REPORT 4 OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH (November 2020) (Resolutions 408-A-19, 411-A-19 and Alternate Resolution 913-I-19) Public Health Impacts of Cannabis Legalization (Reference Committee E)

EXECUTIVE SUMMARY

Objective. To review developments in cannabinoid pharmacology, update relevant sections of Council Report 5-I-17, "Clinical Implications and Policy Considerations of Cannabis Use," and evaluate the public health impacts in states that have legalized cannabis for adult use to determine whether modifications to AMA are warranted.

Methods. English language reports were selected from searches of the PubMed, Google Scholar, and Cochrane Library databases from August 2017 to August 2020 using the (text or MeSh) search terms "marijuana or cannabis or cannabinoid or cannabidiol" in combination with "legalization or laws," and "health," "mental or public health," "addiction or cannabis use disorder," "health effects," "use," "benefits or harms," "youth or adolescents," "edibles," "driving," "taxes," "social equity or justice" and "treatment." Additional articles were identified through related article searches and by manual review of the reference lists of retrieved articles. Websites managed by federal and state agencies, and applicable regulatory and advocacy organizations also were consulted for relevant information.

Results. Thirty-three states have legalized medicinal use of cannabis. Eleven of these states have legalized cannabis for adult use. All 17 states that have not legalized medical use of cannabis allow the use of cannabidiol (CBD) in some way, as does the federal government for CBD products derived from hemp containing $\leq 0.3\%$ Δ -9-tetrahydrocannabinol (THC). The health effects of cannabis and cannabinoids described in Council Report 5-I-17 remain valid; additionally, attention has been drawn to increased cardiovascular risks with cannabis use.

The overall prevalence of cannabis use in the U.S has increased steadily since 2011, mostly among young adults aged 18-25 years and adults 26 years of age and older. Adolescent use has declined during the same time period; findings from state-based surveys in states with legalized adult use contradict to a certain degree patterns reported by national surveys in individual states, but in the fastest growing demographic (18-25 years-old), prevalence of use is highest in states with legalized adult use. Legalization of cannabis for adult use also is associated with increased traffic fatalities, exposures reported to poison control centers (including infants and children), emergency department visits, and cannabis-related hospitalizations. Changes in methods and patterns/intensity of cannabis use in pregnant women are most concerning. Legalization has led to a large decrease in cannabis-related arrests for adults, less so for juveniles, and with limited effects on disparities in that population. States that have legalized cannabis for adult use have garnered increasing revenues on a quarterly/annual basis, with variable portions earmarked for public health measures or designed to address social equity concerns.

Conclusion. Developments in states' retail cannabis market have advanced more rapidly than public health frameworks to minimize harms. Amendments to current AMA policy are recommended to address these developments.

REPORT OF THE COUNCIL ON SCIENCE AND PUBLIC HEALTH

CSAPH Report 4, November 2020

Subject: Public Health Impacts of Cannabis Legalization

(Resolutions 408-A-19, 411-A-19 and Alternate Resolution 913-I-19)

Presented by: Kira A. Geraci-Ciardullo, MD, MPH, Chair

Referred to: Reference Committee E

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INTRODUCTION

This Council report responds to three referred resolutions on cannabis.

Resolution 408-A-19, "Banning Edible Cannabis Products," introduced by the Illinois Delegation and referred to the Board of Trustees, asked:

That our American Medical Association adopt policy supporting a total ban on recreational edible cannabis products;

Resolution 411-A-19, "AMA to Analyze Benefits/Harms of Legalization of Marijuana," introduced by the New York Delegation and referred to the Board of Trustees, asked:

That our American Medical Association review pertinent data from those states that have legalized marijuana; and,

Alternate Resolution 913-I-19, "Public Health Impacts and Unintended Consequences of Legalization and Decriminalization of Cannabis for Medicinal and Recreational Use," was adopted, but an additional proposed resolve, referred to the Board of Trustees, asked:

That our AMA amend Policy H-95.924, "Cannabis Legalization for Recreational Use," by addition and deletion to read as follows:

H-95.924, "Cannabis Legalization of Cannabis Use for Medical or Any Other Purposes for Recreational Use" Our AMA: (1) believes warns that cannabis is a dangerous drug and as such is a serious public health concern; (2) advocates that cannabis and cannabinoid use are a serious public health concern; (2 3) warns against the legalized use and sale of cannabis and cannabinoids due to their potential negative impact on human health believes that the sale of cannabis for recreational use should not be legalized; (3 4) discourages warns against cannabis and cannabinoid use, especially by persons vulnerable to the drug's effects and in high risk populations such as youth, by children, adolescents, pregnant women, and women who are breastfeeding; (4 5) believes strongly advocates that states that have already legalized cannabis for medical purposes or any other purposes (for medical or recreational use or both) should be required to take steps to regulate the product cannabis and cannabinoids effectively in order to protect public health and safety and that laws and regulations related to legalized cannabis use should consistently be evaluated to determine their effectiveness; (5 6) strongly encourages local, state, and federal public health agencies to improve surveillance efforts to ensure data is

available on the short- and long-term health effects of cannabis and cannabinoid use; and (67) supports decriminalization and public health based strategies, rather than incarceration, in the handling of individuals possessing cannabis or cannabinoids for personal use.

This report updates relevant sections of Council Report 5-I-17, "Clinical Implications and Policy Considerations of Cannabis Use," summarizes current state legislation legalizing adult cannabis and cannabinoid use, and reviews other pertinent information and developments in these jurisdictions to evaluate the public health impacts of legalization. The term cannabis will be used throughout when referring to the *Cannabis sativa* plant rather than the slang term marijuana/marihuana, unless the latter is officially included in a title, policy, or otherwise official language.

METHODS

 English language reports were selected from searches of the PubMed, Google Scholar, and Cochrane Library databases from August 2017 to August 2020 using the (text or MeSh) search terms "marijuana or cannabis or cannabinoid or cannabidiol" in combination with "legalization or laws," and "health," "mental or public health," "addiction or cannabis use disorder," "health effects," "use," "benefits or harms," "youth or adolescents," "edibles," "driving," "taxes," "social equity or justice" and "treatment." Additional articles were identified through related article searches and by manual review of the reference lists of retrieved articles. Websites managed by federal and state agencies, and applicable regulatory and advocacy organizations also were consulted for relevant information.

CURRENT AMA AND FEDERATION POLICY

The Council has issued six previous reports on cannabis covering: (1) aspects of research and investigational and therapeutic use (including in-hospital); (2) the juxtaposition of cannabis within the evolution of U.S. national drug control policy; and, (3) the broader clinical implications and policy considerations associated with the proliferation of state-based medicinal and legalized adult use programs. ¹⁻⁶

AMA policy categorizes cannabis as a dangerous drug and public health concern (Policy H-95.924). Accordingly, our AMA supports increased educational programs on the use and misuse of alcohol, marijuana, and controlled substances, including specific measures aimed at K-12 curricula (H-170.992).

With respect to criminal penalties, our AMA believes that public health-based strategies, rather than incarceration, should be utilized in the handling of individuals possessing cannabis for personal use (H-95.924). A plea of cannabis intoxication should not be a defense in any criminal proceedings (H-95.997).

With respect to research, our AMA calls for further adequate and well-controlled studies of marijuana and related cannabinoids in patients who have serious conditions for which preclinical, anecdotal, or controlled evidence suggests possible efficacy (H-95.952). To facilitate the conduct of clinical research and development of cannabinoid-based medicines, the status of marijuana as a federal schedule I controlled substance should be reviewed and relevant federal agencies should implement measures designed to streamline the clinical research process (H-95.952). The consequences of long-term cannabis use in youth, pregnant women and those who are breastfeeding are special concerns. Our AMA discourages cannabis use, especially in these populations (and in those who are otherwise vulnerable to the drug's effects), and supports specific

 point of sale warnings and product labeling about the potential dangers of use during pregnancy and breastfeeding (H-95.924).

In order to promote public health and safety, research on the impact of cannabis legalization and decriminalization also is encouraged and information derived from such activities should be disseminated. Local, state, and federal public health agencies can assist by improving surveillance efforts to capture relevant data on both short-and long-term health effects of cannabis. Our AMA supports the development of resources on the human health effects of cannabis and on methods for counseling and educating patients on cannabis and cannabinoid use (H-95.924).

AMA policy otherwise separates cannabis legalization for medicinal (D-95.969) or recreational use (H-95.924). AMA policy opposes state-based legalization of cannabis for medical use (whether via legislative, ballot, or referendum processes) and supports the traditional federal drug approval process for assessing the safety and efficacy of cannabis-based products for medical use. U.S. Food and Drug Administration (FDA) approved cannabinoid products include:

• Dronabinol (Marinol®) is an oral formulation (capsules) containing synthetic delta-9-tetrahydrocannabinol (THC) approved for the treatment of HIV-wasting and chemotherapy-induced nausea and vomiting when conventional treatments are inadequate; a liquified formulation (Syndros®) also is available.

• Nabilone (Cesamet®), a synthetic THC analogue that activates the endogenous cannabinoid type 1 (CB₁) receptor, is an oral formulation approved for the treatment of the nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

• Cannabidiol (CBD) oral solution (Epidiolex®) is approved for the treatment of seizures associated with Lennox-Gastaut syndrome, Dravet syndrome, and tuberous sclerosis complex in patients one year of age and older. (Note: AMA Policy H-120.926, "Expedited Prescription Cannabidiol Drug Rescheduling," supports legislative and regulatory measures designed to expedite the availability of FDA-approved cannabidiol products and to reassert that patient access should be managed like other prescription-only products.)

 Nabiximols (Sativex®) is a 1:1 ratio of THC and CBD, extracted from specially bred cannabis plants and formulated as an oromucosal spray for the treatment of spasticity in patients with multiple sclerosis. This product is approved in 20 countries, including Canada, but remains investigational in the U.S.

Cannabis products that have not been approved by the FDA (but are marketed for human ingestion in many states) should carry the following warning label: "Marijuana has a high potential for abuse. This product has not been approved by the FDA for preventing or treating any disease process" (D-95.969). Hospitals and health systems also should not recommend the use of such products within their facilities and should educate medical staffs on cannabis use, its effects, and symptoms (withdrawal syndrome) that may appear in patients who abruptly discontinue use. AMA policy also recognizes that physicians may need to engage in a dialogue with their patients about cannabis/cannabinoid use, that such discussions are protected, and that physicians whose behavior conforms to state cannabis laws should not be subject to federal prosecution.

Our AMA also opposes legalizing the sale of cannabis for adult use and supports stronger public health messaging on the health effects of cannabis and cannabinoid inhalation and ingestion (H-95.924). States that have already legalized cannabis (for medical or legalized adult use or both)

should ensure that processes are in place to regulate the product to effectively protect public health and safety with an ongoing evaluation of their effectiveness. A "substantial portion" of tax revenues derived from state-based programs should be used for public health purposes including prevention and treatment of substance use disorders, the aforementioned cannabis-related educational programs, research on the health effects of cannabis use, and public health surveillance efforts.

The AMA also has policy on addressing synthetic cannabinoids and recognizing new psychoactive substances as a public health threat. The Council addressed these substances in detail in its 2017 report, Emerging Drugs of Abuse are a Public Health Threat. Synthetic cannabinoids are outside the scope of this report. Issues relevant to the regulation of CBD are covered in detail in the Council on Science and Health Report on dietary supplements (CSAPH Report 2) being considered at this meeting. As a result, issues related to CBD and are outside of the scope of this report.

Many medical societies in the Federation have taken positions that are consistent with AMA policy. The California Medical Association (CMA) is one exception. It is on record as urging the legalization and regulation of cannabis to allow for greater clinical research, oversight, accountability, and quality control. CMA believes that the most effective way to protect the public's health is to tightly control, track, and regulate cannabis and to comprehensively research and educate the public on its health impacts, not through ineffective prohibition. CMA policy also opposes policies of health plans, health systems, and hospitals with pain management programs that automatically eliminate patients who use therapeutic cannabis.

CANNABIS AND CANNABINOID PRIMER

In order to better understand certain issues surrounding cannabis, substances derived from the plant, their pharmacology, and implications for adult legalization, a brief review is provided.

Cannabis Plant

 Cannabis sativa contains a complex array of chemical compounds, including more than 100 phytocannabinoids that are exclusively produced in cannabis, and more than 200 terpenoids (comprising "essential oils") which are responsible for the aroma of cannabis. Phytocannabinoids and terpenoids are synthesized in secretory cells inside glandular trichomes that are most highly concentrated in unfertilized female flowers. HC is the most concentrated phytocannabinoid and the main psychoactive substance; delta-8-THC is similar in potency to THC, but is normally present in only trace amounts. CBD, which possesses its own pharmacologic profile and lacks THC's intoxicating effects, and cannabinol are the other major phytocannabinoids; CBD is the most common phytocannabinoid in hemp (fiber) plants.

 Other phytocannabinoids of pharmacologic interest include cannabichromene, cannabigerol, tetrahydrocannabaverin, and cannabidivarin.¹¹ These substances have their own pharmacologic profiles, effects of which are largely unstudied in humans.¹¹ Precursor acid forms of the neutral phytocannbinoids, that break down in the presence of heat, exist in the plant and may be available in concentrated forms in dispensaries in some states; other "secondary" phytocannabinoids isolates have become available as well.

Selective Mendelian breeding has created cannabis varieties (termed chemovars or chemotypes) with altered concentrations and ratios of phytocannabinoids and terpenes. General categories based on cannabinoid content have been described as THC-predominant (typical of legalized adult use marketplaces), "balanced" THC and CBD varietals, and CBD-predominant; some strains have been

created that are enriched in specific terpenes. 12 The average THC content of illicit cannabis samples confiscated in the U.S. increased from ~4% to 12% between 1995 and 2014. The majority of advertised cannabis flower products with both state medicinal and legalized adult use programs now exceed 15% THC, and some exceed 20% in states with legalized adult use. Genetic engineering, either via genetic modification of plants or using recombinant DNA in microorganisms (yeast, bacteria, algae) also is being used to increase yields of THC or CBD, or of the lesser studied phytocannabinoids. 14 These developments have implications for both the traditional pharmaceutical industry and the legalized adult use marketplace, and for evaluating both the risks and harms of cannabis and cannabinoid use in the published literature over time.

Endocannabinoid System

Phytocannabinoids exert their effects, in part, via the endogenous cannabinoid (endocannabinoid) system. This system comprises two specific neuromodulators that are arachidonic acid derivatives [anandamide (AEA) and 2-arachidonoylglycerol (2-AG)], enzymes for their biosynthesis and inactivation, and two transmembrane, G-protein coupled cannabinoid receptors (CB₁, CB₂). ^{15,16} CB₁ receptors are enriched and widely distributed in the brain, and to a lesser extent in peripheral tissues, in a region specific manner. ¹⁷⁻²⁰ See Figure 1 for a summary of the functions that have been associated with CB₁ receptors. Expressed mainly peripherally on circulating immune system cells, the spleen, macrophage derived cells, and the liver, CB₂ receptors are normally present in low concentrations in the brain (brainstem and hippocampus), but following injury or inflammation are upregulated in reactive microglia and astrocytes where they inhibit neuroinflammation. ^{15,18,20}

2-AG is an agonist at CB_1 and CB_2 receptors; AEA is a partial agonist at CB_1 receptors and largely inactive at CB_2 receptors. These substances act in a retrograde manner, being released from postsynaptic sites, migrating to presynaptic CB_1 receptors and inhibiting neurotransmitter release, dampening activity within discrete excitatory and inhibitory pathways. ¹⁹

 THC is a partial agonist at CB₁ and CB₂ receptors. ^{18,21} CBD is a partial agonist of the CB₂ receptor, although it also binds to and acts as an antagonist at other non-cannabinoid G-protein receptors. CBD also inhibits the uptake of AEA and its metabolism and activates TRPV receptors and 5HT_{1A} receptors. CBD has low affinity for CB₁ receptors, but in low concentrations is capable of functioning as an effective antagonist (or perhaps as a noncompetitive negative allosteric modulator) of THC and other 2-AG agonists. ^{22,23} Peripherally, activation of CB₂ receptors exerts anti-inflammatory and immunomodulatory effects, mobilizes hematopoietic stem cells, decreases gastrointestinal motility, and reduces visceral pain.

Disposition of THC and Cannabadiol Based on Route of Administration

Based on information obtained in pharmacokinetic studies of approved drug products, oral THC capsules (Marinol®) demonstrate low (6% to 20%) and variable bioavailability among test subjects. Gastric acidity causes some isomerization of THC to the delta-8-derivative and the drug is subject to a significant first pass effect. Peak plasma concentrations of THC are achieved within 1 to 6 hours, but may remain elevated for several hours. $^{24-27}$ Initially, THC is oxidized in the liver to 11-hydroxy-THC, a potent psychoactive metabolite, which undergoes further oxidation to the primary inactive (acidic) metabolite (THC-COOH). Although THC is cleared rapidly by the liver it has a very large volume of distribution (\approx 10 L/kg). 24 Thus, the terminal half-life of THC is on the order of 20 to 36 hours. 24,27 With chronic use, the limiting step for the terminal phase of elimination is redistribution from peripheral tissue storage sites.

Following inhalation, THC and CBD are rapidly absorbed into the blood stream and redistributed. Considerable amounts of the dose contained in one cigarette are lost in sidestream smoke and destroyed by pyrolysis. ^{24,28} Peak blood levels of THC and CBD are achieved at the end of smoking and then decline rapidly over the next 30 minutes.²⁴ The pharmacokinetics of vaporized and smoked cannabinoids are comparable; however, infrequent users report more pronounced effects with vaping than smoking. ^{29,30} Smoked or vaped cannabis is associated with much larger peak plasma THC concentrations, but a shorter duration of effect than orally administered THC. The time course of plasma concentrations after smoking or vaping marijuana is similar to that obtained after intravenous administration.²⁶

Considerably smaller amounts of 11-OH-THC are formed when THC is inhaled, compared with the oral route. ^{24,31} After oral administration of THC, THC-containing edibles, or cannabis-based extracts, the concentrations of THC and 11-OH-THC are much lower than those found upon smoked administration, exhibit marked variability among various preparations, and are slower to reach a peak level; however, they are capable of causing comparable subjective effects and substantial impairment of cognitive/psychomotor functioning. ³¹⁻³⁴

RELEVANT FEDERAL LAW AND POLICY

Under the U.S. Controlled Substances Act (CSA) of 1970, marihuana remains classified as a Schedule I controlled substance, and the DEA and FDA have reinforced that interpretation, meaning it has no currently accepted medical use in treatment in the United States, a lack of accepted safety for use under medical supervision, and a high potential for abuse.^{35,36} The term "marihuana" means all parts of the plant *Cannabis sativa*, whether growing or not; the seeds thereof; the resin extracted from any part of such plant; and every compound, manufacture, salt, derivative, mixture, or preparation of such plant, its seeds or resin.³⁷ As noted in the introduction, FDA has approved three cannabinoid-based prescription medicines

Council Report 5-I-17 discussed legal challenges, federal agency findings, and federal policy recommendations that were intended to manage the conflict between federal and state laws and emerging issues on medical or legalized adult use of cannabis. That discussion remains valid with a few notable exceptions and developments.

 Early in the Trump administration, then-Attorney General Jeff Sessions rescinded existing Department of Justice guidance (the Cole Memorandum) that was intended to make clear that state-legalized cannabis was not an enforcement priority. In response, the House of Representatives approved spending bill amendments in both 2019 and 2020 to block the Department of Justice from using its funding to interfere with the implementation of state, territorial and tribal cannabis programs.

 Also, in 2018, the Agricultural Improvement Act (the 2018 Farm Bill) was passed.³⁸ This law removed hemp from the definition of marihuana in Schedule I of the Controlled Substances Act, thereby legalizing the production of hemp under federal law. The bill defined hemp as any cannabis plant, including derivatives or extracts, that contains less than 0.3 percent of THC.³⁸

STATE LAWS ON CANNABIS

At the state level, trends in law continue to move from legal prohibition, to decriminalization, to the legalization of medical use of cannabis, to cannabis legalized for adult use (commonly referred to as recreational use). ³⁹⁻⁴² To varying degrees these trends have been shaped by arguments that cannabis is less harmful than alcohol and tobacco and may demonstrate certain health benefits; that

arrests and criminal convictions for cannabis possession are disproportionately harmful (including their effect on minoritized populations), and that legalization has the potential to eliminate the illicit market, enable regulation of use (including product potency and purity), reduce prison overcrowding, redistribute law enforcement activities, and raise government revenue.⁴³

California (CA) was the first jurisdiction in the United States (U.S.) to legalize the use of cannabis for medical purposes in 1997. Today, 33 states, the District of Columbia (D.C.), Guam, and Puerto Rico have legalized the use of cannabis for medical purposes through either a legislative process or ballot measure. 39-42 As described in Council Report 5-I-17, these laws vary greatly by jurisdiction from how patients access the product (home cultivated or dispensary), to qualifying conditions, product safety and testing requirements, packaging and labeling requirements, the retail marketplace, and consumption method. In jurisdictions that have legalized cannabis for medicinal use, physicians can "certify" or "recommend" a qualifying patient for the medicinal use of cannabis, but physicians cannot prescribe cannabis for medical purposes because, as a Schedule I Controlled Substance, it is illegal under federal law. Eleven of these states (and four others without medical use of cannabis laws) have decriminalized and removed jail time for possession of small amounts of cannabis. 42

 In 2012, Colorado (CO) and Washington (WA) were the first U.S. jurisdictions to legalize the adult use of cannabis. ^{44,445} At this point, a total of 11 states and D.C. have legalized cannabis for adult use, ten through the ballot measure process, and two (Illinois [IL[and Vermont [VT]) via legislation. ^{39,41} As noted in the 2017 Council report, most of these jurisdictions have created forprofit, commercial cannabis production and distribution markets where the product is sold and taxed; Washington, DC (DC) and VT are exceptions. DC has adopted a "grow and give" model whereby residents are permitted to possess, use, grow, and give away cannabis, but they cannot sell it. ⁴⁶ VT's adult use law, passed in 2018, also allows residents to possess recreational cannabis (1 oz) or grow up to six plants (only two mature at a time) but retail sales are currently not allowed. ⁴⁷ Possession limits for adult use in other states range from 1 to 2.5 oz of usable cannabis flower, with most allowing variable numbers of plants, and limits on the amount of hash, solid or liquid infused products, or concentrates that can be possessed. ³⁹ See Figure 2 for a timeline of legalization and actual implementation.

RETAIL MARKETPLACE: LEGALIZED CANNABIS FOR ADULT USE

As the marketplace for legalization of cannabis for adult use has grown dramatically, an expansive retail environment has developed with "novel cannabis products, formulations and methods of administration."48 Different formulations (extracts, concentrates) of cannabis have emerged that can be smoked, vaporized, or used to create (infused) edibles (e.g., gummy bears, lozenges, candies, lollipops, brownies/cookies/other foods, and beverages), tinctures and oils for consumption, as well as topicals. 49,50 Extracts are a type of concentrate formed by using solvents to wash the cannabinoid-rich trichomes off the plant and remove phytocannabinoids and terpenes. Hydrocarbons (e.g., butane, propane), ethanol, or supercritical fluid extraction using CO₂ are the most common approaches.⁵⁰ Depending on the method, the resulting concentrate comes in various forms (e.g., waxes, shatter, resin), that can be further processed into various textures (e.g., budder, crumble, honeycomb). Concentrates made without the use of solvents are produced using mechanical or physical means to remove and gather trichomes (e.g., hash, kief, rosin). Some dispensaries also feature products enriched in other phytocannabinoids, most commonly CBD, cannabinol, cannabigerol, or tetrahydrocannabinolic acid (THCA) and products that are enriched in certain terpenes. 48 See Table 1 for a graphic display and description.

THE HEALTH EFFECTS OF CANNABIS AND CANNABINOIDS

 The National Academies of Sciences, Engineering, and Medicine (National Academies, NASEM) published a comprehensive report in January 2017 commissioned by federal, state, philanthropic, and nongovernmental organizations, entitled "The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and the Recommendations for Research." The report's recommendations outline priorities for a research agenda and highlight the potential for improvements in data collection efforts and enhanced surveillance capacity.

 The report contained 98 conclusions based on the accumulated evidence related to cannabis or cannabinoid use and health.⁵⁶ It examined a broad range of possible health effects of cannabis and cannabinoids. Health effects examined included those related to cancer; cardiometabolic risk; respiratory disease; immunity; injury and death; prenatal, perinatal, and neonatal exposure; psychosocial and mental health; problem cannabis use; and cannabis use and the misuse of other substances. The findings were organized into 5 evidence categories: conclusive, substantial, moderate, limited, and no/insufficient evidence.

Health Uses: The report found conclusive or substantial evidence that cannabis or cannabinoids are effective: (1) as antiemetics in the treatment of chemotherapy-induced nausea and vomiting (oral cannabinoids); and (2) for improving patient-reported multiple sclerosis spasticity symptoms (oral cannabinoids); and (3) for the treatment of chronic pain in adults (cannabis).

The report found moderate evidence that use of cannabis or cannabinoids: (1) are effective in improving short-term sleep outcomes in individuals with sleep disturbance associated with obstructive sleep apnea syndrome, fibromyalgia, chronic pain, and multiple sclerosis (cannabinoids, primarily nabiximols); (2) are associated with improved cognitive performance among individuals with psychotic disorders (history of use).

 The report also found substantial evidence of a statistical association between cannabis smoking and: (1) more frequent chronic bronchitis episodes (long-term cannabis smoking); (2) increased risk of motor vehicle crashes; (3) lower birth weight of offspring (maternal cannabis smoking); (4) the development of schizophrenia or other psychoses, with the highest risk among the most frequent users; and substantial evidence that initiating use at an earlier age and smoking cigarettes (males) as risk factors for progression to problematic cannabis use.

The report found moderate evidence of a statistical association between cannabis use and: (1) increased risk of overdose injuries, including respiratory distress, among pediatric populations in U.S. states where cannabis is legal; (2) impairment in the cognitive domains of learning, memory, and attention; (3) a number of mental health domains including increased symptoms of mania and hypomania in individuals diagnosed with bipolar disorders (regular cannabis use); small increased risk for the development of depressive disorders; increased incidence of suicidal ideation and suicide attempts with a higher incidence among heavier users; increased incidence of suicide completion; and increased incidence of social anxiety disorder (regular cannabis use).

In general, the findings and conclusions of this report remain valid. Two additional comprehensive systematic reviews have been published since the NASEM report. A review on cannabis-related harms was in substantial agreement with the NASEM report.⁵² This study also called attention to increased cardiovascular risks associated with cannabis use, prenatal exposure and cognitive dysfunction/behavioral disturbances in offspring, and hyperemesis syndrome. Case studies have linked cannabis use to acute myocardial infarction, cardiac arrythmias, cardiomyopathies, stroke, and arteritis, mostly in younger men with few cardiovascular risk factors.⁵³ A scientific statement

issued by the American Heart Association in August 2020 warned that cannabis use may be linked 2 to an increased risk of heart attacks, atrial fibrillation and heart failure.⁵⁴ A recent retrospective analysis of nationwide inpatient data found that cannabis use was an independent predictor for 3 acute myocardial infarction-related hospitalization in adolescents and young adults.⁵⁵ The other review used evidence mapping and appraisal to evaluate published studies on the therapeutic benefits of cannabis and cannabinoids. This study also was in substantial alignment with the NASEM report.⁵⁶

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PUBLIC HEALTH IMPACTS OF STATE LEGALIZATION OF CANNABIS

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Despite the fact that 11 states and D.C. have now legalized the adult use of cannabis, evaluation of the impacts of legalization on health and safety remain somewhat limited. Retail sales have not commenced in ME, and are not allowed in VT and D.C. Insufficient time has elapsed since retail sales commenced in some states (e.g., IL, Michigan [MI], Massachusetts [MA]) to get meaningful results and/or a state program for formal analysis of post-legalization effects has not been created. Importantly some states established a framework for future analysis by evaluating and compiling various baseline measures (pre-legalization) to be used for comparison (e.g., OR, MI, MA).

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Otherwise, CO [through its Department of Public Health and Environment (CDPHE) and appointed Retail Marijuana Public Health Advisory Committee (RMPHAC)] and WA [in partnership with the Washington State Institute for Public Policy (WSIPP)], and two other states (OR and AK), lead the way on having examined state-specific health and safety outcomes and patterns of cannabis use since legalization. State-based data and surveys, as well as national surveys such as the Substance Abuse and Mental Health Services Administration's (SAMHSA) National Survey on Drug Use and Health (NSDUH) and the Center for Disease Control and Prevention's (CDC) Behavioral Risk Factor Surveillance System (BRFSS), Monitoring for the Future (MTF) and Pregnancy Risk Assessment Monitoring System (PRAMS) have been relied on. Where available larger, state representative surveys that have been implemented longitudinally may be more relevant on certain measures.⁵⁷

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General issues being examined include the impact of legalization for the adult use of cannabis on:

- patterns of use by children and adolescents, college and university students, other adults, and pregnant women. In youth, monitoring changes in the perceived risk and social acceptability of cannabis and cannabis advertising also has been emphasized;
- incidents of impaired driving and traffic fatalities;
- cannabis-related hospital or emergency department visits and other cannabis-related (toxic) exposures;
- changes in the incidence, costs and treatment for mental health disorders, including treatment admissions for cannabis use disorder;
- effects on the market for alcohol and other drugs;
- criminal behaviors (including civil penalties, arrests, prosecution and incarceration); and, government revenues and costs of implementing legalization.

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Considerable attention also has been devoted to the association between medicinal and/or legalized adult use and opioid-related measures and outcomes.

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CO has the most extensive state-based data. Their findings are emphasized for some topics, 48 buttressed with comparable data, where available, from other states that have legalized cannabis for adult use.

General Age-Related Patterns Use

In the U.S., the most commonly used illicit drug (based on federal status) in the past year among those aged 12 or older was cannabis, totaling approximately 43.5 million people or 15.9% of the population; nearly 44% of this group are of past month users. The overall prevalence of cannabis use in the U.S. has increased steadily since 2011 (38% increase), accounted for mostly by increased use among young adults aged 18-25, and adults 26 years of age and older. Annual cannabis use is at historic highs (42.5%) since 2013 among 19-22 year-olds (both college and non-college peers). In 2016, 43% past-month cannabis users who were 18 years and older reported daily or near-daily cannabis use (20 or more days per month), a 30% increase since 2002. This pattern of use declined about 23% in adolescents over the same time period. According to the 2019 MTF survey, there has been an uptake in daily use among younger students (grades 8 and 10) since 2017. Based on the BRFSS, daily use of cannabis in adults in CO has increased from 6% in 2014 to 9% in 2018, but the methods of use in CO adults have remained fairly constant.

Adolescent use has declined nationally since 2011, remaining fairly steady from 2015 to 2018.⁵⁸ Combined NSDUH data for 2017-18 suggest that 6.5% or 1.6 million adolescents (12-17 years old) were current (past month) users of cannabis. The prevalence of past month use in this survey was higher than the national average in CO (9.36%) as well as all other states with legalized adult use; six of these states (WA, VT, OR, MA, Nevada, ME) and DC showed increased adolescent use according to NSDSUH, contrary to the national trend.^{58,62}

A nationally representative survey of U.S. adults aged 18 years or older using KnowledgePanel concluded that prevalence of past-year use of any form of cannabis is more common among in states with legalized adult use (20.3%) compared with use in medically legal states (15.4%), and nonlegal states (11.9%). Perceptions of risk from using cannabis also have continued to decrease. An analysis based on the National College Health Assessment survey also concluded that cannabis use has accelerated to a greater degree among students who attend colleges in states with legalization of cannabis for adult use. ⁶⁴

When examining high school students specifically, state surveys have found higher rates of use and different trends than national surveys. CDPHE in conjunction with the Departments of Human Services and Education conducts the statewide Health Kids Survey. In 2019, the overall current or past 30-day marijuana use prevalence among CO high school students was 20.6% (slightly lower than national estimates based on the Youth Risk Behavioral Survey) but not increasing. Similarly, according to the Healthy Youth Survey, past month cannabis use across grades 10 and 12 in WA state has deceased since the legalization of the adult use of cannabis, but the prevalence (~18%) is higher than estimates from national surveys. The OR Health Authority Survey found similar trends (reduced use since legalization) among students in grade 11.67

 Although adolescents who use cannabis still prefer smoking, recent changes in the usual methods of marijuana consumption have been documented with the prevalence of dabbing and vaporizing of concentrates increasing in CO, a pattern reflected across other parts of the country. ⁶⁸ Data from the online international cannabis policy study conducted in 2018 among 16-19 year-olds found that the prevalence of past 30-day vaping of cannabis was 13.8%. Nearly one-third of these users in the U.S. reported vaping cannabis oil and consuming THC solid concentrates such as wax and shatter. ⁶⁹

These reported increases in the vaping of THC oil as a method of consumption are concerning given the CDC's investigation on the national outbreak of lung injury associated with the use of vaping products. Among the cases or deaths reported to CDC (in which substance use was

available), 82% reported using THC-containing products, 33% exclusively. Sixteen percent reported acquiring products only from commercial sources (recreational and/or medical dispensaries, vape or smoke shops, stores, and pop-up shops); most others were obtained from family/friends, dealers, online, or other sources.

Increases that have been reported in daily (or near daily) use and changes in consumption patterns with the use of more concentrated products also presents cause for concern. Respondents who report using cannabis daily consume almost twice as much per day compared with those reporting less frequent use. ⁷¹ In adolescents with no history of heavy cannabis use, the use of cannabis concentrates is associated with progression to persistent use, more so than the use of other cannabis products. ⁷² As noted in CSAPH Report 5-I-17, adolescents are of particular interest in cannabis-policy discussions because the negative health effects of the drug are heightened when use begins in adolescence. In addition to health effects, including the increased risk of cannabis use disorder, evidence also suggests that cannabis use in adolescence and early adulthood is associated with poor social outcomes, including unemployment, lower income, and lower levels of life and relationship satisfaction. ⁷³⁻⁷⁵

Use among Pregnant Women

Cannabis is the most commonly used (illicit) drug during pregnancy, and THC crosses the placenta and is found in breast milk. Endocannabinoids play an important role in fetal neurodevelopment and in postnatal synaptic plasticity. Preclinical and emerging human evidence suggests that prenatal exposure to cannabis may "lead to subtle, persistent changes in targeted aspects of higher-level cognition" and neurobehavioral outcomes in children. However, real world evidence is limited to three longitudinal cohorts, with different designs and outcomes, all of which were initiated at a time of much lower (average) THC exposure from cannabis. Additionally, epigenetic effects of THC have been described.

 The American College of Obstetricians and Gynecologists updated its committee opinion in 2017 reaffirming that prenatal exposure is associated with low birth weight and discouraging physicians from suggesting the use of marijuana during preconception, pregnancy, and lactation. ^{76,82-84} Effects on low birth weight are independent of maternal age, race, ethnicity, level of education and tobacco use during pregnancy. ⁸² Infants exposed to cannabis in utero also may be more likely to end up in the NICU or experience preterm birth. ^{83,85}

Overall, based on NSDUH, cannabis use during pregnancy has doubled over the last 15 years with 7.0% of pregnant women between the ages of 18 and 44 years reporting past-month cannabis use in 2017 compared with 3.4% in 2002; daily or near daily use more than tripled (0.9 to 3.4%). 86 The majority of use was described as "non-medical" and is most prevalent during the first trimester. Pregnant women may use cannabis to help with nausea or to improve mood, are more likely to perceive it as natural and safe, and are unsure or unaware if cannabis is addictive or if risks are associated with prenatal cannabis use. 87

Compared with 2014, PRAMS data for CO showed that among new mothers in 2018, 16.5 percent used cannabis prior to pregnancy (47% increase), 8.2 percent used cannabis during pregnancy (44% increase), and 7.9 percent of breastfeeding mothers used cannabis after delivery (160% increase), all substantially higher than national averages. We umbilical cord sampling for cannabis metabolites detected prenatal use at an even higher rate than self-reported values. Cannabis useduring pregnancy in CO was statistically higher among women with an unintended pregnancy (12.5%) than among women who intended to become pregnant (4.5%). When cannabis useduring pregnancy was compared among different demographics, both education and age showed statistical

differences, whereas race and ethnicity did not. 88 Across three states (AK, CO, WA) that had legalized adult use by 2016, women were more likely to use cannabis during preconception, during the prenatal period, and postpartum, compared with states without legalized adult use. 90 Clinicians can "play a key role in preventing harms associated with cannabis use in pregnancy by educating patients about the potential risks of frequent use, advising all patients who are pregnant to quit cannabis use, and providing patients with safe and effective medically approved ways to improve mood and treat nausea and vomiting in pregnancy."91

Impaired Driving

 A serious consequence of legalizing cannabis for adult use is an increase in traffic crashes and fatalities. Although it is well established that acute THC intoxication impairs driving, CSAPH Report 5-I-17 explained some of the complexities involved with correlating blood concentrations of THC with driving impairment and outcomes, and in establishing legal standards. Unlike alcohol, there is poor correlation between blood or other fluid concentrations of THC or its metabolites and when the cannabis product might have been consumed, and behavioral effects or field sobriety or functional tests for cannabis/THC have not been validated. In CO, about 1 in 5 adults with past month use report driving within 2-3 hours after consumption, a value that has not increased with legalization of cannabis for adult use. 92 In WA among those 18-25 years of age reporting past year cannabis use, more than 40% reported driving with 3 hours of use at last once, with 1 in 7 reporting such driving on at least 6 occasions. 93

In CO and WA, the THC blood limit for an inference of driving impairment is 5 ng/ml in those 21 and older; any detectable amount is considered a violation in individuals less than 21 years of age. Between 2013 and 2018, there has been an increase in traffic deaths in CO in which drivers tested positive for cannabis and an increase in the percentage of all traffic deaths that were presumed to be cannabis related.⁹⁴

Based on an analysis of traffic fatality rates through 2018 obtained from the most recent report of the National Highway Traffic Safety Administration's Fatality Analysis Reporting System, legalization was associated with an increase in traffic fatalities compared with the 5 years preceding legalization among the first 4 states to legalize adult cannabis use (CO, WA, OR, and AK). These states are the only ones that have legalized adult use for which there are at least 2 full years of traffic fatality data available following the opening of retail stores. On a national scale, this rate would translate to an excess 6800 deaths. The calculated rate in this study was comparable to the rate reported after commercialization of retail sales in a previous study of traffic fatalities in CO and WA. Another recent study that examined data through 2017 and extended the comparison period to 2005 found that traffic fatalities increased (at a lower rate than above) in CO but not WA. A trend for increased fatalities also may exist in neighboring jurisdictions.

Cannabis-Related Exposures

Cannabis-related exposures generally refer to the number of human exposures related to either accidental/unintentional or excessive/intentional consumption or inhalation of cannabis and cannabis edibles. Some of these may end up as calls or reports to Poison Control Centers, emergency department visits (which also may report to Poison Control), or hospitalizations.

<u>Poison Control</u>. The number of calls to Rocky Mountain Poison and Drug Safety (serving CO) with a cannabis mention increased five-fold from 2006 to 2017, stabilizing between 2014 and 2017, when 222 reports occurred, and then increasing somewhat again. ⁹⁹ Between January 2017 and June 2020, 973 exposures were reported by healthcare facilities and residences, mostly edibles (44.9%),

followed by the cannabis plant (29.1%) and concentrates (10.7%). Reporting rates for these substances have remained mostly unchanged since the middle of 2018. Patients <5 years old accounted for one-third of these reports, and those 6 to 12 years of age accounted for 9%. ⁹² In CO, there has been a significant increase since 2014, from 6.9% to 11.2%, in the percentage of homes with children 1-14 years old that reported having cannabis or cannabis products in or around the home. ¹⁰⁰ It is estimated that approximately 23,000 homes (or 22.4%) in CO with children 1-14 years old had cannabis in the home with potentially unsafe storage, a rate that has increased 60% since 2014.100

Since retail sales opened in WA in 2014, calls to the WA State Poison Control Center involving cannabis in 2018 have more than doubled from 245 to 497; reports in children ≤5 years of age tripled from 34 to 94 (18.9% of total), and those in children 6-12 years of age more than doubled to 31 (6.2% of total). Thirty-two percent of cannabis exposure calls involved edibles. Because of these trends, particularly among young children, a new logo was required in 2017 on all cannabis edible packaging (Figure 3). After increasing from 2013-2016, calls reported to OR poison control decreased in 2017 and then started increasing again in 2018; approximately 20% of cannabis exposures in 2017 were in children aged 5 years and under. ¹⁰²

Finally, a recent analysis of all 50 states from 2010-2017 found that an increase in cannabis exposures reported to the U.S. National Poison Data System occurred after commercialization (retail sales) in states with legalized adult use. ¹⁰³ The overall magnitude of the increase was 67-77% relative to the pre-legalization average, depending on the composition of comparison states. The relative increases were higher in minors, males, and among those who were classified as suffering medical consequences.

Cannabis-Related Emergency Department Visits and Hospital Admissions

 In addition to emergency department visits and sometimes hospitalizations for unexpected pediatric exposures to cannabis, emergency department visits and hospitalizations can be prompted by acute intoxication leading to drowsiness/lethargy/confusion, dizziness/vertigo/ataxia, psychotic symptoms, agitation or anxiety, and extreme tachycardia or other cardiovascular events. ¹⁰² Chronic use, especially of high potency derivatives, can lead to hyperemesis syndrome, which may require treatment for intractable vomiting, dehydration, and electrolyte abnormalities. ¹⁰⁴ In individuals with a *history* of recreational use, the most common reasons for hospitalization were alcohol and drug rehabilitation or detoxification and psychological/psychiatric evaluation. ¹⁰⁵

In an informative analysis, the CO Department of Public Health analyzed rates of cannabis exposures, diagnoses, and billing codes from 2000 to 2016 per 100,000 hospitalizations. From a baseline rate of 575/100K, hospitalization rates increased steadily to 894/100K when medical cannabis was legalized but not commercialized (2001-2009), experiencing another significant jump to 1,440/100K during the commercialization of medical cannabis (2010-2013), and further increasing again to 2,696 possible cannabis-related hospitalizations per 100,000 during the initial commercial phase of legalized adult use (2014-Sept 2015). An updated analysis indicates that the yearly number of cannabis-related hospitalizations doubled after the initial year of legalized adult use (2013) compared to with 2017. Similar trends were noted in a study of cannabis-related hospitalizations from 2002-2016, a time period covering major changes in WA state policies and marketplace for medical cannabis, legalization for adult use, and then the initial period of retail sales. 107

Cannabis Use Disorder and Related Treatment Admissions

A proportion of people who initiate cannabis use eventually meet the criteria for cannabis use disorder (CUD), although the estimated prevalence varies widely depending on the diagnostic criteria and sampling methods that were used. Nevertheless, CUD influences key brain responses and functions relevant to substance use and it manifests as other substance use disorders based on the reinforcing properties of THC, regardless of method of use or formulation. ¹⁰⁸

Epidemiological data indicate that "the majority of those who use cannabis do not have problems related to their use, but a substantial subset of people (using cannabis/THC) do report experiencing symptoms and consequences consistent with a CUD." Data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) study indicate that the past year prevalence of DSM-IV cannabis abuse and dependence doubled from 1.5% in 2001-02 to 2.9% in 2012-13.¹¹⁰ A similar analysis of NSDUH data (DSM-IV criteria) concluded that past year prevalence was relatively unchanged over the same time period (1.6-1.5%). The disparate findings likely reflect differences in sampling methods (live interview versus online survey) and changes in societal norms over time which may influence respondents. 112 Again, depending on the method, between 11% (NSDUH, 2016) and 30% (NESARC, 2013) past-year cannabis users met DSM-IV criteria for cannabis abuse or dependence. 110,112 A recent meta-analysis using DSM-IV or ICD-9 criteria estimated that individuals who use cannabis have a 1 in 5 risk of developing cannabis abuse or dependence and risks increase if cannabis is initiated early and used frequently.¹¹³ Other data suggest that in individual populations, the prevalence of cannabis abuse or dependence roughly doubles for those who initiate use before 17 years of age, and is much higher for adolescents who use weekly or more often. 114 Among youth and emerging adults in the U.S., prevalence of cannabis use and dependence appears to increase with time since initiation of use. This increase appears to be steeper for youth than emerging adults. The adjusted 12-month prevalence among youth with lifetime cannabis use ranged from 10.9 in the first year after starting cannabis use, increasing in each year to 20.6% in the fourth year and beyond. Values for young adults (aged 18-25) were lower at all times and increased at a lower rate eventually reaching about 10% four years after initiaition.115

 A few previous studies examining the effects of state medical cannabis laws on CUD found mixed results. ^{116,117} A study in CO, WA, OR, and AK based on NSDUH surveys from 2008 to 2016 found a small increase in past year cannabis abuse and dependence among respondents aged 12 to 17 years, and more significant increases in frequent use and abuse or dependence among adults 26 years or older. ¹¹⁸ One look back study of the 2012-2014 NESARC study using DSM-5 criteria for CUD estimated that the prevalence of 12-month and lifetime CUD were 2.5% and 6.3%, respectively. ¹¹⁹

In summary, most of the published longitudinal trends on cannabis use disorder are based on DSM-IV criteria for cannabis abuse and dependence, which were combined into one set of diagnostic criteria for DSM-V. The DSM-V criteria for CUD perform similarly to other substance use disorders. Although little is known about how legalization of cannabis for adult use will impact CUD, the availability of high potency products, easy access (cost and proximity), methods of use that are more appealing than smoking, decreased perceptions of risk, and changes in social norms and marketing, all point to a need for vigilance in this area.

Treatment Admissions

Treatment-seeking for CUD comprises a substantial proportion of all substance use treatment admissions. In 2017, cannabis remains by far the most common substance in adolescents seeking treatment; more than 70% percent of publicly funded treatment admissions in individuals aged 12 to 17 years were for primary cannabis use. 120

Total publicly funded substance use disorder treatment admissions in the U.S. declined about 0.7% from 2007-2017 (see the Treatment Episode Data Set [TEDS-A]). The proportion of cannabis admissions aged 12 years or older increased from 16% in 2007 to 19% in 2010, before declining to 13% percent in 2017. The average age at admission was 27 years among admissions for primary use of cannabis. Non-Hispanic Whites represented 42 percent of admissions, 31 percent were non-Hispanic Blacks, and 20 percent were of Hispanic origin. Consistent with the national picture, cannabis-related treatment admissions in WA declined in the three years following legalization of adult use 2012-2015. In AK, among the approximately 6,800 total people who received public-paid substance dependence treatment in 2018, about 8% (550) received primary treatment for cannabis use disorder, similar to the proportion from 2016-17. In CO, the overall treatment admission rate for those reporting cannabis as the primary drug has decreased every year from 2012-2017, except for a brief uptake in 2014-15 in those 21 years and older.

Opioid Use

Increases in unintentional overdoses and deaths due to illicit fentanyl, heroin and prescription opioids remain the biggest drivers of the unintentional overdose death epidemic. Nearly 70% of the 67,367 deaths in 2018 involved an opioid.

Several ecological or epidemiological studies and convenience survey samples have reported population-level associations between the existence of state medicinal cannabis laws and reductions in opioid-related morbidity/mortality, reduced opioid prescribing in Medicaid and Medicare enrollees, as well as subsets of privately insured individuals, self-reported reductions in opioid use (and risks) among medical users (i.e., substitution of cannabis), and intersections between cannabis use and opioids among drivers, including fatalities. ¹²⁴⁻¹³² Effects of medical cannabis laws on reducing opioid prescriptions and dampening increases in opioid-related deaths have been linked, in part of the presence and density of dispensary distribution within states. ^{126,132}

A review of 25 such studies concluded: 133

• States that with medical cannabis laws have reported a slower rate of increase in opioid overdose deaths which has persisted over time. Findings are strengthened when controlling for operation of state prescription drug monitoring programs and demographics which also influence patterns of use. The relative contribution of treatment for opioid use disorder in such states is not understood.

Some epidemiologic and ecological studies provide evidence that cannabis availability may reduce opioid use and/or harms. Some of these studies are "limited by selection bias, cross sectional designs and reliance on self-reported assessments of the opioid sparing effects of cannabis."

While cannabis availability may reduce opioid consumption, based on urine drug testing in patients on chronic opioid therapy, legalization of the adult use of cannabis led to a small increase in positive cannabinoid test results, but compliance with opioid therapy was unaffected. Additionally, in a cross-sectional study of toxicological testing data of drivers from the 2011–2016 Fatality Analysis Reporting System (FARS) and the 2013–2014 National Roadside Survey of

Alcohol and Drug Use by Drivers (NRS), drivers who tested positive for marijuana were significantly more likely to test positive for prescription opioids.¹³⁵

CO's legalization of the adult use of cannabis resulted in a significant slowing of the upward trend in opioid-related deaths in 2015 after retail sales were initiated. This turned out to be a short-term effect as deaths accelerated again in 2016 and 2017. A more recent study of states with medical cannabis laws and with legalized adult use confirmed previous findings of lower prescription rates in Medicare Part D enrollees, with incremental additional deceases in opioid prescribing in states with legalized adult use. The another study of Medicaid recipients from 2010-2017 among states and D.C., where adult use had been legalized, prescriptions for Schedule III, but not Schedule II opioids were significantly reduced. The another study of Medicaid recipients from 2010-2017 among states and D.C., where adult use had been legalized, prescriptions for Schedule III, but not Schedule III.

Overall, "it remains unclear whether the presumed benefit of legalizing marijuana in reducing opioid-related harms outweighs the policy's externalities, such as its impact on mental health and traffic safety." ¹³²

Social and Criminal Justice

 AMA policy supports decriminalization of cannabis (i.e., reduction in the penalty associated with possession of a small amount of cannabis from a criminal offense subject to arrest to a civil infraction), a view also held by the American Academy of Pediatrics. ¹³⁹ Legalization of adult use allows cannabis and cannabinoid products or their legal sale and the removal of all penalties for possession of small amount of cannabis.

<u>Criminal arrest</u>. One large multistate comparison found that between 2000 and 2016, decriminalization substantially reduced adult and youth arrest rates for cannabis possession (less so for youth), but adult legalization had little or no impact on youth arrest rates. A related outcome that is highly relevant is "whether cannabis legalization can be used to promote social equity and help communities of color that have been and still are disproportionately affected by prohibition." 141

Arrests for cannabis violations have decreased dramatically in states with legalized adult use, falling 90-99% in AK, WA, OR and D.C. ¹⁴² In WA, a study that included data only through the initial period of legal adult sales, found that cannabis arrest rates among both African American and White adults decreased significantly and stayed at a dramatically lower rate after the marijuana retail market opened. Cannabis accounted for nearly half (47%) of all criminal drug use cases processed in calendar year 2012 in WA, a number which dropped dramatically to about 12% of all drug cases handled by the police by 2016. ¹⁴³

 However, relative disparities in cannabis arrest rates for Blacks increased for those of legal age, and remained unchanged for younger adults. Another study in OR found that adult cannabis legalization was associated with an increase in juvenile cannabis allegations, although relative disparities decreased for Black compared with White youth. AK also reported a modest increase in the number of youth who have been referred to juvenile justice systems for cannabis offenses since 2016. Juvenile offenders engage in both cannabis use and polysubstance use at higher rates than the general adolescent population. At 7

<u>Crime Rates</u>. Cannabis laws more broadly, and the legalization of recreational marijuana more specifically, had minimal effects on violent or major crime in CO or WA or on property crime rates through 2015, except for a decline of burglary rates in WA. This contrasts with reports from the CO Bureau of Investigation of modest upticks in property crimes and a more significant increase in

violent crimes beginning in 2016-2018.⁹⁴ Legalization for adult use was associated with increased resolution of serious crimes in WA even though crime rates were steady as policy devoted more resources to their clearance.¹⁴³

Expungement of Prior Cannabis Related Arrests and Convictions. Even with legalization of cannabis for adult use, for those who have a cannabis-related criminal record for a minor offence, the damage persists. Eight states have created a pathway for expungement although it is usually limited to possession, and may have other limiting conditions (e.g., waiting period, no other criminal convictions, petition hurdles). Li included automatic expungement for convictions of possessing 1 oz or less in its bill; individuals can initiate the process and cases are being identified by law enforcement searches; more than 11,000 have been pardoned.

 Social Equity in the Legal Cannabis Business. Some states have established social equity programs to encourage and enable participation (based on a set of criteria) in the cannabis industry by people from communities that have previously been disproportionately harmed by cannabis prohibition and enforcement. MA provides free, statewide, technical assistance, and a training program that provides education, skill-based training, and tools for success in the cannabis industry to applicants; about 4% of cannabis applications in MA were from self-identified minorities. ¹⁴⁹ IL offers technical assistance and support in creating a business plan and applying for a license, and also established lower thresholds for license approval, lower fees and access to low interest loans. ¹⁵⁰ IL also has its "Restore, Renew, Reinvest" program for communities that have been adversely affected by past prohibition efforts. MI offers substantial discounts on applicant, license and permit fees while expanding eligibility to persons with prior cannabis infractions. ¹⁵¹ Certain other states (e.g., OR) also have eliminated prior cannabis convictions as a disqualification. CA established a "Community Reinvestment Fund" to support communities disproportionately affected by past federal and state drug policies.

Governmental Costs and Revenue

 The legalization and commercialization of cannabis results in revenue for states through taxes and fees, but it also comes with costs, both in regulating and enforcement actions and in protecting public health and safety. Of the 9 states with active retail sales, six employ cultivation levies on growers, while all but AK charge an excise tax specifically on cannabis sales. Seven states also charge a general sales tax and/or allow a local option. Once these laws are fully implemented, legalized adult-use cannabis programs have generated significant annual sales that continue to trend upward annually, yielding surpluses from taxes and fees after accounting for the costs to administer the program. States have implemented adult-use regulatory programs for as little as \$1.8 million (AK) up to \$60 million for CA (medical and adult use together). For a summary of state administrative agencies, possession limits for legalized adult use, tax rates, recent tax revenues, and administrative costs see Table 2. In some states (e.g., MA) dispensaries for legalized adult use were closed for a period of time during early phases of the COVID-19 pandemic. While the creation of legalized adult use programs leads to reductions in the number of authorized medical users, the number of medical marijuana patients increased by thousands in MA during COVID closures.

How states distribute their cannabis tax revenues also is of interest. Virtually all states allocate a portion of funds for various cannabis/substance use treatment and education efforts. 152

DISCUSSION

The last 20 years have seen a evolution in state laws increasing access to cannabis and cannabis products to the point where two-thirds of the country now have medical cannabis laws, 11 states

among this group and D.C have legalized the adult use of cannabis, and the other one-third have passed laws allowing the use of CBD in some way; Federal regulations also are now permissive for the use and marketing of certain CBD products.

In trying to evaluate public health impacts in states that have legalized cannabis for adult use, it is important to understand that state retail markets are in different developmental phases to becoming fully established, a process measured in terms of years. All of these states had preexisting, established medical cannabis programs, some more robust than others, especially the states (CO, WA, OR, and to a lesser extent AK) that have provided the most evidence to date. Many studies of the public health impacts of medical cannabis laws exist (and over a longer time period), so it is relevant to question what the appropriate comparison "group" is, especially for states with more recent movement into legalized adult use. In most studies this has been the pre- and post-legalization periods. Some states have set up a process to accomplish this, aided by development of detailed baseline analyses. It is tempting, but premature, to infer that what has happened in the earlier adopter states will be generalizable to other states that have subsequently begun retail sales. One thing that is common is the expansive array of cannabis varietals and novel cannabinoid products and formulations that have been developed, some at very high concentrations, accompanied by an array of administration routes and methods, some posing more health risks to users than others.

As reviewed in this and other reports on this topic, use of cannabis and cannabinoids are associated with some therapeutic benefits, as well as a range of harms and risks of social consequences. In particular, research into the possible therapeutic uses of cannabidiol is in an expansive phase. Harms and risks of social consequences are much more prevalent in the subset of users with generally recognized risk factors including initiation of use at younger ages, high intensity (i.e., frequency and potency) and mode of use. A major difficulty in understanding impacts, risks and benefits of these substances under the umbrella of legalization is the substantial change in potency of products that has occurred over the years, and the range of products now available.

 Nationally, cannabis use has increased in the U.S. among 18-25 year-olds, and adults 26+ but decreased in adolescents. Legalization has not significantly impacted recent patterns of adolescent use, but in the fastest growing demographic (18-25 year-olds), the eight states with highest prevalence of past month use are among those that have legalized adult use (ranging from 30.44% in WA to 37.67% in VT). Although not specific to states with legalized adult use, it will be important to monitor recent changes in products used, methods of consumption, and intensity of use, as these are predictors of several harmful outcomes.

Cannabis use in pregnant women has doubled, and women in states with legalized adult use (by 2016) were more likely to use cannabis during preconception, pregnancy, and postpartum. It also seems clear that individuals who use cannabis, particularly younger adults, are driving under the influence of cannabis or cannabis products at a fairly high rate, that such use is associated with traffic accidents and fatalities, and these occur in higher rates in states with legalized adult use.

A robust finding has been the association of legalized adult use with an increase in reported poison control exposures and cannabis-related hospitalizations. Depending on the state, ingestion is the most common route for these exposures, with 20-33% of these reports involving children under the age of 5. In WA, the median age of children (range 0-9 years) was 2 years (2010-2016).¹⁵⁴ In one study involving a children's hospital in CO, the median age also was 2 years with about half of the exposure due to edibles, usually obtained by the child either due to lack of child-resistant packaging (at the time), poor child supervision or inadequate storage.¹⁵⁵ All states should educate the public in this area and require packaging that is child proof, conveys a meaningful and easily

understood unit of consumption, and that clearly differentiates the cannabis edible from food. Incremental increases in cannabis-related hospitalizations have been associated with both medical cannabis laws and legalization of adult use.

Publicly reported trends in cannabis use disorder and treatment admissions have lagged behind changes in consumption patterns. One would expect increased intensity of use and administration of higher concentrations to eventually become evident. Substantial research into the intersections of cannabis laws and various measures of opioid use and harm has largely been limited to medical cannabis laws; the impact of legalization for adult use, over a sufficient time period is only now being examined. Any protective effects of cannabis availability in this area is probably more than offset by impacts on mental health, cannabis use disorder, driving accidents, and other consequences of cannabis use requiring healthcare and community resources.

Legalization of cannabis for adult use has led to a large decrease in cannabis-related arrests for adults, but racial disparities still exist, especially in youth, where possession and use are still illegal. Overall effects on crime rates appear to be neither protective nor provocative. Some states have set up processes for expungement of prior cannabis-related convictions, mostly with limited success because of cumbersome processes that may interfere with successful minority participation. Some states have also set up specific programs to advance participation in the cannabis industry by people from communities that have been disproportionately harmed by previous prohibition and enforcement, and some have created funding streams for community development and provision of services.

 Ultimately, the full public health impacts of cannabis legalization will involve the intersection of a number of competing interests including; (1) the regulated marketplace, (i.e., product properties, availability/supply, access/price, preventing youth access, combining current medical and "recreational" markets); (2) impacts on still operating illicit markets; (3) similar to alcohol and tobacco, impacts of advertising, labeling, price and taxes on purchase; (4) effectiveness of public health surveillance and monitoring; and, (5) the extent to which education and community outreach can foster changes in risky behaviors that are subject to individual control.

 With respect to behaviors that are subject to individual control, in addition to general abstinence, and avoidance of use in specific populations (e.g., pregnancy, preexisting mental health disorder), the following set of evidence-based measures for lower risk cannabis use have been previously identified: 156

- avoid early age initiation of cannabis use (i.e., definitively before the age of 16 years);
- choose low-potency tetrahydrocannabinol (THC) or balanced THC-to-cannabidiol (CBD)—ratio cannabis products;
- avoid combusted cannabis inhalation and give preference to nonsmoking use methods (e.g., oral solutions/oils, tincture, edibles);
- avoid deep or other risky inhalation practices;
- avoid high-frequency (e.g., daily or near-daily) cannabis use;
- abstain from cannabis-impaired driving, and,
- avoid combining risk behaviors (e.g., early initiation and high-frequency use).

RECOMMENDATIONS

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The Council on Science and Public Health recommends that the following statement be adopted in lieu of Resolution 408-A-19, Resolution 411-A-19, and the additional proposed resolve from Alternate Resolution 913-I-19 and the remainder of the report be filed:

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That Policy H-95.924, "Cannabis Legalization for Recreational Use," be amended by addition and deletion to read as follows:

Cannabis Legalization for Recreational Adult Use (commonly referred to as recreational use)

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Our AMA: (1) believes that cannabis is a dangerous drug and as such is a serious public health concern; (2) believes that the sale of cannabis for recreational adult use should not be legalized: (3) discourages cannabis use, especially by persons vulnerable to the drug's effects and in high-risk populations such as youth, pregnant women, and women who are breastfeeding; (4) believes states that have already legalized cannabis (for medical or recreational adult use or both) should be required to take steps to regulate the product effectively in order to protect public health and safety including but not limited to: regulating retail sales, marketing, and promotion intended to encourage use; limiting the potency of cannabis extracts and concentrates; requiring packaging to convey meaningful and easily understood units of consumption, and requiring that for commercially available edibles, packaging must be child-resistant and come with messaging about the hazards about unintentional ingestion in children and youth. (5) that laws and regulations related to legalized cannabis use should consistently be evaluated to determine their effectiveness; (56) encourages local, state, and federal public health agencies to improve surveillance efforts to ensure data is available on the short- and long-term health effects of cannabis, especially emergency department visits and hospitalizations, impaired driving, and prevalence of psychiatric and addictive disorders, including cannabis use disorder; (67) supports public health based strategies, rather than incarceration, in the handling of individuals possessing cannabis for personal use; (7,8) encourages research on the impact of legalization and decriminalization of cannabis in an effort to promote public health and public safety; (8,9) encourages dissemination of information on the public health impact of legalization and decriminalization of cannabis; (9,10) will advocate for stronger public health messaging on the health effects of cannabis and cannabinoid inhalation and ingestion, with an emphasis on reducing initiation and frequency of cannabis use among adolescents, especially high potency products; use among women who are pregnant or contemplating pregnancy; and avoiding cannabis-impaired driving; (11) supports social equity programs to address the impacts of cannabis prohibition and enforcement policies that have disproportionately impacted marginalized and minoritized communities, and (1012) will coordinate with other health organizations to develop resources on the impact of cannabis on human health and on methods for counseling and educating patients on the use cannabis and cannabinoids.

Fiscal note: Less than \$500

REFERENCES

- 1. Council on Science and Public Health Report 5. Clinical Implications and Policy Considerations of Cannabis Use. American Medical Association, Interim Meeting of the House of Delegates, Honolulu, HI, November 2017.
- 2. Council on Scientific Affairs Report 10. Medical marijuana. American Medical Association, Interim Meeting of the House of Delegates, Dallas, TX, December 1997.
- 3. Council on Scientific Affairs Report 6. Medical marijuana. American Medical Association, Annual Meeting of the House of Delegates, Chicago, IL, June 2001.
- 4. Council on Science and Public Health Report 3. Use of Cannabis for Medicinal Purposes. American Medical Association, Interim Meeting of the House of Delegates, Houston, TX, November 2009.
- 5. Council on Science and Public Health Report 2. A Contemporary View of National Drug Control Policy. American Medical Association, Interim Meeting of the House of Delegates, National Harbor, MD, November 2013.
- 6. Council on Science and Public Health Report 3. Patient Use of Non-FDA Approved Cannabis and Cannabinoid Products in Hospitals. American Medical Association, Interim Meeting of the House of Delegates, November 2019.
- California Medical Association. CA Medical Association announces support for responsible marijuana ballot initiative. February 1, 2016.
 https://www.cmadocs.org/newsroom/news/view/ArticleId/32200/-CA-Medical-Association-announces-support-for-responsible-marijuana-ballot-initiative
- 8. Ross S, ElSohly M. The volatile oil composition of fresh and air-dried buds of Cannabis sativa. *J Nat Prod.* 1996;59:49-51.
- 9. Brenneisen R. Chemistry and analysis of phytocannabinoids and other Cannabis constituents. In: Elsohly M (ed.). *Marijuana and the Cannabinoids*. Humana Press: Totowa, NY. 2007:17-49.
- 10. Razdan RK. Structure-activity relationships in cannabinoids. *Pharmacol Rev.* 1986;38:75-149.
- 11. Russo EB. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Brit J Pharmacol.* 2011;163:1344-64.
- 12. Lewis MA, Russo EB, Smith KM. Pharmacological foundations of cannabis chemovars. *Planta Med.* 2018;84:225-33.
- 13. ElSohly MA, Mehmedic Z, Foster S, Gon C, Chandra S, Church JC: Changes in cannabis potency over the last 2 decades (1995-2014): analysis of current data in the United States. *Biol Psychiatry*. 2016;79:613-19.
- 14. Dolgin E. A boosted crop. *Nature*. 2019;572;S5-7.

- 15. Bie B, Wu J, Foss JF, Naguib M. An overview of the cannabinoid type 2 receptor system and its therapeutic potential. *Curr Opin Anaesthesiol*. 2018;31:407-414.
- 16. Felder CC, Glass M. Cannabinoid receptors and their endogenous agonists. *Annu Rev Pharmacol Toxicol*. 1998;38:179-200.
- 17. Matsuda LA, Lolait SJ, Brownstein MJ, Young AC, Bonner TI. Structure of a cannabinoid receptor and functional expression of the cloned cDNA. *Nature*. 1990;346:561-4.
- 18. Shahbazi F, Grandi V, Banerjee A, Trant JF. Cannabinoids and cannabinoid receptors: The story so far. *iScience*. 2020;23(7). doi.org/10.1016/j.isci.2020.101301.
- 19. Zou S, Kumar U. Cannabinoid receptors and the endocannabinoid system: Signaling and function in the central nervous system. *Int J Mol Sci.* 2018;19:833.
- 20. Mackie, K. Distribution of cannabinoid receptors in the central and peripheral nervous system. *Handb Exp Pharmacol*. 2005;168:299–325.
- 21. Howlett AC, Abood ME. CB1 & CB2 Receptor Pharmacology. *Adv Pharmacol*. 2017;80:169-206.
- 22. Thomas A, Baillie G, Phillips A, et al. Cannabidiol displays unexpectedly high potency as an antagonist of CB₁ and CB₂ receptor agonists *in vitro*. *Br J Pharmacol*. 2007;150:613-23.
- 23. Laprairie R., Bagher A, Kelly M, Denovan-Wright E. Cannabidiol is a negative allosteric modulator of the cannabinoid CB₁ receptor. *Br J Pharmacol*. 2015;172:4790-4805.
- 24. Wall ME, Sadler BM, Brine D, Taylor H, Perez-Reyes M. Metabolism, disposition, and kinetics of delta-9-tetrahydrocannabinol in men and women. *J Clin Pharmacol*. 1983;34:352-63.
- 25. Wall ME, Perez-Reyes M. The metabolism of delta⁹-tetrahydrocannabinol and related cannabinoids in man. *J Clin Pharmacol*. 1981;21:178S-189S.
- 26. Ohlsson A, Lindgren JE, Wahlen A, et al. Plasma delta-9-tetrahydrocannabinol concentrations and clinical effects after oral and intravenous administration and smoking. *Clin Pharmacol Ther.* 1980;28:409-16.
- 27. Marinol® capsules (Dronabinol solution in sesame oil in soft gelatin capsules). Roxane Laboratories, Inc. Columbus, Ohio. Package Insert.
- 28. Davis KH, McDaniel IA, Caddel LW, et al. Some smoking characteristics of marijuana cigarettes. In: Agurell S, Dewey WL, Willette RE, eds. *The Cannabinoids: Chemical, Pharmacologic, and Therapeutic Aspects*. New York: Academic Press; 1984:97-109.
- 29. Newmeyer MN, Swortwood MJ, Barnes AJ, et al. 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. *Clin Chem.* 2016;62:1579–92.

- 30. Spindle TR, Cone EJ, Schlienz NJ, et al. Acute effects of smoked and vaporized cannabis in healthy adults who infrequently use cannabis: a crossover trial. *JAMA Netw Open.* 2018; 1:e184841.
- 31. Huestis MA. Human Cannabinoid Pharmacokinetics. Chem Biodivers. 2007:4:1770-1804.
- 32. Spindle T, Cone E, Herrmann E, et al. Pharmacokinetics of cannabis brownies: A controlled examination of Δ9-tetrahydrocannabinol and metabolites in blood and oral fluid of healthy adult males and females. *J Anal Toxicol*. 2020 Jun 15;doi:10.1093/jat/bkaa067.
- 33. Poyatos L, Pérez-Acevedo A,1Papaseit E, et al. Oral administration of cannabis and Δ-9-tetrahydrocannabinol (THC) preparations: A systematic review. *Medicina*. 2020;56:309.
- 34. Vandrey R, Herrmann ES, Mitchell JM, et al. Pharmacokinetic profile of oral cannabis in humans: blood and oral fluid disposition and relation to pharmacodynamic outcomes. *J Anal Toxicol.* 2017;41:83-99.
- 35. 21 USC 812.
- 36. 81 FR 53687.
- 37. 21 USC 802(16)
- 38. Public Law 115-334. Agriculture Act of 2018.
- 39. Britannica ProCon.org. Legal recreational marijuana states and DC. https://marijuana.procon.org/legal-recreational-marijuana-states-and-dc/. Accessed August 5, 2020.
- 40. Britannica ProCon.org. States with legal cannabidiol (CBD). https://medicalmarijuana.procon.org/states-with-legal-cannabidiol-cbd/. Accessed August 5, 2020.
- 41. Investopedia. Marijuana laws by U.S. state. https://www.investopedia.com/marijuana-legality-by-state-4844504. Accessed August 6, 2020.
- 42. Marijuana Policy Project. State policy. https://www.mpp.org/states/. Accessed August 5, 2020.
- 43. Hall W, Lynskey M. Assessing the public health impacts of legalizing recreational cannabis use: the US experience. *World Psychiatry*. 2020;19:179-96.
- 44. CO Amendment 64. (2012).
- 45. WA I-502. (2012).
- 46. Washington, D.C. Initiative 71. (2014).
- 47. VT S. 22. (2017).

- 48. Spindle T, Bonn-Miller M, Vandrey R. Changing landscape of cannabis: novel products, formulations, and methods of administration. *Curr Opin Psychol*. 2019 Dec;30:98-102. doi: 10.1016/j.copsyc.2019.04.002. Epub 2019 Apr 9.
- 49. Gabrys R. Clearing the Smoke on Cannabis. Edible Cannabis Products, Cannabis Extracts and Cannabis Topicals. Canadian Centre on Substance Abuse, 2020. https://www.ccsa.ca/sites/default/files/2020-05/CCSA-Edible-Cannabis-Extracts-and-Topicals-Report-2020-en.pdf. Accessed August 27, 2020.
- 50. Cannabis concentrates. https://weedmaps.com/learn/products-and-how-to-consume/cannabis-concentrates/. Accessed August 26, 2020.
- 51. The National Academies of Sciences Engineering and Medicine. The Health Effects of Cannabis and Cannabinoids: Current State of Evidence and Recommendations for Research. Washington, DC: The National Academies Press. 2017.
- 52. Campenya E, López-Pelayoa H, Nutt D. The blind men and the elephant: Systematic review of systematic reviews of cannabis use related health harms. *Eur Neuropsychopharm*. 2020;33:1-35.
- 53. Latif Z, Garg N. The impact of marijuana on the cardiovascular system: A review of the most common cardiovascular events associated with marijuana use. *J Clin Med.* 2020;9:1925. doi:10.3390/jcm9061925.
- 54. Page R, Allen L, Kloner R, et al. Medical Marijuana, Recreational Cannabis, and Cardiovascular Health. A Scientific Statement From the American Heart Association. Circulation. 2020;142:00–00. https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000883. Accessed August 27, 2020.
- 55. Patel R, Manocha P, Patel J, Patel R, Tankersley W. Cannabis use is an independent predictor for acute myocardial infarction related hospitalization in younger population. *J Adolesc Health*. 2020;66:79e-85.
- 56. Montero-Oleas N, Arevalo-Rodriguez I, Nuñez-González S, Viteri-García A, Simancas-Racines D. Therapeutic use of cannabis and cannabinoids: an evidence mapping and appraisal of systematic reviews. *BMC Complem Med Therap*. 2020;20:12.
- 57. Midgette G, Reuter P. Has cannabis use among your increased after changes in its legal status? A commentary on use of Monitoring the Future for analyses of changes in state cannabis laws. *Prev Sci.* 2020;21:137-45.
- 58. Substance Abuse and Mental Health Services Administration. (2019). Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health (HHS Publication No. PEP19-5068, NSDUH Series H-54). Rockville, MD: Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. https://www.samhsa.gov/data/. Accessed August 23, 2020.

- 59. 2018 Monitoring the Future: College Students and Young Adults. Drug use trends among college age adults (19-22). https://www.drugabuse.gov/drug-topics/trends-statistics/infographics/drug-alcohol-use-in-college-age-adults-in-2018. Accessed August 24, 2020.
- 60. 2019 Monitoring the Future Survey. High School and Youth Trends.
- 61. Behavioral Risk Factor Surveillance System (BRFSS) data. Colorado adult marijuana users. https://marijuanahealthinfo.colorado.gov/health-data/behavioral-risk-factor-surveillance-system-brfss-data.
- 62. Substance Abuse and Mental Health Services Administration. (2019). 2017-2018 National Surveys on Drug Use and Health: Model-Based Estimated Totals (in Thousands) (50 States and the District of Columbia). https://www.samhsa.gov/data/report/2017-2018-nsduh-state-prevalence-estimates. Accessed August 23, 2020.
- 63. Steigerwald S, Wong PO, Cohen BE, et al. Smoking, vaping, and use of edibles and other forms of marijuana among U.S. adults. *Ann Intern Med.* 2018;169:890-92.
- 64. Bae H, Kerr DC. Marijuana use trends among college students in state with and without legalization of recreational use: initial and longer-term changes from 2008 to 2018. *Addiction*. 2020;115:1115-24.
- 65. Prevalence of past 30-day cannabis use among high school and middle school students in Colorado and the United States. https://marijuanahealthinfo.colorado.gov/health-data/healthy-kids-colorado-survey-hkcs-data. Accessed August 26, 2020
- 66. Dilley J, Richardson S, Kilmer B, et al. Prevalence of cannabis use in youths After legalization in Washington state. *JAMA Ped.* 2019;173;192-93.
- 67. Oregon Health Authority. Youth marijuana use, attitudes and related behaviors in Oregon. https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/MARIJUANA/Documents/fact-sheet-marijuana-youth.pdf. Accessed August 26, 2020.
- 68. Method of marijuana use among high school student-Colorado 2015-2019. https://marijuanahealthinfo.colorado.gov/health-data/healthy-kids-colorado-survey-hkcs-data. Accessed August 26, 2020.
- 69. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C. Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy*. 2020;77: https://doi.org/10.1016/j.drugpo.2020.102698. Accessed August 27, 2020.
- 70. Centers for Disease Control and Prevention. Outbreak of Lung Injury Associated with the Use of E-Cigarette, or Vaping, Products. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html#latest-information. Accessed August 31, 2020.
- 71. Caulkins J, Pardo B, Kilmer B. Intensity of cannabis use: Findings from three online surveys. *Int J Drug Policy*. 2020;79:102740. doi: 10.1016/j.drugpo.2020.102740. Online ahead of print. Accessed August 23, 2020.

- 72. Barrington-Trimis J, Cho J, Ewusi-Boisvert E. Risk of persistence and progression of use of 5 cannabis products after experimentation among adolescents. *JAMA Network Open*. 2020;3:e1919792. doi:10.1001/jamanetworkopen.2019.19792. Accessed August 24, 2020.
- 73. Volkow ND, Baler RD, Compton WM.et al. Adverse health effects of marijuana use. *N Engl J Med.* 2014;370:2219-2227.
- 74. Fergusson DM, Boden JM. Cannabis use and later life outcomes. *Addiction*. 2008;103:969-976.
- 75. Hall W, Lynesky M. Evaluating the public health impacts of legalizing recreational cannabis use in the United States. *Addiction*. 2016;111:1764-1773.
- 76. American College of Obstetricians and Gynecologists. Marijuana use during pregnancy and lactation. Committee Opinion No. 722. *Obstet Gynecol*. 2017;130:e205-09.
- 77. Grant K, Petroff R, Isoherranen N, Stella N, Burbacher T. Cannabis use during pregnancy: Pharmacokinetics and effects on child development. *Pharmacol Ther*. 2018;182:133-51.
- 78. Calvigioni D, Hurd Y, Harkany T, Keimpema E. Neuronal substrates and functional consequences of prenatal cannabis exposure. *Eur Child Adolesc Psychiatry*. 2014;23:931-41.
- 79. Jutras-Aswad D, DiNieri J, Harkany T, Hurd Y. Neurobiological consequences of maternal cannabis on human fetal development and its neuropsychiatric outcome. *Eur Arch Psychiatry Clin Neurosci*. 2009;259:395-412.
- 80. McLemore G, Richardson K. Data from three prospective longitudinal human cohorts of prenatal marijuana exposure and offspring outcomes from the fetal period through young adulthood. *Data in Brief.* 2016;9:753-7.
- 81. Szutorisz H, Hurd Y. High times for cannabis: epigenetic imprint and its legacy on brain and behavior. *Neurosci Biobehav Rev.* 2018;85:93-101.
- 82. Crume TL, Juhl A, Brooks-Russell A, et al. Cannabis use during the perinatal period in a state with legalized recreational and medical marijuana. The association between maternal characteristics, breastfeeding patterns, and neonatal outcome. *J Pediatr.* 197:90-6, 2018.
- 83. Gunn J,1 Rosales C, Center K, et al. Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis. *BMJ Open.* 2016;6:e009986. doi:10.1136/bmjopen-2015-009986.
- 84. Conner SN, Bedell V, Lipsey K, et al. Maternal marijuana use and adverse neonatal outcomes: A systematic review and meta-analysis. *Obstet Gynecol*. 2016;128:713-23.
- 85. Corsi D, Walsh L, Weiss D. Association between self-reported prenatal cannabis use and maternal, perinatal, and neonatal outcomes. *JAMA*. 2019;322:145-52.
- 86. Volkow ND, Han B, Compton WM, et al. Self-reported medical and nonmedical cannabis use among pregnant women in the United States. *JAMA* 2019;322:167-9.

- 87. Chang JC, Tarr JA, Holland CL, et al. Beliefs and attitudes regarding prenatal marijuana use: Perspectives of pregnant women who report use. *Drug Alcohol Depend*. 2019;196:14–20.
- 88. Colorado Pregnancy Risk Assessment Monitoring System. Marijuana use during pregnancy by pregnancy intention. Colorado 2014-2018. https://marijuanahealthinfo.colorado.gov/health-data/pregnancy-risk-assessment-monitoring-system-prams-data. Accessed August 28, 2020.
- 89. Metz T, Silver R, McMillin G. Prenatal marijuana use by self-report and umbilical cord sampling in a state with marijuana legalization. *Obstet Gynecol*. 2019;133: 98–104.
- 90. Skelton K, Hecht A, Benjamin-Neelon S. Recreational cannabis legalization in the US and maternal use during the preconception, prenatal, and postpartum periods. *Int J Environ Res Public Health*. 2020;17:909; doi:10.3390/ijerph17030909.
- 91. Young-Wolff KC, Sarovar V, Tucker L, et al. Self-reported Daily, Weekly, and Monthly Cannabis Use Among Women Before and During Pregnancy. *JAMA Netw Open*. 2019;2(7):e196471. doi:10.1001/jamanetworkopen.2019.6471.
- 92. Colorado Department of Public Health & Environment. THC Concentration in Colorado: Marijuana Health Effects and Public Health Concerns. July 31,2020. https://www.thenmi.org/wp-content/uploads/2020/08/THC-Concentration-in-Colorado-Marijuana- CDPHE-8.3.2020.pdf. Accessed August 21, 2020.
- 93. Washington Young Adult Health Survey. Driving After Marijuana Use. 2014-16. https://www.dshs.wa.gov/sites/default/files/BHSIA/dbh/Research/Young%20adult%20MJ%20survey%206-26-2015.pdf.
- 94. Rocky Mountain High Intensity Drug Trafficking Area. The Legalization of Marijuana in Colorado: The Impact. Volume 6, September 2019.
- 95. Kamer R, Warshafsky S, Kamer G. JAMA Int Med. 180;8:1119-20.
- 96. Aydelotte JD, Mardock AL, Mancheski CA, et al. Fatal crashes in the 5 years after recreational marijuana legalization in Colorado and Washington. *Accid Anal Prev.* 2019;132:105284. doi:10.1016/j.aap.2019.105284.
- 97. Santaella-Tenorio J, Wheeler-Martin K, DiMaggio C, et al. Association of Recreational Cannabis Laws in Colorado and Washington State With Changes in Traffic Fatalities, 2005-2017. *JAMA Intern Med.* 2020;180(8):1061-1068.
- 98. Lane T, Hall W. Traffic fatalities within US states that have legalized recreational cannabis sales and their neighbors. *Addiction*. 2019;114:847-56.
- 99. Colorado Department of Public Safety. Division of Criminal Justice, Office of Research and Statistics. *Impacts of Marijuana Legalization in Colorado*. October 2018
- 100. Colorado Child Health Survey. https://marijuanahealthinfo.colorado.gov/health-data/child-health-survey-chs-data. Accessed August 21, 2020.
- 101. Washington Poison Center. 2018 Annual Data Report: Cannabis. https://www.wapc.org/wp-content/uploads/2018-Cannabis.pdf. Accessed August 21, 2020.

- 102. Oregon Poison Control. Annual Marijuana Cases 2014-2017 By Age. https://www.ohsu.edu/sites/default/files/2018-11/Cannabis-report-FINAL%20november%2018%20PDF.pdf.
- 103. Shi Y, Liang D. The association between recreational cannabis commercialization and cannabis exposures reported to the US National Poison Data System [published online ahead of print, 2020 Feb 20]. *Addiction*. 2020;10.1111/add.15019. doi:10.1111/add.15019.
- 104. Richards JR. Cannabinoid Hyperemesis Syndrome: Pathophysiology and Treatment in the Emergency Department. *J Emerg Med.* 2018;54(3):354-363. doi:10.1016/j.jemermed.2017.12.010
- 105. Desai R, Shamim S, Patel K, et al. Primary causes of hospitalizations and procedures, predictors of in-hospital mortality, and trends in cardiovascular and cerebrovascular events among recreational marijuana users: A five-year nationwide inpatient assessment in the United States. *Cureus*. 10(8):e3195. doi.7759/cureus.3195.
- 106. Colorado Hospital Association (CHA) data. Rates of hospitalizations with marijuana billing codes in Colorado, 2000-2017. https://marijuanahealthinfo.colorado.gov/health-data/colorado-hospital-association-cha-data. Accessed August 29, 2020.
- 107. Close NS. Adverse Health Effects of Marijuana Legalization. Doctoral Thesis. <a href="https://digital.lib.washington.edu/researchworks/bitstream/handle/1773/44809/Close_washington.edu/researchworks/bitstream/handle
- 108. Zehra A, Burns J, Liu C, Wang G. Cannabis addiction and the brain: a review. *J Neuroimmune Pharmacol*. https://doi.org/10.1007/s11481-018-9782-9
- 109. Budney A, Sofis M, Borodovsky J. An update on cannabis use disorder with comment on the impact of policy related to therapeutic and recreational cannabis use. *Eur Arch Psychiatry Clin Neurosci.* 2019; 269:73–86.
- 110. Hasin DS, Saha TD, Kerridge BT, et al. Prevalence of marijuana use disorders in the United States Between 2001-2002 and 2012-2013. *JAMA Psychiatry*. 2015;72(12):1235–1242. doi:10.1001/jamapsychiatry.2015.1858
- 111. SAMHSA. Results from the 2016 national survey on drug use and health: detailed tables Prevalence estimates, standard Errors, P Values, and sample sizes. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality, Rockville, 2017.
- 112. Grucza RA, Agrawal A, Krauss MJ, Cavazos-Rehg PA, Bierut LJ. Recent trends in the prevalence of marijuana use and associated disorders in the United States. *JAMA Psychiatry*. 2016;73:300-01.
- 113. Leung J, Chan G, Hides L, Hall W. What is the prevalence and risk of cannabis use disorders among people who use cannabis? a systematic review and meta-analysis. *Addictive Behaviors*. 2020;109:106479. https://doi.org/10.1016/j.addbeh.2020.106479. Accessed August 29, 2020.

- 114. Silins E, Horwood LJ, Patton GC, et al. Young adult sequelae of adolescent cannabis use: an integrative analysis. *Lancet Psychiatry*. 2014;1:286-93.
- 115. Han B, Compton W, Blanco C, Jones CM. Time since first cannabis use and 12-month prevalence of cannabis use disorder among youth and emerging adults in the United States. *Addiction*. 2019;114: 698-707.
- 116. Smart R, Pacula R. Early evidence of the impact of cannabis legalization on cannabis use, cannabis use disorder, and the use of other substances: Findings from state policy evaluations. *Am J Drug Alcohol Abuse*. 2019;45:644-63.
- 117. Hasin D, Sarvet A, Cerdá M. US adult illicit cannabis use, cannabis use disorder, and medical marijuana laws 1991-1992 to 2012-2013. *JAMA Psychiatry*. 2017;74:579-88.
- 118. Cerdá M, Mauro C, Hamilton A, et al. Association between recreational marijuana legalization in the United States and changes in marijuana use and cannabis use disorder from 2008 to 2016. *JAMA Psychiatry*. doi:10.1001/jamapsychiatry.2019.3254 Published online November 13, 2019.
- 119. Hasin DS, Kerridge BT, Saha TD, et al. Prevalence and correlates of DSM-5 cannabis use disorder, 2012–2013: findings from the national epidemiologic survey on alcohol and related conditions–III. *Am J Psychiatry*. 2016;173:588-599.
- 120. Substance Abuse and Mental Health Services Administration, Center for Behavioral Health Statistics and Quality. Treatment Episode Data Set (TEDS): 2017. Admissions to and Discharges from Publicly-Funded Substance Use Treatment. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2019. https://www.dasis.samhsa.gov/dasis2/teds-pubs/TEDS-2017-R.pdf
- 121. Northwest High Intensity Drug Trafficking Area. Washington State Marijuana Impact Report. Volume 3. August 2017.
- 122. Department of Health and Social Services. Marijuana Use and Public Health in Alaska -2020. Anchorage, Alaska: Office of Substance Misuse and Addiction Prevention, Division of Public Health, Alaska Department of Health and Social Services; January 2020.
- 123. Centers for Disease Control and Prevention. Opioid Overdose. Understanding the Epidemic. https://www.cdc.gov/drugoverdose/epidemic/index.html. Accessed August 31, 2020.
- 124. Bachhuber M, Saloner B, Cunningham C, Barry C. Medical cannabis laws and opioid analgesic overdose. Mortality in the United States, 1999–2010. *JAMA Intern Med.* 2014; 174: 1668-73.
- 125. Bradford AC, Bradford WD, Abraham A, Bagwell Adams G. Association between US state medical cannabis laws and opioid prescribing in the Medicare Part D population. *JAMA Intern Med.* 2018;178:667-72.
- 126. Boehnke KF, Litinas E, Clauw DJ. Medical cannabis use is associated with decreased opiate medication use in a retrospective cross-sectional survey of patients with chronic pain. *J Pain*. 2016;17:739-44.

- 127. Reiman A, Welty M, Solomon P. Cannabis as a substitute for opioid-based pain medication: Patient self-report. *Cannabis Cannabin Res.* 2017;2.1 doi:10.1089/can.2017.0012.
- 128. Bradford A, Bradford WD. Medical marijuana laws reduce prescription medication use in Medicare Part D. *Health Affairs*. 2016;35:1230-36.
- 129. Raji M, Abara NO, Salameh H, et al. Association between cannabis laws and opioid prescriptions among privately insured adults in the US. *Prev Med.* 2019;125:62-8.
- 130. Shia Y, Lianga D, Baob Y, et al. Recreational marijuana legalization and prescription opioids received by Medicaid enrollees. *Drug Alcohol Depend*. 2019;194:13-9.
- 131. Powell D, Pacula RL, Jacobson M. Do medical marijuana laws reduce addictions and deaths related to pain killers? *J Health Econ.* 2018;58:29-42.
- 132. Chihuri S, Li G. State marijuana laws and opioid overdose mortality. *Injury Epidemiol*. 2019;6:38 https://doi.org/10.1186/s40621-019-0213-z.
- 133. Campbell G, Hall W, Nielsen S. What does the ecological and epidemiological evidence indicate about the potential for cannabinoids to reduce opioid use and harms? A comprehensive review. *Int Rev Psychiatry*. 2018;30:91-106.
- 134. Lo SY, Winston-McPherson GN, Starosta AJ, et al. Cannabis legalization does not influence patient compliance with opioid therapy. *Am J Med*. 2019;132:347-53.
- 135. Li G, Chihuri S. Is marijuana use associated with decreased use of prescription opioids? Toxicological findings from two US national samples of drivers. *Sub Abuse Treat Prevent Policy*. 2020;15:12 doi.org/10.1186/s13011-020-00257-7.
- 136. Livingston M, Barnett T, Delcher C, Wagenaar A. Recreational cannabis legalization and opioid-related deaths in Colorado, 2000–2015. *Am J Public Health*. 2017;107:1827-29.
- 137. Wen H, Hockenberry JM. Association of medical and adult-use marijuana laws with opioid prescribing for Medicaid enrollees. *JAMA Intern Med.* 2018;178(5):673-79.
- 138. Shia Y, Lianga D, Bao Y. Recreational marijuana legalization and prescription opioids received by Medicaid enrollees. *Drug Alcohol Depend*. 2019;194:13-19.
- 139. Committee on Substance Abuse, Committee on Adolescence; Committee on Substance Abuse Committee on Adolescence. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics*. 2015;135:584-7.
- 140. Plunk A, Peglow S, Harrell P, Grucza R. Youth and adult arrests for cannabis possession after decriminalization and legalization of cannabis. *JAMA Pediatr*. 2019;173:763-9. doi:10.1001/jamapediatrics.2019.1539.
- 141. Kilmer B1, Kilmer Neel E. Being thoughtful about cannabis legalization and social equity. *World Psychiatry*. 19:2 June 2020;194-5.
- 142. Adinoff B, Reiman A. Implementing social justice in the transition from illicit to legal cannabis. *Am J Drug Alcohol Abuse*. 2019;45:673-88.

- 143. Effects of Marijuana Legalization on Law Enforcement and Crime: Final Report Author(s): Stohr M, Willits D, Makin D et al. Document Number: 255060: July 2020.
- 144. Firth CL, Mahera J, Dilleya J, Darnell A, Lovrich N. Did marijuana legalization in Washington State reduce racial disparities in adult marijuana arrests? *Subst Use Misuse*. 2019; 54:1582-7.
- 145. Firth CL, Hajat A, Dilley J, Braun M, Maher J. Implications of cannabis legalization on juvenile justice outcomes and racial disparities. *Am J Prev Med*. 2020;58:562-9.
- 146. Alaska Department of Health and Social Services. Marijuana Use and Public Health in Alaska
 2020. Anchorage, Alaska: Office of Substance Misuse and Addiction Prevention, Division of Public Health, Alaska Department of Health and Social Services; January 2020.
- 147. Banks DE, Hershberger AR, Pemberton T, et al. Poly-use of cannabis and other substances among juvenile-justice involved youth: variations in psychological and substance-related problems by typology. *Am J Drug Alcohol Abuse*. 2019;45:313-22.
- 148. Lu R, Willits D, Stohr M et al. The cannabis effect on crime: Time-series analysis of crime in Colorado and Washington State, *Justice Quarterly*. 2019. doi:10.1080/07418825.2019.1666903.
- 149. Massachusetts Equity Programs. https://mass-cannabis-control.com/equityprograms/
- 150. Illinois Adult Use Social Equity Program https://www2.illinois.gov/dceo/CannabisEquity/Pages/default.aspx
- 151. Michigan expands parameters of marijuana social equity program. https://mjbizdaily.com/michigan-expands-parameters-of-marijuana-social-equity-program/
- 152. State Cannabis Tax Revenue Distributions as of 2019. https://www.civicfed.org/civic-federation/blog/how-will-illinois-spend-cannabis-revenues.
- 153. Fischer B, Russell C, Rehm J, Leece P. Assessing the public health impact of cannabis legalization in Canada: core outcome indicators towards an 'index' for monitoring and evaluation. *J Public Health* (Oxf). 2019;41(2):412-421. doi:10.1093/pubmed/fdy090
- 154. Thomas A, Von Derau K, Bradford M, et al. Unintentional pediatric marijuana exposures to and after legalization and commercial availability of recreational marijuana in Washington state. *J Emerg Med.* 2019;56:398-404.
- 155. Wang GS, Le Lait MC, Deakyne SJ, Bronstein AC, Bajaj L, Roosevelt G. Unintentional Pediatric Exposures to Marijuana in Colorado, 2009-2015. *JAMA Pediatr*. 2016;170(9):e160971. doi:10.1001/jamapediatrics.2016.0971
- 156. Fischer B, Russell C, Sabioni P, et al. Lower-risk cannabis use guidelines: A comprehensive update of evidence and recommendations [published correction appears in Am J Public Health. 2018 May;108(5):e2]. *Am J Public Health*. 2017;107(8):e1-e12. doi:10.2105/AJPH.2017.303818

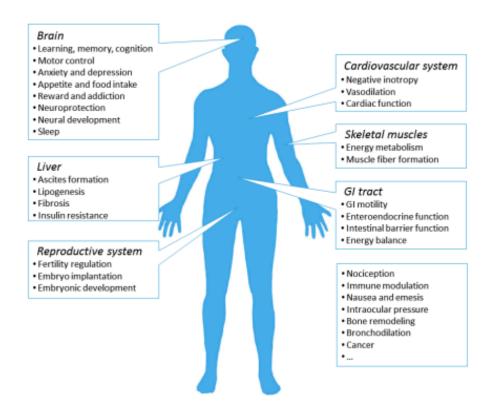


Figure 1. Major localization and associated functions of the CB1 receptor, the majority of which are expressed in the brain from: Zou S, Kumar U. Cannabinoid Receptors and the Endocannabinoid System: Signaling and Function in the Central Nervous System. *Int J Mol Sci.* 2018 Mar 13;19(3):833. doi: 10.3390/ijms19030833. Open Access.

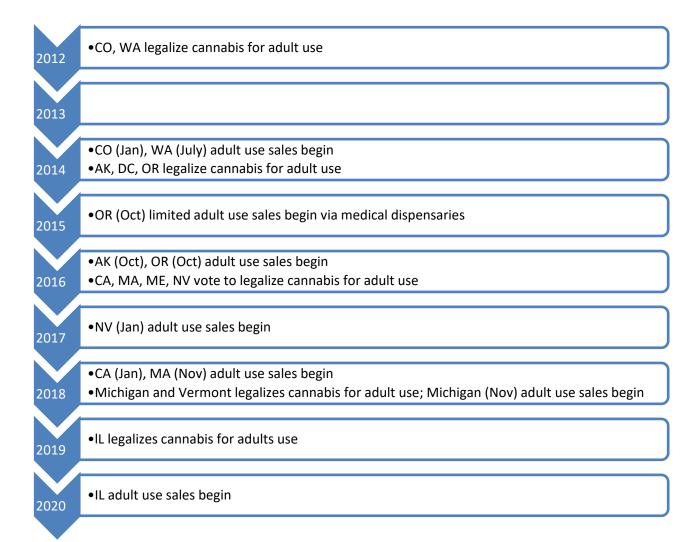


Figure 2. Timeline of legalization and implementation of cannabis for adult use. Constructed figure.



Figure 3. Washington State logo for cannabis edibles. Washington State Liquor and Cannabis Board

Table 1. Summary of cannabis extracts

Product	Description	Method of Use	Average Levels of THC and CBD ²
Hash	No.		
	Hash or hashish is the oldest and best-known type of cannabis extract. It is a light to dark brown substance composed of compressed or purified trichomes, which are the stalked resin glands that contain most of the cannabinoids present in the cannabis plant. Hash that has been pressed is usually solid, whereas water-purified hash develops a paste-like consistency and is often called "bubble melt hash" or "bubble hash."	- Smoked (either alone or mixed in with dried cannabls or tobacco) - Vaped - Dabbed	THC: 40-80% CBD: less than 5%
Kief			
	Kief refers to the collection of trichomes that accumulate when sifted from dried cannabis, often using a three-chamber grinder.	- Smoked (either alone or mixed in with dried cannabis or tobacco)	THC: 40-50% CBD less than 5%
Wax (crumble,	budder)		
16	Wax is a solvent-based (e.g., butane³) extract that is named after its appearance and consistency. Wax varies in level of THC depending on quality, but can contain well over 50% THC. Crumble is the drier and more crumbly form of wax, whereas budder contains a higher moisture content.	- Vaped - Dabbed	THC: 26-70% CBD:
Shatter			
	Shatter is amber and glass-like in appearance and consistency. It is generally high in THC and low in CBD. Compression following the extraction process turns shatter into a substance called "cookie crumble" or "honeycomb."	- Vaped - Dabbed	THC: ~ 70% CBD:
Live Resin			1
	Live resin is made the same way as wax, but with fresh cannabis plant material that has been immediately frozen after harvest. This is the reason for the term "live." This process gives live resin a "more intense and complex" smell and taste, so it is more expensive than typical wax and budder products. The moisture in this extract gives it a slightly different appearance from wax and budder.	- Vaped - Dabbed	THC: 40-50% CBD:
Rosin	V (40.314 No. 3000)		
a se	Rosin refers to cannabis extracts that were made using "rosin tech," which is essentially the application of heat and compression to the resinous sap from cannabis plant matter, most often flower (or bud), kief or hash. This extraction method results in a sappy and translucent cannabis extract that is similar in appearance and composition to shatter. It is believed that rosin can reach comparable THC concentrations to that in solvent-based extracts, but this has yet to be scientifically tested.	- Vaped - Dabbed	THC: ~ 70% CBD:

Product	Description	Method of Use	Average Levels of THC and CBD¹
Tinctures and (Oil Sprays		
	Tinctures and oil sprays are products consisting of a cannable extract, a carrier liquid, such as coconut-derived MCT (medium-chain triglycerides) oil, and sometimes terpenes. These products vary widely in their THC and CBD levels and reasons for use. Tinctures come in plastic or glass buttles with droppers and are administered under the tongue (sublingually). Oil sprays are similarly intended to be sprayed under the tongue.	- Sublingual - Ingested	High THC: THC: 20-30 mg/ml CBD: 0-1 mg/ml High CBD: THC: 0.7-2 mg/ml CBD: 15-55 mg/ml Balanced: THC: 1-12.5 mg/ml CBD: 1-12.5 mg/ml
Softgels and C	apsules		
100	Softgels and capsules are comprised of similar ingredients to that of tinctures and oil sprays: a cannabis extract, a carrier liquid (e.g., MCT) and, sometimes, terpenes. These products vary widely in their THC and CBD levels.	- Ingested	High THC: THC: 2.5–10 mg/capsule CBD: 0–1 mg/capsule Capsules on the illicit market appear to contain up to 100 mg of THC. High CBD: THC: 0–1 mg/capsule CBD: 9–25 mg/capsule Balanced: THC: 2–3 mg/capsule CBD: 2–3 mg/capsule
Vape Cartridge	es and Disposable Pens		
	Vape cartridges and pens contain high concentrated cannable extracts and varying terpene (flavour) profiles. High THC vape products are the most commonly sold. However, it appears that high CBD and "balanced" vape products are becoming increasingly available.	- Vaped	High THC: THC: 70-95% CBD: 0-10% High CBD: THC: 0-5% CBD: 60-70% Balanced: THC: 40-60% CBD: 20-40%

Source: Gabrys R. Canadian Centre on Substance Use and Addiction. Clearing the Smoke on Cannabis Edible Cannabis Products, Cannabis Extracts and Cannabis Topicals. https://www.ccsa.ca/sites/default/files/2020-05/CCSA-Edible-Cannabis-Extracts-and-Topicals-Report-2020-en.pdf.

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Table 2: Tax rates, recent tax revenues, and administrative cost (adult use)

State	Licensing & Tracking	Possession Limits	Taxes	Tax Revenue	Administrative Costs
Colorado	Colorado Dept. of Revenue	1 oz usable, 6 plants (no more than 3 mature), 8 g hash/concentrates; 800 mg edible	Cultivator excise tax of 15% sales to retail stores Retail tax of 15% Local option retail tax up to 8%	>1 billion in tax revenue from initiation to June 2019; \$203 million for Jan-Jun 2020	\$16 million
Washington	Washington State Liquor and Cannabis Board	1 oz usable, 16 oz solid cannabis-infused, 72 oz liquid infused, 7 g concentrates	37% tax on retail sales 6.5% retail sales tax (plus local tax)	\$395 million in 2019; \$248 million thru Jun 2020	\$42 million
Oregon	Oregon Liquor Control Commission	1 oz usable in public, 8 oz homegrown, 4 plants, 16 oz solid, 72 oz liquid-infused, 1 oz hash/extract at home	17% retail sales tax Local option sales tax up to 3%	\$133 million for FY 2020	\$10 million
Alaska	Marijuana Control Board	1 oz usable, 6 plants (no more than 3 mature)	Cultivator excise tax of \$50/oz flowers; \$15/oz stems and leaves; \$25/oz for immature flowers/buds; \$1 per clone	\$24.5 million FY 2020	\$2 million
Nevada	Nevada Dept. of Taxation	1 oz usable, 6 plants, 3.5 g hash/concentrates	Cultivator wholesale excise tax 15% Retail tax 10% Sales tax 6.85% (plus local)	Jul 2019-May 2020, \$95 million in tax revenue	\$3.5 million
California	CalCannabis Cultivations Licensing (CA Dept. of Food & Agriculture	1 oz usable, 6 plants, 8 g hash/concentrates	Cultivator tax of \$9.65/ounce for flowers; \$2.87 ounce for leaves Fresh plant material \$1.35/ounce Excise tax (15% of Retail Sales) Retail sales tax (7.25% plus local)	California passed \$1 billion in cannabis tax revenue two years after launching legal market.	\$61 million
Massachusetts	Massachusetts Cannabis Control Commission	1 oz usable (up to 10 oz secured), 6 plants, 5 g concentrates	10.75% Excise tax on retail sales 6.25% Retail sales tax Local option excise tax of up to 3%	\$122 million in tax revenue collected in the FY 2019- 2020	?
Michigan	Michigan Dept. of Licensing and Regulatory Affairs	2.5 oz usable, 12 plants, 15 g concentrates	10% Retail excise tax 6% State sales tax	Since Dec 2019, \$35 million in excise/sales tax	?

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Illinois	Illinois Dept. of Financial & Professional Regulation	1 oz usable, 5 g hash/concentrates	Cultivator excise tax (7%) on sales to dispensaries Retail Excise Taxes: 10% with THC level of <35%, 25% for THC>35%; 20% on cannabising taxed are due to	\$52.8 million Jan-Jun 2020 with further increase in July	?
			infused products; Local option tax up to 3%		
Maine	Office of Marijuana Policys	2.5 oz usable, up to 15 plants (no more than 3 mature), 6 g hash/concentrates	Cultivator excise tax of \$335 per pound/ \$94 per pound trim/\$1.50 per seedling/\$0.35 per seed Retail sales tax of 10%	Sales on Hold	