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Essays on the Availability, Legality, and Reasons for Using Hemp-Derived Cannabinoid
Products

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for the degree Doctor of Philosophy

in

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by

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LIST OF ABBREVIATIONS

AB	Assembly Bill
aOR	Adjusted Odds Ratio
aRR	Adjusted Risk Ratio
CBD	Cannabidiol
CBG	Cannabigerol
CBN	Cannabinol
CI	Confidence Interval
CSA	Controlled Substances Act
DEA	US Drug Enforcement Agency
EVALI	E-cigarette or Vaping-Associated Lung Injuries
FDA	US Food and Drug Administration
HHC	Hexahydrocannabinol
EMM	Estimated Marginal Mean
IPTW	Inverse Probability of Treatment Weighting
LLT	Lowest Level Term
MedDRA	Medical Dictionary for Regulatory Activities
PT	Preferred Term
SOC	System Organ Class
SMD	Standardized Mean Differences
THC	Tetrahydrocannabinol
US	United States

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ABSTRACT OF THE DISSERTATION

Essays on the Availability, Legality, and Reasons for Using Hemp-Derived Cannabinoid Products

by

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Doctor of Philosophy in Public Health (Epidemiology)

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Background: The passage of the 2018 United States (US) Farm Bill, which separated “hemp” from the definition of “marijuana”, resulted in the growth of a market for hemp-derived cannabinoid products, such as cannabidiol (CBD) and delta-8-THC. Hemp-derived cannabinoid products are those derived from *Cannabis Sativa L.* that contain less than 0.3% delta-9-THC,

which is the main psychoactive compound in marijuana. Although the new and unregulated marketplace of hemp-derived cannabinoid products poses several health risks to consumers, there is a scarcity of data to answer basic epidemiological questions about their use.

Methods: This dissertation is comprised of three chapters. Chapters 2 and 3 utilized data from a nationally representative sample of US adults recruited from the Ipsos KnowledgePanel to describe the characteristics and motivations of hemp-derived cannabinoid product use (Chapter 2) and estimate the association between lifetime use of delta-8-THC and state marijuana use laws and regulations on delta-8-THC, independently and in combination (Chapter 3). Chapter 4 used data from a sample of e-commerce tobacco retailers serving San Diego County to examine the association between hemp-derived cannabinoid product availability and website visits and assess compliance with state hemp regulations.

Results: In Chapter 2 we found that there is heterogeneity among US adults who use hemp-derived cannabinoid products in terms of sociodemographic characteristics, medical versus recreational reasons for use, and specific medical reasons for use. Most adults used CBD for medical reasons and delta-8-THC for recreation. Anxiety and pain were the most frequently reported medical conditions for using hemp-derived cannabinoid products. In Chapter 3 we showed that medical and recreational marijuana use laws and delta-8-THC restrictions were associated with a lower probability of delta-8-THC use. Among states with recreational marijuana use laws, having delta-8-THC restrictions decreased the probability of delta-8-THC use. In Chapter 4 we found that tobacco retailers that offered hemp-derived cannabinoid products received more website visits, and a sizeable number of retailers were out of compliance with state hemp regulations.

Conclusion: These data suggest that hemp-derived cannabinoid products are widely available, used to relieve medical symptoms, and used as a legal substitute to marijuana. Evidence-based education, federal regulations, and better enforcement of existing state laws for hemp-derived cannabinoid products are crucial for ensuring consumer safety and limiting youth access, both essential for protecting public health.

CHAPTER 1: INTRODUCTION

Cannabinoids are a class of chemical compounds that are unique to the marijuana plant (1). All cannabinoids interact with the human endocannabinoid system in various ways and most have not been extensively studied (2, 3). The most well-known and researched cannabinoid is delta-9-tetrahydrocannabinol (delta-9-THC), which is the main psychoactive compound in the marijuana plant and hereafter referred to as marijuana.

Although prior research and policy discussions have focused primarily on delta-9-THC, there are at least 144 other cannabinoids that can be extracted or synthesized from the marijuana plant (4). The passage of the 2018 United States (US) Farm Bill, which separated “hemp” from the definition of “marijuana”, resulted in the growth of a market for cannabinoid products derived from hemp (5). Hemp-derived cannabinoid products are those derived from *Cannabis Sativa L.* that contain less than 0.3% delta-9-THC. The most well-researched and prevalent hemp-derived cannabinoid products are cannabidiol (CBD) and delta-8-tetrahydrocannabinol (delta-8-THC) (6-8). However, there are numerous others, most of which are psychoactive, that are widely available to consumers throughout the US. The remaining portion of the introduction section will delve into the relevant public health literature and the research findings pertaining to hemp-derived cannabinoid products.

Review of Public Health Studies on CBD

Following the passage of the US Farm Bill, major retailers, such as Walgreens, began introducing topical and edible CBD products, resulting in their heightened accessibility across multiple states (9). To date, all US states except Idaho, South Dakota, and Nebraska allow the sale of CBD products under state law, but with different regulations (10). One study has shown

that public interest in CBD has increased across the US since 2015 (6). Despite widespread consumer interest, only one nationally representative study in 2023 has estimated that 21.1% of US adults used CBD in the past year (11).

Nevertheless, there is relatively little evidence on the use of CBD products, and no national estimates of motivations for using them. Several surveys conducted using online convenience samples have described the characteristics, use patterns, and motivations of CBD users, with some of these studies suggesting that products containing CBD may have gained popularity due to their marketing as an alternative option to treat medical conditions (7, 12-15). Furthermore, research examining the e-commerce landscape for CBD products has documented several of tobacco retailers making explicit health claims about the benefits of products containing CBD, even though the Food and Drug Administration (FDA) prohibits such marketing claims and has issued several warning letters to CBD product manufacturers (16).

Review of Public Health Studies on Delta-8-THC and Other Hemp-Derived Cannabinoid Products

Delta-8-THC has a nearly identical chemical structure with delta-9-THC and produces similar psychoactive effects, such as euphoria, visual distortion, and difficulty thinking and speaking (13, 17, 18). While delta-8-THC naturally occurs in *Cannabis Sativa L.* in small amounts, most commercially available delta-8-THC is synthesized from CBD (19).

Online surveys of delta-8-THC consumers have found that the most common routes of administration were eating (64%) and vaping (48%), about half (51%) used delta-8-THC to treat health conditions, and the majority (78%) did not inform their primary provider of their delta-8-THC use (20). Most consumers of delta-8-THC (83%) also reported using marijuana, with many using delta-8-THC as a substitute for marijuana (57%) or as a substitute for pharmaceutical drugs

(59%), which is concerning as delta-8-THC products have not been evaluated or approved for safe use by the FDA (20). However, these prior studies were conducted using online trends data or data from online convenience samples that were not nationally representative and relied on self-reported state of residence. One nationally representative survey estimated that the past-year prevalence of delta-8-THC was 11.9% (11). Another national study found that delta-8-THC may also be commonly used by youth, with 11.4% of 12th-grade students having used delta-8-THC in their lifetime (21). However, both studies did not explore the motivations for using delta-8-THC or other psychoactive hemp-derived cannabinoid products. Therefore, there is a gap in the literature regarding the reasons for using various hemp-derived cannabinoid products, which is especially important if individuals are using them as a substitute for the treatment of medical conditions. Therefore, the aim of paper 1 is to provide the first nationally representative measure of the motivations behind hemp-derived cannabinoid product use.

While some US states have banned or regulated the sale of delta-8-THC, many states do not have any laws in place or have difficulty assessing compliance with and enforcement of existing regulations (22). The absence of federal laws and the minimal state regulations governing the use of hemp-derived cannabinoid products allow for cannabinoid product manufacturers to evade restrictions and regulatory systems that are in place for delta-9-THC products, such as age restrictions and testing requirements (23). Consequently, over 2,000 reports of adverse events linked to delta-8-THC consumption have been received by the FDA and the national poison control centers between December of 2020 and February of 2022, many of which required intervention and involved pediatric patients (24-27). Many of the symptoms presented in adverse events related to delta-8-THC use were similar to those reported for acute delta-9-

THC intoxication (e.g., anxiety and paranoia), but there were several unique symptoms that could have stemmed from unregulated manufacturing methods (e.g., muscle spasms) (28).

Previous studies have shown that public interest in delta-8-THC has increased in recent years across the US (6, 29, 30) and delta-8-THC use was higher in states with restrictions on marijuana use and without restrictions on delta-8-THC, suggesting that delta-8-THC may be used as a legal substitute to marijuana (8, 20, 29, 30). However, there have been no nationally representative studies to date that have examined whether delta-8-THC use is higher in states with restrictions on marijuana use. Therefore, paper 2 aims to assess the association between marijuana use laws, delta-8-THC regulations, and delta-8-THC use.

Hemp-Derived Cannabinoid Product Availability

The availability and promotion of new and loosely regulated substances, such as hemp-derived cannabinoid products, can pose significant health risks to consumers. These products often do not undergo the same testing and quality control procedures as regulated marijuana and tobacco products and are subject to little regulation around their marketing, distribution, and sales (23, 31, 32). Unregulated manufacturers may be potentially exposing users to mislabeled products that may result in poisonings, especially among children, or contaminated products that may result in serious injury, as in the case of e-cigarette or vaping use-associated lung injury (EVALI) (24, 27, 33).

Hemp-derived cannabinoid products are not subject to tobacco or marijuana regulations in most US states. Therefore, tobacco retailers may be able to subvert certain distribution and marketing restrictions (e.g., making explicit health claims about the benefits of tobacco products) by broadening their product range to include hemp-derived cannabinoid products. Prior research has already shown that tobacco retailers, such as vape shops, often sell substances other than

nicotine, including kratom, CBD, and delta-8-THC (16, 34-36). Unlike marijuana products sold within state-controlled marijuana regulatory systems, hemp-derived cannabinoid products are not obligated to adhere to these regulations which, for example, restrict marketing practices that appeal to youth, require products undergo testing for adulterants, or have purchasing age requirements (8, 23, 32).

Many delta-8-THC users obtain their products online or from stores that are not marijuana dispensaries (20). While a few studies have examined the availability of delta-8-THC products in physical stores within states that restrict their sale, the e-commerce marketplace for cannabinoid products has not been assessed. Unlike brick-and-mortar retailers, e-commerce platforms are often not specified within local and state policies governing tobacco product advertising, marketing, and sales (37). Additionally, online retailers may operate across state lines, potentially avoiding local regulations (37, 38). More research is needed to comprehensively assess the landscape of hemp-derived cannabinoid product availability within the online marketplace and to understand how online retailers navigate various tobacco regulatory frameworks and restrictions across different states. For example, California's Assembly Bill 45 (AB-45) prohibits the manufacture or sale of inhalable industrial hemp products, including retailers that offer products through a delivery service (i.e., e-commerce), except for the sole purpose of sale in other states. As a part of this law, inhalable industrial hemp products cannot contain characterizing flavors other than natural terpenes, may not be sold to consumers under 21 years of age, and may not be sold in retail locations in California (39). Therefore, paper 3 aims to examine the availability of hemp-derived cannabinoid products in online vape shops and assess compliance with local regulations in California.

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CHAPTER 2: REASONS FOR USING HEMP-DERIVED CANNABINOID PRODUCTS AMONG US ADULTS

Abstract

Background: The 2018 US Farm Bill resulted in a market for cannabinoid products derived from *Cannabis sativa L.* that contain <0.3% delta-9-THC. Despite limited scientific literature, these products are widely available across the US, often accompanied by unsubstantiated health claims. Understanding the characteristics and motivations of cannabinoid product users is crucial for effective regulation of these products.

Methods: We conducted a cross-sectional survey study of adults 18 years or older using the probability-based Ipsos Knowledge panel, which represents 97% of US households. We assessed lifetime CBD, delta-8-THC, CBN, CBG, and HHC use and awareness. Using multivariate logistic regression models, we investigated associations of demographic and health behavior characteristics with cannabinoid product use. Lastly, we used the Medical Dictionary for Regulatory Activities to system organ class and preferred term categories to code medical reasons for cannabinoid product use.

Results: Delta-8-THC, CBN, CBG, and HHC awareness among U.S. adults was 23.2% (95% CI 20.9-25.7), 22.2% (95% CI 19.8-24.8), 5.0% (95% CI 3.8-6.4), and 3.8% (95% CI 2.9-5.0), respectively. Lifetime use of CBD was 35.2% (95% CI 32.7-37.9), compared with 7.7% (95% CI 6.5-9.1), 4.5% (95% CI 3.7-5.6), 1.3% (95% CI 0.9-1.9), and 1.5% (95% CI 1.0-2.1) for delta-8-THC, CBN, CBG, and HHC, respectively. The most frequently cited preferred terms for CBD use were anxiety (14.7%, 95% CI 13.0-16.6), pain (13.1%, 95% CI 11.5-15.0) and arthralgia (11.2%, 95% CI 9.5-13.2). Anxiety (18.6%, 95% CI 13.3-25.3), pain (15.2%, 95% CI 11.1-20.5) and insomnia (10.7%, 95% CI 7.4-15.3) were the most frequently cited preferred

terms for delta-8-THC use. Insomnia (15.4%, 95% CI 9.6-23.9), pain (11.1%, 95% CI 6.4-18.7) and anxiety (10.9%, 95% CI 6.0-19.0) were the most frequently cited preferred terms for CBN use.

Conclusion: In this nationally representative survey, we show that the use of cannabinoid products is prevalent, with many individuals using them for medical purposes. More research is needed to examine which health outcomes are associated with the use of cannabinoid products. Due to the lack of industry standards for cannabinoid products, additional regulation is crucial to ensure product safety and protect public health.

Introduction

The passage of the 2018 United States (US) Farm Bill, which separated “hemp” from the definition of “marijuana”, resulted in the growth of a market for cannabinoid products (1). Hemp-derived cannabinoid products are those derived from *Cannabis Sativa L.* that contain less than 0.3% delta-9-THC, which is the main psychoactive compound in marijuana. The most well-researched and prevalent hemp-derived cannabinoid products are cannabidiol (CBD) and delta-8-THC. However, there are numerous others, most of which are psychoactive, that are widely available to consumers throughout the US.

The new and unregulated marketplace of hemp-derived cannabinoid products poses several health risks to consumers. First, in US states where marijuana use remains restricted, cannabinoid products, such as delta-8 THC, may be used as substitutes for individuals to achieve similar euphoric effects (i.e., to get “high”) (2,3). Cannabinoid products may not be a safe substitution for marijuana as they are not tested for their safety and may contain adulterants resulting from their synthesis. Already, there have been over 2,000 reports of adverse events linked to delta-8-THC consumption received by the FDA and the National Poison Control

Centers between December 2020 and February 2022, many of which required medical intervention and involved pediatric patients (4–6). Furthermore, many cannabinoid products, such as CBD, might be used to relieve medical symptoms, even though they have not been approved for therapeutic applications (7,8). Therefore, it is critical to understand the prevalence and motivations behind hemp-derived cannabinoid product use.

There is a scarcity of data to answer basic epidemiological questions about hemp-derived cannabinoid products such as: who has used them and why? Most of the scientific literature on hemp-derived cannabinoid products has focused on CBD and delta-8-THC and relies on online surveys that use convenience samples (9–11). Assessment of online communities has shown that people may be using CBD for self-treatment of medical symptoms (7). Although CBD has been approved only for the treatment of epilepsy, in the form of EPIDIOLEX®, retailers that sell CBD have been shown to make unsubstantiated health claims related to its properties (12,13). Reasons for using delta-8-THC have not been extensively assessed, with several convenience sample surveys showing that most adults use it for reasons similar to delta-9-THC (9,10). Nevertheless, there are very few studies about cannabinoid products other than CBD and delta-8-THC, such as cannabitol (CBN), a commercially available cannabinoid that has some limited scientific literature about its use (14,15).

To date, there is only one nationally representative study among US adults that has assessed past-year hemp-derived cannabinoid product use (16). This study estimated the prevalence of past-year CBD, delta-8-THC, CBN, and cannabigerol (CBG) use to be 21.1%, 11.9%, 5.2%, and 4.4%, respectively. However, it did not explore the motivations for use and did not include hexahydrocannabinol (HHC), which is becoming increasingly widespread and has already been linked to adverse events (17). A national study of 12th grade students found that

delta-8-THC may also be commonly used by youth, with 11.4% of adolescents having used delta-8-THC in their lifetime (18). Similar to the first national survey, this study did not examine motivations for delta-8-THC use and did not assess any other hemp-derived cannabinoid products. Therefore, there is a gap in the literature regarding the reasons for using various hemp-derived cannabinoid products, which is especially important if individuals are using them as a substitute for the treatment of medical conditions.

Herein, we estimate the awareness and lifetime use of hemp-derived cannabinoid products using a nationally representative sample of US adults. Furthermore, we identify the characteristics of individuals who use cannabinoid products and their reasons for using these products. Among adults who use hemp-derived products for a medical purpose, we categorize and compare their reasons through the use of a standardized medical dictionary. The results of this study may be used by policymakers to make better-informed decisions about their regulation, and public health officials to develop better education campaigns for consumers.

Methods

Study sample

The study sample consisted of participants in a US National Institute on Drug Abuse-funded survey on CBD use conducted between October and November of 2023. Respondents were recruited from Ipsos KnowledgePanel®, the largest probability-based online panel in the US. The Ipsos KnowledgePanel® consists of about 55,000 panelists whose demographics are weighted to the US census. To recruit panel members, Ipsos uses probability selection algorithms for random-digit telephone dialing and address-based sampling methods. Households without computer and/or internet access are provided with a web-enabled device (e.g., laptop) and free monthly internet access. The KnowledgePanel® is representative of 97% of the adult US general

population, covering all 50 states and Washington DC, and has been widely used to provide representative statistics on drug use in the US (19–22).

The KnowledgePanel® recruited a random sample of 4,505 adults aged 18 years or older to complete the survey, with a survey completion rate of 63.9%. There were 1,525 adults who qualified for the survey. The survey over-sampled CBD users, resulting in 1008 adults who have ever used CBD and 515 adults who have never used CBD. The study sample covered all 50 US states and Washington DC. The survey was administered in both English and Spanish and the average completion time for the survey was 10 minutes. The survey was approved by the Human Research Protections Program at the University of California San Diego.

Measures

Hemp-Derived Cannabinoid Product Awareness and Use. Participants were asked about their familiarity with different cannabinoid products using four separate questions that asked, ‘Before today, have you ever heard of 1) delta-8-THC, 2) cannabitol (CBN), 3) cannabigerol (CBG), and 4) hexahydrocannabinol (HHC)?’ with response options (1 = Yes; 2 = No).

Awareness of cannabidiol (CBD) was not assessed since the sampling method of the survey oversampled CBD users. Those who reported hearing about a cannabinoid product were then asked ‘Have you ever, even once, used 1) CBD, 2) delta-8-THC, 3) CBN, 4) CBG, and 5) HHC?’ with response options (1 = Yes; 2 = No).

Reasons for Hemp-Derived Cannabinoid Product Use. Participants who reported ever using a cannabinoid product, were asked “Which purposes have you ever used 1) CBD, 2) delta-8-THC, 3) CBN, 4) CBG, and 5) HHC products for?” with response options (1 = I have ONLY used the products for medical purposes; 2 = I have ONLY used the products for recreation; 3 = I have used the products for BOTH medical purposes and recreation). Medical purposes were

defined as “to treat or decrease symptoms of a health condition” and recreation was defined as “to get pleasure, feel good, or relax but not to treat a specific condition”. Individuals who reported using a cannabinoid product for medical reasons were asked “What health condition(s) have you taken 1) CBD, 2) delta-8-THC, 3) CBN, 4) CBG, and 5) HHC for?” with the option to input up to 10 different conditions using an open text field.

Socio-demographics. Information was provided by the KnowledgePanel about the sociodemographic characteristics of each respondent.

Age. Age was provided as a categorical variable with four levels: 1) 18-29, 2) 30-44, 3) 45-59, and 4) 60+ years.

Sex. Sex was provided as a dichotomous variable 1) male or 2) female.

Race/ethnicity. Race/ethnicity was provided as a categorical, five-level variable: 1) White, non-Hispanic, 2) Black, non-Hispanic, 3) Other, non-Hispanic, 4) Hispanic and 5) 2+ races, non-Hispanic. For the purposes of this analysis, the Other, non-Hispanic and 2+ races, non-Hispanic were combined.

Education. Education level was provided as a categorical, four-level variable: 1) No high school diploma or GED, 2) High school graduate (high school diploma or the equivalent GED), 3) Some college or Associate degree, and 4) Bachelor’s degree or higher.

Self-reported physical health, mental health, and quality of life. The survey asked each participant to self-rate their physical and mental health and quality of life on a 5-point Likert scale ranging from “1) Poor” to “5) Excellent”. As previously done by other studies using this question (23,24), we categorized all three variables by grouping the “Fair/Poor”, “Good”, and “Very Good/Excellent” categories.

Marijuana Use. The survey asked each participant about their use of other substances. Marijuana use was assessed using the question “In your entire lifetime, have you ever used cannabis (i.e., marijuana) that contained THC?” and collected as a dichotomous variable (yes/no).

Other Drug Use. Other drug use was assessed using the question “In your entire lifetime, have you ever used any of the following substances?” with response options 1) Cocaine or crack, 2) Non-prescription stimulants like methamphetamine or speed, 3) Psychedelics like LSD or psilocybin-containing mushrooms, 4) Empathogens like, MDMA also known as ecstasy or molly, 5) Dissociative substances like ketamine, 6) Any other drugs like heroin, inhalants, or solvents, and 7) None of the categories apply. Endorsement of any category 1-6 use was coded as “other drug use.”

Medical Reasons Coding. The health conditions reported by individuals who used cannabinoid products for medical reasons were coded using a standardized medical language, the Medical Dictionary for Regulatory Activities (MedDRA) (25). MedDRA uses a five-level hierarchical structure with the "System Organ Class" (SOC) at the top. SOC represents terms based on an anatomical or physiological system, etiology, or function. Three levels beneath the SOC is the "Preferred Term" (PT), which represents a distinct medical concept related to a symptom, sign, or disease diagnosis. The lowest tier in the hierarchy is the "Lowest-Level Term" (LLT), which captures how observations are described in the everyday language by a consumer. All LLTs are associated with a single PT and all PTs are associated with a single SOC. The MedDRA hierarchy is shown in Figure 1.

To translate medical reasons for using cannabinoids to MedDRA, three annotators (N.S., K.Y., and W.K.) assigned all medical reasons to MedDRA LLTs. There was no restriction on the

number of medical reasons or LLTs a cannabinoid product could be used for. For example, the medical reason “arthritis and asthma,” would be mapped to the LLTs “Arthritis” and “Asthma”. Annotators had moderate agreement on LLT selections (Cohen’s $K=0.718$), with differences primarily resulting from lexical variations allowed in MedDRA (e.g., MedDRA has distinct LLTs for “difficulty sleeping” and “poor sleep”). Coder agreement was higher at the PT (Cohen’s $K=0.784$) and SOC (Cohen’s $K=0.841$) levels, therefore analyses were performed at these levels.

Statistical analyses

To produce population-based estimates, we used survey weights, which accounted for the oversampling of CBD users in the study design. All percentages were weighted by population parameters based on the findings of the most recent US Current Population Survey. A survey-specific poststratification adjustment was used to account for survey non-response, as well as non-coverage or under-sampling and oversampling resulting from the survey-specific sampling design. All characteristics were categorical and were thus summarized using counts and proportions. Weighted frequencies and the corresponding 95% confidence intervals (CIs) of cannabinoid product awareness and use were calculated to determine the proportion for each of the cannabinoid products assessed. Differences in frequency distributions for each outcome and the sociodemographic, substance use, and self-reported health correlates were examined by cannabinoid product awareness and use.

Among people who endorsed lifetime use of a cannabinoid product, we calculated weighted frequencies and corresponding 95% CIs for the proportion who used the product for medical and recreational purposes. If a respondent reported using a cannabinoid product for both medical reasons and recreation, they were included in the proportion for both categories.

Multivariable analyses were conducted for every hemp-derived cannabinoid product assessed. For each sociodemographic characteristic, the cannabinoid product used (CBD, delta-8-THC, CBN, CBG, HHC) was treated as the outcome and a multivariable log-binomial regression model was used to calculate adjusted odds ratios (aORs) and corresponding 95% CIs adjusting for all other sociodemographic, substance use, and self-reported health factors. All multivariable analyses used complete case analysis. All analyses were performed using R, version 4.1 (R Project for Statistical Computing).

Results

Over a third (35.2% (95% CI 32.7-37.9)) of US adults reported ever using CBD (Table 1). Overall, 23.2% (95% CI 20.9-25.7) of adults had heard of delta-8-THC, and 22.2% (95% CI 19.8-24.8) had heard of CBN compared with 5.0% (95% CI 3.8-6.4) for CBG and 3.8% (95% CI 2.9-5.0) for HHC. Similarly, 7.7% (95% CI 6.5-9.1) reported ever using delta-8-THC compared with 4.5% (95% CI 3.7-5.6), 1.3% (95% CI 0.9-1.9), and 1.5% (95% CI 1.0-2.1) for CBN, CBG, and HHC respectively.

Females reported higher CBD use, while males reported greater use of delta-8-THC, CBN, CBG, and HHC (Table 1). Adults aged 30-44 had the highest use of most hemp-derived cannabinoids, except CBG, which was highest among 18-29-year-olds. Non-Hispanic White adults reported higher CBD and delta-8-THC use, whereas Hispanic adults reported more CBN, CBG, and HHC use. Those with some college education used more CBD and CBG, while those without a high school diploma reported higher delta-8-THC and HHC use, and high school graduates reported higher CBN use. Adults who have used marijuana or other drugs, as well as those rating their quality of life as "fair" or "poor," reported higher use of all hemp-derived

cannabinoids. More adults with "fair" or "poor" physical health used all the assessed hemp-derived cannabinoids except CBG, which was highest among those with "good" physical health. Similarly, more adults with "fair" or "poor" mental health used all assessed cannabinoids except HHC, which was highest among those with "good" mental health.

After adjusting for other sociodemographic characteristics, there were no differences in hemp-derived cannabinoid use by participant race/ethnicity or mental health (Table 5: Supplement A). Female sex, younger age, marijuana and other drug use, and good physical health and quality of life increased the odds of CBD use. Younger age, marijuana use, and other drug use also increased the odds of delta-8-THC use. High school education and marijuana and other drug use increased the odds of CBN use, while some college education and other drug use increased the odds of CBG use. Having no high school degree or some college education, and using other drugs also increased the odds of HHC use.

Significantly more US adults used CBD for medical purposes (71.9%, 95% CI 68.9-74.7) than recreation (47.1%, 95% CI 43.9-50.3). Conversely, more adults used delta-8-THC for recreation (76.1% 95% CI 67.0-83.3) than for medical reasons (50.9; 95% CI 42.6-59.2). Although more people reported using CBN, CBG, and HHC for medical reasons than recreation, the difference in the two proportions was not statistically significant, as denoted by the overlapping confidence intervals (Table 2).

Psychiatric disorders were the most common SOC of medical reasons for using delta-8-THC 48.6% (95%CI 41.3-55.9), CBN 36.8% (95%CI 26.3-48.8), and HHC 46.8% (95%CI 23.7-71.5) while musculoskeletal and connective tissue disorders 35.5% (95%CI 32.3-38.8) were the most common SOC for using CBD and general disorders and administration site conditions 39.5% (95%CI 16.2-68.8) were the most common SOC for using CBG (Table 3). General

disorders and administration site conditions were the second most frequently mentioned SOC for delta-8-THC 20.0% (95%CI 14.1-27.5), CBN 20.3% (95%CI 12.0-32.4), and HHC 16.5% (95%CI 5.3-41.1) while psychiatric disorders were the second most prevalent SOC for using CBD 33.2% (95%CI 30.3-36.3) and CBG 35.5% (95%CI 15.6-62.2).

As shown in Table 4, the most frequently cited PTs for CBD use were anxiety (14.7%, 95% CI 13.0-16.6), pain (13.1%, 95% CI 11.5-15.0), and arthralgia (11.2%, 95% CI 9.5-13.2). Anxiety (18.6%, 95% CI 13.3-25.3), pain (15.2%, 95% CI 11.1-20.5), and insomnia (10.7%, 95% CI 7.4-15.3) were the most frequently cited PTs for delta-8-THC use. Insomnia (15.4%, 95% CI 9.6-23.9), pain (11.1%, 95% CI 6.4-18.7) and anxiety (10.9%, 95% CI 6.0-19.0) were the most frequently cited PTs for CBN use. Interestingly, the most frequently cited PT category for CBG use could not be determined, coded as “unevaluable event”, followed by anxiety (11.1%, 95% CI 6.4-18.7) and pain (11.1%, 95% CI 6.4-18.7). The most commonly cited PTs for HHC use were anxiety (12.0%, 95% CI 3.5-33.7), insomnia (11.3%, 95% CI 2.9-35.3) and pain (10.1%, 95% CI 1.9-40.0). The full list of PTs is shown in Table 6: Supplement B.

Discussion

Our results are consistent with previous research on cannabinoid product awareness and use. We found that lifetime use of CBD among US adults was 35.2%, which aligns with another national survey that showed that 21.1% of US adults used CBD in the past year (16). However, our findings showed a lower prevalence of lifetime delta-8-THC, CBN, and CBG use compared to their estimates of past-year use, likely as a result of differences in the legal status of marijuana in participants’ states of residence between the two studies. To our knowledge, our study was the first to estimate the prevalence of HHC among US adults. Although the prevalence of HHC use

among our study sample was low (1.5%), it is still concerning due to recent cases of HHC-induced psychotic illness, particularly from legally purchased HHC products (17).

We found that the use of substances such as stimulants and hallucinogens was associated with the use of all hemp-derived cannabinoid products assessed and lifetime use of marijuana was associated with CBD, delta-8-THC, and CBN use. While demographic differences were not the focus of the current study, younger age and female sex were associated with an increased odds of CBD use, and younger age was also associated with an increased odds of delta-8-THC use. Similar to our results, a prior online survey found that younger age and marijuana use was associated with delta-8-THC use (9). However, while the previous survey found that identifying as male was associated with delta-8-THC use, we did not observe the same association. This discrepancy is likely because our survey asked about sex at birth, whereas their survey asked about gender identity and included an 'other' option. Although our results show that race/ethnicity was not associated with cannabinoid product use, an online survey found that young adults who self-reported their race as Black or other were less likely to use CBD (26). The inconsistency between the two studies may be due to differences in sample size as well as distributions of participants' race/ethnicity. Our study results show that individuals who rate their physical health and quality of life as “good” have higher odds of using CBD compared to those who rate their physical health and quality of life as “excellent” or “very good”. None of the previous surveys of cannabinoid product users examined mental health, physical health, or quality of life correlates (9,10,16,26).

Similar to online surveys of cannabinoid product users, we found that most individuals who use CBD, delta-8-THC, and CBN for medical reasons use these products for pain and anxiety (7,10,11,27). These medical applications may result from cannabinoid product

manufacturers' health claims about the therapeutic effects of their products for a variety of medical conditions including pain, arthritis, sleep disorders, and anxiety (13). For example, an analysis of over 2 million Twitter posts showed that pain, anxiety disorders, sleep disorders, and stress were the four main therapeutic claims for CBD (28). We found that insomnia was the most common medical reason for CBN use, which is not surprising given that many CBN manufacturers have been shown to make claims about the sleep-promoting effects of CBN (15). Many of the reasons for using hemp-derived cannabinoid products overlapped with reasons for marijuana use (29, 30). For example, findings from the International Cannabis Policy Survey conducted among adults in the US and Canada showed that many adults use marijuana to manage pain (53%), anxiety (52%), and sleep (46%) (29). Overall, our results show that US adults are using cannabinoid products for many different medical conditions, possibly as a result of manufacturers making health claims about these products and similarities between marijuana and cannabinoid products derived from hemp, even though there is a lack of evidence to support these claims.

The current study has some limitations. While the Ipsos KnowledgePanel consists of a nationally representative sample of panelists, the participant characteristics of the proposed study might differ from those of the general US population because our sampling method oversampled those who have ever used CBD. Furthermore, the characteristics of cannabinoid product users and reasons for use were measured in adults, and therefore may not be representative of younger populations. Lastly, we encountered sample size limitations that prevented us from examining individuals who use cannabinoid products more frequently. More studies are needed among established users to elucidate the health impacts of heavy cannabinoid product use.

In summary, our study reveals significant heterogeneity among US adults who use hemp-derived cannabinoid products in terms of sociodemographic characteristics, medical versus recreational reasons for use, and specific medical reasons for use. These differences underscore the complexity of the hemp-derived cannabinoid product landscape and the diverse motivations driving their use. Our findings highlight the need for future research into risk perceptions and health outcomes associated with the use of cannabinoid products. Proper regulation of cannabinoid products is crucial to ensure product safety, accurate labeling, and consistent potency, which are essential for protecting public health.

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Chapter 2, in full, is currently being prepared for submission for publication of the material. Satybaldiyeva, Nora; Yang, Kevin H.; Kepner, Wayne; Leas, Eric C. Nora Satybaldiyeva was the primary investigator and author of this paper.

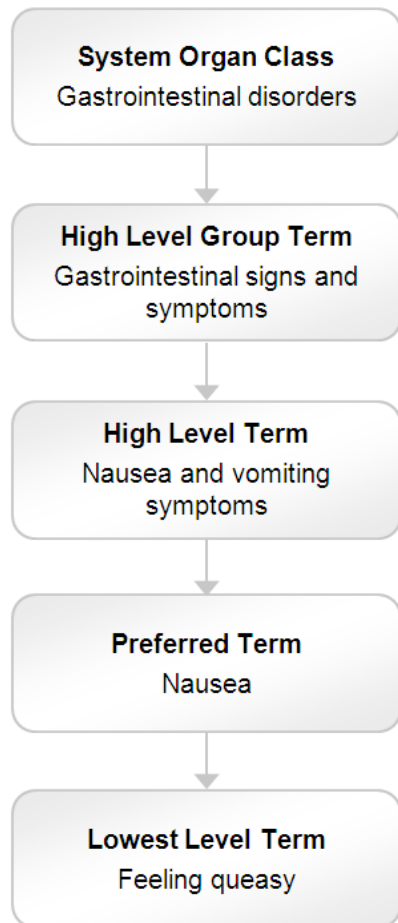


Figure 1: Example of a MedDRA hierarchy used for classifying medical conditions

Table 1: Demographic and behavioral characteristics of US adults by lifetime use of various hemp-derived cannabinoid products (n=1523)

Characteristic	Unweighted n	Overall Sample	CBD Ever Use % (95% CI)	Delta-8-THC Ever Use % (95% CI)	CBN Ever Use % (95% CI)	CBG Ever Use % (95% CI)	HHC Ever Use % (95% CI)
Ever Use			35.2 (32.7-37.9)	7.7 (6.5-9.1)	4.5 (3.7-5.6)	1.3 (0.9-1.9)	1.5 (1.0-2.1)
Sex							
Male	747	48.6 (45.4-51.8)	33.6 (30.1-37.2)	8.5 (6.9-10.4)	5.5 (4.2-7.2)	1.7 (1.0-2.8)	2.1 (1.3-3.3)
Female	776	51.4 (48.2-54.6)	36.8 (33.1-40.6)	6.9 (5.3-9.1)	3.6 (2.6-5.1)	1.0 (0.6-1.7)	0.9 (0.5-1.6)
Age							
18-29	227	19.5 (16.8-22.6)	37.3 (30.6-44.6)	9.7 (6.7-13.9)	4.7 (2.8-8.0)	1.7 (0.7-3.9)	1.5 (0.6-3.8)
30-44	382	25.7 (23.0-28.7)	39.9 (34.5-45.6)	12.1 (9.1-15.9)	5.0 (3.5-7.0)	1.6 (0.8-3.0)	2.6 (1.4-4.7)
45-59	377	23.5 (21.0-26.3)	33.7 (28.9-38.9)	5.8 (4.2-7.9)	4.3 (2.7-6.8)	1.5 (0.7-3.5)	0.9 (0.4-2.0)
60+	537	31.2 (28.4-34.0)	31.2 (27.5-35.2)	4.2 (2.9-6.1)	4.2 (2.8-6.3)	0.7 (0.3-1.5)	0.9 (0.4-1.9)
Race/ethnicity							
White, Non-Hispanic	1,082	61.8 (58.4-65.1)	38.8 (35.7-42.0)	8.6 (7.1-10.2)	4.4 (3.4-5.7)	1.1 (0.7-1.8)	1.2 (0.7-2.1)
Black, Non-Hispanic	148	12.1 (10.0-14.5)	32.3 (25.2-40.3)	7.1 (4.4-11.3)	2.3 (1.0-5.2)	1.1 (0.4-3.6)	1.6 (0.6-4.3)
Other/ 2+ Races, Non-Hispanic	110	9.1 (7.1-11.5)	24.4 (17.3-31.2)	5.9 (1.9-16.7)	5.1 (2.5-9.9)	1.1 (0.1-7.1)	1.6 (0.4-6.6)
Hispanic	183	17.0 (14.4-20.1)	30.2 (23.9-37.4)	5.8 (3.5-9.6)	6.3 (3.8-10.4)	2.3 (1.0-5.2)	2.0 (1.0-4.3)
Education							
No high school diploma or GED	92	9.0 (6.9-11.5)	32.9 (23.5-43.9)	9.0 (5.2-14.9)	3.6 (1.6-7.9)	1.8 (0.7-5.1)	2.8 (1.1-6.9)
High school graduate	396	28.8 (25.9-31.9)	34.2 (29.4-39.4)	8.3 (5.8-11.7)	6.6 (4.6-9.4)	1.5 (0.8-3.0)	1.0 (0.4-2.4)
Some college/ Associate's degree	433	26.6 (24.0-29.4)	39.8 (34.8-45.0)	8.2 (6.2-10.6)	4.0 (2.6-5.9)	1.9 (1.0-3.7)	2.6 (1.4-4.6)
Bachelor's degree or higher	602	35.6 (32.7-38.7)	33.2 (29.5-37.2)	6.5 (4.9-8.7)	3.5 (2.3-5.2)	0.6 (0.3-1.3)	0.6 (0.3-1.4)

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval; GED = General Educational Development
 Other drug use includes stimulant, sedative, and tranquilizer misuse, and cocaine, non-prescription stimulant, psychedelic, empathogen, dissociative substance, and other drug use.

Table 1 continued: Demographic and behavioral characteristics of US adults by lifetime use of various hemp-derived cannabinoid products (n=1523)

Characteristic	Unweighted n	Overall Sample	CBD Ever Use % (95% CI)	Delta-8-THC Ever Use % (95% CI)	CBN Ever Use % (95% CI)	CBG Ever Use % (95% CI)	HHC Ever Use % (95% CI)
Marijuana Use							
Yes	954	46.6 (43.5-49.8)	59.5 (55.1-63.8)	15.8 (13.4-18.5)	8.8 (7.1-10.8)	2.5 (1.7-3.7)	2.8 (1.9-4.0)
No	514	49.3 (46.1-52.5)	12.6 (10.6-14.8)	0.6 (0.2-1.9)	0.8 (0.3-2.2)	0.3 (0.1-1.5)	0.3 (0.1-1.8)
Other Drug Use							
Yes	569	28.5 (25.9-31.3)	55.7 (50.1-61.2)	17.0 (14.0-20.5)	9.7 (7.4-12.5)	3.4 (2.1-5.3)	3.7 (2.3-5.8)
No	954	71.5 (68.7-74.1)	27.1 (24.4-29.8)	4.0 (2.9-5.4)	2.5 (1.7-3.6)	0.5 (0.3-1.0)	0.6 (0.3-1.1)
Physical Health							
Excellent/ Very Good	656	44.9 (41.7-48.1)	29.9 (26.5-33.4)	6.5 (5.0-8.4)	4.2 (3.0-5.8)	1.1 (0.6-2.0)	1.3 (0.8-2.3)
Good	530	34.9 (31.9-38.0)	36.4 (32.0-41.1)	7.4 (5.7-9.6)	4.3 (2.9-6.3)	1.7 (0.9-3.2)	1.3 (0.6-3.0)
Fair/ Poor	319	19.2 (16.8-21.8)	44.5 (37.9-51.3)	11.0 (7.6-15.7)	5.8 (3.7-9.0)	1.0 (0.4-2.3)	2.1 (1.1-3.8)
Mental Health							
Excellent/ Very Good	717	48.2 (45.0-51.4)	29.4 (26.2-32.8)	4.7 (3.5-6.2)	4.2 (3.1-5.8)	0.9 (0.4-1.9)	1.3 (0.8-2.2)
Good	437	29.2 (26.3-32.2)	34.1 (29.5-39)	7.0 (5.3-9.1)	4.7 (3.2-7.0)	1.5 (0.8-2.8)	1.8 (0.9-3.8)
Fair/ Poor	352	21.5 (19.0-24.3)	49.2 (42.3-56)	15.6 (11.7-20.5)	5.2 (3.4-8.0)	2.1 (1.1-3.8)	1.4 (0.7-2.8)
Quality of Life							
Excellent/ Very Good	812	55.5 (52.2-58.6)	28.9 (26.0-32.0)	5.4 (4.1-7.0)	4.0 (3.0-5.5)	1.1 (0.6-1.9)	1.1 (0.6-1.9)
Good	471	29.4 (26.5-32.4)	41.4 (36.2-46.8)	8.5 (6.6-10.9)	4.5 (3.1-6.6)	1.1 (0.6-2.1)	1.2 (0.5-3.0)
Fair/ Poor	224	14.2 (12.1-16.6)	46.1 (38.1-54.2)	14.6 (10.0-20.9)	6.4 (3.8-10.6)	3.0 (1.5-5.9)	3.2 (1.6-6.2)

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval; GED = General Educational Development
Other drug use includes stimulant, sedative, and tranquilizer misuse, and cocaine, non-prescription stimulant, psychedelic, empathogen, dissociative substance, and other drug use.

Table 2: Motivations for hemp-derived cannabinoid product use among a national sample of US adults (n=1523)

Cannabinoid	Ever Use Unweighted n	Reason for Use weighted % (95% CI)	
		Medical	Recreation
Cannabidiol (CBD)	1,008	71.9 (68.9-74.7)	47.1 (43.9-50.3)
Delta-8-THC	191	50.9 (42.6-59.2)	76.1 (67.0-83.3)
Cannabinol (CBN)	112	62.7 (51.7-72.5)	45.2 (35.0-55.9)
Cannabigerol (CBG)†	31	69.8 (51.1-83.6)	46.6 (29.0-65.1)
Hexahydrocannabinol (HHC)†	33	59.8 (40.0-76.8)	54.1 (35.0-72.0)

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval;

Note: Categories do not sum to 100 because participants were allowed to select both medical and recreation use.

†Estimates are unstable as a result of small sample size

Table 3: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA System Organ Class (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA System Organ Class (SOC)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Musculoskeletal and connective tissue disorders	35.5 (32.3-38.8)	15.3 (9.8-23.1)	18.8 (11.0-30.0)	14.6 (4.1-40.8)	15.2 (3.4-47.6)
Psychiatric disorders	33.2 (30.3-36.3)	48.6 (41.3-55.9)	36.8 (26.3-48.8)	35.5 (15.6-62.2)	46.8 (23.7-71.5)
General disorders and administration site conditions	17.1 (15.1-19.3)	20.0 (14.1-27.5)	20.3 (12.0-32.4)	39.5 (16.2-68.8)	16.5 (5.3-41.1)
Nervous system disorders	6.7 (5.4-8.3)	7.8 (4.7-12.9)	6.5 (2.9-14.1)	4.5 (0.9-19.6)	10.3 (1.9-40.7)
Injury, poisoning and procedural complications	1.5 (0.9-2.6)	1.8 (0.3-10.1)	5.1 (1.7-14.6)	-	-
Gastrointestinal disorders	1.3 (0.8-2.2)	3.2 (1.5-6.6)	-	-	-
Skin and subcutaneous tissue disorders	0.8 (0.4-1.6)	-	-	-	-
Surgical and medical procedures	0.5 (0.2-1.2)	0.8 (0.2-3.4)	4.7 (1.6-13.2)	3.3 (0.4-23.4)	11.1 (3.2-32.3)
Metabolism and nutrition disorders	0.5 (0.2-1.0)	-	0.8 (0.1-5.6)	2.5 (0.3-19.9)	-
Infections and infestations	0.4 (0.2-0.9)	-	-	-	-
Reproductive system and breast disorders	0.4 (0.1-1)	-	-	-	-
Respiratory, thoracic and mediastinal disorders	0.4 (0.1-1)	0.6 (0.1-4.1)	-	-	-
Immune system disorders	0.3 (0.1-1)	-	-	-	-
Investigations	0.3 (0.1-0.8)	-	-	-	-
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0.2 (0.1-0.6)	-	4.9 (0.7-27.5)	-	-
Hepatobiliary disorders	0.2 (0-1.1)	-	-	-	-
Eye disorders	0.2 (0-0.7)	1.0 (0.3-4.2)	-	-	-
Congenital, familial and genetic disorders	0.2 (0-0.7)	-	2.0 (0.3-12.6)	-	-
Social circumstances	0.1 (0-0.6)	0.9 (0.1-5.2)	-	-	-
Blood and lymphatic system disorders	0.1 (0-0.5)	-	-	-	-
Vascular disorders	0.1 (0-0.4)	-	-	-	-
Renal and urinary disorders	0.1 (0-0.4)	-	-	-	-
Cardiac disorders	0 (0-0.2)	-	-	-	-

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval

†Estimates are unstable as a result of small sample size

Table 4: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Anxiety	14.7 (13.0-16.6)	18.6 (13.3-25.3)	10.9 (6.0-19.0)	17.3 (5.8-41.8)	12.0 (3.5-33.7)
Pain	13.1 (11.5-15.0)	15.2 (11.1-20.5)	11.1 (6.4-18.7)	14.2 (3.7-41.7)	10.1 (1.9-40.0)
Arthralgia	11.2 (9.5-13.2)	-	6.1 (2.9-12.5)	-	4.8 (0.6-30.2)
Insomnia	9.5 (8.1-11.2)	10.7 (7.4-15.3)	15.4 (9.6-23.9)	-	11.3 (2.9-35.3)
Arthritis	6.9 (5.6-8.5)	-	4.4 (1.9-10.0)	-	-
Back pain	-	4.7 (2.3-9.4)	-	-	-
Depression	-	6.0 (3.3-10.4)	-	-	7.6 (1.6-28.8)
Osteoarthritis	-	-	-	4.0 (0.8-18.1)	-
Sleep disorder	-	-	-	5.8 (1.2-23.3)	-
Unevaluable event	-	-	-	25.4 (5.6-66.3)	-

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval;

†Estimates are unstable as a result of small sample size

Note: Only top 5 PTs are presented for each cannabinoid product. For the full list of PTs, refer to Supplemental Table 2.

Table 5: Supplement A: Demographic and behavioral characteristics associated with lifetime hemp-derived cannabinoid product use among a national sample of US adults (n=1498)

Characteristic	CBD Ever Use aOR (95% CI)†	Delta-8-THC Ever Use aOR (95% CI)†	CBN Ever Use aOR (95% CI)†	CBG Ever Use aOR (95% CI)†*	HHC Ever Use aOR (95% CI)†*
Sex					
Male	Ref	Ref	Ref	Ref	Ref
Female	1.36 (1.02-1.81)	0.83 (0.57-1.21)	0.76 (0.47-1.22)	0.78 (0.38-1.63)	0.50 (0.21-1.18)
Age					
18-29	Ref	Ref	Ref	Ref	Ref
30-44	0.61 (0.38-0.97)	0.80 (0.46-1.39)	0.75 (0.37-1.51)	0.76 (0.25-2.34)	1.15 (0.40-3.32)
45-59	0.57 (0.36-0.91)	0.40 (0.23-0.71)	0.71 (0.33-1.52)	0.66 (0.21-2.06)	0.30 (0.08-1.18)
60+	0.48 (0.31-0.75)	0.32 (0.18-0.59)	0.71 (0.33-1.49)	0.40 (0.11-1.39)	0.36 (0.11-1.18)
Race/ethnicity					
White, Non-Hispanic	Ref	Ref	Ref	Ref	Ref
Black, Non-Hispanic	0.88 (0.54-1.42)	1.05 (0.57-1.95)	0.66 (0.27-1.62)	1.37 (0.36-5.17)	1.65 (0.47-5.81)
Other/2+ Races, Non-Hispanic	0.59 (0.34-1.03)	0.87 (0.26-2.84)	1.74 (0.79-3.84)	1.11 (0.24-5.09)	1.92 (0.47-7.85)
Hispanic	0.85 (0.53-1.36)	0.66 (0.32-1.39)	1.75 (0.84-3.63)	2.47 (0.97-6.31)	1.69 (0.58-4.94)
Education					
No high school diploma/ GED	0.67 (0.35-1.29)	1.05 (0.48-2.30)	1.02 (0.33-3.12)	1.73 (0.32-9.17)	5.29 (1.32-21.18)
High school graduate	0.96 (0.66-1.41)	1.45 (0.77-2.75)	2.37 (1.23-4.55)	2.31 (0.66-8.07)	1.56 (0.48-5.08)
Some college/ Associate's degree	1.34 (0.95-1.89)	1.46 (0.87-2.45)	1.21 (0.62-2.35)	3.17 (1.06-9.48)	4.68 (1.64-13.38)
Bachelor's degree or higher	Ref	Ref	Ref	Ref	Ref
Marijuana Use					
Yes	9.11 (6.70-12.39)	20.81 (6.81-63.56)	10.61 (3.62-31.11)	5.48 (0.79-37.92)	5.47 (0.56-53.64)
No	Ref	Ref	Ref	Ref	Ref

CBD = cannabidiol; CI = confidence interval; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; Ref= reference group.

Other drug use includes stimulant, sedative, and tranquilizer misuse, and cocaine, non-prescription stimulant, psychedelic, empathogen, dissociative substance, and other drug use.

† adjusts for all listed variables

*Estimates are unstable as a result of small sample size

Table 5: Supplement A continued: Demographic and behavioral characteristics associated with lifetime hemp-derived cannabinoid product use among a national sample of US adults (n=1498)

Characteristic	CBD Ever Use aOR (95% CI)†	Delta-8-THC Ever Use aOR (95% CI)†	CBN Ever Use aOR (95% CI)†	CBG Ever Use aOR (95% CI)†*	HHC Ever Use aOR (95% CI)†*
Other Drug Use					
Yes	1.55 (1.13-2.14)	2.14 (1.36-3.36)	2.00 (1.19-3.37)	3.55 (1.07-11.77)	3.49 (1.04-11.71)
No	Ref	Ref	Ref	Ref	Ref
Physical Health					
Excellent/ Very Good	Ref	Ref	Ref	Ref	Ref
Good	1.42 (1.00-2.01)	0.89 (0.51-1.54)	0.97 (0.50-1.86)	1.19 (0.36-3.96)	0.77 (0.30-1.94)
Fair/ Poor	1.21 (0.76-1.92)	0.64 (0.33-1.25)	0.94 (0.38-2.33)	0.18 (0.03-1.14)	0.51 (0.10-2.55)
Mental Health					
Excellent/ Very Good	Ref	Ref	Ref	Ref	Ref
Good	0.74 (0.49-1.10)	1.32 (0.72-2.42)	0.95 (0.48-1.87)	1.51 (0.44-5.18)	1.06 (0.43-2.61)
Fair/ Poor	1.04 (0.62-1.72)	2.03 (0.92-4.46)	0.51 (0.24-1.08)	1.29 (0.31-5.32)	0.20 (0.05-0.81)
Quality of Life					
Excellent/ Very Good	Ref	Ref	Ref	Ref	Ref
Good	1.56 (1.05-2.32)	1.00 (0.55-1.80)	0.92 (0.45-1.91)	0.62 (0.17-2.25)	1.03 (0.40-2.62)
Fair/ Poor	1.57 (0.87-2.84)	1.43 (0.67-3.07)	1.32 (0.47-3.70)	2.91 (0.72-11.69)	5.22 (1.15-23.66)

CBD = cannabidiol; CI = confidence interval; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; Ref= reference group.

Other drug use includes stimulant, sedative, and tranquilizer misuse, and cocaine, non-prescription stimulant, psychedelic, empathogen, dissociative substance, and other drug use.

† adjusts for all listed variables

*Estimates are unstable as a result of small sample size

Table 6: Supplement B: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Anxiety	14.7 (13.0-16.6)	18.6 (13.3-25.3)	10.9 (6.0-19.0)	17.3 (5.8-41.8)	10.9 (6.0-19.0)
Pain	13.1 (11.5-15.0)	15.2 (11.1-20.5)	11.1 (6.4-18.7)	14.2 (3.7-41.7)	11.1 (6.4-18.7)
Arthralgia	11.2 (9.5-13.2)	3.8 (1.8-7.5)	6.1 (2.9-12.5)	3.3 (0.4-23.4)	6.1 (2.9-12.5)
Insomnia	9.5 (8.1-11.2)	10.7 (7.4-15.3)	15.4 (9.6-23.9)	2.9 (0.3-23.8)	15.4 (9.6-23.9)
Back pain	7.1 (5.8-8.6)	4.7 (2.3-9.4)	3.3 (1.1-9.0)	-	3.3 (1.1-9.0)
Arthritis	6.9 (5.6-8.5)	2.7 (1.2-6.0)	4.4 (1.9-10.0)	3.3 (0.4-23.4)	4.4 (1.9-10.0)
Myalgia	5.2 (4.0-6.6)	1.2 (0.4-3.7)	1.7 (0.5-5.4)	1.9 (0.2-16.8)	1.7 (0.5-5.4)
Depression	3.7 (2.8-4.9)	6.0 (3.3-10.4)	3.5 (1.4-8.5)	2.9 (0.3-21.1)	3.5 (1.4-8.5)
Headache	1.8 (1.2-2.7)	1.9 (0.7-5.3)	0.6 (0.1-4.2)	-	0.6 (0.1-4.2)
Migraine	1.6 (1.0-2.4)	1.6 (0.4-5.4)	-	2.0 (0.2-16.4)	-
Unevaluable event	1.6 (0.9-3.0)	2.6 (0.7-9.0)	5.6 (1.3-20.8)	25.4 (5.6-66.3)	5.6 (1.3-20.8)
PTSD	1.3 (0.8-2.1)	1.5 (0.4-5.2)	1.0 (0.1-6.9)	-	1.0 (0.1-6.9)
Stress	1.3 (0.8-2.2)	3.0 (1.3-6.4)	1.7 (0.4-6.7)	2.9 (0.3-22.6)	1.7 (0.4-6.7)
Inflammation	1.1 (0.6-1.8)	-	2.4 (0.7-7.3)	-	2.4 (0.7-7.3)
Fibromyalgia	0.9 (0.5-1.7)	-	1.2 (0.3-4.8)	-	1.2 (0.3-4.8)
Feeling of relaxation	0.7 (0.4-1.3)	0.6 (0.1-4.4)	-	-	-
Neck pain	0.6 (0.3-1.2)	-	-	-	-
Neuropathy peripheral	0.6 (0.3-1.1)	0.4 (0.1-3.1)	2.3 (0.8-7.1)	-	2.3 (0.8-7.1)
Rheumatoid arthritis	0.6 (0.3-1.3)	0.6 (0.1-4.2)	-	-	-
Sleep disorder	0.6 (0.3-1.3)	0.9 (0.2-3.7)	1.3 (0.3-5.6)	5.8 (1.2-23.3)	1.3 (0.3-5.6)
Osteoarthritis	0.5 (0.3-1.1)	0.3 (0.0-2.5)	-	4.0 (0.8-18.1)	-
Seizure	0.5 (0.2-1.2)	0.7 (0.1-4.8)	1.0 (0.1-7.1)	-	1.0 (0.1-7.1)
Attention deficit hyperactivity disorder	0.4 (0.1-1.0)	2.4 (0.8-6.5)	-	-	-
Epilepsy	0.4 (0.2-0.9)	0.4 (0.1-3.2)	0.7 (0.1-5.0)	2.5 (0.3-19.9)	0.7 (0.1-5.0)
Multiple sclerosis	0.4 (0.1-1.0)	-	-	-	-

PTSD = Post-traumatic stress disorder; CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

Table 6: Supplement B continued: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Neuralgia	0.4 (0.2-0.9)	-	-	-	-
Sciatica	0.4 (0.2-0.9)	0.5 (0.1-3.7)	-	-	-
Muscle spasms	0.3 (0.1-0.7)	-	-	-	-
Dysmenorrhoea	0.3 (0.1-0.9)	-	-	-	-
Skin disorder	0.3 (0.1-0.7)	-	-	-	-
Joint injury	0.3 (0.1-1.0)	-	-	-	-
Mental disorder	0.3 (0.1-1.0)	1.3 (0.3-5.3)	2.0 (0.3-12.6)	-	2.0 (0.3-12.6)
Parkinson's disease	0.3 (0.1-0.7)	0.4 (0.1-2.7)	1.3 (0.3-5.4)	-	1.3 (0.3-5.4)
Intervertebral disc degeneration	0.3 (0.1-0.8)	0.4 (0.1-3.1)	-	2.0 (0.2-16.4)	-
Decreased appetite	0.2 (0.0-0.7)	-	0.8 (0.1-5.6)	-	0.8 (0.1-5.6)
Autism spectrum disorder	0.2 (0.0-0.8)	0.6 (0.1-4.6)	1.0 (0.1-7.2)	3.6 (0.4-27.9)	1.0 (0.1-7.2)
Crohn's disease	0.2 (0.1-0.7)	0.8 (0.2-3.5)	-	-	-
Diabetes mellitus	0.2 (0.0-0.6)	-	-	-	-
Dyspepsia	0.2 (0.0-0.8)	-	-	-	-
Dry skin	0.2 (0.1-0.9)	-	-	-	-
Gastrointestinal pain	0.2 (0.1-0.8)	-	-	-	-
Glaucoma	0.2 (0.0-0.7)	0.5 (0.1-3.8)	-	-	-
Pain in extremity	0.2 (0.0-0.6)	0.4 (0.1-3.3)	-	-	-
Musculoskeletal stiffness	0.2 (0.1-0.7)	-	-	-	-
Nervousness	0.2 (0.0-0.7)	0.6 (0.1-4.4)	-	-	-
Panic attack	0.2 (0.0-0.6)	0.5 (0.1-3.6)	-	-	-
Plantar fasciitis	0.2 (0.0-0.6)	-	-	-	-
Psoriasis	0.2 (0.0-0.6)	-	-	-	-
Weight	0.2 (0.0-0.6)	-	-	-	-
General physical health deterioration	0.2 (0.0-0.7)	-	-	-	-

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

Table 6: Supplement B continued: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Muscle strain	0.2 (0.1-0.7)	0.9 (0.1-5.2)	-	-	-
Limb injury	0.2 (0.0-0.8)	-	-	-	-
Alopecia	0.1 (0.0-0.5)	-	-	-	-
Ankle fracture	0.1 (0.0-0.8)	-	-	-	-
Polyarthritis	0.1 (0.0-0.5)	-	-	-	-
Contusion	0.1 (0.0-0.8)	-	-	-	-
Bursitis	0.1 (0.0-0.9)	-	1.2 (0.2-8.6)	-	1.2 (0.2-8.6)
Neoplasm malignant	0.1 (0.0-0.5)	-	4.9 (0.7-27.5)	-	4.9 (0.7-27.5)
Ex-tobacco user	0.1 (0.0-0.6)	-	-	-	-
Chronic hepatitis	0.1 (0.0-0.6)	-	-	-	-
Cystitis interstitial	0.1 (0.0-0.4)	-	-	-	-
Nasopharyngitis	0.1 (0.0-0.5)	-	-	-	-
Disturbance in attention	0.1 (0.0-0.6)	0.5 (0.1-3.7)	-	-	-
Constipation	0.1 (0.0-0.4)	-	-	-	-
Chronic obstructive pulmonary disease	0.1 (0.0-0.5)	-	-	-	-
Ehlers-Danlos syndrome	0.1 (0.0-0.5)	-	-	-	-
Epstein-Barr virus infection	0.1 (0.0-0.5)	-	-	-	-
Malaise	0.1 (0.0-0.7)	-	-	-	-
Generalised anxiety disorder	0.1 (0.0-0.6)	0.5 (0.1-3.9)	-	-	-
Gastroesophageal reflux disease	0.1 (0.0-0.6)	0.5 (0.1-3.6)	-	-	-
Gout	0.1 (0.0-0.5)	-	-	-	-
Hip arthroplasty	0.1 (0.0-0.9)	-	0.9 (0.1-6.4)	3.3 (0.4-23.4)	0.9 (0.1-6.4)
HIV infection	0.1 (0.0-0.5)	-	-	-	-
Hypertension	0.1 (0.0-0.4)	-	-	-	-
Injection site pain	0.1 (0.0-0.9)	-	1.2 (0.2-8.4)	-	1.2 (0.2-8.4)

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

Table 6: Supplement B continued: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95 % CI)	weighted % (95 % CI)	weighted % (95 % CI)	weighted % (95 % CI)	weighted % (95 % CI)
Irritable bowel syndrome	0.1 (0.0-0.5)	-	-	-	-
Antibiotic therapy	0.1 (0.0-0.6)	-	-	-	-
Lyme disease	0.1 (0.0-0.5)	-	-	-	-
Euphoric mood	0.1 (0.0-0.6)	-	-	-	-
Mood swings	0.1 (0.0-0.6)	-	-	-	-
Muscle injury	0.1 (0.0-0.4)	-	-	-	-
Nausea	0.1 (0.0-0.6)	1.5 (0.4-5.1)	-	-	-
Nerve injury	0.1 (0.0-0.5)	-	-	-	-
Osteoporosis	0.1 (0.0-0.6)	0.5 (0.1-3.9)	0.8 (0.1-6.0)	-	0.8 (0.1-6.0)
Psoriatic arthropathy	0.1 (0.0-0.4)	-	-	-	-
Restless legs syndrome	0.1 (0.0-0.6)	0.5 (0.1-3.6)	-	-	-
Rotator cuff syndrome	0.1 (0.0-0.6)	-	-	-	-
Osteochondrosis	0.1 (0.0-0.5)	-	-	-	-
Schizophrenia	0.1 (0.0-0.9)	-	-	-	-
Sciatic nerve injury	0.1 (0.0-0.9)	-	1.2 (0.2-8.6)	-	1.2 (0.2-8.6)
Herpes zoster	0.1 (0.0-0.4)	-	-	-	-
Sickle cell disease	0.1 (0.0-0.7)	-	-	-	-
Sleep apnoea syndrome	0.1 (0.0-0.8)	-	-	-	-
Poor quality sleep	0.1 (0.0-0.5)	-	-	-	-
Abdominal pain upper	0.1 (0.0-0.7)	-	-	-	-
Cerebrovascular accident	0.1 (0.0-0.5)	0.4 (0.1-3.0)	-	-	-
Surgery	0.1 (0.0-0.6)	0.4 (0.1-2.8)	-	-	-
Peripheral swelling	0.1 (0.0-0.6)	-	-	-	-
Tendonitis	0.1 (0.0-0.5)	-	-	-	-
Epicondylitis	0.1 (0.0-0.4)	-	-	-	-

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

Table 6: Supplement B continued: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Temporomandibular pain and dysfunction syndrome	0.1 (0.0-0.6)	-	-	-	-
Tremor	0.1 (0.0-0.6)	-	-	-	-
Immunodeficiency	0.1 (0.0-0.6)	-	-	-	-
Weight decreased	0.1 (0.0-0.5)	-	-	-	-
Post-traumatic neck syndrome	0.1 (0.0-0.4)	-	-	-	-
Pain of skin	0.1 (0.0-0.5)	-	-	-	-
Muscle tightness	0.1 (0.0-0.4)	-	-	-	-
Wound	0.1 (0.0-0.5)	-	-	-	-
Routine health maintenance	0.1 (0.0-0.8)	-	-	-	-
Procedural pain	0.1 (0.0-0.5)	-	3.2 (0.6-14.5)	-	3.2 (0.6-14.5)
Bipolar disorder	0.1 (0.0-0.9)	0.6 (0.1-4.4)	-	-	-
Autoimmune disorder	0.1 (0.0-0.6)	-	-	-	-
Spondylolisthesis	0.1 (0.0-0.7)	0.6 (0.1-4.6)	-	-	-
Bone loss	0.1 (0.0-1.0)	-	-	-	-
Mast cell activation syndrome	0.1 (0.0-0.5)	-	-	-	-
Delusion of parasitosis	0.1 (0.0-0.5)	-	-	-	-
Sleep deficit	0.1 (0.0-0.6)	-	-	-	-
Major depression	0.1 (0.0-0.5)	-	-	-	-
Knee arthroplasty	0.1 (0.0-0.4)	-	0.8 (0.1-5.6)	-	0.8 (0.1-5.6)
Alcoholism	0.1 (0.0-0.4)	0.3 (0.0-2.5)	-	-	-
Ankylosing spondylitis	0.1 (0.0-0.8)	-	-	-	-
Asthma	0.1 (0.0-0.6)	0.6 (0.1-4.1)	-	-	-
Blood pressure measurement	0.1 (0.0-0.4)	-	-	-	-
Hepatic cirrhosis	0.1 (0.0-0.6)	-	-	-	-
Cyst	0.1 (0.0-0.6)	-	-	-	-

CBD = cannabidiol; delta-8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

Table 6: Supplement B continued: Medical reasons for use among hemp-derived cannabinoid product users by MedDRA Preferred Term (n=704)

	CBD	Delta-8-THC	CBN	CBG†	HHC†
MedDRA Preferred Term (PT)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)	weighted % (95% CI)
Endometriosis	0.1 (0.0-0.6)	-	-	-	-
Hypersensitivity	0.1 (0.0-1.0)	-	-	-	-
Radiculopathy	0.1 (0.0-0.5)	-	0.7 (0.1-4.7)	-	0.7 (0.1-4.7)
Chemotherapy	0.1 (0.0-0.5)	-	2.5 (0.4-14.9)	-	2.5 (0.4-14.9)
Menopause	0.1 (0.0-0.5)	-	-	-	-
Borderline personality disorder	0.1 (0.0-0.9)	-	-	-	-
Breast cancer	0.1 (0.0-0.5)	-	-	-	-
Chronic hepatitis B	0.1 (0.0-0.6)	-	-	-	-
Joint stiffness	0.1 (0.0-0.6)	-	-	-	-
Toothache	0.1 (0.0-1.0)	-	-	-	-
Thinking abnormal	-	0.5 (0.1-3.6)	-	-	-
Back injury	-	-	0.7 (0.1-4.7)	-	0.7 (0.1-4.7)
Cachexia	-	-	-	2.5 (0.3-19.9)	-
Carpal tunnel syndrome	-	0.5 (0.1-3.7)	-	-	-
Cerebral palsy	-	-	2.0 (0.3-12.6)	-	2.0 (0.3-12.6)
Colitis	-	0.5 (0.1-3.3)	-	-	-
Injury	0.0 (0.0-0.4)	-	-	-	-
Hepatic cancer	0.0 (0.0-0.2)	-	-	-	-
Asthenia	-	1.6 (0.2-10.5)	-	-	-
Lymphoma	0.0 (0.0-0.2)	-	-	-	-
Analgesic therapy	-	0.4 (0.1-3.2)	-	-	-
Vision blurred	-	0.5 (0.1-3.7)	-	-	-
Underweight	0.0 (0.0-0.3)	-	-	-	-
Anhedonia	-	0.6 (0.1-4.1)	-	-	-
Ligament sprain	-	0.9 (0.1-5.2)	-	-	-
Substance use	-	0.9 (0.1-5.2)	-	-	-
Pain management	-	-	0.5 (0.1-4.0)	-	0.5 (0.1-4.0)

CBD = cannabidiol; delta -8-THC = delta-8-tetrahydrocannabinol; CBN = cannabinol; CBG = cannabigerol; HHC = hexahydrocannabinol; CI = confidence interval.

†Estimates are unstable as a result of small sample size

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CHAPTER 3: STATE MARIJUANA AND DELTA-8-THC LEGISLATION AND DELTA-8-THC USE IN THE US

Abstract

Importance: Delta-8-THC is a cannabinoid with a nearly identical chemical structure to delta-9-THC that produces similar psychotropic effects and has gained popularity since the passage of the 2018 US Farm Bill. The absence of federal laws and the minimal state regulations governing delta-8-THC has allowed manufacturers to evade restrictions and regulatory systems in place for marijuana products.

Objective: To determine whether lifetime delta-8-THC use is higher among US adults residing in states with restrictive marijuana laws and lower among those residing in states with restrictions on delta-8-THC sales.

Design: This cross-sectional study surveyed a probability-based online panel of US adults from October to November of 2023 and used inverse probability of treatment weighting to calculate adjusted risk ratios (aRRs).

Setting: All 50 US states and Washington DC.

Participants: Participants were recruited from Ipsos KnowledgePanel, a probability-based online panel of US adults.

Exposures: State marijuana (recreational, medical, illegal) and delta-8-THC (any restrictions, no restrictions) laws.

Outcome: Lifetime use of delta-8-THC.

Results: States where marijuana use was illegal had the highest prevalence of delta-8-THC use (11.2%; 95% CI 8.8-14.2), followed by states with medical (6.6%; 95% CI 4.7-9.2), and recreational (6.4%; 95% CI 4.7-8.6) marijuana laws. Over twice as many adults used delta-8-THC in states without any delta-8-THC restrictions at 10.7% (95% CI 8.7-13.0), compared to states with delta-8-THC restrictions at 4.7% (95% CI 3.5 - 6.3). Compared to states where marijuana use was fully illegal, adults in states with medical marijuana laws had a 75% lower probability of using delta-8-THC (aRR=0.57; 95% CI 0.37-0.88), and those in states with recreational marijuana laws had a 85% lower probability (aRR=0.54; 95% CI 0.37-0.79). Delta-8-THC restrictions decreased the probability of use by 117% (aRR=0.46; 95% CI 0.32-0.67). In states with recreational marijuana laws and delta-8-THC restrictions, the probability of delta-8-THC use was 170% lower (aRR=0.37; 95% CI 0.20-0.70) compared to recreational states without any delta-8-THC restrictions.

Conclusions and Relevance: States with stronger restrictions on marijuana have higher rates of delta-8-THC use, but restrictions on delta-8-THC are associated with lower rates of delta-8-THC use.

Introduction

Delta-8-tetrahydrocannabinol (delta-8-THC) is a chemical compound that is structurally similar to the primary psychotropic compound found in marijuana, delta-9-tetrahydrocannabinol (delta-9-THC) and produces comparable psychotropic effects (1,2). Although delta-8-THC naturally occurs in *Cannabis Sativa L.* in small quantities, it can also be easily synthesized from cannabidiol (CBD) (3). CBD is abundantly bioavailable in “hemp,” which is defined under the 2018 Farm Bill as *Cannabis Sativa L.* and *Cannabis Sativa L.* derivatives containing $\leq 0.3\%$ delta-9-THC. Many US manufacturers have argued that products containing delta-8-THC

produced from hemp-derived CBD can be legally sold throughout the US under federal and most state laws, opening an essentially unregulated market for psychotropic marijuana products.

Some steps have been taken to regulate psychotropic hemp-derived products at the federal level. For example, the Drug Enforcement Agency (DEA) classifies delta-8-THC as an analog of delta-9-THC, implying that it falls under similar regulatory restrictions (4). However, it is unclear which governing body is responsible to enforce these regulations as the DEA has not actively pursued regulatory actions against the production and sale of delta-8-THC products. Given that the 2018 Farm Bill is set to expire on September 30, 2024, the 2024 Farm Bill is currently being revised to include provisions such as imposing a limit on “total THC” and excluding cannabinoids not naturally produced in the marijuana plant, which would both address delta-8-THC (5). However, the US Congress is continuing to debate these proposed changes as they have both supporters and detractors. In the meantime, several US states have taken delta-8-THC regulation into their own hands. To date, 27 US states and Washington D.C. have banned or regulated delta-8-THC sales, while 23 states have no restrictions in place or struggle with enforcement (6–8).

Loose regulations governing the use and sale of delta-8-THC has allowed manufacturers to evade restrictions on marijuana products, presenting public health challenges (9). Recent analyses show inconsistencies between product labels and actual delta-8-THC content (10). Unlike marijuana products, delta-8-THC lacks age restrictions in many jurisdictions throughout the US. A recent case report described a 7-year-old boy who experienced asystole after ingesting 5 gummies that contained a total of 75 mg of delta-8-THC, highlighting risks to children (11). Between December 2020 and February 2022, over 2,000 adverse events linked to delta-8-THC were reported to the FDA and the poison control centers, many of which required intervention

and involved pediatric patients (12–15). A case series of delta-8-THC-related adverse events found that these adverse events were very similar to those resulting from marijuana intoxication (16), raising concerns about whether delta-8-THC should be regulated by jurisdictions as a hemp or marijuana product.

Limited research exists on delta-8-THC interest and use by state policies. Two previous studies using online search queries have shown that public interest in delta-8-THC has increased in recent years across the US and delta-8-THC interest was higher in states with restrictions on marijuana use, suggesting its use as a legal substitute (17,18). A survey conducted using an online convenience sample of US adults who use marijuana also found higher delta-8-THC use in states where marijuana use was not legal for recreational purposes and states without restrictions on delta-8-THC products (19); however, the study was conducted when few states had any delta-8 THC restrictions, relied on self-reported state of residence, and did not examine the interplay of state marijuana use laws and delta-8-THC regulations.

Herein, we utilized a nationally representative panel to measure delta-8-THC use by state marijuana use laws and delta-8-THC regulations (both independently and in combination). In addition, we used inverse probability of treatment weighting (IPTW) to test associations between delta-8-THC use and state regulations around marijuana and delta-8-THC. The use of IPTW ensures that our estimates of the impact of state regulations on delta-8-THC use are adequately adjusted for individual factors related to a person's state of residence and are also related to self-selected use of delta-8-THC (e.g., age) (19–21).

Methods

Study sample

The study sample consisted of participants in a cross-sectional survey on CBD use conducted between October and November of 2023. Respondents were recruited from Ipsos KnowledgePanel®, the largest probability-based online panel in the US. The Ipsos KnowledgePanel® consists of about 55,000 panelists whose demographics are weighted to the US census. To recruit panel members, Ipsos uses probability selection algorithms for random-digit telephone dialing and address-based sampling methods. Households without computer and/or internet access are provided with a web-enabled device (e.g., laptop). and free monthly internet access. The KnowledgePanel is representative of 97% of the adult US general population, covering all 50 states and Washington DC, and has been widely used to provide representative statistics on drug use in the US (22–25).

For this study, Ipsos recruited a random sample of 4,505 KnowledgePanel® adults aged 18 years or older to complete the survey, with a survey completion rate of 63.9%. There were 1,523 adults who qualified for the survey. The survey over-sampled CBD users, resulting in 1008 adults who have ever used CBD and 515 adults who have never used CBD. The study sample covered all 50 US states and Washington DC. The survey was administered in both English and Spanish and the average completion time for the survey was ~10 minutes. The Human Research Protections Program at the University of California San Diego considered the study exempt human subject research.

Measures

Outcome

Delta-8-THC Ever Use. Participants were asked were asked ‘Have you ever, even once, used delta-8-THC?’ with response options (1 = Yes; 2 = No).; those who responded “yes” to the previous question were categorized as having ever used delta-8-THC.

Exposure

Marijuana Use Policies. Each state was categorized as “fully illegal”, “medical”, or “recreational” based on the state regulations at the time of the survey (Table 10: Supplement A) (26,27). The fully illegal marijuana use law category consists of states where marijuana use is not permitted for medical or recreational purposes and is not decriminalized. Medical marijuana use includes states where marijuana use is only legal for medical purposes if an individual has a qualifying condition. At the time of the survey administration, marijuana use was medicinally legal in 38 US states, among which there are 12 states where marijuana use is medicinally legal but not legal for recreational use, which were included in the medical marijuana use laws category in this analysis (Figure 2). The recreational marijuana use law category refers to the use of marijuana for non-medical, personal, or recreational use. In all these states, retailers must have a license from the state to sell marijuana products and sales are regulated and taxed by the states in various ways.

Delta-8-THC Restrictions. US state restrictions on products containing delta-8-THC and/or delta-8-THC use at the time of the survey were obtained from the website CBD Oracle (28). Their data showed that delta-8 THC was banned in 17 states and Washington D.C., severely restricted in 7 states, and substantially regulated in 3 states. All of these categories were coded as having “any” delta-8-THC restrictions. The remaining 23 states were categorized as having “none” (Figure 3).

Covariates

Age. Age was provided as a continuous variable ranging from 18 to 93.

Sex. Sex was provided as a dichotomous variable: 1) male or 2) female.

Race/ethnicity. Race/ethnicity was provided as a categorical, five-level variable: 1) Non-Hispanic (NH) White, 2) NH Black, 3) NH Other including 2+ races, and 4) Hispanic.

Education. Education level was provided as a categorical, four-level variable: 1) no high school diploma or General Educational Development (GED), 2) high school graduate (high school diploma or the equivalent GED), 3) some college or Associate's degree, and 4) Bachelor's degree or higher.

Marijuana use. The survey asked each participant about their substance use. Marijuana use was assessed using the question "In your entire lifetime, have you ever used cannabis (i.e., marijuana) that contained THC?" (yes/no).

Other drug use. Other drug use was assessed using the question "In your entire lifetime, have you ever used any of the following substances?" with response options 1) Cocaine or crack, 2) Non-prescription stimulants like methamphetamine or speed, 3) Psychedelics like LSD or psilocybin-containing mushrooms, 4) Empathogens like, MDMA also known as ecstasy or molly, 5) Dissociative substances like ketamine, 6) Any other drugs like heroin, inhalants, or solvents, and 7) None of the categories apply. Use of any of the substances was coded "yes" and none was coded "no".

Self-reported physical health, mental health, and quality of life. The survey asked each participant to self-report their general physical and mental health as well as their quality of life on a 5-point Likert scale ranging from "1) Poor" to "5) Excellent".

Statistical analyses

To produce population-based estimates, we used survey weights constructed by Ipsos, which accounted for the oversampling of CBD users in the study design. All percentages were weighted by population parameters based on the findings of the most recent US Current

Population Survey. A survey-specific poststratification adjustment was used to account for survey non-response, as well as non-coverage or under-sampling and oversampling resulting from the survey-specific sampling design. Weighted frequencies and the corresponding 95% confidence intervals (CIs) of lifetime delta-8-THC use were calculated. Differences in frequency distributions for lifetime delta-8-THC use were examined across the different state policy categories. Complete case analyses were conducted as $\leq 3.6\%$ of observations were missing from any variable (Table 11: Supplement B).

To calculate propensity scores, separate logistic models were fit to predict six comparisons of state policies: 1) marijuana use fully illegal vs medical marijuana use laws, 2) marijuana use fully illegal vs recreational marijuana use laws, 3) any delta-8-THC restrictions vs none, 4) among states where marijuana use is illegal, any delta-8-THC restrictions vs none, 5) among states with medical marijuana use laws, any delta-8-THC restrictions vs none, and 6) among states with recreational marijuana use laws, any delta-8-THC restrictions vs none. Predictors in these models included all potential confounders and, as recommended (29), the Ipsos-constructed survey weights. Stabilized inverse propensity score weights were computed with the resulting propensity scores (30). Diagnostics of the resulting distributions of stabilized weights suggested no evidence of non-positivity or of misspecification of the propensity score model as all means were near 1.0 and there were no extreme observations (Table 12: Supplement C) (31). The resulting stabilized weights were multiplied by the Ipsos-constructed survey weights to form a final weight for subsequent balance assessments and effect estimation (29).

To assess balance between the state policy groups, weighted standardized mean differences (SMD) of each potential confounder were computed between the exposed and unexposed groups before and after including the stabilized inverse propensity scores with the

composite weights (32). We chose a conventional threshold of the absolute value of the SMD below 0.2, as an indicator of good balance (33). The impact of state policies on delta-8-THC use was estimated through adjusted risk ratios (aRR) and 95% CIs obtained from log-binomial models (34) using IPTW with lifetime use of delta-8-THC as the outcome and state policy category as the exposure. All analyses were performed using R, version 4.1 (R Project for Statistical Computing), and weighted analyses were conducted using the R package ‘survey’ (35).

Results

A total of 7.7% (95% CI 6.5-9.1) of US adults reported using delta-8-THC in their lifetime, representing 19.3 million individuals (Table 7). The prevalence of delta-8-THC use was highest among adults who resided in US states where marijuana use was fully illegal (11.2% (95% CI 8.8-14.2), followed by states where medical marijuana use was permitted (6.6%; 95% CI: 4.7-9.2), and recreational marijuana use was permitted (6.4%; 95% CI 4.7-8.6). Overall, the prevalence of delta-8-THC was twice as high in states without delta-8-THC restrictions (10.7%; 95% CI 8.7-13.0), compared to states with delta-8-THC restrictions (4.7%; 95% CI 3.5-6.3). The prevalence of delta-8-THC use was also higher among states without delta-8-THC restrictions at each level of state marijuana use restrictions. For example, among US adults residing in states where marijuana use was illegal, the prevalence of delta-8-THC use was double for those residing in state without any restrictions (10.5%; 95% CI 6.7-16.1) compared with state that did have restrictions on delta-8-THC (4.4%; 95% CI: 2.9-6.5).

In the dataset weighted with only the Ipsos-provided survey weights, a comparison of the SMDs identified imbalance across the marijuana use laws and delta-8-THC restriction groups on several of the assessed covariates (Table 8). Among states where marijuana use was fully illegal,

imbalance (using $SMD > |0.2|$ as an a priori threshold) was observed for states with delta-8-THC restrictions versus those without delta-8-THC restrictions on the age, physical health, mental health, and quality of life variables. The mean age ($SMD=0.43$), physical health rating ($SMD=0.26$), mental health rating ($SMD=0.21$), and quality of life rating ($SMD=0.28$) were all higher in states with delta-8-THC restrictions. Within states with recreational marijuana use laws, there was an imbalance between states with and without delta-8-THC restrictions on the NH-White race variable, where a smaller proportion of NH-White individuals lived in states with delta-8-THC restrictions ($SMD= -0.21$). Although the comparisons were imbalanced using the composite weights, IPTW improved the comparability of comparison groups for every variable we assessed, including the propensity scores, resulting in SMDs that were closer to 0 (Table 8). The final IPTW comparisons were well balanced, as SMDs for all variables and the propensity scores were $< |0.2|$, the conventional threshold, for all comparisons.

Table 9 presents the IPTW-adjusted associations between delta-8-THC use and state marijuana use laws and delta-8-THC restrictions. Compared to states where marijuana use is fully illegal, adults in states with medical marijuana laws had an 75% lower probability of using delta-8-THC ($aRR=0.57$; 95% CI 0.37-0.88), and those in states with recreational marijuana laws had a 127% lower probability of using delta-8-THC ($aRR=0.54$; 95% CI 0.37-0.79). Residing in a state with delta-8-THC restrictions (vs no restrictions). decreased the probability of delta-8-THC use by 117% ($aRR=0.46$; 95% CI 0.32-0.67). Adults residing in states with recreation marijuana use laws and delta-8-THC restrictions had a 170% lower probability of using delta-8-THC ($aRR=0.37$; 95% CI 0.20-0.70) compared to those in states with recreation marijuana but without delta-8-THC restrictions. Similarly, individuals in states where marijuana use is fully illegal and there are restrictions on delta-8-THC had a 127% lower probability of using delta-8-

THC (aRR=0.44; 95% CI 0.18-1.07) than those in states where marijuana use is fully illegal but without any restrictions on delta-8-THC, although this association was imprecise. Surprisingly, adults residing in states with medical marijuana use laws and delta-8-THC restrictions had an 66% higher probability of using delta-8-THC (aRR=1.66; 95% CI 0.72-3.84) compared to those in states with medical marijuana but without delta-8-THC restrictions, but this association was also not statistically significant.

Discussion

These results suggest that approximately 19.3 million US adults have tried using delta-8-THC, with the prevalence of use varying considerable by the regulatory status of marijuana and hemp-derived products across use states. The prevalence of delta-8-THC use was highest among adults who resided in states like Indiana, Texas and West Virginia, where marijuana use remains fully illegal but hemp-derived delta-8-THC products can be sold without restrictions. However, restrictions on the sale of delta-8-THC was associated with a lower prevalence of use among all categories of marijuana regulation, including fully illegal, medicinal use, legal recreational use.

Our results are consistent with previous research on delta-8-THC use and public interest across varying state policies. Confirming results of public interest (17,18), the data suggest that delta-8-THC use was highest among states where marijuana use was illegal. Similar to an online survey of current delta-8-THC users, we found that those who resided in states with restrictions on sales of delta-8-THC were less likely to use it (19). The lower rates of delta-8-THC use among states with strict policies around marijuana use further support the hypothesis that delta-8-THC might be fulfilling the demand for legal THC in areas where marijuana use is prohibited. State regulations on delta-8-THC products often include age, sales, and marketing restrictions (9,36), which may limit their availability and access and therefore result in lower rates of delta-8-

THC use. Furthermore, there may be differences in public health messaging around the potential risks associated with marijuana in states with medical and recreational legalization, which could extend to hemp-derived psychotropic compound found in marijuana, like delta-8-THC.

Currently, the legal status of delta-8-THC at the federal level remains unclear and is disjointed across US states. Although the DEA has added delta-8-THC as a controlled substance under “Tetrahydrocannabinols”, it remains unclear whether this decision is legally binding or whether the DEA is responsible or will enforce it (4). The pending revisions to the 2024 Farm Bill concerning delta-8 THC and other psychotropic hemp-derived products combined with the current ambiguity around federal enforcement, leave it to individual US states to establish their own laws regarding delta-8-THC (9). Our findings suggest that states with more stringent regulations or bans on delta-8-THC products have lower prevalence of delta-8-THC use. While the legality of hemp-derived cannabinoid products is under question at the federal level, state delta-8-THC restrictions could be used as effective tools to mitigate potential adverse effects that may be associated with delta-8-THC use (12,16). These policies should encompass all derived cannabinoid products, regardless of what substance (i.e., hemp, marijuana) or process they are derived from to prevent future loopholes.

The current study has some limitations. Given the small sample size of our study, we were unable to examine other frequencies (e.g., past month). of delta-8-THC use, which may provide more current information on the effectiveness of state policies. Larger studies are needed among current and established delta-8-THC users to elucidate the impacts of state policies. Although the Ipsos KnowledgePanel used address-based sampling methods to obtain a nationally representative sample, the participant characteristics within each US state might not be representative of the residents for that given state. In this study, delta-8-THC use was measured

among US adults. More research is needed to examine the impact of state marijuana and delta-8-THC policies on delta-8-THC use among youth.

In conclusion, these results suggest that delta-8-THC use is highest in environments that are most restrictive to the use of marijuana. However, US state delta-8-THC restrictions, separately and in combination with marijuana use laws, are associated with lower prevalence of delta-8-THC. Policy makers should consider the appropriate mix marijuana and hemp policies to maximize patient safety and minimize risk.

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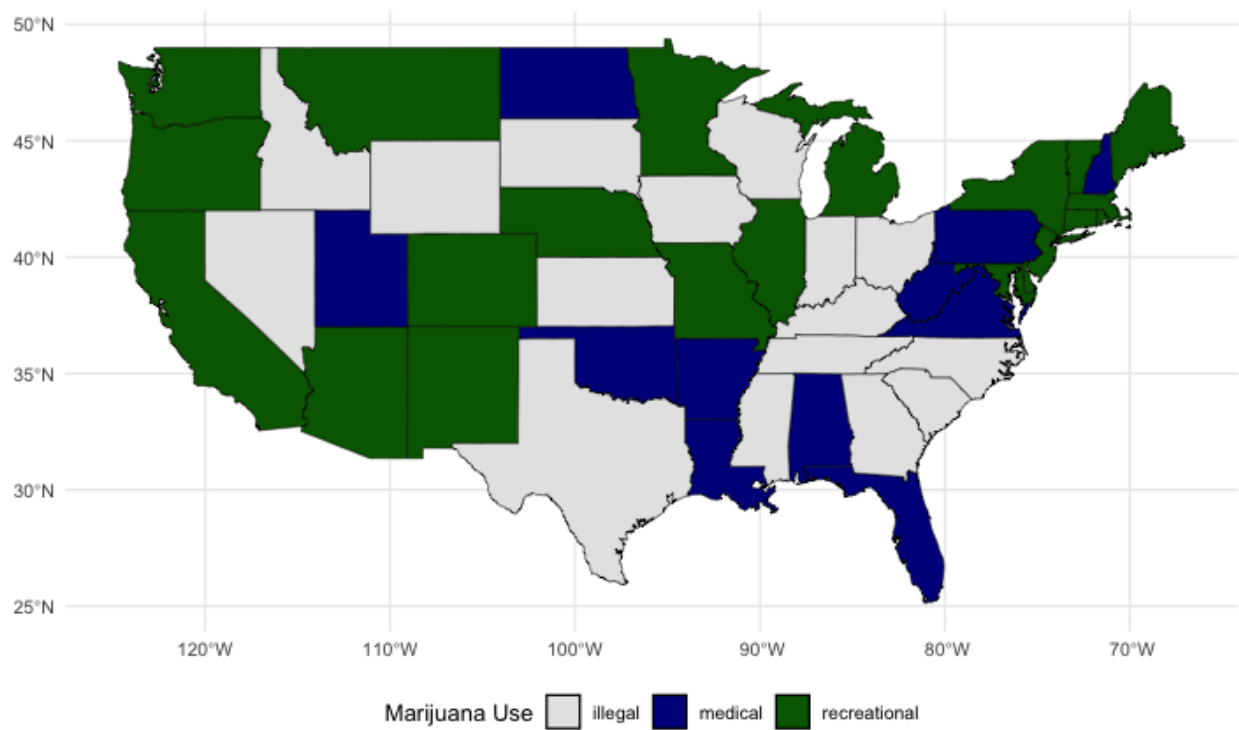


Figure 2: Map of US states by marijuana use policies.

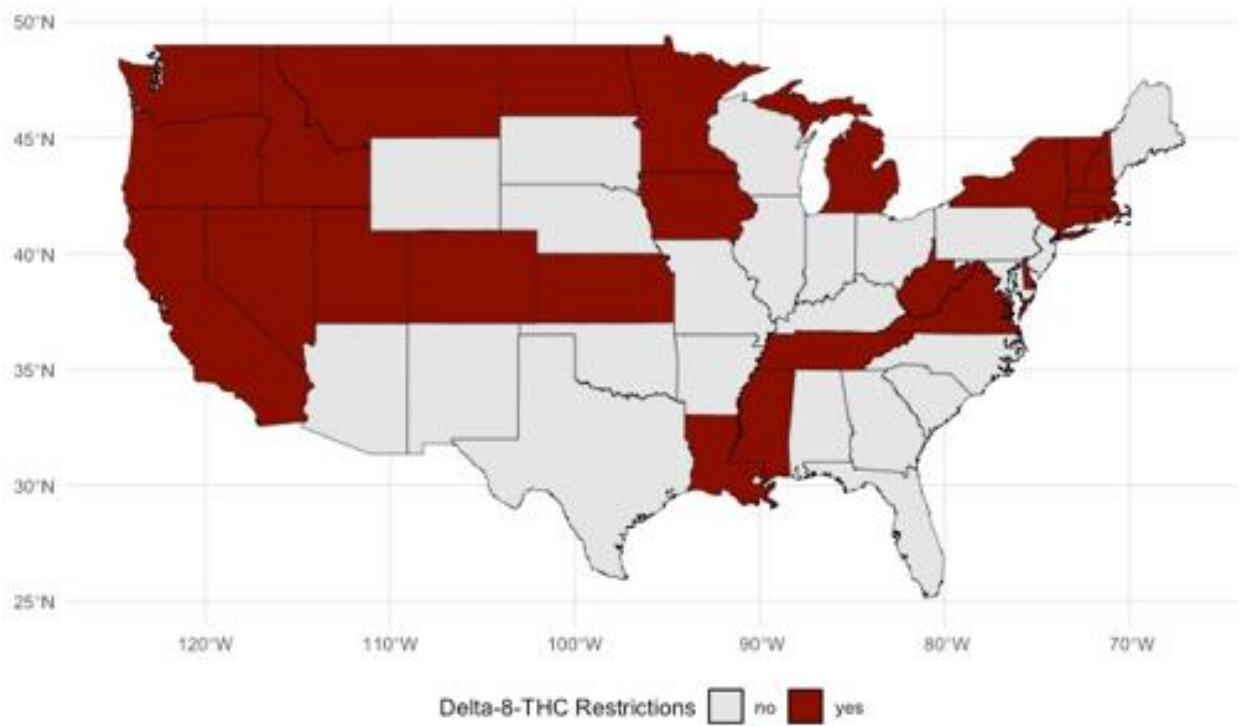


Figure 3: Map of US states by delta-8-THC sales restrictions.

Table 7: Prevalence of delta-8-THC use by state marijuana use laws and delta-8-THC restrictions among a national sample of US adults (n=1523)

State Policies	Overall Sample	Delta-8-THC Ever Use
	n	Prevalence % (95% CI)
Overall	1523	7.7 (6.5-9.1)
Marijuana Use Laws		
Fully Illegal	426	11.2 (8.8 - 14.2)
Medical	329	6.6 (4.7 - 9.2)
Recreational	768	6.4 (4.7 - 8.6)
Delta-8-THC Restrictions		
Any	726	4.7 (3.5 - 6.3)
None	797	10.7 (8.7 - 13.0)
Marijuana Use Fully Illegal		
With Delta-8-THC Restrictions	68	6.1 (2.8 - 13.0)
Without Delta-8-THC Restrictions	358	12.1 (9.4 - 15.4)
Medical Marijuana Use Laws		
With Delta-8-THC Restrictions	105	5.5 (3.0 - 9.9)
Without Delta-8-THC Restrictions	224	7.2 (4.8 - 10.7)
Recreational Marijuana Use Laws		
With Delta-8-THC Restrictions	553	4.4 (3.0 - 6.4)
Without Delta-8-THC Restrictions	215	11.6 (7.2 - 18.2)

All estimates were weighted using Ipsos-provided population weights.

Table 8: Standardized mean differences showing balance improvement obtained by weighting the propensity scores for state policy comparisons

	Marijuana Use Fully Illegal vs Recreational Marijuana Use Laws		Marijuana Use Fully Illegal vs Medical Marijuana Use Laws		Delta-8-THC Restrictions Any vs None		Marijuana Use Fully Illegal with vs without Delta-8-THC Restrictions		Medical Marijuana Use Laws with vs without Delta-8-THC Restrictions		Recreational Marijuana Use Laws with vs without Delta-8-THC Restrictions	
Covariate	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W
Propensity score	0.53	0.00	0.35	0.00	0.39	0.01	0.83	0.09	0.93	-0.03	0.59	0.05
Female sex	-0.01	-0.01	0.02	0.01	-0.09	0.00	-0.11	0.03	0.04	0.01	-0.17	-0.01
Age	0.04	0.01	0.20	-0.01	0.04	0.00	0.43	0.16	-0.08	0.01	-0.03	-0.04
Race/ Ethnicity												
White	-0.04	0.00	0.01	0.00	-0.09	0.00	0.18	0.12	-0.06	0.02	-0.20	-0.02
Black	-0.06	0.00	0.02	0.00	-0.01	0.00	0.00	-0.03	0.13	0.00	0.00	-0.01
Other/2+ more	0.07	0.00	0.01	0.00	0.07	0.00	-0.05	0.02	0.03	0.00	0.09	0.02
Hispanic	0.03	0.00	-0.04	0.00	0.03	0.00	-0.13	-0.10	-0.10	-0.03	0.11	0.02
Education												
No high school diploma or GED	-0.01	0.00	-0.05	-0.01	0.00	0.00	-0.11	-0.01	0.04	0.00	0.02	0.02
High school graduate	-0.08	0.00	-0.01	0.00	-0.06	0.00	0.05	-0.01	-0.11	0.03	-0.01	-0.01
Some college/ Associate's degree	0.00	0.00	0.01	0.00	-0.01	0.00	0.08	0.01	-0.09	-0.02	0.00	0.00
Bachelor's degree or higher	0.09	0.00	0.05	0.00	0.06	0.00	-0.02	0.02	0.16	-0.03	0.00	0.00
Lifetime marijuana use	0.07	0.00	0.03	0.00	-0.02	0.00	-0.07	0.05	-0.10	0.03	-0.06	-0.01

IPTW = inverse probability of treatment weighting.

Table 8 continued: Standardized mean differences showing balance improvement obtained by weighting the propensity scores for state policy comparisons

	Marijuana Use Fully Illegal vs Recreational Marijuana Use Laws		Marijuana Use Fully Illegal vs Medical Marijuana Use Laws		Delta-8-THC Restrictions Any vs None		Marijuana Use Fully Illegal with vs without Delta-8-THC Restrictions		Medical Marijuana Use Laws with vs without Delta-8-THC Restrictions		Recreational Marijuana Use Laws with vs without Delta-8-THC Restrictions	
Covariate	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W	Composi te	IPT W
Lifetime other drug use	0.03	0.01	0.03	0.00	0.03	0.00	0.01	0.07	-0.03	-0.01	0.05	0.03
Physical health	0.10	0.00	0.18	0.01	0.07	-0.01	0.26	-0.05	-0.17	-0.04	0.07	0.02
Mental health	0.09	0.00	0.15	0.01	0.11	0.00	0.21	-0.10	0.00	-0.03	0.13	0.00
Quality of life	0.09	0.00	0.14	0.01	0.08	0.00	0.28	-0.14	-0.06	0.00	0.07	0.02
Living in a non-metropolitan area	-0.12	0.00	0.00	0.00	-0.06	0.00	0.02	0.05	0.10	0.01	-0.05	0.00

IPTW = inverse probability of treatment weighting.

Table 9: Probability of using delta-8-THC by state policy

State Policies	Delta-8-THC Ever Use
	IPTW aRR (95% CI)
Marijuana Use Laws	
Fully Illegal	ref
Medical	0.57 (0.37-0.88)
Recreational	0.54 (0.37-0.79)
Delta-8-THC Restrictions	
None	ref
Any	0.46 (0.32-0.66)
Marijuana Use Fully Illegal	
Without Delta-8-THC Restrictions	ref
With Delta-8-THC Restrictions	0.44 (0.18-1.07)
Medical Marijuana Use Laws	
Without Delta-8-THC Restrictions	ref
With Delta-8-THC Restrictions	1.66 (0.72-3.84)
Recreational Marijuana Use Laws	
Without Delta-8-THC Restrictions	ref
With Delta-8-THC Restrictions	0.36 (0.19-0.67)

All estimates were calculated using inverse probability of treatment weighting.
 RR= Risk ratio; CI= confidence interval

Table 10: Supplement A: State marijuana use laws and delta-8-THC restrictions

State	Marijuana Use Laws	Delta-8-THC Restrictions
Alabama	Medical	No
Alaska	Recreational	Yes
Arizona	Recreational	No
Arkansas	Medical	No
California	Recreational	Yes*
Colorado	Recreational	Yes
Connecticut	Recreational	Yes*
Delaware	Recreational	Yes
Florida	Medical	No
Georgia	Fully Illegal	No
Hawaii	Medical	Yes
Idaho	Fully Illegal	Yes
Illinois	Recreational	No
Indiana	Fully Illegal	No
Iowa	Fully Illegal	Yes
Kansas	Fully Illegal	Yes
Kentucky	Fully Illegal	No
Louisiana	Medical	Yes
Maine	Recreational	No
Maryland	Recreational	No
Massachusetts	Recreational	Yes
Michigan	Recreational	Yes
Minnesota	Recreational	Yes
Mississippi	Fully Illegal	Yes
Missouri	Recreational	No
Montana	Recreational	Yes
Nebraska	Fully Illegal	No
Nevada	Recreational	Yes
New Hampshire	Medical	Yes
New Jersey	Recreational	Yes
New Mexico	Recreational	No
New York	Recreational	Yes
North Carolina	Fully Illegal	No
North Dakota	Medical	Yes
Ohio	Fully Illegal	No

*sold in regulated marijuana dispensaries

Table 10 continued: Supplement A: State marijuana use laws and delta-8-THC restrictions

State	Marijuana Use Laws	Delta-8-THC Restrictions
Oklahoma	Medical	No
Oregon	Recreational	Yes
Pennsylvania	Medical	No
Rhode Island	Recreational	Yes
South Carolina	Fully Illegal	No
South Dakota	Fully Illegal	No
Tennessee	Fully Illegal	Yes
Texas	Fully Illegal	No
Utah	Medical	Yes
Vermont	Recreational	Yes
Virginia	Medical	Yes
Washington	Recreational	Yes
West Virginia	Medical	Yes
Wisconsin	Fully Illegal	No
Wyoming	Fully Illegal	No
Washington D.C.	Recreational	Yes

*sold in regulated marijuana dispensaries

Table 11: Supplement B: Description of missingness by sample characteristics among a national sample of US adults (n=1523)

Variable	Missing (%)
Sex	0.0
Age (continuous)	0.0
Race/ Ethnicity	0.0
Education	0.0
Lifetime marijuana use	3.6
Lifetime other drug use	0.0
Self-reported physical health, score of 1 (excellent) to 5 (poor)	1.2
Self-reported mental health, score of 1 (excellent) to 5 (poor)	1.1
Self-reported quality of life, score of 1 (excellent) to 5 (poor)	1.1
Metropolitan area status	0.0

Table 12: Supplement C: Distributions of stabilized weights.

Analytical Comparison	n	mean	CV	P1	P99	Min	Max
Marijuana Use Fully Illegal vs Recreational Marijuana Use Laws	1117	1.01	0.27	0.54	2.10	0.45	2.77
Marijuana Use Fully Illegal vs Medical Marijuana Use Laws	707	1.01	0.17	0.73	1.48	0.68	2.12
Delta-8-THC Restrictions Any vs None	1415	1.01	0.20	0.66	1.77	0.62	2.15
Marijuana Use Fully Illegal with vs without Delta-8-THC Restrictions	409	1.04	0.66	0.48	1.95	0.29	10.00
Medical Marijuana Use Laws with vs without Delta-8-THC Restrictions	298	1.07	0.51	0.43	3.15	0.37	4.04
Recreational Marijuana Use Laws with vs without Delta-8-THC Restrictions	708	1.02	0.29	0.55	2.25	0.47	3.47

CV = Coefficient of Variation; P1 = 1st Percentile; P99 = 99th Percentile

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CHAPTER 4: ONLINE VAPE SHOPS THAT SELL HEMP-DERIVED CANNABINOID PRODUCTS RECEIVE MORE WEBSITE VISITS

Abstract

Objective: To determine the proportion of online vape shops that offer hemp-derived cannabinoid products in a large metropolitan area (San Diego, California), whether these vape shops comply with California state hemp regulations (i.e., bans on flavored and inhalable hemp products), and estimate whether these shops receive more website traffic.

Methods: We obtained a comprehensive sample of vape shops (n=109) using browser-based (i.e., Google Search) and web-based (i.e., Google Maps and Yelp) searches in San Diego and conducted a content analysis of their websites to identify hemp-derived cannabinoid products offered for mail-order purchasing. Using website traffic data, we examined the association between hemp-derived cannabinoid product availability and monthly website visits.

Results: Among the 109 online vape shops in the study sample, 35.8% offered hemp-derived cannabinoid products for mail-order purchase and 26.6% sold flavored and inhalable hemp products. Compared to vape shops that did not offer hemp-derived cannabinoid products (Mean: 23,619; 95% CI: 23,605-23,634), those offering flavored and inhalable hemp products received 2.5 times more monthly website visits (Mean: 57,950; 95% CI: 57,913-57,986) and those offering any hemp-derived cannabinoid products received 5.5 times more monthly website visits (Mean: 130,694; 95% CI: 130,607-130,782).

Conclusion: The prevalence of flavored and inhalable hemp-derived cannabinoid products, despite being prohibited under California's industrial hemp regulations, highlights the need for additional enforcement measures to ensure retailer compliance. The higher website traffic observed among vape shops offering cannabinoid products may be indicative of a greater

advantage for retailers selling hemp-derived cannabinoid products compared to those selling nicotine or tobacco products alone.

Introduction

Cannabinoids are chemical compounds that naturally occur at various levels in all species of *Cannabis Sativa L.* (1). However, since the passage of the 2018 Farm Bill in the United States (US), *Cannabis Sativa L.* and its derived cannabinoids can legally be classified as either “hemp” or “marijuana” based on their concentration of delta-9-tetrahydrocannabinol (delta-9-THC), with plants or derivatives containing $\leq 0.3\%$ delta-9-THC considered “hemp” and those with $> 0.3\%$ delta-9-THC considered “marijuana” (i.e., cannabis) (2). A critical drug policy question is whether it is legal to sell cannabinoids derived from hemp to produce psychotropic chemical analogs to delta-9-THC, such as Δ^8 tetrahydrocannabinol (delta-8-THC) (3). Many manufacturers have interpreted the 2018 Farm Bill as implying that hemp derivatives are legal so long as they contain $\leq 0.3\%$ delta-9-THC. However, the Drug Enforcement Agency (DEA) has refuted this assumption in some communications but has yet to take broad-sweeping actions against hemp product manufacturers (4). This legal ambiguity about products like delta-8-THC has created a new market for ‘hemp-derived’ cannabinoid products in the US (5–10).

The availability of hemp-derived cannabinoid products in inhalable modalities, such as vapes, has created regulatory complexities that overlap with tobacco regulation. Almost all retailers in Fort Worth, Texas with an alcohol, tobacco, or cannabidiol (CBD) license that sold delta-8-THC (96%) offered product types that were intended to be smoked or vaped (7). Furthermore, an assessment of online retailers of psychotropic cannabinoid products showed that most of the modalities offered were inhalable, such as disposable vapes (43%), vape carts (18%), and pre-rolls (7%) (11). The overlap in modes of use between tobacco and cannabinoid products

can interfere with efforts to pinpoint culprit products during vaping-related outbreaks, such as the e-cigarette or vaping-associated lung injuries (EVALI) outbreak, in which many cases vaped a combination of cannabinoid and tobacco products (12,13). Although tobacco product manufacturers are required to submit product applications to the Food and Drug Administration (FDA) before they can market and distribute them in the US, the FDA does not have a similar framework for hemp-derived cannabinoid products. However, the FDA has taken some actions to protect public health by issuing warning letters to companies marketing inhalable CBD products and delta-8-THC products (14). The interchangeability of vaping products can also create loopholes in regulation. For example, although several US states have banned flavored nicotine vapes to tackle nicotine vaping among youth, similar regulations for hemp-derived cannabinoid products are rare (15), even though cannabinoid product use is prevalent among US youth (16).

The lack of quality and safety standards for hemp-derived cannabinoid products may also have public health impacts. Without established quality assurance standards, hemp-derived cannabinoid products can be mislabeled, may include more than 0.3% delta-9-THC, and may include harmful contaminants (17,18). For example, one assessment of commercially available CBD products in the US found that most (74%) of these products were inaccurately labeled, and several contained heavy metals, residual solvents, and pesticides that violated regulatory thresholds (18). Similarly, a toxicological analysis of 27 vaping products containing delta-8-THC found that all of the products had mislabeled the delta-8-THC content contained and contained side-products such as heavy metals, and many products contained unlabeled cutting agents (17). There were over 2,000 reports of adverse events linked to delta-8-THC consumption received by the FDA and the National Poison Control Centers between December 2020 and February 2022,

many of which required medical intervention and involved pediatric patients (19–21). Many of the symptoms presented in adverse events related to delta-8-THC use were similar to those reported for acute delta-9-THC intoxication (e.g., anxiety and paranoia), but there were several unique symptoms that could have stemmed from unregulated manufacturing methods (e.g., muscle spasms) (22).

Given the existing regulatory challenges and health risks associated with hemp-derived cannabinoid products, very little is known about how vape shops, specifically those with an online presence, have responded to their growing popularity. Prior research has already shown that tobacco retailers, including vape shops, often sell substances other than nicotine, including kratom, CBD, and delta-8-THC (6,7,23–25). A recent review of 520 vape shops across the US found that 74% offered psychotropic cannabinoid products for sale (26). Inhalable cannabinoid products with characterizing flavors may be sold by online vape shops as a way of circumventing local regulations for flavored tobacco products (27). Online retailers, which frequently use e-commerce platforms, are often not included in the definition of “retailers” within local and state policies governing tobacco products (28). Therefore, online retailers may operate across state lines, potentially avoiding local regulations, such as state bans on flavored tobacco products. There are jurisdictions in which online retailers are subject to laws governing certain products. For example, California’s Assembly Bill 45 (AB-45) prohibits the manufacture or sale of inhalable industrial hemp products, including retailers that offer products through a delivery service (i.e., e-commerce), except for the sole purpose of sale in other states. As a part of this law, inhalable industrial hemp products cannot contain characterizing flavors other than natural terpenes, may not be sold to consumers under 21 years of age, and may not be sold in retail

locations in California (29). However, to our knowledge, no surveillance of flavored and inhalable cannabinoid products to inform enforcement activity has been conducted.

To inform policy around cannabinoid products, we describe the availability of hemp-derived cannabinoid products in online tobacco retailers in California. Furthermore, we evaluate compliance with a local law that restricts flavored and inhalable hemp product sales. Since vape shops may be offering hemp-derived cannabinoid products as a way of generating business, we used web traffic data for the websites in our study sample to compare traffic according to whether they offer hemp-derived cannabinoid products or not. The findings may inform policy recommendations for regulating the online marketplace of cannabinoid products derived from hemp.

Methods

Study Sample

We obtained a comprehensive sample of vape shops (n=109) with e-commerce websites using browser-based and web-based searches in San Diego County from March to August of 2023 (Figure 4). The focus on San Diego County allowed for the assessment of compliance with California's AB-45. We excluded all vape shops that did not allow for mail-order purchase of vaping products on their website (n=472).

Sample Derivation

The focus on San Diego County allowed for the assessment of compliance with California's AB-45. We excluded all vape shops that did not allow for mail-order purchase of vaping products on their website (n=472).

Sample Derivation

The comprehensive sample included retailers that had a physical retail location in San Diego County (“map-based”) as well as an online-only retailers (“browser-based”). Map-based retailers were identified using the Google Maps and Yelp Application Programming Interfaces (APIs) with locations set in San Diego County. Two separate lists of vape shops from Yelp and Google Maps were merged using street addresses and zip codes to link common records. The merged dataset consisted of 311 unique vape shops, of which 166 contained uniform resource locators (URLs) to a website. Browser-based retailers were collected using Google searches for 5 terms indicative of shopping, including “buy”, “order”, “shop”, “retailer”, or “sale”, in combination with a vaping or product-indicative term (i.e., “vape”, “e-cig”, “JUUL”, “NJOY”). Searches were performed using a Google Chrome browser with the location of searches positioned to the geographic center point of each jurisdiction within San Diego County. Google searches initially yielded 106,400 search results, of which 481 were unique URLs. After merging the unique URLs across search strategies (n=580) and removing URLs to websites that did not allow for mail-order purchasing of vape products (n=471), we retained 109 online vape shops for further content analysis.

Content Analysis

We visited all the e-commerce websites included in our final analytic sample to conduct a content analysis. Following a previous protocol used to study online vaping retailers and other online content discussing delta-8-THC (e.g., Reddit posts), we developed a codebook and four independent, trained coders (N.S., R.H., T.M., and N.M) working in teams of two coded websites to determine whether and what type of hemp-derived cannabinoid products the retailer sold while using an automated archiving software (30). After review, we calculated agreement

between the two coders (31), flagged disagreements by comparing labels, and reviewed and adjudicated (R.H.) any website with discordance using the saved archive.

Hemp-derived Cannabinoid Product Availability

Using the list of all retailers (map-based and browser-based), we identified retailers with e-commerce websites that allowed for mail-order purchasing of hemp-derived cannabinoid products. For every retailer, coders were first asked “Does the website sell hemp-derived products?” with response options “yes” and “no”. If a website was coded as selling hemp-derived products, 10 additional questions were asked to collect information about the different types of cannabinoid products available. Each of the 10 questions was presented in a similar format, “Does the website sell... 1) Cannabidiol (CBD), 2) Δ 8 Tetrahydrocannabinol (delta-8-THC), 3) Hexahydrocannabinol (HHC), 4) Tetrahydrocannabinol acetate (THC-O), 5) Δ 10 Tetrahydrocannabinol (delta-10-THC), 6) Cannabinol (CBN), 7) Cannabigerol (CBG), 8) Hemp products (cannabinoids not defined), 9) Hemp legal Δ 9 Tetrahydrocannabinol (Containing < 0.3% delta-9-THC), and 10) Other Product not mentioned.” There was high agreement between the two pairs of independent coders for all the cannabinoid product-related measures (Table 13). Coder agreement for the availability of specific cannabinoids in vape shops was high, with prevalence-bias-adjusted kappas ranging from 0.80 to 1.00.

Inhalable and Flavored Hemp-derived Cannabinoid Products

Among websites selling hemp-derived cannabinoid products, we collected information on whether any of the cannabinoid products offered by the retailer were inhalable (e.g., disposable vapes, e-liquid) and contained a characterizing flavor (e.g., “honeydew ice”). Cannabinoid products containing natural terpene flavors only (e.g., limonene) were not coded as flavored because they are permitted under California’s AB-45. Flavored and inhalable cannabinoid

product availability was assessed similarly to cannabinoid product availability using 10 separate questions: “Does the website sell... 1) Cannabidiol (CBD), 2) Δ 8 Tetrahydrocannabinol (delta-8-THC), 3) Hexahydrocannabinol (HHC), 4) Tetrahydrocannabinol acetate (THC-O), 5) Δ 10 Tetrahydrocannabinol (delta-10-THC), 6) Cannabinol (CBN), 7) Cannabigerol (CBG), 8) Hemp products (cannabinoids not defined), 9) Hemp legal Δ 9 Tetrahydrocannabinol (Containing < 0.3% delta-9-THC), and 10) Other” products that are inhalable and advertised with flavor descriptors?”. There was high coder agreement for inhalable and flavored varieties of each cannabinoid, with prevalence-bias-adjusted kappas ranging from 0.76 to 0.93.

Website Traffic

We purchased a six-month report from Semrush (www.semrush.com) that provided an estimate of the number of monthly website visits to each website in our final analytic sample (March 2023 through August 2023). Semrush calculated the estimated monthly visits nationally for each website. Across the six months reflected in the report, there was a total of 28,193,827 website visits directed from Google searches to the websites in our sample.

Statistical Analyses

We calculated the percentage of retailers that allowed for mail-order purchasing of hemp-derived cannabinoid products. Among retailers that permitted mail-order purchasing of hemp-derived cannabinoid products, we identified the proportion of vape shops that offered inhalable hemp products with non-terpene-derived flavors and were, therefore, non-compliant with California’s AB-45.

To compare the website traffic of retailers that offered hemp-derived cannabinoid products and those that did not, we ran a hierarchical Poisson regression model with web traffic as the dependent variable, availability of hemp-derived products as the independent variable, and

adjustment for retailer type. Web traffic was operationalized as a continuous variable measured as the average number of visits over the six-month period for each retailer and the retailer ID variable was included to account for the fact that the number of visits is grouped by retailer. Hemp-derived cannabinoid product availability was a three-level variable categorized as 1) none, 2) inhalable and flavored hemp-derived products offered, or 3) hemp-derived products offered but not inhalable and flavored. Retailer type was a dichotomous variable categorized as map-based and browser-based. We also report the web traffic estimated marginal means and corresponding 95% confidence intervals for the three-level hemp-derived cannabinoid product availability variable by retailer type. All analyses were performed using R V.3.6.1 and $\alpha=0.05$.

Results

Among the 109 online vape shops in the study sample, 35.8% offered a hemp-derived cannabinoid product for mail-order purchase (Table 14). The most common cannabinoids listed as main ingredients among the retailers were CBD (32.1%), delta-8-THC (20.2%), hemp-compliant delta-9-THC (17.4%), HHC (16.5%), CBG (14.7%), delta-10-THC (13.8%), THC-O (10.1%), and CBN (10.1%). There were 12 “other” cannabinoid products sold by the vape shops including Tetrahydrocannabiphorol (10.1%), Hexahydrocannabiphorol (3.7%), Delta-9 tetrahydrocannabutol (3.7%), Tetrahydrocannabinolic acid (2.8%), Delta-6-THC (2.8%), THC-X (1.8%), Delta-11-THC (2.8%), Cannabidivarin (0.9%), Delta-7-THC (0.9%), Tetrahydrocannabinol monomethylether (0.9%), Hydrox-4-phc (0.9%), and Tetrahydrocannabivarin (0.9%).

Over a quarter of the retailers (26.6%) sold flavored and inhalable hemp-derived cannabinoid products (Table 14). Each of the cannabinoids identified was offered in flavored and inhalable form within our sample of online vape shops. There were 21.1% of retailers offering

flavored and inhalable products containing CBD, 18.3% containing delta-8-THC, 14.7% containing HHC, 13.8% containing hemp-compliant delta-9-THC and delta-10-THC, 11.0% containing THC-O, 9.2% containing CBN, and 7.3% containing CBG. All of the 12 “other” cannabinoid products (e.g., delta-6-THC and tetrahydrocannabiphorol) sold by the vape shops were offered in flavored and inhalable form.

Online vape shops that sold inhalable and flavored hemp-derived cannabinoid products received 2.5 times more average monthly website visits (Mean: 57,950; 95% CI: 57,913-57,986) than vape shops that did not offer any cannabinoid products for sale (Mean: 23,619; 95% CI: 3,605-23,634). Similarly, vape shops that sold cannabinoid products, not including those that were inhalable and flavored, had average monthly visit rates that were 5.5 times higher (Mean: 130,694; 95% CI: 130,607-130,782) than vape shops that did not sell any cannabinoid products. The association between cannabinoid product availability and average website visits was similar across the two types of retailers examined within the study sample (Table 15). After adjusting for retailer type, offering cannabinoid products, both inhalable and flavored and not inhalable and flavored, was positively associated with a greater number of monthly website visits compared to not offering any cannabinoid products (Table 16: Supplement A).

Discussion

We found that just over a third of the online vape shops in this sample online vape shops serving San Diego County offered hemp-derived cannabinoid products and just over a quarter offered flavored and inhalable hemp-derived cannabinoid products, despite these being prohibited under California’s AB-45. Vape shops that offered hemp-derived cannabinoid products received significantly more monthly website visits compared to those that did not offer

any hemp-derived products, suggesting that selling hemp-derived cannabinoid products may be more advantageous for business compared with selling nicotine alone.

The availability of hemp-derived cannabinoid products among our sample of online vape shops in San Diego County is consistent with previous research on CBD and delta-8-THC products in retail settings (7,24,26). For example, a study from 2021 found that 37% of online vape shops sold products containing CBD, with the majority offering inhalable products, which is similar to the proportion of retailers that offered a cannabinoid product for mail-order purchase in our sample (24). Among a sample of map-based retailers in Fort Worth, Texas in 2021, 11% reported selling delta-8-THC, a much smaller proportion than that found within our sample (20.2%) (7). This discrepancy may be due to their inclusion of retail locations with alcohol and CBD licenses, resulting in a larger sample of total retailers. Lastly, our results show that hemp-derived cannabinoid product availability among online vape shops is similar to those with a physical location, as a recent study of vape shops in the US found that 50% of vape shops with a physical location in California sold psychotropic cannabinoid products (26).

More than 1 in 4 vape online vape shops in San Diego were non-compliant with California's AB-45, which pertains to industrial hemp products, as they offered hemp-derived cannabinoid products that were inhalable and flavored. Furthermore, the online vape shops out of compliance with AB-45 had greater website traffic, which highlights the need for strengthened regulation of flavored and inhalable hemp-derived cannabinoid product sales. One mechanism for addressing non-compliance may be through an already established model of compliance monitoring used by the County of San Diego Tobacco Retail Licensing program.

Our finding of a dozen “other” hemp-derived cannabinoid products sold by online vape shops raises several concerns given that there is scarce scientific literature on these products and their safety profile. Given that previous research has shown several adverse events associated with delta-8-THC use, the use of these “other” cannabinoid products, many of which are mildly psychotropic, may result in similar negative health outcomes, such as anxiety, paranoia, and respiratory issues (22). Similar to popular cannabinoids, such as delta-8-THC, there is likely a lack of regulatory oversight and quality control in the production of these “other” cannabinoid products.

There are several strengths and limitations to the current study. A notable strength is our use of a comprehensive sample that includes retailers with websites returned in the first two pages of a Google Search in San Diego County, as previous research has shown that over 70% of users click a link on the first page of Google results (32). This approach minimizes sampling bias, which is a common issue in prior studies that focused on brick-and-mortar retailers. However, the restriction of our sample to San Diego County limits the generalizability of our findings to the overall US population as well as other jurisdictions throughout California, since vape shops in different parts of the state may be subject to varying local sales restrictions. For example, 6 of 19 total jurisdictions within San Diego County have adopted flavor restrictions on menthol cigarettes and flavored vaping products (33). Given that psychotropic hemp-derived cannabinoid products are widely available in vape shops throughout the US (26), our study findings need to be replicated in other states with different regulations around the sale of hemp-derived cannabinoid products. An additional strength of the current study is the ability to measure the association between website visits and the types of products available for sale by that website. Although the measure of website traffic allows us to expand on previous research in

the field of e-commerce tobacco retailer surveillance, the 6-month measure of website visits in the current study serves as a proxy for vape shop popularity. We did not measure the number of sales or purchases made for any of the websites in the current study.

Conclusion

We found that a sizeable proportion of online vape shops sold hemp-derived cannabinoid products, most of which were psychotropic. Most online vape shops that sold hemp-derived cannabinoid products offered them in flavored and inhalable modalities, which are prohibited under California's AB-45, which governs industrial hemp products. Notably, vape shops that offered cannabinoid products had a higher number of monthly website visits, which may underscore their popularity with consumers. The availability of hemp-derived cannabinoid products among online vape shops raises multiple public health and policy concerns, such as the lack of standardized safety measures and the absence of marketing regulations for these products. Our findings highlight the need for strengthened regulations of online vape shops offering hemp-derived cannabinoid products to prevent potential public health issues resulting from their sale.

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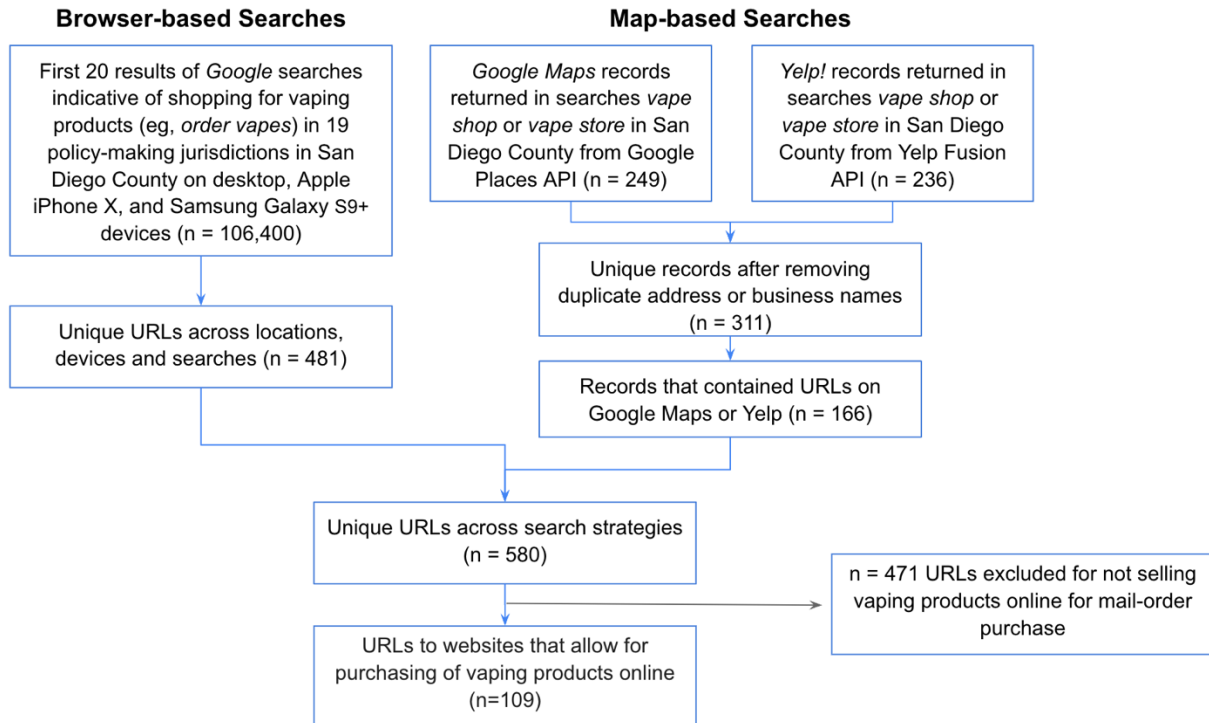


Figure 4: Derivation of study sample of online vape shops offering products for mail-order purchase

Table 13: Agreement and reliability between two independent coders for cannabinoid product-related measures.

Cannabinoid	Agreement (%)	adjusted kappa [†]
Any	0.91	0.82
Cannabidiol (CBD)	0.90	0.80
<i>Inhalable + Flavored CBD</i>	0.94	0.89
Delta-8-THC	0.96	0.93
<i>Inhalable + Flavored delta-8-THC</i>	0.95	0.91
Hexahydrocannabinol (HHC)	0.96	0.93
<i>Inhalable + Flavored HHC</i>	0.95	0.91
Tetrahydrocannabinol acetate (THCO)	0.96	0.93
<i>Inhalable + Flavored THCO</i>	0.96	0.93
Delta-10-THC	0.95	0.91
<i>Inhalable + Flavored delta-10-THC</i>	0.94	0.89
Cannabinol (CBN)	0.95	0.91
<i>Inhalable + Flavored CBN</i>	0.95	0.91
Cannabigerol (CBG)	0.95	0.91
<i>Inhalable + Flavored CBG</i>	0.94	0.89
Hemp-compliant delta-9-THC	0.93	0.85
<i>Inhalable + Flavored hemp-compliant delta-9-THC</i>	0.93	0.85
Other	1.00	1.00
<i>Inhalable + Flavored other cannabinoid</i>	0.88	0.76

[†]The kappa statistic is adjusted for the low prevalence of cannabinoid product availability among vape shops in the study sample.

Table 14: Cannabinoids listed as main ingredients among all online vape shops in the study sample, by product type (n=109).

Cannabinoid	Any products <i>column %</i>	Flavored and inhalable products <i>column %</i>
Any	35.8	26.6
Cannabidiol (CBD)	32.1	21.1
Delta-8-THC	20.2	18.3
Hemp-compliant delta-9-THC	17.4	13.8
Hexahydrocannabinol (HHC)	16.5	14.7
Cannabigerol (CBG)	14.7	7.3
Delta-10-THC	13.8	13.8
Tetrahydrocannabinol acetate (THCO)	10.1	11.0
Cannabinol (CBN)	10.1	9.2
Tetrahydrocannabiphorol (THCP)	10.1	10.1
Hexahydrocannabiphorol (HHCP)	3.7	3.7
Delta-9 tetrahydrocannabutol (THCB)	3.7	3.7
Tetrahydrocannabinolic acid (THCA)	2.8	2.8
Delta-6-THC	2.8	2.8
THC-X	1.8	1.8
Delta-11-THC	2.8	2.8
Cannabidivarin (CBDV)	0.9	0.9
Delta-7-THC	0.9	0.9
Tetrahydrocannabinol monomethylether (THCM)	0.9	0.9
Hydrox-4-phc (PHC)	0.9	0.9
Tetrahydrocannabivarin (THCV)	0.9	0.9

Note: THC-X is a manufactured cannabinoid.

Table 15: Average monthly website traffic for categories of cannabinoid product availability, overall and by retailer type, among online vape shops in the study sample (n=109).

	Overall	Map-Based Retailers	Browser-Based Retailers
Cannabinoid Products Offered	EMM (95% CI)	EMM (95% CI)	EMM (95% CI)
None	23,619 (23,605-23,634)	1,306 (1,302-1,310)	30,914 (30,895-30,934)
Inhalable and Flavored	57,950 (57,913-57,986)	2,953 (2,943-2,962)	69,906 (69,862-69,950)
Not Inhalable or Flavored	130,694 (130,607-130,782)	8,470 (8,444-8,496)	200,537 (200,403-200,672)

Abbreviations: EMM, Estimated Marginal Mean; CI, Confidence Interval

Table 16: Supplement A: Association between types of cannabinoid products offered and average monthly website traffic, adjusting for retailer type among online vape shops in the study sample (n=109).

	Beta	Standard error	t value	p-value
Cannabinoid Products Offered				
None	Ref			
Inhalable and Flavored	30348	11932	2.54	0.011
Not Inhalable or Flavored	113962	17306	6.59	<0.001
Retailer Type				
Brick-and-click	Ref			
Click-only	58734	12042	4.88	<0.001

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CHAPTER 5: CONCLUSION

The passage of the 2018 United States (US) Farm Bill, which separated “hemp” from the definition of “marijuana”, resulted in the growth of a market for hemp-derived cannabinoid products. Hemp-derived cannabinoid products are those derived from *Cannabis Sativa L.* that contain less than 0.3% delta-9-THC, which is the main psychoactive compound in marijuana. Although the new and unregulated marketplace of hemp-derived cannabinoid products poses several health risks to consumers, there is a scarcity of data to answer basic epidemiological questions about their use, reasons for use, and availability.

In Chapter 2, we used a nationally representative sample of US adults to estimate the lifetime use of hemp-derived cannabinoid products and compare the reasons for their use. We found that the use of hemp-derived cannabinoid products is prevalent and there is significant heterogeneity among US adults who use these products in terms of sociodemographic characteristics, medical versus recreational reasons for use, and specific medical reasons for use. Most adults used CBD for medical reasons and delta-8-THC for recreation. Anxiety and pain were among the top three most frequently reported medical conditions for using all of the hemp-derived cannabinoid products assessed. Delta-8-THC, cannabitol (CBN), and hexahydrocannabinol (HHC) were commonly used to treat insomnia while CBD was used to treat arthralgia (i.e., joint pain). These results highlight the need for public health education regarding the use of hemp-derived cannabinoids for the treatment of medical conditions.

In Chapter 3, we used the same sample to estimate the association between lifetime use of delta-8-THC and state marijuana use laws and regulations on delta-8-THC, independently and in combination. We found that the prevalence of delta-8-THC use was lower in states with medical and recreational marijuana use laws and restrictions on delta-8-THC. Our inverse probability of

treatment weighting (IPTW)-adjusted effect estimates showed that medical and recreational marijuana use laws and delta-8-THC restrictions were associated with a lower probability of delta-8-THC use. Furthermore, among states with recreational marijuana use laws, having delta-8-THC restrictions decreased the probability of delta-8-THC use compared to not having any restrictions. Our findings suggest that state restrictions on delta-8-THC may be effective, especially among states with a regulatory framework for legal marijuana products.

In Chapter 4, we conducted a content analysis of e-commerce tobacco retailers serving San Diego County to identify the types of hemp-derived cannabinoid products offered and assess compliance with state hemp regulations. We also used website traffic data to examine the association between product availability and website visits. We found that a sizeable number of retailers were out of compliance with state regulations. Furthermore, tobacco retailers that offered hemp-derived cannabinoid products received more website visits, suggesting an advantage for those selling cannabinoid products compared to those selling nicotine or tobacco products alone. Our findings highlight the need for additional enforcement measures to ensure tobacco retailer compliance with state regulations around hemp.

These studies provide critical contributions to the existing body of literature on hemp-derived cannabinoid products by providing the first nationally representative estimates of the reasons for their use, quantifying the relationship between state regulations and the use of one of the most popular cannabinoids (delta-8-THC) and measuring compliance among retailers in a state with regulations on hemp products. Future research should explore risk perceptions and health outcomes associated with the use of hemp-derived cannabinoid products. Evidence-based education, additional regulations, and better enforcement of existing state laws for hemp-derived

cannabinoid products are crucial for ensuring consumer safety and limiting youth access, both essential for protecting public health.