

High Tetrahydrocannabinol (THC) Cannabis and Effects on the Human Body: More Research Needed.

A Legislative Report and Considerations for Research
and Policy.

October 2021

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The Commission’s Research Department would like to formally acknowledge Dr. Alexandra F. Kritikos, whose recent dissertation work provided vast background on and future directions for medicinal cannabis concentration research and implications for both research and policy.

Suggested bibliographic reference format:

Doonan SM., Laramie O., & Johnson JK. (2021, October). High Tetrahydrocannabinol (THC) Cannabis and Effects on the Human Body—More Research Needed. *A Legislative Report and Considerations for Research and Policy*. Worcester, MA: *Massachusetts Cannabis Control Commission*.

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Main Findings

Potency Research Barriers

- There are major political and practical barriers to conducting research with cannabis products.
- Much of the English-language literature base, to date, uses cannabis with low THC, which does not reflect most products sold in legal markets in the United States.
- Current English-language literature lacks standardization, making cross-study comparisons challenging.

Data from Legal Market

- Massachusetts sales data is currently limited for these research purposes. Thus, we stratify products by product category as an imperfect tool to examine demand for higher THC products (e.g., concentrates, vape products).
- Demand is high for vapes and concentrate products. In May 2020, vapes and concentrates made up 23% of sales in the medical market and 27% of sales in the adult-use market.

Literature Overview

- Potency refers to the amount of a substance needed to achieve a particular effect.
- To examine the impact of cannabis potency on the human body, a sole focus on THC content is an incomplete measure.
- High doses of THC are associated with greater harms in some populations. Harms are greater for youth and young adults compared to adults.
- Evidence is insufficient to recommend a THC potency limitation ("cap") at this time. More work is needed to understand potential unintended consequences of limits, including potential impacts on equity, and how other components of the cannabis plant work to enhance or reduce the effects of THC in humans.

I. Purpose

This report has been prepared in response to St. 2017, c. 55, § 30 (f):

The commission shall investigate, in conjunction with the department of public health, the effects of marijuana and marijuana products with a high potency of tetrahydrocannabinol on the human body and recommend whether there should be restrictions on the potency of tetrahydrocannabinol in marijuana and marijuana products.

The Commission is unable to directly investigate the effects of tetrahydrocannabinol (THC) on the human body due to research barriers around using the cannabis plant, the feasibility of isolating one chemical component in the cannabis plant, and federal restrictions on human testing. This report synthesizes the myriad of barriers and limitations to our collective understanding of THC. The report includes a high-level literature review and an assessment of industry data in Massachusetts to examine market share of potentially high THC products. Based on this assessment, Commission staff pose considerations for the Commonwealth, other states, and researchers, which would permit a better understanding of THC potency to assist lawmakers and regulators in making evidence-based policy decisions in the future.

The Commission follows the Colorado Department of Public Health and Environment’s recent research report in interpreting the “potency of THC” as “THC concentration.”¹ THC concentration is typically measured in percentage of THC for inhaled products and in milligrams of THC for edible products and infused drinks.² However, as others have identified, understanding effects based on THC alone is limited as it does not account for other cannabinoids, such as cannabidiol (“CBD”), which may moderate psychoactive effects.³

II. Executive Summary

This legislative report, *High Tetrahydrocannabinol (THC) Cannabis and Effects on the Human Body: More Research Needed. A Legislative Report and Considerations for Massachusetts* (“report”) has been prepared in response to the enabling legislation in St. 2017, c. 55.

The enabling legislation, St. 2017, c. 55, §30 (f), requires the Commission to assess the effects of marijuana and marijuana products with a high potency of THC on the human body and recommend whether there should be restrictions on THC potency in marijuana and marijuana products. “Potency of THC” is defined as “THC concentration” throughout this report.

To fulfill this legislative requirement, the Commission analyzed medical and adult-use sales data by cannabis product category and conducted a high-level scoping literature review, including

literature reviews and meta-analyses of relevant scientific and gray literature that reports on health effects of high-THC cannabis. The Massachusetts Department of Public Health reviewed the report.

This report finds that there is high demand for cannabis products with high-THC concentrations in the legal market [see Section X. Results]. The scientific literature is limited by research restrictions and data limitations [see Section VII. Challenges to conducting research and Methods: Data Considerations]. Higher concentrations of THC outside of a medical cannabis setting are associated with greater harms for some populations.⁴ Among non-medical adult-users (“recreational”), consumption of products with high THC concentrations is likely associated with greater risks, but current evidence is incomplete. Among non-medical youth users, the use of highly potent THC products carries risks [See Section XI. Literature Overview]. Among medical cannabis users, evidence is currently insufficient to draw conclusions regarding high THC concentration and effect on the human body.

After assessment of the available Massachusetts data and literature pertaining to cannabis THC concentration limits for consumption and manufacturing purposes, scientific evidence is not sufficient to recommend a specific concentration limitation [see Section X. Methods and Section X. Results]. However, the Commission follows the National Institute on Drug Abuse (“NIDA”)’s expertise in recommending five milligrams of THC as the standard unit for research and reporting purposes.

Commission staff conclude that evidence is not sufficient to recommend a concentration limit currently [see Section XIV. Conclusion and Recommendation]. The Commonwealth may wish to increase scientific surveillance capacity to monitor high-THC cannabis product use [see Section XVI. Considerations].

To address some of the current data limitations, Commission staff offer multiple considerations to increase data capacity [see Section XV. Considerations]. A reassessment in the future may be warranted as the scientific evidence matures.

III. What is Cannabis?

Cannabis (“marijuana”) is the term often used in the United States (U.S.) to define the components of several cannabis plant varieties, including Cannabis Indica and Cannabis Sativa. Although cannabis varietal names and the cultural terminology for cannabis (*e.g., marijuana, ganja, grass, hash, pot, weed*) are often used interchangeably, the term *cannabis* is used for purposes of this report.

Cannabinoids are important biological markers unique to the cannabis plant and refer specifically to a group of varying molecules (terpenophenolic compounds) that bind to cannabinoid receptors in the body.^{5,6} There are more than 100 known cannabinoids.⁵ The ratio of two cannabinoids, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), in an individual plant contribute to its discrete chemical phenotype.

There are three major chemical phenotypes: (1) Chemotype I, where there is a high THC concentration, (2) Chemotype II, where CBD is the prevalent cannabinoid and THC is lower, and (3) Chemotype III, where there is a low THC concentration.⁵

Cannabinoids are categorized as: (1) endogenous (endocannabinoids), (2) synthetic cannabinoids, and (3) phytocannabinoids. THC and CBD are phytocannabinoids and have particular importance for understanding cannabis concentration. THC is the main intoxicating component of cannabis contributing to cognitive effects, potential medicinal effects, and substance use dependence potential.⁷ THC binds to cannabinoid receptors, CB₁ and CB₂, in the brain and body and has the potential for therapeutic and adverse acute and long-term effects. Such effects can include impairment of cognitive functions, analgesia, intoxication, short-term memory loss, muscle relaxant, and anti-inflammatory effects.⁸

Less is known about other cannabinoid profiles and their impacts on the human body. Recently, Delta-8-Tetrahydrocannabinol, another cannabinoid is gaining public attention, but a comprehensive understanding of the full range of cannabinoids is not yet known. Further assessment of effects of other cannabinoids which have potential for adverse outcomes, such as Delta-8-Tetrahydrocannabinol, may be warranted in the future as science better understands the effects of other cannabinoids and cannabinoid profiles.

IV. What is Potency?

Potency refers to the amount of a substance needed to achieve a particular effect. However, the unique characteristic of cannabis means that there is no specific dose that can reliably achieve a particular effect across individuals. A recent report by the Colorado Department of Public Health and Environment describes this phenomenon:

Although “potency” is the term commonly used to describe THC concentration or content, it has a different pharmacologic meaning. The proper use of the term potency is used to express the activity of a drug, in terms of the amount required to produce a defined effect. The term “potency” is inaccurate when discussing marijuana clinical effects since the active compound, THC, is the same in all marijuana products, and the effect on cannabinoid receptors is therefore consistent across products, on the cellular level. Since the effects of THC are subjective, differing between individuals and

dependent on mode of use, a known amount to produce a defined effect does not exist. Misuse of the term potency in this way may also give a false sense that any risk has been mitigated due to testing the relationship of amount to effect. Increasing the concentration of THC can lead to an increase in the dose consumed. Even low doses may affect some individuals in adverse ways, though as dose increases, risk increases.¹

Thus, Commission staff similarly interpret THC potency as THC concentration, for which reliable measures exist. Per the Colorado Department of Public Health and Environment's work, THC concentration is defined as, "THC content per volume or weight of marijuana products, usually measured in milligrams or percentage."¹ THC concentration is typically measured in percentage of THC for inhaled products and in milligrams of THC for edible products and infused drinks.² Dose or dosage refers to the amount of THC consumed at one time point.¹

To date, Massachusetts regulations set dosage restrictions for only one cannabis product type: edibles. A single serving may not contain more than 5.5 milligrams of THC (which includes a 10% allowed variance) and a single package of multiple edibles may not contain more than 20 servings. For all products, Massachusetts requires labeling which identifies the product's cannabinoid profile (i.e., the amounts, expressed as the dry-weight percentages, of delta-9-THC, CBD, tetrahydrocannabinol acid and cannabidiol acid in a Marijuana product) (935 CMR 500.000).

As of May 2021, new guidance from NIDA to cannabis researchers declared a standard dose of 5 milligrams of THC to be used for human research.⁹ The purpose of this standardization is to allow for greater comparability between studies; ultimately increasing scientific knowledge and better reflecting the marketplace and real world application.¹⁰

However, assessing THC alone is inadequate as it does not account for other cannabinoids, such as CBD, which may moderate or otherwise interact with psychoactive effects of THC, or the other less studied chemical components of the cannabis plant [see [Section III. What is Cannabis?](#)]. Nonetheless, the Commission focuses this report on THC concentration as it is the most well-understood cannabinoid implicated in cannabis' psychoactive effects on the human body in the scientific literature and is best represented in currently available data.

V. Increasing THC Concentration in Cannabis

The scientific literature shows that THC concentration in cannabis grown in North America has increased.^{11,12} An analysis of cannabis seized by the Drug Enforcement Administration (DEA) from 1995 to 2014 shows this increase.⁶ In the seized sample, average THC concentration increased from 4% in 1995 to 12% in 2014, whereas CBD concentration decreased during this timeframe.⁶

In the legal adult-use markets, researchers observe a similar trend toward increasing THC concentrations in the short-term but also show some evidence of tapering off. For example, Jikomes and Zoorob (2018) examined THC concentrations in cannabis flower using legal sales data from Washington State. Researchers found the THC concentration in flower increased from 2014-2015, then stabilized from 2015-2017 [see Section XVII. Appendix Table 3].¹³

Research across several states with regulated cannabis sales also identify a trend toward increasing market share of higher concentrated THC cannabis products (i.e., extracts) while observing a decline in market share of flower [see Section XI. Literature Overview]. As cannabis legalization policies precede scientific knowledge, research on the varied impacts of high THC cannabis and newer modes of consuming high THC cannabis (e.g., dabbing) are critical.

Most scientific studies are based on low-THC cannabis as products available for research historically have lower THC concentrations than legally sold products [see Section VII: Challenges to conducting research with cannabis]. The extent to which the current literature findings will apply to high THC cannabis is unknown. Studies are further limited by a lack of standardization in THC dosage, which makes comparisons between studies challenging. However, recent action by NIDA to create a standard dose of 5 milligrams of THC for research purposes may help rectify part of this challenge going forward.⁹

NIDA Director, Dr. Nora Volkow, states: “Adoption of a standard unit for measuring and reporting purposes will facilitate data interpretation and will make it possible to design experiments on drug effects that have real-world relevance, as well as make it easier to translate that research into policy and clinical practice.” Further clarifying that, “a standard unit is not a limit, nor any kind of recommendation for consumption that would apply to consumers or to dispensaries; it is simply a unit of measure to help facilitate cannabis research. Similar standard measures have also been applied for other substances.”¹⁰

VI. Brief History of Cannabis Laws

International

Worldwide, cannabis has been used for religious, recreational, and therapeutic purposes for thousands of years, although it has been predominantly illegal since the 1961 United Nations (U.N.) Single Convention on Narcotic Drugs.

National: United States

In the U.S., cannabis cultivation and use were legal under federal and state laws throughout most of modern American history. The first evidence of cannabis use in the U.S. was in 1611, when hemp was produced for its fiber and seed. Its therapeutic use was introduced into Western medicine by Irish physician, William Brooke O'Shaughnessy, in 1839. Cannabis's therapeutic potential was recognized by some U.S. physicians in the 1840s. From 1850 to 1941, cannabis was included in the *United States Pharmacopeia*, an official list of public standards for recognized medicinal drugs. The use of medicinal cannabis decreased as the development of other pharmaceuticals increased (e.g., *aspirin, morphine, and other opium-derived drugs*).

Social reform policies in the 20th century aimed to reduce recreational use of many substances, including cannabis. An increase in cannabis use from 1910-1920 led 29 states, including Massachusetts, to pass laws prohibiting the possession or sale of cannabis. State-level changes in cannabis policy led to its inclusion in the 1940's amendment to two federal policies: The Uniform Narcotic Drug Act of 1932 and the Marihuana Tax Act of 1937. The Marihuana Tax Act of 1937 moved toward federal criminalization through exorbitant fines for cannabis use, possession, and cultivation.

The Federal Controlled Substance Act (CSA) of 1970 replaced the Marihuana Tax Act and made it additionally illegal under federal law for physicians to prescribe cannabis medicinally. Despite the increasing stringency of federal cannabis policies over time, use of cannabis continued.

In 1971, President Richard Nixon declared a War on Drugs, proclaiming: "America's public enemy number one in the United States is drug abuse. In order to fight and defeat this enemy, it is necessary to wage a new, all-out offensive." The purpose of Nixon's "War on Drugs" policies were to combat drug abuse on both the supply and demand sides. However, a disproportionate number of these policies focused on criminal justice enforcement and punishment for drug offenses thus, creating systematic changes in the criminal justice system. These policies assisted in creating both the "Law and Order" (i.e., politicization of crime) and "Crime and Punishment" (i.e., a culmination of fear of street crime that created a "morally and justified" reason for the heavy punitive response to drug crime) phenomena.

Currently under the CSA, the DEA classifies cannabis as a Schedule 1 drug, the most restrictive ranking ("scheduling") on par with heroin, contending that it has: (1) a high potential for abuse, (2) no current accepted medical use in the U.S., and (3) a lack of accepted safety for use under medical supervision. Since 1970, there have been multiple efforts by activists, researchers, and others to reschedule cannabis at the federal level, including in recent months with the [Cannabis Administration and Opportunity Act](#).

The U.S. Food and Drug Administration (FDA) is responsible for the oversight and implementation of the 1906 Pure Food and Drug Act, which prevents the manufacture, sale, or transportation of adulterated, misbranded, poisonous, or deleterious foods, drugs, medicines, and liquors. The FDA's role in the regulation of drugs, which includes cannabis and cannabis-derived products [e.g., Marinol (i.e., dronabinol), Cesamet (i.e., nabilone), Syndros (i.e., dronabinol), Epidiolex (i.e., cannabidiol)], includes a review to determine whether proposed drug products are safe and effective for their intended use before products can go to market. The FDA has not approved the cannabis plant for the treatment of any disease, symptom, or condition with exception of approved medicines that include cannabis extracts approved to treat specific medical conditions.¹⁴

State Level

There are three types of cannabis-use policies enacted at the state or local level in the U.S. that allow for regulation despite cannabis' federal status: (1) decriminalization but not regulation or legalization, (2) medicinal cannabis legalization, and (3) recreational or adult-use cannabis legalization.

The first wave of cannabis policy change was decriminalization, which differs from legalization, and was defined in 1972 by the National Commission on Marijuana and Drug Abuse, as policies replacing criminal sanctions for the possession for personal use or casual distribution of cannabis in small amounts with civil fines. States with decriminalization designate offenses as low-level misdemeanors without jail sentences for qualifying offenses or a civil infraction.

Since 1996, 36 states, the District of Columbia (D.C.), and four territories have enacted varying laws legalizing comprehensive medicinal cannabis programs,¹⁵ which include four main features: (1) protection from criminal penalties for using cannabis for a medical purpose; (2) access to cannabis through home cultivation, dispensaries, or some other system; (3) allowance for a variety of strains and/or consumption methods; and (4) allowance for either smoking or vaporization of some type of cannabis product, plant material, or extract. An additional 12 states permit use of "low THC, high CBD" products for medicinal reasons or as a legal defense in limited situations.¹⁵ These states are not considered "medical cannabis" states.

Since 2012, 17 states, D.C., and two territories have enacted varying laws legalizing small amounts of cannabis for non-medical, adult-use by adults 21 years old or older.¹⁶

It is important to note that since 1996, cannabis legalization policies (i.e., medicinal and non-medicinal adult-use) have been enacted at the state level, creating a heterogenous patchwork of policies, provisions, liberalization of provisions, regulation, enforcement, and fidelity of

enforcement across states. THC concentration caps vary across states and potentially within states.¹⁷

These differences and limitations in regulation and cultivation of cannabis sale and use make research into THC's effects on the human body difficult to examine. Until recently, very few states, and only those with regulated cannabis markets, have undertaken research into how cannabis use affects users. In the U.S., we found no evidence or report of clinical research covering this broad topic. These research limitations contribute to gray areas and hinder regulators from making evidence-based decisions about THC concentration caps and other matters.

Legal Background: Commonwealth of Massachusetts

Massachusetts enacted and implemented three types of cannabis policy changes in three waves of ballot initiatives: cannabis decriminalization in 2008 with Question 2, "*The Sensible Marijuana Policy Initiative*"; medicinal cannabis legalization in 2012 with Question 3, "*An Initiative Petition for a Law for the Humanitarian Medical Use of Marijuana*"; and non-medical adult-use cannabis legalization in 2016 with Question 4, "*Massachusetts Legalization, Regulation and Taxation of Marijuana Initiative*".

i. State Laws Governing the Cultivation, Production, Transportation, or Sale of Medical and Adult-Use Cannabis

- St. 2008, c. 387: *An Act Establishing A Sensible State Marijuana Policy*
<https://malegislature.gov/Laws/SessionLaws/Acts/2008/Chapter387>
- St. 2012, c. 369: *An Act for The Humanitarian Medical Use of Marijuana*
<https://malegislature.gov/Laws/SessionLaws/Acts/2012/Chapter369>
- St. 2016, c. 334: *The Regulation and Taxation of Marijuana Act*
<https://malegislature.gov/Laws/SessionLaws/Acts/2016/Chapter334>
- St. 2017, c. 55: *An Act to Ensure Safe Access to Marijuana*
<https://malegislature.gov/Laws/SessionLaws/Acts/2017/Chapter55>
- M.G.L. c. 94G: Regulation of the Use and Distribution of Marijuana Not Medically Prescribed: <https://malegislature.gov/laws/generallaws/parti/titlexv/chapter94g>
- M.G.L. c. 94I: Medical Use of Marijuana:
<https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXV/Chapter94i>

ii. State Laws Governing Controlled Substances

- M.G.L. c. 94C: *Controlled Substances*
<https://malegislature.gov/Laws/GeneralLaws/PartI/TitleXV/Chapter94C>

iii. Current Cannabis Regulations

- 935 CMR 500.00: *Adult Use of Marijuana* https://masscannabiscontrol.com/wp-content/uploads/2021/05/210416_Adult_Use_Regulations.pdf
- 935 CMR 501.000: *Medical Use of Marijuana* https://masscannabiscontrol.com/wp-content/uploads/2021/05/210416_Medical_Use_Regulations.pdf

iv. Sub-Regulatory Guidance

- *Commission Guidance Documents* <https://masscannabiscontrol.com/public-documents/guidance-documents/>

VII. Challenges to Conducting Research with Cannabis

As discussed above, in the U.S., there are major barriers to conducting research with cannabis products. These challenges contribute to the current gaps in the scientific literature surrounding the impacts of high-THC concentration cannabis products on the human body and severely limit the ability to enact evidence-based policy decisions. A recent article in the *New England Journal of Medicine*, Zarrabi et al., (2020), describes these barriers.¹⁸ In short, the DEA currently classifies cannabis as a Schedule 1 drug meaning there is no (federally) accepted medical use and a high potential for abuse. Researchers trying to conduct studies that involve human cannabis consumption, including clinical trials, must obtain FDA and DEA approval. These processes can take a year or longer.¹⁸ A recent federal report by the U.S. Senate Caucus on International Narcotics Control (2021) states that the maximum time it should take for schedule 1 registration is 47 days, and the DEA reports an average of 52 days for completed applications. Applications deemed incomplete (about 70% of submitted applications), have a substantially delayed processing time.¹⁹ Researchers are also subject to background checks and research site visits.¹⁹

After approval, the researchers can only use cannabis approved by NIDA, and grown and managed by the University of Mississippi, the only federally approved cultivator of cannabis for research purposes.¹⁸ This supply does not mirror the array of products and THC concentrations sold at cannabis retailers (or in the illicit market) or the variety and regional differences in cannabis, and the quality of products may be poor.¹⁸ Further, any changes to the research protocol requiring review and approval by the FDA or DEA will slow the research process further.¹⁹ Given the limitations on the cannabis from the University of Mississippi, if a researcher was able to navigate the regulatory barriers, institution-specific barriers, and Institutional Review Board (IRB) processes, the researcher's study findings may have limited utility for understanding cannabis' effects on humans.¹⁸

In March 2020, NIDA issued a [Request for Information \(RFI\)](#) regarding the establishment of a standard dose of THC to facilitate cannabis research. In May 2021, NIDA, along with the National Cancer Institute, the National Heart, Lung, and Blood Institute, and the National



Institute of Mental Health, published a notice in the National Institute of Health (NIH) Guide directing researchers funded by these institutes to measure and report their findings from clinical research on cannabis using a standard unit of THC of 5 milligrams. The purpose of this standardization is to allow for greater comparability between studies, ultimately increasing scientific knowledge and increasing real-world application, including translating research into policy and clinical practice.¹⁰

The implementation of a standard unit for measuring and reporting purposes in research will permit researchers to design experiments on cannabis effects that could have real-world relevance, facilitate more precise data interpretation, and begin to translate the spectrum of research conducted into evidence-based policy and clinical practice. The challenge remains, however, for researchers to access cannabis products like what are currently available to consumers in the U.S.

VIII. Medicinal Cannabis Research Considerations

Given the beforementioned challenges of using cannabis for research, the current state of research on the medical efficacy of cannabis to treat specified disorders and symptoms is mixed and varied.

A recent dissertation study conducted by Dr. Alexandra F. Kritikos comprehensively assesses medical cannabis laws and provisions, medicinal patients and concentration levels of products purchased, gaps in research, and effects on policy in New York State. Dr. Kritikos' study pioneers the use of sales data from dispensaries and provides a unique opportunity to investigate medical cannabis use from an alternative perspective. In her work, she discusses critical points relevant to concentration.

Kritikos (2021) states that cannabis is a plant consisting of more than 100 chemical components, which does not meet the standards required for medicinal approval of other medications by the FDA. Further, Kritikos reports that most research on the therapeutic efficacy of cannabis has been conducted using oral preparations formulated by pharmaceutical companies, not inhaled preparation common to many users. Preparations include dronabinol (Marinol) and nabilone (Cesamet), synthetic analogs of THC, and nabiximols (Sativex), a cannabis-derived oromucosal spray containing THC and CBD in a 1:1 ratio.^{20,21}

There is insufficient research evidence on the short- and long-term health effects of THC and CBD products, especially under legalization, which expedited the production of novel cannabis products and high THC concentrations compared to those products used in clinical trials, which are usually a lower concentration THC.^{20,22,23} This finding is relevant for those accessing medical cannabis through the “gray market.” Recent research suggests that “gray market” access to medical cannabis is increasingly common among Massachusetts youth in treatment for cannabis use disorders, warranting additional research.²⁴

Kritikos (2021) further sheds light on how cannabis legalization has impacted innovation in cannabis manufacturing and cultivation to produce varying cannabinoid profiles. Similarly, regulated markets have resulted in modes of administration, which changed the ways cannabis is consumed: “Cannabis potency and modes of consumption have evolved quickly since it first became legalized. Medicalization brought new products (e.g., edibles, tablets), new potency levels, and new modes of consumption (e.g., vaping).”²⁰

Changing THC concentration cannabinoid profiles of available legal market products and modes of consumption are specifically important for youth, who face greater risks than adults do when it comes to cannabis use and high THC concentration cannabis use.⁴ Additional considerations should be made for both the medical efficacy for treating youth medical patients with high-THC products, as well as the potential for diverted use among youth [see Section XV. Considerations: (1) Research Consideration #s 2, 3; (2) Policy and Regulatory Considerations, All States Considerations #s 3, 4, 6, 8; and (3) Policy and Regulatory Considerations, Massachusetts Consideration #1].

Unlike medications approved through the formal data-driven process by the FDA, currently, there is no clear optimal dosing information of cannabis in its approved medical conditions,²⁰ which vary across states. The newly enacted standardized THC dose for research may help alleviate this fundamental limitation as it pertains to THC; however, further research will still be needed to assess interactions with other cannabis chemical components, varying routes of administration, and variations in the test subjects.¹⁰

In an important statement, Kritikos explains that, “despite the lack of scientific research in the legalized markets, medical cannabis use is now common in clinical practice, and physicians are increasingly faced with questions from patients about cannabis and its medical applications. Therefore, providers and policy makers must understand both the scientific rationale and the practical implications of medical cannabis laws.”²⁰ This highlights a critical call for researchers and policymakers alike.

IX. Methods

This report consists of data analysis and a high-level literature overview. As high-quality reviews on this topic have previously been conducted, we focused our literature search primarily on peer reviewed literature and on relevant gray literature (i.e., reports and articles that were not published through academic reviewed journals, such as government reports).

Data Considerations

The Commission considered multiple data sources for inclusion in this report. We largely relied on the report, “[*Special Report: Evaluating the Impact of Cannabis Legalization in*](#)

Massachusetts: State of the Data” to identify potential surveillance data sources.²⁵ Only one surveillance source considered for inclusion, the [International Cannabis Policy Study](#), asks participants to report THC concentrations for cannabis products they consume. However, a study of consumer knowledge about the THC and CBD levels of the products that they use found consumer knowledge was low. These authors conclude: “... despite the potential utility of collected self-reported data on THC and CBD levels in population based surveys, the accuracy of these data is dubious and should be interpreted with considerable caution.”³ This suggests that consumer education is necessary before self-reported cannabinoid profiles have broader utility for surveillance purposes [see [Section XV. Considerations: Educational Considerations #1](#)].³ In light of this knowledge gap and in order to align with other states’ efforts, we focus this report on the cannabis product types that are more likely to have high THC concentrations as an attempt to isolate use of high-concentration cannabis products.

There is not a universal definition of cannabis product types likely to have high THC concentrations. For example, Colorado’s recent state report on THC concentration included smoking, eating, drinking, vaporizing, or dabbing cannabis among the methods of cannabis consumption for a statewide survey (i.e., Behavioral Risk Factor Surveillance System (BRFSS)). The authors noted: “The only method of use on BRFSS that can provide an unbiased estimate of adult use of high concentrated THC products is dabbing.”¹ Alternatively, a report from Washington State took a broader approach and examined the prevalence of consumption by dabbing, eating, and vaping in their state BRFSS.¹¹ For the purposes of the Commission’s report, and due to our data classification, we follow Washington State’s broader approach. We consider *potentially high THC cannabis products* as cannabis concentrates, vaping products, and edibles. We are limited to using potentially high THC cannabis product categories, because the data’s current form does not allow us to extract THC concentrations without an exhaustive manual process³ [see [Section XV. Considerations: Policy and Regulatory Considerations: Massachusetts: Considerations #1](#)]. The approach is further limited as individual products with lower amounts of THC (e.g., an edible with a low THC concentration) in potentially high THC categories cannot be differentiated.

While sales data is one way to understand consumer behavior, it does not capture home-grown or illicit market use. To address this limitation and to better triangulate trends in potentially high THC cannabis consumption, other states’ reports leverage an optional cannabis (“marijuana”) module in BRFSS. This module contains cannabis behavior questions and is a strong surveillance measure because participants are a generalizable state sample. Unfortunately, the Massachusetts BRFSS does not include an optional cannabis module which asks about the mode of cannabis use.²⁶ While Massachusetts does add in multiple optional questions related to cannabis, mode of use, or other measure(s) which could identify potentially high THC products are not currently available for surveillance purposes. Thus, we do not include data from BRFSS



in this report³ [see Section XV. Considerations: Policy and Regulatory Considerations: Massachusetts: Consideration #4].

At the time of writing, other key surveillance data sources, including Massachusetts's Youth Risk Behavior Surveillance System (YRBSS) do not ask about mode of use (excluding 2015 National YRBSS that asked about method of use).²⁶ Likewise, the Massachusetts Youth Health Survey (YMS) does not ask a question about mode of cannabis use.²⁶ At the time of last assessment in 2019, the Massachusetts Pregnancy Risk Assessment Monitoring System (PRAMS), a surveillance system for pregnant people, had not added an optional module about cannabis use.²⁵

Due to these limitations, this report solely relies on the Commission's collected data on legal medical and adult-use sales by product category [see methods below].

Sales Data

Massachusetts collects a wide range of data in its mandatory seed-to-sale tracking system of record (i.e., Metrc). Licensed Marijuana Establishments must input data for all plants (i.e., immature, vegetative, flowering) and for all packages made from each batch of cannabis. For each package, licensees must input an item name, product category, quantity, and unit of measure. Stringent testing protocols are required for all cannabis products, and unique identifiers allow for traceability back to a product's original tested batch. Within this system, all cannabis and cannabis products are linked to specific licensees, and cannabis products can be traced back to the original cultivation.

In Massachusetts, regulated medical cannabis sales began in June 2015, and adult-use cannabis sales began in November 2018.

For this report, we extracted Massachusetts medical sales data from May 1, 2019 to March 31, 2021, and adult-use sales data from December 1, 2018 to March 31, 2021. The start date for the data on medical sales is later than adult-use because medical dispensaries were not required to use Metrc until September 2019, after the Commission became responsible for regulation of medical- and adult-use entities.

Specifically, we extracted the total sales in dollars for each product category and total units of the product sold for each month in the study timeframe. Medical market sales represent patient and caregiver purchases and are presented separately from consumer sales in the adult-use market.

Each cannabis product is classified as one of the following product categories: Buds, Concentrate, Concentrate (each), Infused edible, Infused (non-edible), Kief, Raw pre-roll,

Infused pre-roll, Infused Beverage, Shake/Trim, Shake/Trim (by strain), Suppository, Vape Product, and Waste. The column “Waste” was dropped from analysis as this indicates a product was destroyed and not sold to a consumer. There is no specific codebook or definitions for each of these categories, therefore, different retailers may classify similar products differently.

Product classification options changed since the seed-to-sale tracking system began. Use of the product categories for “pre-rolls” began in March 2019. Wide use of the product category “Vape Product” occurred in December 2019 for both the non-medical adult-use and medical markets. Before this was an option, most retailers were classifying vape products under the category “Concentrate (each),” therefore, to maintain comparability across the time frame, we created a new category, “Vape and Concentrate (each),” which sums the totals in “Concentrate (each)” and “Vape Product.” This allows comparability from before December 2019 to after. The product category “Infused Beverage” was also an added classification; its use began in February 2021.

For clarity in reporting purposes and visuals, we collapse the product categories that made up 1% or less of total sales into the category “Other product.” Other contains the following categories: “Concentrate,” “Infused (nonedible),” “Infused Beverage,” “Infused Pre-rolls”, “Kief”, “Shake/trim”, “Shake/trim (by strain)”, and “Suppository”. After these data cleaning steps, the final analytic dataset had five product categories: “Vapes and concentrate (each) merged”, “Raw pre-rolls”, “Buds”, “Infused edibles”, and “Other”.

In the scientific literature, Smart et al. (2017) use Washington State seed-to-sale data and operationalize market share by product type in the following way: “... product categories are calculated as percent of total tax-inclusive expenditures in the market ...” [online supplementary appendix].²⁷ We follow this conceptualization but calculate market share for each product type as the percent of total expenditures *excluding* tax, as the tax dollar amount is not included Massachusetts data [See Report, [Feasibility of Alternative Tax Schemes: A Legislative Report and Recommendation for Massachusetts](#), for detailed information on Massachusetts’ cannabis tax structure]. Similarly, we calculate the share of total units as the percent of total units for each product category. Due to time and financial constraints, we present only descriptive findings and follow Firth et al. (2019) in displaying findings through a stacked area chart showing total sales per month on the vertical axis (e.g., Tables 1 and 3)² and follow Davenport (2019) in displaying findings through a 100% stacked area chart showing the percent of total monthly sales that each product type represents (e.g., Tables 2 and 4).²⁸

Several major changes occurred during this study period, which could impact product type trends. The Centers for Disease Control and Prevention (CDC) began standardized data collection to investigate e-cigarette or vaping product use-associated lung injury (EVALI), a novel public health threat, in August 2019 and identified a peak in EVALI cases in September 2019. The CDC stopped collecting data on EVALI in February 2020 due to the identification of



the primary cause and the decline in cases.²⁹ In Massachusetts, Governor Baker and then the Commission quarantined all vape products from September 24, 2019 through December 12, 2019, meaning no vape products could be sold in stores. On December 12, 2019, the Commission allowed vapes manufactured after December 12, 2019, to be sold in stores and on August 4, 2020, the Commission allowed vapes manufactured before December 12, 2019, to be sold in stores subject to a re-testing and remediation process. The COVID-19 pandemic also began during this study timeframe. Notably, in Massachusetts, a pandemic-related emergency order temporarily halted adult-use sales from March 24, 2020, through May 24, 2020. The medical market remained open during this time.

Peer-review Literature Review

The Commission staff conducted targeted searches of peer-reviewed scientific literature in March and April 2021 on PubMed and Google Scholar. The search terms included “cannabis,” “cannabis use,” “psychological disorders,” “mental health,” “potency,” “THC,” “high potency,” “literature review,” “risk factors,” and “cannabinoids”, and prioritized literature reviews published from 2008 to 2021. [Appendix Table 1]

In May 2021, Commission staff conducted targeted searches in Google Scholar and through reference review of identified articles to identify articles that use legal seed-to-sale tracking systems to examine product and concentration trends. The search terms included: “cannabis,” “potency,” “THC,” “seed-to-sale,” “legal market,” “recreational legalization,” and “Washington.” [Appendix Table 3]

Gray Report Review

Staff also conducted a secondary search for relevant gray literature (*i.e., reports and articles that were not published through academic reviewed journals*) through targeted Google searches. Search terms included the following: “THC concentration,” “report,” “THC,” “cannabis,” “high-potency,” “marijuana,” and “potency.”

This part of the search prioritized governmental reports and was limited to reports written in English. Staff also conducted reference review and searched author reference libraries. [Appendix Table 2]

X. Results

Medical-use Sales

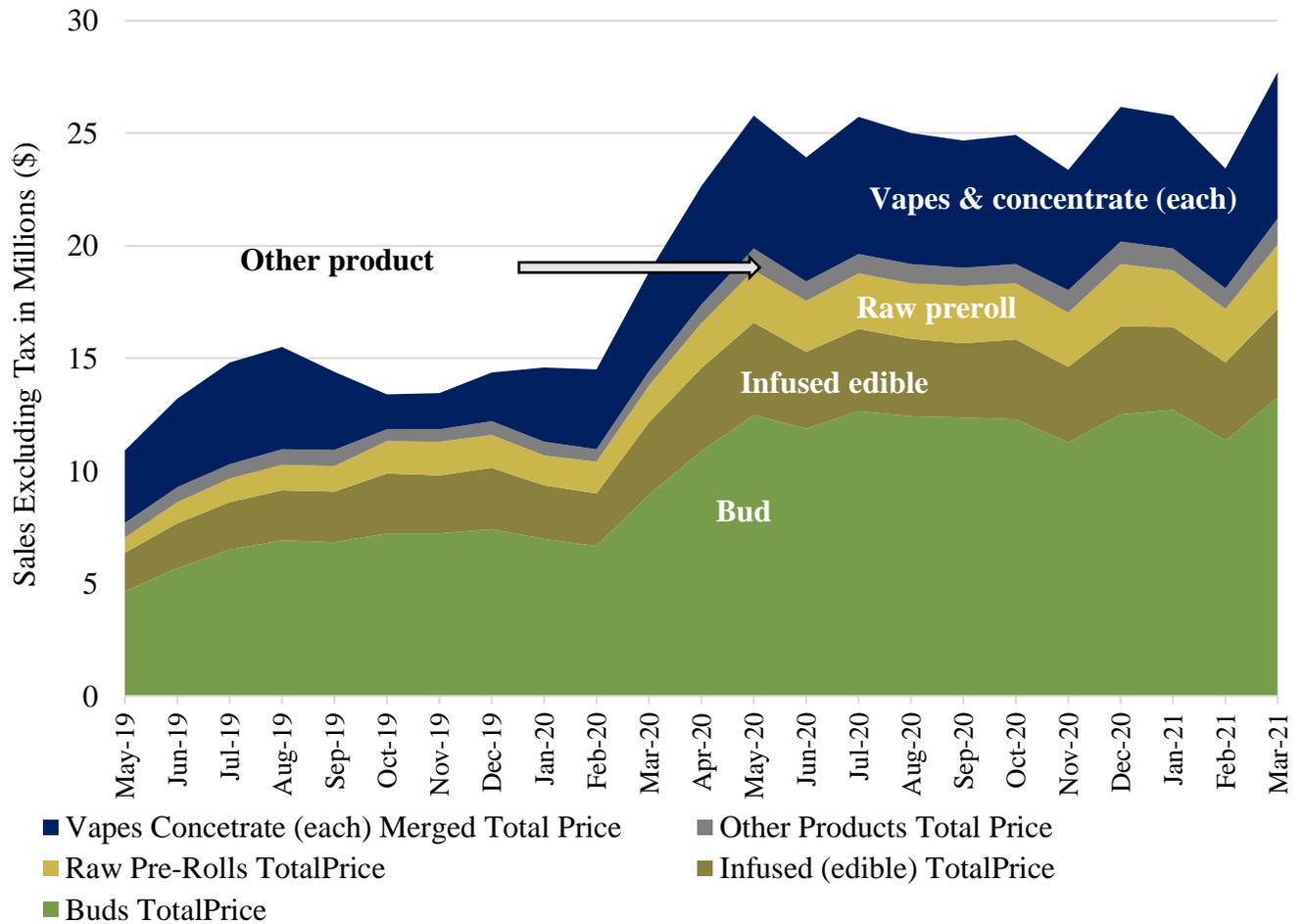
Tables 1 and 2 show medical sales stratified by product category per month. Table 1 shows the total sales in millions of dollars on the left Y-axis (vertical). Table 2 shows the percentage of

total sales on the left Y-axis (vertical). For example, if there were 50 million sales in Month X, the highest point for the month on Table 1 would be level with 50 million and 100% on Table 2 would equal 50 million.

Concentrates and vape products typically have higher THC concentrations as compared to buds. In May 2019, vapes and concentrate (each) made up 30% of total sales, and in May 2020, vapes and concentrate (each) made up 23% of total sales. However, during the EVALI public health crisis and the Commission's quarantine on vape products, vapes and concentrates as a percentage of total sales fell to between 12-15% from October 2019 through December 2019.

In May 2019, buds made up 43% of total medical cannabis sales, and in May 2020, buds made up 48% of total medical sales. Edibles made up 16% of sales at both time points, and raw pre-roll made up 6% (May 2019) to 9% (May 2020) of sales.

Table 1. Total Dollars Spent on Medical Cannabis by Product Type (in millions per month)



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

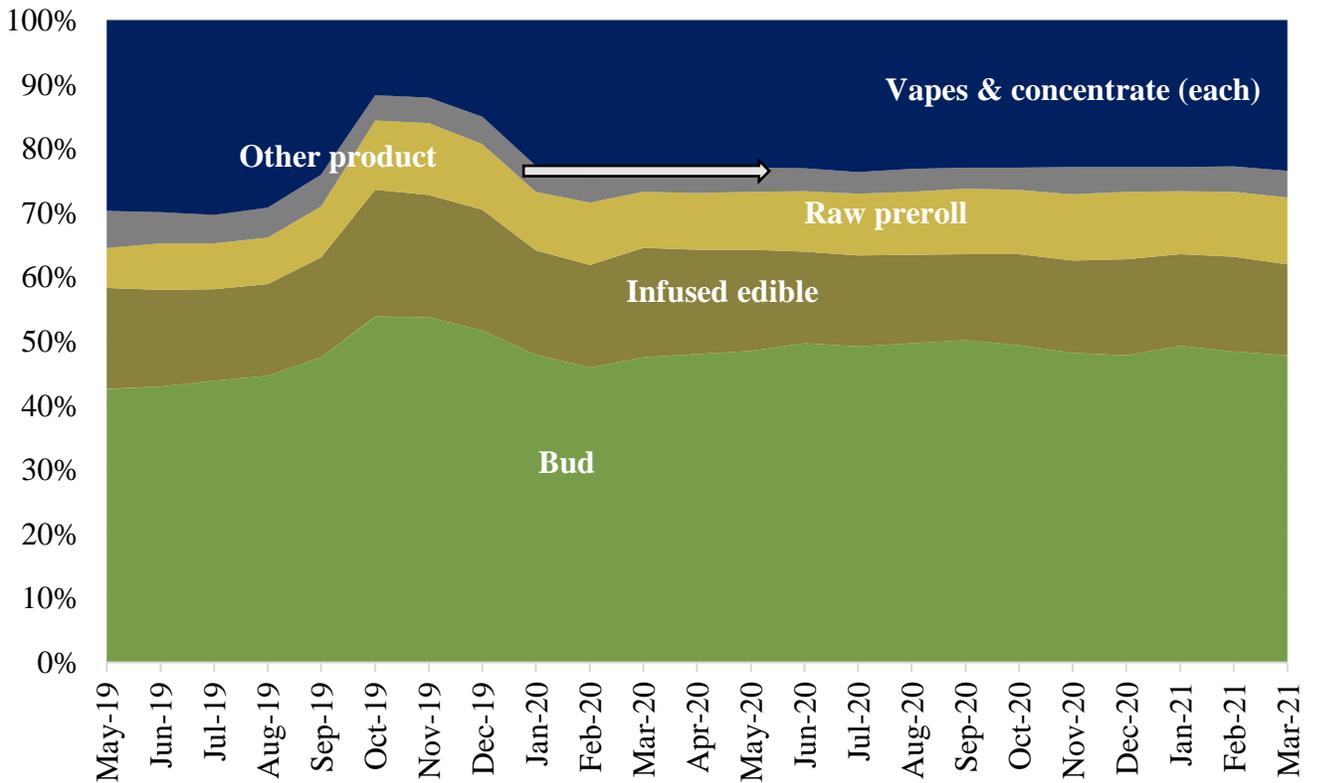
Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Table 2. Percent of Total Monthly Medical Sales by Product Type



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

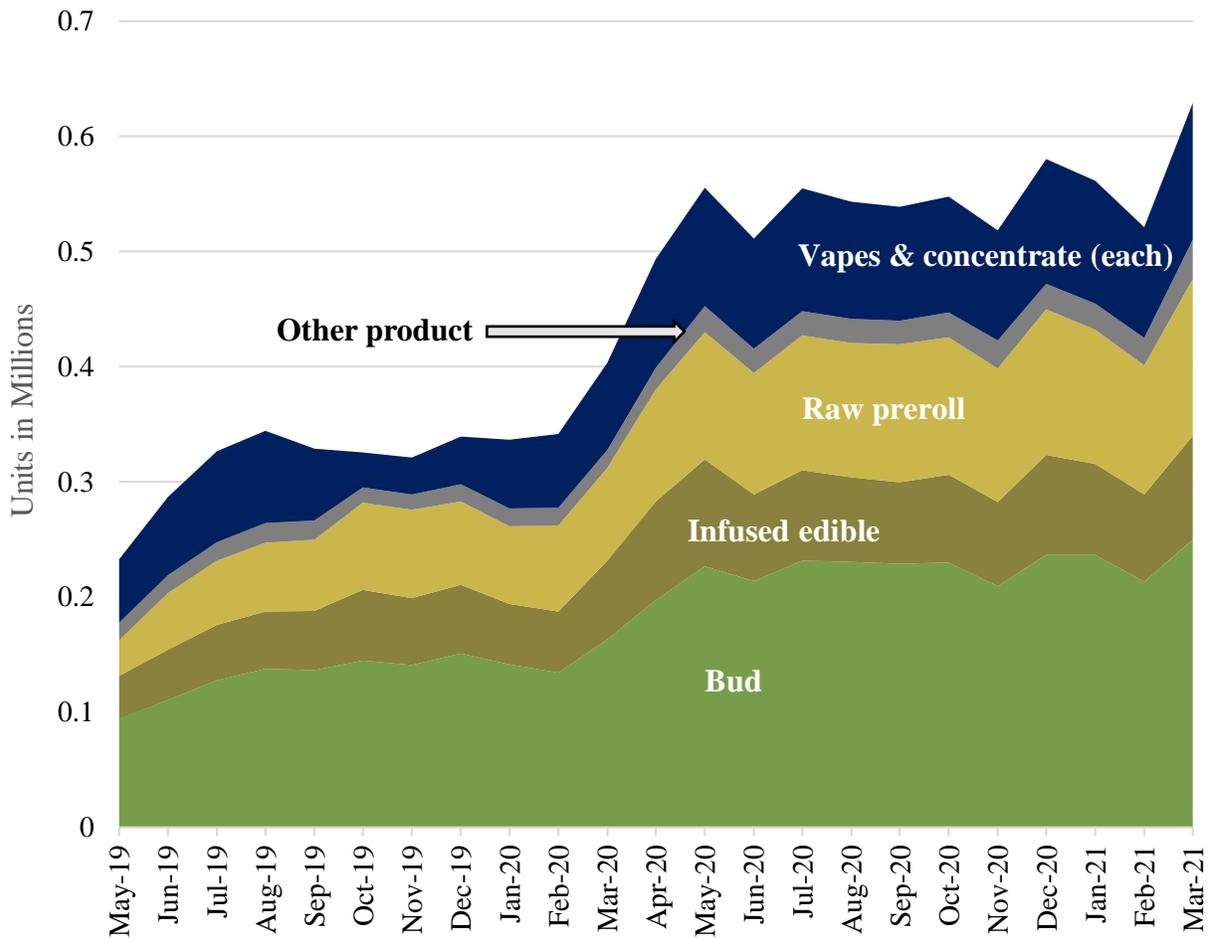
Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Tables 3 and 4 show medical product units by product category per month. Units refer to each package sold (e.g., one package of edibles) or each “unit” of bud (i.e., 1 gram of strain A and 1 gram of strain B is two units while 2 grams of strain A is one unit.). Table 3 shows the total units by product category per month. Table 4 shows the percentage that each product category made up of the total units of cannabis product sold in the medical cannabis market per month.

In May 2019, vapes and concentrate (each) made up 24% of total units sold, and in May 2020, vapes and concentrate (each) made up 18% of total units sold. However, during the EVALI public health crisis and Commission quarantine on vape products [see [Section X. Methods for more detail](#)], vapes and concentrates as a percentage of total units sold fell to between 9-12% from October 2019 through December 2019.

In May 2019, buds made up 41% of total cannabis units sold, and in May 2020, buds also made up 41% of total units sold. During the same time points, edibles made up 16% (May 2019)-17% (May 2020) of units sold. Raw pre-rolls made up 13% (May 2019) to 20% (May 2020) of units sold.

Table 3. Monthly Medical Units Sold by Product Type (millions)



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

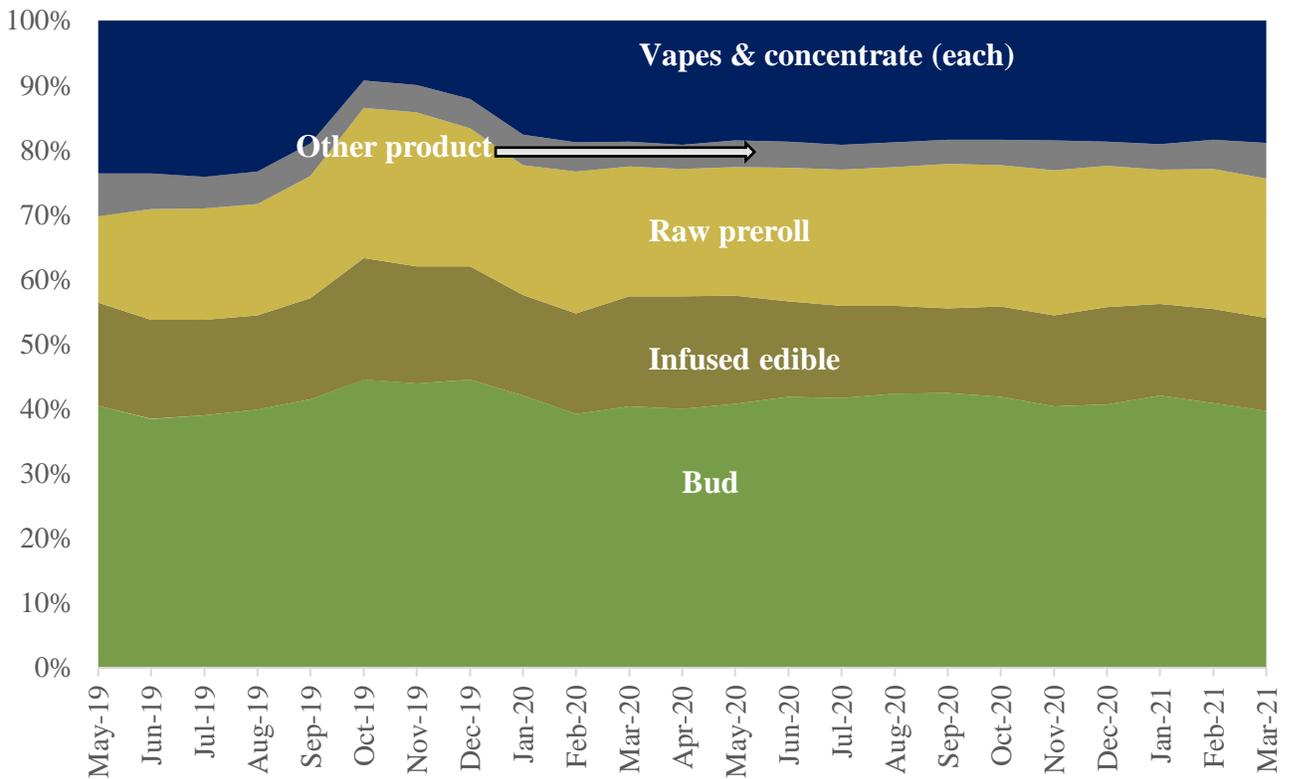
Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Table 4. Percent of Total Monthly Medical Units by Product Type



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Adult-use Sales

Tables 5 and 6 show adult-use sales by product category per month. Table 5 shows the total sales in millions of dollars on the left Y-axis (vertical). For example, if there were 50 million sales in Month X, the highest point for the month on Table 5 would be level with 50 million and 100% on Table 6 would equal 50 million.

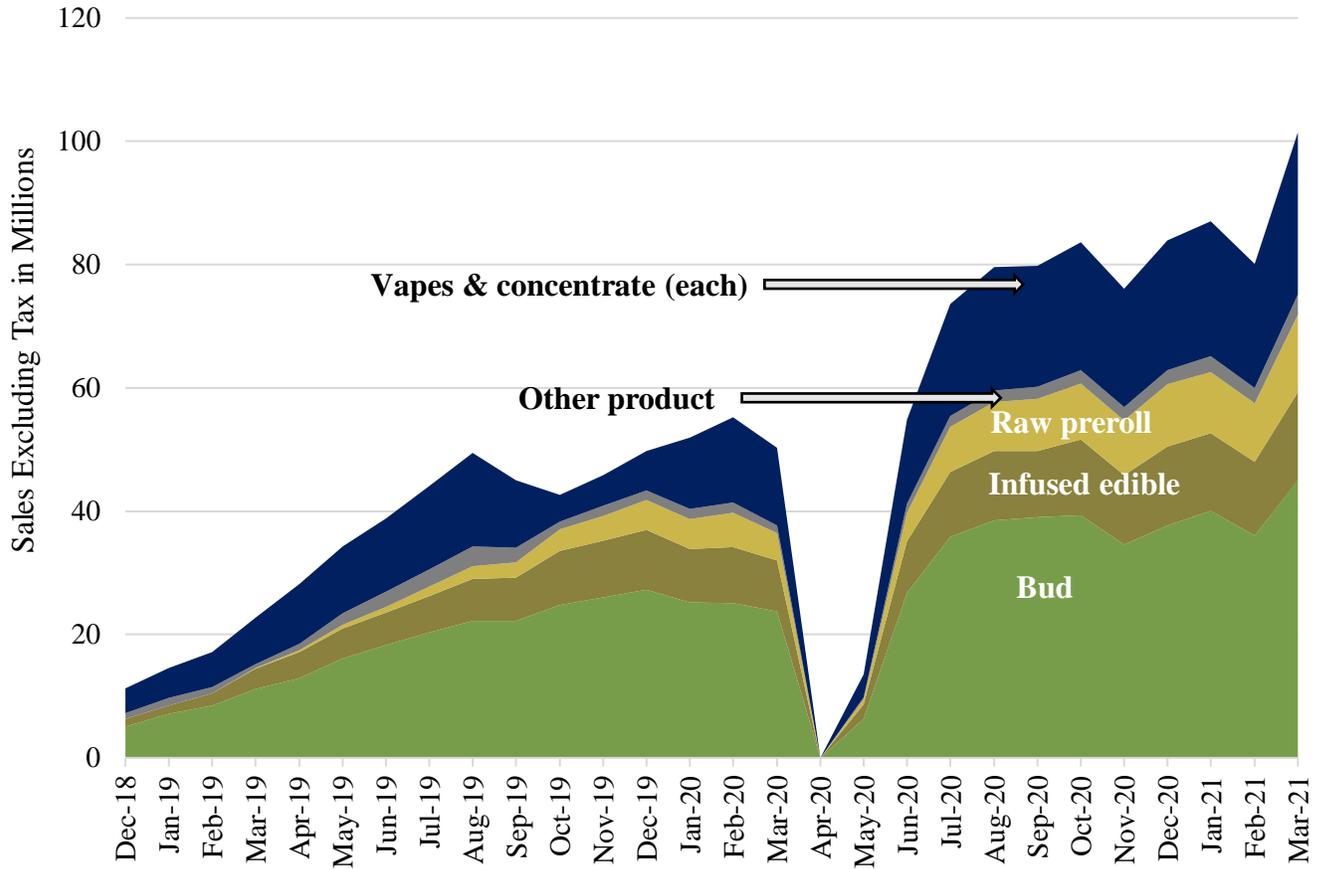
There were no sales in April 2019, due to a COVID-19-related emergency order which required adult-use retailers to temporarily halt sales.

Table 6 shows the percent that each product category made up out of the total dollars spent that month.

In December 2018, vapes and concentrate (each) made up 35% of total adult-use sales, and in December 2020, vapes and concentrate (each) made up 25% of total sales. However, during the EVALI public health crisis and Commission quarantine on vape products, vapes and concentrates as a percentage of total sales fell to between 10-13% from October 2019 through December 2019.

In December 2018, buds made up 45% of total adult-use cannabis sales, and in December 2020, buds also made up 45% of total adult-use sales. During the same time points, infused edibles made up 12% (December 2018)-15% (December 2020) of total sales. Raw pre-rolls made up 12% of sales in December 2020.

Table 5. Total Dollars Spent on Adult-use Cannabis by Product Type (in millions per month)



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

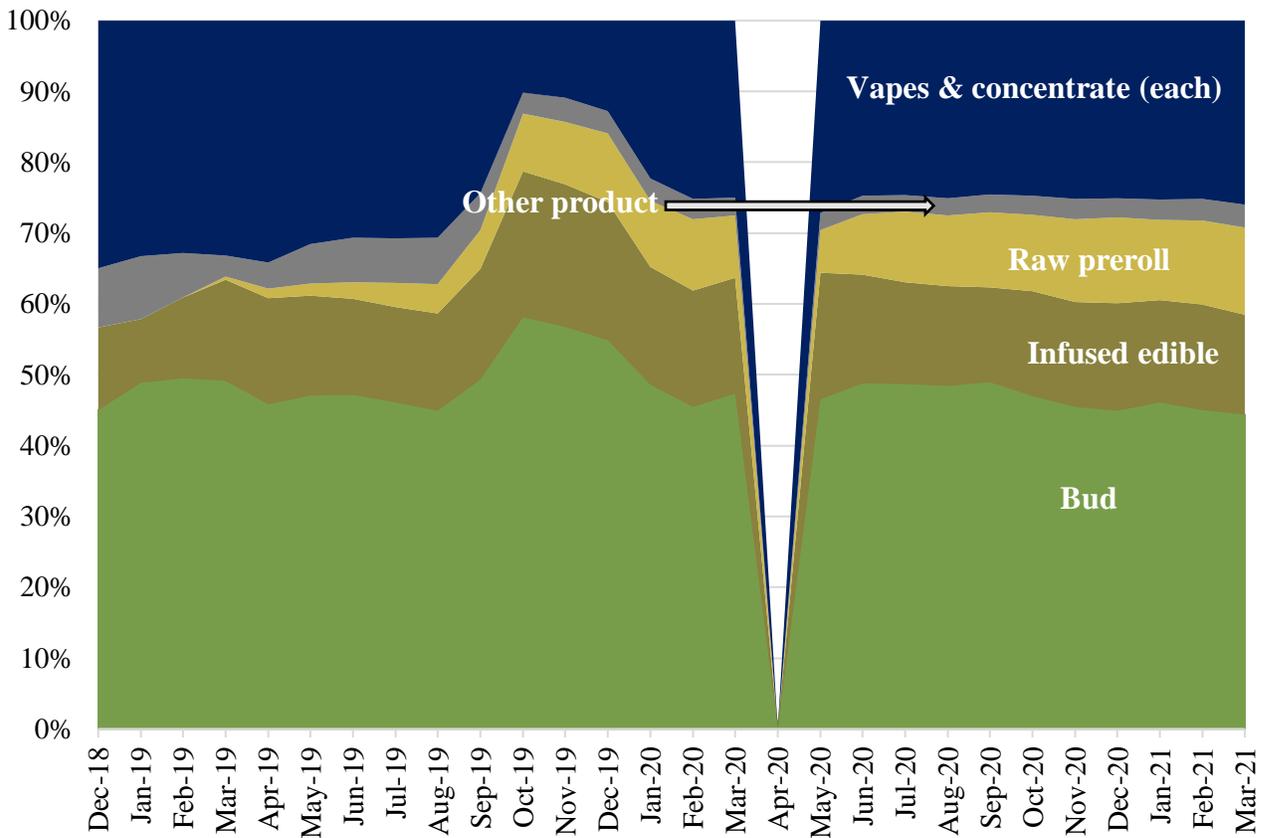
Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Table 6. Percent of Total Monthly Adult-use Sales by Product Type



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

For comparison to the timeframes reported in medical-use results section: in May 2019, vapes and concentrates (each) made up 32% of sales and in May 2020, vapes and concentrate (each) made up 27% of sales.

Tables 7 and 8 shows adult-use product units by product category per month. Units refer to each package sold (e.g., one package of edibles) or each “unit” of bud (i.e., 1 gram of strain A and 1 gram of strain B is two units while 2 grams of strain A is one unit).

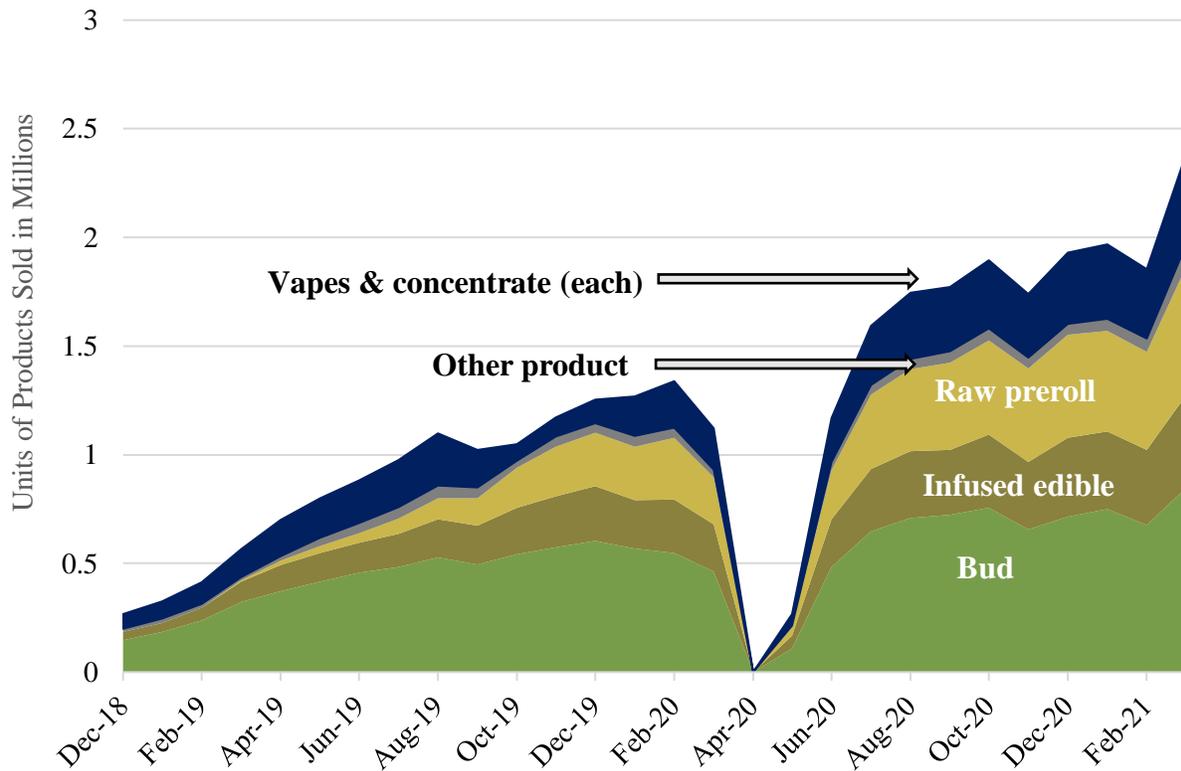
Table 7 shows the total units by product category per month. Table 8 shows the percentage that each product category made up of the total units of cannabis product sold in the legal non-medical adult-use cannabis market per month. There were no units of cannabis products sold in April 2019, due to a COVID-19-related emergency order which required adult-use retailers to temporarily halt sales.

In the non-medical adult-use market, the percentage of units sold that are buds have declined since 2018. In December 2018, buds made up 55% of total cannabis units sold, and in December 2020, buds made up 37% of total units sold.

In December 2018, vapes and concentrate (each) made up 25% of total units sold, and in December 2020, vapes and concentrate (each) made up 17% of total units sold. However, during the EVALI public health crisis and Commission quarantine on vape products [see [Section IX. Methods](#)], the percent that vapes and concentrates made up of total units sold fell to between 7-9% from October 2019 through December 2019.

In December 2018, infused edibles made up 15% of total units sold, and in December 2020, infused edibles made up 19% of total units sold. In December 2020, Raw pre-rolls made up 25% of units sold.

Table 7. Total Cannabis Units by Product Type (in millions per month)



Notes:

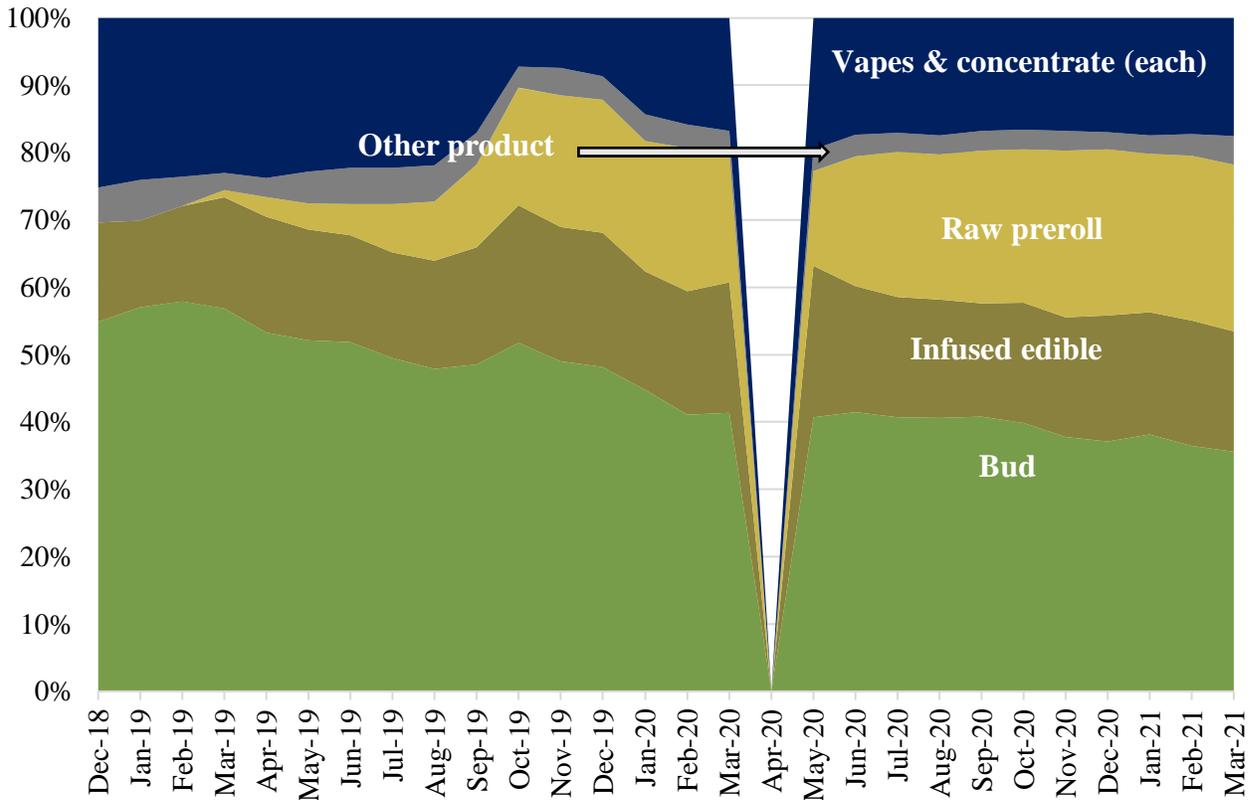
From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

Table 8. Percentage of Total Units of Cannabis Product Sold by Product Type (per month)



Notes:

From top to bottom: blue shaded section represents products classified as vapes or concentrate (each), gray shaded section represents products classified as other product [see note below], yellow shaded section represents products classified as raw pre-rolls, brown shaded section represents product classified as infused edibles, and green shaded section represents products classified as buds.

Raw pre-rolls category began to be used in March 2019, and April 2019 was the first month it was used for the entirety of the month.

Vape products category began to be used in December 2019.

Sales are not inclusive of tax.

Other products include: Concentrate, Infused (nonedible), Infused Beverage, Infused Pre-rolls, Kief, Shake/trim, Shake/trim (by strain), and Suppository.

XI. Literature Overview – THC Health Effects

The purpose of this section is to identify studies and reports about the effects of high THC cannabis on the human body in medical and adult-use contexts. Literature includes both peer-review scientific articles and gray literature, such as government reports.

Medical Cannabis

At the time of this report in May 2021, 36 states, D.C., and four territories have some form of legal cannabis use (medicinal or adult-use).¹⁵ The increase in availability of cannabis products has created further need to research and assess the efficacy of cannabis use for medicinal purposes, including consideration of specific THC and CBD concentrations.³⁰ The most comprehensive review of the evidence regarding the health effects of cannabis was published in 2017 by the National Academies of Sciences, Engineering, and Medicine. The report “*The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research*” considered 10,700 abstracts on the effects of medicinal cannabis for a variety of diseases, illnesses, and disorders. The authors then narrowed down the abstracts by quality and date published.²¹

Researchers found approximately 100 different conclusions after extensive review of the relevant literature. The findings were separated into categories depending on the weight of evidence, including: Conclusive Evidence; Substantial Evidence; Moderate Evidence; Limited Evidence; and No or Insufficient Evidence to Support the Association. The authors formulated four recommendations based on the collection of evidence. The first recommendation states that to develop comprehensive evidence, public agencies, philanthropic and professional organizations, private companies, and clinical and public health research groups should provide funding and support for a national cannabis research agenda. The second recommendation seeks to improve research quality by suggesting that the U.S. Department of Health and Human Services (HHS), NIH, and CDC jointly fund a workshop to develop a set of research standards. The third recommendation asks for improved surveillance capacity. Finally, the authors suggests that the CDC, NIH, and FDA address the barriers to this realm of research.²¹

As a result of the gaps in research on health effects of cannabis and cannabinoids, we do not draw a conclusion regarding the effects of high THC medical cannabis on the human body [see Section VIII. Medicinal Cannabis Research Considerations], and instead offer considerations to increase research capacity [see Section XV. Considerations].

Non-medical Adult-use Cannabis

The average THC concentration in cannabis increased in past decades,^{12,31} although major variation in products and raw plants exist.³² Studies of legal cannabis identify an early trend

toward increasing THC concentrations in flower.²⁷ For example, Jikomes and Zoorob found that in Washington's legal market, THC concentration in flower increased from 2014 to 2015, then stabilized from 2015 to 2017.¹³ Concentrates from cannabis flower did not show a trend toward increasing THC concentration after 2015.¹³

Researchers also identify a shift in market share toward cannabis product types with traditionally higher THC concentrations (i.e., inhalable extracts or concentrates increasing in market share) and a decreasing market share of flower.^{2,13,27,28,33} Thus, Commission staff conclude that there is substantial demand for cannabis products with high THC content.

Next, Commission staff assessed relevant literature reviews and gray literature reports examining high THC cannabis products and health effects [see Section XVII. Appendix Tables 1 and 2]. We framed this review by using the Lower Risk Cannabis Use Guidelines, a public health tool based on systemic literature reviews.³⁴ These guidelines identify that the use of lower THC cannabis products and products with a high CBD:THC ratio as one evidence-based strategy to reduce cannabis-related harms.

High THC content products are generally associated with higher risks of various (acute and chronic) mental and behavioral problem outcomes. For public health, clinical health, and safety, users should know the nature and composition of the cannabis products, and ideally use cannabis products with low THC content. Given the evidence of CBD's attenuating effects on some THC-related outcomes, it is advisable to use cannabis containing high CBD:THC ratios. [Evidence Grade: Substantial.]³⁴

Staff identified two high-quality government reports assessing THC in products in Colorado and Washington State. The Colorado report concluded:

Evidence is moderate to strong concerning THC concentration and the association with mental health effects in adolescents, young adults and adults... Specific to THC concentrate products, evidence is insufficient when examining the association to dependence and acute health effects. Our ability to make unbiased, evidence-based statements on the potential health effects of marijuana products containing high THC concentration is limited until further scientific research can be conducted and the evidence shared or published. Therefore, in the best interest of public health, we suggest funding research to answer these questions.¹

The Washington report concluded:

Research available to date documents that THC content in cannabis products contributes to adverse health effects in a dose-response manner. This increased risk imposed from

using higher potency cannabis products is particularly concerning for young users and those with certain pre-existing mental health conditions. To further our understanding on the impact of high-THC content cannabis products, more research is needed.⁴

Regarding the requirement to examine whether THC concentration should be capped in cannabis and cannabis products, we reviewed articles for policy options and analysis pertaining to cannabis THC concentrations limits. In these reports, researchers identify multiple policy mechanisms that could impact THC concentrations in the legal market, including, tax based on concentration, concentration related price floors, THC concentration limits, initial restrictions on edibles and high-THC products, dose/serving size labeling requirements, and data collection requirements to monitor trends and harms.^{27,35} However, specific assessment of these policy options and potential unintended consequences have not been extensively studied; therefore, Commission staff do not find sufficient evidence to recommend a concentration cap, especially in light of potential unintended consequences discussed below.

XII. Illicit Market Considerations

Researchers are beginning to study regulatory options regarding concentration.³⁶ For example, Shover and Humphreys (2020), state that a concentration cap on products sold in the legal market could limit harms related to consumption of high-concentration products and development of new high-potent products until the science catches up with policy.³⁷ However, authors acknowledge that conversely, a concentration cap could incentive illicit market cannabis consumption and do not recommend a ban on certain product types.³⁷

As legal sales data from Washington, Oregon, Nevada, and Massachusetts show, there is substantial demand for high-THC concentration cannabis and product types.^{2,13,27,28,33} Restricting access in the legal markets could incentivize consumers to turn to the illicit markets. This could result in public health harms associated with unregulated and untested products in the illicit market (i.e., illegally produced and illegally sold “black market”). It could also negatively impact social equity effects through reliance on enforcement mechanisms to curb illicit market sales, such as fines and arrests.³⁸ Such harms may disproportionately impact people and communities most harmed by cannabis prohibition due to the racial and ethnic inequities in cannabis prohibition enforcement.

XIII. Limitations

There are many limitations to this report, which are outlined below.

Data and Analysis

This report includes only legal sales data on cannabis product types. There is no knowledge of what percentage of products under the “potentially high THC products” category, such as concentrates and vape products, are high THC. Importantly, the extent of the illicit market activity (i.e., legally produced but illegally sold “gray market” or illegally produced and sold “black market”) and home-grown products involving high THC cannabis products are unknown.

Literature

The peer-review literature is relatively sparse on the impact of high-THC cannabis on the human body. Beyond barriers to using cannabis for research, the makeup of cannabis, which includes over 100 chemical components, makes isolating the effect of one of these components, such as THC, difficult. Due to time, financial, and language restraints, this report reviewed English-language literature related to high-THC cannabis, but the Commission did not conduct a comprehensive literature review of all studies available. Nonetheless, the number of review articles and quality work from other governmental agencies (e.g., Colorado and Washington), provide strong overviews of the current evidence basis.

The major barriers to conduct cannabis research with products [see Section VII. Challenges to Conducting Research with Cannabis] are a contributing factor to this limited knowledge base. Gray literature, including governmental reports, complete some of these gaps but are limited by the lack of peer-review, sample size, and comparability.

XIV. Conclusion and Recommendation

After an assessment of the available Massachusetts data and current literature pertaining to the effects of high THC cannabis on the human body and concentration limits for consumption and manufacturing purposes, Commission staff find that evidence is not sufficient to recommend a specific concentration cap at this time [see Section IX. Methods and Section X. Results].

We additionally conclude that THC concentration in cannabis has increased and that there is substantial demand for cannabis products with high THC content in the legal markets. As a result of the gaps in the research, we do not draw a conclusion regarding the effects of high-THC medical cannabis on the human body [see Section VIII. Medicinal Cannabis Research Considerations]. Instead, staff offer considerations to increase research capacity [see Section XV. Considerations] for evidence-based decisions regarding THC limits in the future. Non-medical use of high THC products and greater doses of cannabis products by some populations appear associated with greater health and public safety risks than lower dose use; however, additional research is needed. Based on current finding, THC use presents some health risks for youth, and risks appear greater for youth using high-THC cannabis products.⁴

To address some current data limitations, Commission staff offer multiple considerations to increase data capacity [see [Section XV. Considerations](#)]. A reassessment may be warranted as the scientific evidence basis matures in the future as additional research is conducted.

XV. Considerations

Research Considerations

Policy preceding science is a fundamental limitation in the Commission’s ability to make evidence-based policy decisions. For this reason, below are key research considerations based on gaps in the current knowledge of THC concentration.

Consideration 1: Research could assess the newly enacted 5 milligram THC research dose with varying concentrations of other chemical components in cannabis plants, specifically CBD, to assess differential effects regarding interactions and cannabinoid ratios (“cannabinoid profiles”).^{10,20,39} [see [Section VII. Challenges to Conducting Research with Cannabis](#)].

Consideration 2: Research could assess how patients in the current regulated markets use medical cannabis for varying illnesses and symptoms, including dosage, modes of administration, THC concentration, and differential effects.²⁰ [see [Section VIII. Medicinal Cannabis Research Considerations](#)]. This assessment would both permit policymakers to better understand the concentration of products used by medical patients by their conditions and assist researchers in designing future studies.

Consideration 3: Researchers and clinicians could develop guidelines on how to administer medical cannabis of varying concentration, including indicators of potential side effects, and effectiveness for specified conditions.²⁰ [see [Section VIII. Medicinal Cannabis Research Considerations](#)]. It is also important to consider the labeling and packaging of products to ensure that patients understand the concentration dosage of their prescription. This would assist medical providers to be able to guide patients in more safe and effective ways to consume cannabis for medicinal treatment.

Consideration 4: Researchers could study policy mechanisms that could impact THC concentrations in the legal market, including tax based on concentration, concentration related price floors, THC limits, initial restrictions on edibles and high-THC products, dose or serving size labeling requirements, and data collection requirements to monitor trends and harms.^{27,35} [see [Section XI. Literature Overview—THC Health Effects](#)].

Consideration 5: Research could assess how THC concentration levels in the legal market(s) affect purchasing and consumption behaviors in both the legal and illicit markets [see [Section XIII. Limitations](#)]. This assessment would help guide policy decisions in harm reduction ways to

prevent adverse clinical and public health effects (i.e., prevent increased cannabis use disorders, cannabis induced psychosis, and health care utilization) and public safety effects (i.e., eliminating illicit market activity and prevent criminal justice incident inequalities).

Consideration 6: Alternative data sources, such as sales data and seed-to-sale data, could be used for future research. These metrics would provide a more accurate picture of how patients are using medicinal cannabis.

Policy and Regulatory Considerations

All States

Consideration 1: States enacting and implementing cannabis policies for medicinal and/or adult-use could implement effective seed-to-sale tracking to monitor legal cannabis throughout the production lifecycle, including testing of each batch’s cannabinoid profile, including THC concentration [see Section IX. Methods]. In regard to concentration, seed-to-sale tracking permits comprehensive monitoring of product purchase behaviors and sales, which helps facilitate research and guide policymakers and regulators on varying issues, including surveilling high concentration cannabis products through the legal supply chain, enforcing concentration-related regulations, collecting concentration-based taxes (if applicable), preventing high-concentration product diversion to youth, who may experience disproportionate harm from its use, and help to inform research to eliminate the illicit market²⁰ [see Section VIII. Medicinal Cannabis Research Considerations].

Consideration 2: Similar to Massachusetts, other states with comprehensive seed-to-sale tracking systems could consider building databases to allow for public health and safety purposes in addition to compliance purposes, like the Commission’s [Open Data Platform](#).

Consideration 3: Similar to New York, other states’ medicinal cannabis regulations could require that patients’ condition and symptoms are included in the seed-to-sale tracking system, which allows linkage of that information to medical cannabis purchasing behaviors.²⁰ This may help facilitate research, including assessment of effective THC concentration of cannabis products and modes of administration for treating specified illnesses and symptoms [see Section VIII. Medicinal Cannabis Research Considerations]. Additionally, platforms should track all concentration levels and pricing in order for research to better evaluate patient utilization.

Consideration 4: Recent research at Boston Children’s Hospital finds increased access/use of diverted medical market cannabis from the regulated market to youth in sample of youth in outpatient treatment for cannabis use in Massachusetts²⁴ [see Section VIII. Medicinal Cannabis Research Considerations]. To prevent this diversion, specifically for high-THC cannabis, which is more harmful to some youth (i.e., youth without medical need),⁴ states could limit high-THC

cannabis products in the medical market to specify efficacious medical conditions, such as cancer pain, to dispense high-THC cannabis to those within a specified age bracket, such as 18-21 or 18-25 [see [Section VIII. Medicinal Cannabis Research Considerations](#)]. To enact this, however, would require better research on which types of cannabis and cannabis products, and specified cannabinoid profiles, are advised for which medical conditions (see “Consideration 6”).

Consideration 5: States could license and regulate research facilities conducting research using the cannabis plant [see the Commission’s [Guidance on Licensure and Research License FAQ](#)]. The Commission licenses Marijuana Research Facilities as well as issues Research Permits (i.e., research projects to be conducted within the licensed facilities). This process could expedite research hindered by barriers to conducting research with cannabis from the only federally approved cultivator, the University of Mississippi.

Consideration 6: States could develop evidence-based cannabis prescribing guidelines for cannabis products based on the currently available scientific evidence and in collaboration with clinicians and cannabis researchers²⁰ [see [Section VIII. Medicinal Cannabis Research Considerations](#)]. This would permit more effective prescribing of products, including THC concentration, to medical patients with specified diagnoses, illnesses, and symptoms for which scientific studies have shown efficacy.

Consideration 7: States could implement additional taxes on non-medical, high-THC cannabis. This public health-based approach would theoretically disincentivize buyers from purchasing higher THC cannabis, potentially averting adverse effects of non-medical high-THC cannabis use; however, there are implementation challenges to this approach [see [Report, *Feasibility of Alternative Tax Schemes: A Legislative Report and Recommendation for Massachusetts*](#)].

Consideration 8: States could implement regulations to only permit high-THC cannabis products for medical patients, and more specifically for medical patients with specified diagnoses, illnesses, and symptoms for which scientific studies have shown efficacy; however, assessment(s) of unintended consequences is warranted [see [Section VIII. Medicinal Cannabis Research Considerations](#)]. Additionally, assessments of medical efficacy specifically for youth are warranted.

Massachusetts

Consideration 1: The Commission could change its data collection process to link cannabinoid concentrates to product sales, as the current mechanism requires hand-coding [see [Section IX. Methods and Section XIII. Limitations](#)]. Better linkage could enable precise research regarding the specific levels of THC, CBD, and other cannabinoids in products to accurately classify “high THC concentration” products.

Consideration 2: The Commission could work with its seed-to-sale tracking vendor to provide definitions for each of the cannabis product type classification categories which could increase data quality and reliability [see Section IX. Methods]. This would increase the utility of tracking data for research purposes.

Consideration 3: The Commission could continue its work to increase research capacity within the state, such as the implementation and regulation of Research Facility Licensing and Research Permits, and advocate for decreasing federal barriers in cannabis research.

Consideration 4: The Commonwealth could add the Marijuana Module to [BRFSS](#). There are costs associated with adding additional questions [see Section IX. Methods].

Consideration 5: The Commonwealth could add cannabis questions to [YRBSS](#) and [YHS](#). There are costs associated with adding additional questions [see Section IX. Methods].

Consideration 6: The Commonwealth could add cannabis questions to PRAMS. There are costs associated with adding additional questions [see Section IX. Methods].

Consideration 7: The Commonwealth could use industry seed-to-sale tracking data combined with the Regional Center for Poison Control and Prevention out of Boston Children’s Hospital to surveil both high THC concentration cannabis among youth and potential diversion from the legal medicinal market [see Section VIII. Medicinal Cannabis Research Considerations].

Consideration 7: Massachusetts could develop and add a section on high-THC cannabis products for inclusion in the Responsible Vendor Training (RVT) curriculum, notably, the Advanced Core Curriculum to be implemented in July 2022 [see Section IX. Methods].

Education Considerations

Consideration 1: Research shows that most cannabis consumers do not fully understand labeling and what constitutes high THC concentration products³ [see Section IX. Methods]. To increase understanding, the Commission could create additional public awareness materials or build upon its campaign, “More About Marijuana,” to educate consumers on what constitutes high-THC concentration cannabis.

Consideration 2: States’ medical societies (e.g., Mass Medical Society) and educational programs could add cannabis as medicine to clinical and training curriculums, ensuring providers are educated in the current state of data of cannabis efficacy and concentration [see Section VIII. Medicinal Cannabis Research Considerations].

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XVII. Appendix

I. Acronyms

Acronyms	Term
BRFSS	Behavioral Risk Surveillance Factor System
CBD	Cannabidiol
CDC	Center for Disease Control
COVID-19	Coronavirus Disease
CSA	The Federal Controlled Substances Act of 1970
D.C.	District of Columbia
DEA	U.S Drug Enforcement Agency
DPH	Department of Public Health
EVALI	E-Cigarette or Vaping Associated Lung Injury
FDA	U.S. Food and Drug Administration
HHS	U.S Health and Human Services
IRB	Internal Review Board
NIDA	National Institute on Drug Abuse
NIH	National Institute of Health
PRAMS	Pregnancy Risk Assessment Monitoring System
THC	Tetrahydrocannabinol
U.S.	United States
YMS	Youth Health Survey

II. Literature Search Tables

Table 1. Literature Search Results—THC Health Effects: Peer-reviewed literature reviews

Study	Methods	Outcomes	Findings	Limitations	doi
Increasing delta-9-tetrahydrocannabinol (Δ -9-THC) content in herbal cannabis over time: systematic review and meta-analysis. Cascini et al. 2012.	Literature review and meta-analysis	Cannabis THC concentrations	Cannabis potency is increasing.	Review is limited by inconsistencies across studies included (e.g., cannabis sample differences and methods differences).	10.2174/1874473711205010032
Changes in delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) concentrations in cannabis over time: systematic review and meta-analysis. Freeman et al. 2020.	Literature review and meta-analysis	Cannabis THC and CBD concentrations	Cannabis THC concentrations have increased from 1970 to 2017. CBD concentrations have remained stable.	Limited data on CBD.	10.1111/add.15253
Cannabis Legalization and Acute Harms from High Potency Cannabis Products: A Narrative Review and Recommendations for Public Health. Matheson and Le Foll 2020.	Literature overview	Examined impacts of cannabis product diversification	Authors provide three approaches to minimize harm: (1) early restriction of cannabis edibles and high-potency products; (2) clear and consistent labelling that communicates dose/serving size and health risks; (3) implementation of robust data collection frameworks to monitor harms	Review is limited by gaps in the literature	10.3389/fpsy.2020.591979
Cannabis Potency and Contamination: A Review of the Literature. McLaren et al. 2008	Literature review	Examined cannabis potency and contamination	Cannabis potency in the U.S. has increased. There is wide variation in product potency. Studies that report CBD find lowered CBD levels. Mixed evidence for titration patterns.	Studies do not always report CBD levels; and The sample sizes of cannabis products may not be representative.	10.1111/j.1360-0443.2008.02230.x
What Do You Know About Maryjane? A systematic review of the current data on the THC:CBD ratio. Zeyl, et al. 2020	Literature review	Literature regarding THC:CBD ratios, percentages, and/or weighted amounts	THC:CBD ratios included – 1:0, 22:1, 2:1, 1:1, 1:6, 1:9, 1:20, 1:33, 1:50, and 0:1. No substantive conclusions can be drawn from current literature.	Relatively few studies meeting inclusion criteria. Current research limited by lack of blinding.	10.1080/10826084.2020.1731547

Biomarkers for the effects of cannabis and THC in healthy volunteers. Zuurman, et al. 2008	Literature review	Asses which biomarkers are found useful in early cannabinoid drug development, and how cannabis affects different central nervous system functions	Cannabis/THC affected a wide range of Central Nervous System domains. Some CNS domains showed indications of depression at lower potency and stimulation at higher potency.	Test standardization needed	10.1111/j.1365-2125.2008.03329.x
Cannabis Use and its Association with Psychological Disorders. Urtis, et al. 2020.	Literature Review and Meta-Analysis	Connections between Cannabis Use and various mental illnesses such as psychosis, depression, and anxiety	“Cannabis Use disorder is highly prevalent in individuals with mental illness”, Connections between cannabis use and psychosis, depression, and anxiety require further investigation.	“It may possible to conduct structured studies of cannabis dosage in patients using medical cannabis.”	Cannabis Use and its Association with Psychological Disorders (nih.gov)
Medical cannabis and mental health: A guided systematic review	Literature Review and Meta-Analysis	“Considers the potential influences of the use of cannabis for therapeutic purposes on areas of interest to mental health professionals”	Cannabis has potential for the treatment of PTSD and substance abuse disorders. Cannabis use does not appear to increase risk of harm to self or others. More research is needed to characterize the mental health impact of medical cannabis.	None listed.	10.1016/j.cpr.2016.10.002

Table 2. Literature Search Results—THC Health Effects: Gray literature

Report	Potency definition	Sample	Methods	Relevant outcomes assessed	Findings	Link
THC Concentration in Colorado Marijuana: Health Effects and Public Health Concerns. <i>Colorado Department of Public Health and Environment (CDPHE) (2020).</i>	“THC potency” is interpreted as THC concentration”	Colorado youth and adults	Prevalence and rate estimates of varying consumption outcomes; literature review	Poison control center exposures and associated product type; BRFSS method of use by product type and concentration; Literature review of health effects	Moderate evidence that individuals who use marijuana with THC concentration >10% THC are more likely than non-users to be diagnosed with a psychotic disorder, such as schizophrenia; Substantial evidence that THC intoxication can cause acute psychotic symptoms, which are worse with higher dose; Moderate evidence that adolescents/young adults who use marijuana with higher THC concentration (>10% THC) are more likely than non-users to continue use; Moderate evidence that adolescents/young adults who use marijuana with higher THC concentration (>10% THC) are more likely than non-users to develop future mental health symptoms and disorders; Insufficient evidence to determine whether or not the use of THC concentrates is more likely to result in adverse acute health effects than the use of other forms of marijuana; and Insufficient evidence to determine whether or not the use of THC concentrates is more likely to result in adverse acute health effects than the use of other types of marijuana.	https://www.thenmi.org/wp-content/uploads/2020/08/THC-Concentration-in-Colorado-Marijuana-CDPHE-8.3.2020.pdf
Cannabis Concentration and Health Risks: A report for the Washington State Prevention Research Subcommittee (PRSC). <i>Joint University of Washington and Washington State University Workgroup (2020).</i>	“Potency of cannabis is typically defined by the amount of THC within cannabis products, with varying cut-offs; and more recently by mode of cannabis administration of high THC potency manufactured products such as cannabis concentrates (wax, shatter), and liquid extracts used in vaping devices and infused edibles (candy or cookies).”	Washington adults and youth	Literature review and study overviews	Epidemiology of dabbing, vaping, edible behaviors; contaminants; observation study of real-world use; poison control center data; traffic safety; cannabis use disorder, potency and psychotic disorders; adolescent use; use during pregnancy	“THC content of cannabis products contributes to adverse health effects in a dose-response manner” Concentrate use in increasing in WA; High-potency cannabis use can have adverse lifelong effects; Youth are at particularly risk of adverse effects; Marginalized populations may be more adversely impacted; and Evidence of dose-response effect between THC concentration and health effects.	https://adai.uw.edu/wordpress/wp-content/uploads/2020/11/Cannabis-Concentration-and-Health-Risks-2020.pdf
The Health Effects of Cannabis and	“The amount of drug required to produce a	-	Literature review of various topics	Various health outcomes	National data on non-herb cannabis lacks	https://www.nap.edu/catalog/24625/the-health-effects-

Cannabinoids: The Current State of Evidence and Recommendations for Research. <i>National Academies of Sciences, Engineering, and Medicine.</i> (2017).	specific level of effect."					of-cannabis-and-cannabinoids-the-current-state
Cannabis Policy: Public Health and Safety Issues and Recommendations. <i>United States Senate Caucus on International Narcotics Control.</i> (2021).	-	-	Literature overview of various topics	Impacts of increasing cannabis potency	THC concentration in cannabis has increased products with high THC may be associated with acute intoxication, poison control calls, Cannabinoid Hyperemesis, emergency room visits, addiction and dependence, psychosis, increasing near-daily use. More research is needed on short and long-term effects of high THC cannabis.	https://www.drugcaucus.senate.gov/content/cannabis-policy-public-health-and-safety-issues-and-recommendations

Note: The Massachusetts Department of Public Health recommends the following reports for further background information:

- (1) [Marijuana Baseline Health Study \(2019\)](#);
- (2) [The Safety and Generally Recognized as Safe \(GRAS\) Status of the Proposed Use of Hulled Hemp Seeds in Human Food.](https://www.fda.gov/files/food/published/GRAS-Notice-765.pdf)
- (3) [National Toxicology Program \(NTP\). Toxicology and Carcinogenesis Studies of 1-Trans-Delta9-Tetrahydrocannabinol. TR 446.](#)

Table 3. Legal sales data to examine market share and/or THC concentration

Article	State(s) and timeframe	Relevant methods	Relevant outcomes assessed	Findings	Limitations	doi
Variation in cannabis potency & prices in a newly legal market: Evidence from 30 million cannabis sales in Washington State. Smart et al. 2017.	Washington state (2014-2016)	Variation and potency trends (for flower and concentrate) assessed through descriptive statistics and linear regressions. Hedonic price regression to examine price relationships.	Product type variation and trends, potency variation and trends, impact of potency on price	Flower's market share has declined from 2014 to 2016, while cannabis extracts have increased; THC concentrations for flower are higher than illicit market estimates; High THC flower has increased in market share of flower products sold; and a one percentage point increase in THC potency associated with a 1–2% price increase.	Potency analysis for flower and inhalation extract only.	10.1111/add.13886
Big data on a big new market: Insights from Washington State's legal cannabis market Caulkins et al. 2018.	Washington state (2014-2016)	Descriptive statistics and data visualization methods.	Price across product types. Potency across product types. Market share of product types. Relationship between price and potency.	Average THC concentration for flower was 20%; Average concentration for extracts was 70%; and Wax/shatter/resin/dab segment showed fastest growth in WA market during study time frame.	No information about the consumer; and Potency levels for edibles not included due to inconsistent reporting.	10.1016/j.drugpo.2018.03.031
The Cannabinoid Content of Legal Cannabis in Washington State Varies Systematically Across Testing Facilities and Popular Consumer Products. Jikomes and Zoorob 2018.	Washington state (2014-2017)	Stains identified in seed-to-sale data matched to Leafly data and classified by chemotype.	THC and CBD concentrations in flower and concentrate product. Between lab differences in cannabinoid concentrations.	Of the three chemotypes, most WA legal cannabis falls in Chemotype 1 (i.e., high THC, low CBD); Measurement varies across testing labs; Mean THC flower increased from 2014-2015 and plateaued from 2015-2017; and Similarly, researchers find mean THC concentrates have not increased from 2015-2017.	Limited by quality and inconsistency of reporting in data accessed.	10.1038/s41598-018-22755-2
Price and product variation in Washington's recreational cannabis market. Davenport 2019.	Washington state (2014-2017)	Text-analytic methods to estimate potency for edibles and identify product subgroups.	Potency patterns and trends, including estimating potency for edibles.	Market share of flower is decreasing, while share for extracts is increasing; and High CBD chemotypes are increasing in popularity but are still uncommon.	Potency data reliability concerns; Data availability, present analysis limited to WA state only; and Data not available after 2017.	10.1016/j.drugpo.2019.08.004
How high: differences in the developments of cannabis markets in two legalized states. Firth et al. 2020.	Washington state (2014-2016) and Oregon (2016-2018)	Descriptive statistics and data visualization methods.	Product variety, product potency, price trends	Market share of flower decreased in WA and OR; and Cannabis products with high THC are cheaper than those with high CBD.	Data availability and comparability differences between states.	10.1016/j.drugpo.2019.102611

Availability, retail price and potency of legal and illegal cannabis in Canada after recreational cannabis legalization. Mahamad et al. 2020.	Canada (2018)	Descriptive statistics of retail data from retailer websites and Weedmaps.	Potency of legal and illicit products	Average THC concentrations is increasing; and On average, illicit herb was higher THC potency than legal herb.	Data was largely obtained through website review, accuracy was unknown.	10.1111/dar.13069
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