DEPARTMENT OF HEALTH

Post-Traumatic Stress Disorder Patients in the Minnesota Medical Cannabis Program: Experiences of Enrollees During the First Five Months

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Executive Summary

In May of 2014 Minnesota became the 22nd state to create a medical cannabis program. Distribution of extracted cannabis products in liquid or oil form to qualified, enrolled patients began July 1, 2015. Post-traumatic stress disorder (PTSD) was added to the list of qualifying conditions for the program effective August 1, 2017. This report draws on data from enrollment, purchasing, symptom and side effect ratings at time of each purchase, and survey results to describe the experience of patients newly enrolled in the program for PTSD during the first five months it was a qualifying condition.

Participation

Between August 1 – December 31, 2017 a total of 751 patients enrolled in the program under the qualifying condition of PTSD. Note that patients who took advantage of pre-enrollment during the month of July were given an effective enrollment date of August 1 for this report. Most of the patients (65%) were between the ages of 25 and 49, 2% were <18, and 6% were ≥ 65 years. 53% were male. Distribution by race/ethnicity generally matched the state's demographics for White (85%) and Black (6%); the Native American proportion (4%) was somewhat larger than in 2014 Census Bureau estimates for the state, and Asian (1%) somewhat smaller. Some patients were certified for one or more qualifying conditions in addition to PTSD; intractable pain was by far the most common (n=123; 16%).

Most patients (68%) live within the Twin Cities metro region, based on first three digits of zip code; 7% live in the St. Cloud region, 6% in the Duluth region, 5% in the Willmar region, and 4% each in the Rochester and Mankato regions. The program allows patients to have one or more parents or non-parent caregivers who register with the program and then are allowed to transport and administer a patient's medical cannabis. Only 1% of patients had a registered caregiver, 2% had a registered parent or legal guardian, and 3% had either a registered parent/legal guardian or a registered caregiver. By patient self-report the primary cause of PTSD for the majority of patients (71%) was non-military in nature, with 13% reporting military and 6% reporting both military and non-military. Seventy five patients (10%) indicated they preferred not to answer this question.

A total of 107 health care practitioners registered with the program and certified for PTSD the 751 patients covered in this report; 72% were physicians, 20% were advanced practice registered nurses, and 8% were physician assistants. Most of the physicians (69%) were primary care physicians and 17% were psychiatrists.

Medical Cannabis Use Patterns

Each patient's medical cannabis purchasing transactions during their first enrollment year were analyzed. A total of 15,538 products were purchased through 9,529 transactions. For analytic purposes, products were classified according to the ratio of delta-9-tetrahydrocannabinol (THC) to cannabidiol (CBD) as follows:

- Very High THC:CBD (100:1 or higher)

- High THC:CBD (>4:1 up to 99:1)
- Balanced THC:CBD (1:1 Up to 4:1)
- High CBD:THC (≥1:1 up to 99:1)
- Very High CBD:THC (100:1 or higher)

Products for inhalation (vaporized oil) accounted for 71% of products purchased, products for enteral administration (swallowed – includes capsules and oral solutions) accounted for 24%, oromucosal products accounted for 4%, and topical products 2%. When all routes of administration are combined, Very High THC:CBD products accounted for 55% of all product purchases, followed by Balanced products (27%), High THC:CBD products (9%), High CBD:THC products (9%), and Very High CBD:THC (<1%).

Examining purchasing history across all patients is very complex for reasons that include experimentation with different products over time. As a first approach to assessing routine use of products, most frequently purchased products were examined for each patient. For 25% of patients, two or more products were purchased the same number of times. The product types that emerged as most frequently purchased were Very High THC:CBD vaporization oil (45%), balanced vaporization oil (7%), and balanced enteral preparations (6%).

Benefits

Information on patient benefits comes from the Patient Self-Evaluation (PSE) completed by patients prior to each medical cannabis purchase and from patient and health care practitioner surveys. At enrollment and in the patient surveys patients are asked to complete a questionnaire on PTSD symptoms called the PTSD Checklist for DSM-5 (PCL-5). The PCL-5 is a 20-item self-report measure that assess 20 DSM-5 (Diagnostic and Statistical Manual of Mental Disorders – 5th edition) symptoms of PTSD. The PCL-5 was developed by the National Center for PTSD, part of the U. S. Department of Veteran Affairs. Among its purposes is monitoring symptom change before and after treatment. Results of analyses of the PSE and survey data (including PCL-5) indicate perceptions of a high degree of benefit for the majority of the patients.

At enrollment, 96% of the 751 PTSD patients included in this report scored above 33 points, meeting the cut-point for provisional PTSD diagnosis. Comparing PCL-5 score at enrollment and at 3 months, for the 51% who responded to the survey 3 months after their first medical cannabis purchase, shows many experienced substantial benefit. Literature has shown that a clinically meaningful difference in PCL-5 scores measured at different times amounts to a difference of 10-20 points. Between 50% and 71% (depending on whether a reduction of 20 points or 10 points is used) of respondents saw a clinically meaningful improvement in PTSD symptoms. Change in PCL-5 score appeared to be similar across groups based on primary cause of PTSD. Because those who completed the 3-month survey and those who did not were similar in demographics and in enrollment PCL-5 score, we can have some confidence that the change in PCL-5 score seen for survey responders is representative of the entire group.

Patients responded to a survey question asking them how much benefit they believe they received from using medical cannabis on a scale from 1 (no benefit) to 7 (great deal of benefit). Across all responding patients, 76% indicated a benefit rating of 6 or 7. A small but important proportion of patients indicated little or no benefit: 4% gave a rating of 1,2, or 3. When patients were asked what the most important benefit was for them, 23% indicated anxiety reduction, 16% improved sleep, 13% improved mood and/or emotional regulation, and 12% pain reduction. Survey response rate from health care practitioners was less than hoped for; HCP surveys for only 21% of the patients had benefit rating information. HCP ratings on the completed surveys were quite similar to patient ratings.

An important part of this report is the verbatim comments written by patients, and the reader is encouraged to review these comments in *Appendix A: Patient-Reported Benefits from Medical Cannabis*. Examples of these comments include:

- "Fewer periods of dissociation due to increased mindfulness, being able to tolerate processing trauma in therapy without dissociating, improved sleep, improved transition from sleeping to wakefulness, decreased body pain, eating more, not isolating from friends and family as much, being able to tend to my house more."
- "Sleeping has been AMAZING, pain is way down, not helping my anxiety as much as I would like, but nothing is perfect."
- "Controlled doses. I used cannabis before this program in such an uncontrolled dosage that it affected my other medications. The control of the cartridge has been extremely helpful."
- "Being able to go to work with less anxiety and feeling like I can function. No more night terrors and screaming in my sleep."
- "Able to leave the house easier. I have PTSD and being on any road can make me anxious and hyper-vigilant. Using medical cannabis makes that feeling go away for the most part. Before medical cannabis it felt like anyone and anything could be a threat. After, it allows me to remain calm and either ignore or remove thoughts and feelings like that. It eases my general anxiety and depression overall so I'm able to take less of my as needed medications like diazepam, propanerol, and hydroxyzine. Overall, it has reduced my stress levels which helps me think clearer and be a more productive father and husband. I'm grateful for it."
- "Feeling less anxious and having to deal with less chronic pain has overall improved my quality of life a great deal. I have more moments of happiness and it's opened up many doors to me that I have had shut for a long time."
- "Better sleep, better appetite, I'm not so angry all the time. My memories don't seem to bother me like they used to. This has been a life changer for me!"
- "Since starting medical cannabis it's like I've been given a fair chance to treat my PTSD symptoms I've struggled with over a decade now. My family sees a night and day difference and it's easier to communicate with them. I've since found a part-time job

with flexible hours to work around starting college in January, 2018. The only hope I have is that it becomes more affordable as I'm barely able to afford it now."

- "Increased appetite, increased attention, better quality sleep, helps me stay grounded after trauma therapy, more sleep, increased confidence, new job, new career direction."

The PTSD patients included in this report had a high burden of symptoms. When they initiated program participation, a majority had at least moderate levels of anxiety (96%), disturbed sleep (91%), depression (84%), fatigue (84%), pain (69%), and lack of appetite (60%). For 6 of the 8 symptoms measured, among those with at least moderate levels of the symptom at baseline, between 32% (fatigue) and 48% (lack of appetite), both achieved ≥30% symptom reduction within four months and retained that level of improvement over the following four months. The percentage was a bit lower for pain (27%) and a bit higher for vomiting (56%).

Adverse Side Effects

The proportion of patients with at least one physical or mental adverse effect varied from 11% in the PSE data to 21% in HCP surveys to 26% in patient surveys. Most patients with at least one adverse effect experienced only one. The vast majority of all reported adverse effects were mild or moderate in severity as reported on the PSE (82%) or a score of 1 through 5 on the 7-point severity scale used in patient (95%) and HCP (94%) surveys.

The most common adverse effects were dry mouth, increased appetite, anxiety, drowsiness, and fatigue. Anxiety was reported somewhat more frequently (n=12; 1.7%) than in prior reports of enrolled patients, and 8 of the 12 patients rated the anxiety as severe. Patients were asked to report symptoms they thought were likely caused by medical cannabis products. It is possible some reported anxiety that was part of their PTSD symptoms. However, a few survey comments specifically attributed increased anxiety to use of medical cannabis products, with some suggestion this was THC dose dependent. There was also one comment about increased anxiety with use of a high CBD:THC product. No serious adverse events (life threatening or requiring hospitalization) were reported for this group of patients during the observation period.

1. Patients and Caregivers Registered During the First Five Months of PTSD Enrollment

Qualifying Condition

On August 1, 2017, post-traumatic stress disorder (PTSD) became a qualifying medical condition for the Minnesota Medical Cannabis program. In the subsequent five months (August 2017-Decemter 2017), a total of 751 patients were enrolled in the program under the qualifying condition of PTSD.

The most common additional qualifying condition was intractable pain (n = 123; 16.4%), followed by severe and persistent muscle spasms (n = 50; 6.7%). Table 1.1 shows the frequency of additional qualifying medical conditions within the cohort.

Table 1.1. Count of PTSD Patients with Additional Qualifying Medical Conditions.

Conditions	Count (%)
Intractable Pain	123 (16.4%)
Muscle Spasms	50 (6.7%)
Cancer	4 (0.5%)
Inflammatory Bowel Disease, incl. Crohn's Disease	3 (0.4%)
Seizures	3 (0.4%)
Glaucoma	1 (0.1%)
Tourette Syndrome	1 (0.1%)

Age and Gender

Of the 751 patients enrolled for the first time and certified for PTSD, 345 (45.9%) were female, 396 (52.7%) were male, and 10 (1.3%) did not respond. See Table 1.2 for breakdown of patient gender by age category. The largest proportion of patients were between the ages of 25 and 49 (65% of PTSD patients).

Table 1.2. Patient Counts by Age and Gender (N = 751).

Age (yrs)	N	Female (%)	Male (%)	Prefer Not to Answer (%)
0-4	0	0 (0.0%)	0 (0.0%)	0 (0.0%)
5-17	15	8 (53.3%)	6 (40.0%)	1 (6.7%)
18-24	55	21 (38.2%)	31 (56.4%)	3 (5.5%)
25-35	255	108 (42.4%)	143 (56.1%)	4 (1.6%)
36-49	233	109 (46.8%)	122 (52.4%)	2 (0.9%)
50-64	148	91 (61.5%)	57 (38.5%)	0 (0.0%)
65+	45	8 (17.8%)	37 (82.2%)	0 (0.0%)
Total	751	345 (45.9%)	396 (52.7%)	10 (1.3%)

Note: Percentages are calculated based on the total count of patients in each age category.

Race and Ethnicity

PTSD patients enrolled in the first five months were predominately white (n = 635; 84.6%); 6% were black, 4% were Native American, and 5% did not respond (Table 1.3). Patients were given the option to select multiple race categories, so the counts reflect some patients more than once.

Table 1.3. Self-Reported Race and Ethnicity for PTSD Patients (N = 751).

Race and Ethnicity	Count (%)
White	635 (84.6%)
Black	46 (6.1%)
Native American	32 (4.3%)
Asian	6 (0.8%)
Pacific Islander	1 (0.1%)
Other Race	18 (2.4%)
Race Unknown	8 (1.1%)
Hispanic Ethnicity	22 (2.9%)

Note: Patients could select more than one race/ethnicity and may be represented more than once each in this table.

39 (5.2%) patients declined to indicate race.
26 (3.5%) selected two or more races.
25 (3.3%) patients declined to answer Hispanic ethnicity question.

Registered Caregivers and Parents/Legal Guardians

If a patient is unable to pick up their medication from a cannabis patient center or is unable to administer the medication, their certifying health care practitioner may also specify the patient's need for a designated caregiver within the registry (check a box during the patient's certification to allow a patient to have a caregiver). This allows the enrolled patient to invite another person to serve as a caregiver. Caregivers subsequently undergo a background check and register with the program. Registered caregivers can then legally obtain and possess the patient's medical cannabis on their behalf. Additionally, parents or legal guardians of patients can register with the program to act as caregiver and pick up or possess medication on behalf of the patient. Table 1.4 shows the proportion of patients who have registered caregivers or parents/legal guardians registered to pick up medication on behalf of the patient.

Table 1.4. Patients with caregiver(s) and/or parent(s)/legal guardian(s) registered in the program.

Patients with Caregiver(s) or Parent/Legal Guardian(s)	Count (%)
Patients with Registered Caregiver(s)	8 (1.1%)
Patients with Registered Parent/Legal Guardian(s)	16 (2.1%)
Patients with Caregiver(s) or Parent/Legal Guardian(s)	24 (3.2%)

Geographic Distribution

At the time of registration, patients provide their home address for verification of Minnesota residency. Home addresses are retained in the patient's online registry account but are not retained in the research database; in lieu of home address, patient ZIP codes are accessible for research purposes. The general geographic distribution of patients was examined using patient-reported ZIP codes; the first three digits of ZIP codes compose a prefix which corresponds to an approximate geographic region[1]. The U.S. Postal Service assigns to each prefix labels that match the major city within the region and approximate surrounding cities; these region labels are shown in Table 1.5, along with the count of patients living in the corresponding ZIP codes.

Most patients live within the Twin Cities metro ZIP code region (68%); 7% of patients live in the Saint Cloud region, 5% live in the Willmar region and 4% live in the Mankato region and Rochester region.

Table 1.5. PTSD Patients by ZIP Code Region (First Three Number Prefixes).

ZIP Region	ZIP Prefixes	Count (%)
Minneapolis	553,554,555	304 (40.5%)
St. Paul	550,551	208 (27.7%)
St. Cloud	563	51 (6.8%)
Duluth	556,557,558	46 (6.1%)
Willmar	562	35 (4.7%)
Mankato	560,561	30 (4.0%)
Rochester	559	28 (3.7%)
Detroit Lakes	565	17 (2.3%)
Brainerd	564	16 (2.1%)
Bemidji	566	12 (1.6%)
Grand Forks	567	4 (0.5%)

[1] https://pe.usps.com/Archive/HTML/DMMArchive20050106/print/L002.htm

Primary Cause of PTSD

When a patient registers for the program, they are asked to provide the primary cause of the PTSD they are experiencing. Patients must select one of the following options: a) military-related, b) non-military-related, c) both military- and non-military-related, or d) prefer not to answer.

The most common cause for PTSD was non-military in nature (71%) followed by military-related PTSD (13%). See Table 1.6.

Table 1.6. Primary Cause of PTSD.

Primary Cause of PTSD	Count (%)
Non-Military	531 (70.7%)
Military	100 (13.3%)
Both Military and Non-Military	45 (6.0%)
Prefer Not to Answer	75 10.0%)

2. Registered Healthcare Practitioners Certifying Early PTSD Patients

The Minnesota Medical Cannabis program outlines a set of qualifying medical conditions which make a patient eligible for enrollment in the program. By Minnesota statute, a patient must be certified by a Minnesota-licensed physician, physician assistant (PA), or advanced practice registered nurse (APRN) as having one or more of the qualifying conditions. A Minnesota practitioner with appropriate credentials must first register with the Minnesota Medical Cannabis program before they can certify patients for the program: practitioners complete a short online form with their name and clinic information to register. Office of Medical Cannabis staff verify the provider's entered information and their Drug Enforcement Agency license prior to approving the practitioner to certify patients. This chapter will describe registered healthcare practitioners who certified patients under the qualifying condition of PTSD who were approved within the first five months of when PTSD was added as a qualifying condition (August 2017-December 2017).

Healthcare Practitioners by Type

A total of 107 healthcare practitioners (HCPs) who registered in the Minnesota Medical Cannabis program certified patients under PTSD who enrolled in the program prior to December 31, 2017. Of these HCPs, 77 (72%) were physicians, 9 (8%) were PAs and 21 (20%) were APRNs (Table 2.1).

Table 2.1. Certifying healthcare practitioners for the first five months of PTSD, by type.

Healthcare Practitioner Type	Count (%)
Physician	77 (72%)
Physician Assistant	9 (8%)
Advanced Practice Registered Nurse	21 (20%)
Total	107

Certifying Physician Specialty

The Minnesota Board of Medical Practice lists information on Minnesota-licensed physicians and physician assistants. Included in self-reported "Area of Specialty" information indicating a physician's certifications from the American Board of Medical Specialties or American Osteopathic Specialty Boards. While physician assistant specialty information is infrequently provided, physicians often list multiple certifications. For example, physicians practicing as infectious disease specialists may list certifications in the area of Internal Medicine and Infectious Disease. A variety of specialties were represented among physicians certifying PTSD patients, including Primary Care and Psychiatry (Table 2.3). One physician who is licensed in Minnesota and registered in the program does not have any listed specialties with the Board of Medical Practice; this physician is therefore excluded from Table 2.3. The most common specialty category for physicians who certified this group of PTSD patients was primary care

(n=56, 69%), including family medicine (n=41; 53%), internal medicine (n=14; 18%) and pediatrics (n=1; 1%), followed by Psychiatry (n=12; 4%).

Table 2.3. Count of physicians by specialty type.

Physician Specialty Type	Count (%)
Primary Care	56 (73%)
Psychiatry	13 (17%)
Physical Medicine and Rehabilitation	3 (4%)
Anesthesiology	2 (3%)
Hospice/Palliative Medicine	1 (1%)
Pain Medicine	1 (1%)

3. Medical Cannabis Use Patterns

Medical cannabis purchasing data is captured for enrolled MN patients through the online registry. For this report, purchasing data were extracted for PTSD patients enrolled between August 1 – December 31, 2017. All purchases that occurred within each patient's first enrollment year were retained, which showed:

- 9,529 purchasing transactions consisting of:
- 15,538 product purchases, which
- Represented 725 patients (96.5% of the PTSD cohort)

Products included in this dataset were categorized according to their route of administration and ratio of THC to CBD contained in the product. Routes of administration include enteral, inhalation, oromucosal, and topical routes of entry into the body (see Box 3.1). THC:CBD ratios ranged from products very high in THC to CBD to those very high in CBD to THC, as well as everything in between (Box 3.1).

Box 3.1. Definitions of Medical Cannabis Product Ratio Categories and Routes of Administration.

Medical Cannabis Products Categorized by THC:CBD Ratio:

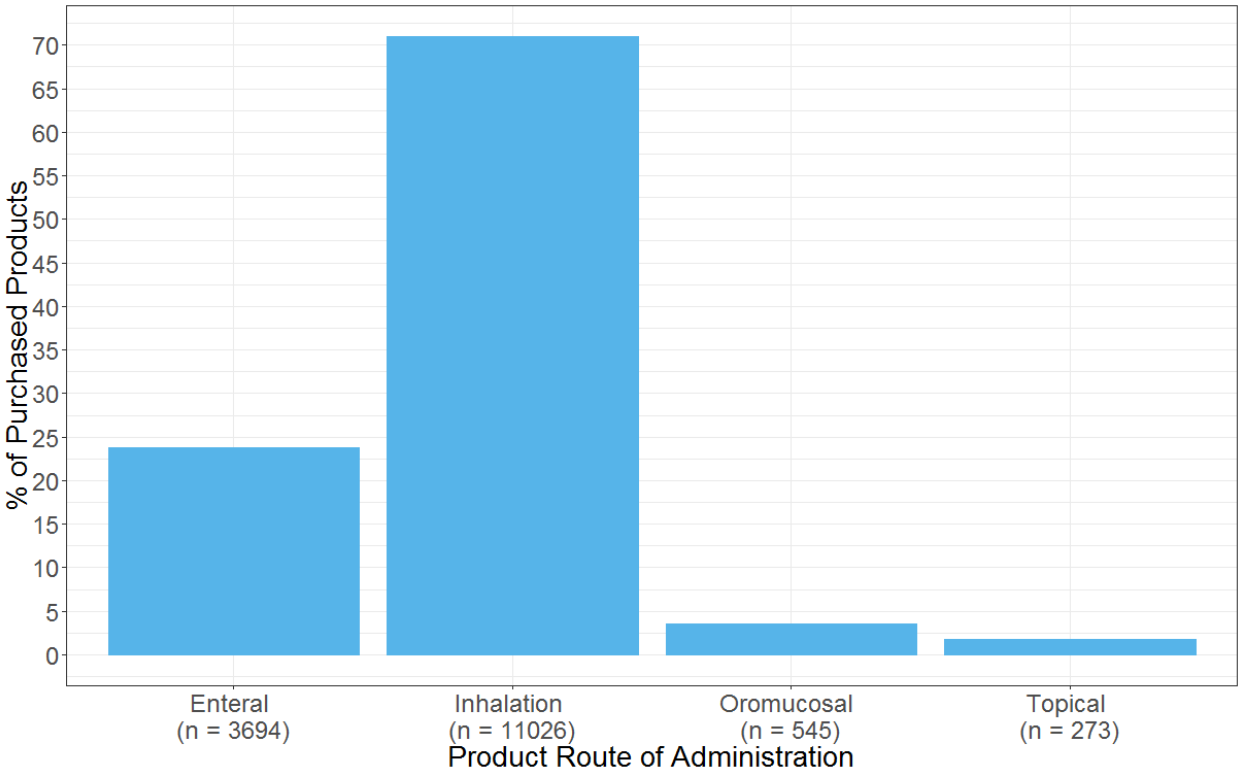
- **Very High THC to CBD** = 100:1 or higher
- **High THC to CBD** = >4:1 up to 99:1
- **Balanced** = 1:1 up to 4:1
- **High CBD to THC** = ≥1:1 up to 99:1
- **Very High CBD to THC** = 100:1 or higher

Product Routes of Administration (ROA):

- **Enteral:** entry through the gastrointestinal tract via swallowing (e.g., capsules, oral solutions)
- **Inhalation:** oils vaporized into lungs
- **Oromucosal:** sublingual sprays and tinctures absorbed through cheek/oral mucosa.
- **Topical:** applied to body surface (e.g., balms)

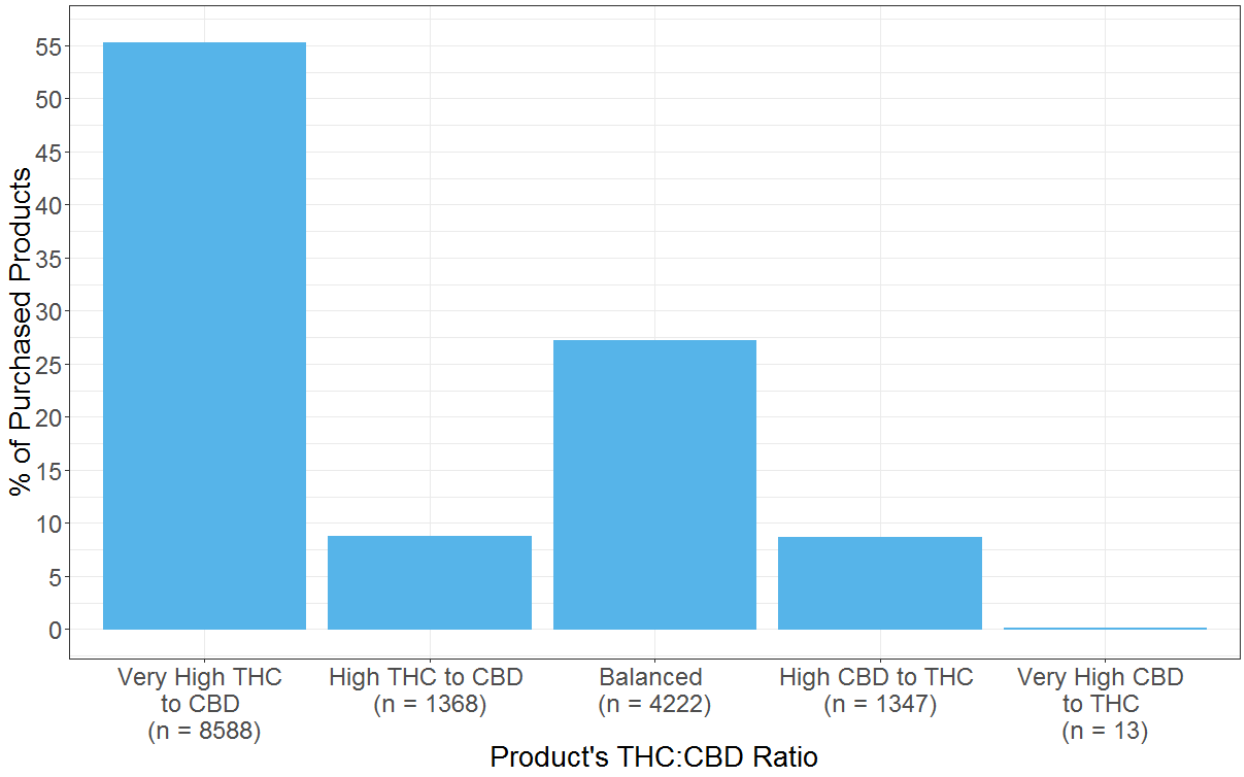
Analysis of purchased products indicates that the majority of purchases (71.0%) were intended for inhalation and 23.8% for enteral administration. Together, these routes accounted for 95% of all products purchased. Oromucosal and topical products together accounted for less than 10% of all products purchased (respectively at 3.5% and 1.8% of all purchases). See Figure 3.1.

Figure 3.1. Product Transactions Categorized by the Product's Route of Administration (out of 15,538 Products).



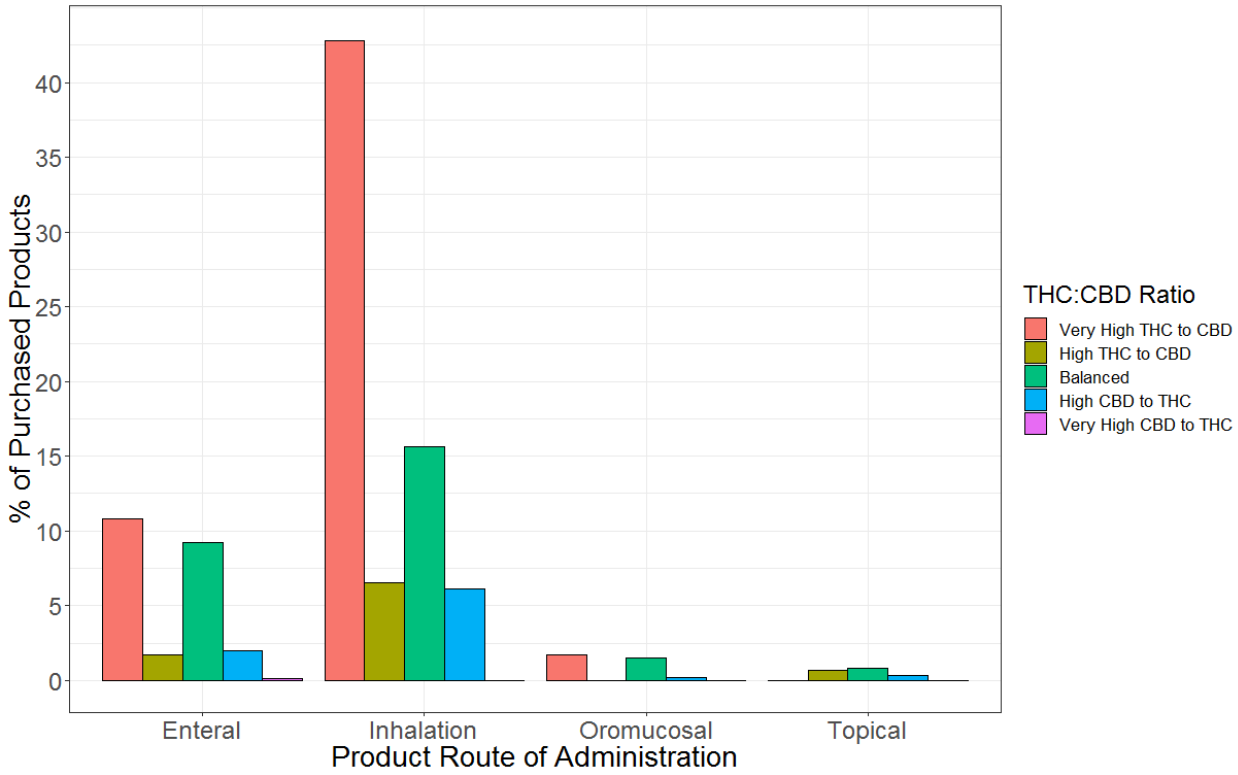
Analysis of products stratified by the THC:CBD ratio showed that products with Very High THC:CBD ratios were purchased most frequently (55.3% of all product purchases), followed by Balanced products (27.2%). High THC:CBD products and High CBD:THC products respectively accounted for 8.8% and 8.7% of all product transactions, with Very High CBD:THC products accounting for 0.1% of all products purchased. See Figure 3.2.

Figure 3.2. Product Transactions Categorized by THC:CBD Ratio (out of 15,538 Products).



Product transactions were also examined by the products' THC:CBD ratio as a function of route of administration (see Figure 3.3 below). Very High THC:CBD and Balanced products were most frequently purchased among enterally, inhaled, and oromucosal products.

Figure 3.3. Product Transactions Categorized by THC:CBD Ratio and Route of Administration (out of 15,538 Products).



Analyzing purchasing patterns across patients is complicated in that there may be some experimentation involved when purchasing medical cannabis to find a dosage and formulation a patient believes is working for them. Another layer of complexity is the fact that products that patients have an affinity for may not necessarily be purchased in the same transaction. Therefore, understanding what is routinely used requires some careful thought and standardized operationalization of what would be considered 'routine' medication. As a first step, this report will present products most frequently purchased by patients. This particular approach is simplistic, but the idea is to continue to refine the operational definition of routine use over time in subsequent analyses.

All products purchased by any given patient were quantified by the number of times they were purchased. The most frequently purchased product(s) was then categorized according to their route of administration and THC:CBD ratio. For each product identified as most frequently purchased, the following calculations were performed within each patient across purchases of that product: summing of intended days supply of product usage, summing of THC dosages (mg), and summing of CBD dosages (mg). From these summed values, daily THC and CBD consumption of the product(s) purchased most frequently was calculated by dividing the summed THC dose and CBD dose by the summed days supply for each patient. Patients who most frequently purchased the same product type(s) had their calculated daily THC and CBD dosages averaged together. This data is displayed in Table 3.1.

Table 3.1 identifies the most frequently purchased product types with an “X”, along with the percentage of patients identified as having purchased that product most frequently (see 2nd column from right). The average daily THC and CBD dose for the patients who purchased the same product type most frequently are indicated in the right-most column. According to the data, 75.4% of all patients (n = 725) purchased product(s) from one ROA-THC:CBD ratio category most frequently (see rows with one “X”). Forty-five percent all patients making purchases most frequently purchased vaporized product(s) with Very High THC:CBD, followed by Balanced vaporized (7.2%) and Balanced enteral (5.7%) product types.

Table 3.1. Product Type(s) Most Frequently Purchased by Each Patient (out of 725 Patients), along with Average Daily THC/CBD dose (mg).

Enteral					Inhalation					Oromucosal					Topical						
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	% of PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
					X															45.2 (326)	111.6 mg / 0.9 mg
							X													7.2 (52)	60.6 mg / 43.3 mg
		X																		5.7 (41)	24.4 mg / 20.3 mg
X																				5.5 (40)	28.0 mg / 0.2 mg
					X		X													4.4 (32)	136.8 mg / 36.7 mg
								X												4.2 (30)	5.1 mg / 81.8 mg
						X														2.5 (18)	137.6 mg / 6.0 mg
			X																	2.1 (15)	7.3 mg / 154.5 mg
					X			X												1.5 (11)	67.8 mg / 89.6 mg
		X			X		X													1.2 (9)	188.3 mg / 47.8 mg
										X										1.2 (9)	59.2 mg / 0.2 mg
	X																			1.1 (8)	78.3 mg / 8.4 mg
												X								1.1 (8)	39.9 mg / 32.1 mg
X					X															0.7 (5)	87.5 mg / 0.7 mg
					X	X														0.7 (5)	248.2 mg / 8.6 mg
X		X			X		X													0.6 (4)	163.9 mg / 47.1 mg
X		X																		0.6 (4)	35.5 mg / 8.2 mg
X			X																	0.6 (4)	19.5 mg / 116.6 mg
	X				X															0.6 (4)	105.0 mg / 5.6 mg
		X	X																	0.6 (4)	23.3 mg / 101.1 mg
					X	X	X													0.6 (4)	307.8 mg / 46.9 mg
X					X			X												0.4 (3)	81.7 mg / 74.0 mg
X								X												0.4 (3)	23.0 mg / 88.2 mg
X												X								0.4 (3)	69.9 mg / 42.5 mg
			X				X													0.4 (3)	43.8 mg / 98.7 mg
					X		X	X												0.4 (3)	129.9 mg / 146.2 mg
					X					X										0.4 (3)	221.6 mg / 1.9 mg
							X	X												0.4 (3)	53.2 mg / 124.3 mg
													X							0.4 (3)	7.3 mg / 138.5 mg
X					X		X													0.3 (2)	163.2 mg / 50.1 mg
	X	X																		0.3 (2)	68.4 mg / 39.3 mg
		X	X		X		X													0.3 (2)	197.0 mg / 131.5 mg
		X			X	X	X													0.3 (2)	193.9 mg / 43.2 mg
		X			X		X									X				0.3 (2)	248.8 mg / 41.7 mg
		X						X												0.3 (2)	25.8 mg / 111.4 mg
						X	X													0.3 (2)	75.8 mg / 43.5 mg
								X				X								0.3 (2)	37.6 mg / 121.2 mg

Table 3.1 continued. Product Type(s) Most Frequently Purchased by Each Patient (out of 725 Patients), along with Average Daily THC/CBD dose (mg).

Enteral					Inhalation					Oromucosal					Topical						
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	% of PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
										X		X								0.3 (2)	86.3 mg / 36.5 mg
X	X				X															0.1 (1)	109.7 mg / 6.5 mg
X	X																			0.1 (1)	106.9 mg / 6.2 mg
X		X					X			X										0.1 (1)	132.4 mg / 52.1 mg
X			X		X													X		0.1 (1)	115.0 mg / 110.2 mg
X					X					X										0.1 (1)	97.0 mg / 0.7 mg
X					X											X				0.1 (1)	270.0 mg / 5.5 mg
X						X														0.1 (1)	74.4 mg / 2.6 mg
X							X			X							X			0.1 (1)	127.8 mg / 58.0 mg
X							X													0.1 (1)	76.7 mg / 11.8 mg
X										X		X								0.1 (1)	96.3 mg / 36.5 mg
	X	X			X		X													0.1 (1)	219.3 mg / 47.7 mg
	X	X			X															0.1 (1)	68.0 mg / 22.8 mg
	X		X		X															0.1 (1)	298.6 mg / 49.6 mg
	X				X	X	X									X				0.1 (1)	387.6 mg / 53.9 mg
	X				X	X	X													0.1 (1)	263.8 mg / 39.6 mg
	X					X														0.1 (1)	264.2 mg / 15.0 mg
		X	X		X	X	X	X		X							X			0.1 (1)	592.1 mg / 333.4 mg
		X	X		X	X	X													0.1 (1)	449.7 mg / 133.3 mg
		X	X		X		X	X					X							0.1 (1)	180.3 mg / 356.8 mg
		X	X					X				X								0.1 (1)	97.6 mg / 356.9 mg
		X	X									X					X			0.1 (1)	104.1 mg / 180.1 mg
		X			X		X			X		X								0.1 (1)	242.7 mg / 41.4 mg
		X			X		X										X			0.1 (1)	111.8 mg / 61.6 mg
		X			X		X											X		0.1 (1)	188.2 mg / 60.8 mg
		X			X															0.1 (1)	80.5 mg / 45.3 mg
		X				X	X													0.1 (1)	124.0 mg / 24.5 mg
		X					X													0.1 (1)	149.8 mg / 37.5 mg
		X								X										0.1 (1)	46.3 mg / 15.2 mg
		X										X								0.1 (1)	48.2 mg / 48.2 mg
			X		X		X			X										0.1 (1)	289.8 mg / 349.5 mg
			X		X		X						X							0.1 (1)	101.7 mg / 182.3 mg
			X		X		X													0.1 (1)	168.1 mg / 95.4 mg
			X		X															0.1 (1)	85.8 mg / 47.9 mg
			X					X												0.1 (1)	15.1 mg / 130.7 mg
			X									X								0.1 (1)	35.8 mg / 198.7 mg

Table 3.1 continued. Product Type(s) Most Frequently Purchased by Each Patient (out of 725 Patients), along with Average Daily THC/CBD dose (mg).

Enteral					Inhalation					Oromucosal					Topical						
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	% of PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X																0.1 (1)	1.9 mg / 342.9 mg
					X	X	X									X				0.1 (1)	310.0 mg / 107.2 mg
					X	X	X										X			0.1 (1)	197.5 mg / 44.9 mg
					X	X				X										0.1 (1)	167.5 mg / 4.1 mg
					X		X									X				0.1 (1)	210.2 mg / 56.9 mg
					X		X										X			0.1 (1)	121.1 mg / 58.4 mg
					X			X									X			0.1 (1)	70.7 mg / 107.2 mg
							X			X		X								0.1 (1)	248.8 mg / 124.0 mg
							X			X										0.1 (1)	107.4 mg / 34.5 mg
							X						X							0.1 (1)	104.2 mg / 104.2 mg
								X		X										0.1 (1)	54.4 mg / 88.2 mg
																X				0.1 (1)	15.0 mg / 4.3 mg

4. Benefits

Summary

Information on patient benefits comes from the Patient Self-Evaluation (PSE) completed by patients prior to each medical cannabis purchase and from patient and health care practitioner surveys. At enrollment and in the patient surveys patients are asked to complete a questionnaire on PTSD symptoms called the PTSD Checklist for DSM-5 (PCL-5). The PCL-5 is a 20-item self-report measure that assess 20 DSM-5 (Diagnostic and Statistical Manual of Mental Disorders – 5th edition) symptoms of PTSD. The PCL-5 was developed by the National Center for PTSD, part of the U. S. Department of Veteran Affairs. Among its purposes is monitoring symptom change before and after treatment. For details on the PCL-5 see: U.S. Department of Veterans Affairs - PTSD: National Center for PTSD (https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp)

Survey Data

At enrollment, 96% of the 751 PTSD patients included in this report scored above 33 points, meeting the cut-point for provisional PTSD diagnosis. Comparing PCL-5 score at enrollment and at 3 months, for the 51% who responded to the survey 3 months after their first medical cannabis purchase, shows many experienced substantial benefit. Literature has shown that a clinically meaningful difference in PCL-5 scores measured at different times amounts to a difference of 10-20 points. Between 50% and 71% (depending on whether a reduction of 20 points or 10 points is used) of respondents saw a clinically meaningful improvement in PTSD symptoms. Because those who completed the 3-month survey and those who did not were similar in demographics and in enrollment PCL-5 score, we can have some confidence that the change in PCL-5 score seen for survey responders is representative of the entire group.

Patients responded to a survey question asking them how much benefit they believe they received from using medical cannabis on a scale from 1 (no benefit) to 7 (great deal of benefit). Across all responding patients, 76% indicated a benefit rating of 6 or 7. A small but important proportion of patients indicated little or no benefit: 4% gave a rating of 1,2, or 3. When patients were asked what the most important benefit was for them, 23% indicated anxiety reduction, 16% improved sleep, 13% improved mood and/or emotional regulation, and 12% pain reduction. Survey response rate from health care practitioners was less than hoped for; HCP surveys for only 21% of the patients had benefit rating information. HCP ratings on the completed surveys were quite similar to patient ratings.

An important part of this report is the verbatim comments written by patients, and the reader is encouraged to review these comments in *Appendix A: Patient-Reported Benefits from Medical Cannabis*. Examples of these comments include:

- “Fewer periods of dissociation due to increased mindfulness, being able to tolerate processing trauma in therapy without dissociating, improved sleep, improved transition from sleeping to wakefulness, decreased body pain, eating more, not isolating from friends and family as much, being able to tend to my house more.”
- “Sleeping has been AMAZING, pain is way down, not helping my anxiety as much as I would like, but nothing is perfect.”

- "Controlled doses. I used cannabis before this program in such an uncontrolled dosage that it affected my other medications. The control of the cartridge has been extremely helpful."
- "Being able to go to work with less anxiety and feeling like I can function. No more night terrors and screaming in my sleep."
- "Able to leave the house easier. I have PTSD and being on any road can make me anxious and hyper-vigilant. Using medical cannabis makes that feeling go away for the most part. Before medical cannabis it felt like anyone and anything could be a threat. After, it allows me to remain calm and either ignore or remove thoughts and feelings like that. It eases my general anxiety and depression overall so I'm able to take less of my as needed medications like diazepam, propanerol, and hydroxyzine. Overall, it has reduced my stress levels which helps me think clearer and be a more productive father and husband. I'm grateful for it."
- "Feeling less anxious and having to deal with less chronic pain has overall improved my quality of life a great deal. I have more moments of happiness and it's opened up many doors to me that I have had shut for a long time."
- "Better sleep, better appetite, I'm not so angry all the time. My memories don't seem to bother me like they used to. This has been a life changer for me!"
- "Since starting medical cannabis it's like I've been given a fair chance to treat my PTSD symptoms I've struggled with over a decade now. My family sees a night and day difference and it's easier to communicate with them. I've since found a part-time job with flexible hours to work around starting college in January, 2018. The only hope I have is that it becomes more affordable as I'm barely able to afford it now."
- "Increased appetited, increased attention, better quality sleep, helps me stay grounded after trauma therapy, more sleep, increased confidence, new job, new career direction."

Patient Self-Evaluation Data

The PTSD patients included in this report had a high burden of symptoms. When they initiated program participation, a majority had at least moderate levels of anxiety (96%), disturbed sleep (91%), depression (84%), fatigue (84%), and lack of appetite (60%). For 6 of the 8 symptoms measured, among those with at least moderate levels of the symptom at baseline, between 32% (fatigue) and 48% (lack of appetite), both achieved ≥30% symptom reduction within four months and retained that level of improvement over the following four months. The percentage was a bit lower for pain (27%) and a bit higher for vomiting (56%).

Benefits Reported on Patient Experience Survey and Health Care Practitioner Survey

In addition to collecting data on severity of symptoms related to each patient's qualifying condition or conditions before each medical cannabis purchase, the Office of Medical Cannabis sought to gain a qualitative understanding of patient-reported benefits and harms of program participation. Utilizing expertise within the Minnesota Department of Health, the Office of Medical Cannabis developed a Patient Experience survey, which captures information on benefits and harms of program participation. A parallel survey for each patient was developed for their certifying health care practitioner, which captures similar information from the clinician's perspective. The surveys include scaled response and open-response questions; health care practitioners were also asked to provide any clinical observations they noted about the patient's experience with medical cannabis. Healthcare providers familiar with the program provided feedback as part of the development process.

When PTSD became a qualifying condition in the Minnesota Medical Cannabis program, the PTSD Checklist for DSM-5 (PCL-5) was integrated into the patient enrollment process for patients certified for PTSD. The PCL-5 was also integrated into the Patient Experience Survey for patients certified for PTSD. The PCL-5 is a 20-item self-report measure that assess 20 DSM-5 (Diagnostic and Statistical Manual of Mental Disorders – 5th edition) symptoms of PTSD. The PCL-5 was developed by the National Center for PTSD, part of the U. S. Department of Veteran Affairs. Among its purposes is monitoring symptom change before and after treatment. For each of the 20 symptoms patients are asked how much the symptom bothered them in the past month, from 0=Not at All to 4=Extremely.

Survey Methodology

The surveys are provided through an online platform; in the patient's first program year they are sent to patients three months, then six months after the patient's first medical cannabis purchase and are sent to healthcare practitioners six months after the patient's first medical cannabis purchase. Patients and healthcare practitioners access the surveys through the subject's registry page and through introductory emails containing unique links. To maximize survey submission rates, the survey can be submitted with incomplete responses to any of the questions. Each of the surveys is available online to the recipient for 45 days. Patient recipients receive reminder emails after one week; after two weeks with no response, paper copies of surveys are mailed to the recipient. For patients without online access the full process is accomplished by phone or mail.

Patients were required to complete all items in the PCL-5 in order to submit a survey; surveys returned with incomplete responses (n=15) to the PCL-5 questions were excluded from analyses.

PTSD patients were asked to report the cause(s) of their PTSD as military related, non-military related, both military-related and non military-related. Patients were also allowed to respond, "Prefer not to answer." Based on their response, patients were placed into three groups:

Military (patients who reported military-related PTSD and both military-related and non-military related PTSD); Non-Military (patients who reported non military-related PTSD and both military-related and non-military related PTSD) and No Response (patients who did not report a PTSD cause).

Survey Data Preparation

Patients and their certifying HCPs were asked to report the benefits and negative effects, if any, they have experienced as a result of medical cannabis treatment (in order of importance to the patient.) Survey responses from patients and health care practitioners on perceived benefits and perceived negative effects were reported in free-text format; each response was individually reviewed and classified into a category of benefit or negative effects. Reported benefits typically included either direct improvement of symptoms related to the patient's qualifying condition or more general improvements in health or quality of life, referred to in this report as global health benefits. Many responses included more than one type of benefit; in these cases, the first reported benefit was presumed to be the most important benefit. In this report, we examine both overall perceptions of benefit, as well as type of reported benefit.

Analysis of PCL-5 assessment data was performed using a cut-point score of 33 or greater as a provisional PTSD diagnosis, and in comparing a patient's baseline PCL-5 score to their 3-month survey PCL-5 score, two thresholds of PCL-5 score reduction were used as a marker of clinically meaningful improvement: ≥10 points and ≥20 points[2]. Baseline scores, 3-month survey scores and the percent of patients who experienced a clinically meaningful improvement at the time of the 3-month survey were reported.

Patient-Reported Benefits

Of 751 patients certified for PTSD between August 2017-December 2017, 381 (50.7%) responded to a survey sent 3 months after the patient's first purchase. Response rates by age category varied somewhat, with a slight underrepresentation of young adult patients (Table 4.1). Response rates by race/ethnicity also varied and tended to underrepresent minority groups, particularly Asian, black or American Indian patients (Table 4.2). Response rates varied by reported cause of PTSD; patients with either military related PTSD or non-military-related PTSD were more likely to respond to the 3-month survey than patients who did not report a PTSD cause or who reported both causes of PTSD (Table 4.3).

[2] "PTSD Checklist for DSM-5 (PCL-5)": https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp

Table 4.1. Patient response rates by age group.

Age Group	Total	Patient Responses
0-4 yrs	0	-
5-17 yrs	15	8 (53%)
18-24 yrs	55	24 (44%)
25-35 yrs	255	134 (53%)
36-49 yrs	233	108 (46%)
50-64 yrs	148	73 (49%)
65+ yrs	45	34 (51%)

Table 4.2. Patient survey response rate by race and ethnicity.

Race/Ethnicity	Total	Patient Responses
American Indian	32	14 (44%)
Asian	6	2 (33%)
Black	46	19 (41%)
Hawaiian	1	1 (100%)
White	637	337 (53%)
Hispanic	22	14 (64%)
Other	18	10 (56%)

Table 4.3. Response Rates by Reported Cause of PTSD.

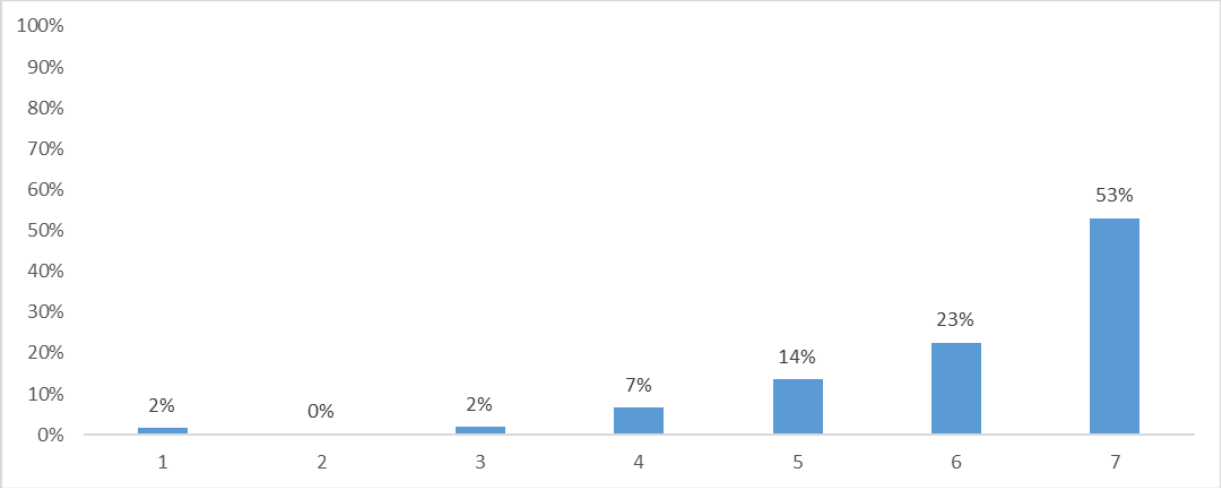
Reported Cause of PTSD	Total	Patient Responses
Military Related PTSD	100	52 (52%)
Non-Military Related PTSD	531	280 (53%)
Military and Non-Military Related PTSD	45	21 (47%)
No Response	75	28 (37%)

Patient Perceptions of Benefit from Medical Cannabis

The Patient Experience survey asks patients to report how much benefit they have experienced as a result of medical cannabis, on a scale from 1 (representing no benefit) to 7 (representing a great deal of benefit). Patients are also asked to report the types of benefits they have experienced as a result of medical cannabis. Figure 4.1 shows the distribution of scores on the benefit scale from respondents- the percentages use the total number of survey respondents as the denominator, though in a small number of cases (n=2) surveys were returned incomplete and did not report a benefit score.

Of 381 patients who responded to the survey, 288 patients (76%) reported a benefit score of 6 or 7, indicating a high degree of benefit from medical cannabis.

Figure 4.1. Patient-Perceived Benefit in Survey Respondents (N=381).



Patient responses regarding types of benefits experienced as a result of medical cannabis treatment are shown in Table 4.4. Table 4.4 shows the most important benefits reported by patients, as determined from the order of benefits listed.

Of 381 patient respondents, 88 (23%) reported anxiety reduction as the most important benefit from medical cannabis (Table 4.4). In addition to a general reference to improvement in PTSD symptoms (8%), patients most often reported improved sleep (16%), improved mood and/or emotional regulation (13%) and pain reduction (12%) as the most important benefit. Among respondents, 46 (12%) did not specify any benefits (though in a few cases they reported benefit scores of ≥2). Thirteen patients reported miscellaneous benefits, such as legal access to cannabis or benefits to other health conditions. In a few other cases, patients reported a benefit without an accompanying benefit score; these responses are reflected in the total number of responses in each category but not in the breakdown of responses by scores. A full

tabulation of patient-reported benefit statements can be found in *Appendix A: Patient-Reported Benefits from Medical Cannabis.*

Table 4.4. Most important benefits reported by patients, by benefit score.

	Scores by Most Important Benefit Type: N (%)							
Most Important Benefit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**Total**
Anxiety Reduction	-	-	2 (1%)	8 (2%)	7 (2%)	22 (6%)	49 (13%)	88 (23%)
Appetite Improvement	-	-	-	1 (<1%)	1 (<1%)	-	2 (1%)	4 (1%)
Depression Reduction	-	-	-	-	1 (<1%)	-	2 (1%)	3 (1%)
Improved Mood/Emotional Regulation	-	1 (<1%)	-	4 (1%)	6 (2%)	12 (3%)	26 (6%)	49 (13%)
Improved Cognition/Alertness	-	-	-	-	-	2 (1%)	8 (2%)	10 (3%)
Nausea/Vomiting Reduction	-	-	-	1 (<1%)	-	1 (<1%)	1 (<1%)	3 (1%)
Reduction/Elimination of Other Medications	-	-	-	1 (<1%)	1 (<1%)	2 (1%)	9 (2%)	13 (3%)
Pain Reduction	-	-	-	1 (<1%)	9 (2%)	11 (3%)	23 (6%)	44 (12%)
Improved Physical Functioning/Mobility	-	-	-	-	-	1 (<1%)	1 (<1%)	2 (1%)
PTSD Symptom Reduction	1 (<1%)	-	-	1 (<1%)	3 (1%)	3 (1%)	24 (6%)	32 (8%)
Improved Quality of Life	-	-	-	-	-	2 (1%)	8 (2%)	10 (3%)
Improved Sleep	-	-	2 (1%)	5 (1%)	11 (3%)	17 (5%)	27 (6%)	62 (16%)
Seizure Reduction	-	-	-	-	-	2 (1%)	-	2 (1%)

Healthcare Practitioner-Reported Benefits

For 751 patients certified for PTSD between August 2017-December 2017, 345 healthcare practitioner surveys were completed 6 months after the patient's first purchase. Review of submitted HCP responses revealed that in many cases, healthcare practitioners indicated they had not seen the patient since certification and therefore they had no clinical updates to provide; these surveys were eliminated (n=182), and the remaining 163 (21.2% of cohort) were included in analyses described below.

Healthcare practitioner response rates by patient age category varied slightly and tended to more fully represent younger patients (Table 4.5). Response rates were roughly similar across patient race/ethnicity groups (Table 4.6).

Table 4.5. Healthcare practitioner survey response rates by patient age group.

Age Group	Total	Responses by Patient Category
0-4 yrs	0	-
5-17 yrs	15	8 (53%)
18-24 yrs	52	15 (29%)
25-35 yrs	244	57 (23%)
36-49 yrs	226	49 (22%)
50-64 yrs	144	24 (17%)
65+ yrs	45	10 (22%)

Table 4.6. Healthcare practitioner survey response rates by patient race and ethnicity.

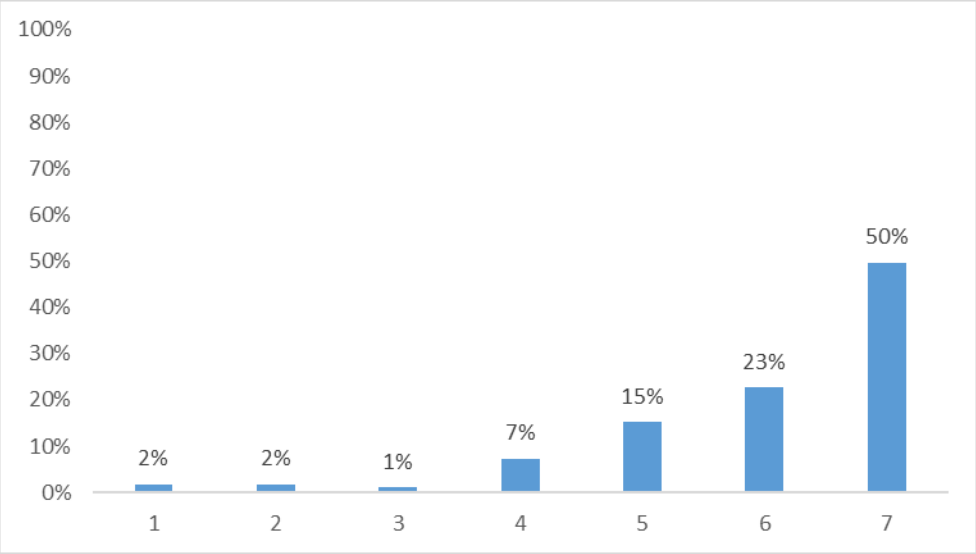
Race/Ethnicity	Total	Responses by Patient Category
American Indian	32	7 (22%)
Asian	5	1 (20%)
Black	43	9 (21%)
Hawaiian	1	0 (0%)
White	621	140 (23%)
Hispanic	19	4 (21%)
Other	16	4 (25%)

Healthcare Practitioner Perceptions of Benefit from Medical Cannabis

The Healthcare Practitioner survey asks HCPs to report how much benefit they believe the patient has experienced as a result of medical cannabis, on a scale from 1 (representing no benefit) to 7 (representing a great deal of benefit). They are also asked to report the types of benefits the patient experienced as a result of medical cannabis. Figure 4.2 shows the distribution of scores on the benefit scale from respondents- the percentages use the total number of survey respondents as the denominator.

Of 163 completed surveys, 118 (72%) reported a patient benefit score of 6 or 7, indicating a high degree of benefit from medical cannabis (Figure 4.2).

Figure 4.2. Healthcare Practitioner-Perceived Benefit in Survey Respondents (N=163).



Healthcare practitioner survey responses regarding types of benefits experienced as a result of medical cannabis treatment are shown in Table 4.7. Table 4.7 shows the most important benefits reported by healthcare practitioners, as determined from the order of benefits listed.

Of 163 HCP respondents, 32 (20%) reported anxiety reduction as the most important benefit from medical cannabis (Table 4.7). In addition to a general reference to improvement in PTSD symptoms (11%), HCPs most often reported improved sleep (12%), improved mood and/or emotional regulation (12%) and pain reduction (11%) as the most important benefit. Among respondents, 48 (30%) did not specify any benefits (though in a few cases they reported benefit scores of ≥2). A full compilation of healthcare practitioner-reported benefit statements is available in *Appendix B: Healthcare Practitioner-Reported Benefits from Medical Cannabis.*

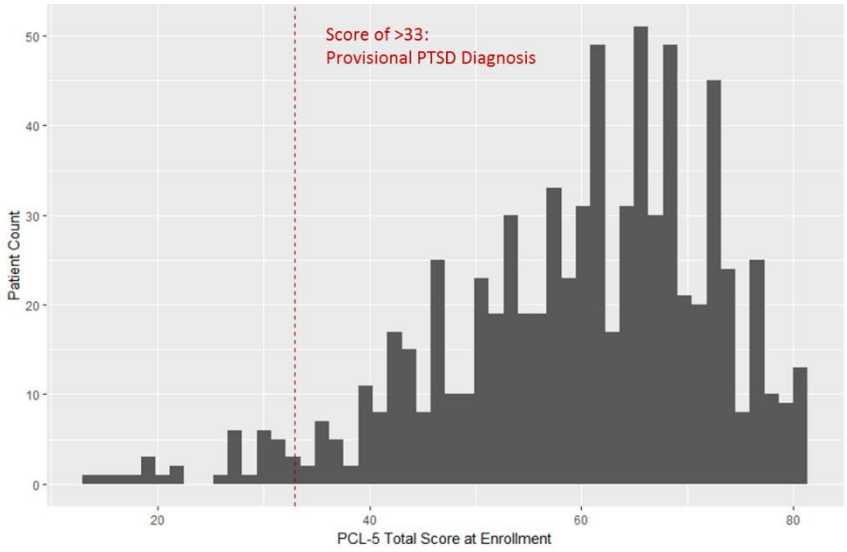
Table 4.7. Most important benefits reported by healthcare practitioners, by benefit score.

	Scores by Most Important Benefit Type: N (%)							
	1	**2**	**3**	**4**	**5**	**6**	**7**	**Total**
Anxiety Reduction	-	-	-	4 (2%)	1 (1%)	4 (2%)	23 (14%)	32 (20%)
Appetite Improvement	-	-	-	-	-	-	1 (1%)	1 (1%)
Depression Reduction	-	-	-	-	-	-	1 (1%)	1 (1%)
Improved Mood/Emotional Regulation	-	1 (1%)	-	2 (1%)	2 (1%)	4 (2%)	10 (6%)	19 (12%)
Nausea/Vomiting Reduction	-	-	-		-	-	1 (1%)	1 (1%)
Reduction/Elimination of Other Medications	-	-	-	-	1 (1%)	-	1 (1%)	2 (1%)
Pain Reduction	-	-	1 (1%)	1 (1%)	4 (2%)	2 (1%)	10 (6%)	18 (11%)
Improved Physical Functioning/Mobility	-	-	-	-	-	-	1 (1%)	1 (1%)
PTSD Symptom Reduction	-	-	1 (1%)	1 (1%)	3 (2%)	6 (4%)	7 (4%)	18 (11%)
Improved Quality of Life	-	-	-	-	1 (1%)	1 (1%)	-	2 (1%)
Improved Sleep	-	1 (1%)	-	-	4 (2%)	7 (4%)	7 (4%)	19 (12%)
Tic Reduction	-	-	-	-	-	1 (1%)	-	1 (1%)

PTSD Checklist for DSM-5 Results at Enrollment and 3 Months After First Purchase

All patients who are certified for PTSD by an HCP are required to complete a PCL-5 assessment prior to enrollment in order to complete the registration process. Figure 4.3 shows PCL-5 scores at enrollment for PTSD cohort patients (n=751). Overall, 719 patients (96%) scored above 33 points, meeting the cut-point for provisional PTSD diagnosis. Mean PCL-5 score at enrollment was 59.6 (SD=12.7); median PCL-5 score at enrollment was 61.

Figure 4.3. PTSD Patient PCL-5 Scores at Enrollment (N=751).



Only patients who completed the survey at 3 months after first purchase provided a PCL-5 score for comparison against enrollment score; therefore, enrollment PCL-5 scores were stratified by response status (responder to 3 month survey vs. non-responder to 3 month survey) for examination and the two groups showed no differences in enrollment PCL-5 score (Figure 4.4, $p>0.1$). Mean (SD) among responders was 59.3 (13.0); mean (SD) among non-responders was 59.9 (12.5), with no significant differences between the two groups ($p>0.1$).

Patient PCL-5 scores at enrollment and at 3-month survey are shown for survey responders in Figure 4.5. Among responders, mean PCL-5 score (SD) at enrollment was 59.3 (13.0); at 3 months after first purchase, mean PCL-5 score (SD) was 38.3 (17.7). The changes from baseline to 3 months among survey responders increased the proportion under the >33 point threshold for provisional diagnosis of PTSD to 39% (4% at baseline for both survey responders and for all patients).

Figure 4.4. Enrollment PCL-5 Scores, Stratified by 3-Month Survey Response Status (N=751).

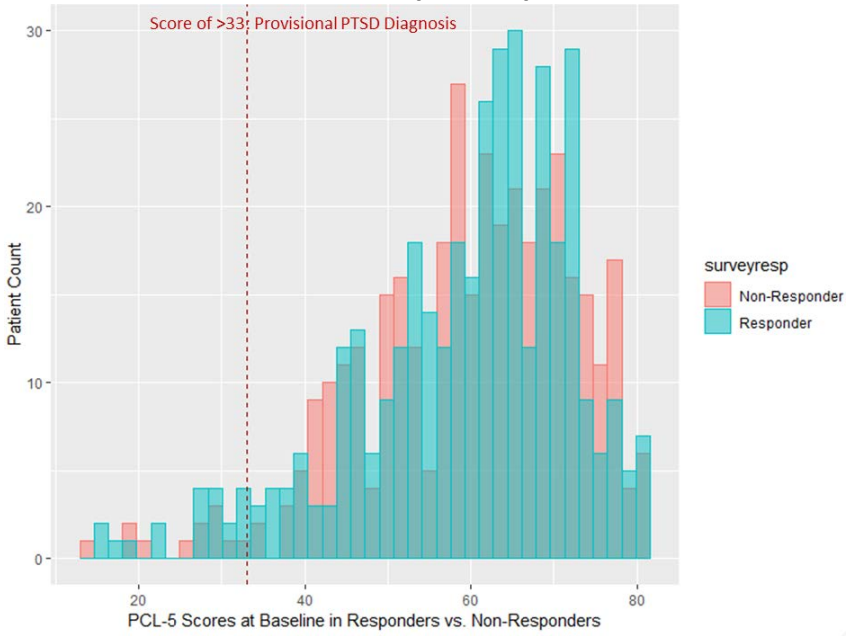


Figure 4.5. Enrollment PCL-5 Scores and 3-Month Survey PCL-5 Scores Among 3-Month Survey Responders (N=381).

PCL-5 Scores by PTSD Cause

Enrollment PCL-5 scores and 3-month PCL-5 scores for survey respondents were further stratified by reported PTSD cause (military, non-military or no response). Figure 4.6 shows distribution of PCL-5 enrollment and 3-month scores for each PTSD cause group. In the military PTSD group (n=73), mean PCL-5 score (SD) at enrollment was 59.2 (12.2); mean PCL-5 score (SD) at 3-month survey was 36.8 (15.1). In the non-military PTSD group (n=301), mean PCL-5 score (SD) at enrollment was 59.1 (12.9); mean PCL-5 score (SD) at 3-month survey was 38.1 (18.2). In the no-response PTSD group (n=28), mean PCL-5 score (SD) at enrollment was 59.5 (16.2); mean PCL-5 score (SD) at 3-month survey was 40.4 (18.0). Generally, enrollment PCL-5 scores were similar across PTSD cause groups, and 3-month survey PCL-5 scores were similar across PTSD cause groups, but PCL-5 scores were generally lower in each group at the 3-month survey time, compared to at enrollment.

Figure 4.6. Enrollment PCL-5 Scores and 3-Month Survey PCL-5 Scores Among 3-Month Survey Responders, by Reported PTSD Cause (N=381).

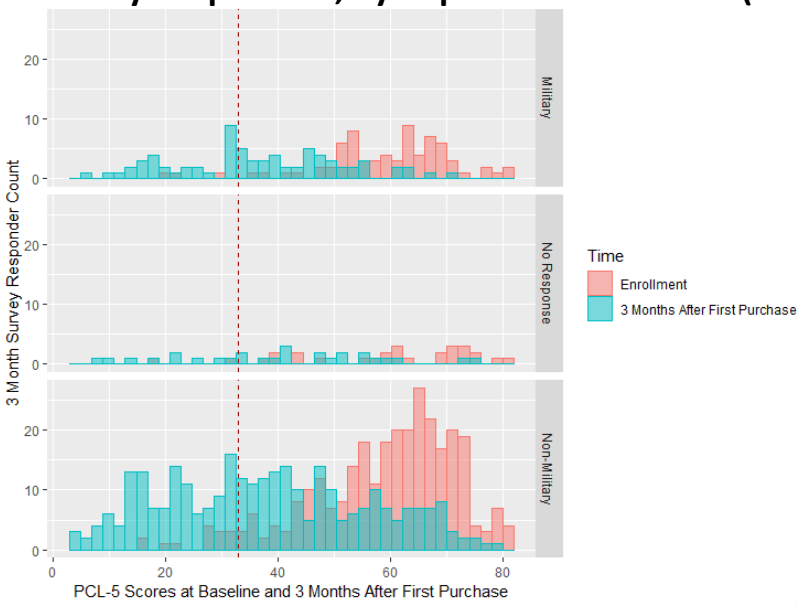
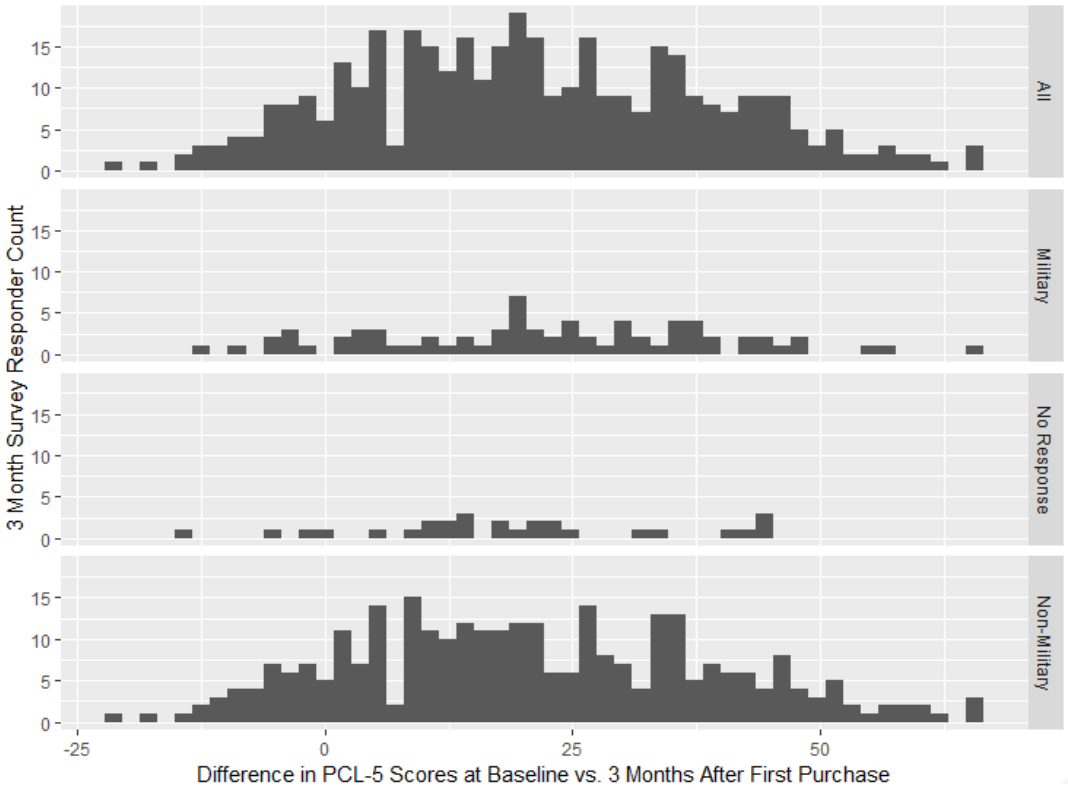


Figure 4.7 shows the difference between baseline PCL-5 score and 3-month PCL-5 score for each survey respondent (overall and stratified by PTSD cause), where positive values indicate symptom improvement and negative values indicate symptom worsening. Overall mean difference (SD) was 21.1 (17.8); in the military cause PTSD group, mean difference (SD) was 22.4 (17.0) and in the non-military cause PTSD group, mean difference (SD) was 21.0 (18.1). Mean difference (SD) in the "No Response" group was 19.1 (15.5).

Literature has shown that a clinically meaningful difference in PCL-5 scores measured at different times amounts to a difference of 10-20 points[3]. Score differences between enrollment PCL-5 and 3-month PCL-5 were calculated for each survey respondent; Table 4.8 shows the percent of survey respondents who demonstrated a decrease of ≥10 points and the percent who demonstrated a decrease ≥20 points. Among all survey respondents (n=381), 272 (71%) saw ≥10 points improvement when comparing enrollment PCL-5 scores to 3-month PCL-5 scores. The military PTSD cause respondents were more likely to experience this improvement than non-military PTSD cause respondents. When a decrease of ≥20 points is used as a threshold, 50% showed this level of improvement overall (58% in military-related PTSD and 50% in non-military-related PTSD).

Figure 4.7. Difference between Enrollment PCL-5 Scores and 3-Month Survey PCL-5 Scores Among 3-Month Survey Responders, by Reported PTSD Cause (N=381)



[3] "PTSD Checklist for DSM-5 (PCL-5)": https://www.ptsd.va.gov/professional/assessment/adult-sr/ptsd-checklist.asp

Table 4.8. Percent of Survey Respondents Experiencing ≥10 Point and ≥20 Point Improvement in PCL-5 Scores at 3-Month Survey PCL-5 Scores, by Reported PTSD Cause (N=381).

PTSD Cause	N	Patients with ≥10 point improvement over 3 months	Patients with ≥20 point improvement over 3 months
All Causes	381	272 (71%)	191 (50%)
Military Related PTSD	73	55 (75%)	42 (58%)
Non-Military Related PTSD	301	211 (70%)	149 (50%)
No Response	28	22 (79%)	12 (43%)

PCL-5 Symptom Clusters at Enrollment and 3-Month Survey

The PCL-5's 20 items can be broken down into four symptom clusters, each corresponding to a DSM-5 criterion: intrusive symptoms (Criterion B), avoidance (Criterion C), negative alterations in cognition and mood (Criterion D) and alterations in arousal and reactivity (Criterion E). Presence of each criterion can be determined by at least one item in symptom clusters B, C and D and at least two items in symptom cluster E scored at 2 ("Moderately" endorsed) or higher.

Figure 4.8 compares PCL-5 overall scores and symptom cluster results at enrollment and 3-month survey for survey respondents (n=381). The following proportions of patients are reported:

- Meeting the >33 cut-point for provisional PTSD diagnosis
- Meeting PTSD diagnostic Criteria B-E based on symptom cluster scores
- Meeting Criterion B (intrusive symptoms) based on symptom cluster B scores
- Meeting Criterion C (avoidance) based on symptom cluster C scores
- Meeting Criterion D (negative alterations in cognition and mood) based on symptom cluster D scores and
- Meeting Criterion E (alterations in arousal and reactivity) based on symptom cluster E scores

At enrollment PCL-5, 95% of respondents met the >33 cut-point for provisional PTSD diagnosis and met all 4 criteria for PTSD diagnosis assessed in the PCL-5; at the 3-month survey these

proportions dropped to 59% and 61%, respectively. Individual criteria were more frequently met at enrollment and at the 3-month survey; Criterion E (alterations in arousal and reactivity) showed the largest difference between prevalence at enrollment vs. 3-month survey (98% vs. 73%).

Figure 4.8. Proportion of survey respondents at enrollment and 3-month PCL meeting PTSD diagnostic criteria.

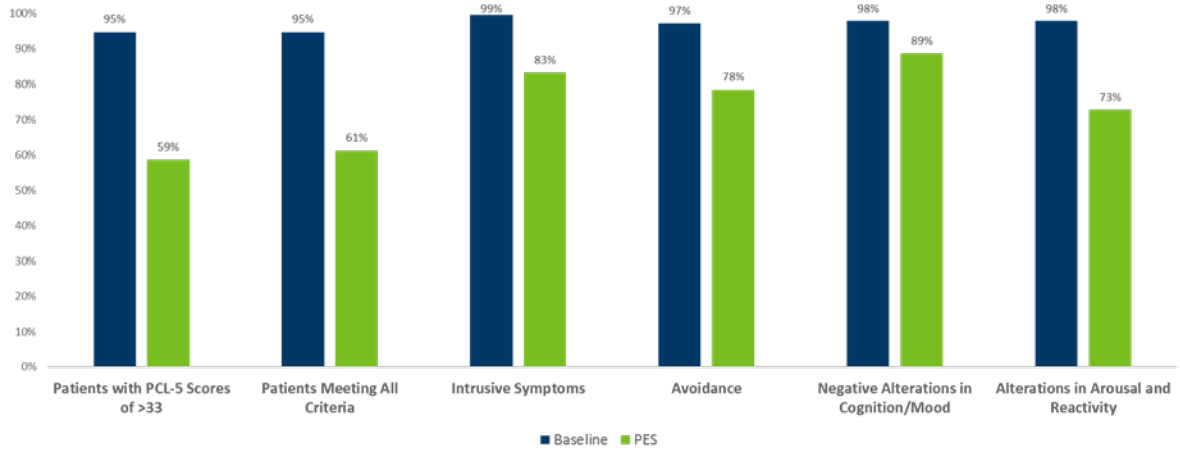
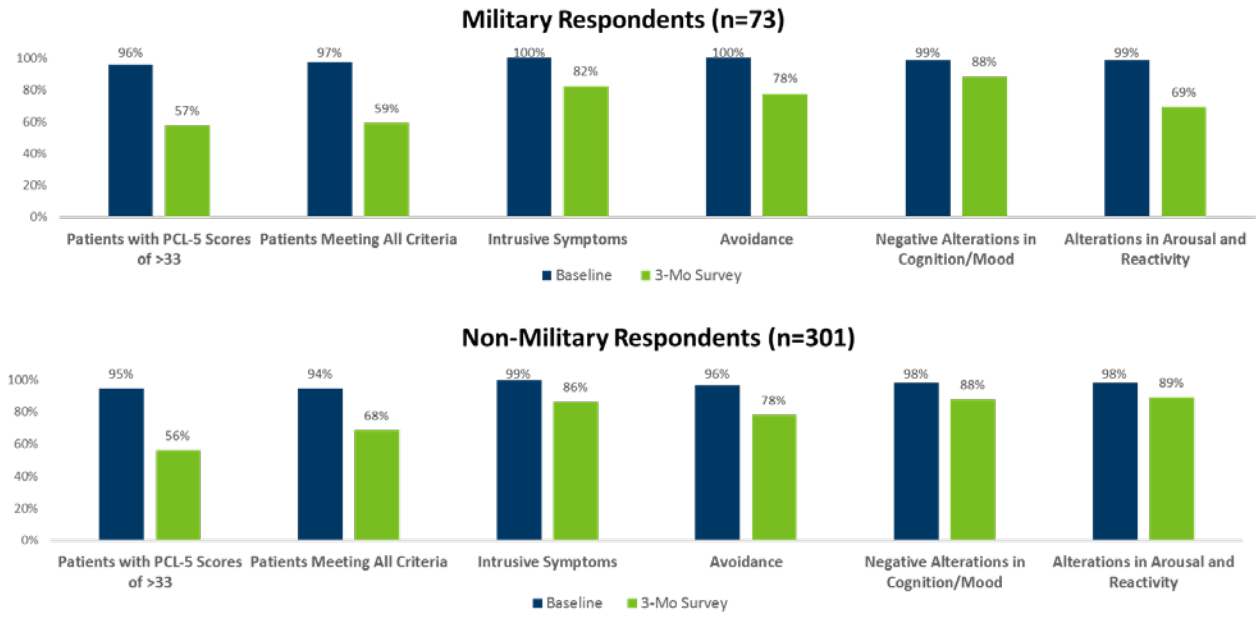


Figure 4.9 compares PCL-5 overall scores and symptom cluster results at enrollment and 3-month survey within the military and non-military PTSD cause groups. Results were generally similar between military and non-military groups, but notable differences were observed: reduction in percentage of patients meeting all four PTSD criteria was larger for the military group (97% to 59%) than the non-military group (94% to 68%). Proportions of patients meeting individual criteria were similar in military and non-military groups with the exception of Criterion E (alterations in arousal and reactivity) where percentage meeting Criterion E was similar at enrollment but different at 3-month survey (69% in military group, 89% in non-military group).

Figure 4.9. Proportion of survey respondents at enrollment and 3-month PCL meeting PTSD diagnostic criteria, stratified by PTSD cause (military and non-military).



Medical Cannabis Products Purchased Immediately Prior to 3-Month Survey

Patients responding to both the enrollment and 3-month PCL-5 survey (n = 381) were split into those who exhibited improvement of ≥10 points (called responders in this section; n = 272) and those who did not (called non-responders in this section; n = 109). An analysis was conducted to describe the medical cannabis products that were purchased immediately preceding the date they submitted their 3-month survey. Medical cannabis products were categorized according to the following: a) ratio of THC to CBD contained in the product and b) route of administration. See Box 4.1 below for ROA and THC:CBD ratio definitions.

Box. 4.1. Definitions of Medical Cannabis Product Ratios and Route of Administration.

Medical Cannabis Products Categorized by THC:CBD Ratio:

- **Very High THC to CBD** = 100:1 or higher
- **High THC to CBD** = >4:1 up to 99:1
- **Balanced** = 1:1 up to 4:1
- **High CBD to THC** = ≥1:1 up to 99:1
- **Very High CBD to THC** = 100:1 or higher

Product Routes of Administration (ROA):

- **Enteral:** entry through the gastrointestinal tract via swallowing (e.g., capsules, oral solutions)
- **Inhalation:** oils vaporized into lungs
- **Oromucosal:** sublingual sprays and tinctures absorbed through cheek/oral mucosa.
- Topical: **applied to body surface (e.g., balms)**

Tables 4.9 and 4.10 tally product types purchased immediately preceding the date the 3-month PCL-5 survey was submitted, along with providing the average daily THC (mg) and CBD (mg) for each grouping of products. Table 4.9 presents product types for patients who achieved ≥10 point reduction in PCL-5 score. Table 4.10 presents patients who did not achieve ≥10 point reduction. Column headers indicate the ROA-THC:CBD ratio combinations that products can be categorized into. The "X"s in a particular row indicates product(s) that were purchased in the transaction that preceded the 3-month PCL-5 submission. The second-most column from the right indicates the percentage and number of patients who bought the products marked with an "X." The right-most column indicates the average daily THC (mg) and CBD (mg) across the patients who purchased that product or combination of products.

The data generally indicates little variability between product types that were purchased between patients who did and those who did not achieve ≥10 point PCL-5 score reduction, including the average daily THC and CBD dosages. Therefore, at the descriptive-level, those who achieved clinically meaningful improvement on the 3-month PCL-5 (based on 10 point reduction) did not necessarily purchase anything drastically different from those who did not exhibit clinically meaningful improvements on the same survey.

Among the most common product types (or combinations) were:

- Very high THC:CBD inhalation product only (#1 for both groups)
- Very high THC:CBD inhalation product and balanced inhalation product (#2 for both groups)
- Balanced inhalation product only (#3 for responders and #4 for non-responders)
- High THC:CBD inhalation product only (#4 for responders and #6 for non-responders)

- Very high THC:CBD inhalation product and very high THC:CBD inhalation product (#5 for responders and #5 for non-responders)

Table 4.9. Products Purchased Just Prior to 3-Month PCL-5 Submission: Patients Who Achieved ≥10 Point Reduction in PCL-5 Score.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												25.0 (68)	124.9 mg / 1.2 mg
				X		X										6.6 (18)	168.9 mg / 35.0 mg
						X										5.5 (15)	74.1 mg / 43.6 mg
					X											4.8 (13)	196.8 mg / 9.9 mg
X				X												4.4 (12)	130.9 mg / 1.2 mg
				X			X									3.7 (10)	85.3 mg / 82.3 mg
		X		X		X										2.6 (7)	296.3 mg / 99.3 mg
							X									2.6 (7)	6.1 mg / 85.5 mg
X		X														2.2 (6)	60.6 mg / 26.7 mg
X				X		X										1.8 (5)	111.4 mg / 37.1 mg
X																1.8 (5)	31.9 mg / 0.2 mg
	X			X												1.8 (5)	120.6 mg / 7.6 mg
		X														1.8 (5)	20.9 mg / 17.3 mg
	X															1.5 (4)	51.7 mg / 6.4 mg
		X	X													1.5 (4)	18.9 mg / 122.6 mg
		X		X												1.5 (4)	93.9 mg / 29.4 mg
		X				X										1.5 (4)	88.4 mg / 59.5 mg
			X													1.5 (4)	6.1 mg / 120.9 mg
				X	X											1.5 (4)	247.9 mg / 4.6 mg
				X		X	X									1.5 (4)	121.4 mg / 129.6 mg
				X				X								1.5 (4)	140.6 mg / 1.1 mg
X				X			X									1.1 (3)	81.9 mg / 91.1 mg
			X			X										1.1 (3)	68.1 mg / 98.0 mg
										X						1.1 (3)	45.0 mg / 25.8 mg
X		X		X												0.7 (2)	198.6 mg / 50.4 mg
X			X													0.7 (2)	42.5 mg / 87.7 mg
X						X										0.7 (2)	61.2 mg / 24.5 mg
		X						X								0.7 (2)	68.2 mg / 30.7 mg
		X								X						0.7 (2)	49.1 mg / 30.3 mg
			X				X									0.7 (2)	13.5 mg / 205.5 mg
				X			X			X						0.7 (2)	103.3 mg / 110.3 mg
						X	X									0.7 (2)	71.1 mg / 110.6 mg
								X		X						0.7 (2)	95.0 mg / 40.2 mg

Table 4.9 continued. Products Purchased Just Prior to 3-Month PCL-5 Submission: Patients Who Achieved ≥10 Point Reduction in PCL-5 Score.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
X	X			X		X										0.4 (1)	129.7 mg / 41.8 mg
X	X				X											0.4 (1)	118.0 mg / 5.7 mg
X	X															0.4 (1)	58.8 mg / 9.1 mg
X		X	X	X	X											0.4 (1)	128.6 mg / 64.2 mg
X		X	X													0.4 (1)	52.0 mg / 70.2 mg
X		X				X								X		0.4 (1)	99.9 mg / 89.9 mg
X			X	X												0.4 (1)	235.0 mg / 802.0 mg
X			X					X								0.4 (1)	114.0 mg / 80.3 mg
X				X	X											0.4 (1)	98.2 mg / 1.7 mg
X					X											0.4 (1)	155.0 mg / 3.4 mg
X						X									X	0.4 (1)	99.6 mg / 86.4 mg
X							X			X						0.4 (1)	61.4 mg / 109.9 mg
X							X							X		0.4 (1)	43.2 mg / 106.8 mg
X							X									0.4 (1)	24.4 mg / 88.1 mg
X								X		X						0.4 (1)	96.3 mg / 36.5 mg
X										X						0.4 (1)	56.3 mg / 36.5 mg
X														X		0.4 (1)	41.4 mg / 21.5 mg
	X	X														0.4 (1)	37.5 mg / 8.1 mg
	X		X	X		X										0.4 (1)	158.3 mg / 87.5 mg
	X			X	X			X								0.4 (1)	827.1 mg / 29.6 mg
	X			X		X										0.4 (1)	181.3 mg / 23.0 mg
	X						X									0.4 (1)	33.7 mg / 80.4 mg
	X												X			0.4 (1)	46.3 mg / 10.1 mg
		X			X	X										0.4 (1)	401.7 mg / 55.6 mg
		X								X				X		0.4 (1)	66.8 mg / 66.8 mg
			X					X								0.4 (1)	29.0 mg / 80.1 mg

Table 4.9 continued. Products Purchased Just Prior to 3-Month PCL-5 Submission: Patients Who Achieved ≥10 Point Reduction in PCL-5 Score.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X	X	X										0.4 (1)	158.3 mg / 43.9 mg
				X	X								X			0.4 (1)	240.0 mg / 13.0 mg
				X										X		0.4 (1)	72.7 mg / 14.9 mg
					X	X										0.4 (1)	75.0 mg / 13.9 mg
					X								X			0.4 (1)	121.3 mg / 10.5 mg
						X				X						0.4 (1)	137.5 mg / 81.3 mg
						X					X			X	X	0.4 (1)	57.3 mg / 137.6 mg
							X	X		X						0.4 (1)	52.0 mg / 109.7 mg
							X							X		0.4 (1)	25.1 mg / 94.8 mg
								X								0.4 (1)	50.0 mg / 0.2 mg
														X		0.4 (1)	30.0 mg / 30.0 mg

Table 4.10. Products Purchased Just Prior to 3-Month PCL-5 Submission: Patients Who Did Not Achieve ≥10 Point Reduction in PCL-5 Score.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												36.7 (40)	141.0 mg / 1.2 mg
				X		X										11.9 (13)	182.5 mg / 48.3 mg
		X														5.5 (6)	25.2 mg / 13.9 mg
						X										4.6 (5)	95.4 mg / 45.4 mg
X				X												3.7 (4)	158.5 mg / 0.9 mg
					X											3.7 (4)	91.1 mg / 4.5 mg
X																2.8 (3)	15.0 mg / 0.1 mg
				X			X									2.8 (3)	67.0 mg / 74.0 mg
X				X		X										1.8 (2)	115.7 mg / 37.0 mg
	X			X												1.8 (2)	298.3 mg / 15.7 mg
X		X		X		X										0.9 (1)	265.7 mg / 96.0 mg
X			X													0.9 (1)	12.0 mg / 80.0 mg
X				X		X	X									0.9 (1)	123.3 mg / 110.5 mg
X				X			X									0.9 (1)	128.7 mg / 74.4 mg
X					X											0.9 (1)	184.5 mg / 8.5 mg
X						X										0.9 (1)	28.2 mg / 18.2 mg
X										X						0.9 (1)	51.3 mg / 36.5 mg
	X	X		X	X	X										0.9 (1)	507.1 mg / 115.4 mg
	X	X														0.9 (1)	85.3 mg / 37.8 mg
	X			X	X											0.9 (1)	156.3 mg / 8.1 mg
		X	X													0.9 (1)	13.3 mg / 163.3 mg
		X		X	X	X					X					0.9 (1)	314.2 mg / 203.3 mg
		X		X		X										0.9 (1)	204.3 mg / 34.4 mg
		X		X												0.9 (1)	107.3 mg / 6.4 mg
		X				X							X	X		0.9 (1)	169.8 mg / 91.1 mg
		X				X										0.9 (1)	90.7 mg / 22.7 mg
				X	X	X										0.9 (1)	430.0 mg / 76.2 mg
				X		X	X			X						0.9 (1)	50.4 mg / 68.8 mg

Table 4.10 continued. Products Purchased Just Prior to 3-Month PCL-5 Submission: Patients Who Did Not Achieve ≥10 Point Reduction in PCL-5 Score.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X		X	X									0.9 (1)	103.3 mg / 110.3 mg
				X		X					X					0.9 (1)	236.3 mg / 189.7 mg
						X	X									0.9 (1)	40.0 mg / 109.7 mg
						X		X								0.9 (1)	86.3 mg / 36.5 mg
						X									X	0.9 (1)	173.8 mg / 65.4 mg
								X		X						0.9 (1)	86.3 mg / 36.5 mg
								X								0.9 (1)	50.0 mg / 0.2 mg
										X						0.9 (1)	36.3 mg / 36.3 mg
													X			0.9 (1)	40.0 mg / 11.3 mg

Benefits Reported on Patient Experience Survey and Health Care Practitioner Survey: Conclusions

For 751 patients certified for PTSD and enrolled in the medical cannabis program from July-Dec 2017, 381 (51%) had patient survey responses and PCL-5 data and 163 (22%) had HCP survey responses to report on the patient's program experience. Most patient and HCP responders reported that patients experienced a high degree of benefit from medical cannabis: 53% of patient surveys and 50% of HCP surveys reported the highest level of benefit. Patients and HCPs reported reduced anxiety, improved sleep and improved mood/emotional regulation as the most important benefits from medical cannabis. Comparison of PCL-5 scores at baseline compared to at the time of the 3-month survey showed that between 50% and 71% (depending on whether a reduction of 20 points or 10 points is used) of respondents saw a clinically meaningful improvement in PTSD symptoms 3 months after their first purchase. Patients reporting military as a PTSD cause may be more likely to see reduction of symptoms, as measured by the PCL-5, than patients reporting non-military PTSD causes- especially for symptoms related to alterations in arousal and reactivity.

Benefits Reported on the Patient Self-Evaluation

A separate source of information on patient benefits apart from the Patient Experience Survey (discussed in previous section) is from symptom data provided on the Patient Self-Evaluation (PSE). The PSE is required for patients to complete prior to every medical cannabis purchase, including prior to the patient's first purchase of medical cannabis. This allows the opportunity to understand the symptom status of the patient at the outset of program participation (symptom baseline) and how it is changing over time with their medical cannabis use.

All patients, including PTSD patients, receive a standard set of symptom questions (the "standard 8"). This symptom measure and results will be discussed in this section for PTSD patients enrolled in the program from August 1, 2017 through December 31, 2017.

Standard 8 Symptom Data

All patients, regardless of their certified condition(s), receive a set of 8 symptom questions which are answered on a 0-10 numerical rating scale (NRS), with 0 indicating absence of the symptom to 10 indicating that the symptom is as bad as the patient can imagine (see Box 4.2). Therefore, higher scores indicate greater symptom severity. Patients are asked to rate symptom severity over the past 24 hours.

Box 4.2. Listing of the Standard 8 Symptom Measures that all Patients Answer, Including Response Options Available to Patients.

Standard 8 Symptom Measures:

Anxiety	Fatigue
Lack of Appetite	Nausea
Depression	Pain
Disturbed Sleep	Vomiting

Response Options (0-10 Numerical Rating Scale):

0 1 2 3 4 5 6 7 8 9 10

Symptom not present — Symptom as bad as one can imagine

Research Objectives

To understand the degree of benefits each patient obtained during their participation in the program, the following three questions were explored for each Standard 8 symptom measure:

Question 1

Of those patients who experienced moderate to severe symptoms at baseline (score of 4 or higher at baseline), what percentage of them experienced at least a 30% improvement in symptoms within 4-months of their first medical cannabis purchase? The threshold of ≥30% reduction on a 0-10 point scale was chosen for the Standard 8 because this threshold has been documented in clinical trials to represent clinically meaningful change – especially for pain reduction and spasticity reduction. Examples of ≥30% change include moving from a score of 10 to a score of 7, from a 9 to 6, from 8 to 5, from 7 to 4, etc.

Question 2

If a patient achieved at least a 30% improvement on symptoms within 4-months of their first medical cannabis purchase (determined in Question 1), what percentage of them will, on average, still maintain that level of improvement in the four months following that initial 30% symptom improvement? [Four-month follow-up period]

Question 3

What medical cannabis products were purchased just *prior* to the patient's first report of ≥30% improvement on the PSE? What was the average daily intake of delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) for these product types?

Question 1 – Methodology

All patients who scored 4 or higher at baseline were identified as those experiencing moderate to severe symptoms, and all symptom responses that were submitted within 4 months of their first medical cannabis purchase were retained for analysis. In this dataset, each patient's standard 8 responses that were submitted within this initial 4-month period were compared to their baseline responses. If a patient achieved at least a 30% improvement on a given symptom anytime during this initial 4-month period, the patient was counted as achieving clinically meaningful improvement on that symptom within 4 months of their first medical cannabis purchase.

Calculating the percentage of patients who achieved ≥30% symptom improvement within 4 months of their first medical cannabis purchase was done in the following way: the number of patients achieving ≥30% symptom improvement within 4 months was divided by the number of patients who made a first purchase (all patients with a baseline PSE submission). This allows for a conservative estimate of symptom benefit since a patient may have discontinued purchasing medical cannabis because of lack of effectiveness.

Of the PTSD patients in this cohort (n = 751), 96.5% of them (n = 725) were included in the symptom analysis reported here. The 26 patients that were excluded from analysis had not made any purchases (and therefore, had not submitted any PSE data).

Question 2 – Methodology

For patients who achieved ≥30% improvement in symptoms within 4-months of their first purchase, a follow-up 4-month period was identified to ascertain whether those patients, on average, maintained those improvements. To do this, the first instance of ≥30% symptom improvement was identified within the first 4-months of their first purchase – from that date, 4 months were added on from that date to determine the 4-month follow-up period.

Question 3 – Methodology

Products that were purchased just *prior* to each patient's initial ≥30% symptom improvement were identified and categorized by their THC:CBD ratio and route of administration (ROA). See Box 4.3 for definitions of these categories.

Box. 4.3. Categories to Describe Medical Cannabis Products Purchased by Patients.

Medical Cannabis Products Categorized by THC:CBD Ratio:

- **Very High THC to CBD** = 100:1 or higher
- **High THC to CBD** = >4:1 up to 99:1
- **Balanced** = 1:1 up to 4:1
- **High CBD to THC** = ≥1:1 up to 99:1
- **Very High CBD to THC** = 100:1 or higher

Product Routes of Administration (ROA):

- **Enteral:** entry through the gastrointestinal tract via swallowing (e.g., capsules, oral solutions)
- **Inhalation:** oils vaporized into lungs
- **Oromucosal:** sublingual sprays and tinctures absorbed through cheek/oral mucosa.
- **Topical:** applied to body surface (e.g., balms)

Results: Standard 8 Measures

Table 4.11 below lists the Standard 8 symptom measures along with results on symptom improvement and persistence in patients who experienced at least moderate to severe symptoms at baseline (n = 725). This table addresses Questions 1 and 2 of the research objective for this section of the report. The third column from the left shows the percentage of patients experiencing moderate to severe symptoms for any given Standard 8 measure—these are the patients that were followed through the course of the analysis. Results suggest that, apart from vomiting and nausea, the majority of patients experience high symptom burden – ranging from 60% experiencing moderate to severe lack in appetite at baseline to 96% experiencing moderate to severe anxiety at baseline.

The fourth column in Table 4.11 displays the percentage of patients (among those who experienced moderate to severe symptoms at baseline) who achieved at least a 30% improvement in symptoms within 4-months of their first purchase compared to their baseline measure. For five out of eight symptoms, the percentage of patients achieving at least a 30% improvement in symptoms within 4-months were in the 60% range (fatigue, anxiety, depression, disturbed sleep, nausea), with over 70% of patients achieving ≥30% improvement in 4-months for lack of appetite and vomiting. Half the patients (50%) achieved ≥30% improvement in pain within 4-months of first purchase. Of patients who experienced ≥30% symptom improvement in 4-months, over half will, on average, show persistence of that improvement in the follow-up 4-month period for all 8 symptoms (column 6).

Table 4.11. Standard 8 Symptom Benefits in PTSD Patients.

			INITIAL 4-MONTH PERIOD	FOLLOW-UP PERIOD		
	Standard 8 Symptom Measure	**% of Patients Reporting at Moderate to Severe Levels at Baseline (n)**	**% of Patients Achieving ≥30% Symptom Improvement within 4 months of First Purchase out of all Moderate to Severe Baseline Scorers (n)**	**# of Patients with Data in 4-mo Period Following initial ≥30% Symptom Improvement**	**% of Patients Who Achieved ≥30% Symptom Improvement that Maintained it for at least 4 months (n)**	**% of Patients that Both Achieved ≥30% Symptom Improvement and Retained that Degree of Improvement for at least 4 months.**
PTSD Patients (n = 725)	Anxiety	96.1 (697)	60.1 (419)	380	59.2 (248)	35.6
	Appetite Lack	60.4 (438)	72.6 (318)	285	65.4 (208)	47.5
	Depression	84.0 (609)	65.7 (400)	366	63.5 (254)	41.7
	Disturbed Sleep	90.6 (657)	65.9 (433)	390	64.7 (280)	42.6
	Fatigue	83.7 (607)	59.5 (361)	319	54.3 (196)	32.3
	Nausea	36.6 (265)	68.7 (182)	162	67.0 (122)	46.0
	Pain	68.8 (499)	50.1 (250)	227	53.6 (134)	26.9
	Vomiting	16.8 (122)	75.4 (92)	82	73.9 (68)	55.7

Medical Cannabis Use Preceding Initial Symptom Improvement

To describe what medical cannabis products patients used just prior to their initial symptom improvement, all patients who achieved ≥30% symptom improvement were identified (patients in Column 4 of Table 4.11). The purchasing transaction immediately preceding each patient's initial ≥30% improvement was extracted, with all products purchased in that transaction categorized according to the products' intended route of administration (ROA) and THC:CBD content ratio.

Tables 4.12 – 4.19 show the top 7 medical cannabis product type(s) purchased by patients just prior to achieving the initial ≥30% symptom improvement for all standard 8 measures. The top 7 accounted for 55%-59% of all product type purchases by patients. Based on the top 7 across symptom measures, inhaled and enteral product types were most common. The top 7 showed that very high THC:CBD inhaled products appeared in over half the patients across all symptoms in conjunction with some other inhaled or enteral product type.

Table 4.12. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Anxiety Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												11.2 (46)	117.5 mg / 9.2 mg
		X		X		X										11.0 (45)	305.9 mg / 138.1 mg
				X		X										10.0 (41)	227.5 mg / 63.4 mg
				X			X									10.0 (41)	70.0 mg / 20.1 mg
X				X												7.6 (31)	117.1 mg / 9.7 mg
X				X			X									3.7 (15)	81.7 mg / 20.6 mg
		X		X												3.7 (15)	130.2 mg / 26.4 mg

Table 4.13. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Lack of Appetite Measure.

Enteral					Inhalation					Oromucosal					Topical						
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
					X															12.5 (39)	107.6 mg / 8.5 mg
X					X															9.9 (31)	118.6 mg / 9.9 mg
		X			X		X													9.9 (31)	305.4 mg / 136.6 mg
					X		X													9.9 (31)	242.3 mg / 70.5 mg
					X			X												8.7 (27)	72.8 mg / 19.7 mg
X					X		X													4.8 (15)	173.3 mg / 41.0 mg
		X			X															3.2 (10)	135.1 mg / 32.2 mg

Table 4.14. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Depression Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												12.0 (47)	111.0 mg / 9.2 mg
		X		X		X										11.2 (44)	305.2 mg / 139.3 mg
				X		X										9.9 (39)	229.2 mg / 61.8 mg
				X			X									8.9 (35)	70.9 mg / 20.2 mg
X				X												7.1 (28)	113.0 mg / 9.5 mg
X				X		X										3.6 (14)	152.9 mg / 34.2 mg
		X		X												3.6 (14)	143.1 mg / 27.5 mg

Table 4.15. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Disturbed Sleep Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												12.0 (51)	113.5 mg / 8.6 mg
		X		X		X										10.4 (44)	318.5 mg / 142.5 mg
X				X												8.7 (37)	117.4 mg / 10.4 mg
				X		X										8.7 (37)	214.5 mg / 60.7 mg
				X			X									8.3 (35)	69.5 mg / 19.0 mg
		X		X												4.0 (17)	129.1 mg / 27.3 mg
X				X			X									3.1 (13)	81.5 mg / 20.9 mg

Table 4.16. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Fatigue Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												12.1 (43)	103.2 mg / 9.0 mg
		X		X		X										11.5 (41)	299.8 mg / 137.7 mg
				X			X									10.1 (36)	69.8 mg / 19.8 mg
X				X												8.4 (30)	116.2 mg / 9.3 mg
				X		X										7.3 (26)	210.5 mg / 57.0 mg
X				X			X									3.9 (14)	82.3 mg / 20.6 mg
		X		X												3.4 (12)	113.9 mg / 14.3 mg

Table 4.17. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Nausea Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
				X												14.0 (25)	121.9 mg / 9.7 mg
		X		X		X										10.6 (19)	299.7 mg / 140.6 mg
				X		X										8.4 (15)	245.0 mg / 58.1 mg
X				X												7.8 (14)	96.5 mg / 8.0 mg
				X			X									6.1 (11)	74.5 mg / 19.3 mg
X				X		X										5.0 (9)	179.1 mg / 46.0 mg
X				X			X									2.8 (5)	74.0 mg / 18.6 mg

Table 4.18. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Pain Measure.

Enteral					Inhalation					Oromucosal					Topical						
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
		X			X		X													11.0 (27)	300.4 mg / 133.3 mg
					X		X													11.0 (27)	223.5 mg / 63.2 mg
					X															10.6 (26)	122.1 mg / 10.2 mg
X					X															8.6 (21)	114.5 mg / 10.4 mg
					X			X												8.6 (21)	69.3 mg / 20.0 mg
X					X		X													4.1 (10)	139.2 mg / 39.0 mg
X					X			X												4.1 (10)	81.5 mg / 19.2 mg

Table 4.19. Top 7 Medical Cannabis Product Type(s) Purchased by PTSD Patients Just Prior to Achieving Initial 30% Reduction on Standard 8 Vomiting Measure.

Enteral				Inhalation				Oromucosal				Topical					
Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	Very High THC to CBD	High THC to CBD	Balanced	High CBD to THC	% PTs (n)	Avg Daily THC Use (mg) / Avg Daily CBD Use (mg)
		X		X		X										12.2 (11)	325.6 mg / 134.2 mg
X				X												11.1 (10)	98.9 mg / 7.7 mg
				X												8.9 (8)	186.5 mg / 13.8 mg
				X			X									7.8 (7)	81.1 mg / 20.5 mg
X				X		X										6.7 (6)	189.7 mg / 47.0 mg
				X		X										5.6 (5)	201.9 mg / 53.5 mg
		X		X												4.4 (4)	181.6 mg / 44.4 mg

Benefits Reported on the Patient Self-Evaluation: Conclusions

Results on the Standard 8 measures suggest high symptom burden in enrolled PTSD patients. Roughly 32-48% of patients initially experiencing moderate to severe symptoms both achieved and maintained at least a 30% reduction in symptoms. The proportion was a bit lower for pain (27%) and a bit higher for vomiting (56%).

5. Adverse Side Effects

Summary

This chapter provides insight into the frequency and severity of adverse (negative) side effects through three sources of information: the Patient Self-Evaluation (PSE) completed by the patient prior to each medical cannabis purchase, patient and health care practitioner (HCP) surveys, and adverse event reports to the two medical cannabis manufacturers.

The three information resources tell a similar story- one quite similar to what was reported in two previous comprehensive reports on cohorts of enrolled patients: a substantial minority of patients experienced adverse physical or mental effects of some kind, and in the majority of cases they were of mild to moderate intensity. The proportion of patients with at least one physical or mental adverse effect varied from 11% in the PSE data to 21% in HCP surveys to 26% in patient surveys. Most patients with at least one adverse effect experienced only one.

The vast majority of all reported adverse effects were mild or moderate in severity as reported on the PSE (82%) or a score of 1 through 5 on the 7-point severity scale used in patient (95%) and HCP (94%) surveys. The most common adverse effects were dry mouth, increased appetite, anxiety, drowsiness, and fatigue. An assessment of the 29 patients reporting severe adverse events, meaning "interrupts usual daily activities," found no apparent pattern in patient age or type of medical cannabis product used – taking into consideration the very large share of patients who used vaporized high or very high THC:CBD products as part of their regimen. Anxiety was reported somewhat more frequently (n=12; 1.7%) than in prior reports of enrolled patients, and 8 of the 12 patients rated the anxiety as severe. Patients were asked to report symptoms they thought were likely caused by medical cannabis products. It is possible some reported anxiety that was part of their PTSD symptoms. However, a few survey comments specifically attributed increased anxiety to use of medical cannabis products, with some suggestion this was THC dose dependent. There was also one comment about increased anxiety with use of a high CBD:THC product.

No serious adverse events (life threatening or requiring hospitalization) were reported for this group of patients during the observation period.

Some limitations of the data should be mentioned. For example, when the patient completes a Patient Self-Evaluation and has it reviewed in consultation with pharmacist staff, the completeness and accuracy of reported side effects ultimately depend on the attention and good communication of the patient. Perhaps a more significant risk for under-reporting through PSE data is the situation when a patient has an intolerable side effect and decides to make no more purchases of medical cannabis. If the patient doesn't go to a cannabis patient center for another purchase, the patient doesn't fill out another PSE, so the side effect is not documented through this mechanism.

Though the limitations mentioned in the paragraph above might undercount the frequency of physical and mental adverse effects to some degree, their impact does not seem likely to significantly change the main conclusion of the analyses reported in this section: the safety profile of the medical cannabis products available through the Minnesota program continues to appear quite favorable. However, there is a suggestion that medical cannabis products might exacerbate anxiety in a small percentage of PTSD patients.

Adverse Side Effects on the Patient Self-Evaluation

Patients have the opportunity to report adverse side effects they attribute to medical cannabis use on the Patient Self-Evaluation (PSE), which is administered prior to every medical cannabis purchase. Information collected at this time include what the effect is (patients can choose from a dropdown menu of options or manually write in), the severity of the side effect (see Box 5.1. for definitions), and any additional comments they'd like to provide regarding the side effect (additional comments are optional). During a patient's visit to a Cannabis Patient Center (CPC) to purchase medical cannabis, the pharmacist can review the patient's completed Patient Self-Evaluation (PSE) and also discuss side effects that were reported by the patient to factor it into any recommendations on medical cannabis dosing and formulation.

Box 5.1. Definitions on Severity for Adverse Side Effect Reporting.

Adverse Side Effect Severity: Definitions
Mild: Symptoms do not interfere with daily activities. **Moderate:** Symptoms may interfere with daily activities. **Severe:** Symptoms interrupt usual daily activities.

Note: These definitions are provided to patients when completing the adverse side effect section of the Patient Self-Evaluation.

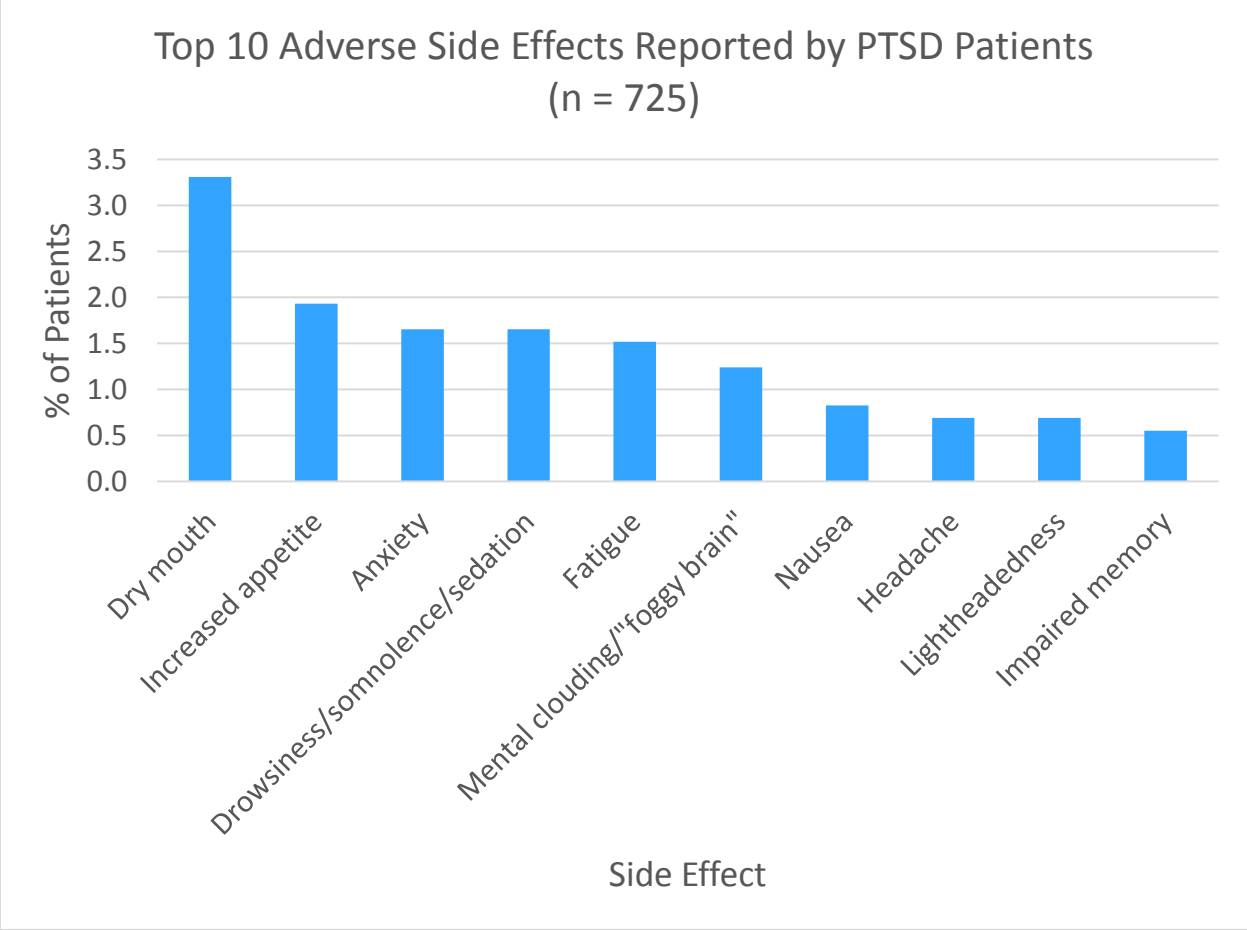
Adverse side effects were examined among the 751 PTSD-certified who enrolled in the medical cannabis program from August 1, 2017 through December 31, 2017. For this report, all side effect data submitted within 4 months of each patient's first medical cannabis purchase were analyzed. In the cases where patients had written in their side effects (as opposed to choosing a dropdown menu option), each entry was evaluated carefully and adjudicated as best as possible for analytical purposes.

Of the 751 patients in this cohort report, 725 patients (97% of the PTSD cohort) had submitted any PSE data within 4 months of their first medical cannabis purchase. Of this patient subset, 76 patients (10.5%) reported adverse side effects. These responses from the 76 patients were further processed so that each unique side effect was captured once in the dataset for each patient and at the highest severity level reported. In other words, if a patient reported the same side effect multiple times, only one of those responses was kept in the analysis at the highest severity level reported. This resulted in a total of 158 side effect responses submitted by these 76 patients.

Of patients reporting side effects (n = 76), most (61.8%) reported one unique side effect, with 84.2% of all patients reporting three or fewer different side effects within four months of their first medical cannabis purchase.

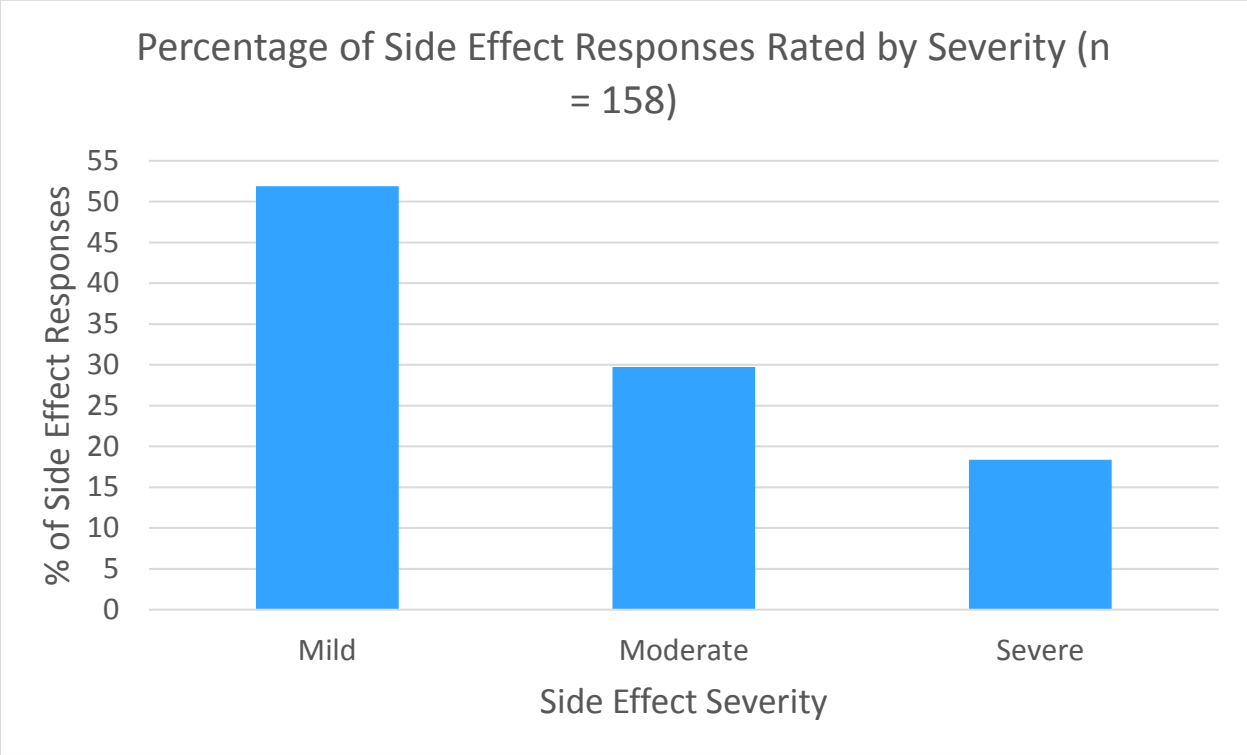
The most commonly reported side effects amongst patients were Dry Mouth, Increased Appetite, Anxiety, and Drowsiness/Somnolence/Sedation. Figure 5.1 shows a rank ordering of the top 10 most frequently reported side effects out of the 725 patients who submitted PSE data.

Figure 5.1. Top 10 Most Commonly Reported Adverse Side Effects Across Patients (n = 725).



All 158 side effect responses submitted by the 76 patients were stratified by the severity in which they were reported. Mild side effects represented 51.9% of all responses (n = 82), moderate side effects representing 29.7% of responses (n = 47), and severe side effects representing 18.4% of all responses (n = 29). See Figure 5.2.

Figure 5.2. Distribution of Side Effect Responses by Reported Severity (n = 158).



Severe Adverse Side Effects

Of the 158 side effect responses submitted, 29 of them were rated as severe (18.4% of all responses). Table 5.1 shows all side effects reported by the 725 patients who submitted PSE data, along with a column to indicate the percentage and count of patients who reported a given side effect as severe. Of the top 10 side effects reported, anxiety was reported most frequently as a severe side effect; 67% of the patients who reported anxiety as an adverse side effect reported it as severe.

Table 5.1. Patient Counts by Reported Side Effect and the Percentage of those Indicating Side Effect was Severe.

Side Effect	# of PTs Reporting	% of PTs Reporting as Severe (n)
Dry mouth	24	4.2 (1)
Increased appetite	14	7.1 (1)
Anxiety	12	66.7 (8)
Drowsiness/somnolence/sedation	12	25.0 (3)
Fatigue	11	18.2 (2)
Mental clouding/"foggy brain"	9	0.0 (0)
Nausea	6	16.7 (1)
Headache	5	0.0 (0)
Lightheadedness	5	0.0 (0)
Impaired memory	4	0.0 (0)
Abdominal/epigastric pain	3	0.0 (0)
Coughing/lung irritation	3	0.0 (0)
Dizziness	3	0.0 (0)
Euphoria (intense feeling of well-being or pleasure)	3	66.7 (2)
Insomnia	3	33.3 (1)
Panic attack	3	33.3 (1)
Paranoia	3	0.0 (0)
Asthenia(muscle weakness)	2	0.0 (0)
Chest pain	2	0.0 (0)
Diarrhea	2	0.0 (0)
Numbness	2	0.0 (0)
Tachycardia (rapid heart rate)	2	0.0 (0)
Tinnitus (ringing in the ears)	2	0.0 (0)

Side Effect	# of PTs Reporting	% of PTs Reporting as Severe (n)
Bizarre dreams or nightmares	1	0.0 (0)
Burning/tingling skin	1	0.0 (0)
Depression	1	100.0 (1)
Difficulty concentrating	1	0.0 (0)
Dry eyes	1	0.0 (0)
Dysphoria (intense feeling of unease or unpleasantness)	1	0.0 (0)
Euphoria	1	100.0 (1)
Exacerbation of COPD symptoms	1	100.0 (1)
Eye muscle twitching	1	0.0 (0)
Heartburn	1	0.0 (0)
Hypoglycemia	1	100.0 (1)
Increased agitation	1	0.0 (0)
Increased light sensitivity	1	0.0 (0)
Increased number of bowel movements	1	0.0 (0)
Increased urinary frequency	1	0.0 (0)
Increased yelling	1	100.0 (1)
Involuntary movements	1	100.0 (1)
Muscle spasms	1	0.0 (0)
Returning of tics	1	100.0 (1)
Slurred speech	1	0.0 (0)
Stomach bloating	1	100.0 (1)
Tremors	1	0.0 (0)
Vomiting	1	100.0 (1)

Adverse Side Effects Reported on the Patient Self-Evaluation: Conclusions

Ninety-seven percent of the PTSD cohort submitted at least one Patient Self-Evaluation (725 out of 751 patients in the cohort) within 4-months of their first medical cannabis purchase. Of these 725 patients, 76 (10.5%) of them reported adverse side effects in that 4-month period, submitting a total of 158 side effect responses. Unlike other cohorts thus far examined (cohorts collapsing across conditions or the cohort report on Intractable Pain patients), anxiety appeared as one of the top adverse side effects reported on the PSE even if reported infrequently (reported in 1.7% of the 725 patients). In addition, of the most frequently-reported side effects, anxiety was reported most frequently as severe. Anxiety can be a prominent symptom in PTSD and it is possible that some of the reports of severe anxiety as a side effect could in actuality be part of the patient's PTSD condition – though instructions do ask patients to report adverse side effects the patients believes might be due to medical cannabis.

Adverse Side Effects Reported on Surveys

Patient-Reported Negative Effects of Medical Cannabis

The Patient Experience survey asks respondents to report the degree, or severity, of any negative effects they believe the patient received from using medical cannabis, on a scale from 1 (no negative effects) to 7 (a great deal of negative effects). The survey then asked the respondent to describe, in their own words, the negative effect(s) they have experienced. Table 5.2 shows the distribution of negative effects by severity score within three broad categories: physical side effects (including dry mouth, fatigue, headache, dizziness, blurred vision); mental side effects (including mental clouding, paranoia, sedation or symptoms related to "high"); and issues related to accessing the medications (distance to distribution center, inconvenient operating hours for distribution centers, etc.). Based on anticipated reports on the high cost of medication, patients were asked to report on the affordability of the medication separately. However, some patients included cost in their estimation of the most significant negative effects related to medical cannabis; these reports are excluded from Table 5.2 but included in *Appendix C: Patient-Reported Negative Effects*.

Of 751 patients certified for PTSD between August 2017-December 2017, 381 (50.7%) responded to a survey sent 3 months after the patient's first purchase. Of 381 completed patient surveys, 379 responses (99%) included a negative effects score and 370 (97%) included a response regarding type of negative effect, including comments stating "no negative effect." Of 379 negative effect scale responses, 245 (65%) reported a score of 1, or "no negative effect." A total of 98 responses (26% of all patient responses) reported physical or mental negative effects. These reports generally mirrored side effects reported in clinical trials of medical cannabis (see "A Review of Medical Cannabis Studies relating to Chemical Compositions and Dosages for Qualifying Medical Conditions (http://www.health.state.mn.us/topics/cannabis/practitioners/compdosagerpt.pdf)" on the Office of Medical Cannabis website). Reports of the most severe negative physical and mental effects were as follows: scores of 7 (great deal of negative effects) were associated with a report of severe depression and suicidality (n=1) and severe allergic reaction (n=1). Scores of 6 were associated with reported grogginess upon waking (n=1), interactions with other medication (n=1), and coughing (n=1). Scores of 5 which reported physical negative effects included tinnitus (n=1), extreme fatigue (n=1), impaired memory and confusion (n=1), and "spaciness" (n=1).

Apart from physical or mental negative effects, some patients reported issues related to program access, including distance to the nearest cannabis patient center (n=10). A full listing of patient-reported negative effect comments is available in *Appendix C: Patient-Reported Negative Effects.*

Table 5.2. Summary of most significant negative effects experienced by the patient, per patient reports.

Most Important Negative Effect Type	1	2	3	4	5	6	7	Total
Mental Effect	1 (<1%)	19 (5%)	6 (2%)	5 (1%)	2 (1%)	1 (<1%)	1 (<1%)	35 (9%)
Physical Side Effect	12 (3%)	31 (8%)	7 (2%)	8 (2%)	2 (1%)	2 (1%)	1 (<1%)	63 (17%)
Access	2 (1%)	5 (1%)	-	-	2 (1%)	-	1 (<1%)	10 (3%)

Note: Results are broken down by negative effect scale scores. Percentages are calculated based on the total number of patient survey responses received (n=381).

HCP-Reported Negative Effects from Medical Cannabis

Like the Patient Experience survey, the HCP survey asks respondents to report the degree, or severity, of any negative effects they believe the patient received from using medical cannabis, on a scale from 1 (no negative effects) to 7 (a great deal of negative effects). The survey then asked the respondent to describe, in their own words, the negative effect(s) they have experienced. Table 5.3 shows the distribution of negative effects by severity score within three broad categories: physical side effects (including dry mouth, fatigue, headache, dizziness, blurred vision); mental side effects (including mental clouding, paranoia, sedation or symptoms related to "high"); and issues related to accessing the medications (long distance to distribution center, inconvenient operating hours for distribution centers, etc.).

For 751 patients certified for PTSD between August 2017-December 2017, 345 healthcare practitioner surveys were completed 6 months after the patient's first purchase. Review of submitted HCP responses revealed that in many cases, healthcare practitioners indicated they had not seen the patient since certification and therefore they had no clinical updates to provide; these surveys were eliminated (n=182), and the remaining 163 (21.2% of cohort) were included in analyses described below. Of 163 total HCP survey responses, 160 responses (98%) included a negative effects score and 67 responses (41%) included a response regarding type of negative effect, including comments stating "no negative effect." Of 160 negative effect scale responses, 116 (73%) reported a score of 1, or "no negative effect." This includes one report of a physical side effect. There were 33 HCP reports (20% of all HCP survey responses) of physical or mental negative effects resulting from medical cannabis treatment. As seen in the patient survey results, these generally mirrored side effects described in clinical trials. Healthcare providers describing negative effects with high scores reported the following: a score of 7 was associated with a report of increased anxiety and panic attack (n=1) and "increased emotional lability" (n=1). A full listing of all negative effect comments from HCPs can be found in *Appendix D: HCP-Reported Negative Effects.*

Table 5.3. Summary of most significant negative effects experienced by the patient, per HCP reports.

Most Important Negative Effect Type	1	2	3	4	5	6	7	Total
Mental Effect	-	7 (4%)	5 (3%)	-	-	-	2 (1%)	14 (9%)
Physical Side Effect	1 (1%)	14 (9%)	4 (2%)	-	-	-	-	19 (12%)

Note: Results are broken down by negative effect scale scores. Percentages are calculated based on the total number of HCP survey responses received (n=163).

Adverse Side Effects Reported on Surveys: Conclusions

Based on data from surveys completed by patients and their certifying healthcare practitioners three months after the patient's first medical cannabis purchase, 25% of patient respondents report physical or mental side effects related to medical cannabis use. A minority of healthcare provider responders (20%) report physical or mental side effects. Both groups describe negative effects related to medical cannabis use including the cost of products and issues related to accessing medicine. Most patients and HCPs reporting physical or mental side effects report low degrees of severity (negative effect scale scores of 1-3).