THC Concentration in Colorado Marijuana

Health Effects and Public Health Concerns

July 31, 2020

COLORADO
Department of Public
Health & Environment

www.marijuanahealthinfo.colorado.gov

Contents

Abstract

The Retail Marijuana Public Health Advisory Committee through the Colorado Department of Public Health and Environment were asked by the Colorado General Assembly to produce a report on the scientific findings pertaining to "…tetrahydrocannabinol (THC) potency of marijuana and any related health effects" by July 31, 2020. This report provides a brief history of marijuana in Colorado, including the roles state agencies play and what actions are taken to protect consumer health and safety. Background is provided on the chemical makeup of marijuana and the large variety of products available on the regulated market described. "THC potency" is interpreted as THC concentration, with further explanation of this definition provided. The variation of THC concentration among marijuana products is addressed as well as the various methods of marijuana product consumption and the importance of considering the frequency of marijuana use when examining health effects. Most importantly, this report provides summaries of current scientific evidence and data that works to inform our understanding of the potential of adverse health effects associated with high concentration THC products. Informed by this evidence or the lack thereof, this report concludes with recommendations to better educate, inform, and protect the people of Colorado.

Statement of concern

The regulated marijuana industry in Colorado produces a large variety of retail products that contain a high concentration of tetrahydrocannabinol or THC, the most psychoactive substance found in marijuana. The clinical effects of marijuana are dictated by the dose of THC, and to a lesser extent, other cannabinoids which will not be discussed in this report. Other factors might include individual response and marijuana product type. THC concentration, commonly called "potency", refers to the content of THC in the marijuana product expressed as either a percentage (%) or milligram (mg) dose per serving for some products, including edible products. Products containing a high THC concentration raise public health concern because increased dose may lead to higher potential for adverse health effects in consumers of these products.

Introduction

About this report

During the 2019 Colorado legislative session, the General Assembly requested the Colorado Department of Public Health and Environment (CDPHE) to study "…tetrahydrocannabinol (THC) potency of marijuana and any health effects".[1] In a request for information submitted through the Long Bill in Footnote 88a, CDPHE was instructed to have the Retail Marijuana Public Health Advisory Committee (RMPHAC) review the scientific literature, plus relevant data, and present a report with recommendations to the General Assembly by July 31, 2020. This white paper serves as the requested report.

In response to this request, it should be noted that both CDPHE and the RMPHAC interpret the term "THC potency" as the concentration of THC in marijuana or marijuana products. Although "potency" is the term commonly used to describe THC concentration or content, it has a different pharmacologic meaning. The proper use of the term potency is used to express the activity of a drug, in terms of the amount required to produce a defined effect.[2] The term "potency" is inaccurate when discussing marijuana clinical effects since the active compound, THC, is the same in all marijuana products, and the effect on cannabinoid receptors is therefore consistent across products, on the cellular level. Since the effects of THC are subjective, differing between individuals and dependent on mode of use, a known amount to produce a defined effect does not exist. Misuse of the term potency in this way may also give a false sense that any risk has been mitigated due to testing the relationship of amount to effect. Increasing the concentration of THC can lead to an increase in the dose consumed. Even low doses may affect some individuals in adverse ways, though as dose increases, risk increases.

This report is reflective of literature available and reviewed as of March 2020, and data available as of August 2020. CDPHE and the RMPHAC consistently search and review the published literature on a quarterly basis. Data are analyzed as new data is released. As new evidence emerges on topics covered by this committee, including THC concentration and/or specific marijuana product types, the RMPHAC will update statements and recommendations made in this report. Updates are made regularly by CDPHE and posted to the website www.marijuanahealthinfo.colorado.gov.

Definitions

- <u>Trichomes</u> - part of marijuana plant containing cannabinoids, such as THC and CBD.

- <u>Cannabinoid</u>- compounds found in marijuana, such as THC and CBD.

- <u>THC-A or Δ-9-tetrahydrocannabinolic acid</u> - non-psychoactive precursor of THC that is activated (i.e. decarboxylated) by heat energy to form THC.

- <u>THC or Active THC or Δ-9-tetrahydrocannabinol</u> - a prominent cannabinoid of marijuana and the primary psychoactive compound found within the marijuana plant.

- <u>CBD or Cannabidiol</u> - a prominent non-intoxicating cannabinoid of marijuana.

- <u>THC Concentrate</u> - product created by using extraction methods that condense trichomes and separates them from marijuana plant material. Contains concentrated amounts of cannabinoids, including THC.

- <u>THC Concentration</u> - THC content per volume or weight of marijuana products, usually measured in milligrams or percentage.

- <u>Potency</u> - an expression of the activity of a drug, in terms of the amount required to produce a defined effect.

- <u>Dose or Dosage</u>- specified amount of THC taken (inhaled or milligrams consumed) at one point in time.

- <u>Method of marijuana use</u> - The manner in which marijuana is consumed.

Background

History of marijuana in Colorado

Colorado has a 20-year history in the legalization of marijuana. Marijuana, a federally illegal, Schedule I drug that contains psychoactive THC, was first legalized in Colorado for medicinal purposes only. Added to the state constitution through Amendment 20 in 2000, only certain listed medical conditions may be treated using medical marijuana recommended by a physician.[3] In 2012, non-medical marijuana intended for adult consumption was proposed on Amendment 64 and passed with 53% of the vote.[4] Amendment 64 also instituted the large-scale production and sale of marijuana.[5] On January 1, 2014 Colorado became the first state in the nation to open retail stores selling regulated, adult-use marijuana.

State agency roles

Both state and local government agencies in Colorado have roles in the regulation and safety of marijuana. At the state level, the Colorado Department of Revenue's Marijuana Enforcement Division (MED) has authority over the production, distribution and sale of marijuana.[5] The Marijuana Health Monitoring Program at CDPHE is responsible for monitoring marijuana use trends across the state and the emerging scientific evidence of health effects related to marijuana use.[6] At the local level, jurisdictions have authority to require additional licenses and may enact laws that build upon rules and regulations set at the state level to protect public health and safety.[5]

The MED dictates in rule and regulation what marijuana products are allowable. A current list of allowable products, that includes marijuana concentrate, may be found in the Colorado Code of Regulations, Marijuana Enforcement Division, 1 CCR 212-3.[7] These rules and regulations are updated through the rulemaking process that includes input from stakeholders, including industry representatives, state agencies, subject matter experts and the public. CDPHE regularly participates during the rulemaking process to offer consultation from its subject matter experts on topics that pertain to public health. Consumer safety and education, laboratory testing, youth and unintentional consumption prevention, and environmental impacts are all topics that CDPHE has provided input on to minimize the occurrence of adverse health effects and outcomes.

CDPHE is required by statute to monitor health effects of retail marijuana use in order to protect both marijuana consumers and the general public.[6] This is accomplished through analysis of various data sources and regular review of peer-reviewed literature by a panel of health experts, the RMPHAC. Through the work of the RMPHAC, the department issues Evidence Statements and Public Health Statements on the health effects of marijuana use that are based on the evidence found in the current scientific literature. Evidence Statements and Public Health Statements are referenced and discussed throughout this paper. All statements on health effects have been approved by the RMPHAC. The work of the RMPHAC and CDPHE is presented to the legislature, Department of Revenue, and Board of Health as a report summary every two years. The next report summary is due January 31, 2021, however the work of the RMPHAC is regularly updated throughout the year and current information may be accessed at www.marijuanahealthinfo.colorado.gov .

What the state does to protect consumers

The state of Colorado has enacted laws and regulations that are intended to protect consumers of marijuana products. The MED has rules and regulations that aim to inform and protect consumers of marijuana. A few rules of note that intend to protect and inform consumers include; placing THC "potency" (concentration) test results on marijuana product packaging labels, requiring a "potency" (concentration) statement of total THC and cannabidiol (CBD) for all concentrate products and flower, and requiring a warning statement on the container or marketing label that says "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" and "Use of marijuana may impair your ability to drive a car or operate machinery."[7] During 2019 Rulemaking, marijuana stores were required to notify MED or CDPHE of any reports of adverse health effects reported to them by consumers. The MED also has authority to issue Health and Safety Advisories when any marijuana product is thought to be a threat to public health or safety.[7] CDPHE is regularly consulted during this process.

The chemical makeup of marijuana

Marijuana contains hundreds of cannabinoids, with Δ-9- tetrahydrocannabinol (THC) and cannabidiol (CBD) being the two most prominent.[8] THC is the primary psychoactive compound found within the marijuana plant and can be defined by two primary types: THCA, Δ-9-tetrahydrocannabinolic acid, which is a non-psychoactive precursor that is decarboxylated by heat energy to form THC, Δ-9-

tetrahydrocannabinol, which is psychoactive. THC concentration refers to the content of THC per unit of weight or volume, and is usually expressed as a percentage (%), but may also be expressed in milligrams (mg).[9] "Total THC" means the sum of the percentage by weight of THCA multiplied by 0.877 plus the percentage by weight of THC i.e., Total THC = (%THCA x 0.877) + % THC.[7] The 0.877 is used to account for the difference of molecular weight between THCA and THC and this equation assumes 100% decarboxylation of THCA to active THC.[9]

Variety of marijuana products

The marijuana industry in Colorado produces high quality marijuana and a wide variety of products produced from marijuana extract. Marijuana flower is the part of the plant that contains the most THC-containing trichomes. Flower is considered the most valuable part of the plant and is primarily sold as a smokable product. There are hundreds of varieties of marijuana flower regularly cultivated and sold on the regulated market in Colorado. According to the 2018 Colorado Market Size and Demand Update, flower accounted for the majority of all marijuana sales in the state.[10]

There are also many products sold on the regulated market that are produced using marijuana plant extract. The marijuana industry uses extraction methods to separate THC-containing trichomes from parts of the plant that otherwise would be waste. Specialized machinery that uses a combination of heat and pressure, solvents (e.g. butane, propane, ethanol, isopropyl alcohol, etc.) or water produces relatively small batches of marijuana extract that contains concentrated levels of THC. The resulting extract may be used in the production of many THC-containing products, such as vaping liquids, edibles, tinctures, topicals or alternative use products like inhalers or nasal sprays.

Marijuana extract may also be further refined to produce various forms of concentrate products. Concentrate products are intended to be consumed in pure concentrated form. The consistency of the product can vary and is often given a name that reflects its appearance, like wax, shatter, or budder. The MED refers to these products as "marijuana concentrates".[7] For clarity purposes, we refer to these products as THC concentrates throughout this paper.

THC concentration of marijuana products in Colorado

Marijuana flower produced in Colorado and other legalized states is known to contain higher concentrations of THC than what has been reported previously from other regulated sources. According to the 2018 Colorado Market Size and Demand Update report, marijuana flower in Colorado contained an average of 19.6% THC per gram (Upper limit 35%) in 2017 and has remained relatively stable since 2014.[10] By comparison, flower produced for research purposes by the University Mississippi for the National Institute of Drug Abuse averages 4.14%.[11] Looking at Colorado specifically, a 2020 study by Cash et al. found 92.94% of all products sold in retail marijuana stores to have >15% THC.[12]

The content of THC in concentrate products is substantially higher than flower. The 2018 Colorado Market Size and Demand Update report shows the percentage of THC in concentrate products steadily increased over the years; in 2014, concentrate averaged 56.6% THC compared to an average of 68.6% THC (Upper limit 90%) in 2017.[10] Some retail marijuana stores advertise up to 95% THC in concentrate products.[13]

In contrast to THC concentrate products, the THC content in retail marijuana edible products has decreased. This was due to policy changes for edible products in 2016, which set the maximum THC concentration (measured as dose in milligrams) in retail edible products to 10mg dose THC per individual serving, with a maximum of 100mg per package.[14] This change was prompted after public health concern was raised due to reports of THC overconsumption in adults and unintentional or accidental THC consumption by children.[15,16]

Scientific literature shows a trend of increasing THC concentration happening worldwide and it appears to be increasing on a yearly basis. Cascini et al. (2012) conducted a systematic review of scientific literature published between 1970 and 2009 and found a significant association between average THC content of marijuana flower and year. Average increase of mean THC concentration between 1970 and 2010 was 4.7% and this rise has been more rapid in the last decade. Studies specific to the United States have shown similar results.[17] ElSohly et al. (2016) used DEA confiscated marijuana flower samples from 1995 to 2014 and found a trend of increasing THC concentration from ~4% in 1995 to ~12% in 2014.[18] Specifically related to THC concentrates, a 2019 study by Chandra et

al. used DEA confiscated samples to find an average THC content increased from 6.7% in 2008 to 55.7% in 2017, with fluctuation in between.[19] These articles provide evidence that average THC concentration in marijuana products has increased and is associated with time.

Method of use

The method of marijuana use is the manner in which the marijuana is consumed. Certain methods of use can give insight as to which marijuana products are being consumed. For example, eating or drinking marijuana indicates only products containing active THC (i.e. edibles) are consumed in order for the effects of the THC to be felt. Similarly, dabbing marijuana is indicative of THC concentrate use. However, method of use does not always dictate what type of marijuana product(s) are being consumed. For example, vaporizing can involve either THC concentrates or flower. In an effort to help the reader understand the difference in each method of use, we define the most common methods of marijuana use in the following list:

- Smoking, the most traditional method of use, involves marijuana flower rolled in cigarette paper or tobacco leaves (i.e. joint or blunt respectively), or inserted into the bowl of a pipe or bong. The flower is combusted by applying flame and the smoke inhaled.

- Eating/Drinking or Oral Administration involves marijuana edible products or tinctures that contain active THC that is ingested orally. Effects of edibles are delayed but last longer compared to those of smoking.

- Lotions/salves/topicals contain active THC and are applied to the skin surface.

- Vaporizing involves devices (e.g. pen) that contain internal coils that are heated by a battery supply. Vaping liquid containing THC concentrate or flower comes into contact with the heated coils and produces a vapor that is inhaled.

- Dabbing, also considered a form of vaporization, involves a device that has a metal or ceramic plate that is heated prior to placing THC concentrate directly onto the plate's surface to produce an inhalable vapor.

- Alternative use products, such as inhalers and nasal sprays, contain THC concentrate mixed with other inactive ingredients to produce a fine, mist-like product that can be inhaled through either the mouth or nose.

Frequency of use

As with all substance use, frequency of use plays an important role in subsequent health effects. A 2020 study by Hines et al. found the use of high THC concentration marijuana products to be associated with at least weekly marijuana use, when compared to those using lower THC concentration marijuana (aOR 4.38, 95% CI 2.89-6.63).[20] In another study Bidwell et al. (2018) studied characteristics of people using THC concentrates on the legal markets in the United States. Those reporting frequent use of concentrate products reported using marijuana (of any form) an average of 6.04 days per week, compared to 4.16 days for marijuana users who never use concentrate products. Furthermore, frequent concentrate users reported a higher per-day use frequency than flower-only marijuana users.[21]

Data

Health effects data

CDPHE is statutorily tasked with collecting data specific to marijuana related health effects and marijuana use trends. Over the years CDPHE has worked with its partners to explore data sources that contain information relevant to marijuana health monitoring purposes. Although we have been successful in identifying data sources that contain useful data on marijuana use, there are few sources that contain detailed information needed to distinguish the type of marijuana product consumed and the THC concentration of those products. A prime example is the Colorado Hospital Association (CHA) data set. CHA provides CDPHE with the largest and most complete surveillance data set containing information on hospital and emergency department visits from most hospitals around the state. These data contain billing codes, from which valuable information is extracted, including information on visits involving marijuana. Since the primary purpose of these codes are for billing purposes, they only contain information specific to the medical procedure or condition. These codes do not contain the level of detail that distinguishes the marijuana product type, percentage THC, or whether the hospital visit was attributable to THC. Therefore these data do not appear in this report.

Rocky Mountain Poison and Drug Safety (RMPDS) serves as the regional poison center for Colorado. RMPDS has been providing CDPHE data on the number of marijuana exposures since 2014. In 2017 CDPHE granted RMPDS additional funds to collect more detailed information from callers reporting marijuana exposures. Detailed data now attempted to be collected includes type of marijuana product consumed. A limitation to these data is that they are voluntarily reported by callers and cannot capture the true prevalence of use patterns. Additionally, detailed information is not always known by the caller, who may be a friend, family member, or healthcare personnel who are calling the poison center on the patient's behalf.

RMPDS collects information on exposures and opens a case number to be followed. The generic codes in the Table 1 define an exposure due to marijuana. Each unique patient under a case number is considered a "case". Marijuana cases usually have multiple generic codes present. Each case can have multiple substance exposures.

Table 1: RMPDS generic codes and descriptions for marijuana exposures and the associated marijuana product type and THC concentration

Generic Code	Generic Code Description	Marijuana Product Type	High THC Concentration
0083000	Marijuana: Dried Plant	Plant	Unknown
0310033	eCigarettes: Marijuana Device Without Added Flavors	Electronic device/liquids	Unknown
0310034	eCigarettes: Marijuana Device With Added Flavors	Electronic device/liquids	Unknown
0310035	eCigarettes: Marijuana Liquid Without Added Flavors	Electronic device/liquids	Unknown
0310036	eCigarettes: Marijuana Liquid With Added Flavors	Electronic device/liquids	Unknown
0310096	eCigarettes: Marijuana Device Flavor Unknown	Electronic device/liquids	Unknown
0310097	eCigarettes: Marijuana Liquid Flavor Unknown	Electronic device/liquids	Unknown
0310121	Marijuana: Edible Preparation	Edible	Unknown
0310122	Marijuana: Oral Capsule or Pill Preparation	Oral capsule/pill	Unknown
0310123	Marijuana: Undried Plant	Plant	Unknown
0310124	Marijuana: Concentrated Extract (Including Oils and Tinctures)	Concentrate	Yes
0310125	Marijuana: Topical Preparation	Topical	Unknown
0310126	Marijuana: Other or Unknown Preparation	Other/Unknown	Unknown
0310146	Cannabidiol (CBD)	CBD	None
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020. Data Source: Rocky Mountain Poison and Drug Safety.			

Exposures

Most often marijuana exposures are not a single exposure. A marijuana exposure can have multiple generic codes including polysubstance exposures. Concentrated THC product exposures were determined using the generic code for concentrated extract (0310124). From January 2017 through June 2020, 973 human exposures with at least one marijuana generic code present were sent to CDPHE using an enhanced surveillance collection project from RMPDS.

In total there were 975 marijuana generic codes described in Table 2 by product type. Almost 75% of marijuana exposures reported to RMPDS were from edibles (44.9%) and marijuana plant (29.1%). There were 104 (10.7%) concentrate extract exposures since 2017. Further description of the marijuana product gathered through the call are in Figure 1. Of the concentrated extracts, 31.7% were described as either concentrated marijuana/THC and 21.2% were oils. No concentrated extracts were tinctures.

The number of marijuana exposures due to the top three marijuana associated exposure (edibles, plant, or concentrated extracts) has remained unchanged starting in Q3 of 2018 (Figure 2). Since 2017, most exposures have been due to either edibles or marijuana plant. Exposure to concentrated extracts have consistently remained lower than edible and marijuana plant exposures.

Table 2: Count of marijuana exposures by product type reported to RMPDS, Colorado January 2017 - June 2020

Marijuana Product Type	Exposures Number (%)
Edible	438 (44.9%)
Plant	284 (29.1%)
Concentrate	104 (10.7%)
Other/Unknown	85 (8.7%)
CBD	34 (3.5%)
Electronic device/liquids	27 (2.8%)
Topical	-*
Oral capsule/pill	-*
Total marijuana exposures	975 (100%)

-*Suppressed due to low number count.
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Rocky Mountain Poison and Drug Safety.

Figure 1: Count and descriptions of marijuana product types associated with marijuana codes reported to RMPDS, Colorado January 2017 - June 2020
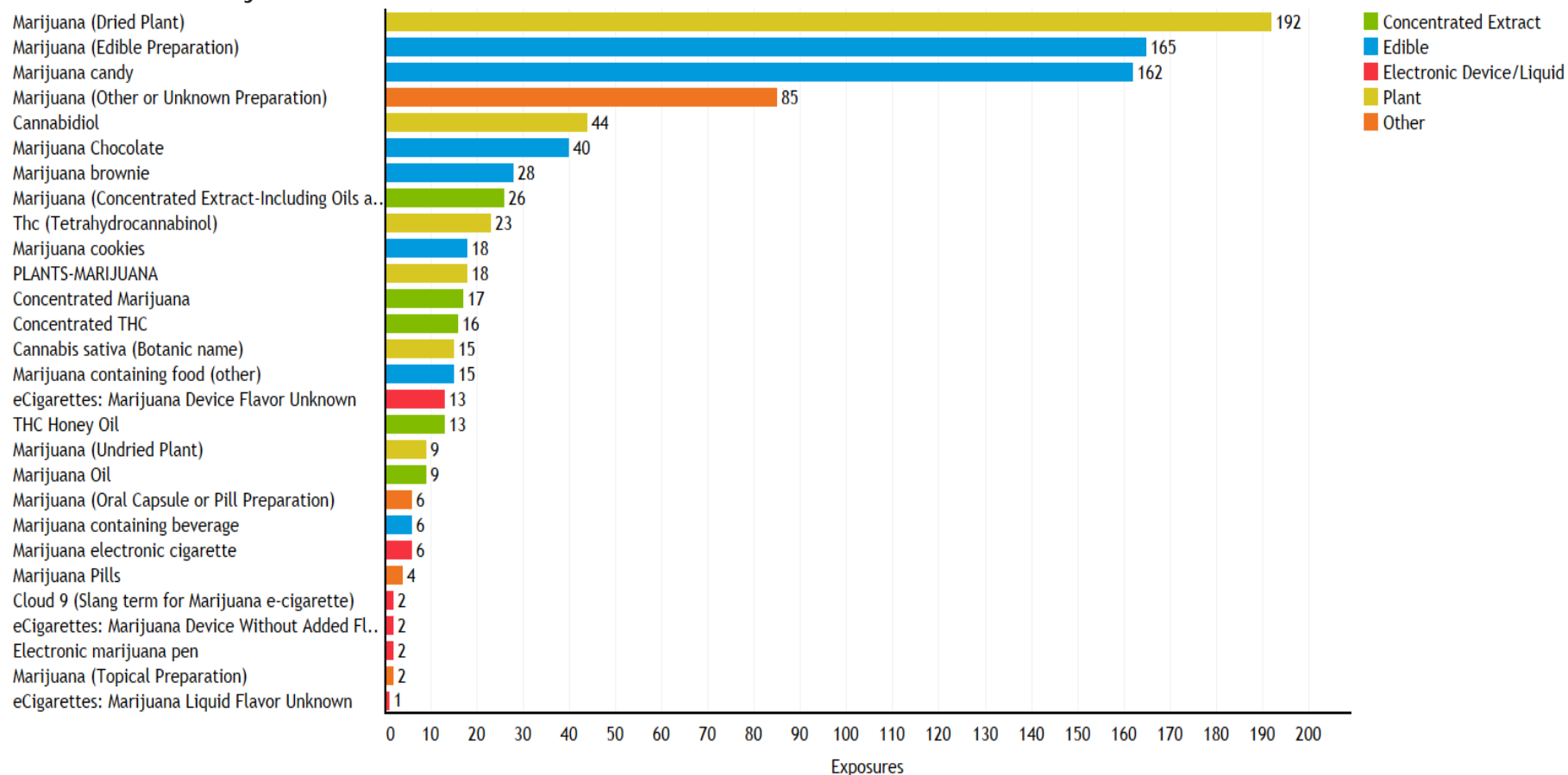
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Rocky Mountain Poison and Drug Safety.

Figure 2: Quarterly count of top three marijuana exposures reported to RMPDS, Colorado January 2017 - June 2020

Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Rocky Mountain Poison and Drug Safety.

Cases

A concentrate case is exclusive and considered a case if the generic code was present despite the possibility of multiple substance exposures. There were 104 unique concentrate cases from January 2017 to June 2020. Information about the caller is collected, including caller location site and whether or not the caller is associated with a healthcare facility. There were no meaningful differences in the proportion of concentrate exposures reported by call site (11.3% health care facility vs. 10.1% residential, Table 3). Among all concentrate cases reported to the poison center 54.8% were called-in by a health care facility, similar to other marijuana product type cases. Of those called in by a health care facility, 79% were calling from a hospital and 17.5% called from an emergency clinic, also similar to other marijuana product type cases.

Table 3: Call site of cases reported to RMPDS, Colorado January 2017 - June 2020

	Concentrate Cases (n=104) N (%)	Other Marijuana Product Type Cases (n=869) N (%)	Total (n=973) N (% Concentrate)
Call Site*			
Health care facility**	57 (54.8%)	447 (51.4%)	504 (11.3%)
Residential	43 (41.4%)	381 (43.8%)	424 (10.1%)
Occupational	-*	11 (1.3%)	-*
Other	-*	30 (3.5%)	-*
Health Care Facility**			
Emergency Clinic	10 (17.5%)	60 (13.4%)	70 (14.2%)
Hospital	45 (79.0%)	363 (81.2%)	408 (11.0%)
Provider Office	-*	8 (1.8%)	-*
Other Health Facility	-*	16 (3.6%)	-*

*Caller's location
**Caller associated with a health care facility.
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
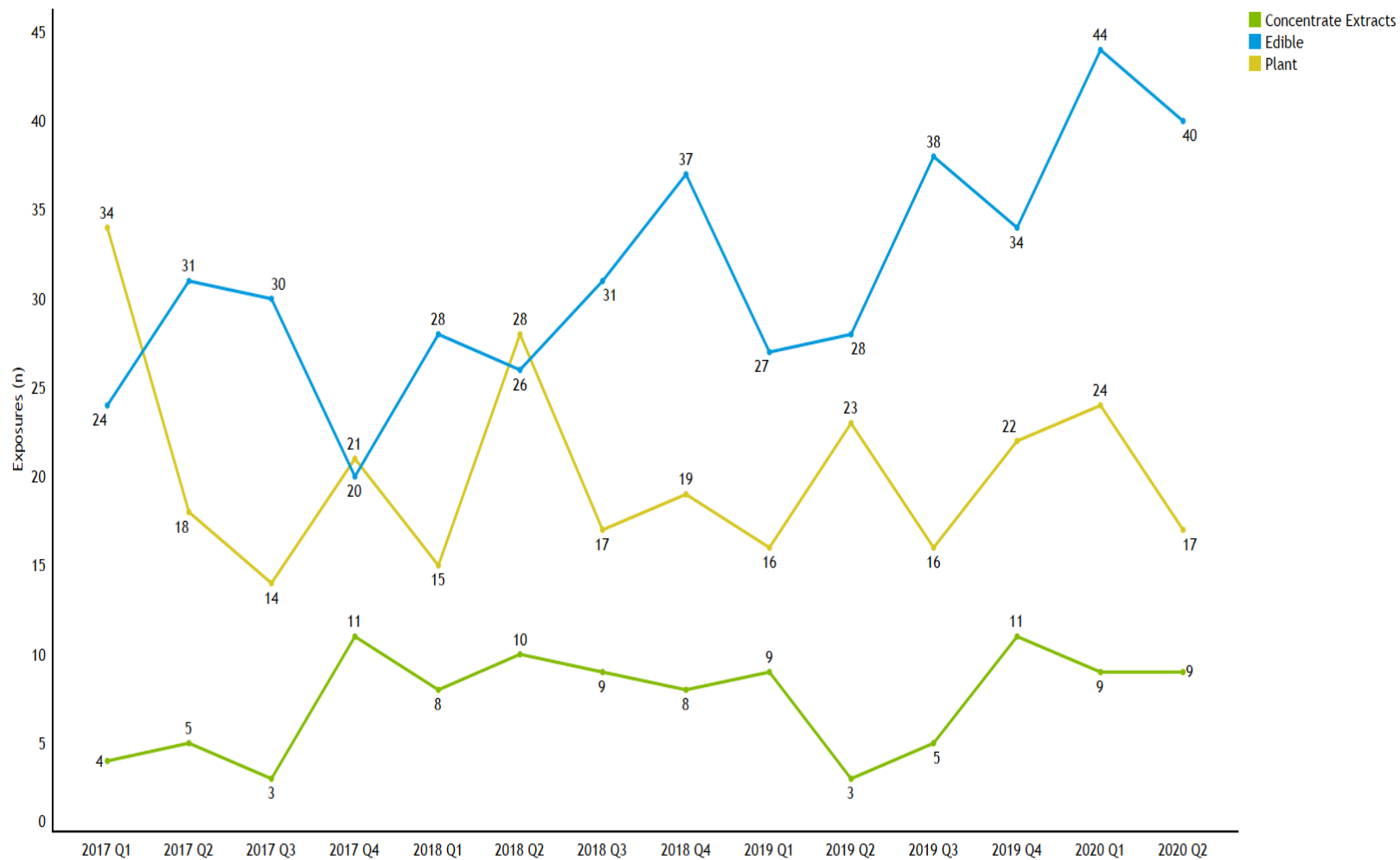Data Source: Rocky Mountain Poison and Drug Safety.

Table 4 compares the demographics of concentrated cases to other marijuana product type cases. It also contains the medical outcome, which is based upon available information on the symptoms exhibited, symptom severity and duration following an exposure. Among concentrated cases, the highest percentage of cases were between 13 and 20 years old (32.7%) followed by those aged less than 5 years old (27.6%). Compared to other marijuana product type cases, the highest percentage of cases were less than 5 years old (36.0%) and then cases ages 13 through 20 years (22.0%). Concentrate cases under the legal age to use retail marijuana (21 years) contributed to 10.7% of total marijuana cases. There were no differences based on gender. Interestingly, population surveys have found general marijuana use to be more prevalent in males (20.2% [18.5, 21.8] compared to 14.9% [13.4, 16.5]; BRFSS 2018), and regardless of concentrate exposure there are no differences between males and females. This finding may suggest that marijuana exposures may affect females more or a result of females being more likely to seek care. The majority of concentrate case outcomes resulted in minor (48.1%) or no effect (22.1%). However, concentrate cases contributed to over a quarter (26.1%) of the major medical outcomes associated with marijuana, but causality cannot be determined.

Table 4: Demographics of marijuana concentrate cases compared to other marijuana product type cases reported to RMPDS, Colorado January 2017 - June 2020

Demographic	Concentrate Cases (n=104) N (%)	Other Marijuana Product Type Cases (n=869) N (%)	Total (n=973) N (% Concentrate)
Age			
0-5 years	27 (27.6%)	297 (36.0%)	324 (8.3%)
6-12 years	8 (8.2%)	81 (9.8%)	89 (9.0%)
13-20 years	32 (32.7%)	183 (22.0%)	215 (14.9%)
21-29 years	11 (11.2%)	87 (10.6%)	98 (11.2%)
30 + years	20 (20.4%)	176 (21.4%)	196 (10.2%)
Legal Consumption Age			
Less than 21 years	67 (67.0%)	561 (66.2%)	628 (10.7%)
Older than 21 years	33 (33.0%)	287 (33.8%)	320 (10.3%)
Gender			
Male	50 (48.1%)	460 (52.9%)	510 (9.8%)
Female	54 (51.9%)	398 (45.8%)	451 (12.0%)
Medical Outcome			
Confirmed non-exposure/unrelated	-*	19 (2.2%)	-*
No effect	23 (22.1%)	129 (14.8%)	152 (15.1%)
Minor effect	50 (48.1%)	427 (49.1%)	477 (10.5%)
Moderate effect	16 (15.4%)	166 (19.1%)	182 (8.8%)
Major effect	6 (5.8%)	17 (2.0%)	23 (26.1%)
Unknown	7 (6.7%)	111 (12.8%)	118 (5.9%)

-* Suppressed
Percentages may not add up to total sample size due to unknown demographics.
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Rocky Mountain Poison and Drug Safety.

Table 5 compares medical outcomes and intentionality of concentrate cases to other marijuana product type cases among cases between the ages of 13 and 20. Exposure intention refers to whether the exposure was knowingly intended or not. There were no meaningful differences between concentrate cases and other marijuana product type cases. Overall cases in this age group had minor or moderate effects. Major effects were split between concentrate cases and other marijuana product type cases, each contributed to half (50.0%) of the major outcomes. However, causality cannot be determined. All cases in this age range had high intentional use of marijuana. Concentrate cases contributed to 16.1% of intentional use exposures.

Table 5: Medical outcome and exposure intention of concentrate cases and other marijuana product type cases, ages 13 to 20 years, reported to RMPDS, Colorado January 2017 - June 2020

	Concentrate Cases (n=32) N (%)	Other Marijuana Product Type Cases (n=183) N (%)	Total (n=215) N (% Concentrate)
Medical Outcome			
Confirmed non-exposure/unrelated	-*	-*	-*
No effect	-*	13 (7.1%)	-*
Minor effect	14 (43.8%)	98 (53.6%)	112 (12.5%)
Moderate effect	8 (25.0%)	49 (26.8%)	57 (14.0%)
Major effect	5 (15.6%)	5 (2.7%)	10 (50.0%)
Unknown	-*	14 (7.7%)	-*
Exposure Intention			
Unintentional	-*	10 (5.5%)	384 (7.6%)
Intentional	29 (90.6%)	153 (83.6%)	192 (16.1%)
Unknown	-*	20 (10.9%)	52 (13.5%)

Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020. Data Source: Rocky Mountain Poison and Drug Safety.

Marijuana use trend data

CDPHE monitors population use of marijuana in Colorado using the Healthy Kids Colorado Survey (HKCS) and Behavioral Risk Factor Surveillance Survey (BRFSS). Both surveys target specific populations and ask questions on marijuana use in the past 30 days, method(s) of use, and frequency of use. These population health surveys do not currently ask respondents to identify marijuana product type or percentage of THC most commonly used. Therefore, the prevalence of high concentration THC use in Colorado cannot be directly determined from these data sources. Note: 2019 Health Kids Colorado Survey will be provided in a supplement separate from this report.

Colorado adults

BRFSS asks adults 18 and older about marijuana use in the past 30 days. Adults who consumed marijuana one or more days are then asked to select all methods used for marijuana in the past 30 days. Method options on BRFSS include the following: smoke, eat, drink, vaporize, dab, some other way, not sure, or refused. Method questions on BRFSS provide some examples on the type of marijuana product used with the method, but does not provide information on the percentage of THC present (see Table 6).

Table 6: Colorado BRFSS marijuana method of use question options and associated method of use, marijuana product types and THC concentration

Survey Question	Method of Use	Associated Product Types	High THC Concentration
Smoke it? (for example: in a joint, bong, pipe, or blunt)	Smoked	Unspecified/Multiple	Unknown
Eat it? (for example, in brownies, cakes, cookies, or candy)	Ingestion	Edibles	Unknown
Drink it? (for example, in tea, cola, alcohol)	Ingestion	Edibles	Unknown
Vaporize it? (for example in an e-cigarette-like vaporizer)	Vaporized	Unspecified/Multiple	Unknown
Dab it? (for example using butane hash oil, wax or concentrates)	Dabbed	Butane hash oil, wax, concentrates	Yes
Was it used in some other way?	Other way	Unknown	Unknown

Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Behavioral Risk Factor Surveillance System (BRFSS)

The only method of use on BRFSS that can provide an unbiased estimate of adult use of high concentrated THC products is dabbing. Methods are examined by any method of reported use, multiple methods of use, and single method of use. See Table 7 for how the types of use can be interpreted for the Colorado adult population. BRFSS survey responses from 2017 and 2018 were combined to provide more stable estimates due to the small sample size of adults that dabbed concentrates. Prevalence is the average prevalence for the combined years 2017 and 2018. Population estimates are weighted and statistical significance was determined using margins of error and overlapping confidence intervals.

Table 7: Method of use interpretations for Colorado adults, BRFSS 2017-2018

Method of Use	Colorado Adults
Any Method of Use	The averaged prevalence (2017-2018) of Colorado adults that used at least one method to consume marijuana at least once in the past 30 days. They may or may not have used the method along with additional methods.
Multiple Methods of Use	The averaged prevalence (2017-2018) of Colorado adults that used multiple different methods to consume at least once in the past 30 days.
Single Method of Use	The averaged prevalence (2017-2018) of Colorado adults that used only one method to consume marijuana at least once in the past 30 days.

Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Behavioral Risk Factor Surveillance System (BRFSS).

Across 2017 and 2018, 8.2% (7.6, 8.8) of Colorado adults used multiple methods to consume marijuana (Table 8). The most common methods of marijuana use were smoking and ingestion. Among adults, any use of smoking as a method was 13.7% (13.0, 14.4), with 7.5% (6.9, 8.1) using multiple methods along with smoking and 6.2% (5.7, 6.7) only smoking. Any consumption of marijuana by ingestion was 6.6% (6.1, 7.2), but the majority (5.2% [4.8, 5.7]) used other methods along with ingestion. The third most used method was vaporizing marijuana (4.8% [4.4, 5.3]), but this method was again used by the majority in conjunction with other methods. Across 2017 and 2018, 3.7% (3.3, 4.1) of Colorado adults dabbed concentrated THC products. However, dabbing was mostly used along with other methods and only 0.1% (0.0, 0.2) dabbed concentrates exclusively.

Table 8: Method of marijuana use among Colorado adults, BRFSS 2017-2018

Method of Use Chosen on Survey	Any Method of Use % (95% Confidence Intervals)	Multiple Methods of Use % (95% Confidence Intervals)	Single Method of Use % (95% Confidence Intervals)
Did not use marijuana in past 30 days	83.5% (82.7, 84.3)	83.5% (82.7, 84.3)	83.5% (82.7, 84.3)
Smoked	13.7% (13.0, 14.4)	7.5% (6.9, 8.1)	6.2% (5.7, 6.7)
Ingestion (Ate/Drank)	6.6% (6.1, 7.2)	5.2% (4.8, 5.7)	1.3% (1.1, 1.6)
Vaporized	4.8% (4.4, 5.0)	4.6% (4.1, 5.0)	0.3% (0.2, 0.4)
Dabbed	3.7% (3.3, 4.1)	3.6% (3.2, 4.0)	0.1% (0.1, 0.2)
Other methods	1.3% (1.1, 1.5)	1.0% (0.8, 1.2)	0.3% (0.3, 0.4)
Multiple methods	N/A	N/A	8.2% (7.6, 8.8)

Estimates may not add to total any use due to rounding and suppression of unknown/unsure responses
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Behavioral Risk Factor Surveillance System (BRFSS).

Since legalization of retail marijuana, there have been increases in various methods of use among Colorado Adults (Figure 3). In 2018, there were increases in smoking (14.4% [13.3, 15.4]) and ingestion of edibles (7.0% [6.2, 7.8]) compared to 2015 (11.0% [10.0, 12.1]; 4.7% [4.0, 5.5]). In 2018, dabbing concentrates significantly increased to 4.1% (3.5, 4.8) from 2.4% (1.8, 3.0).

Figure 3: Annual prevalence of marijuana use methods among Colorado adults, BRFSS 2015-2018
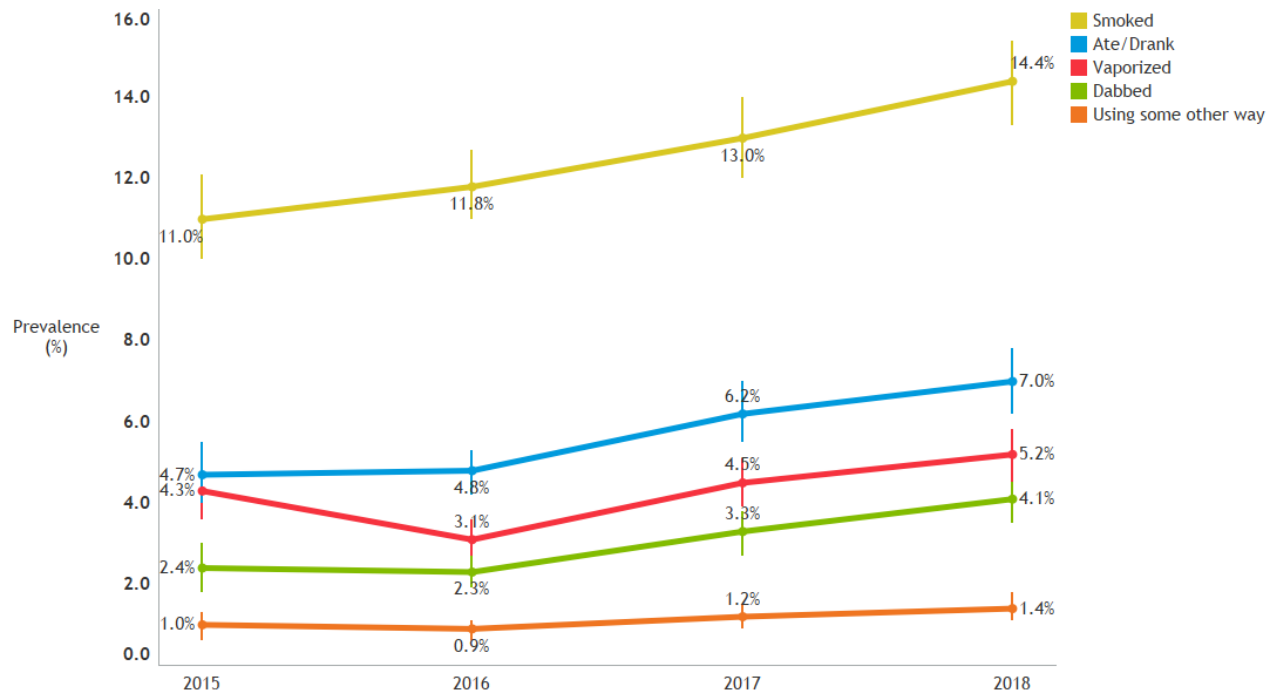
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020. Data Source: Behavioral Risk Factor Surveillance System (BRFSS).

Adult current users

Further analyses examining frequency of use are among the subset of the populations that used marijuana in the past 30 days (current users). Frequency of use questions ask respondents to estimate how many days in the past 30 days they used <u>ANY</u> type of marijuana product. Respondents provide a number (1 through 30). Frequency of use among adults is determined by combining days into monthly, weekly, near daily, or daily use (30 days). Due to small sample sizes of single use and higher prevalence of multiple method use to consume marijuana, frequency is stratified by any use of a method. These analyses do not provide estimates for frequency of concentrate use specifically.

Among current adult marijuana users in Colorado, half (49.4%) were monthly to weekly users and half (50.6%) were daily or near daily users. Those who reported dabbing had the greatest difference in prevalence; among adults who reported dabbing, 83.8% reported dabbing daily or near daily compared to 16.17% who dabbed monthly or weekly. Regardless of the method of use, daily or near daily use was more prevalent than monthly or weekly use (Table 9). This could be due to more daily and near daily adult users choosing to use multiple methods to consume marijuana versus just a single

method (Figure 4). Those that smoked (56.0% vs. 44.0%) or ingested edibles (54.4% vs. 45.6%) were slightly more likely to use daily or almost daily. Daily or almost daily users are significantly more likely to use multiple methods (67.7% (63.0, 72.4]) than adults using one method (32.3% [27.6, 37.0]).

Table 9: Frequency of marijuana use by any use method among current adult marijuana users, Colorado, BRFSS 2017-2018

Any Method of Use	Weighted Mean Days of Use (95% Confidence Intervals)	Monthly or Weekly [A] % (95% Confidence Intervals)	Daily or Near Daily [B] % (95% Confidence Intervals)
Smoked	18.5 (17.8, 19.2)	44.0% (41.1, 46.9)	56.0% (53.1, 58.9)
Ate/Drank	18.0 (17.0, 19.0)	45.6% (41.6, 49.7)	54.4% (50.3, 58.4)
Vaporized	21.4 (20.4, 22.5)	32.6% (28.0, 37.1)	67.4% (62.9, 72.0)
Dabbed	25.6 (24.6, 26.6)	16.2% (12.0, 20.4)	83.8% (79.6, 88.0)
Other methods	21.0 (19.1, 22.8)	35.0% (27.3, 42.8)	65.0% (57.2, 72.8)
Total	17.1 (16.5, 17.7)	49.4% (46.8, 52.0)	50.6% (48.0, 53.2)

Estimates do not add to total due to multiple selection of methods
A Used 1-19 days in the past 30 days
B Used 20 or more days in the past 30 days
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Behavioral Risk Factor Surveillance System (BRFSS).

Figure 4: Frequency of marijuana use by single or multiple methods of use among current adult marijuana users, Colorado, BRFSS 2017-2018
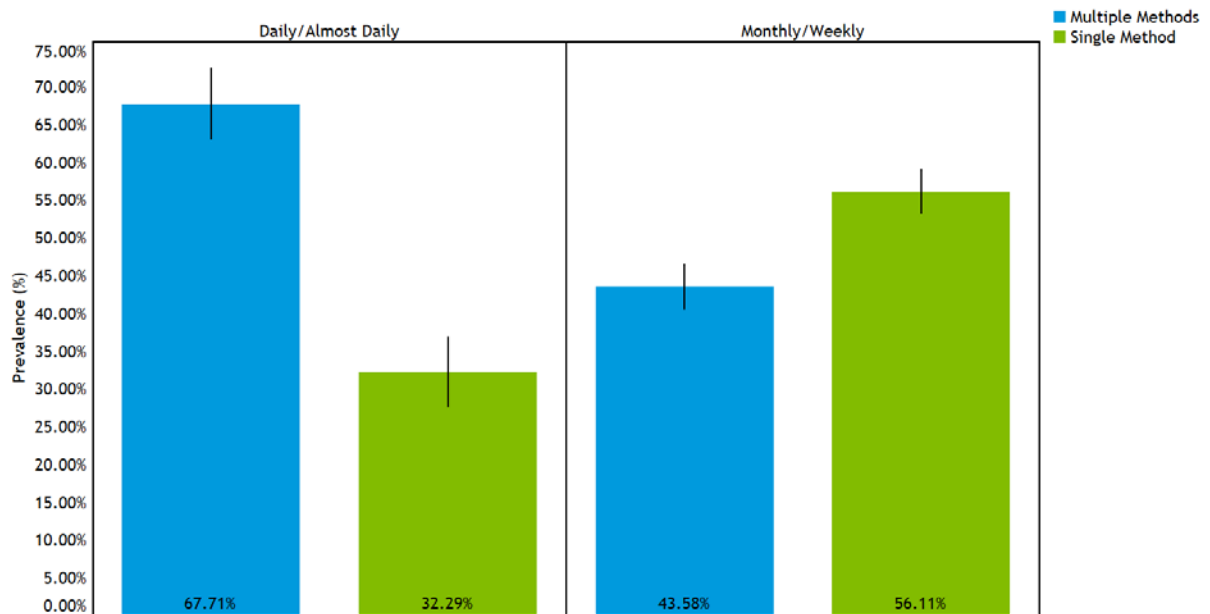
Produced by: Marijuana Health Monitoring Program, Colorado Department of Public Health & Environment 2020.
Data Source: Behavioral Risk Factor Surveillance System (BRFSS).

Data limitations

A major limitation of using population surveys to determine prevalence of high concentrated THC use is that questions on marijuana product type and percentage of THC usually used is not collected. Dabbing as a method is typically associated with concentrates, but many other methods can be used to consume high concentrated THC products. Additionally, the purpose of frequency of use questions is for marijuana consumption in general and not for specific product types. These survey questions help monitor patterns of marijuana use.

Surveillance of health outcomes due to highly concentrated THC products is limited. Marijuana poison center calls are small in comparison to other substances and often are polysubstance exposures. Causality between concentrated THC exposures and major medical outcomes cannot be determined from these data.

Data conclusions

Method of marijuana consumption in Colorado varies between the adult and youth populations. For Colorado adults 18 and older, 8.2% used multiple methods to consume marijuana during 2017 and 2018 combined. The average prevalence of dabbing concentrates during that time was 3.7%, with only 0.1% of the population dabbing THC concentrates exclusively.

Frequency of use is an important consideration when determining health outcomes. If a current user is using infrequently, then the possibility of adverse health effects is lower compared to more frequent users. Among current adult marijuana users 83.8% dabbed, and 67.4% vaporized marijuana daily or near daily. Daily or near daily users are also more likely to use multiple methods for consumption use. Frequency of days used does not determine frequency of concentrated THC consumption and higher prevalence is likely correlated with multiple method users rather than method of use.

Examining adverse health effects through poison center calls, only 10.7% had a marijuana concentrated extract code and there have been no major changes in number of exposures since 2017. Age was the only major difference between cases, and concentrate cases had a higher percentage of adolescents between 13 and 20 years old (32.7% compared to 22.0%). Adolescents in this age group had high percentages of intentional use regardless of marijuana product type. 90.6% of concentrate cases and 83.6% of the other marijuana product types were intentionally using the substances.

Literature review of health effects

Overview of the systematic literature review process

The Marijuana Health Monitoring Program (MHMP) and the Retail Marijuana Public Health Advisory Committee (RMPHAC) are tasked with reviewing the latest peer-reviewed literature articles published.[6] The scientific literature is systematically searched and reviewed on a quarterly basis. The quality of key findings from each article are graded as high, medium or low based on the study's strengths and limitations. The findings are then compiled by topic and the RMPHAC decides the overall level of evidence strength for that topic. Evidence levels range from insufficient to substantial. Definitions for each level and further information about the methodology of this systematic process may be found at www.marijuanahealthinfo.colorado.gov/process.

Following are health topic categories containing Evidence Statements that have been approved by the RMPHAC and are supported by CDPHE. Each Evidence Statement is reflective of the current state of evidence on that specific health effect and the association with high THC concentration or specific marijuana product. These associations should not be interpreted as causal. Below each statement is a list of the peer-reviewed articles with the key findings of evidence that supports the statement. The articles are organized by quality rating (High, Medium and Low). At the end of each list of articles is a summary of the overall evidence.

THC concentration and mental health effects

Adults

- Evidence Statement: We found MODERATE evidence that individuals who use marijuana with THC concentration >10% are more likely than non-users to be diagnosed with a psychotic disorder, such as schizophrenia.

- Public Health Statement: No public health statement at this time.

    o High - none

    o Medium

- Di Forti 2015 - Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: a case-control study[22]

  - Individuals who reported smoking more potent marijuana (average THC 12.9%) were at 2.91 (95% CI 1.52-3.60) greater odds of developing first episode psychosis compared to those who never used.

  - This relationship was not significant for individuals who used lower concentration marijuana compared to those who never used.

- Di Forti 2019 - The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): a multicentre case-control study[23]

  - Lifetime use (ever use of cannabis) of high concentration cannabis (> 10% THC) was associated with a psychotic disorder compared with no lifetime use of cannabis (OR 1.6, 95% CI 1.2-2.2), while uswe of low concentration cannabis (≤10% THC) was questionable (OR 1.1, 95% CI 0.9-1.5).

  - Daily cannabis use was associated with increased odds of psychotic disorder compared with never users (aOR 3.2, 95% CI 2.2 - 4.1), increasing to nearly five-times increased odds for daily use of high-potency types of cannabis (aOR 4.8, 95% CI 2.5-6.3).

  o Low

  - Sideli 2018 - Interaction between cannabis consumption and childhood cannabis abuse in psychotic disorders: preliminary findings on the role of different patterns of cannabis use.[24]

    - Use of cannabis with higher THC content (12-18% THC) was associated with diagnosis of a psychotic disorder in adulthood, regardless of childhood cannabis abuse status. (aOR 2.16, 95%CI 1.15-4.06 w/o childhood cannabis abuse and aOR 3.46, 95%CI 1.34-8.97 w/ childhood cannabis abuse).

- Evidence Statement: We found SUBSTANTIAL evidence that THC intoxication can cause acute psychotic symptoms, which are worse with higher doses.

- Public Health Statement: THC, a component of marijuana, can cause acute psychotic symptoms such as hallucinations, paranoia, delusional beliefs, and feeling emotionally unresponsive during intoxication. These symptoms are worse with higher doses.

  - High

    - D'Souza 2004 - The psychotomimetic effects of IV THC in healthy individuals: implications for psychosis[25]

      - THC acutely causes both positive and negative psychotic symptoms, as well as subjective and objective dissociative symptoms - all in a dose-dependent manner (5mg vs 2.5mg THC).

      - All other articles linked to this evidence statement only support evidence that THC intoxication can cause acute psychotic symptoms, not that these symptoms are worse with higher doses (5mg vs 2.5mg THC).

Current literature shows that adults who use marijuana classified as containing high concentrations of THC (>10% THC) are more likely than non-marijuana-users to be diagnosed with a psychotic disorder, such as schizophrenia. In a 2015 study by Di Forti et al., individuals who reported using marijuana products with higher THC concentration (average 12.9% THC) had greater odds of developing first episode psychosis compared to those who never use marijuana products.[22] This relationship remained after controlling for individual demographic factors and any other substance use. However, for participants that reported using lower THC concentration marijuana products (~3.6% THC), this relationship was not maintained, signaling that higher THC concentration may be the catalyst for this relationship.

A 2004 study by D'Souza et al., found that THC can induce positive and negative psychotic symptoms, as well as dissociative symptoms, and this relationship exhibits a dose-dependent manner.[25] Numerous studies have also shown this association between THC intoxication and psychotic symptoms, however, evaluation of the effect that dose variation may influence this relationship needs further evidence.

The relationship between marijuana with high THC concentration (>10% THC) and being diagnosed with a psychotic disorder was further explored in a 2018 study by Sideli et al. and a 2019 study by Di Forti et al.[23,24] Sideli et al., sought to examine if childhood abuse affected the interaction between marijuana use and later diagnosis of a psychotic disorder in adulthood. They found that regardless of childhood abuse status, use of high THC concentration marijuana products (12-18% THC) were associated with diagnosis of a psychotic disorder.[24] In the 2019 study by Di Forti et al., they sought to explore frequency of use, along with THC concentration, and their associations with psychotic disorder diagnosis in adulthood. Daily use of any marijuana products was associated with a psychotic disorder, however daily use of high THC concentration products (>10% THC) was more strongly associated (OR 4.8; 95% CI 2.5-6.3) than daily use of low THC concentration products (≤10% THC) (OR 2.2; 95% CI 1.4-3.6) when compared to never using marijuana. On the other end of the frequency spectrum, ever use of high THC concentration marijuana was associated with a psychotic disorder (OR 1.6; 95% CI 1.2-2.2), while ever use of low THC concentration marijuana was questionable (OR 1.1; 95% CI 0.9-1.5), when compared to no lifetime use of marijuana.[23]

Adolescents and young adults

- Evidence Statement: We found MODERATE evidence that adolescents/young adults who use marijuana with higher THC concentration (>10% THC) are more likely than non-users to continue use.

- Evidence Statement: We found MODERATE evidence that adolescents/young adults who use marijuana with higher THC concentration (>10% THC) are more likely than non-users to develop future mental health symptoms and disorders.

- Public Health Statement: High THC concentration marijuana use by adolescents and young adults is associated with continued use and development of future mental health symptoms and disorders.

  o High - none

  o Medium

    ▪ Di Forti 2015 - Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis[22]

- Individuals who started using cannabis at ages younger than 15 years had increased risk of psychotic disorders compared with those who never used cannabis (aOR 1.55; 95% CI 1.00-1.39).

- Frequent use of high concentration (~12.9% THC) cannabis and starting at a young age increased risk of psychotic disorders.

- Di Forti 2019 – The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe: a multicenter case-control study[23]

  - Compared to never users, those who had started using high concentration cannabis by age 15 years showed a doubling of risk (OR 2.3, 95% CI 1.4-3.1) for psychotic disorder, without evidence of interaction (p=0.63).

- Hines 2020 - Association of high-potency cannabis (flower only) use with mental health and substance use in adolescence[20]

  - Use of high concentration (>10% THC) cannabis during adolescence was associated with a moderate elevation in likelihood of generalized anxiety disorder (GAD) at age 24 (OR 1.77; 95% CI 1.09-2.86) and this association was strengthened after adjusting for socio demographic variables, depression symptoms at 14yo, and frequency of cannabis use (aOR 1.92; 95% CI 1.11-3.32)

  - Use of high concentration cannabis was associated with participants reporting frequent or distressing psychotic experiences (OR 1.81; 95% CI 1.01-3.24), however this association was weakened after adjusting for frequency of cannabis use.

  - People reporting the use of high concentration cannabis were about 4 times as likely to report having recently experienced problems associated with their cannabis use, when compared to people using **low concentration (≤10% THC) cannabis products (aOR 4.08, 95% CI 1.41-11.81)**

  - After adjusting for age at onset of cannabis use or for early adolescent measure of psychopathologic conditions and frequency of cannabis

use, high concentration cannabis was associated with increases in the likelihood of frequent cannabis use, and the likelihood of experiencing GAD.

- Association between high concentration cannabis use and reporting using cannabis at least weekly, compared with those reporting use of lower concentration cannabis (aOR 4.38, 95% CI 2.89-6.63).

- Barrington-Trimis 2020 - Risk of persistence and progression of use of five cannabis products after experimentation among adolescents[26]

  - Association of cannabis use at baseline with the mean number of days of use across 6- and 12-month follow-up surveys was significantly stronger for concentrate (RR 9.42; 95% CI 2.02 - 35.50)

  - Stronger associations of progression of cannabis use were observed for cannabis concentrate than for any other cannabis product in models adjusted for poly-cannabis product use and demographic characteristics.

  - Suggests that concentrated cannabis use may carry a higher risk of continued and more frequent cannabis use among adolescents who are in the early stages of use and do not use heavily yet

Research suggests that the use of high THC concentration marijuana products by adolescents and young adults may carry more risks than use by mature adults. Di Forti et al., (2015) found that adolescent and young adult patients presenting with first-episode psychosis were more likely, than non-using patients, to have started using marijuana at age 15 or before.[22] Similarly, a study by Hines et al. in 2020 sought to describe the association of high THC concentration marijuana use with mental health and substance use outcomes in adolescence. Using high THC concentration marijuana was associated with reportedly using marijuana at least weekly (aOR 4.38; 95% CI 2.89-6.63) and recently experiencing problems associated with their marijuana use (aOR 4.08; 95%CI 1.41-11.81), when compared to those using low THC concentration marijuana.[20] Barrington-Trimis et al. (2020) sought to define progression of marijuana use by adolescents depending on the type of product used. Use of THC concentrates was strongly associated with persistence of use at 6- and 12-month follow-up surveys (RR 9.42; 95% CI 2.02-35.50), when compared to other forms of marijuana use.[26]

Similar to mature adults, a study by Hines et al. (2020) found that adolescents who use high THC concentration marijuana were more likely to report psychotic experiences (OR 1.81; 95% CI 1.01-3.24), however, this association was weakened when accounting for frequency of marijuana use. This suggests that using high THC concentration marijuana and increased frequency of use may both contribute to subsequent psychotic experiences for adolescents.[20] Hines et al. (2020) also looked at other mental health outcomes, such as depression and generalized anxiety disorder (GAD) in adolescents using marijuana with high THC concentration, compared to those using marijuana not classified as containing high THC concentration. They found that use of marijuana with high THC concentration was associated with GAD (aOR 1.92; 95% CI 1.11-3.32), but no association was found for depression. Overall, their findings show marijuana use with high THC concentrations was associated with increases in the likelihood of frequent cannabis use and experiencing GAD; when adjusting for onset age of marijuana use, early adolescent psychopathologic conditions, and frequency of marijuana use.[20]

THC blood levels resulting from different exposures

THC blood levels are an important measure for understanding marijuana pharmacokinetics, or how our body metabolizes a drug. This understanding is useful for developing methods of marijuana use detection and a general concept of how acute use affects impairment.[27] This understanding is more important than ever with the extensive variety of marijuana use methods available to consumers today. Studies of this subject will commonly report findings as either a measure of whole blood or plasma (one component of whole blood). THC and its metabolites are in much higher concentrations in plasma, which is why many studies report this measurement. However, whole blood is the standard specimen used for drug testing (to determine driving under the influence, for example) and is typically more readily available for analysis.[28]

Flower

- Evidence Statement: We found SUBSTANTIAL evidence that inhaling more than about 10mg THC (or 10-20% of a currently available marijuana cigarette) is likely to yield whole blood THC concentrations near or above 5 ng/mL within 10 minutes.

- Public Health Statement: Smoking or vaporizing more than 10mg THC, or consuming an edible marijuana product with more than 15mg THC can lead to a blood THC level above 5ng/mL, which can be used to support a conviction for driving under the influence.

- o High

    - Berghaus 2011 - Meta-analysis of empirical studies concerning the effects of medicines and illegal drugs including pharmacokinetics on safe driving[29]

        - Peak whole blood THC concentration of 44 ng/mL occurred a mean of 7 minutes after smoking 15mg THC.

    - Ramaekers 2006 - Cognition and motor control as a function of Delta-9-THC concentration in serum and oral fluid: limits of impairment[30]

        - Measured whole blood THC levels of 29 ng/mL and 47.6 ng/mL five minutes after smoking 250 mcg/kg (17.5 mg/70 kg) and 500 mcg/kg (35 mg/70 kg), respectively

    - Huestis 1992 - Blood cannabinoids. I. Absorption of THC and formation of 11-OH-THC and THCCOOH during and after smoking marijuana[31]

        - A single inhalation of a 1.75% or 3.55% THC cigarette (cigarette weight not specified) produced immediate (within 12 minutes) mean whole blood THC concentrations of 3.5 and 9.1 ng/mL, respectively.

        - There was wide inter-individual variation in THC levels despite use of a paced smoking protocol.

    - Reeve 1983 - Plasma concentrations of delta-9-tetrahydrocannabinol and impaired motor function[32]

        - Measured whole blood THC levels of 0-66 ng/mL five minutes after 19 subjects (infrequent marijuana users) smoked whatever portion of an 18 mg THC cigarette produced a reasonable subjective high.

        - Mean whole blood THC level at 5 minutes post-smoking was 22.1 ng/mL. Two subjects had 2.5 and 3.5 ng/mL THC levels at baseline (before smoking).

- o Low

    - Spindle 2019 - Acute pharmacokinetic profile of smoked and vaporized cannabis in human blood and oral fluid[27]

- Mean THC concentration at 10min after smoking 10mg THC was 3.76 ng/ml (0-21 ng/ml), and after vaporizing 10mg THC was 7.53 ng/ml (0-18 ng/ml)

- Mean THC concentration at 10min after smoking 25mg THC was 10.24 ng/ml (0-38 ng/ml), and after vaporizing 25mg THC was 14.36 ng/ml (1-33 ng/ml)

Due to the diverse nature of marijuana products and methods of use it is important to differentiate resulting blood levels of THC. Smoking marijuana flower is still considered the most traditional method of consuming marijuana and involves rolling flower into cigarette paper or tobacco leaves. Current research provides substantial evidence that inhaling more than about 10mg of THC, an amount equal to part (10-20%) of a currently available marijuana cigarette, is likely to yield whole blood THC concentrations of 5 ng/mL or higher within 10 minutes of smoking. From the studies included it is clear that THC blood levels can vary widely depending on many factors, such as amount consumed and an individual's tolerance, but this provides a good baseline measurement.

Edibles

- Evidence Statement: We found MODERATE evidence that ingesting more than about 15 mg THC is capable of yielding a whole blood THC concentration > 5ng/mL.

- Public Health Statement: Smoking or vaporizing more than 10mg THC, or consuming an edible marijuana product with more than 15mg THC can lead to a blood THC level above 5ng/mL, which can be used to support a conviction for driving under the influence.

  - High

    - Lile 2013 - Pharmacokinetic and pharmacodynamic profile of supratherapeutic oral doses of delta(9)-THC in cannabis users[33]

      - Mean peak whole blood THC levels exceeded 5 ng/mL only at oral doses >45mg, however, there was large inter-individual variability and some subjects yielded levels >5ng/mL at doses of 15mg and 30mg.

- Menetrey 2005 - Assessment of driving capability through the use of clinical and psychomotor tests in relation to blood cannabinoids levels following oral administration of 20mg dronabinol or of a cannabis decoction made with 20 or 60mg THC[34]

  - Found mean peak whole blood THC concentrations of 2.8 ng/mL (range undetectable to 5.6) after dronabinol 20 mg, 3.8 ng/mL (range 1.5-8.3) after milk decoction containing 16.5 mg THC, and 8.4 ng/mL (range 3.9-13.1) after milk decoction containing 45.7 mg THC.

- Evidence Statement: We found SUBSTANTIAL evidence that it takes up to 4 hours after ingesting marijuana to reach peak blood THC concentrations.

- Public Health Statement: Smoking or vaporizing more than 10mg THC, or consuming an edible marijuana product with more than 15mg THC can lead to a blood THC level above 5ng/mL, which can be used to support a conviction for driving under the influence.

  o Medium

    - Vandrey 2017 - Pharmacokinetic Profile of Oral Cannabis in Humans: Blood and Oral Fluid Disposition and Relation to Pharmacodynamic Outcomes[35]

      - The time of maximum blood THC level (Tmax) ranged from 1hr to 6hr post dose, with most occurring at 1-3hr (only one subject at 4hr and one at 6hr).

      - The time of first positive blood THC ranged from 0.5hr to 2hr post dose, with most occurring at 1hr.

      - The maximum blood THC levels (Cmax) did not exceed 5ng/mL.

    - Newmeyer 2017 - Cannabis Edibles: Blood and Oral Fluid Cannabinoid Pharmacokinetics and Evaluation of Oral Fluid Screening Devices for Predicting Delta(9)-Tetrahydrocannabinol in Blood and Oral Fluid following Cannabis Brownie Administration[36]

      - The time of maximum blood THC level (Tmax) following oral THC ranged from 1hr to 3.5hr post dose for frequent users and 1hr to 5hr post dose for occasional users.

- The maximum blood THC levels (Cmax) ranged from 3.2-14.3 ng/mL for occasional users and 8.0-36.1 ng/ml for frequent users.

- Newmeyer 2016 - Free and Glucuronide Whole Blood Cannabinoids' Pharmacokinetics after Controlled Smoked, Vaporized, and Oral Cannabis Administration in Frequent and Occasional Cannabis Users: Identification of Recent Cannabis Intake[37]

  - The time of maximum blood THC level (Tmax) following oral THC ranged from 1.5hr to 3.5hr post dose for both frequent and occasional users.

  - The maximum blood THC levels (Cmax) ranged from 3.6-22.5 ng/mL for occasional users and 4.7-34.8 ng/ml for frequent users.

- Lile 2013 - Pharmacokinetic and pharmacodynamic profile of supratherapeutic oral doses of Delta(9) -THC in cannabis users[33]

  - Doses produced physiologic (elevated heart rate) and behavioral effects reported previously. Peak plasma THC concentrations occurred between 2 and 4 hours post-ingestion.

- Bosker 2012 - Medicinal Delta(9)-tetrahydrocannabinol (dronabinol) impairs on-the-road driving performance of occasional and heavy cannabis users but is not detected in Standard Field Sobriety Tests[38]

  - Peak THC concentrations at 1.5 hours (tested 1.5, 4.25, and 6 hours post ingestion).

- Curran 2002 - Cognitive and subjective dose-response effects of acute oral delta-9-tetrahydrocannabinol (THC) in infrequent cannabis users[39]

  - Reported peak plasma concentrations at two hours post ingestion, with a mean peak for 15mg dose of approximately 4.75 ng/mL and a mean peak for 7.5mg dose of approximately 1.25 ng/mL.

Marijuana products classified as edibles come in a wide variety, such as cookies, drinks, candy, and tinctures. However, they all contain active THC that is ingested orally. Active THC is measured as

milligrams (mg) THC per serving in edibles as opposed to percentage (%) THC. Edibles are also metabolized in the body differently from inhalable marijuana products. This is especially important to understanding resulting blood levels of ingested THC. Currently, we have moderate evidence that ingesting more than about 15 mg THC is capable of yielding a whole blood THC concentration > 5 ng/mL. A 2013 study by Lile et al. found mean peak whole blood THC levels only exceeded 5 ng/mL only when taking doses greater than 45mg. However, they also described large inter-individual variability between subjects, with some having blood levels > 5 ng/mL at doses of 15mg and 30mg.[33]

Another key factor with edible metabolism is the amount of time after ingestion before effects begin and when peak blood THC concentrations are reached. There is substantial evidence that it may take up to 4 hours after ingesting marijuana to reach peak blood THC concentrations. However, there is variability between individuals, including within groups of frequent or occasional users as well. Newmeyer et al. (2017) found time of maximum blood THC level after ingesting marijuana ranged from 1 - 3.5 hours post dose for frequent users and 1 - 5 hours post dose for occasional users.[36] Coinciding with a longer time to peak blood levels is the longer duration of action that users will experience with edibles; leading to prolonged symptoms and subsequently more opportunity for adverse drug events.[49] As edibles continue to grow in popularity among the public, we can expect research efforts to further explore this relationship between edibles and blood THC levels.

Vaporized

- Evidence Statement: We found MODERATE evidence that inhaling vaporized marijuana yields blood THC levels that are similar to those produced by smoking the same dose.

- Public Health Statement: Smoking or vaporizing more than 10mg THC, or consuming an edible marijuana product with more than 15mg THC can lead to a blood THC level above 5ng/mL, which can be used to support a conviction for driving under the influence.

    o High

        ▪ Abrams 2007 - Vaporization as a smokeless cannabis delivery system: a pilot study[40]

- Found similar plasma concentrations of THC by vaporization and smoking through 360 minutes post-dosing, except for higher concentrations by vaporization at 30 and 60 minutes

- Peak plasma concentrations (at 2 minutes) and systemic doses (area under the concentration-time curves) were not significantly different. Subjective effects were similar between the vaporizing subjects and the smoking subjects. Performance effects were not examined.

- Plasma concentrations of THC are similar to those obtained by smoking, but bioequivalence has not been fully established.

o Low

- Spindle 2019 - Acute pharmacokinetic profile of smoked and vaporized cannabis in human blood and oral fluid[27]

  - Mean THC concentration at 10min after smoking 10mg THC was 3.76 ng/ml (0-21 ng/ml), and after vaporizing 10mg THC was 7.53 ng/ml (0-18 ng/ml)

  - Mean THC concentration at 10min after smoking 25mg THC was 10.24 ng/ml (0-38 ng/ml), and after vaporizing 25mg THC was 14.36 ng/ml (1-33 ng/ml)

- Newmeyer 2016 - Free and Glucuronide Whole Blood Cannabinoids' Pharmacokinetics after Controlled Smoked, Vaporized, and Oral Cannabis Administration in Frequent and Occasional Cannabis Users: Identification of Recent Cannabis Intake[37]

  - Among occasional users, the maximum blood THC levels (Cmax) were NOT statistically different after vaporizing (mean 47.8 ng/mL, range 5.2-137 ng/mL) or smoking (mean 51.6 ng/mL, range 1.3-174).

  - Among frequent users, the maximum blood THC levels (Cmax) WERE statistically different after vaporizing (mean 87.1 ng/mL, range 24.7-170 ng/mL) and smoking (mean 153 ng/mL, range 52.8-471).

- The time of maximum blood THC level (Tmax) was no different for smoked or vaporized MJ, in occasional or frequent users. All subjects reached Tmax by 0.17hr (10 minutes).

Along with concentrates, vaporizing marijuana has emerged as a method of use in more recent years. Vaporizing involves using a device (e.g. pen) that heats vaping liquid containing THC concentrate or flower that is inhaled. Currently, we found moderate evidence that inhaling vaporized marijuana yields blood THC levels that are similar to those produced by smoking the same dose. In a 2007 study, Abrams et al. described similar plasma concentrations of THC for vaporizing and smoking throughout the 6 hours measured after using marijuana. Also, subjective effects of marijuana were similar between the vaporizing and smoking groups of participants.[40]

THC concentrates

- Evidence Statement: We found LIMITED evidence that inhaling THC concentrate yields higher blood levels of active and later inactive THC, when compared to smoking marijuana flower.

- Public Health Statement: Inhaling THC concentrate may be associated with higher blood levels of THC when compared to smoking marijuana flower.

  - High - none

  - Medium

    - Bidwell 2020 - Naturalistic administration of cannabis flower and concentrates: cannabinoid blood levels, subjective intoxication, cognition, and motor function[41]

      - Concentrate users had higher levels of inactive THC (THC-COOH) measured at baseline, and active THC (delta-9 + 11-OH-THC) measured at acute post-use and one-hour post use compared to flower users (concentrate average of 320ng/mL, flower average of 143ng/mL).

In a 2020 study by Bidwell et al., concentrate users were found to have higher levels of inactive THC (THC-COOH) at baseline, and active THC (Δ-9 + 11-OH-THC) measured right after use and one-hour after use, compared to flower users. However, despite higher levels of THC, subjective intoxication

levels were not significantly different between flower and concentrate groups. They also measured for neurobehavioral impairment differences between concentrate and flower users, such as verbal recall memory, working memory, and balance. Performance on measures of verbal memory and balance worsened with acute use of marijuana. However, no differences were observed across other cognitive measures and, despite blood levels differences, no effect of marijuana type was observed.[41] More research is needed to evaluate how THC blood levels correlate with health effects, but this provides an interesting perspective on how THC blood levels coincide with subjective effects of marijuana. THC blood levels are an especially important measurement when discussing motor vehicle crash risk.

THC concentrates

Dependence

- Evidence Statement: We found INSUFFICIENT evidence to determine whether or not individuals who use THC concentrates are more likely to report symptoms of cannabis use disorder than those who use only non-concentrate marijuana products.

- Public Health Statement: No public health statement at this time.

    o High - none

    o Medium - none

    o Low

        ▪ Loflin 2014 - A new method of cannabis ingestion: the dangers of dabs?[42]

            • Adults perceive flower cannabis use as safer overall compared to dabbing (significance found).

            • Dab users report significant increases in withdrawal and tolerance compared to flower users.

            • Users do not experience more negative consequences or accidents (burns/fires) due to their dabbing use (no significance found).

        ▪ Meier 2017 - Associations between butane hash oil use and cannabis-related problems[43]

- College students who used butane hash oil (dab, wax, shatter, budder, etc.) had higher scores for physical dependence than those who used other types of marijuana and did not use BHO.

Another important aspect of health related to marijuana use is dependence or symptoms of cannabis use disorder. Currently, evidence available is insufficient to make a determination on whether or not use of THC concentrates (high % THC) marijuana products are associated with a higher likelihood of experiencing reporting symptoms of cannabis use disorder. Two studies explored this relationship, and did find an association, but more evidence is needed to strengthen this connection. Loflin & Earleywine (2014) explored concentrates, or dabs, (high % THC) through a self-report survey. Adult users reported perceiving flower marijuana use as a safer overall product than concentrates, even though users did not report experiencing more problems or accidents due to dabbing. However, withdrawal and tolerance effects were significantly increased according to self-report from THC concentrate users, when compared to flower marijuana.[42] In support of this, a 2017 study by Meier, found those who used Butane Hash Oil (BHO) were more likely to receive high scores for physical dependence to marijuana than people who used other types of marijuana, and did not use BHO.[43]

Acute health effects

- Evidence Statement: While there have been multiple reports of severe adverse health effects requiring hospitalization following the use of THC concentrates, we found INSUFFICIENT evidence to determine whether or not the use of THC concentrates is more likely to result in adverse acute health effects than the use of other types of marijuana.

- Public Health Statement: No public health statement at this time.

    o High - none

    o Medium - none

    o Low

        ▪ Chan 2017 - User characteristics and effect profile of Butane Hash Oil: an extremely high concentration cannabis concentrate[44]

            • Higher depression and number of other substances used (BHO > high THC concentration cannabis > cannabis use with no BHO or high THC concentration cannabis).

- o Case series/report

  - ▪ McMahon 2016 - Severe pneumonitis after inhalation of BHO[45]

    - • One case of severe pneumonitis requiring intubation.

  - ▪ Pierre 2016 - Cannabis-induced psychosis associated with high potency "wax dabs".[46]

    - • Two cases of severe paranoia resulting in psychiatric hospitalization.

  - ▪ Schneberk 2015 - Hot wax[47]

    - • One case of severe paranoia and injury after jumping from a moving car.

While there have been no formal studies conducted on the subject, there have been case reports of severe adverse acute health effects after the use of THC concentrates. However, these few case studies provide overall insufficient evidence to determine if using this type of marijuana product is more likely than other types of marijuana to result in adverse acute health effects. A 2017 study by Chan et al., defined user profiles of BHO, a type of concentrate THC product, compared to users of other products. They found higher depression and number of other substances used among BHO users.[44] Other case reports have described people experiencing severe paranoia resulting in psychiatric hospitalization after using BHO and one case of severe pneumonitis.

Preparation and device failure leading to burn injury

- • Evidence Statement: Numerous cases reported show that home butane extraction of hash oil [a type of marijuana concentrate] has resulted in severe burns requiring hospitalization.

- • Public Health Statement: Extracting hash oil yourself with flammable substances can cause severe burns requiring hospitalization.

  - o 7 case reports/series with numerous individual cases included (N = 163, total assuming no overlap)[50-56]

- • Evidence Statement: Numerous cases reported show that electronic vaporizing devices have failed (exploded), resulting in cases of trauma and burn injury.

- Public Health Statement: Electronic smoking or vaporizing devices can explode, causing serious injury.

    o 2 case reports/series (N = 4, no overlap, 2 cases involving burns while device not in use, 2 cases involve trauma resulting from explosion while in use)[57,58]

When discussing products with high THC concentration, such as concentrates or "dabs," it is important to mention potential injuries related to the equipment or devices required to consume THC concentrate and home-production of THC concentrate. Stogner and Miller (2015) stated harms of dabbing, or using concentrate THC products, include using a butane torch and the higher temperature of heat required to vaporize this specific type of marijuana product.[48] Additionally, numerous case reports have shown that conducting home butane extraction of hash oil (a type of marijuana concentrate) has resulted in burns severe enough to require hospitalization. There have also been many case reports that have shown electronic smoking devices (one method of concentrate use) have failed or exploded, resulting in trauma and burn injury. As with any type of substance use, we cannot ignore the physical or traumatic injuries that may result from equipment or devices when using or attempting to produce these concentrated products.

Discussion and recommendations

Six years after retail marijuana was legalized in Colorado it is apparent that progress has occurred quicker in the marijuana industry than in science. The sheer quantity and variety of marijuana products available on the retail market place is proof of this rapid advancement. In contrast, few studies have been conducted that examine the impact different product types with differing THC concentrations have on human health. Our search of the peer-reviewed literature was encompassing of all health topics and all marijuana product types. However our most recent search did not yield results in the health topics areas of pregnancy and breastfeeding, cardiovascular effects, cancer, gastrointestinal effects, reproductive health effects, respiratory effects, or second and third-hand smoke/aerosol exposure. The lack of evidence in these areas paired with the little evidence that was found in other topics of interest limits our ability to assess the full health impact of these products at this time. Though it is clear that use of products with high concentrations of THC are associated with higher rates of psychiatric disorders, such as schizophrenia, psychosis, and generalized anxiety disorder.

CDPHE and the Retail Marijuana Public Health Advisory Committee acknowledge and share concern about the health and safety of the consumption of highly concentrated THC products available in Colorado. In effort to better address these concerns we make the following recommendations;

Education

➢ Increase awareness, education and understanding of THC concentration.

➢ Increase adult consumer awareness and education about the risks of mental health effects from using marijuana products with high THC concentration.

➢ Increase adolescent and young adult prevention efforts with emphasis on the risk of developing future mental health symptoms and/or disorders from using products with high THC concentration and/or with more frequent marijuana use.

➢ Encourage use of the term THC concentration in place of potency.

➢ Increase clinician and local public health knowledge on the importance of collecting information on marijuana product type and THC content (% or mg THC).

Research

Prioritize public health research in the follow areas concerning THC concentration;

➢ Investigate the relationship between mental health effects and THC concentration, dose and frequency of use.

➢ Further investigate how varying THC concentration of different marijuana products affects THC blood levels, subsequent intoxication, and health.

➢ Investigate acute health effects related to marijuana use and document the marijuana products involved and THC concentration.

➢ Encourage research studies that utilize products from Colorado with varying THC concentration.

➢ Determine thresholds for what should be considered low and high THC concentrations.

Surveillance

➢ Continue surveillance efforts surrounding adolescent and young adult use of marijuana products containing high THC concentration.

➢ Improve data by collecting information on marijuana product type and THC content (% or mg THC) and encourage healthcare systems and providers to collect this information.

➢ Develop and validate survey questions that can be used to inform on three key areas; product type, THC content (% or mg THC), and number of times used per day.

➢ Monitor rates of adverse events stratified by product type.

➢ Monitor THC concentration among marijuana products available on the regulated retail market in Colorado.

Conclusion

In Colorado, almost all retail marijuana products contain high THC concentration, rarely containing less than 10% THC. Evidence is moderate to strong concerning THC concentration and the association with mental health effects in adolescents, young adults and adults. When examining specific types of marijuana products and the impact on blood THC levels, the evidence is strong for marijuana flower, moderate for both edibles and vaporized products and limited for THC concentrate products. Specific to THC concentrate products, evidence is insufficient when examining the association to dependence and acute health effects. Our ability to make unbiased, evidence-based statements on the potential health effects of marijuana products containing high THC concentration is limited until further scientific research can be conducted and the evidence shared or published. Therefore, in the best interest of public health, we suggest funding research to answer these questions. We will diligently continue to monitor the scientific literature, conduct surveillance activities, and update our statements and recommendations as more evidence becomes available.

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