MINNESOTA
OFFICE OF CANNABIS MANAGEMENT

Obstructive Sleep Apnea Patients in the Minnesota Medical Cannabis Program

Experience of Enrollees During the First Five Years

May 2025

Obstructive Sleep Apnea Patients in the Minnesota Medical Cannabis Program: Experience of Enrollees During the First Five Years

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Executive Summary

Obstructive sleep apnea (OSA) is a disorder characterized by episodes of complete (apnea) or partial (hypopnea) collapse of the upper airway during sleep that ultimately reduces airflow. These episodes cause a progressive asphyxia that increasingly stimulates breathing efforts against the collapsed airway until the individual is awakened (Spicuzza et al., 2015). This can have other physiological consequences such as fragmented sleep, intermittent hypoxia, and fluctuations in heart rhythm, blood pressure, and intrathoracic pressure. Long term, OSA can cause hypertension and cardiovascular morbidities, reduced cognitive function, decreased mood and quality of life, impaired performance at work and driving, and premature death (Peppard et al., 2013).

OSA was added as an approved qualifying condition to the Minnesota Medical Cannabis Program in August 2018. This report examines the experiences of patients qualified for OSA in the Minnesota's medical cannabis program through demographic information, medical cannabis product purchases, benefits experienced from medical cannabis, and adverse side effects.

Participation

A total of 3,102 patients enrolled in the Minnesota Medical Cannabis Program for the first time with obstructive sleep apnea (OSA) between August 1, 2018, and July 31, 2023. Of those enrolled, 2,982 (96.1%) patients made a medical cannabis purchase in the program. This report will only focus on patients who made at least one medical cannabis purchase.

A majority of the cohort self-identified as male (n = 2,256; 76.2%) compared to female (n = 671; 22.7%). The average age of patients at enrollment into the program was 49 years old, ranging from 13 to 97 years old. A majority of patients self-identified as white (84.6%), followed by Black, African, or African American (3.3%), and two or more races (2.6%). More than half of patients live in the Twin Cities metro region (71.3%), followed by the St. Cloud region (6.4%).

Medical cannabis use patterns

Each patient's medical cannabis purchasing transactions during their first enrollment year were analyzed, including 33,920 purchasing transactions consisting of 104,602 medical cannabis products purchased. Products are classified by their route of administration (how a product enters the body) and THC and CBD content. The most common route of administration for purchased products was inhalation (breathing in). Products in this category include raw cannabis flower and vape oil products. They accounted for 64.2% of all products purchased. Enteral products, which pass through the gastrointestinal tract, including gummies, capsules, powders mixed with water and oral solutions, were the second most common products purchased, accounting for 29.2% of purchases. Oromucosal (absorption through oral mucosa) and topical (absorption through skin) products were the least commonly purchased, accounting for 4.8% and 1.9% of purchased products, respectively. High THC products were the most popular products among all routes of administration.

Benefits

Prior to each purchase, patients are asked to fill out a patient self-evaluation (PSE). The PSE asks patients to rate the severity of eight standard symptoms in the past 24 hours on a scale from 0 to 10. The standard eight symptoms include anxiety, lack of appetite, depression, disturbed sleep, fatigue, nausea, pain, and vomiting. In this report, a ≥30% decrease in symptom score from enrollment score was considered to be a clinically significant change.

Disturbed sleep and fatigue were the most common symptoms reported among patients, with 93.0% and 86.8% of patients reporting moderate to severe scores at baseline, respectively. Among patients with moderate to severe disturbed sleep, 60.8% saw a ≥30% reduction in disturbed sleep symptoms within four months. Of those patients with data after initial improvement, 73.6% maintained ≥30% improvement in their disturbed sleep for at least four months after initial improvement. Overall, of the 2,749 patients with moderate to severe disturbed sleep, approximately 39.4% were able to both achieve ≥30% reduction and maintain it for at least four months. For patients with moderate to severe fatigue, 33.5% of patients were able to both achieve ≥30% reduction and maintain it for at least four months.

Among the other standard eight symptoms, more than one-third of patients with moderate to severe depression (39.8%), and anxiety (36.7%) at baseline were able to both achieve ≥30% reduction and maintain it for at least four months. Pain symptoms saw the least improvement with only 23.1% of patients with moderate to severe pain at baseline were able to both achieve ≥30% reduction and maintain it for at least four months.

Adverse side effects

In addition to symptom questions, the PSE also includes questions about adverse side effects. Only 16.5% (n = 488) of obstructive sleep apnea patients reported adverse side effects on their PSE. More than half reported one unique side effect (n = 320; 65.6%), with 92.2% reporting three or fewer unique side effects within one year of their first medical cannabis purchase. The majority (75.5%) of side effects reported were mild, and the most common side effect was dry mouth. Only 3.7% of patient-reported side effects were severe, the most commonly reported severe side effects were fatigue and headache.

1. Introduction

In May 2014, Minnesota became the 22nd state to create a medical cannabis program. Distribution of cannabis products to qualified enrolled patients began July 1, 2015. Minnesota's medical cannabis program is distinct from those in nearly all other states due to the fact that the Minnesota Office of Cannabis Management is required to study and learn from the experience of participants. Minnesota's online registry, which integrates information from patients, certifying healthcare practitioners and manufacturers, continuously captures program data. Data elements from the registry have been selected to create a de-identified research dataset for reporting and research. This report draws on aspects of that research dataset to describe the experience of patients newly enrolled in the program for obstructive sleep apnea between August 1, 2018, and July 31, 2023. This corresponds with the first five years that obstructive sleep apnea was recognized as a qualifying condition in Minnesota's medical cannabis program.

Obstructive sleep apnea (OSA) is a sleep disorder characterized by repetitive episodes of complete (apnea) or partial (hypopnea) collapse of the upper airway (mainly the oropharyngeal tract) during sleep, with a consequent cessation/reduction of the airflow. The obstructive events cause a progressive asphyxia that increasingly stimulates breathing efforts against the collapsed airway, typically until the person is awakened (Spicuzza et al., 2015). These episodes cause acute physiological disruptions including fragmented sleep, intermittent hypoxia, and exaggerated fluctuations in heart rhythm, blood pressure, and intrathoracic pressure. Over time, the acute disruptions evolve into long-term sequelae such as hypertension and cardiovascular morbidities, reduced cognitive function, decreased mood and quality of life, impaired performance at work and while driving, and premature death (Peppard et al., 2013).

Obstructive sleep apnea was approved as a qualifying medical condition for Minnesota's medical cannabis program on August 1, 2018. This report details patient experience in Minnesota's medical cannabis program. Cannabis and Obstructive Sleep Apnea. Cannabis is thought to reduce apneas and stabilize respiration during sleep by suppressing vagal nerve activity (Carley et al., 2002). Studies in rats found injection with dronabinol, a synthetic delta-9-tetrahydrocannabinol (THC), reduced apneas (Calik et al., 2014; Calik & Carley, 2017; Carley et al., 2002). Relatively few studies have investigated the benefits of cannabis for patients with obstructive sleep apnea. One proof-of-concept trial in humans found improved apnea-hypopnea index scores in patients after starting dronabinol treatment. However, this was a small study with only 17 participants (Prasad et al., 2013). In another clinical trial, obstructive sleep apnea patients who were given dronabinol before bedtime reported improved sleep and improved apnea-hypopnea index scores compared to patients receiving placebo treatment (Carley et al., 2017). This was a larger study with 73 participants and a placebo treatment group. However, more research is needed to determine if cannabis is an effective therapeutic agent for obstructive sleep apnea patients.

2. Description of Patients Enrolled

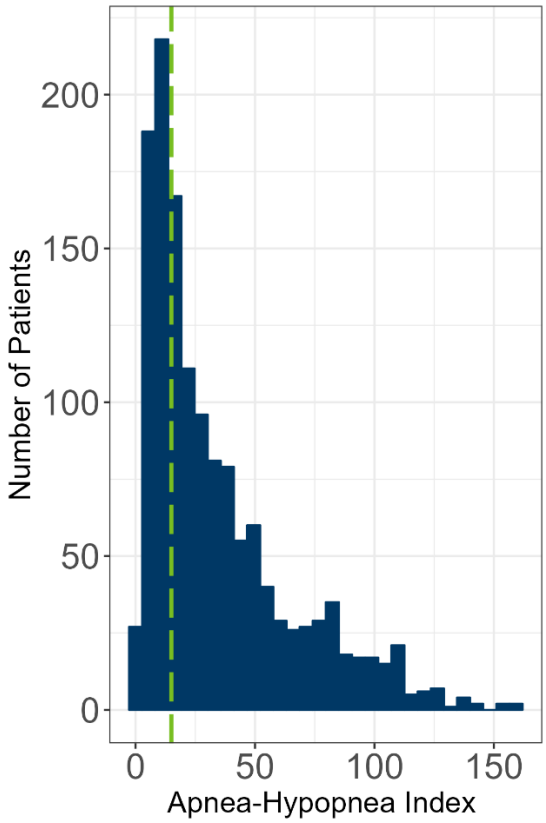
Qualifying condition

A total of 2,982 patients were enrolled with obstructive sleep apnea in Minnesota's medical cannabis program and purchased medical cannabis between August 1, 2018, and July 31, 2023. The cutoff of July 31, 2023, was selected to allow eight months of follow-up to investigate the benefits of medical cannabis use.

Upon certification for obstructive sleep apnea, healthcare providers are encouraged to provide sleep study data for the patient. These data include date and results of their latest sleep study. Among this cohort of obstructive sleep apnea patients, 78.5% (n = 2,341) provided the date of their last sleep study. The median time between sleep study and certification for medical cannabis is three years (interquartile range (IQR): 6 years).

The Apnea-hypopnea Index (AHI) provides an average of the number of apneas and hypopneas that occur per hour of sleep. A patient is considered to have moderate OSA with an AHI of 15-30, and severe OSA with a score higher than 30. AHI score from the latest sleep study was provided for 46.4% (n = 1,385) of patients. Median AHI prior to certification was 23.9 (IQR: 36.9; minimum: 0.1; maximum: 159.4) (Figure 2.1). Based on these AHI measures, a majority of patients who provided AHI score have moderate to severe obstructive sleep apnea (66.2%; n = 917) (Goyal & Johnson, 2017).

Figure 2.1. Distribution of Apnea-Hypopnea Index (AHI) among patients at first certification for medical cannabis. Dashed line represents threshold of AHI score for moderate to severe sleep apnea.



Additional qualifying conditions

Many patients were also qualified for other conditions, most commonly intractable pain (n = 691; 23.3%), chronic pain (n = 490; 16.5%), and post-traumatic stress disorder (n = 284; 9.6%) (Table 1.1). Nearly two-thirds (65.7%, n = 1,946) of patients were only qualified for obstructive sleep apnea.

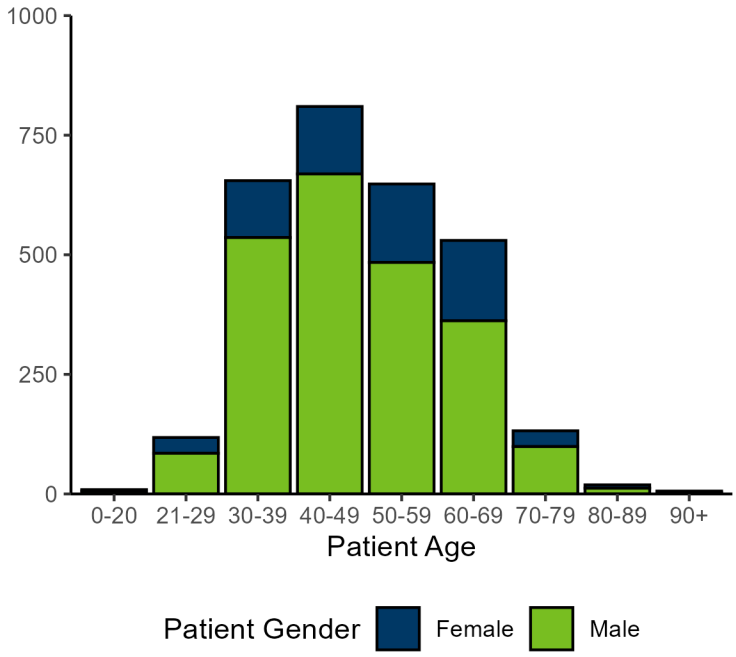
Table 2.1. Count of additional qualifying conditions

Additional qualifying condition	Number of patients (%)
Intractable pain	691 (23.3)
Chronic pain	490 (16.5)
Post-traumatic stress disorder	284 (9.6)
Severe and persistent muscle spasms	265 (8.9%)
Inflammatory bowel disease, incl. Crohn's disease	32 (1.1)
Seizures	23 (0.8)
Cancer with severe or chronic pain	22 (0.7)
Glaucoma	19 (0.6)
Autism spectrum disorder	14 (0.5)
Other qualifying condition	21 (0.6)

Gender and age

More than three-quarters of obstructive sleep apnea patients identified as male (n = 2,256; 76.2%) compared to female (n = 671, 22.7%), while 35 (1.2%) preferred not to answer. The estimated gender ratio of obstructive sleep apnea in the general population is 2:1, male to female (Franklin & Lindberg, 2015). The average age of patients at enrollment was 49 years old (standard deviation: 12.7 years). The youngest patient was 13 years old, while the oldest was 97 years old (Appendix A, table A1). Figure 2.2 depicts the age of patients by gender.

Figure 2.2. Age of patients by gender



Race and ethnicity

Obstructive sleep apnea patients self-identified predominantly as white (n = 2,506; 84.6%); 3.3% as Black, African, or African American; 1.7% as American Indian or Alaskan Native; 0.6% as Asian; 1.7% as another race; 2.6% identified as two or more races; and 3.5% (n = 103) identified as having Hispanic ethnicity (Table 2.4). This population is representative of the overall medical cannabis registry and Minnesota population with regards to white, American Indian or Alaska Native identifying patients and patients that identify with two or more races. However, there are fewer Black, African, or African American patients with OSA (3.3%), compared to the overall registry (5.9%) (*Minnesota Medical Cannabis Dashboard*, 2024) and Minnesota population (7.4%) (*Minnesota Medical Cannabis Dashboard*, 2024) (Table 2.4). The proportion of Asian patients with OSA (0.9%) is representative of the overall registry (0.9%), but not the Minnesota population (5.4%) (*Minnesota Medical Cannabis Dashboard*, 2024).

Table 2.4. Self-reported race for obstructive sleep apnea patients

Race	Number of patients (%)
White	2506 (84.6)
Black, African or African American	98 (3.3)
American Indian or Alaska Native	50 (1.7)
Asian	28 (0.9)
Other race	49 (1.7)
Two or more races	77 (2.6)
No answer or unknown	154 (5.2)

Geographic distribution

When registering for Minnesota's medical cannabis program, patients provide their home address to verify Minnesota residency. The general geographic distribution of patients was examined using patient-reported ZIP codes; the first three digits of ZIP codes compose a prefix that corresponds to an approximate geographic region. 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 A2, along with the count of patients living in the corresponding ZIP codes. The majority of obstructive sleep apnea patients are located in the Twin Cities metro ZIP region, Minneapolis 41.3% and St. Paul 30.0%; 6.4% live in the St. Cloud region, 5.5% in the Rochester region, and 4.5% in the Duluth region (Table A2).

3. Medical Cannabis Use Patterns

Description of purchased products

Purchasing data for medical cannabis is captured by Minnesota's medical cannabis program. For this report, purchasing data were extracted for all obstructive sleep apnea patients enrolled for the first time between August 1, 2018, and July 31, 2023. This report describes all purchases made within their first year in the program. For patients whose first enrollment year had not yet ended at the time of data extraction (April 8, 2024), all purchases prior to that date were retained. The query provided a dataset containing:

- 33,920 sales transactions consisting of:
- 104,602 product purchases, which
- represented 2,962 patients.

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. As of this report, products that include raw cannabis flower (e.g. ground flower, flower, pre-roll products) do not include THC or CBD concentration in milligrams and cannot be classified by THC:CBD ratio in the same way as other products. They are instead classified by relative values of THC and CBD by percent of product weight.

Medical Cannabis Products Categorized by THC:CBD Content 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

Medical Cannabis Flower Products Categorized by Relative Values of THC and CBD:

Values measured as % by product weight

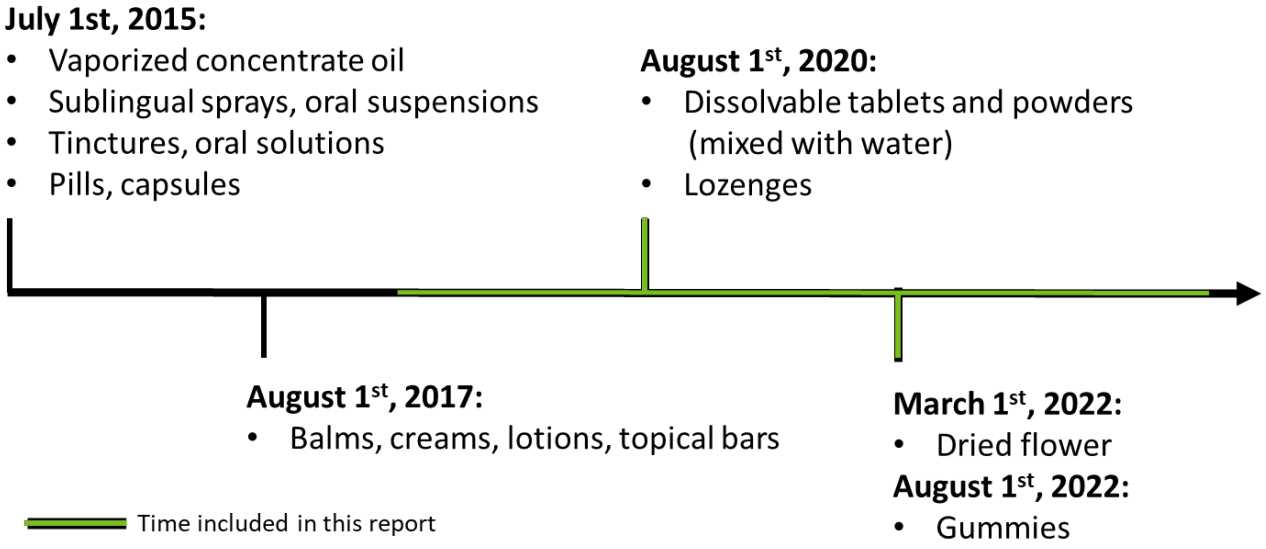
- **High THC:** >15%
- **Medium THC:** 5 to 15%
- **Low THC:** <5%
- **High CBD:** >10%
- **Medium CBD:** 1 to 10%
- **Low CBD:** <1% or trace amount

Product Routes of Administration (ROA):

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

Product delivery methods available through Minnesota's medical cannabis program are decided on by the Office of Cannabis Management through a petition process. Therefore, cannabis product availability has evolved throughout the time covered by this report. During the time covered in this report, dissolvable tablets and powders, lozenges, dried cannabis flower, and gummies were introduced as available products. The timeline of products availability is shown in Figure 3.1.

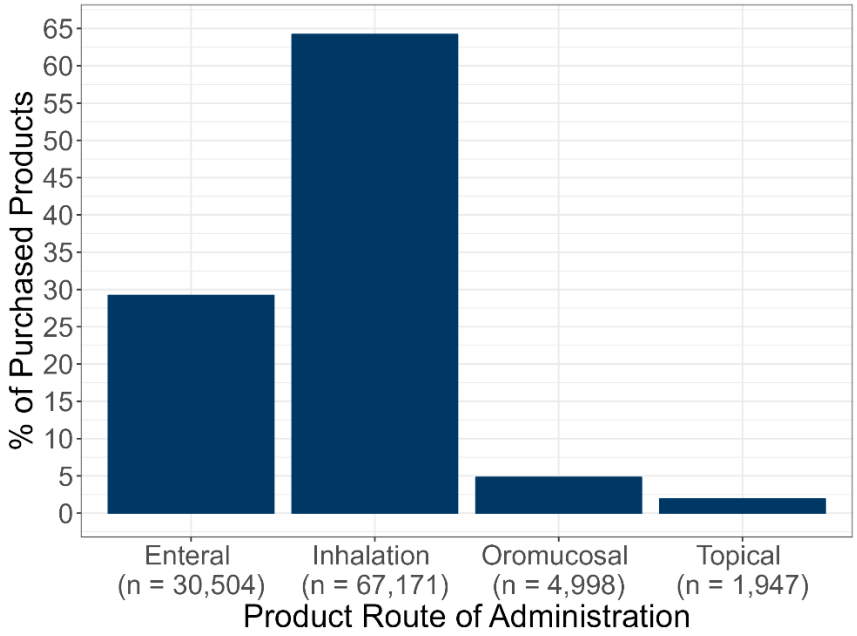
Figure 3.1. Timeline of product availability in the Minnesota Medical Cannabis Program



Route of administration

Products intended for inhalation, including raw flower, ground flower, and pre-rolls, were the most popular with obstructive sleep apnea patients accounting for 64.2% of all products purchased. Enteral products, including gummies, capsules, and oral solutions, made up 29.2% of products purchased. Oromucosal and topical products were less popular, accounting for 4.8% and 1.9% of purchased products, respectively (Figure 3.2).

Figure 3.2. Product transactions categorized by product's intended route of administration

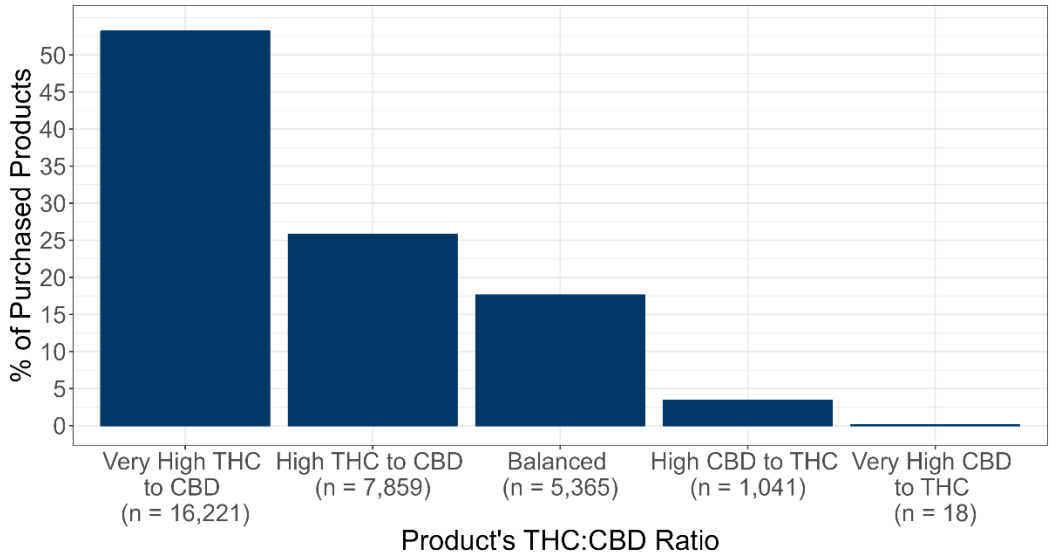


THC:CBD Ratio

Enteral products

Capsules and tablets were the most popular enteral products, accounting for 58.8% of products, followed by gummies or chews (29.5%), and oral solutions (11.7%). A majority of these products have a very high THC to CBD ratio (n = 16,221; 53.2%), followed by high THC to CBD (n = 7,859; 25.8%), and balanced THC to CBD ratio (n = 5,365; 17.6%). High and very high CBD to THC ratio products accounted for less than 5% of enteral products purchased (Figure 3.3).

Figure 3.3. Enteral product transactions categorized by product's THC:CBD ratio.



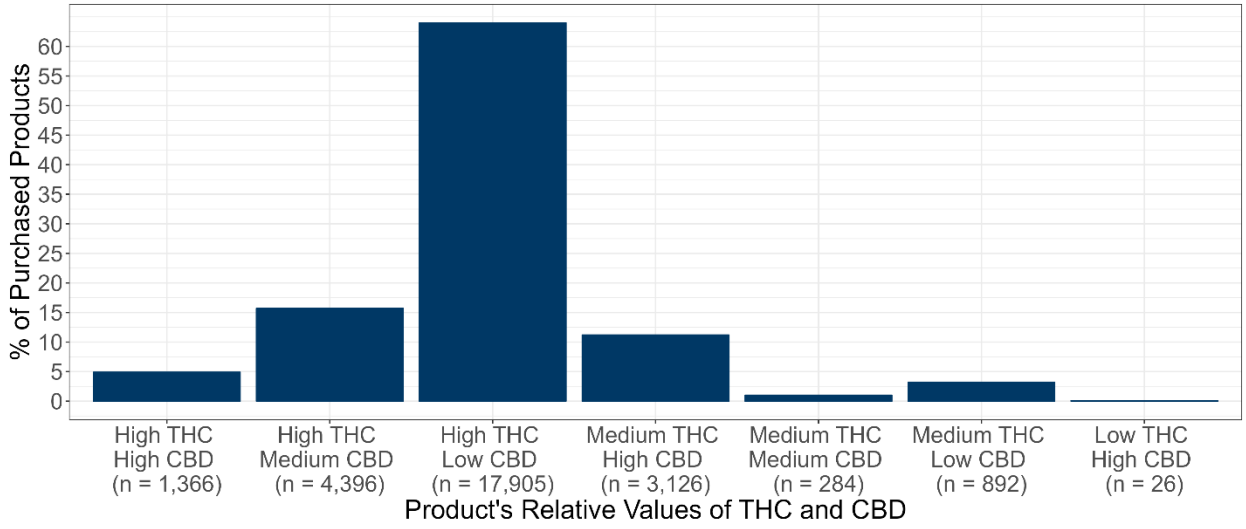
Inhalation Products

Inhalation products sold in Minnesota's medical cannabis program fall into two groups: flower products and vaporization products. Dried flower products were added as an approved delivery method March 1, 2022, (Figure 3.1) and make up 41.8% of all inhalation products purchased by obstructive sleep apnea patients. Flower products include flower (69.4%) and pre-rolls (30.7%).

Manufacturers do not report milligrams of THC and CBD in their flower products; instead, they report an approximate percentage of THC and CBD by product weight. Therefore, these products could not be categorized by THC:CBD ratio and are instead categorized by relative values of THC and CBD (Box 3.1).

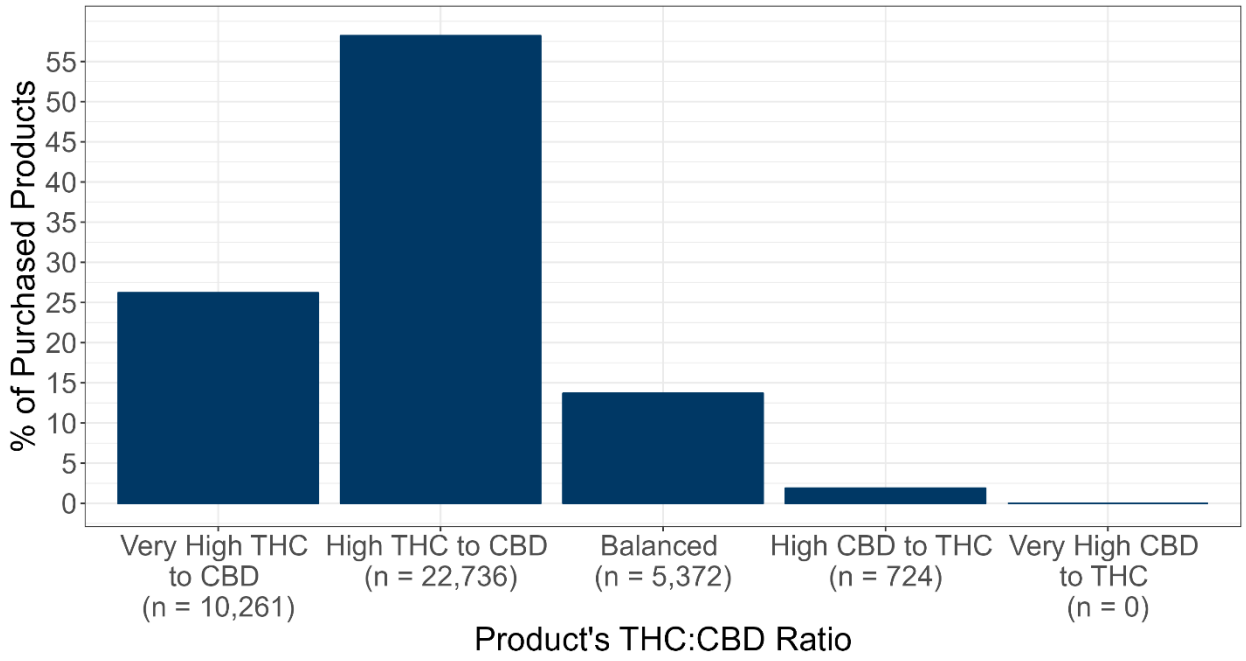
A majority of flower products purchased had high THC/low CBD (63.8%), followed by high THC/medium CBD (15.9%) and medium THC/high CBD (11.1%) products (Figure 3.4).

Figure 3.4. Inhalation flower product transactions organized by relative values of the THC and CBD



Vaporization products include vape cartridges (92.9%), oils (7.0%), and syringes (0.1%). A majority of vaporization products had a high THC:CBD ratio (58.2%), followed by very high THC:CBD ratio (26.2%). Less than 15% of products purchased were balanced (13.7%) or high CBD:THC (1.9%) (Figure 3.5).

Figure 3.5. Inhalation vaporization product transactions organized by product's THC:CBD ratio.

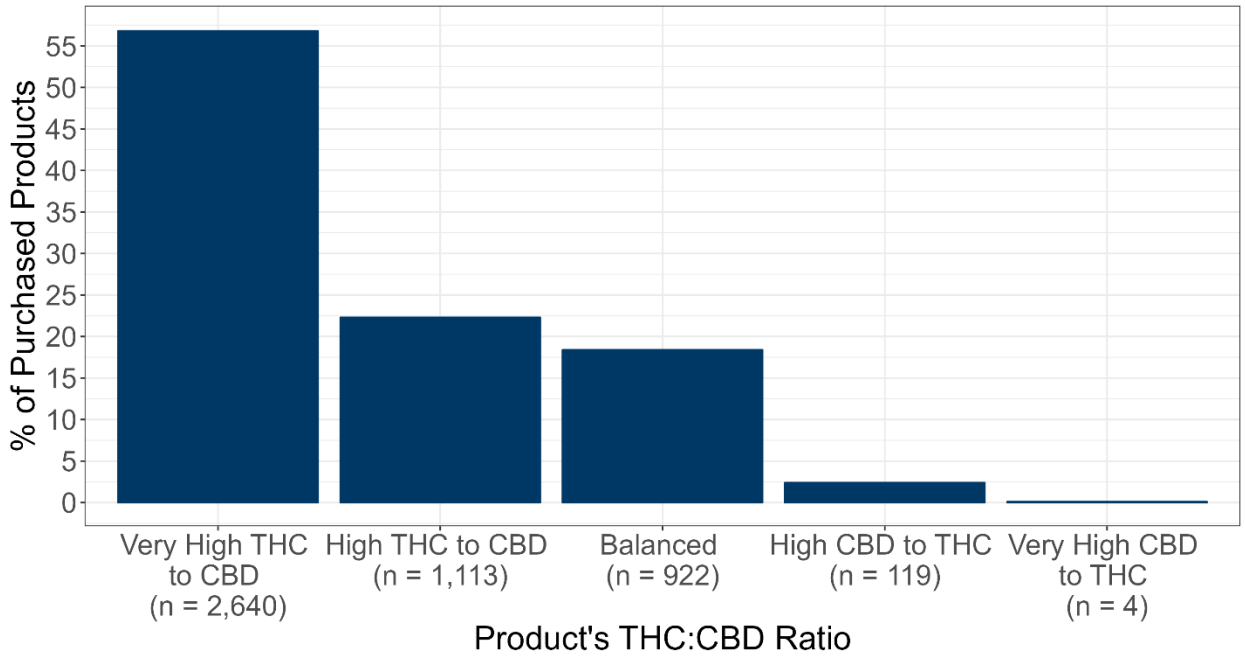


Oromucosal products

Oromucosal products include lozenges (31.0%), sublingual sprays (49.5%), and tinctures (19.5%). A majority of oromucosal products were very high THC:CBD ratio (56.8%), followed by

high THC:CBD ratio (23.3%) and balanced (18.4%) products. Majority CBD products made up less than 3% of all oromucosal sales (Figure 3.6).

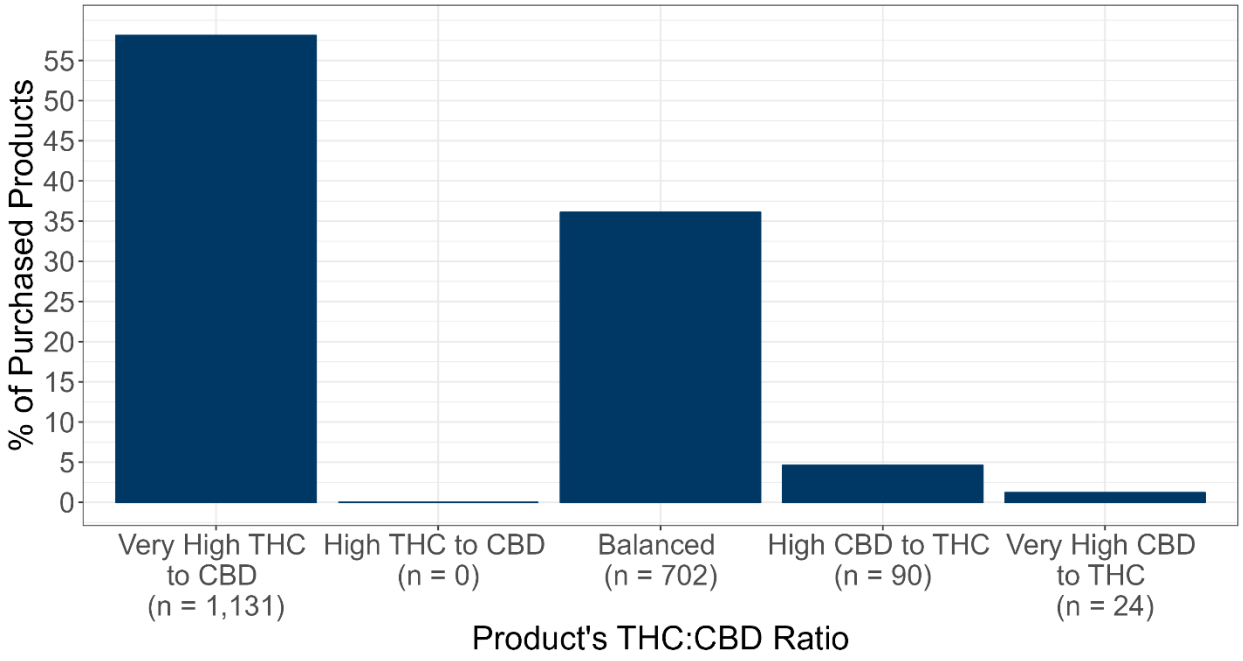
Figure 3.6. Oromucosal product transactions categorized by product's THC:CBD ratio



Topical products

Topical medical cannabis products include balms (38.7%), bars (27.0%), and gel creams (34.3%). A majority of purchased topical products had a very high THC:CBD ratio (58.1%), followed by balanced products (36.1%). Majority CBD products accounted for 5.8% of all topical products purchased (Figure 3.6).

Figure 3.7. Topical product transactions categorized by product's THC:CBD ratio



4. Benefits

Benefit received from medical cannabis

All patients enrolled in Minnesota's medical cannabis program must complete a patient self-evaluation (PSE) prior to each medical cannabis purchase. The PSE asks patients about their symptoms and concerns about medical cannabis to facilitate a discussion with their medical cannabis pharmacist before making their next purchase. Patients are asked about new medication, a set of eight standard symptoms, side effects, and any perceived benefits from using medical cannabis.

Below are a sample of quotes from obstructive sleep apnea patients in Minnesota's medical cannabis program when asked about the benefits of medical cannabis.

- *"Increased length of time asleep. Easier time tolerating CPAP."*
- *"Relaxing sleep, relief of sleep apnea side effects, lower anxiety, less stress and fatigue, better home life."*
- *"1. Sleep deeper 2. Sleep longer 3. More energy in the morning."*
- *"Sleep is still great. Getting through a full night – waking up fulfilled. Anxiety is the big helper. Between therapy, cannabis, and my support system, I feel I can handle most of what life throws at me."*
- *"Reduced anxiety and increased compliance with my CPAP mask; decreased pain."*

Length of time in Minnesota's Medical Cannabis Program

Medical cannabis patients may leave the program at any time by either formally removing themselves from the registry, not renewing their medical cannabis certification, or patients simply stop purchasing. Patients cite cost of medical cannabis, inaccessibility of medical cannabis dispensaries, and ineffectiveness for their symptoms as major reasons for leaving the program.

Length of time in Minnesota's medical cannabis program was calculated as time from a patient's first medical cannabis purchase to their most recent patient self-evaluation. All patients included in this report had the opportunity to be in the program for at least eight months. Among pain patients described in this report, (n = 2,962), 5.6% (n = 165) only purchased medical cannabis one time before leaving the program, 8.1% (n = 241) were in the program between 1-4 months, 7.0% (n = 208) were in the program between 5-8 months, and 79.3% (n = 2,348) were in the program for more than eight months. Among patients who were only qualified for obstructive sleep apnea, 80.8% stayed in the program for more than eight months, compared to 76.2% of patients with multiple qualifying conditions.

Standard eight symptoms

All patients, regardless of their certified condition(s), receive a set of eight 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 4.1). Therefore, higher scores indicate greater symptom severity. Scores greater than or equal to 4 indicate moderate to severe symptoms. Patients are asked to rate symptom severity over the *past 24 hours*.

Box 4.1. Listing of the standard eight symptom measures that all patients answer, including the responses options available to patients.

Standard 8 Symptom Measures:

Anxiety	Fatigue
Lack of Appetite	Nausea
Depression	Pain
Disturbed Sleep	Vomiting

Response Options (0 – 10 NRS):

0 1 2 3 4 5 6 7 8 9 10

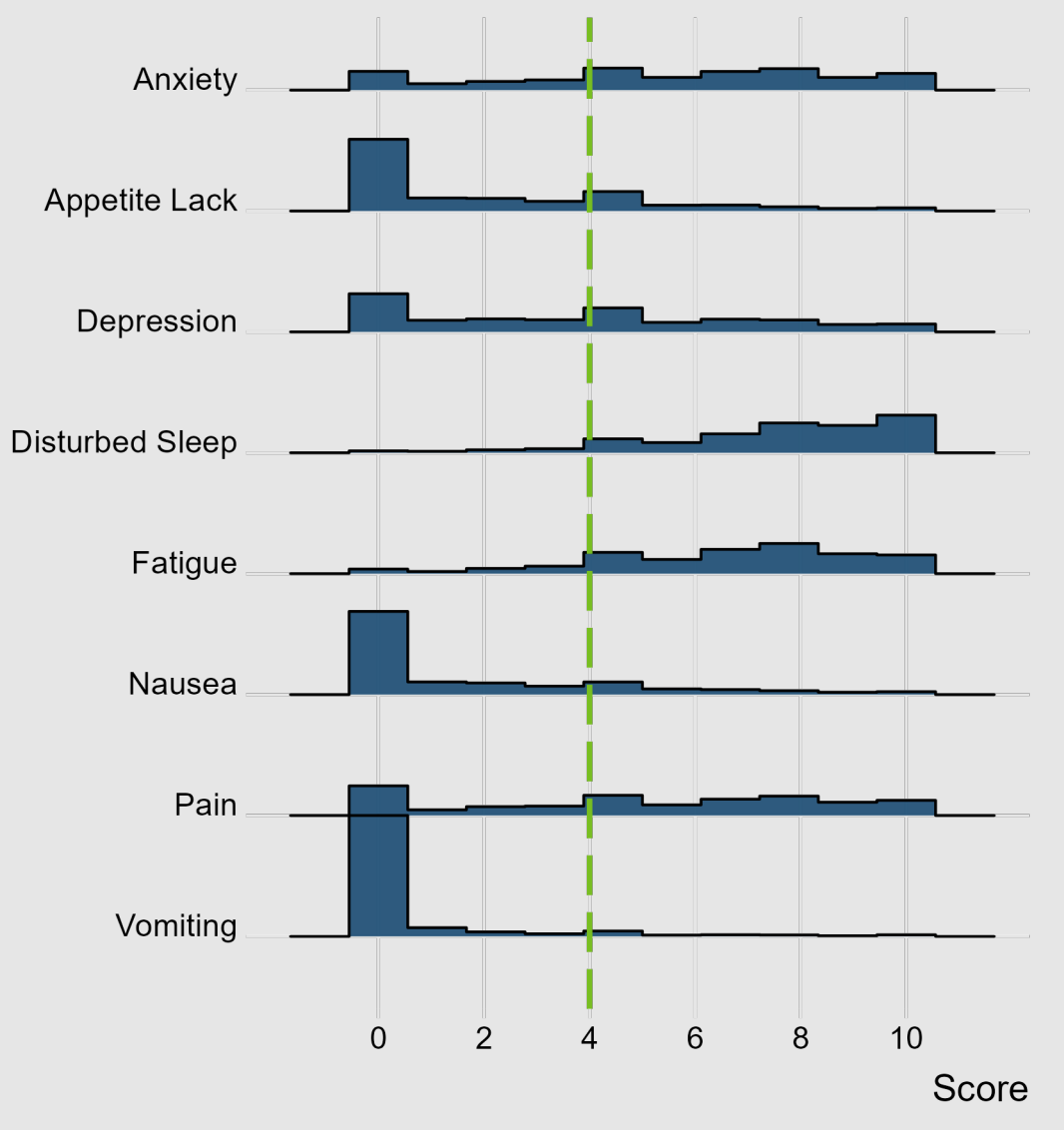
Symptom not present — Symptom as bad as one can image

The threshold of ≥30% reduction on a 0-10 point scale was chosen for the standard eight 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 9 to 6, from 8 to 5, from 7 to 4, etc.

Symptoms at enrollment in Minnesota's Medical Cannabis Program

Among obstructive sleep apnea patients, 93.0% (n = 2,749) reported moderate to severe disturbed sleep scores at enrollment (Table 4.1A). The average disturbed sleep score at enrollment was 7.7 (standard deviation (SD): 2.3) and was not different between patients who were only certified for obstructive sleep apnea compared with patients who were certified for obstructive sleep apnea among other conditions (Figure 4.1; Table A3). As expected, fatigue was the next most common symptom with 86.8% (n = 2,566) of patients reporting moderate to severe scores at baseline (Table 4.1A). Patients with obstructive sleep apnea among other conditions report higher fatigue scores (mean: 7.11; SD: 2.45), compared to patients only qualified for obstructive sleep apnea (mean: 6.53; SD: 2.57) (Table A3). Average and standard deviation of all baseline standard eight symptom scores are found in Table A3.

Figure 4.1. Distribution of standard eight symptom scores at enrollment. A score of four or greater indicates that symptom is of moderate to severe intensity.



Changes in symptoms

Among all obstructive sleep apnea patients with moderate to severe disturbed sleep scores at enrollment, 60.8% (n = 1,672) reported a ≥30% reduction in disturbed sleep score within four months (Table 4.1). Among all patients who saw improvement in disturbed sleep score within four months, 73.6% (n = 1,084) were able to maintain that improvement for at least four months (Table 4.1). Overall, 39.4% of patients with moderate to severe disturbed sleep score were able to achieve and maintain ≥30% reduction disturbed sleep score (Table 4.1). Initial improvement in disturbed sleep score within four months of first medical cannabis purchase was not significantly different between patients only qualified for obstructive sleep apnea and patients who have additional qualifying conditions ($X^2(1, N = 2,749) = 0.28$, $p = 0.598$; Table A4). However, there was a significant difference in proportion of patients

who experienced maintained improvement of disturbed sleep score for at least four months between patients only qualified for obstructive sleep apnea and patients with other qualifying conditions. Maintained improvement was reported by 77.0% (n = 752) of patients with only obstructive sleep apnea, compared to 66.8% (n = 332) of patients with other qualifying conditions ($X^2(1, N = 1,473) = 17.27$, $p < 0.001$; Table A5).

Overall, 33.5% of patients were able to achieve and maintain ≥30% improvement in fatigue scores. Initial improvement in fatigue score was significantly different between patients with only obstructive sleep apnea (n = 969; 58.4%) and patients with other qualifying conditions (n = 449; 49.4%) ($X^2(1, N = 2,566) = 18.84$, $p < 0.001$; Table A4). Maintained improvement of fatigue score was also significantly different between those two groups ($X^2(1, N = 1,253) = 11.58$, $p < 0.001$; Table A5), 71.8% (n = 610) of patients with only obstructive sleep apnea compared to 62.0% (n = 250) of patients with other qualifying conditions (Table 4.1, Table A5).

Change in symptoms among patients who stayed in the program at least eight months

As discussed above, proportions of patients who were able to achieve ≥30% symptom relief and maintain it for at least four months is a conservative estimate that does not account for patients leaving the program. The above proportions are calculated assuming no loss to follow-up, using the number of patients with moderate to severe scores at baseline as the denominator.

Patients in Minnesota's medical cannabis program may leave the program at any time by either formally removing themselves from the registry, not renewing their certification, or by simply stopping purchasing cannabis products. Patients cite cost of medical cannabis, inaccessibility of medical cannabis dispensaries, and ineffectiveness for their symptoms as major reasons for leaving the program in optional surveys given by OCM.

Length of time in Minnesota's medical cannabis program was calculated as time from a patients' first medical cannabis purchase to their most recent patient self-evaluation. All patients included in this report had the opportunity to participate in the program for at least eight months. Among obstructive sleep apnea patients described in this report (n = 2,962), 5.6% (n = 165) only purchased medical cannabis one time before leaving the program, 8.2% (n = 242) purchased multiple times and participated in the program between 1-4 months, 7.6% (n = 225) were in the program between 5-8 months, and 78.7% (n = 2,330) were in the program for more than eight months.

To investigate benefits received from medical cannabis among obstructive sleep apnea patients who remained in Minnesota's medical cannabis program for at least eight months, we performed the same analysis described in the above section. Among patients who were in the program for at least eight months who had moderate to severe disturbed sleep scores at baseline, 45.6% (n = 996) were able to achieve ≥30% symptom improvement and maintain it for at least four months, compared to 39.4% among all patients. This increase in proportion of patients achieving and maintaining symptom relief was seen in all standard eight symptoms (Table 4.2).

It is important to note that patients who choose to stop participating in Minnesota's medical cannabis program do not have to give a reason for leaving the program. Therefore, it is possible that patients may

leave because they are not experiencing symptom relief which may artificially inflate the proportion of patients experiencing symptom relief compared to the true proportion if all patients remained in the program for at least eight months. We provide both the conservative estimate using all patients who enrolled in the program as the denominator, as well as the liberal estimates using only patients who remained in the program from eight months knowing that the true value may lie somewhere in the middle.

This report found patients were able to improve their symptoms of sleep disturbance and fatigue after starting medical cannabis. The data used in this report do not speak to whether medical cannabis specifically targets mechanisms that contribute to symptoms of obstructive sleep apnea. Additionally, as this population does not have a group that does not use medical cannabis, or a control group, this report cannot compare symptom relief to an unexposed population.

Table 4.1. Standard eight symptoms benefits in obstructive sleep apnea patients A) All patients with obstructive sleep apnea. B) Patients with only obstructive sleep apnea. C) Patients with obstructive sleep apnea among other conditions.

A) All patients with obstructive sleep apnea

Standard eight symptom measure	n (%) of patients reporting at moderate to severe levels at baseline	n (%) of patients with ≥30% symptom improvement within 4 months, among those who had moderate to severe levels at baseline	# of patients with data in 4-month period following initial ≥30% symptom improvement	n (%) of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	2079 (70.3)	1228 (59.1)	1082	761 (70.3)	36.7%
Appetite lack	822 (27.8)	545 (66.3)	480	363 (75.6)	44.2%
Depression	1464 (49.5)	916 (62.6)	814	583 (71.6)	39.8%
Disturbed sleep	2749 (93.0)	1672 (60.8)	1473	1084 (73.6)	39.4%
Fatigue	2566 (86.8)	1418 (55.3)	1253	860 (68.6)	33.5%
Nausea	647 (21.9)	434 (67.1)	379	290 (76.5)	44.8%
Pain	1890 (63.9)	830 (43.9)	728	436 (59.9)	23.1%
Vomiting	234 (7.9)	179 (76.5)	153	124 (81.0)	53.0%

B) Patients with only obstructive sleep apnea

Standard eight symptom measure	n (%) of patients reporting at moderate to severe levels at baseline	n (%) of patients with ≥30% symptom improvement within 4 months, among those who had moderate to severe levels at baseline	# of patients with data in 4-month period following initial ≥30% symptom improvement	n (%) of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	1267 (65.2)	761 (60.1)	681	499 (73.3)	39.4%
Appetite lack	409 (21.0)	282 (68.9)	251	204 (81.3)	49.9%
Depression	825 (42.5)	528 (64.0)	474	348 (73.4)	42.2%
Disturbed sleep	1812 (93.3)	1109 (61.2)	976	752 (77.0)	41.5%
Fatigue	1658 (85.3)	969 (58.4)	850	610 (71.8)	36.8%
Nausea	314 (16.2)	208 (66.2)	183	143 (78.1)	45.5%
Pain	968 (49.8)	451 (46.6)	394	278 (70.6)	28.7%
Vomiting	108 (5.6)	84 (77.8)	71	57 (80.3)	52.8%

C) Patients with obstructive sleep apnea among other conditions

Standard eight symptom measure	n (%) of patients reporting at moderate to severe levels at baseline	n (%) of patients with ≥30% symptom improvement within 4 months, among those who had moderate to severe levels at baseline	# of patients with data in 4-month period following initial ≥30% symptom improvement	n (%) of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	812 (80.1)	467 (57.5)	401	262 (65.3)	32.3%
Appetite lack	413 (40.7)	263 (63.7)	229	159 (69.4)	38.5%
Depression	639 (63.0)	388 (60.7)	340	235 (69.1)	36.8%
Disturbed sleep	937 (92.4)	563 (60.1)	497	332 (66.8)	35.4%
Fatigue	908 (89.5)	449 (49.4)	403	250 (62.0)	27.5%
Nausea	333 (32.8)	226 (67.9)	196	147 (75.0)	44.1%
Pain	922 (90.9)	379 (41.1)	334	158 (47.3)	17.1%
Vomiting	126 (12.4)	95 (75.4)	82	67 (81.7)	53.2%

Table 4.2. Benefits in the Standard eight symptoms among patients who remained in the Minnesota Medical Program for at least eight months. A) All patients with obstructive sleep apnea. B) Patients with only obstructive sleep apnea. C) Patients with obstructive sleep apnea among other conditions.

A) All patients with obstructive sleep apnea

Standard eight symptom measure	n of patients who stayed in the program at least eight months reporting moderate to severe levels at baseline	n of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	1640	692	42.2%
Appetite Lack	643	333	51.8%
Depression	1136	522	46.0%
Disturbed sleep	2184	996	45.6%
Fatigue	2033	781	38.4%
Nausea	643	265	41.2%
Pain	1485	392	26.4%
Vomiting	191	118	61.8%

B) Patients with only obstructive sleep apnea

Standard eight symptom measure	# of patients who stayed in the program at least eight months reporting moderate to severe levels at baseline	n of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	1019	456	44.7%
Appetite lack	331	192	58.0%
Depression	649	309	47.6%
Disturbed sleep	1465	697	47.6%
Fatigue	1339	559	41.7%
Nausea	331	134	40.5%
Pain	773	253	32.7%
Vomiting	91	56	61.5%

C) Patients with obstructive sleep apnea among other conditions

Standard eight symptom measure	# of patients who stayed in the program at least eight months reporting moderate to severe levels at baseline	n of patients who achieved ≥30% symptom improvement that maintained it for at least 4 months	% of patients that both achieved ≥30% symptom improvement and retained that degree of improvement for at least 4 months
Anxiety	621	236	38.0%
Appetite lack	312	141	45.2%
Depression	487	213	43.7%
Disturbed sleep	719	299	41.6%
Fatigue	694	222	32.0%
Nausea	312	131	42.0%
Pain	712	139	19.5%
Vomiting	100	62	62.0%

5. Adverse Side Effects

In addition to reporting benefits of medical cannabis and rating condition symptoms, the patient self-evaluation (PSE) is also used to report adverse side effects of medical cannabis use. Prior to each medical cannabis purchase, patients must fill out their PSE and include any adverse side effects experiences. At the medical cannabis dispensary, patients can discuss these side effects and any other concerns with the medical cannabis pharmacist. Each adverse side effect is rated by the patient as mild, moderate, or severe. Mild is defined as symptoms do not interfere with daily activities. Moderate is defined as symptoms may interfere with daily activities. Severe is defined as symptoms interrupt usual daily activities.

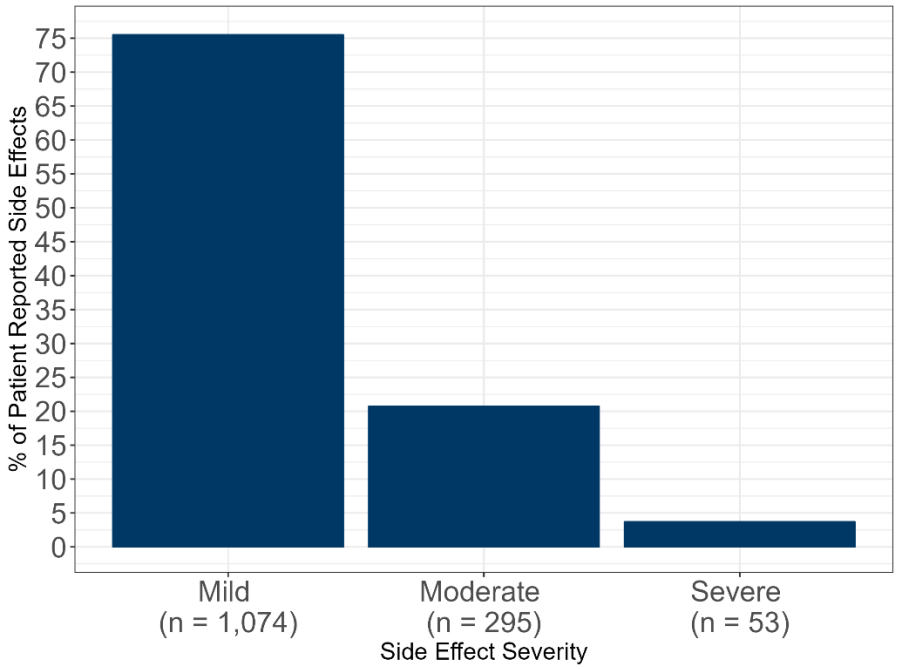
For this report, side effect data from the PSE were extracted for all obstructive sleep apnea patients enrolled for the first time between August 1, 2018, and April 15, 2024. This report describes all purchases that occurred within the first year. For patients whose first enrollment year had not yet ended at the time of data extraction (April 15, 2024), all purchasing transactions prior to that date were retained. This query produced:

- 1,422 patient reported side effects from
- 488 (16.5%) patients.

A major limitation of these data is loss to follow-up. If a patient had a side effect after taking medical cannabis and decided not to purchase again there is no record of the last side effect. Therefore, there is likely underreporting of moderate to severe side effects thorough the PSE. However, patients, caregivers, and health care practitioners can report side effects directly to the medical cannabis manufacturer. These reports are reported to the Office of Cannabis Management, but do not include identifying information and cannot be connected to a specific patient.

Of patients reporting side effects in a PSE (n = 488), over half (n = 320; 65.6%) reported one unique side effect, with 92.2% reporting three or fewer unique side effects within one year of their first medical cannabis purchase. A vast majority of the reported side effects were mild (n = 1,074; 75.5%), 20.7% were moderate (n = 295), and only 3.7% were reported to be severe (n = 53) (Figure 5.1).

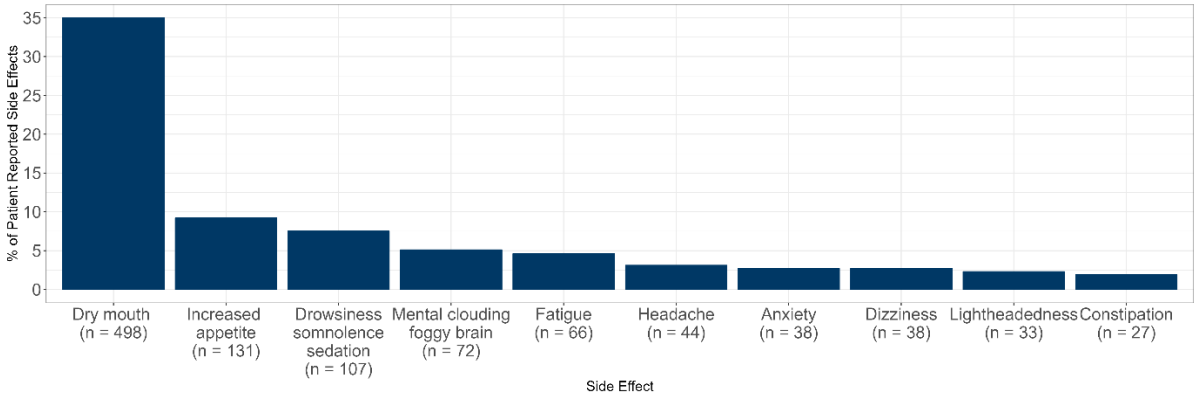
Figure 5.1. Severity of patient-reported side effects



Most commonly reported side effects

The most commonly reported side effect was dry mouth, accounting for 35.0% (n = 498) of all reported side effects. Other commonly reported side effects include increased appetite, drowsiness/somnolence/sedation, and mental clouding or brain fog. Figure 5.2 illustrates the top 10 reported side effects. A full list of reported side effects can be found in the appendix (Table A6). "Other side effect" was the second most commonly reported side effect (n = 181).

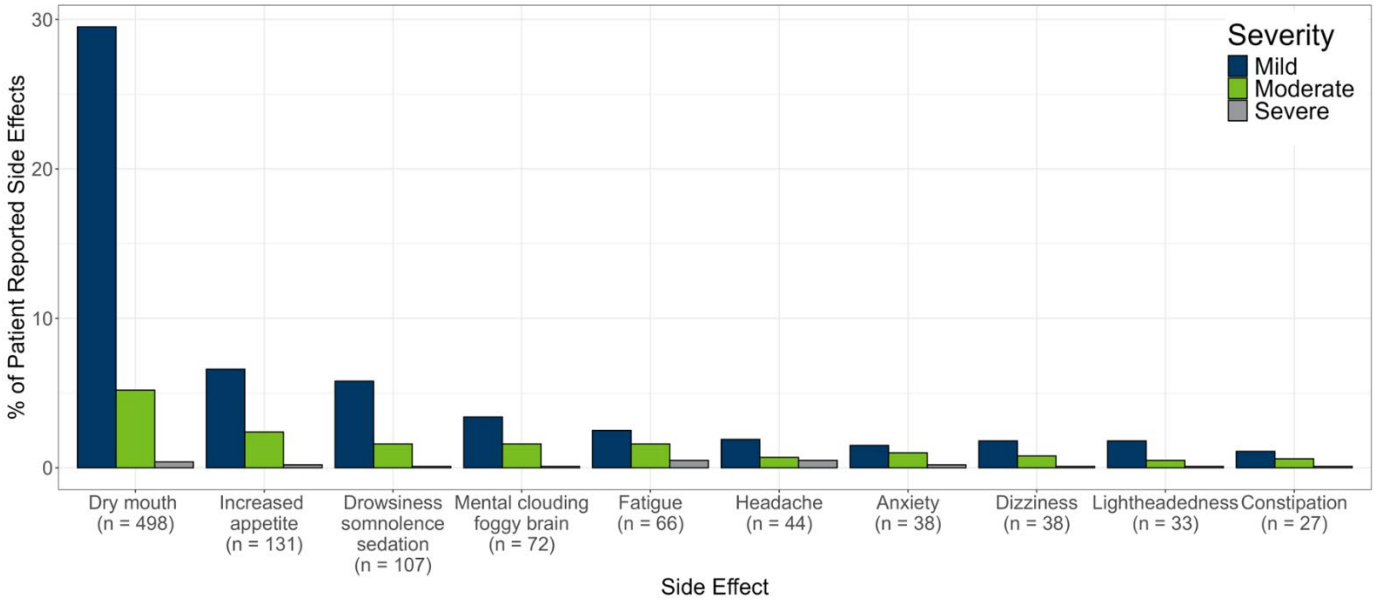
Figure 5.2. Top 10 most commonly reported adverse side effects



Common side effects x severity

Among the top 10 most commonly reported side effects, most were mild, followed by moderate and few were severe (Figure 5.3).

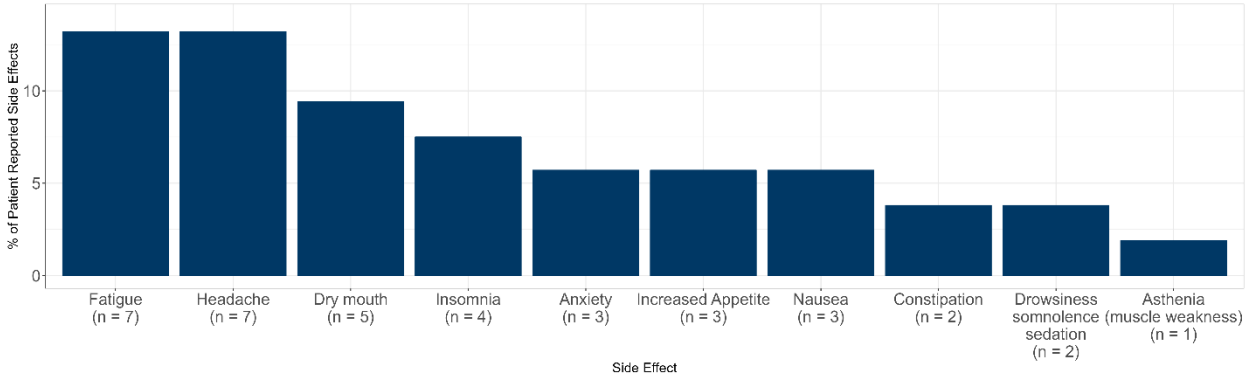
Figure 5.3. Top 10 most reported side effects by severity



Severe adverse side effects

Through the PSE, 53 side effects were reported as severe by 41 patients. Compared to the whole cohort, patient reporting a severe side effect were more likely to be female (48.8% vs. 22.7%). Fatigue and headache were the most common severe side effects (n = 7, 13.2%), dry mouth (n = 5, 9.4%), and insomnia (n = 4, 7.5%) (Figure 5.4).

Figure 5.4. Top 10 side effects reported as severe



Appendix A. Additional Tables

Table A1. Number of patients in each age category at enrollment by gender.

Age Category	Female	Male	Total
0-20	3	6	9
21-29	33	85	118
30-39	119	536	655
40-49	141	669	810
50-59	164	484	648
60-69	168	362	530
70-79	33	99	132
80-89	7	12	19
90+	3	3	6

Table A2. Obstructive sleep apnea patients by ZIP code region (first three number prefixes).

ZIP Region	ZIP Prefixes	Count (%)
Saint Paul	550,551	890 (30.0)
Minneapolis	553,554,555	1,224 (41.3)
Duluth	556,557,558	134 (4.5)
Rochester	559	162 (5.5)
Mankato	560,561	113 (3.8)
Willmar	562	64 (2.2)
Saint Cloud	563	190 (6.4)
Brainerd	564	73 (2.5)
Detroit Lakes	565	77 (2.6)
Bemidji	566	19 (0.6)
Grand Forks	567	13 (0.4)

Table A3. Mean and standard deviation of standard eight symptom scores at baseline among patients only qualified for obstructive sleep apnea and those with other qualifying conditions

Standard eight symptom	OSA only	OSA and other conditions	Total
n size	1,943	1,014	2,957
Anxiety (mean (SD))	5.05 (3.25)	6.37 (3.06)	5.50 (3.25)
Appetite Lack (mean (SD))	1.72 (2.48)	3.06 (3.16)	2.18 (2.81)
Depression (mean (SD))	3.31 (3.17)	4.87 (3.26)	3.85 (3.29)
Disturbed Sleep (mean (SD))	7.67 (2.26)	7.69 (2.38)	7.68 (2.30)
Fatigue (mean (SD))	6.53 (2.57)	7.11 (2.45)	6.73 (2.55)
Nausea (mean (SD))	1.41 (2.43)	2.60 (3.04)	1.82 (2.72)
Pain (mean (SD))	3.75 (3.21)	7.51 (2.53)	5.04 (3.48)
Vomiting (mean (SD))	0.49 (1.53)	1.06 (2.33)	0.68 (1.86)

Table A4. N (%) of patients with ≥30% standard eight symptom improvement within four months, among those who had moderate to severe levels at baseline. Pearson's chi-square test between patients only qualified for obstructive sleep apnea and those with other qualifying conditions.

Standard eight symptom	OSA only	OSA and other conditions	Chi-Square P-Value
Anxiety	761 (60.1)	467 (57.5)	0.268
Appetite lack	282 (68.9)	263 (63.7)	0.128
Depression	528 (64.0)	388 (60.7)	0.218
Disturbed sleep	1109 (61.2)	563 (60.1)	0.598
Fatigue	969 (58.4)	449 (49.4)	**<0.001**
Nausea	208 (66.2)	226 (67.9)	0.722
Pain	451 (46.6)	379 (41.1)	**0.019**
Vomiting	84 (77.8)	95 (75.4)	0.784

Table A5. N (%) of Patients who achieved ≥30% standard eight symptom improvement that maintained it for at least four months. Pearson's chi-square test between patients only qualified for obstructive sleep apnea and those with other qualifying conditions.

Standard eight symptom	OSA Only	OSA and other conditions	Chi-Square P-Value
Anxiety	499 (73.3)	262 (65.3)	**0.007**
Appetite lack	204 (81.3)	159 (69.4)	**0.004**
Depression	348 (73.4)	235 (69.1)	0.207
Disturbed sleep	752 (77.0)	332 (66.8)	**<0.001**
Fatigue	610 (71.8)	250 (62.0)	**<0.001**
Nausea	143 (78.1)	147 (75.0)	0.549
Pain	278 (70.6)	158 (47.3)	**<0.001**
Vomiting	57 (80.3)	67 (81.7)	0.986

Table A6. Count and percentage of all reported side effects by patients in their first year

Side Effect	N (%)
Dry mouth	498 (35.0)
Other	181 (12.7)
Increased appetite	131 (9.2)
Drowsiness/somnolence/sedation	107 (7.5)
Mental clouding/"foggy brain"	72 (5.1)
Fatigue	66 (4.6)
Headache	44 (3.1)
Anxiety	38 (2.7)
Dizziness	38 (2.7)
Lightheadedness	33 (2.3)
Constipation	27 (1.9)
Euphoria (intense feeling of well-being or pleasure)	27 (1.9)
Nausea	27 (1.9)
Insomnia	18 (1.3)
Impaired memory	15 (1.1)
Tinnitus (ringing in the ears)	15 (1.1)

Side Effect	N (%)
Abdominal/epigastric pain	13 (0.9)
Difficulty concentrating	11 (0.8)
Paranoia	11 (0.8)
Blurred vision	10 (0.7)
Diarrhea	9 (0.6)
Tachycardia (rapid heart rate)	8 (0.6)
Confusion	6 (0.4)
Asthenia (muscle weakness)	3 (0.2)
Numbness	3 (0.2)
Tremor	3 (0.2)
Chest pain	1 (0.1)
Disorientation	1 (0.1)
Dysphoria (intense feeling of unease or unpleasantness)	2 (0.1)
Panic attack	2 (0.1)
Slurred speech	2 (0.1)

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