Medical Cannabis and Cannabinoids

Preclinical Science and Clinical Studies - Research Article

Med Cannabis Cannabinoids 2023;6:77–88
DOI: 10.1159/000531666

Received: February 6, 2023
Accepted: May 31, 2023
Published online: August 16, 2023

Long-Term, Self-Dosing CBD Users: Indications, Dosage, and Self-Perceptions on General Health/Symptoms and Drug Use

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Keywords
Cannabidiol · Indications · Dosage · Health · Drug use

Abstract
Introduction: Self-dosing of off-the-shelf cannabidiol (CBD) for a myriad of health conditions is common in the USA. These CBD products are often mislabeled, suggesting that much less or much more CBD is being consumed than indicated on the label. This study examined the relationship between long-term self-dosing of CBD and (a) indications and, when a verified concentration of CBD is being consumed, (b) the daily CBD dosage, (c) the impact on general health and symptoms, and (d) over-the-counter (OTC) and prescription (Rx) drug usage. ***Methods:*** US adults 18–75 years of age who had used unverified CBD products for >1 month were recruited to participate in this decentralized, observational, IRB-approved study and provided a concentration-verified CBD product of their choice from 15 different vendors for 4 weeks. Prior to receiving product, they were queried on their primary reason for use (PRfU), primary symptom for use (PSfU), general health score (GHS), symptom score (SS), OTC and Rx drug use, and daily CBD dose. Individuals were queried daily on OTC and Rx drug use and CBD dose and weekly on SS and GHS prior to (pre-CBD) and after (post-CBD) ingestion of CBD on that day. ***Results:*** The PRfU included chronic pain, mental health, general health and wellness, sleep disorders, the central nervous system, digestive health, and others, while the PSfU included anxiety, back and/or joint pain, sleep, inflammation, and others. The mean daily dose was normally distributed, with a mean, median, and range of 53.1, 40.8, 8–390 mg/day, respectively. For both GHS and SS, the post-CBD was significantly higher than the pre-CBD score for each category of PRfU. The GHS scores did not change over the study, but pre- and post-CBD SS improved over time, with pre-improving more than post-CBD SS. The percentage of individuals decreasing or completely stopping OTC drugs or Rx drugs over the 4 weeks was 31.2% and 19.2%, respectively, with those taking CBD for chronic pain, decreasing drug use the most. OTC and Rx drug usage decreased when the CBD dose was changed and when GHS and SS improved. ***Conclusion:*** Pain, mental health (primarily anxiety/stress), and sleep are the most common reasons for CBD use. Self-administration of CBD reduced OTC and Rx drug usage at daily doses less than those reported in controlled studies. CBD self-administration significantly improves self-perception of general health and decreases symptom severity, and as these improve, fewer OTC and Rx drugs are used.

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Introduction

Cannabidiol (CBD) access and use are increasing rapidly, and it is widely available to millions of users in coffee shops, CBD shops, and tobacco stores in the USA [1]. In a survey of 253 patients with pain, many reported positive outcomes for pain and for a myriad of other conditions when self-medicating with CBD [2]. Reports on social media indicate that 90% of users claim they are self-medicating for diagnosable conditions such as psychiatric illness, sleep conditions, and neurological impairments [3]. There is a substantial need for evidence-based studies focusing on the epidemiology and effects of CBD use [4–7].

Numerous studies have found that only 12–46% of CBD products in retail stores are labeled correctly, with the CBD concentration varying from 17% to 159% of the label claim [8–10]. One study [9] found that 75% of the products have less CBD than the label claim, while another [10] found that 58% had more CBD than the label claim, suggesting that many individuals who are self-dosing with CBD are ingesting much less or much more CBD than they suspect. The purpose of this research was to examine the relationship between long-term self-dosing of CBD and (1) indications (primary reasons for use [PRfUs]) and, when a verified concentration of CBD is being consumed, (2) daily CBD dosage, (3) the impact on one's self-perception of general health and symptoms, and (4) the impact on the use of over-the-counter (OTC) and prescription (Rx) drugs.

Methods

Adults 18–75 years of age across the USA were recruited to participate in this decentralized observational study, which was reviewed and approved by Advarra and ethically conducted in accordance with the World Medical Association Declaration of Helsinki. Data were obtained from an app-based 21CFR Part 11 decentralized clinical study platform (Validcare Study), which was used to securely automate consent, inclusion/exclusion criteria, and collect data for the current study and other studies [8]. Inclusion criteria required individuals to have been taking CBD for a minimum of 30 days prior to entering the study. Exclusion criteria included liver impairment or disease, allergies to cannabinoids, marijuana use in the last 30 days, and any of the following drugs known to elevate liver enzymes in the last 30 days: valproate, vitamin A, clobazam, cyclosporine, phenytoin, fluvoxamine, isoniazid, ritonavir, clarithromycin, diltiazem, erythromycin, grapefruit juice, itraconazole, ketoconazole, nefazodone, ritonavir, telithromycin, or verapamil.

Sixteen companies supplied 39 different oral CBD products (liquid, capsules/pills, gummies, and drink additives) for this study, all of which were unblinded with their original labels which included the CBD composition (full spectrum, broad spectrum, or CBD isolate), concentration, and manufacturers' serving size and daily dosage recommendations. All products were analyzed for cannabinoid, terpene, heavy metal, and pesticide contents to ensure safety and confirm that the cannabinoid content was within ±10% of what was listed on the labeling. Per the manufacturer's labeling, the concentrations of CBD In the liquid products ranged from 10 to 100 mg/mL, and the amount of CBD per serving in the liquid products ranged from 10 to 50 mg, in capsules/pills from 24 to 100, in gummies from 23 to 30 mg, and in drink additives from 24 to 34 mg.

Individuals were recruited from lists supplied by participating companies, research organizations, and industry newsletter subscribers. After signing the consent form, meeting the inclusion/exclusion criteria, the following initial data were collected: weight, height, age, sex, medical history, reasons for taking CBD, present symptoms for which CBD was being taken, daily dosage, length of time they had been taking CBD, form of CBD, composition of CBD, current prescribed (Rx) and OTC medications, medical and medication history, number and type of other therapies they had been using for the last 30 days. Participants were asked weekly for changes in any of these data. The dosage, frequency, and total daily intake of CBD were determined solely by the participants, reported daily, and could be changed at any time during the study period. Individuals were supplied with a product of their choice from the list of products.

The primary measures for the current study included the PRfU, primary symptom for use (PSfU), general health score (GHS) (Likert scale), symptom score (SS) (categorical), OTC and Rx drug use, and daily CBD dose. To measure whether CBD improved the general health of participants during the study, 1 day each week they were asked to rate their overall GHS before (pre-CBD) and after CBD (post-CBD) self-administration on a linear categorical scale from 0 to 5 (0 = very poor and 5 = excellent). Similarly, to measure the impact of CBD on symptoms, 1 day every week, participants were asked if they were suffering from any of a list of symptoms and, if so, to rate their condition before and after taking CBD that day. Similar to the GHS, the participants were asked to rate the severity of the symptoms before and after taking CBD on a scale of 0–5 (0 = very severe and 5 = no symptoms). Participants who reported the same ailment for three or more of the 4 weeks were grouped together to analyze the effect of CBD on that symptom.

Descriptive and comparative statistics were analyzed using IBM SPSS Statistics v27. Repeated measures were used to analyze the GHS and SS. Bonferroni post hoc tests were performed only when significant omnibus tests were present. Whenever Mauchly's test indicated that the assumption of sphericity had been violated, the Greenhouse-Geisser correction was used. When the numbers of individuals in a PRfU category were too small to meet power requirements, the individuals in those categories were combined with the "Other" category for statistical comparisons.

This study is an analysis of data obtained from a larger study of the effect of CBD on liver function, sleepiness, and, in males, testosterone levels which was conducted to assist the FDA in understanding whether a medical safety issue exists with self-dosing of CBD in an unregulated fashion. The study was authorized as observational only and could not be interventional as that would have required an IND for each product in this study. The FDA required that the study participants be given

Table 1. Average age of participants by PRfU

Primary reason for use	Number of subjects	Age	
		mean	SD
Chronic pain	316	51.6[a]	12.31
Mental health	253	38.5[a]	10.73
General health and wellness	234	46.1	12.87
Sleep	121	45.7	13.29
Other	236	46.5	13.24

[a]Significantly different from all others $p < 0.001$.

Table 2. Average daily dose of CBD by PRfU

Primary reason for use	Number of subjects	CBD daily dose, mg/day	
		mean	SD[a]
Chronic pain	279	61.4[1]	37.19
Mental health	226	48.2[2]	30.49
Sleep disorders	221	48.3[2]	35.87
General health and wellness	113	49.0[2]	33.67
Other	215	54.0[3]	49.45

[1]Significantly different from [2]($p < 0.005$) and trending different from [3]($p = 0.0578$). [a]SD, standard deviation.

CBD products where the concentrations of CBD were known and verified, and a control group (individuals continuing to dose with their own OTC CBD products) could not be included.

Results

A total of 1,160 individuals (64.6% female, $n = 749$; 35.4% male, $n = 411$) participated in the study and provided data, although not everyone provided information for all data points. The average number of subjects per brand was 72.5 ± 31.3 with a range of 14–145. There was no statistical difference in the normally distributed ages of females compared to males (46.2 ± 13.34 and 45.4 ± 12.81, respectively; $p = 0.310$).

Reasons for Using CBD

The self-reported primary reasons for use ($n = 1,160$) were as follows: chronic pain ($n = 316$, 27.2%), mental health ($n = 253$, 21.8%), general health and wellness ($n = 234$, 20.2%), sleep disorders ($n = 121$, 10.4%), the central nervous system ($n = 34$, 2.9%), digestive health ($n = 21$, 1.8%), and other ($n = 180$, 16.7%). One-way ANOVA showed a significant difference in age across PRfU ($F(4, 1041) = 33.88$, $p < 0.001$) (Table 1). Within the PRfU category of chronic pain, back pain (31.3%), joint pain (28.2%), and arthritis (23.1%) were the 3 most common detailed reasons for use given by the participants; for mental health, anxiety/stress (81.4%) and depression (7.9%) were the most common; for general health and wellness, cognitive focus/alertness (37.2%), energy/fatigue (25.2%), and performance (15.0%) were most common; for sleep disorders, insomnia/sleeplessness (86.0%) and restless leg syndrome (5.8%) were most common; for central nervous systems, fibromyalgia (50.0%), muscle spasms (8.8%) and seizures/epilepsy (8.8%) were most common; for digestive health, irritable bowel (57.1%), Crohn's disease (9.5%), ulcerative colitis (4.8%) and diverticulosis (4.8%) were most common; and for other, inflammation (23.8%), premenopausal symptoms (11.9%), and Lyme disease (9.5%) were most common.

Daily CBD Dose

A total of 106 participants reported using nano-formulated, full-spectrum CBD (9.1%), and 1,054 reported using non-nano-formulated CBD product (90.9%). One-way ANOVA revealed that the daily dose of participants taking the nano-formulated, full-spectrum product was significantly lower (mean = 7.60, SD = 3.03) than those taking the full-spectrum product (mean = 53.01, SD = 38.48): $F(1,158) = 78.13$, $p < 0.001$. For participants taking a nano-formulated product, one-way ANOVA revealed that the daily CBD dosages were not significantly different between the PRfU categories, $F(4, 101) = 0.551$, $p = 0.699$. Additionally, daily CBD dosage was not significantly correlated with age ($r(106) = 0.080$, $p = 0.415$). Therefore, in all further analyses of CBD dosing, individuals taking the nano-formulated products were excluded.

The daily dose of participants taking non-nano CBD was generally normally distributed with a mean, median, and range of 53.1, 40.8, 8–390 mg/day, respectively. During the study, 27.8% of the participants changed their daily dose, with 5.4% decreasing and 22.5% increasing their daily dose. The majority (98.7%) made the change in the first week of the 4-week study; therefore, all analyses of daily dose were based on the final dose taken. There was no difference in the percentage of individuals who changed their dose among the different PRfU groups ($p = 0.280$). Using one-way ANOVA, the mean daily dose of CBD varied significantly depending on the PRfU, with those with chronic pain taking more CBD than all other

Table 3. GHSs pre- and post-CBD treatment by PRfU (ANOVA)

PRfU	Number of subjects	Pre-CBD		Post-CBD		ANOVA *p* values		
		mean	SE[1]	mean	SE	pre-post	time	PP*time[2]
General health and wellness	134	3.01	0.099	3.36	0.093	<0.001	0.682	0.241
Mental health	65	2.70	0.146	3.04	0.156	<0.001	0.814	0.297
Chronic pain	47	2.81	0.169	3.21	0.149	<0.001	0.225	0.296
Sleep disorders	33	2.87	0.190	3.18	0.180	0.022	0.204	0.72
Other	58	3.22	0.172	3.42	0.166	<0.001	0.884	0.646
Total: all PRfu[3]	337	2.94	0.164	3.27	0.062	<0.001	0.403	0.913

[1]SE, standard error. [2]PP*time, pre-post CBD*time. [3]PRfU, primary reason for use.

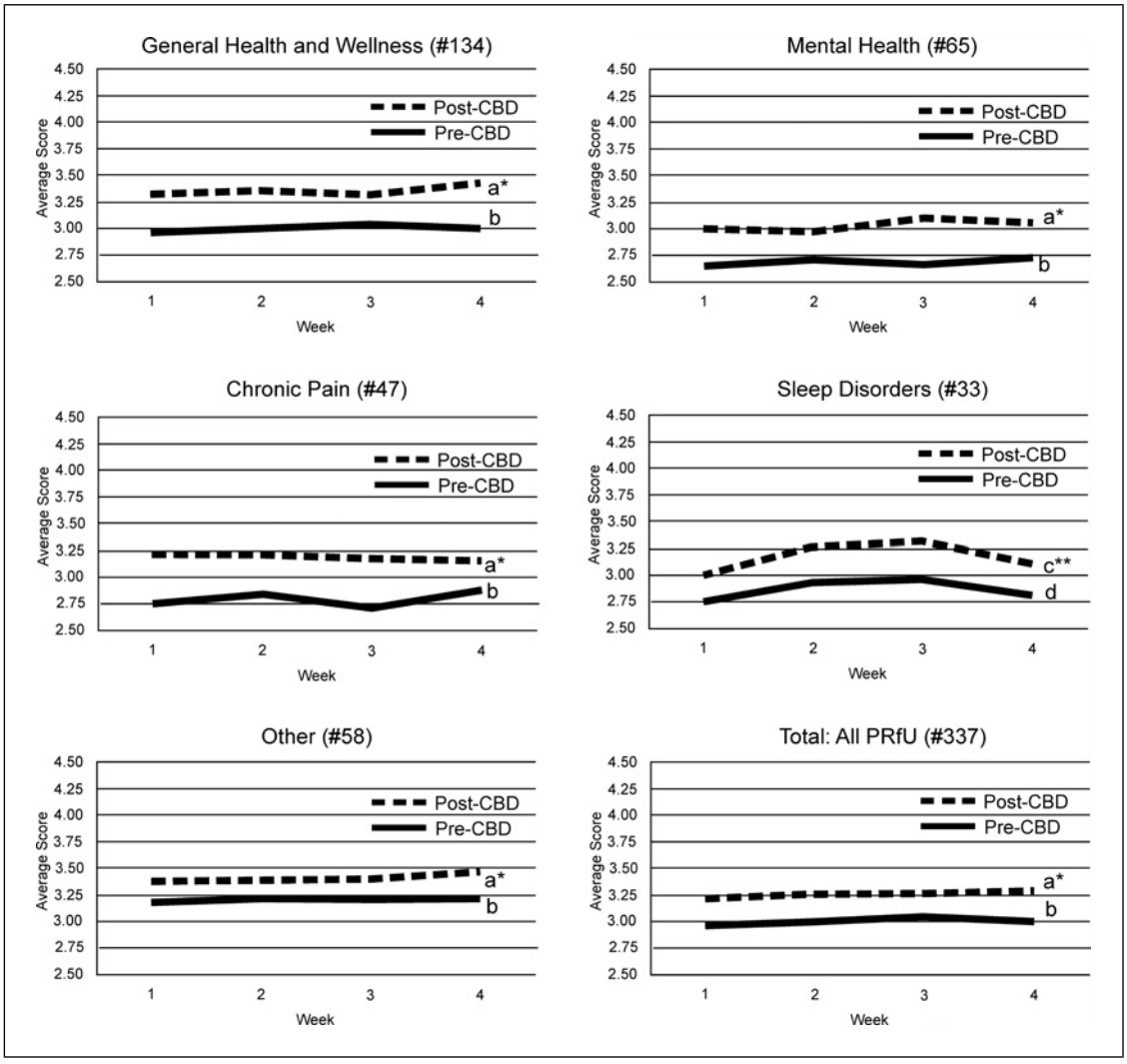

Fig. 1. Changes in pre- and post-CBD GHSs over the 4 weeks of the study for different primary reasons for use (PRfU) and for all PRfU. Pre-to-post CBD differences are significant (a vs. b: $p < 0.001$, c vs. d: $p = 0.022$) for all PRfU but neither the pre-CBD nor the post-CBD scores changed over the 4 weeks (number of individuals in each group in parentheses).

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Table 4. SSs pre- and post-CBD treatment by PRfU (ANOVA)

PRfU	Number of subjects	Pre-CBD		Post-CBD		*p* values		
		mean	SE[1]	mean	SE	pre-post	time	PP*time
Chronic pain	177	2.83	0.057	3.75	0.047	<0.001	<0.001	<0.001
Mental health	133	2.95	0.067	3.97	0.048	<0.001	<0.001	0.002
Sleep disorders	57	3.29	0.091	4.18	0.097	<0.001	<0.001	0.031
General health and wellness	23	3.21	0.165	3.96	0.093	<0.001	<0.001	<0.001
Other	85	2.89	1.099	3.80	0.089	<0.001	0.115	0.002
Total: all PRfu[3]	475	2.95	0.037	3.88	0.030	<0.001	<0.001	<0.001

[1]SE, standard error. [2]PP*time, pre-post CBD*time. [3]PRfU, primary reason for use.

PRfUs and those taking CBD for mental health, sleep disorders, and general health and wellness taking the same amounts, but less than those taking CBD for other reasons (Table 2).

GHS and SS

There were 337 individuals who entered GHSs for all 4 weeks of the study. For all PRfU (all subjects) and for each category of PRfU, the average score after taking CBD (post-CBD) significantly improved (higher) from the pre-CBD score, but the magnitude of the change in score was small and ranged from 0.047 to 0.589 (Table 3). Neither the pre- nor post-CBD scores varied significantly over the 4 weeks (time), as shown in Figure 1.

SSs for each of the 4 weeks were reported by 475 individuals. Overall (total: all PRfU) and for all of the individual PRfU, except Central Nervous System and Digestive Health, the SSs significantly improved (increased) after taking CBD; both the pre- and post-CBD scores significantly increased over time, and the pre-CBD score increased significantly more than the post-CBD score (Table 4). In the CNS and Digestive Health categories, the SSs significantly increased over time. The effects of time on the SSs are shown in Figure 2.

OTC and Rx Drug Use

Of the 858 individuals taking OTC drugs, 172 (19.9%) decreased their usage, 96 (11.2) stopped OTC usage completely, and the remainder (68.8%) continued their previous rate of usage. The percentage of individuals who decreased or stopped their OTC drugs varied significantly by PRfU (p = 0.003). Of the 767 individuals taking Rx drugs, 5 individuals (0.7%) increased the amount of Rx drug usage during the study, 78 (10.2%) decreased their usage, 69 (9.0%) stopped OTC usage completely, and the remainder (80.2%) continued their previous rate of usage. The percentage of individuals who decreased or stopped their OTC or Rx drugs varied significantly by PRfU (p = 0.003 and 0.005, respectively) (Table 5). The reduction in OTC usage was significantly correlated with the reduction in Rx usage ($r(708) = 0.434$, $p < 0.001$), as shown in Figure 3.

Using χ^2 analysis, the reduction in OTC and Rx Drug usage was significantly greater if the CBD dose was either increased or decreased ($p < 0.001$), as shown in Figure 4. Using one-way ANOVA, reductions in OTC use were significantly positively associated with pre-to-post GHS improvement (p = 0.014) but not with pre-to-post SS improvement (p = 0.455), as shown in Figure 5. The reduction in Rx drug use was significantly positively associated with improvement in pre-to-post CBD in both GHS and SS ($p < 0.001$ and p = 0.043, respectively), as shown in Figure 5.

Using one-way ANOVA, pre-to-post SS improvement was positively associated with the number of doses of CBD taken per day ($F = 2.119$, $p = 0.035$) but not with the daily dose of CBD ($F = 0.009$, $p = 0.993$). Pre-to post-GHS improvement was associated with neither the number of doses per day nor the daily CBD dose.

Discussion

Reasons for Using CBD

This study found that the main reasons for which individuals self-administer CBD were pain, mental health, general health and wellness, and sleep, and that low daily doses of CBD significantly improved self-perception of health and symptoms, resulting in a significant decrease in OTC and Rx drug usage. The age of the participants in this study was normally distributed, and the 65:35 ratio of females to males is consistent with

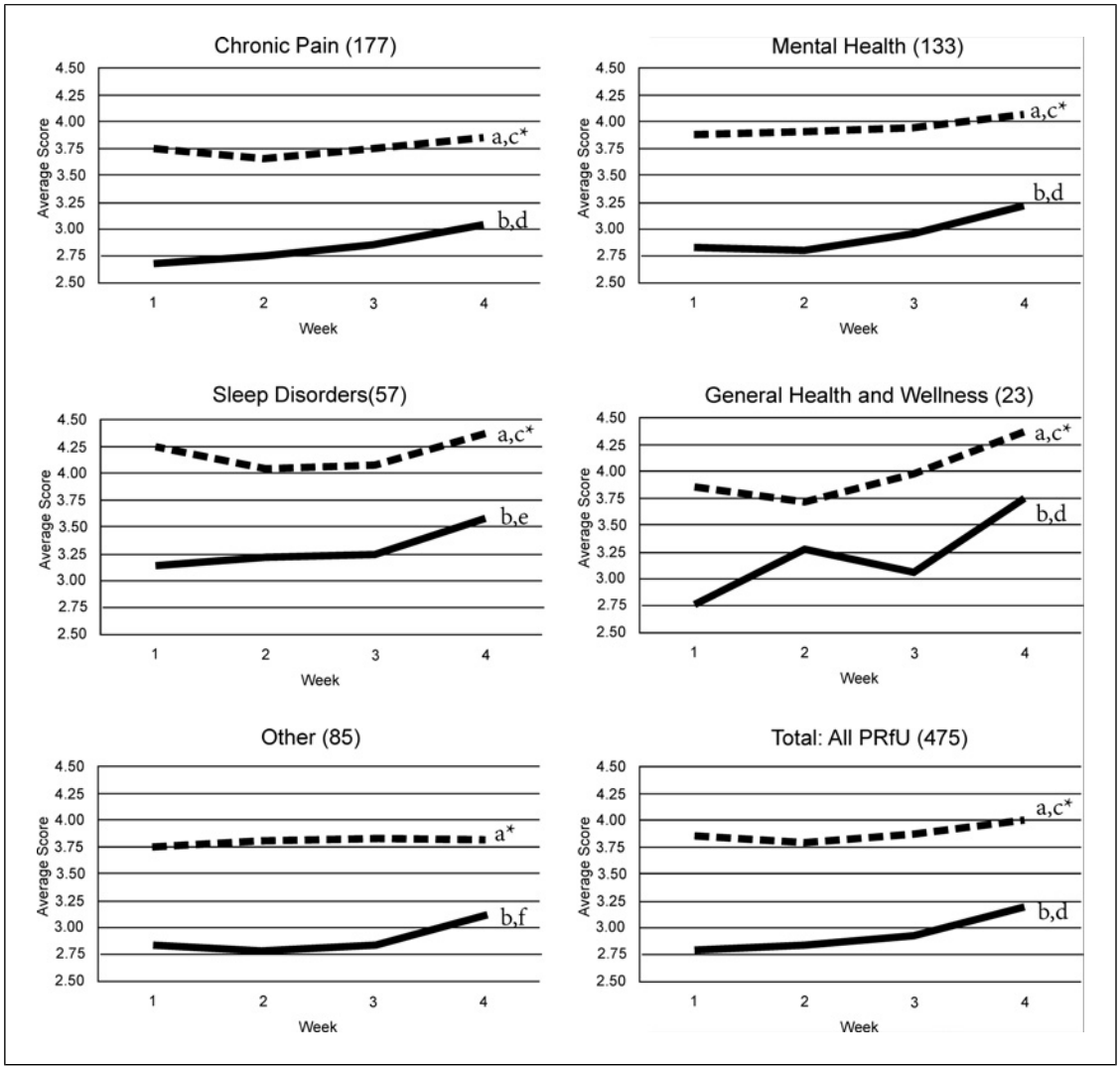

Fig. 2. Changes in pre- and post-CBD SSs over the 4 weeks of the study for different primary reasons for use (PRfU) and for all PRfU. Pre-to-post CBD differences (*a vs. b are significant ($p < 0.001$) for all PRfU and both the pre-CBD nor the post-CBD scores improved over the 4 weeks in all PRfU except for Other ($p < 0.001$) with the pre-CBD scores improving more than the post-CBD scores in all PRfU (d: $p < 0.001$, e: $p = 0.031$, f: $p = 0.002$) (number of individuals in each group in parentheses).

other studies of the usage of CBD in general populations [11–13]. Similar to other studies, the most common conditions for which CBD are being taken are pain, mental health (primarily anxiety/stress), general health and wellness, and sleep, while digestive health and central nervous system conditions are cited as reasons for its use by significantly fewer individuals [12–16]. As in the Moltke study [12], individuals taking CBD for chronic pain were significantly older, whereas those taking CBD for mental health (primarily anxiety and stress) were significantly younger than those taking CBD for other reasons. In this study, 15.6% take CBD for the conditions of cognitive focus/alertness, energy/fatigue, and performance, which is also similar to Moltke's findings [9, 12]. These findings suggest that the individuals in this study are characteristic of adult CBD users in the US population.

GHS and SS

In the present study, individuals reported that their GHS and SS significantly improved after CBD administration. This is consistent with findings of an internet

Table 5. Change in OTC and Rx drug usage by primary reasons for use

PRfU	Over-the-counter (OTC) drug usage				Prescription (Rx) drug usage			
	increased, %	no change, %	decreased, %	stopped, %	increased, %	no change, %	decreased, %	stopped, %
Chronic pain	0.0	57.7	26.2	16.2	1.7	73.8	14.3	10.1
Other	0.0	67.5	23.1	9.5	0.6	75.9	11.7	11.7
Sleep disorders	0.0	74.7	15.8	9.5	0.0	86.6	7.3	6.1
General health and wellness	0.0	75.3	15.6	9.1	0.0	92.2	4.7	3.1
Mental health	0.0	77.7	14.0	8.4	0.0	80.9	8.3	10.8

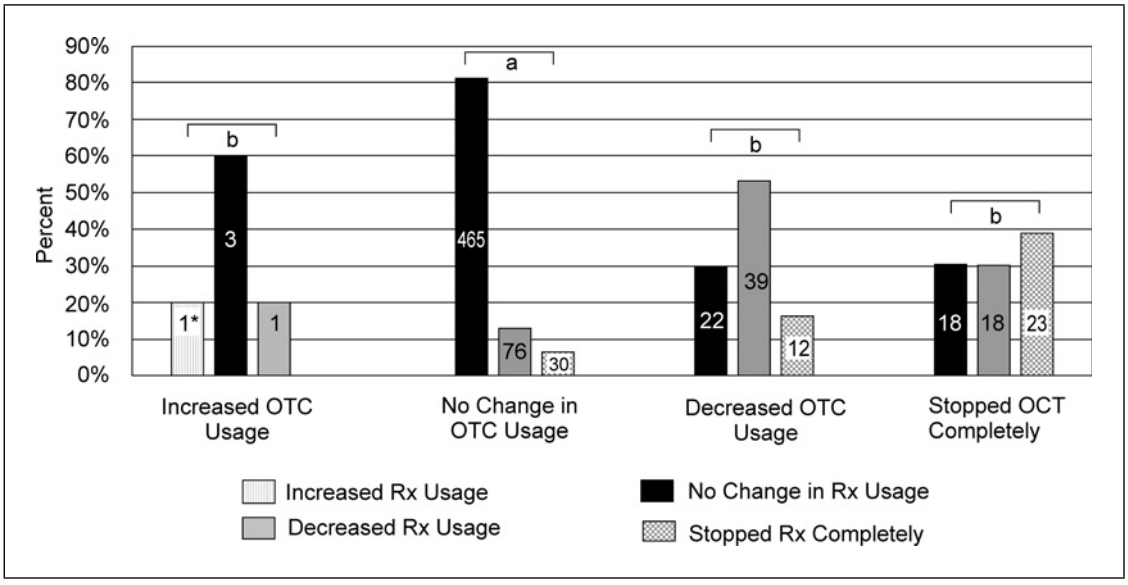

Fig. 3. Change in OCT drug usage by change in Rx drug usage. When OCT drug usage either increased or decreased, Rx drug usage significantly increased or decreased, also (a vs. b: $p < 0.001$) *Number of individuals.

survey which reported that long-term CBD users felt that CBD treated their medical condition "well" to "very well." [13] The pre-CBD and post-CBD GHS did not change significantly during the 4 weeks of treatment, either overall or within different PRfUs. However, except for the category of Other, both the pre-CBD and post-CBD SS improved for all PRfU categories over the 4 weeks of the study. In addition, for all PRfU categories, the pre-CBD SS improved significantly more than the post-CBD scores over the 4 weeks. While participants in this study did not feel that their general health improved over the 4 weeks of this study, they felt that their symptoms improved significantly over the 4 weeks, and the more their symptoms improved, the fewer OTC and Rx drugs they ingested. The improvement in symptoms was also correlated with an increase in the number of CBD doses per day, but not the total amount of CBD being taken. This is not unexpected as to obtain a reasonable steady state of CBD concentration in the blood, CBD must be taken ×2 per day rather than just once [17, 18].

OTC and Rx Drug Use

Thirty-one percent (31%) of the participants in this study decreased or stopped their use of OTC drugs, and 19.2% decreased or stopped the use of Rx drugs during the 4 weeks of the study. Individuals taking CBD for chronic pain had the largest decrease in OTC usage, with 42.4% decreasing or stopping OCT drug use and 24.4% decreasing or stopping Rx drug use. These findings are consistent with those from an internet survey in which

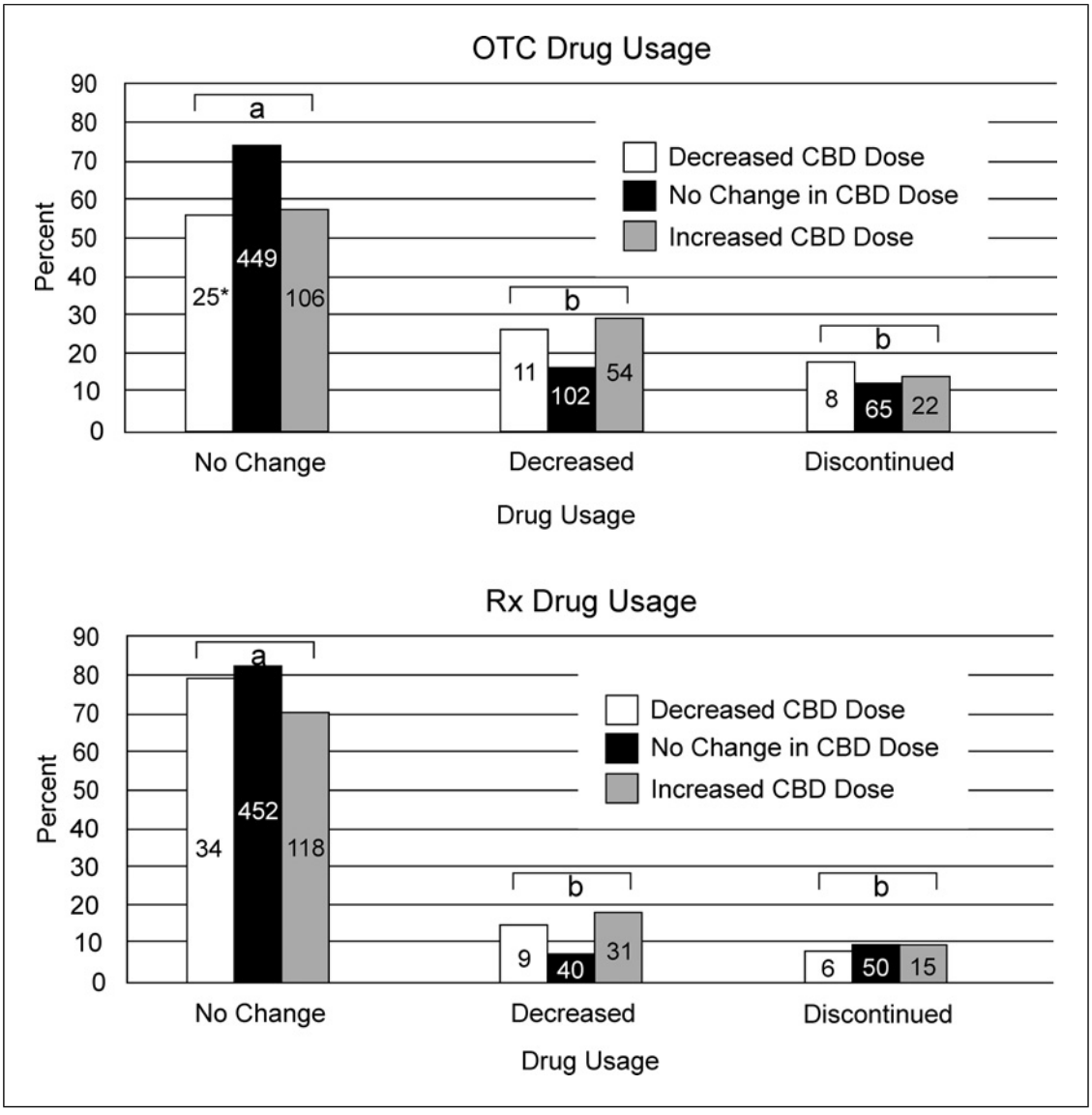

Fig. 4. OTC and Rx drug usage by CBD dose change. When the CBD dose was increased or decreased after starting verified CBD concentration products, the use of OTC and Rx drugs was reduced (a significantly different from b, $p < 0.001$). *Number of individuals.

36% of respondents stated CBD treats their medical condition "very well by itself" and that individuals taking CBD for pain most frequently reported the CBD treated their medical condition "very well by itself" or "moderately well by itself [13]."

Over ¼ of the participants changed their daily dose of CBD after obtaining the CBD supplied by the study. A higher percentage of participants who changed their daily dose of CBD also reduced their use of OTC and Rx drugs, often reducing or stopping both OTC and Rx drug use. The reason for this change is not known, but it is possible that, in the month before taking the product provided in this study, the individuals that changed their dosage had been taking a product where the CBD concentration was mislabeled, as up to 88% of the CBD products commercially available in the USA are often mislabeled [10].

Daily CBD Dose

To our knowledge, this is the first published survey of self-dosing CBD users, where the amount of CBD in the products has been known and verified, and the amount of CBD being ingested was reported and recorded daily

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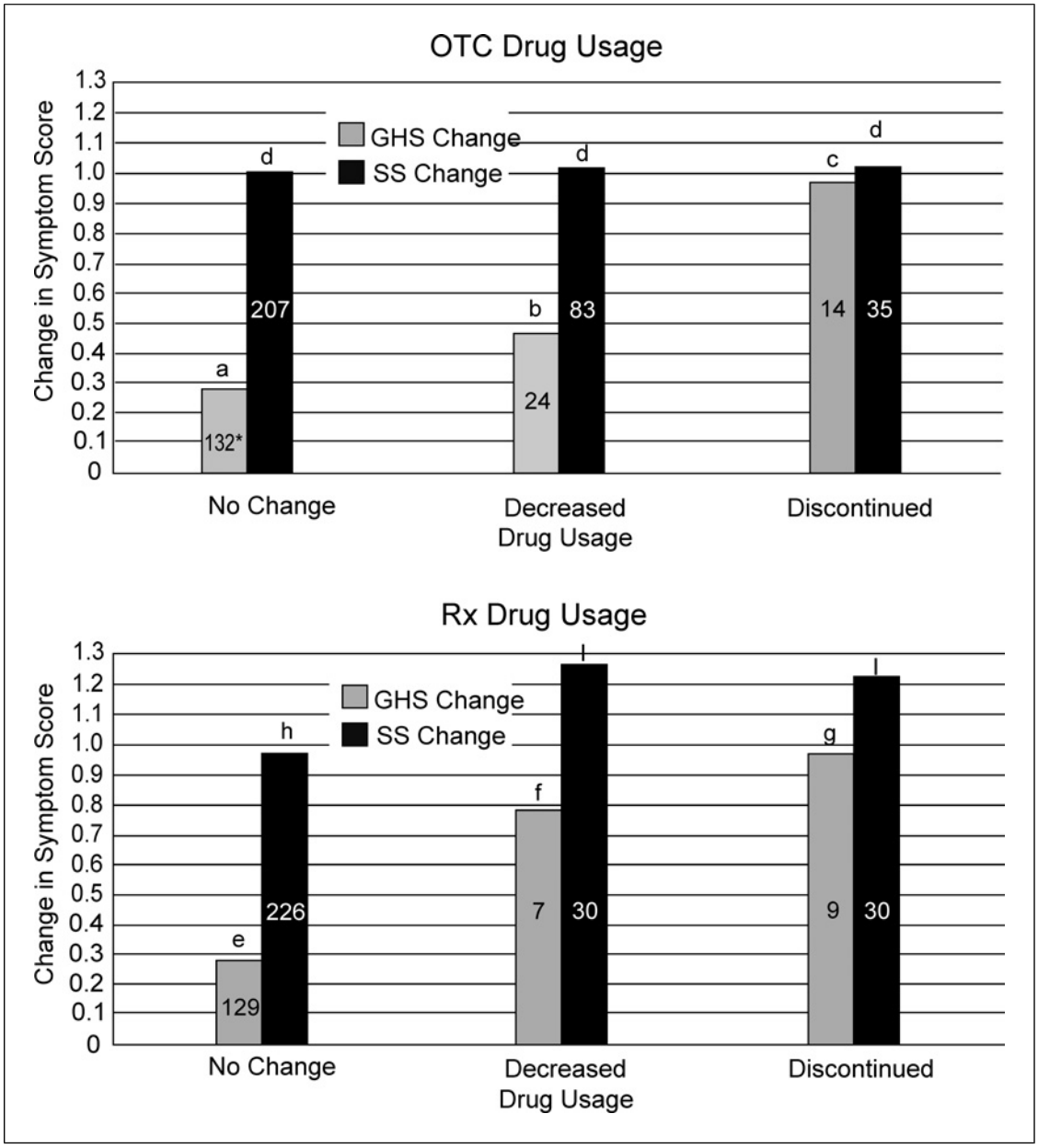

Fig. 5. OTC and RX drug usage changes by change in general health scores (GHS) and symptom scores (SS). Individuals that decreased or discontinued their Rx drug usage had significantly more improvement in GHS (e–g, $p < 0.001$) and SS (h, i, $p = 0.043$), while individuals who decreased or discontinued their OTC drug usage had more significantly more improvement in only their GHS (a–c, $p = 0.014$. *Number of individuals.

by the users. Individuals consuming nano-formulated CBD took significantly less CBD than those taking non-nano CBD, a finding reported by others and thought to be due to increased absorption [18–22]. The average daily dosage of non-nano CBD in this study was 53 mg/day, with a range of 8–390 mg/day. Using data from another study where self-dosing CBD users were asked to estimate their daily dose, the average daily dose was 61 mg/day and with a range from 0 to 200+ [12]. Since orally administered non-prescription products typically recommend daily doses well below 150 [14, 23], it is not surprising that the vast majority of self-dosing CBD users were ingesting CBD daily doses in this range [14, 23].

In the present study, individuals reported that their GHS and SS significantly improved each day after ingesting CBD. This is consistent with an internet survey which reported that long-term, self-dosing CBD users felt that CBD treated their medical condition "well" to "very well [13]. However, in a recent review of controlled trials of low-dose oral CBD, CBD was been found to have little to no effect on the condition being studied if the CBD daily dose was less than 300 mg/dL [24]. In all of these controlled trials, all individuals were given the same daily dose of CBD, and statistical analysis methods that did not account for between-person variability were used. When statistical methods that account for between-person variability (repeated measures, linear mixed effects modeling, etc.) are used, a different conclusion may be obtained, as occurred in 2 recent studies, where low-dose CBD was effective in reducing anxiety in patients with anxiety [25, 26].

When given the same oral dose, maximum CBD blood levels can vary tremendously with the differences increasing with increasing dose [27–29]. Maximum CBD blood levels ranged from 0.2 to 2.6 ng/mL when individuals were given 5.4 mg of CBD orally [28], from 1.1 to 11 ng/mL when given 40 mg [27], and from 0 to 50 ng/mL when given 100 mg [29]. Internet sites recommend that, when self-dosing CBD, individuals should start with a low daily dose (10–40 mg/day) and gradually increase the amount until the individual feels that it's effectively treating their symptoms [30, 31]. The mean, median, and range of daily dose in this study and the daily improvement in GHS and SS suggest that most individuals in this study are and/or have been following a dosing procedure similar to the recommendations found on the internet. One can theorize that individuals self-dosing CBD increase their dose until they reach a CBD blood level that is adequate to resolve the condition being treated. A recent study in chronic pain patients who self-dosed CBD found that low-dose CBD (range: 15–60 mg/day) significantly improved pain and sleep quality and reduced opioid use [32].

An additional explanation as to why individuals self-dosing with CBD have a positive response to their condition(s) for which they are consuming CBD is the concept of covariant conditions. The conditions for which most individuals consume CBD are pain (a perception), anxiety/stress (a mental condition), sleep disorders (an altered mental/physical state), and general health and wellness (a perception) are all covariant conditions (i.e., when one of these conditions worsens or improves, it causes one or more of the other conditions to worsen or improve). In several studies of low-dose CBD use, improvement in covariant conditions often was reported, whether or not CBD was deemed effective for the primary condition being studied [25, 32–36]. In this study, the self-perception of symptoms improved over time in both the pre-CBD and post-CBD scores, but the pre-CBD scores improved significantly more than the post-CBD scores. Two possible explanations for the greater improvement in pre-CBD SS are: (1) this may be due to cumulative improvements in covariant conditions over time, or (2) the conditions causing the symptoms are truly improving.

However, it is entirely possible that many, or at least a portion, of the findings in this study are the result of psychological priming causing a placebo effect (i.e., the survey questions administered on the app led the participants to consider their symptoms more deeply than they would otherwise, causing them to believe in the treatment and evaluate their symptoms as improving). However, the consistency of the improvement in SS after taking CBD every day and length of time many of these individuals have been taking CBD for their symptoms/conditions suggest that something other than strict placebo effects are present when low-dose CBD is self-administered. Many of the positive findings in this study that occurred after the individuals began ingesting the verified CBD products that were supplied by the study were completely unexpected and needed to be studied by using a control group as described in the methods.

Conclusions

Pain, mental health (primarily anxiety/stress), and sleep are the most common reasons for using CBD, and individuals consuming nano-formulated CBD self-administered significantly less CBD than those taking non-nano CBD. Self-administration of CBD reduced OTC and Rx drug usage at daily doses less than those used in controlled studies. CBD significantly improves self-perception of general health and decreases symptom severity, and the more general health and symptoms improve, the fewer OTC and Rx drugs are used.

Acknowledgments

The authors would like to thank Validcare, LLC, for its CRO services including use of their app-based clinical platform.

Statement of Ethics

This study was carried out in accordance with the guidelines on human experimentation in accordance with the Declaration of Helsinki of the World Medical Association. This study protocol

was reviewed and approved by the Institutional Review Board, Advarra, approval number 00043515. Signed informed consent was obtained from all participants before beginning the study.

Conflict of Interest Statements

1. Robert Kaufmann has served as a consultant for Shaman Botanicals, LLC, and Validcare, LLC, and as a speaker for Shaman Botanicals, LLC.
2. Amber Harris Bozer, Amanda Kube Jotte, and Keith Aqua have no conflicts of interest to declare.

Funding Sources

Funding for this project was provided by Asterra Labs, Care by Design, CBDistillery, CBD American Shaman, Cannacraft, Charlotte's Web, Columbia Care, Garden of Life, Global Widget, HempFusion, Impact Naturals, Kannaway, Kazmira, Medterra CBD, Oncuity LLC, and SunMed CBD.

Author Contributions

1. Robert Kaufmann was the study project manager, designed and wrote the protocol, and was the primary author of the manuscript.
2. Amber Harris Bozer assisted with data analysis, interpretation, writing, and final approval.
3. Amanda Kube Jotte performed the statistical calculations and assisted with analysis, writing, and final approval.
4. Keith Aqua was the primary investigator for the study that directed data acquisition, intellectual content review, and final approval.

Data Availability Statements

For legal reasons, the dataset is not available for public viewing but can be made available on request for confirmation of statistics if requested by an accredited peer-reviewed committee or government agency. Further inquiries can be directed to the corresponding authors.

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