



## Cannabidiol (CBD) and other drug use among young adults who use cannabis in Los Angeles

Ekaterina V. Fedorova<sup>a,\*</sup>, Carolyn F. Wong<sup>b,c,d</sup>, Janna Ataiants<sup>a</sup>, Ellen Iverson<sup>b,c</sup>, Bridgid M. Conn<sup>b</sup>, Stephen E. Lankenau<sup>a</sup>

<sup>a</sup> Drexel University, Dornsife School of Public Health, Department of Community Health and Prevention, 3215 Market Street, Philadelphia, PA, 19104, United States

<sup>b</sup> University of Southern California, Keck School of Medicine, Department of Pediatrics, 4650 Sunset Blvd., Los Angeles, CA, 90027, United States

<sup>c</sup> Children's Hospital Los Angeles, Division of Adolescent Medicine, 4650 Sunset Blvd., MS #2, Los Angeles, CA, 90027, United States

<sup>d</sup> Children's Hospital Los Angeles, Division of Research on Children, Youth, & Families, 4650 Sunset Blvd., MS #2, Los Angeles, CA, 90027, United States

### ARTICLE INFO

#### Keywords:

Medical marijuana  
Cannabidiol  
Drug use  
Young adults

### ABSTRACT

**Introduction:** Cannabidiol (CBD) is purportedly a promising therapeutic agent to provide relief for a variety of medical conditions with mild or no psychoactive effects. However, little is known about young adults who use cannabis and CBD-dominant products, and associations between CBD use and other drug use.

**Methods:** Young adults (aged 24–32) who currently used cannabis ( $n = 239$ ) were surveyed in Los Angeles in March 2019 through March 2020. The sample was divided into CBD-dominant (at least 1:1 CBD:THC ratio) and THC-dominant product users. We described CBD forms, reasons and conditions for CBD use and examined between-group differences in sociodemographic characteristics, cannabis practices, health and other drug use. **Results:** CBD-dominant users were more likely to be female, use cannabis at lower frequency and amount (except for edible/drinkable/oral products), self-report medical motivation for cannabis use, use cannabis for pain and report more health problems. Oil, flower, topicals and sprays/drops/tinctures were the most prevalent CBD forms. Psychological problems and pain were commonly reported conditions and medical reasons for CBD use. CBD-dominant users were more likely to report illicit drug use, where psilocybin use was markedly different between the two groups.

**Conclusions:** CBD use was associated with health histories and motivations linked to pain and psychological problems. Positive association between CBD use and illicit drug use may indicate self-medication for psychological conditions. Future studies should evaluate the effectiveness of various CBD forms and dose regimens for treatment of pain and psychological problems, and as a potential intervention for decreasing other drug use and associated harms.

### 1. Introduction

Cannabidiol (CBD) is the second most prevalent compound in the *Cannabis sativa* plant after tetrahydrocannabinol (THC). CBD was discovered in 1940, long before the isolation of THC in 1964, but started gaining popularity only around 2016 (Bonaccorso et al., 2019; Leas et al., 2019; Sexton et al., 2016). CBD is non-psychoactive, has low abuse and addiction potential (Englund et al., 2013; Freeman et al., 2019; Iseger and Bossong, 2015; Schoedel et al., 2018; Wheeler et al., 2020). Unlike THC, CBD does not produce anxiety, panic, or psychotic symptoms in high doses (Freeman et al., 2019; Iffland and Grotenhermen, 2017). In the U.S., CBD is available in three forms: hemp-derived,

cannabis-derived, and pharmaceutical-grade products, with CBD to THC ratio content ranging from CBD-only, CBD-dominant, or balanced (1:1 CBD:THC), to THC-dominant CBD products (Corroon and Kight, 2018; Freeman et al., 2019; Hello, 2017).

The legal status of CBD products has been in flux (Corroon and Phillips, 2018). The 2014 Farm Bill exempted hemp-derived CBD with less than 0.3 % THC content from the Drug Enforcement Administration's (DEA) controlled substances list, while cannabis-derived CBD is still classified as a Schedule I controlled substance (Corroon and Kight, 2018; DEA, 2021). Currently, selling CBD products as a dietary supplement and promoting it as a drug with healing properties is prohibited by the U.S. Food and Drug Administration (FDA) (U.S. Food and Drug

\* Corresponding author.

E-mail address: [evf26@drexel.edu](mailto:evf26@drexel.edu) (E.V. Fedorova).

<https://doi.org/10.1016/j.drugalcdep.2021.108648>

Received 14 December 2020; Received in revised form 9 February 2021; Accepted 14 February 2021

Available online 22 February 2021

0376-8716/© 2021 Elsevier B.V. All rights reserved.

**Administration (FDA, 2021).** The FDA has sent numerous warning letters to producers who have marketed their CBD products as a medicine (Corroon and Kight, 2018). Hemp-derived CBD products are sold in a variety of forms over-the-counter and online across the U.S., while cannabis-derived CBD products are available through storefronts in states that legalized medical or recreational cannabis use (Corroon and Phillips, 2018). California is among the states that offer a full spectrum of CBD products over-the-counter and through medical and recreational cannabis dispensaries as medical cannabis has been legal since 1996 and recreational cannabis for adults over 21 years of age became legal in November 2016.

CBD has been suggested as a promising therapeutic agent for a range of clinical applications (Crippa et al., 2018). Since 2001, over two hundred clinical trials have been investigating the use of CBD in treatment of seizures, cancer, post-traumatic stress disorder, and other health conditions (NIH U.S. National Library of Medicine, 2020). However, the only FDA-approved CBD product is Epidolex developed for the treatment of two rare pediatric epilepsies (Sholler et al., 2020). Evidence of CBD benefits for other ailments (i.e., anxiety, depression, sleep disorder, pain, addiction) is limited and inconclusive as results from different studies are conflicting or lack support from controlled studies with sufficient sample sizes (Arndt and de Wit, 2017; Hunter et al., 2018; Hurd et al., 2019; Pokorski et al., 2017; Sholler et al., 2020; Silote et al., 2019; Solowij et al., 2018; Vigil et al., 2018; Zuardi et al., 2017). Moreover, most of the clinical studies have investigated CBD as an isolated compound, whereas the cannabis entourage theory suggests that synergistic therapeutic effect of multiple compounds found in the cannabis plant is above the effect produced by any single compound (Russo, 2011; Sholler et al., 2020; Spindle et al., 2019). Therefore, findings from clinical trials have limited external validity, unlike studies under naturalistic conditions (Vigil et al., 2018).

Evidence on CBD use in naturalistic settings started to emerge in 2015, including industry reports focused on licensed medical cannabis patients (MCP) (Care by Design, 2015; Hello, 2017) and observational studies of self-described CBD users (Corroon and Phillips, 2018; Wheeler et al., 2020). Only one study reported on patterns of CBD use among young adults (Wheeler et al., 2020). As the CBD industry quickly evolves, more CBD products in various forms have become available on the market to cater to all consumer types (Hello, 2017; Leas et al., 2019). Many CBD-dominant products are being sold in forms similar to THC-dominant cannabis products (i.e., CBD oil, CBD flower, CBD edibles) (Hello, 2017; Spindle et al., 2019). According to an industry report on adult MCP, oil, followed by flower, tinctures and topicals were the most popular CBD forms, which is similar to the findings on cannabis forms reported by young adult MCP and non-patient users (Hello, 2017; Lankenau et al., 2017b). In contrast, among young adult self-described CBD users, edibles were the top CBD form followed by tinctures, oil and topicals (Wheeler et al., 2020).

CBD use is especially common among people who use cannabis medicinally (Corroon and Phillips, 2018; Morean and Lederman, 2019; Zeiger et al., 2019). Anxiety, depression, insomnia and pain have been the top reported reasons for CBD use among MCP and self-described CBD users (Care by Design, 2015; Corroon and Phillips, 2018; Hello, 2017; Wheeler et al., 2020). Notably, psychological problems (i.e., stress, insomnia) were the leading motivations for use among younger CBD users (Wheeler et al., 2020), while pain was the most prevalent reason for use within a sample of older CBD users (Corroon and Phillips, 2018). CBD as a substitute or adjunctive therapy to traditional medications was another commonly reported reason for use among adult MCP who perceived CBD as more effective in managing certain health conditions compared to over-the-counter or prescribed medications (Hello, 2017). Some adult MCP used CBD products to cope with addiction (Care by Design, 2015).

Despite CBD's potential as a substitute for other substances, no published study has examined patterns of illicit drug use among CBD-dominant product users, and how those patterns differ from THC-

dominant product users. This is an especially important area of inquiry as young adults have the highest rates of illicit drug use (Substance Abuse and Mental Health Services Administration (SAMHSA, 2019). Given this gap in the literature in addition to increasing rates of CBD use and its potential to reduce use of other substances (Care by Design, 2015; Hello, 2017; Hurd et al., 2019; Leas et al., 2019), the current study was undertaken to describe patterns of CBD use among young adults who use cannabis, and determine the extent to which CBD use is associated with licit (alcohol, tobacco, prescribed medications) and illicit drug use.

## 2. Methods

The study was approved by the Institutional Review Boards at Drexel University and Children's Hospital Los Angeles. All participants provided a consent to be surveyed in this study.

### 2.1. Study sample

The current study utilized the fifth wave of the quantitative data (n = 260) collected between 2019–2020 from the ongoing Cannabis, Health and Young Adults (CHAYA) longitudinal cohort study (Lankenau et al., 2017b) when we first introduced questions related to CBD use in response to growing interest in CBD and its perceived efficacy. The wave 1 (baseline) (n = 366) sample consisted of 18- to 26-year-old young adults who currently used cannabis residing in the Los Angeles metro area who either had a current valid medical cannabis recommendation issued in California (medical cannabis patients or MCP, n = 210) or had never had a medical cannabis recommendation (non-patient users or NPU, n = 156). Study participants were administered annual quantitative surveys (see (Lankenau et al., 2017a) for additional details on recruitment and characteristics of the baseline sample).

### 2.2. Data collection

Wave 1 quantitative sample was recruited and surveyed in-person between February 2014 and April 2015. Wave 5 quantitative survey was administered online through Research Electronic Data Capture (REDCap) between March 2019 and March 2020.

### 2.3. Measures

Data on key socio-demographic characteristics (i.e., age, gender and race/ethnicity) were collected at wave 1, while educational level and income were assessed annually (Lankenau et al., 2017b).

Use of CBD products with varying CBD:THC ratio was assessed with the following item: *In the past 90 days, have you used any of the following marijuana products that contain CBD [check all that apply]?* Answer options were as following: (1) *hemp-derived CBD product (no THC)*; (2) *mostly CBD product (some THC)*; (3) *half CBD/half THC product*; (4) *some CBD product (mostly THC)*; (5) *none of the products I have used had CBD in it.* Measures assessing CBD use also included questions about CBD forms (e.g., bud/flower, tinctures, edibles), reasons for CBD product use, and health conditions CBD products were used for. Measures of past 90-day cannabis use included days of cannabis use (range 0–90), hits per day (i.e., pull of a pipe, joint, bong, etc.), times per day for using edible/drinkable/oral cannabis products, vaping cannabis oil (yes/no), and reasons for cannabis use. Microdosing was defined as past 12-month consumption of small amounts of marijuana, e.g., 2.5 mg, one hit, one bite, to experience the benefits of THC while limiting the high. Those who had a current valid medical cannabis recommendation at wave 5 were classified as MCP. A dichotomous self-reported medical cannabis use motivation variable was created representing those who reported using cannabis for exclusively or primarily medical, or equally medical and recreational reasons, relative to those who reported using cannabis for primarily or exclusively recreational reasons. Past 12-month physical

**Table 1**  
Sociodemographic characteristics and health conditions of young adults who use cannabis (n = 239).

	Total n = 239 %(n)	CBD-dominant n = 101 %(n)	THC-dominant n = 138 %(n)
Age, mean (SD)	25.3(2.5)	25.4(2.6)	25.2(2.3)
Gender/sex at birth			
Male*	61.5(147)	51.5(52)	68.8(95)
Ethnicity			
Hispanic/Latino	45.1(106)	44.3(43)	45.7(63)
Non-Hispanic race			
White	27.7(65)	33.0(32)	23.9(33)
Black/African American	17.4(41)	12.4(12)	21.0(29)
Multi-Racial	6.4(15)	6.2(6)	6.5(9)
Asian/Pacific Islander	3.4(8)	4.1(4)	2.9(4)
Education			
Some college or above	82.0(191)	85.0(85)	79.7(106)
Annual income			
Below \$25,000	46.4(102)	53.2(50)	41.3(52)
Health conditions in the past 12 months			
Pain (chronic, back pain, migraines)*	39.7(95)	51.5(52)	31.2(43)
Sleep, mood or other psychological problems (such as insomnia, depression)	54.0(129)	62.4(63)	47.8(66)
Nausea or other gastrointestinal problems (such as gastritis, peptic ulcer)	21.3(51)	26.7(27)	17.4(24)
None*	33.5(80)	24.8(25)	39.9(55)

\* p < 0.05.

and psychological health was assessed through the following multiple-choice question: *Have you experienced any physical or psychological problems in the past 12 months in the following area?* This question was followed by a list of potential health problems including pain, psychological and gastrointestinal problems.

Other drug use measures included questions about licit (i.e., alcohol, tobacco, prescribed medications) and illicit (e.g., street and club drugs, and prescription medications misuse) drug use. Alcohol, tobacco, illicit drug use and prescription drug misuse were assessed with the following question: *In the past 12 months, have you used any of the following drugs when they were not prescribed to you or that you took only for the experience or feeling it caused (including to get high or to self-medicate)?* Affirmative responses were followed by the question: *How long has it been since you last used [drug name]?* Responses were dichotomized into yes/no indicating presence or absence of use in the past 90 days. Past 90-day users of illicit drugs and misusers of prescription drugs were asked to select the most frequently used/misused drug and reasons for use/misuse. Prescribed medications question assessed medications prescribed for any injury or health condition in the past 12 months.

#### 2.4. Data analysis

The analytical sample was comprised of young adults (n = 239) who reported past 90-day cannabis use (21 out of 260 (8.1 %) wave 5 participants did not report past 90-day cannabis use). First, CBD users were categorized based on the highest level of CBD content in CBD products used in the past 90 days into four mutually exclusive subgroups: *CBD only* (hemp-derived), *Mostly CBD*, *Half CBD/half THC*, and *Some CBD* product users. For example, *CBD only* users could also report using products with lower CBD content (e.g., mostly CBD, half CBD/half THC, some CBD, or THC only products), while *Mostly CBD* users could also report using half CBD/half THC, some CBD, or THC only products. Then, sample was divided into two groups: CBD-dominant (i.e., *CBD only*, *Mostly CBD* and *Half CBD/half THC* subgroups) and THC-dominant (i.e., *Some CBD* and *THC only* subgroups) product users (Hello, 2017).

The four CBD user subgroups were described by generating frequencies for past 90-day use of CBD forms, reasons and health conditions for CBD use. Differences on key demographic characteristics, health, and cannabis use practices between CBD-dominant and THC-dominant groups were examined with chi-square test for binary and Kruskal-Wallis test for count (i.e., days, hits, times per day) variables. Associations between CBD-dominant product use and other drug use were assessed through logistic regression models which were adjusted

for age, gender or race/ethnicity if outcome was associated with either demographic variable at p < 0.1 level. Given a large number of statistical tests, correction for multiple testing was implemented (Benjamini and Hochberg, 1995).

All analyses were performed in SAS, version 9.4.

### 3. Results

The mean age within the sample was 25.3 years old (Table 1). Participants were predominantly male (61.5 %), of Hispanic/Latino ethnicity (45.1 %), and educated (82.0 % reported some college or above). Almost half (46.4 %) of the participants reported annual income below \$25,000. CBD-dominant users (n = 101, 42.3 %), compared to THC-dominant users (n = 138, 57.7 %), were less likely to be males (p < 0.05) and had higher prevalence of non-Hispanic Whites and lower prevalence of non-Hispanic Blacks/African Americans (though this was not statistically significant). CBD-dominant users were more likely to report at least one health condition in the past 12 months compared to THC-dominant users (75.2 % vs. 60.1 %, p < 0.05). Of those reporting health conditions, significantly more CBD-dominant users reported pain (51.5 % vs. 31.2 %, p < 0.05).

Among THC-dominant users, 50 % were within *Some CBD* subgroup (Table 2). The following subgroups were identified within CBD-dominant user group: *CBD only* (56.4 %), *Mostly CBD* (17.8 %), and *Half CBD/half THC* (25.7 %) users. *CBD only* subgroup had the highest prevalence of CBD creams/topical use (36.8 %), *Mostly CBD* subgroup reported the greatest use of CBD bud/flower (50.0 %), CBD oil (44.4 %), and CBD sprays/drops/tinctures (38.9 %). *Half CBD/half THC* subgroup had highest proportion of CBD edibles (26.9 %) and CBD drinks (26.9 %) users, while CBD bud/flower (34.6 %) and CBD oil (30.8 %) were commonly reported CBD forms within this subgroup. Relief from physical pain, feeling uptight or anxious, and help with sleep were the top three medical reasons for CBD use reported by over a half of CBD-dominant users. THC-dominant group reported the lowest prevalence of CBD use for medical reasons (except for CBD use to relieve feeling uptight or anxious) compared to the other three CBD subgroups. Sleep, mood, or other psychological problems followed by pain were the top two reported health conditions for CBD use. Proportions of users using CBD for pain, sleep, mood, or other psychological problems were lowest among THC-dominant users.

CBD-dominant users, relative to THC-dominant users, reported fewer cannabis days (57.3 vs. 64.9, p < 0.05) and hits per day (12.9 vs. 17.5, p < 0.05), while more times per day for edible/drinkable/oral cannabis

**Table 2**  
CBD use practices of young adult CBD users (n = 171).

	CBD-dominant			THC-dominant	
	CBD only n = 57 %(n)	Mostly CBD n = 18 %(n)	Half CBD/ half THC n = 26 %(n)	Total n = 101 %(n)	Some CBD n = 69 %(n)
<i>CBD forms</i>					
Creams/topical	36.8(21)	27.8(5)	15.4(4)	29.7(30)	24.6(17)
Sprays/drops/tinctures	33.3(19)	38.9(7)	11.5(3)	28.7(29)	17.4(12)
Oils	29.8(17)	44.4(8)	30.8(8)	32.7(33)	29.0(20)
Bud/flower/pre-rolled	26.3(15)	50.0(9)	34.6(9)	32.7(33)	42.0(29)
Drinks	19.3(11)	0.0(0)	26.9(7)	17.8(18)	8.7(6)
Edibles	17.5(10)	22.2(4)	26.9(7)	20.8(21)	26.1(18)
Pills/capsules	10.5(6)	5.6(1)	11.5(3)	9.9(10)	5.8(4)
Concentrates (wax, shatter, dab)	7.0(4)	16.7(3)	11.5(3)	9.9(10)	14.5(10)
Patch/transdermal	0.0(0)	0.0(0)	0.0(0)	0.0(0)	2.9(2)
<i>Reasons for CBD use</i>					
To relieve physical pain	61.4(35)	66.7(12)	61.5(16)	62.4(63)	50.7(35)
To relieve feeling uptight or anxious	52.6(30)	38.9(7)	23.1(6)	42.6(43)	29.0(20)
To help sleep	42.1(24)	38.9(7)	42.3(11)	41.6(42)	29.0(20)
To cope with feeling depressed	17.5(10)	16.7(3)	15.4(4)	16.8(17)	11.6(8)
<i>Health conditions used CBD for</i>					
Pain (chronic, back pain, migraines)	63.2(36)	50.0(9)	57.7(15)	59.4(60)	49.3(34)
Sleep, mood, or other psychological problems (such as insomnia, depression)	71.9(41)	66.7(12)	57.7(15)	67.3(68)	40.6(28)
Nausea or other gastrointestinal problems (such as gastritis, peptic ulcer)	28.1(16)	11.1(2)	23.1(6)	23.8(24)	11.6(8)
None	7.0(4)	5.6(1)	7.7(2)	6.9(7)	26.1(18)

products (5.3 vs. 2.6,  $p < 0.05$ ) (Table 3). CBD-dominant users were more likely to microdose cannabis (55.1 % vs. 35.4 %,  $p < 0.05$ ), report vaping cannabis oil (56.4 % vs. 38.4 %,  $p < 0.05$ ), use cannabis to relieve physical pain (65.3 % vs. 48.6 %,  $p < 0.05$ ), and self-report medical cannabis use (72.7 % vs. 48.0 %,  $p < 0.01$ ).

In the adjusted regression models, CBD-dominant product use predicted greater likelihood of any illicit drug use (AOR = 2.1,  $p < 0.05$ ) (Table 4). The greatest difference was observed for psilocybin use with past 90-day prevalence of 19.8 % within CBD-dominant vs. 4.4 % within THC-dominant users. About half of the psilocybin users reported it as the most frequently used drug in the past 90 days. Among them, majority of the CBD-dominant users reported psilocybin use to cope with anxiety, depression, or both.

#### 4. Discussion

This is the first study characterizing use of CBD products with varying CBD content and corresponding CBD forms, health-related reasons for CBD use, and examining differences in cannabis use

characteristics and associations with other drug use among young adults who used CBD-dominant and THC-dominant cannabis products.

The sample consisted of two groups: CBD-dominant (42.3 %) (CBD only, Mostly CBD and Half CBD/half THC subgroups) and THC-dominant (57.7 %) (Some CBD and THC only subgroups) product users. Earlier report on CBD use among adult MCP also indicated that while CBD product use was common, THC product use still predominated (Hello, 2017). Similar to other studies, a majority of CBD-dominant product users reported having some college education, annual income below \$25,000, self-identifying as Hispanic/Latino or non-Hispanic White, and were more likely to be female compared to THC-dominant product users (Boehnke et al., 2019; Corroon and Phillips, 2018; Hello, 2017; Wheeler et al., 2020; Zeiger et al., 2019). While no age differences were observed between the two user groups, earlier studies with greater age variability within their samples reported an association between CBD use and older age (Corroon and Phillips, 2018; Zeiger et al., 2019).

Consistent with the industry report on CBD use among MCP (Hello, 2017), flower, oil and edibles were common CBD forms among THC-dominant users, while use of CBD creams/topical,

**Table 3**  
Cannabis use practices by CBD-dominant and THC-dominant user groups (n = 239).

	Total n = 239 mean(SD)	CBD-dominant n = 101 mean(SD)	THC-dominant n = 138 mean(SD)
<i>Cannabis days*</i>	61.7(33.1)	57.3(33.1)	64.9(32.8)
<i>Hits per day (pull of a pipe, joint, bong)*</i>	15.5(19.4)	12.9(17.7)	17.5(20.5)
<i>Time per day for edible/drinkable/oral cannabis products*</i>	3.8(10.6)	5.3(13.4)	2.6(7.7)
	%(n)	%(n)	%(n)
<i>Microdosing*</i>	43.9(100)	55.1(54)	35.4(46)
<i>Vaping cannabis oil*</i>	46.0(110)	56.4(57)	38.4(53)
<i>Medical Cannabis Patient</i>	11.7(28)	7.9(8)	14.5(20)
<i>Self-reported medical cannabis use**</i>	58.9(132)	72.7(72)	48.0(60)
<i>Reasons for cannabis use</i>			
To help sleep	61.5(147)	66.3(67)	58.0(80)
To relieve physical pain*	55.6(133)	65.3(66)	48.6(67)
To relieve feeling uptight or anxious	51.0(122)	50.5(51)	51.4(71)
To cope with feeling depressed	35.1(84)	36.6(37)	34.1(47)

\*  $p < 0.05$ .

\*\*  $p < 0.01$ .

**Table 4**  
Other drug use outcomes by CBD-dominant and THC-dominant user groups (n = 239).

	CBD-dominant n = 101 %(n)	THC-dominant n = 138 %(n)	OR (95 % CI)
<i>Licit drug use</i>			
Alcohol	55.6(55)	52.9(72)	1.1(0.7–1.9)
Cigarette	35.4(35)	29.1(39)	1.3(0.8–2.3)
E-cigarette <sup>1,2,3</sup>	22.4(22)	12.5(17)	2.0(0.9–4.4)
<i>Prescribed medications</i>			
Any medication <sup>1,2</sup>	16.8(17)	9.4(13)	1.3(0.6–3.1)
Opioids	8.9(9)	3.6(5)	
Tranquilizers	5.9(6)	2.9(4)	
Stimulants	6.9(7)	1.4(2)	
Sleeping pills	4.0(4)	2.2(3)	
Antidepressants	9.9(10)	5.1(7)	
<i>Rx drug misuse</i>			
Any Rx drug misuse <sup>1,2,4</sup>	21.8(22)	8.0(11)	2.6(1.1–5.9)
Opioids	5.9(6)	1.4(2)	
Tranquilizers	5.9(6)	2.9(4)	
Stimulants	5.9(6)	2.9(4)	
Muscle relaxants	6.9(7)	0.7(1)	
Sleeping pills	3.0(3)	0.7(1)	
Antidepressants	2.0(2)	0.7(1)	
<i>Illicit drug use</i>			
Any illicit drug use <sup>1,5,*</sup>	34.7(35)	19.6(27)	2.1(1.2–3.9)
LSD	8.0(8)	4.3(6)	
Psilocybin <sup>6</sup>	19.8(20)	4.4(6)	
MDMA	7.9(8)	5.1(7)	
GHB	0.0(0)	0.7(1)	
Cocaine	15.0(15)	13.1(18)	
Methamphetamine	1.0(1)	0.0(0)	
Ketamine	2.0(2)	0.7(1)	

\* p < 0.05.

<sup>1</sup> Adjusted for non-Hispanic White.

<sup>2</sup> Adjusted for gender.

<sup>3</sup> Adjusted to vaping cannabis oil.

<sup>4</sup> Adjusted for prescribed any medication.

<sup>5</sup> None reported past 12-month use of heroin, fentanyl, crack, synthetic cathinone, synthetic cannabis or salvia.

<sup>6</sup> Highest proportion (11.9 %) of users/misusers illicit/prescription drugs named psilocybin as a drug used most frequently in the past 90 days; 55 % (n = 11) of CBD-dominant psilocybin users, 50 % (n = 3) of THC-dominant psilocybin users reported psilocybin being the most frequent drug they used in the past 90 days; among them, n = 8 among CBD-dominant users and n = 1 among THC-dominant users used psilocybin to cope with anxiety or depression or both.

sprays/drops/tinctures and drinks was more prevalent within subgroups of CBD-dominant users. Previous studies found that medicinally-oriented CBD-dominant and THC-dominant cannabis use was associated with use of topical and sublingual (i.e., sprays/drops/tinctures) forms, which may indicate desire for more prolonged therapeutic effects with less or no euphoria (Boehnke et al., 2019; Corroon and Phillips, 2018; Jorge et al., 2011; Maccallum and Russo, 2018).

Pain was the most prevalent reason for use among CBD-dominant product users, which is not surprising given that products with higher CBD content were reported to be more effective in pain management than THC-dominant products (Hello, 2017). Moreover, there is evidence that high THC dosage may even worsen pain (Wallace et al., 2007). However, in some cases, THC-dominant products (i.e., flower via smoking) may be preferred due to a more rapid pain relief over commonly reported oral and topical CBD products with delayed onset (Bruni et al., 2018; Hello, 2017). Furthermore, over 90 % of CBD-dominant users reported using CBD to treat one or more health conditions. Similar to a previous study on young adult CBD users (Wheeler et al., 2020), psychological problems followed by pain were the most common conditions for CBD use. Importantly, CBD-dominant and THC-dominant products have been used for very similar reasons and conditions, i.e., sleep, mood problems, and pain (Corroon and Phillips, 2018; Hello, 2017; Lankenau et al., 2017a; Tran and Kavuluru, 2020; Walsh et al., 2013). However, CBD products could be preferred over THC-dominant products due to perceived legality (i.e., hemp) and

better safety profile (i.e., lower addiction potential and lower probability of experiencing anxiety, paranoia or other THC-related adverse effects), and perceived ability to pass a cannabis drug test (Englund et al., 2013; Freeman et al., 2019; Schoedel et al., 2018; Wheeler et al., 2020).

Overall, compared to THC-dominant users, a greater proportion of CBD-dominant users reported using CBD for medical reasons and to treat physical or psychological health conditions. Our findings highlight differences between CBD-dominant and THC-dominant users and provide justification for further analysis focusing on the differences between these two groups given the similarities between *CBD only*, *Mostly CBD* and *Half CBD/half THC* subgroups. Moreover, the current conceptualization of CBD use is similar to the earlier industry report that defined CBD-dominant products as 1:1 CBD:THC ratio, namely half CBD/half THC, or higher (Hello, 2017).

In terms of differences in cannabis use practices, CBD-dominant users reported significantly fewer days of cannabis use and used cannabis forms associated with medical uses (i.e., edibles, drinks, and other oral products) significantly more times per day, while THC-dominant users reported significantly more hits per day when using cannabis forms more prevalent among recreational users (i.e., flower via a pipe or joint; Boehnke et al., 2019; Corroon and Phillips, 2018; Pacula et al., 2016). These findings provide a potential explanation for discrepancies in the results from previous studies reporting a negative association between medicinal CBD use and regular cannabis use (Corroon and Phillips, 2018), while a positive association between medicinal orientation and

more frequent cannabis use (Choi et al., 2017; Metrik et al., 2018), since these studies did not differentiate frequency of use between cannabis forms with varying CBD:THC concentrations. Additionally, CBD-dominant users were more likely to microdose cannabis (e.g., use no more than 2.5 mg at a time), suggesting more responsible, functional, and medicinally oriented cannabis use (Dussault and Bardi, 2017; Johnstad, 2018; Webb et al., 2019).

Prevalence of other drug use across almost all licit and illicit drugs was consistently higher among CBD-dominant users. The greatest difference in licit drug use was observed for e-cigarette use. This may be partially explained by a perceived safety of vaping compared to combustible modes (despite recent reports on health hazards of vaping; (Mcgee and Goldschmidt, 2019; Saxena et al., 2018), similar to CBD-dominant products perceived as being safer than THC-dominant products (Chapman and Wu, 2015; Wheeler et al., 2020).

Greater history of prescribed medications and prescription drug misuse among CBD-dominant users is consistent with greater prevalence of health conditions within this group. Receiving a prescription commonly precedes misuse since medications are frequently misused for the same reason that they were prescribed (Lankenau et al., 2012; Lipari et al., 2017). Moreover, concurrent use of CBD products and prescription medications has been described in the literature as a way to reduce the dose of traditional medications that have more serious adverse effects (Iffland and Grotenhermen, 2017). Additionally, some users might perceive THC-dominant products as more effective for the management of specific physical and psychological health conditions than CBD-dominant products, therefore, eliminating the need for use and misuse of prescription medications. For instance, analgesic properties of THC and its role as a substitute for prescription opioids have been well established, while evidence on CBD use for pain and its ability to stem opioid use is still emerging (Capano et al., 2020; Hill et al., 2017; Khan et al., 2019). Furthermore, comparative effectiveness of THC-dominant versus CBD-dominant products for a range of health problems is yet to be studied (Hello, 2017). Surprisingly, CBD use was associated with illicit drug use. In our early reports and other studies, medicinal orientation towards cannabis use was consistently protective against illicit drug use (Fedorova et al., 2019, 2020a, 2020b; Metrik et al., 2018; Morean and Lederman, 2019; Roy-Byrne et al., 2015). On the other hand, medicinal uses of CBD-dominant (Corroon and Phillips, 2018; Wheeler et al., 2020) and THC-dominant products appear to be common among CBD users. Therefore, similar protective effect of CBD use on illicit drug use might be expected. Upon closer inspection, the association of CBD use with illicit drug use appeared to be driven by psilocybin use. Interestingly, almost half of CBD-dominant users reported using psilocybin to cope with anxiety or depression or both. Indeed, significant and sustained improvement in anxiety and depressive symptoms after psilocybin administration was also observed in recent controlled studies (Goldberg et al., 2020; Reiche et al., 2018).

Our findings present several implications for researchers, healthcare practitioners and industry workers. Given increasing prevalence of CBD use, future studies should explore the efficacy of various CBD forms and CBD:THC ratios for treatment of the most prevalent health conditions CBD was reported being used for in the current study, including pain, anxiety, and sleep problems. Increased rates of prescription and illicit drug use and misuse among CBD users call for more research on drug interactions, and the extent to which CBD can replace or reduce the use of the latter (Sholler et al., 2020; Wheeler et al., 2020). Finally, our study showed that CBD product use may have the potential to reduce harms to respiratory system associated with cannabis smoking given that CBD users reported significantly less frequent use of combustible cannabis forms (Ammerman et al., 2015). Health practitioners and dispensary staff can educate people who currently use cannabis about non-combustible forms of CBD as well as THC products as healthier alternatives.

This study has several limitations that should be noted. First, our results may not be generalizable to young adult CBD users in the general

population since the study sample was not randomly selected, and it was comprised of young adults who currently used cannabis. Second, our study was conducted in a setting with increased access to CBD products with varying CBD:THC ratio, as medical and recreational cannabis use are both legal in California. Therefore, our findings may not be applicable to states with less progressive legal environments around cannabis use. Third, questions about CBD isolate product use were not included in the survey instrument. However, CBD isolate users could select 'hemp-derived CBD (no THC)' based on the lack of THC in these products. Fourth, we did not assess exact CBD:THC ratio of the products used by study participants, which might provide with greater insight into CBD's efficacy under naturalistic conditions. However, given that the labeling of THC content in CBD products has been found in many cases to be incorrect (Bonn-Miller et al., 2017; Care by Design, 2015; Gurley et al., 2020), the current approach to categorize CBD product type as categorical or binary seems reasonable, until more reliable standards are adhered in the industry.

## 5. Conclusions

The use of CBD-dominant products is relatively common among young adults who use cannabis and will likely grow as cannabis markets evolve. Our findings demonstrate high prevalence of health conditions (i.e., pain, anxiety, sleep problems), and medicinally-oriented CBD and cannabis use among young adult CBD-dominant product users. CBD use was associated with less frequent cannabis use via combustible modes of administration. Association of CBD use with illicit drug use may suggest self-medication for psychological problems. Future studies should investigate the efficacy of various CBD forms and concentrations for specific health conditions in naturalistic settings, drug interactions, and CBD's potential to reduce the use of other substances with less favorable safety profiles.

## Contributors

Authors Wong, Iverson and Lankenau developed the study design and protocol. Author Fedorova conducted literature review, statistical analysis and wrote the first draft of the manuscript. Authors Fedorova, Wong, Ataiants, Conn and Lankenau contributed to statistical analysis. All authors contributed to revisions of the draft and have approved the final manuscript.

## Role of funding source

The study was funded by a grant from the National Institute on Drug Abuse (DA034067). This manuscript is the sole responsibility of the authors and does not reflect the views of the National Institute on Drug Abuse.

## Declaration of Competing Interest

The authors report no declarations of interest.

## Acknowledgements

The authors would like to acknowledge the project's Community Advisory Board and the following individuals who supported the development of this manuscript: Meagan Suen, Ana Francisco, Marina Mills and Maral Shahinian.

## References

- Ammerman, S., Ryan, S., Adelman, W.P., 2015. The impact of marijuana policies on youth: clinical, research, and legal update. *Pediatrics* 135, e669-785. <https://doi.org/10.1542/peds.2014-4147>.

- Arndt, D.L., de Wit, H., 2017. Cannabidiol does not dampen responses to emotional stimuli in healthy adults. *Cannabis Cannabinoid Res.* 2, 105–113. <https://doi.org/10.1089/can.2017.0014>.
- Benjamini, Y., Hochberg, Y., 1995. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J. R. Stat. Soc. Ser. B* 57, 289–300. <https://doi.org/https://www.jstor.org/stable/2346101>.
- Boehnke, K.F., Scott, J.R., Litinas, E., Sisley, S., Clauw, D.J., Goesling, J., Williams, D.A., 2019. Cannabis use preferences and decision-making among a cross-sectional cohort of medical cannabis patients with chronic pain. *J. Pain* 20, 1362–1372. <https://doi.org/10.1016/j.jpain.2019.05.009>.
- Bonaccorso, S., Ricciardi, A., Zangani, C., Chiappini, S., 2019. Cannabidiol (CBD) use in psychiatric disorders: a systematic review. *Neurotoxicology* 74, 282–298. <https://doi.org/10.1016/j.neuro.2019.08.002>.
- Bonn-Miller, M.O., Loflin, M.J., Thomas, B.F., Marcu, J.P., Hyke, T., Vandrey, R., 2017. Labeling accuracy of cannabidiol extracts sold online. *JAMA* 318, 1708–1709.
- Bruni, N., Della Pepa, C., Oliaro-Bosso, S., Pessione, E., Gastaldi, D., Dosio, F., 2018. Cannabinoid delivery systems for pain and inflammation treatment. *Molecules* 23, 1–25. <https://doi.org/10.3390/molecules23102478>, 2478.
- Capano, A., Weaver, R., Burkman, E., 2020. Evaluation of the effects of CBD hemp extract on opioid use and quality of life indicators in chronic pain patients: a prospective cohort study. *Postgrad. Med.* 132, 56–61. <https://doi.org/10.1080/00325481.2019.1685298>.
- Care by Design, 2015. *CBD Patient Survey*.
- Chapman, S.L., Wu, L.-T., 2015. E-cigarette prevalence and correlates of use among adolescents versus adults: a review and comparison. *J. Psychiatr. Res.* 54, 43–54. <https://doi.org/10.1016/j.jpsychires.2014.03.005>.
- Choi, N.G., Dinitto, D.M., Marti, C.N., 2017. Nonmedical versus medical marijuana use among three age groups of adults: associations with mental and physical health status. *Am. J. Addict.* 26, 697–706. <https://doi.org/10.1111/ajad.12598>.
- Corroon, J., Kight, R., 2018. Regulatory status of cannabidiol in the United States: a perspective. *Cannabis Cannabinoid Res.* 3, 190–194. <https://doi.org/10.1089/can.2018.0030>.
- Corroon, J., Phillips, J.A., 2018. A Cross-sectional study of cannabidiol users. *Cannabis Cannabinoid Res.* 3, 152–161. <https://doi.org/10.1089/can.2018.0006>.
- Crippa, J.A., Guimarães, F.S., Campos, A.C., Zuardi, A.W., 2018. Translational investigation of the therapeutic potential of cannabidiol (CBD): toward a new age. *Front. Immunol.* 9, 1–16. <https://doi.org/10.3389/fimmu.2018.02009>.
- Drug Enforcement Administration (DEA), 2021. *Drug Scheduling*. Accessed February 9, 2021. <https://www.dea.gov/drug-scheduling>.
- Dussault, D., Bardi, G., 2017. *Ganja Yoga: a Practical Guide to Conscious Relaxation, Soothing Pain Relief and Enlightened Self-discovery*. Hay House, Inc. HarperCollins Publishers, New York, NY.
- Englund, A., Morrison, P.D., Nottage, J., Hague, D., Kane, F., Bonaccorso, S., Stone, J.M., Reichenberg, A., Brenneisen, R., Holt, D., Feilding, A., Walker, L., Murray, R.M., Kapur, S., 2013. Cannabidiol inhibits THC-elicited paranoid symptoms and hippocampal-dependent memory impairment. *J. Psychopharmacol.* 27, 19–27. <https://doi.org/10.1177/0269881112460109>.
- Fedorova, E.V., Schrage, S.M., Robinson, L.F., Cepeda, A., Wong, C.F., Iverson, E., Lankenau, S.E., 2019. Illicit drug use and prescription drug misuse among young adult medical cannabis patients and non-patient users in Los Angeles. *Drug Alcohol Depend.* 198, 21–27. <https://doi.org/10.1016/j.drugalcdep.2019.01.026>.
- Fedorova, E.V., Roth, A.M., Cepeda, A., Wong, C.F., Iverson, E., Lankenau, S.E., 2020a. The role of life events/contextual factors and cannabis use in patterns of other drug use among young adult cannabis users in Los Angeles: a qualitative inquiry. *J. Drug Issues* 50, 157–172. <https://doi.org/10.1177/0022042619900205>.
- Fedorova, E.V., Schrage, S.M., Robinson, L.F., Roth, A.M., Wong, C.F., Iverson, E., Lankenau, S.E., 2020b. Developmental trajectories of illicit drug use, prescription drug misuse and cannabis practices among young adult cannabis users in Los Angeles. *Drug Alcohol Rev.* 39, 743–752. <https://doi.org/10.1111/dar.13078>.
- Freeman, A.M., Petrilli, K., Lees, R., Hindocha, C., Mokrysz, C., Curran, H.V., Saunders, R., Freeman, T.P., 2019. How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. *Neurosci. Biobehav. Rev.* 107, 696–712. <https://doi.org/10.1016/j.neubiorev.2019.09.036>.
- Goldberg, S.B., Pace, B.T., Nicholas, C.R., Raison, C.L., Hutson, P.R., 2020. The experimental effects of psilocybin on symptoms of anxiety and depression: a meta-analysis. *Psychiatry Res.* 284, 112749. <https://doi.org/10.1016/j.psychres.2020.112749>.
- Gurley, B.J., Murphy, T.P., Gul, W., Walker, L.A., Elsohly, M., 2020. Content versus label claims in cannabidiol (CBD)-containing products obtained from commercial outlets in the state of Mississippi. *J. Diet. Suppl.* 17, 1–9. <https://doi.org/10.1080/19390211.2020.1766634>.
- Hello, M.D., 2017. *Understanding Cannabidiol/CBD*. Industry Expert Report. The Brightfield Group.
- Hill, K.P., Palastro, M.D., Johnson, B., Ditre, J.W., 2017. Cannabis and pain: a clinical review. *Cannabis Cannabinoid Res.* 2, 96–104. <https://doi.org/10.1089/can.2017.0017>.
- Hunter, D., Oldfield, G., Tich, N., Messenheimer, J., Sebree, T., 2018. Synthetic transdermal cannabidiol for the treatment of knee pain due to osteoarthritis. *Osteoarthr. Cartil.* 26, S26. <https://doi.org/10.1016/j.joca.2018.02.067>.
- Hurd, Y.L., Spriggs, S., Alishayev, J., Winkel, G., Gurgov, K., Kudrich, C., Opreacu, A.M., Salsitz, E., 2019. Cannabidiol for the reduction of cue-induced craving and anxiety in drug-abstinent individuals with heroin use disorder: a double-blind randomized placebo-controlled trial. *Am. J. Psychiatry* 176, 911–922. <https://doi.org/10.1176/appi.ajp.2019.18101191>.
- Iffland, K., Grotenhermen, F., 2017. An update on safety and side effects of cannabidiol: a review of clinical data and relevant animal studies. *Cannabis Cannabinoid Res.* 2, 139–154. <https://doi.org/10.1089/can.2016.0034>.
- Iseger, T.A., Bossong, M.G., 2015. A systematic review of the antipsychotic properties of cannabidiol in humans. *Schizophr. Res.* 162, 153–161. <https://doi.org/10.1016/j.schres.2015.01.033>.
- Johnstad, P.G., 2018. Powerful substances in tiny amounts: an interview study of psychedelic microdosing. *Nord. Stud. Alcohol Drugs* 35, 39–51. <https://doi.org/10.1177/1455072517753339>.
- Jorge, L.L., Feres, C.C., Teles, V.E., 2011. Topical preparations for pain relief: efficacy and patient adherence. *J. Pain Res.* 4, 11–24. <https://doi.org/10.2147/JPR.S9492>.
- Khan, S.P., Pickens, T.A., Berlau, D.J., 2019. Perspectives on cannabis as a substitute for opioid analgesics. *Pain Manag.* 9, 191–203. <https://doi.org/10.2217/pmt-2018-0051>.
- Lankenau, S.E., Schrage, S.M., Silva, K., Kecojevic, A., Bloom, J.J., Wong, C., Iverson, E., 2012. Misuse of prescription and illicit drugs among high-risk young adults in Los Angeles and New York. *J. Public Health Res.* 1, 22–30.
- Lankenau, S.E., Ataiants, J., Mohanty, S., Schrage, S., Iverson, E., Wong, C.F., 2017a. Health conditions and motivations for marijuana use among young adult medical marijuana patients and non-patient marijuana users. *Drug Alcohol Rev.* 37, 237–246. <https://doi.org/10.1111/dar.12534>.
- Lankenau, S.E., Fedorova, E.V., Reed, M., Schrage, S.M., Iverson, E., Wong, C.F., 2017b. Marijuana practices and patterns of use among young adult medical marijuana patients and non-patient marijuana users. *Drug Alcohol Depend.* 170, 181–188. <https://doi.org/10.1016/j.drugalcdep.2016.10.025>.
- Leas, E.C., Nobles, A.L., Caputi, T.L., Dredze, M., Smith, D.M., Ayers, J.W., 2019. Trends in internet searches for cannabidiol (CBD) in the United States. *JAMA Netw. Open* 2, 1–4. <https://doi.org/10.1001/jamanetworkopen.2019.13853>.
- Lipari, R.N., Williams, M., Van Horn, S.L., 2017. *Why Do Adults Misuse Prescription Drugs? In the CBHSQ Report*. Substance Abuse and Mental Health Services Administration, US.
- Maccallum, C.A., Russo, E.B., 2018. Practical considerations in medical cannabis administration and dosing. *J. Intern. Med.* 49, 12–19. <https://doi.org/10.1016/j.ejim.2018.01.004>.
- Mcgee, P.L., Goldschmidt, K., 2019. E-cigarettes and vaping: what do pediatric nurses need to know? *J. Pediatr. Nurs.* 46, 121–123. <https://doi.org/10.1016/j.pedn.2019.02.027>.
- Metrik, J., Bassett, S.S., Aston, E.R., Jackson, K.M., Borsari, B., 2018. Medicinal versus recreational cannabis use among returning veterans. *Transl. Issues Psychol. Sci.* 4, 6–20. <https://doi.org/10.1037/tps0000133>.
- Morean, M.E., Lederman, I.R., 2019. Prevalence and correlates of medical cannabis patients' use of cannabis for recreational purposes. *Addict. Behav.* 93, 233–239. <https://doi.org/10.1016/j.addbeh.2019.02.003>.
- National Institute of Health (NIH), U.S. National Library of Medicine, 2020. *ClinicalTrials.gov*. Accessed February 9, 2021. <https://clinicaltrials.gov/ct2/results?cond=&term=cannabidiol&cntry=&state=&city=&dist>.
- Pacula, R., Jacobson, M., Maksabedian, E.J., 2016. In the weeds: a baseline view of cannabis use among legalizing states and their neighbours. *Addiction* 111, 973–980. <https://doi.org/10.1111/add.13282>.
- Pokorski, I., Clement, N., Phung, N., Weltman, M., Fu, S., Copeland, J., 2017. Cannabidiol in the management of in-patient cannabis withdrawal: clinical case series. *Future Neurol.* 12, 133–140. <https://doi.org/10.2217/fnl-2016-0035>.
- Reiche, S., Hermle, L., Gutwinski, S., Jungaberle, H., Gasser, P., Majič, T., 2018. Serotonergic hallucinogens in the treatment of anxiety and depression in patients suffering from a life-threatening disease: a systematic review. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 81, 1–10. <https://doi.org/10.1016/j.pnpbp.2017.09.012>.
- Roy-Byrne, P., Maynard, C., Bumgardner, K., Krupski, A., Dunn, C., West, I.I., Donovan, D., Atkins, D.C., Ries, R., 2015. Are medical marijuana users different from recreational users? The view from primary care. *Am. J. Addict.* 24, 599–606. <https://doi.org/10.1111/ajad.12270>.
- Russo, E.B., 2011. Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. *Br. J. Pharmacol.* 163, 1344–1364. <https://doi.org/10.1111/j.1476-5381.2011.01238.x>.
- Saxena, S., Kong, L., Pecht, M.G., 2018. Exploding e-cigarettes: a battery safety issue. *IEEE Access* 6, 21442–21466. <https://doi.org/10.1109/ACCESS.2018.2821142>.
- Schoedel, K.A., Szeto, I., Setnik, B., Sellers, E.M., Levy-cooperman, N., Mills, C., Etges, T., Somerville, K., 2018. Abuse potential assessment of cannabidiol (CBD) in recreational polydrug users: a randomized, double-blind, controlled trial. *Epilepsy Behav.* 88, 162–171. <https://doi.org/10.1016/j.yebeh.2018.07.027>.
- Sexton, M., Cuttler, C., Finnell, J.S., Mischley, L.K., 2016. A cross-sectional survey of medical cannabis users: patterns of use and perceived efficacy. *Cannabis Cannabinoid Res.* 1, 131–138. <https://doi.org/10.1089/can.2016.0007>.
- Sholler, D.J., Schoene, L., Spindle, T.R., 2020. Therapeutic efficacy of cannabidiol (CBD): a review of the evidence from clinical trials and human laboratory studies. *Curr. Addict. Rep.* <https://doi.org/10.1007/s40429-020-00326-8>.
- Silote, G.P., Sartim, A., Sales, A., Eskelund, A., Guimarães, F.S., Wegener, G., Joca, S., 2019. Emerging evidence for the antidepressant effect of cannabidiol and the underlying molecular mechanisms. *J. Chem. Neuroanat.* 98, 104–116. <https://doi.org/10.1016/j.jchemneu.2019.04.006>.
- Solowij, N., Broyd, S.J., Beale, C., Prick, J., Greenwood, L., van Hell, H., Suo, C., Galettis, P., Pai, N., Fu, S., Croft, R.J., Martin, J.H., Murat, Y., 2018. Therapeutic effects of prolonged cannabidiol treatment on psychological symptoms and cognitive function in regular cannabis users: a pragmatic open-label clinical trial. *Cannabis Cannabinoid Res.* 3, 21–35. <https://doi.org/10.1089/can.2017.0043>.

- Spindle, T.R., Bonn-miller, M.O., Vandrey, R., 2019. Changing landscape of cannabis: novel products, formulations, and methods of administration. *Curr. Opin. Psychol.* 30, 98–102. <https://doi.org/10.1016/j.copsyc.2019.04.002>.
- Substance Abuse and Mental Health Services Administration (SAMHSA), 2019. *Results from the 2018 National Survey on Drug Use and Health: Detailed Tables*. Rockville, MD.
- Tran, T., Kavuluru, R., 2020. Social media surveillance for perceived therapeutic effects of cannabidiol (CBD) products. *Int. J. Drug Policy* 77, 102688. <https://doi.org/10.1016/j.drugpo.2020.102688>.
- U.S. Food and Drug Administration (FDA), 2021. Public Health Focus. FDA Regulation of Cannabis and Cannabis-derived Products, Including Cannabidiol (CBD). Accessed February 9, 2021. <https://www.fda.gov/news-events/public-health-focus/fda-regulation-cannabis-and-cannabis-derived-products-including-cannabidiol-cbd>.
- Vigil, J.M., Stith, S.S., Diviant, J.P., Brockelman, F., Keeling, K., Hall, B., 2018. Effectiveness of raw, natural medical cannabis flower for treating insomnia under naturalistic conditions. *Medicines* 5, 75. <https://doi.org/10.3390/medicines5030075>.
- Wallace, M., Schulteis, G., Atkinson, H.J., Wolfson, T., Lazzaretto, D., Bentley, H., Gouaux, B., Abramson, I., 2007. Dose-dependent effects of smoked cannabis on capsaicin-induced pain and hyperalgesia in healthy volunteers. *Anesthesiol. J. Am. Soc. Anesthesiol.* 107, 785–796. <https://doi.org/10.1097/01.anes.0000286986.92475.b7>.
- Walsh, Z., Callaway, R., Belle-Isle, L., Capler, R., Kay, R., Lucas, P., Holtzman, S., 2013. Cannabis for therapeutic purposes: patient characteristics, access, and reasons for use. *Int. J. Drug Policy* 24, 511–516. <https://doi.org/10.1016/j.drugpo.2013.08.010>.
- Webb, M., Copes, H., Hendricks, P.S., 2019. Narrative identity, rationality, and microdosing classic psychedelics. *Int. J. Drug Policy* 70, 33–39. <https://doi.org/10.1016/j.drugpo.2019.04.013>.
- Wheeler, M., Merten, J.W., Gordon, B.T., Hamadi, H., 2020. CBD (cannabidiol) product attitudes, knowledge, and use among young adults. *Subst. Use Misuse* 55, 1138–1145. <https://doi.org/10.1080/10826084.2020.1729201>.
- Zeiger, J.S., Silvers, W.S., Flegler, E.M., Zeiger, R.S., 2019. Cannabis use in active athletes: behaviors related to subjective effects. *PLoS One* 14, e0218998. <https://doi.org/10.1371/journal.pone.0218998>.
- Zuardi, A.W., Rodrigues, N.P., Silva, A.L., Bernardo, S.A., Hallak, J.E.C., Guimarães, F.S., Crippa, J.A.S., Gould, R.W., Albert, K., 2017. Inverted U-shaped dose-response curve of the anxiolytic effect of cannabidiol during public speaking in real life. *Front. Pharmacol.* 8, 259. <https://doi.org/10.3389/fphar.2017.00259>.