

Article

# Characteristics of Older Adults Who Were Early Adopters of Medical Cannabis in the Florida Medical Marijuana Use Registry

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Abstract: Use of medical marijuana is increasing in the United States and older adults are the fastest growing user group. There is little information about the characteristics and outcomes related to medical marijuana use. This study is a descriptive analysis of older adults (aged  $\geq$ 50 years old) who were early adopters of a medical marijuana program in the U.S. state of Florida. Per state legislation, initial and follow-up treatment plans were submitted to the University of Florida College of Pharmacy. Data collection included demographics, clinical history, medical conditions, substance use history, prescription history, and health status. Follow-up treatment plans noted changes in the chief complaint and actions taken since the initial visit. Of the state's 7548 registered users between August 2016 and July 2017, N = 4447 (58.9%) were older adults. Patients utilized cannabidiol (CBD)-only preparations (45%), preparations that had both tetrahydrocannabinol (THC) and CBD (33.3%) or were recorded to use both CBD-only and THC + CBD products (21.7%). The chief complaints indicating medical cannabis treatment were musculoskeletal disorders and spasms (48.4%) and chronic pain (45.4%). Among other prescription medications, patients utilized antidepressants (23.8%), anxiolytics and benzodiazepines (23.5%), opioids (28.6%), and cardiovascular agents (27.9%). Among all drug classes with potential sedating effects, 44.8% of the cohort were exposed to at least one. Patients with follow-up visits (27.5%) exhibited marked improvement as assessed by the authorizing physicians. However, the patient registry lacked detailed records and linkable information to other data resources to achieve complete follow up in order to assess safety or efficacy. Future improvements to registries are needed to more adequately capture patient information to fill knowledge gaps related to the safety and effectiveness of medical marijuana, particularly in the older adult population.

**Keywords:** medical marijuana; cannabis; cannabidiol; CBD; THC; tetrahydrocannabinol; older adults; safety; effectiveness

## 1. Introduction

Cannabis use is increasing among medically complex individuals. The vast majority of cannabis use is recreational; however, there is an increasing number of adults who use cannabis and cannabis-derived substances for medical and complementary health purposes. Increased use corresponds with expanding



access through state medical cannabis programs, broad consumer marketing and use of cannabidiol (CBD) products. There is a continued increase in public support of legalization at the individual state level, whereas cannabis remains illegal (i.e., Schedule 1) at the national level [1–3]. State programs range from what is deemed a "comprehensive" program that allows both CBD and tetrahydrocannabinol (THC) use (N = 33 states), programs that restrict the amount of THC allowed and promote CBD-only products (N = 13 states), and four states (ID, SD, NE, KS) which have no program in place [1]. Currently, 11 states have also legalized recreational cannabis for use by adults [1]. Florida was the 22nd state in the U.S. to legalize access to medical marijuana—the third largest state with one of the largest and fastest growing populations of older adults.

In 2018, state-based medical cannabis programs were estimated to include over 2.1 million legal medical cannabis patients. Enrollment in these programs varies by state, with a range of 1 to >38 patients per 1000 residents [4]. Medical cannabis users represent approximately 10% of adult cannabis users [5]. Practically all state programs have specified conditions for which medical cannabis can be used. These conditions include epilepsy/seizures, chronic pain, nausea/vomiting, muscle spasms, inflammatory conditions, Alzheimer's disease, Parkinson's disease, and cancer [1]. These conditions are highly prevalent among older adults who are likely to have complex medical profiles and pharmacotherapeutic regimens [6–10]. A recent national survey reported increased odds of about 50% for past year marijuana use among patients with history of stroke, heart disease, asthma, chronic pulmonary disease, diabetes, arthritis, renal disease, cancer, and depression among medical cannabis users [1].

The Baby Boomer generation (~55–75 years old), which represents the fastest growing segment of the population in terms of substance use and abuse in general, are more likely to be comfortable with cannabis use compared to their parents' generation due to social or personal exposure earlier in life [12,13]. Data from the period 2006–2013 suggest a 250% increase in cannabis use among those 65+ and nearly a 60% increase among those 50–64 years old—numbers that are likely to have increased as more states legalize medical and recreational cannabis programs [9]. Prevalence estimates of cannabis use in the past year for these age groups are approximately 3% and 9%, respectively [14]. Among older adults, 75% consider cannabis use to have no or only slight health risks if used once or twice a week [14]. Thus, it appears that older adults regard cannabis as generally safe and are rapidly adopting cannabis into their health and medical regimens.

This study described the characteristics of older adult patients, aged  $\geq$ 50 years old, who were licensed to use medical marijuana during the early implementation period of the Florida medical marijuana program between 2016 and 2017 and followed these individuals from treatment initiation to the point of a follow-up encounter.

## 2. Methods

This was a retrospective analysis of initial and follow-up treatment plan forms electronically submitted by providers to the University of Florida College of Pharmacy (UF-COP) between 01 August 2016 and 31 July 2017. The forms were created to meet the Compassionate Medical Cannabis Act (CCA) statutory requirements by a team of outcomes researchers, health policy experts and physicians and pharmacists with expertise in psychiatry, neurology, and pain medicine. The authorizing physician completed the initial and follow-up treatment plans and submitted the forms electronically via a secured portal maintained by the UF-COP. The forms received covered visit dates during the period in which CBD-only cannabis was available associated with the 2014 CCA legislation as well as a period of time when the Amendment 2 legislation was approved, but not yet fully implemented.

The data elements collected on the initial treatment plan forms are the date of treatment plan submission and information on the patient, provider, and the cannabis order. All treatment forms were automatically de-identified upon electronic submission. For each patient, a unique registry identification number was generated for longitudinal tracking. Patient data collected were demographics (i.e., age, race/ethnicity), clinical history, medical conditions, history of substance use (i.e., alcohol, tobacco, illicit

drugs), prescription medication history, and a patient's health condition score assessed by the provider on a scale of 1–7 which is based on the Clinical Global Impression Severity Scale [15]. The clinical history included the indication or indications for cannabis treatment, herein referred to as the chief complaint. For the cannabis order, information covered the date of order, the dosing regimen, the type of cannabis (CBD-only, THC + CBD, or both types of products), the planned duration, the treatment plan goal and the plan for monitoring of patient's symptoms, and a planned follow-up encounter date.

Data collected on the follow-up treatment form include the patient's registry identification number, the date of treatment plan submission, the date of last patient encounter, changes in the cannabis order since last treatment plan, changes in the chief complaint, hospitalization history since last treatment plan, changes in the patient's comorbidities or current medications since last treatment plan, indicators of tolerance or reaction to cannabis, discontinuation of cannabis use during the last quarter, and the provider's assessed patient condition score compared with the initial condition on a scale of 1–7.

We analyzed all electronically submitted forms of registry patients aged 50 to 100 years who attended at least an initial visit. Forms were excluded when providers submitted blank forms and when data entries were erroneous or invalid. Free-text data entries, such as chief complaints, medical treatments, and planned treatment duration were manually reviewed and summarized into clinically meaningful categories. Chief complaint categories were based on the medical conditions listed in the current law and on broader disease categories found to be prominent. Categories for medications were determined by therapeutic classifications that were found to be prominent. The planned treatment duration was categorized into appropriate time intervals determined by all possible entries.

#### Data Analysis

We calculated descriptive statistics of patient and treatment characteristics and examined frequency counts, sample means, and proportions. Analyses were conducted with SAS version 9.4 statistical software (SAS Institute Inc, Cary, NC, USA). This study was approved by the institutional review and privacy board of the University of Florida with a waiver of informed consent and HIPAA authorization.

## 3. Results

There were N = 4447 older adults registered in Florida's medical marijuana treatment registry of a total of 7548 registered (Table 1). Of these, 2662 (59.9%) were 50–64, 1238 (27.8%) were 65–74, and 547 (12.3%) were 75 years old or older. Registered users were predominantly of white race (87.5%). Physician-assessed conditions indicated that most patients were moderately ill or worse and low-THC cannabis (i.e., CBD) was the most common treatment choice (45%) compared to medical cannabis (33.3%) or a combination of the two (21.7%). Most patients were given a planned duration of treatment of 12 months or less.

Chief complaints indicating medical marijuana use were primarily related to pain including musculoskeletal disorders, spasms, and chronic pain (Table 2). Cancer was indicated for 15.5% of all patients. Non-pain-related conditions included epilepsy or seizures (2.9%), glaucoma (2%), autoimmune disorders (3.2%) post-traumatic stress disorder (10%), multiple sclerosis (2.7%), Parkinson's disease (4.5%), amyotrophic lateral sclerosis (ALS; 0.5%) and Crohn's disease (1.2%). Psychological disorders were prevalent in 13.2% of patients and post-traumatic stress disorder in an additional 10%. These chief complaints were not mutually exclusive, and providers could have identified more than one per patient. Other conditions, such as sleep disorders (7%) and headaches or migraines (10.4%), were also common.

			Age Group			
Characteristic, N (%)	Total (N = 4447)	50–64 Years (N = 2662)	65–74 Years (N = 1238)	75+ Years (N = 547)		
Age, mean (SD)	63.4 (9.17)	57.3 (4.17)	68.8 (2.71)	80.9 (5.37)		
Race						
White	3893 (87.5)	2290 (86.0)	1115 (90.1)	488 (89.2)		
Black	157 (3.5)	118 (4.4)	29 (2.3)	***		
Hispanic, Latino or Spanish	203 (4.6)	121 (4.6)	52 (4.2)	30 (5.5)		
Other/Unknown <sup>‡</sup>	194 (4.4)	133 (5.0)	42 (3.4)	19 (3.5)		
F	Patient condition ass	essed by provider				
Normal, not at all ill	195 (4.4)	111 (4.1)	61 (4.9)	23 (4.2)		
Borderline ill	99 (2.2)	59 (2.2)	20 (1.6)	20 (3.7)		
Mildly ill	588 (13.2)	359 (13.5)	167 (13.5)	62 (11.3)		
Moderately ill	1909 (42.9)	1150 (43.2)	512 (41.4)	247 (45.1)		
Markedly ill	1156 (26.0)	715 (26.9)	317 (25.6)	124 (22.7)		
Severely ill	412 (9.3)	224 (8.4)	130 (10.5)	58 (10.6)		
Among the most extremely ill	88 (2.0)	44 (1.7)	31 (2.5)	13 (2.4)		
History of substance use						
Alcohol	628 (14.1)	406 (15.3)	160 (12.9)	62 (11.3)		
Smoking	444 (10.0)	323 (12.1)	202 (8.2)	20 (3.7)		
Illicit drugs	162 (3.6)	118 (4.4)	42 (3.4)	***		
	Cannabis type	e ordered <sup>±</sup>				
Medical cannabis	1481 (33.3)	926 (34.8)	409 (33.1)	146 (26.7)		
Low-THC cannabis	2000 (45.0)	1172 (44.0)	534 (43.1)	294 (53.7)		
Both low-THC and medical cannabis	966 (21.7)	564 (21.2)	295 (23.8)	107 (19.6)		
Planned order duration						
<1 month	469 (10.6)	288 (10.8)	110 (8.9)	71 (13.0)		
1–3 months	1919 (43.2)	1209 (45.4)	515 (41.6)	195 (35.7)		
3–12 months	382 (8.6)	238 (8.9)	109 (8.8)	35 (6.4)		
>12 months or indefinitely	1343 (30.2)	739 (27.8)	406 (32.8)	198 (36.2)		
Not specified	334 (7.5)	188 (7.1)	98 (7.9)	48 (8.8)		

Table 1. Characteristics of Florida medical marijuana registry patients at the initial treatment visit by
cannabis type ordered.

<sup>†</sup> Includes Asian, Native Hawaiian, Pacific Islander, American Indian, or Alaska Native. SD = standard deviation. <sup>±</sup> Medical cannabis not explicitly defined by Florida law. Low-THC cannabis defined by Florida law as "containing no more than 0.8 percent of tetrahydrocannabinol (THC) and at least 10 percent of cannabidiol (CBD)". \*\*\* cell count  $\leq 10$ .

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			Age Group	
Chief Complaint <sup>+</sup> , N (%)	Total (N = 7548)	50–64 Years (N = 2662)	65–74 Years (N = 1238)	75+ Years (N = 547)
Musculoskeletal disorders and spasms	2154 (48.4)	1348 (50.6)	534 (43.1)	272 (49.7)
Cancer	691 (15.5)	350 (13.2)	235 (19.0)	106 (19.4)
Epilepsy or seizures	130 (2.9)	93 (3.5)	30 (2.4)	***
Glaucoma	87 (2.0)	41 (1.5)	30 (2.4)	16 (2.9)
Autoimmune or immune disorders <sup>±</sup>	142 (3.2)	104 (3.9)	29 (2.3)	***
Post-traumatic stress disorder (PTSD)	444 (10.0)	298 (11.2)	136 (11.0)	***
Amyotrophic lateral sclerosis (ALS)	24 (0.5)	***	***	***
Crohn's disease	52 (1.2)	33 (1.2)	15 (1.2)	***
Parkinson's disease	201 (4.5)	51 (1.9)	92 (7.4)	58 (10.6)
Multiple sclerosis (MS)	121 (2.7)	***	***	***
Chronic pain	2019 (45.4)	1242 (46.7)	520 (42.0)	257 (47.0)
Back, spine, or neck conditions	696 (15.7)	475 (17.8)	147 (11.9)	74 (13.5)
Major brain and head injuries	149 (3.4)	***	***	***
Gastrointestinal conditions	225 (5.1)	137 (5.2)	69 (5.6)	19 (3.5)
Headaches or migraines	461 (10.4)	318 (12.0)	93 (7.5)	50 (9.1)
Other nervous system and neurological disorders	486 (10.9)	269 (10.1)	123 (9.9)	94 (17.2)
Psychological disorders (excl. PTSD)	589 (13.2)	376 (14.1)	158 (12.8)	55 (10.1)
Sleep disorders	310 (7.0)	199 (7.5)	82 (6.6)	29 (5.3)
Others	35 (0.8)	***	***	***

**Table 2.** Characteristics of Florida medical marijuana registry patients at the initial treatment visit by cannabis type ordered.

<sup>+</sup> Chief complaints are not mutually exclusive; more than one condition per patient possible. <sup>±</sup> Including HIV/AIDS; excluding MS and Crohn's disease. \*\*\* Data suppressed due to low cell count < 11.

On average, registered patients used approximately 2.5 other medications with medians of 3 (interquartile range 0–4) for all age groups (Table 3). With regards to concomitant medication use, more than 20% of all patients utilized antidepressants (23.8%), anxiolytics and benzodiazepines (23.5%), opioids (28.6%), and cardiovascular agents (27.9%). Among all drug classes with potential sedating effects, 44.8% of the cohort were exposed to at least one.

	Age Group				
Medication Class, N (%)	Total (N = 4447)	50–64 Years (N = 2662)	65–74 Years (N = 1238)	75+ Years (N = 547)	
Number of medications per patient, mean (SD), IQR	2.4 (2.54) 3 (0–4)	2.4 (2.52) 3 (0–4)	2.4 (2.57) 3 (0–4)	2.3 (2.58) 3 (0–4)	
Antidepressants	1060 (23.8)	670 (25.2)	289 (23.4)	101 (18.5)	
Antipsychotics	128 (2.9)	82 (3.1)	35 (2.8)	11 (2.0)	
Anxiolytics and benzodiazepines	1046 (23.5)	674 (25.3)	285 (23.0)	87 (15.9)	
Mood stabilizers	37 (0.8)	***	***	***	
Stimulants and amphetamines	124 (2.8)	***	***	***	
Hypnotics and sedatives	292 (6.6)	168 (6.3)	98 (7.9)	26 (4.8)	
Opioids <sup>±</sup>	1271 (28.6)	863 (32.4)	296 (23.9)	112 (20.5)	
Non-opioid analgesics	861 (19.4)	512 (19.2)	229 (18.5)	120 (21.9)	
Skeletal muscle relaxants	611 (13.7)	458 (17.2)	127 (10.3)	26 (4.8)	
Other musculoskeletal agents <sup>++</sup>	133 (3.0)	73 (2.7)	38 (3.1)	22 (4.0)	
Anticonvulsants and antiepileptics	760 (17.1)	496 (18.6)	176 (14.2)	88 (16.1)	
Anti-Parkinson	162 (3.6)	58 (2.2)	69 (5.6)	35 (6.4)	
Other neurological agents <sup>±±</sup>	71 (1.6)	39 (1.5)	21 (1.7)	11 (2.0)	
Antiemetics	200 (4.5)	128 (4.8)	56 (4.5)	16 (2.9)	
Other GI agents	217 (4.9)	135 (5.1)	58 (4.7)	24 (4.4)	
Cardiovascular agents	1241 (27.9)	623 (23.4)	417 (33.7)	201 (36.8)	
Antidiabetic agents	271 (6.1)	147 (5.5)	92 (7.4)	32 (5.9)	
Hematologic agents	126 (2.8)	52 (2.0)	51 (4.1)	23 (4.2)	
Hormonal agents and steroids	596 (13.4)	319 (12.0)	198 (16.0)	79 (14.4)	
Genitourinary agents	264 (5.9)	99 (3.7)	100 (8.1)	65 (11.9)	
Respiratory agents	181 (4.1)	90 (3.4)	60 (4.9)	31 (5.7)	
Chemotherapeutic agents	102 (2.3)	***	***	***	
Autoimmune agents	75 (1.7)	***	***	***	
Antivirals incl. HIV medications	40 (0.9)	***	***	***	
Anti-infective agents	50 (1.1)	***	***	***	
Ophthalmic and glaucoma medications	51 (1.2)	17 (0.6)	18 (1.5)	16 (2.9)	
OTC medications, vitamins, supplements and others	348 (8.2)	204 (7.6)	111 (9.0)	48 (8.8)	

**Table 3.** All concomitant prescription medication classes reported to be used by Florida medical marijuana registry patients at the initial treatment visit <sup>†</sup>.

SD = standard deviation; IQR = interquartile range. <sup>†</sup> Medications are not mutually exclusive, more than one medication per patient possible. <sup>±</sup> Includes combination products containing an opioid; <sup>††</sup> Includes medications for multiple sclerosis. <sup>±±</sup> Includes triptans and medications for Alzheimer's disease. <sup>\*\*\*</sup> Data suppressed due to low cell count < 11.

Of the 4447 with an initial visit, only 1225 (27.5%) of patients had a second visit treatment plan recorded (Table 4). The majority (72.7%) of patients were recorded to have an improved chief complaint with less than 3% with a worsened complaint. In open response feedback, available for only 85 visits, physicians noted several instances of reduced medication use since initiation of medical marijuana. Noteworthy, were mentions of reduced or stopped opioid medications, improved sleep quality, reduction of medications for sleep, and reduced anxiety medications. Adverse effects were also noted in 16 entries, which included hallucinations, respiratory side effects due to vaped products, sedation or "loopy" feelings, and worsened insomnia. Further, 33 entries were noted in patients who discontinued medical marijuana, which primarily noted inability to afford treatment, preference to not travel with a potentially illegal product, and ineffective treatment. Free text submissions are shown in the Appendix A Figures A1–A4.

Total (N = 1225)	Yes (%)			
Follow-Up Question Since Last Treatment Visit				
Changes in chief complaint since last visit?	10.0%			
Changes in alcohol, smoking, or illicit drug use since last visit? <sup>†</sup>	1.4%			
Changes in comorbidities since last visit?	1.7%			
Hospitalizations since last visit?	2.9%			
Changes in current medications since last visit?	10.0%			
Were there indicators of reaction to cannabis since last visit? <sup>‡</sup>	2.0%			
Did the patient discontinue cannabis use?	4.6%			
Patient Condition Since the Initiation of Treatment Comp	pared to Condition Initially Assessed			
Very much improved	10.8%			
Much improved	31.4%			
Minimally improved	30.5%			
No change from baseline	24.7%			
Minimally worse	1.4%			
Much worse	0.9%			
Very much worse	0.4%			

**Table 4.** Summary of the follow-up information reported by Florida medical marijuana registry patients at a follow-up visit after treatment initiation for total follow-up sample.

<sup>+</sup> Missing N = 62. <sup>‡</sup> Adverse drug reactions, patient-reported problems, medications holds, ER visits, or hospitalizations.

# 4. Discussion

In the state of Florida, there were relatively few initiators of medical marijuana in the first years of implementation but more than one-half were older adults aged  $\geq$ 50 years. The chief complaints indicating medical marijuana use were primarily related to pain conditions. Other recorded medication use was common and, notably, nearly one-half of registered patients use other potentially sedating medications. Adherence to treatment appeared low, with approximately 1 in 4 patients having a recorded follow-up visit, though the brief treatment plan collection window may not have captured all follow-up visits.

Early adopters may not be completely generalizable to more contemporary late adopters in lifestyle and clinical factors. Nevertheless, several noteworthy concerns are evident even in this sample. Both THC and CBD containing products have high potential to induce side effects of sedation, lethargy, or other altered mental states. In our cohort, nearly one-half used at least one medication such as antidepressants, anti-anxiety, and other classes known to cause sedation. In older adults, this is particularly troubling due to increased sensitivity and higher incidence of negative sequelae that are related to sedation (e.g., falls and fractures). Further, THC-containing pharmaceutical products in other non-U.S. countries are contraindicated in patients with heart disease [16]. In our sample, nearly 1 in 3 patients used cardiovascular medications and may be at risk for additional complications with medical marijuana treatment. Improvements noted in this cohort for the chief complaints as well as reductions in other medications deserve additional research to understand if this is causal. Alternative reasons these improvements were observed may include natural disease progression or attrition of those who did not experience benefit.

The public seems to assume the safety of cannabis and its constituents from a long history of recreational use in mostly younger persons or personal use earlier in life [17,18]. Cannabis is generally viewed as a safer alternative to prescription drugs due to its natural origin and because it has become ubiquitous throughout the U.S. via medical and recreational legalization [19]. Safety is further assumed given that consumer CBD-based products are widely available over the counter for recreational and complementary health uses. However, cannabis has been found to have low-quality evidence for any benefit in a myriad of conditions but has been associated with up to 3-fold higher odds of experiencing adverse drug effects [20,21].

Cannabis is a complex botanical product with broad pharmacologic activity and effects on other medications. Whole cannabis and hemp (with low THC composition) plants contain more than 500 phytoconstituents including, but not limited to, approximately 120 cannabinoids [22,23]. Cannabis-derived substances like CBD are delivered as a purified product, cannabinoid combinations (e.g., CBD:THC) or consumed as part of the whole cannabis or hemp plant [22,23]. Alone, the main cannabinoids CBD and THC have established metabolic routes, absorption/elimination characteristics, and known interactions with drug metabolizing enzymes. Thus, cannabis has potential to cause pharmacokinetic drug–drug interactions as either an inhibitor or inducer of these enzymes [24,25]. Cannabinoids have similar pharmacodynamic properties as many common medications. Constituents in cannabis have significant biological effects, e.g., sedation and somnolence, which can be potentiated with concomitant medications with similar effects (e.g., opioids or benzodiazepines), specifically referred to as pharmacodynamic drug-drug interactions [26,27]. These effects are characterized as both the target effects (e.g., pain relief) that drive patients to seek therapy with cannabis as well as adverse drug events (ADEs) related to cannabis and its components (e.g., psychiatric events). These have included somnolence, sedation, acute psychiatric events (paranoia, hallucination, euphoria), cognitive and memory impairment, insomnia, gait disturbances, suicidal thoughts or behaviors, tachycardia, vertigo, and anorexia [16,21,28,29].

ADEs are a major concern among older adults. Older adults are at an increased risk of ADEs due to pathophysiological changes (e.g., sarcopenia, renal/hepatic dysfunction), polypharmacy, and comorbid conditions [30,31]. The aging brain loses significant volume per decade and places older adults at more susceptibility to neurological ADEs as well as the effects of illicit drugs—including cannabis [32]. Older adults (>50 years) are the largest consumers of prescription medications with 67% using  $\ge 5$  prescription drugs, 40% using at least one over-the-counter drug, 60% using a dietary supplement—all numbers which increase throughout aging [33]. In older adults, the estimated prevalence of at least one potential drug–drug interactions in current regimens is 50% and is as high as 80% in certain clinical groups, with up to 1 in 4 patients at risk for  $\geq$ 4 drug–drug interactions [34–37]. Many prescription drugs have unclear risk/benefit profiles in older users and have led to clinical tools (e.g., Beers Criteria, STOPP/START, anticholinergic burden scales) [38-41] to avoid certain medications or avoid specific drug-disease interactions in order to minimize ADEs. In older adults, ADEs disproportionately contribute to severe health outcomes. ADEs are associated with between 3% and 30% of all hospital admissions and ADEs increase the risk of emergency department visits, increased in-hospital morbidity and mortality, and increased health care expenditure [38,41–50]. It is estimated that up to 50% of all ADEs are avoidable, preventable, or ameliorable in that they can either be prevented through selecting alternative therapies to avoid drug-drug interactions or can be reduced through dose reductions or preventive measures against side effects [44,51–53]. The addition of medical cannabis to the armamentarium of treatments for a variety of conditions in older adults deserves further research not only for its potential benefits, but also to fully assess the risks associated with ADEs.

## Limitations

This study included a convenience cohort of older adult medical cannabis users in Florida captured via a physician-provided treatment plan registry. The registry was discontinued due to statutory changes, which did not allow sufficient follow up of patients. Limited patient information was available such as comorbid conditions and medication use, which may have been underreported in the registry. Few follow-up treatment plans were submitted and, thus, assessment of patient outcomes including improvements or adverse effects was not thorough. A new patient registry will be developed in Florida by the Consortium of Medical Marijuana Clinical Outcomes Research, established by state legislature in 2019, to enable better data capture and linkage to other clinical outcome data to improve these limitations.

## 5. Conclusions

Older adults made up more than one-half of all early adopters of medical cannabis. Chronic pain was the most common treatment indication. Registered users were also prescribed several other medications which point to possibilities of drug–drug and drug–disease interactions. Follow up was limited and was likely due to a number of factors including a limited follow-up time, physician non-compliance submitting treatment plans, patients discontinuing medical cannabis, or patient death. Among patients with a follow-up treatment plan, most reported improved conditions and reductions of other medications but some reported side effects or lack of treatment effects. Further research is needed to fill knowledge gaps regarding the safety and effectiveness of medical cannabis for the myriad conditions for which it is being utilized by older patients.

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Conflicts of Interest: The authors declare no conflict of interest.

#### Appendix A

Free-text entries of follow-up treatment plans indicating changes in chief complaints, medications, and patient experiences after an initial treatment with medical marijuana (Figures A1–A4).

current\_medication\_change\_why

Added Atorvastatin 20mg QD, Amlodipine 5mg QD, Valsartan 80mg QD, Effient 10mg QD Added morphine and lorazepam by hospice prescription Began Chemotherapy Crelyn for stomach cramping and to aid digestion Currently taking bentyl and zofran for diarrhea. Suspect due to doubled magnesium dose DC'D LISINOPRIL, CARVEDILOL INCREASED 10 18.5 MG BID, HUMULIN INCREASED TO 65 U. HUMULIN R INCREASED NOON DOSE INCREASED TO 15 U AND PM DOSE INCREASED TO 25 U. ENTRESTO 49-51 MG BID. SPIRONOLACTONE 25 MG DAILY DRONABINOL 10MG DAILY PRN, OMEPRAZOLE 20 MG BID, NUCYNTA 50 MG PRN, MELATONIN DC'D. STOOL SOFTENER 100 MG 2 GELS DAILY, CEPHALEXAN 250 MG PO TID FOR 5 DAYS. OXYBUTYNIN 5 MG TID Decreased dose of pain medications Decreased pain medicine intake Decreased pain meds and patches by 50 Decreased the Xanax dose Decreased the use of opiate medication. Decreased to 25 mcg fentanyl patches, oxycodone 10 mg bid instead of percocet q 6hrs, add xanex 0.5 mg q hs. Depakote ER 500mgs 2 tab bid changed to Depakote ER 500mg 3 qhs and patient is no longer on Clonazepam ODT. Diazepam 10mg TID Gabapentin decreased from 600 tid to 300 TID. Norco between 3-5 doses per day (pre-cannabis always 5/day). Ativan prn use has decreased in frequency. Off abilify. Patient has stpped celebrex and gabapentin as not needing for pain. Patient is also checking with PCP about decreasing lisinopril as BP has been improved (patient thinks pain level was causing reactive HTN which is now resolved). reactive HIN which is now resolved). Patient is now off roxycodone, oxycodone, and baclofen! Off Trazadone for sleep. Has not needed imitrex for breakthrough headaches, or zofran for nausea. Patient is now using less Xanax only 1 mg daily at bedtime when necessary, has completely discontinued baclofen 10 mg and tramadol 50 mg Patient reduced her need of opiates Patient stopped all opioids 2 months ago Patient stopped taking Ambien and decreased taking Seroquel Patient stopped taking Percocet and MS Prochlorperazine for nausea Pt no longer takes BP meds Reduced ibuprofen and pain meds Setraline increased to 150 mg bid. Abilify increased to 30mg Started new cancer treatments every 2 weeks. Stopped hydromorphone (didn't want to be on opiates any longer, took 2 weeks to wean off) Stopped hydromorphone (didn't want to be on opiates any longer, took 2 weeks to wean off) Stopped librax and reglan. Stopped metformin, off hydralazine. Stopped solumedrol premedicaton of IVIG, Will be starting soriatane for psoriasis. Stopped primadone for tremor Taking 5 mg valium daily instead of 10 mg. Paxil is 10 mg instead of 20 The patient has stopped taking fentanyl, methadone, serotonin inhibitor Was off lisinopril for low BP, now back on amlodypine and intermittent lisinopril. Able to decrease alprazolam to 1-2 doses daily instead of 3. Was able to decrease opiate doses when using cannabis consistently, but has not been able to afford cannabis due to unexpected car and roof expenses, so b d/c cymbalta, change to celexa, progesterone increased to 500 decreased 2 mg Clonazepam to 1.5mg QHS 2.5 weeks ago with some insomnia relief felt on current therapy decreased his fentanyl patch from 75mcg to 50mcg decreased use of current prescribed medications, in half dilaudid to xtampza er , added topomax pt's pain mngmt physician changed medication fioricet for headaches increased lexapro to 20 mg daily less narcotics less pain medication lisinopril-hctz changed to just lisinopril pcp removed hctz. no longer taking oxycodone or fentanyl no longer taking triazadone odd depakote, switch to zyprexa off marinol off morphine. decreased blood pressure and diabetic meds. off phenteramine and orphenadrine, taking Norco 5 2-3 times daily. has HCTZ to take 3 times per week if BP elevated but has not needed. on pap machine

Figure A1. Reasons for Change in Current Medication Noted During Follow-Up Visits; *N* = 85 entries.

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chief complaint change why marked improvement improved Symptoms improved All symptoms improved Symptoms decreased deceased 75 relief of pain and muscle spasms but continued issues with PTSD/anxiety causing insomina All symptoms have decreased All symptoms the same but improved significantly Cancer progressing Doing better symptoms decreased He has had improvement with the low THC - CBD. His pain score 5/10. we will increase to get better capture. He has noted a significant decrease in headaches and decreased pain in neck. The headaches are still doing better His current pain is 4/10. He is still off the clonazepam. He rates it at an 8 out of 10. He did better w/ the capsule over the tincture He was able to decrease pain pill intake when he had long capsule and slept better. Her muscle spasms have decreased. She has been able to stop her amitriptyline. Increased whole body pain Increased whole body pain Inhalational 20mg Stimes; oral 20mg 3times, patient preferred route of administration Less nausea after chemo, appetitie has increased. Coughing less, feeling stronger Less pain/neuropathy, Less RA pain, no recurrence of squamous cell skin cancer MARKED IMPROVEMENT PARKED IMPROVEMENT PT symptoms have decreased. Patient does have a new symptoms of tunnel vision Pain 6/10 She is decreasing morphine intake she is down to 45mg TID (from 60mg). Pain decreased. Sleeping better. Pain has improved since starting the low THC- however she still has pain at night with insomnia, but has helped her with her ADLS Patient continues with PTSD symptoms, reports CBD alone has been helpful for anxiety, but has not helped with sleep or nightmares. Additionally reports joint pain in knees and hands Patient diagnosed with Multiple Myeloma since last treatment plan. She is undergoing Chemotherapy Patient did not want to follow protocol of increasing dosage after short time trials, complained the the bottles were the same when delivered and the strength was never correct. Patient did not want to come for appointments. Stated the pharmacy told her she should be given the strongest strength. Complained of delivery charges and payment for office visits. Stated Marijuana was helping her, but told the secretary it was not working at all. Patient reports sleeping improved and as well as anxiety. Has noticed anti inflammatory effects of CBD, back pain not as severe and able to pick up dirty laundry and put on shoes and socks with more ease. more ease. Patient was able to open eyes fully without pain within 7 days of beginning the CBD REPORTS USING LESS INSULIN-LESS PRESERVATIVE-BETTER MOVEMENT-SLEEPY SIDE AFFECT REPORTED Recent CT scan revealed no metabolically active tumors. Eating and sleeping better. Still taking chemo for lung CA Recent liver scan shows no tumors. Same symptoms but all symptoms have improved She has anxiety, muscle spasm, pain from hip fracture, trouble sleeping She has anxiety, muscle spasm, pain from hip fracture, trouble sleeping Significant improvement, with cancer resolution Skin cancers diminishing in size and healing Skin lesions resolving with topical cannabis product Spasms in extremities are rare now. Pain has decreased. Start of chemotherapy lead to severe nausea and loss of appetite Still has a same symptoms but much less pain Symptoms Controlled Symptoms are the same but controlled Symptoms have decreased Symptoms have decreased Symptoms have improved with the CED treatment. We are increasing to get better capture. THERE WAS A SHORTAGE OF SUPPLY. PATIENT HAS BEEN OFF OF HER MEDICATION FOR A FEW WEEKS. SHE IS BACK TO HER ORIGINAL USE OF NARCOTICS AND IS NOT DOING WELL. SHE ALSO HAD A DETERIORATION IN HER MEDICAL CONDITION. HER CADAVER BONE GRAFT IS BEING REJECTED (IN HER NECK) The severe nerve pain in left cheek has diminished and precancerous lesions on arms have resolved add dx of glaucoma recently diagnosed by opthomologist chronic pain chronic pain and muscle spasm failed narcotics, cortisone spine injections and cervical fusion decreased anxiety decreased intensity and frequency of muscle spasms her low back complaints have decreased. she feels more relaxed improvement in mood improvement in mood increased due to disease progression low THC ineffective for pain relief marked improvement, gave up methadone! and ativan! and quit smoking marked improvement, decrease in spasms and shakes marked improvement, no longer taking trazadone, marked improvement, relaxes muscles, helps reduce headaches, reduces anxiety and depression marked improvement, significantly relieves muscle and joint pain marked improvement, significantly relieves muscle and joint pain markedimprovement more pain, less sleep motor skills improved neuropathy is better off of oxycodone, reduced back pain pain complaints pain has decreased from 8 to 4 muscle spasms have decreased progression of CA pt has been diagnosed with breast cancer would like to try THC for Breast cancer there has being slight improvement with increase of dosage tremors have diminished since starting the cannabis products worsening muscle spasms and uncontrolled by previous dose

**Figure A2.** Changes in the Original Chief Complain/Indicated Condition During Follow-Up Visits; *N* = 95 entries.

tolerance or reactions why

2 ER visits related to opiate withdrawal symptoms, needed IVF and K supplementation (due to sweats, nausea, and diarrhea with OPIATE withdrawal) Mild dry mouth but has not decreased patient's use One ER visit for headache, had low BG, oral hypoglycemics stopped. Patient reports burning feeling in her chest following inhalation route of administration. Vape cannabis triggered some facial pain to her aberrant trigeminal nerve Yes with 2mg dose didnt work. felt loopy hallucinations increased THC worsened insomnia keidney stone surgery july/2017 spinal stimulator june/2017 mild cough with vape patient feels more depressed patient feels more depressed patient reported having a headache after using low-the Cannabis pt has sensitivity taking full dose has not found right route of administantion that is working for him yet. trouble using pen, charging issues had to replace pen new pen having trouble with activation and holding charge. vape usage causes gagging cough. \*ape usage causes gagging cough.

**Figure A3.** Documentation of Adverse Drug Reactions to Cannabis or Other Patient-Reported Problems with Treatment During Follow-Up Visits; N = 16 entries.

discontinue\_cannabis\_why

No help 1 WEEK WITH OUT MEDICATION DUE TO VAPE PEN NOT WORKING HAD CHARGING ISSUES. COST PT WAS UNABLE TO AFFORD COST OF MED MJ Can't afford, but was very helpful Discontinued inhaled THC due to adverse reaction. HE WASN'T SURE THERE WAS A GOOD VALUE; NOW, HE HAS CHANGED HIS MIND He only took medical cannabis during the last two months. NO Help Never obtained the needed notes from specialists. Never started. NO Help. PT D/C BECAUSE OF CONCERNS WITH PSA 'S STILL RELIANT ON MED MJ. Patient could not afford CBD but plans to restart CBD Patient had decided to stop CBD, but may restart in the future Patient was never able to start cannabis treatment due to waiting for registry card Pt ran out- had to go out of town- so follow up was later than planned but was not on purpose the instant due to be be deciment to the particulation of the particula She insisted she be given the maximum dosage without building towards an increase of strength. She was going out of the country so she was given marijuana of the same strength for a longer period of time because she would not be available to monitor an increase in dosage. She did not fill this order. Was unable to purchase it on the month of deceased discontinued the cannabis for 4 days to try Gabapentin. Left me very groggy and started the cannabis again while titrating off the Gabapentin. does not appear to have gotten product but did not follow up or contact office to inform us of change he did not notice any difference when taking 30mg daily (orally) i think so but has not followed up to confirm pt had traveled d/c use while travelling was only able to use intermittantly. pt has been taveling did not want to bring. 3weeks no use. pt not using consistantly uses as needed. may go day or so so without till needed for tremors, sleep, anxiety. inneffective brown out unable to afford enough but is doing ok she received a medication that was not palatable and could not tolerate it. stopped using CBD low dose THC as failed to control pain there was a lack of CED:THC RSO 1:1 and the patient received inconsistent therapy; in spite of which, he has returned to work and is pain free. was out of town in a state that it is illegal for several weeks

**Figure A4.** Reasons for Discontinuation of Cannabis During Follow-up Visits; N = 33 entries.

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