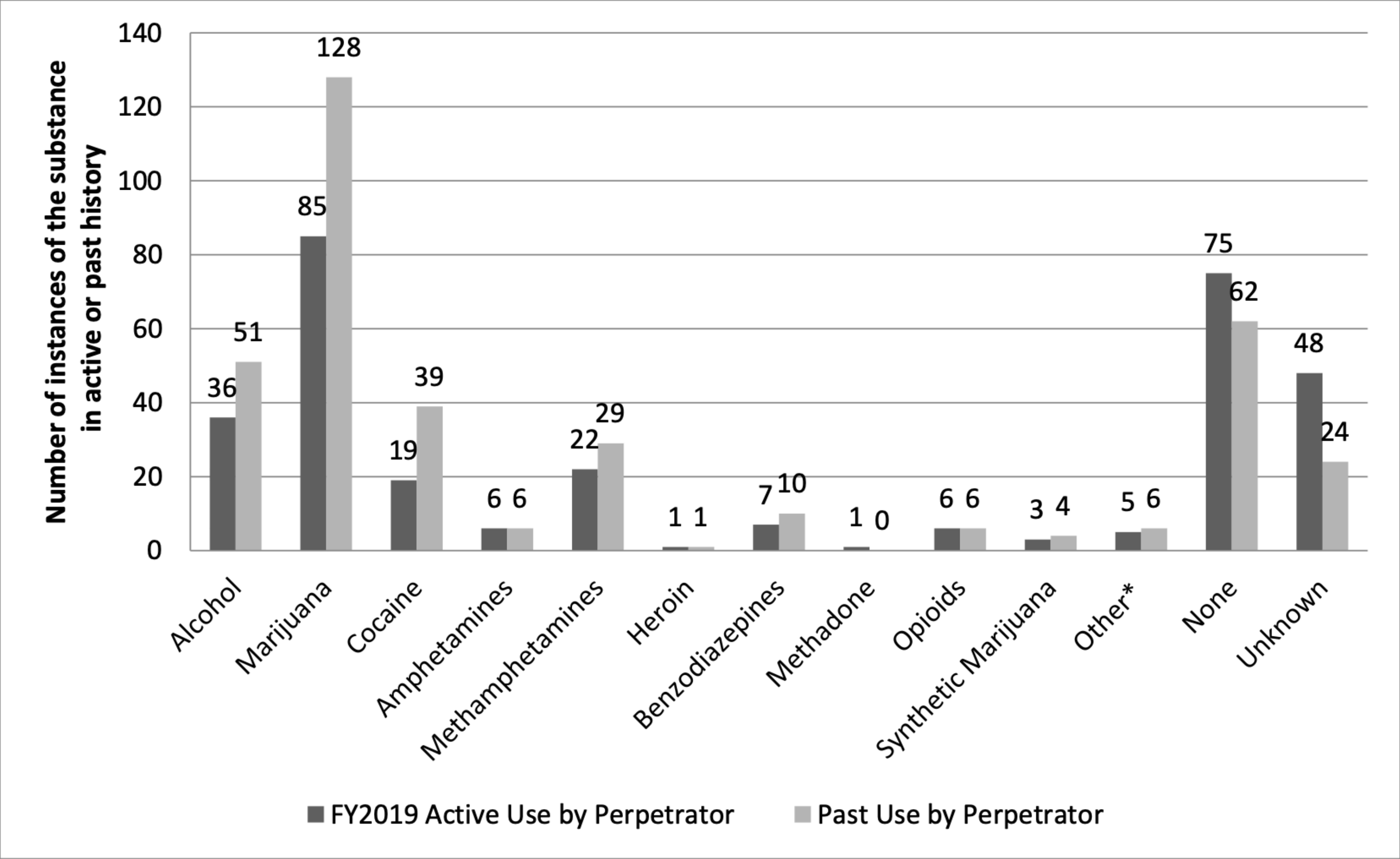
Altered electrical
systems and wiring

Hazards for First Responders



Tripping / entanglement hazards

Figure 11. Confirmed Child Abuse or Neglect Fatality by Substance Abuse by Perpetrator

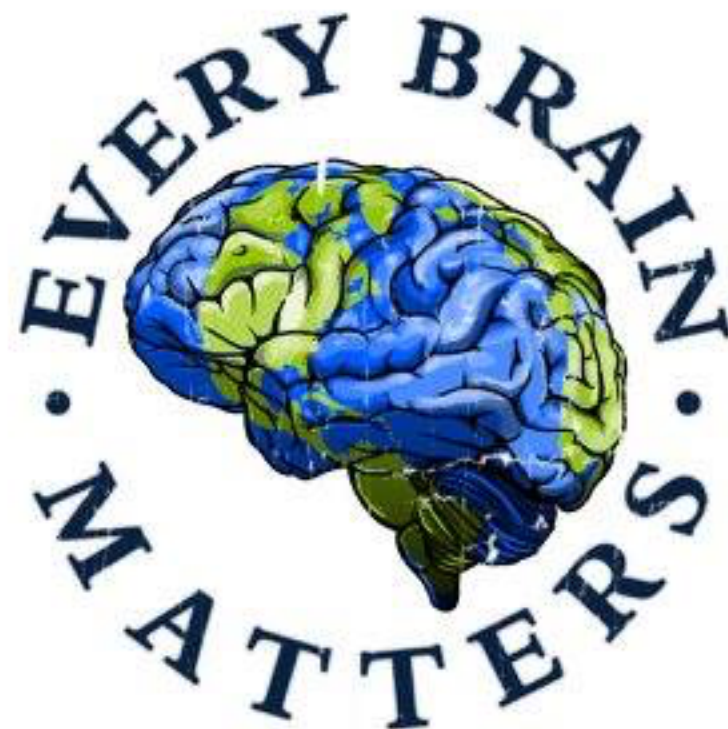


*Other includes lighter fluid, Kratom, ecstasy, morphine and Benadryl.

Out of all the drugs that can induce psychosis, cannabis has the highest conversion rate to bi-polar or schizophrenia.

<u>Drug</u>	<u>Conversion Rate</u>
cannabis	47.00%
amphetamines	30.00%
hallucinogens	24.00%
opioids	21.00%
alcohol	5.00%

<https://ajp.psychiatryonline.org/doi/10.1176/appi.ajp.2017.17020223>



EveryBrainMatters.org



Kevin Neal, California

- Marijuana grower
- **Killed 5 people**, including his wife who he stuffed in a hole under his mobile home
- Went to a **nearby school** and opened fire but no access into the school
- Injured 14 others
- Likely associated mental health issues
- Prior run-ins with the law

CVT CENTRAL VALLEY TOXICOLOGY, INC.	
Case Name: Neal, Kevin	TOXICOLOGY NUMBER: CVT-17-12040
Specimen Description:	9.5 ml femoral blood (2 gray top vials), 14 ml central blood (1 gray top vial, 1 red top vial & 1 lavender top vial), 2.5 ml vitreous humor & 3.75 ml urine each labeled "Neal, Kevin; Tehama County Coroner; 17-02057; Drawn at autopsy; 11/15/2017"
Delivered by Tricor	Date 01-Dec-17
Received by Bill Posey	Date 01-Dec-17
Request: Complete Drug Screen & THC	Agency Case # 17-02057
Requesting Agency Tehama County Coroner P.O. Box 729 Red Bluff CA 96080	Report To Tehama County Coroner P.O. Box 729 Red Bluff CA 96080

Specimen: Femoral Blood Sample	RESULTS
Complete Drug Screen: Specific drug assay for THC performed.	No common acidic, neutral or basic drugs detected.
	No Ethyl Alcohol detected.
Cannabinoids (THC metabolite) by Immunoassay = Positive	
delta-9-THC	= 97 ng/mL
delta-9-THC-COOH	= 37 ng/mL
delta-9-THC-OH	= 3.7 ng/mL

Action Plan

- Marijuana is not a medication. Marijuana is a plant
- Support FDA drug-development process for cannabinoids, including evidence-based dosing guidelines of cannabis-based medications
- Support potency cap (15% THC)
- Eliminate home grows: breeding ground for illegal activity
- Track, monitor, and document public health impact (health care utilization, ER, birth defects, etc)

Action Plan

- Mandatory drug testing for all violent crimes (cannabis induced psychosis)
- Monitor adolescent use closely
- Discourage smoking and vaping (EVALI)
- Discourage use during pregnancy and lactation
- Drug testing/toxicology on all suicides, including adolescents
- Monitor marijuana-related driving fatalities

COVID: FOLLOW THE SCIENCE



POT: FOLLOW THE MONEY

For More Information

- Feel free to send me an email with questions
 - kfinn@springsrehab.net
- For more information please visit the International Academy on the Science and Impacts of Cannabis
 - IASIC1.org

Kenneth Finn *Editor*
Cannabis in Medicine
An Evidence Based Approach

Legalization of marijuana is becoming increasingly prominent in the United States and around the world. While there is some discussion of the relationship between marijuana and overall health, a comprehensive resource that outlines the medical literature for several organ systems, as well as non-medical societal effects, has yet to be seen. While all physicians strive to practice evidence-based medicine, many clinicians aren't aware of the facts surrounding cannabis and are guided by public opinion.

This first of its kind book is a comprehensive compilation of multiple facets of cannabis recommendation, use and effects from a variety of different perspectives. Comprised of chapters dedicated to separate fields of medicine, this evidence-based guide outlines the current data, or lack thereof, as well as the need for further study. The book begins with a general overview of the neurobiology and pharmacology of THC and hemp. It then delves into various medical concerns that plague specific disciplines of medicine such as psychiatry, cardiology, gastrointestinal and neurology, among others. The end of the book focuses on non-medical concerns such as public health and safety, driving impairment and legal implications.

Comprised of case studies and meta-analyses, *Cannabinoids in Medicine: An Evidence-Based Approach* provides clinicians with a concise, evidence-based guide to various health concerns related to the use of marijuana. By addressing non-medical concerns, this book is also a useful resource for professionals working in the public health and legal fields.

Finn *Ed.*



Cannabis in Medicine

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Editor

<https://www.springer.com/us/book/9783030459673>