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Improved Post-Traumatic Stress Disorder Symptoms and Related Sleep Disturbances after Initiation of Medical Marijuana Use: Evidence from a Prospective Single Arm Pilot Study

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Keywords
Medical marijuana · Cannabis · Post-traumatic stress disorder · Sleep · Sleep quality

Abstract
Introduction: Post-traumatic stress disorder (PTSD) is a debilitating disorder experienced by a subgroup of individuals following a life-threatening trauma. Several US states have passed laws permitting the medical use of marijuana (MMJ) by individuals with PTSD, despite very little scientific indication on the appropriateness of marijuana as a therapy for PTSD. This prospective pilot study of adults with confirmed PTSD in Florida (FL) investigated whether PTSD symptoms, sleep quality, affect, and general physical and mental health/well-being improved post-initiation of MMJ treatment. ***Methods:*** Participants, $N = 15$, were recruited from two MMJ clinics in Gainesville and Jacksonville, FL. To be eligible, participants had to be 18 years of age or older, not currently on MMJ, and willing to abstain from recreational marijuana, if using any, until the State Medical Cannabis Card was obtained, screen positive for PTSD. Participants were assessed at baseline (pre-MMJ initiation) and 30 and 70 days post-MMJ initiation using the Pittsburgh Sleep Quality Index (PSQI), PTSD Checklist for DSM-5 (PCL-5), Positive and Negative Affect Schedule (PANAS), PROMIS Global Health V1.2, and semi-structured marijuana and other substance use assessment. ***Results:*** PTSD symptom severity as measured by total PCL-5 score improved significantly at 30- and 70-day follow-ups. Similarly, statistically significant reductions in nightmares were reported at 30- and 70-day follow-ups. Corresponding improvements in sleep were noticed with participants reporting increased duration of sleep hours, sleep quality, sleep efficiency, and total PSQI score. Likewise, negative affect and global mental health improved significantly at follow-up. According to the post hoc analyses, the most statistically significant changes occurred between baseline and 30-day follow-up. The exception to this pattern was nightmares, which did not show significant improvement until day 70. ***Conclusion:*** The findings of this study highlight the potential of MMJ in improving patient outcomes for those with PTSD, particularly concerning sleep disturbances, which often do not respond to currently available treatments.

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Introduction

Post-traumatic stress disorder (PTSD) is a debilitating disorder experienced by a subgroup of individuals following a life-threatening trauma, such as sexual and physical assault, natural disasters, and military combat. The National Comorbidity Survey Replication estimated the lifetime prevalence of PTSD among adult Americans to be 6.8% [1]. Current past-year PTSD prevalence was estimated at 3.5% [2]. The common symptoms of PTSD include re-experiencing, avoidance, negative alterations in cognition and mood, and severe comorbid sleep disturbances. Between 70 and 91% of people with PTSD report having difficulty falling or staying asleep [3]. Nightmares are reported by 19–71% of people, contributing to worsening of mood, PTSD severity, and quality of life [3]. Nightmares associated with PTSD are often a residual symptom that remains difficult to treat despite improvements in other domains [4]. Literature suggests that disturbed sleep can contribute to maladaptive stress and trauma responses and may constitute a modifiable risk factor for poor psychiatric outcomes [5]. These sleep problems are often resistant to treatment and exert a strong negative influence on the quality of life. Self-reported poor sleep after trauma exposure has been identified as a predictor of subsequent PTSD severity [6–8].

Clinical practice guidelines recommend trauma-focused psychotherapies as first-line treatments for PTSD [9, 10]; however, a significant proportion of patients who complete these treatments fail to improve or are left with residual symptoms [11, 12]. Moreover, access to these treatments is limited [13], and dropout rates are high [14]. In response to overwhelming demand for additional treatment options, several US states have passed laws permitting the medical use of marijuana (MMJ) by individuals with PTSD, despite very little scientific indication on the appropriateness of marijuana as a therapy for PTSD. In the state of Florida, PTSD has been a qualifying condition for MMJ since January 2017 per state statutes. A review of the present literature on MMJ in the treatment of PTSD shows about 13 studies that evaluated several different MMJ and cannabinoid medications. These included studies of nabilone (a synthetic THC analogue) [15–17], Δ9-tetrahydrocannabinol (THC) [18–20], cannabidiol (CBD) [21], and CBD + THC [22–26]. Only one randomized placebo-controlled trial compared outcomes from smoked, herbal cannabis with high THC, high CBD, and an equal ratio of THC + CBD against a placebo [27]. The findings of these studies yielded controversial results with a few studies showing significant reductions in PTSD symptoms and nightmares and other studies showing no effect or worsening of symptoms. Research conducted so far in this area has had several limitations. Most studies have been heterogeneous in methodology (e.g., with respect to participant characteristics, use of a control group, and unspecified dosages and routes of marijuana administration). In addition, the potential for recall bias in PTSD symptoms and sleep quality has been glaring in almost all studies [28, 29].

We conducted a pilot prospective study of adults with confirmed PTSD who were initiating MMJ use in Florida based on a framework that has proven that disturbances in effect lead to poor sleep, which, in turn, worsens PTSD symptoms [30]. Built on this framework, we evaluated whether PTSD symptoms, sleep quality, effect, and general physical and mental health/well-being improved at 30- and 70-days post-initiation of MMJ treatment by applying both survey and ecological momentary assessment methods at different time points. For this manuscript, only the survey data obtained at three timepoints, baseline, 30-day follow-up, and 70-day follow-up, were analyzed and reported.

Materials and Methods

Sample

Eligible participants were recruited from two MMJ clinics in Gainesville and Jacksonville, Florida. Only new patients who contacted the clinics for evaluation and were new applicants for a state of Florida Medical Cannabis Card were considered for this study. To be eligible, participants had to be 18 years of age or older, not currently on MMJ, willing to abstain from recreational marijuana, if using any, until the State Medical Cannabis Card was obtained, screen positive for PTSD, and have a smartphone. The study protocol was reviewed and approved by the University of Florida Institutional Review Board (UF-IRB).

Procedure

Study participants were recruited between February and December 2020, during the time of the start of the COVID-19 epidemic. Due to COVID-19 restrictions, participant recruitment and assessment methods were amended to support telephone screening and virtual assessments. The eligibility screening was done via phone, the baseline and 70-day assessments were conducted virtually via Zoom, and the 30-day survey was completed by the participant via REDCap as per the original plan. MMJ clinicians at the participating two MMJ clinics in North Central Florida were briefed about the study purposes, eligibility criteria, and assessment methods. Providers explained the study to all potentially eligible participants, provided them with the UF IRB-approved study flyer, and asked them to provide contact information on an IRB-approved "permission to contact form" if they were interested. The study interviewer contacted clinics regularly to obtain the contact information of patients interested in

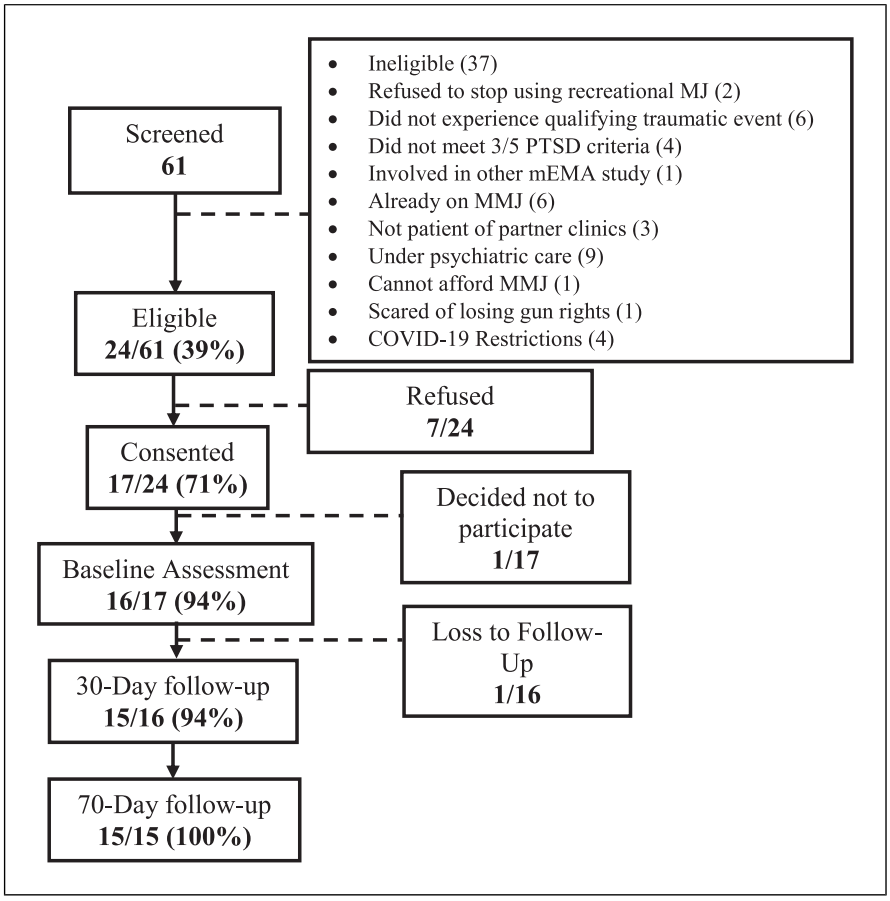

Fig. 1. Participant recruitment flowchart.

participating and later contacted the participants over the phone to screen them for eligibility. We screened 61 individuals, of whom 24 were eligible (shown in Fig. 1). Of those eligible, 17 consented to participate in the study and were enrolled. One participant withdrew after providing informed consent because they decided not to start MMJ. The remaining 16 participants all completed the baseline assessment. One participant was lost to follow-up after the baseline survey due to unknown reasons. Each of the remaining 15 (94%) participants completed all study assessments at 30- and 70-day follow-up. These follow-up timepoints were selected based on the experience of our consultant MMJ practitioners who suggested that most patients take up to 3 weeks after initiating MMJ to adjust their dosage and achieve a stable dose 30 days after MMJ initiation.

Assessments

The following assessments were used in this study at baseline and at 30- and 70-day follow-up:

Pittsburgh Sleep Quality Index (PSQI)

PSQI is a self-rated 19-item questionnaire that assesses subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction over a 1-month time interval [31]. Higher scores on PSQI indicate worse sleep quality.

PTSD Checklist for DSM-5 (PCL-5)

Developed by the US Department of Veterans Affairs, National Center for PTSD, the PCL-5 is a 20-item self-report measure that assesses the 20 DSM-5 symptoms of PTSD in the past 30 days [32, 33]. The PCL-5 has a variety of purposes, including monitoring symptom change during and after treatment, screening individuals for PTSD, and making a provisional PTSD diagnosis.

Positive and Negative Affect Schedule (PANAS)

The PANAS, developed by Watson and Clark [34] (1994), is a 20-item self-report questionnaire assessing two dimensions of affect, positive and negative, in the past 30 days. The PANAS has good psychometric properties. Higher scores represent higher levels of positive and negative affect, and the scores on each domain range from 5 to 50.

PROMIS Global Health V1.2

The NIH-developed PROMIS Global Health is a standardized, self-reported, profile-based health status measurement with 10 self-reported global health items (general health, quality of life, physical health, mental health, social satisfaction, physical activities, pain, fatigue, social activities, and emotional distress) that summarize general perceptions of health [35]. Global physical and mental health scores can range from 4 to 20, with higher scores indicating better health.

Marijuana and Other Substance Use Assessment

A semi-structured assessment developed for this study was used to assess the use of marijuana and other substances, including the use of alcohol. For marijuana, the age of onset (if used prior), frequency, route of administration, date of last use, and money spent on marijuana products in the past and present were asked. For MMJ, the assessment captured the number of products used, and for each product, the mode of administration, frequency of use, and THC-CBD ratio were asked.

Data Analysis

As a preliminary step, the survey data were reviewed to rectify any data entry errors and prepared for analysis. We applied descriptive statistics on the demographics and all variables to understand the demographic characteristics of the sample and also to understand the response patterns. We applied correlations between the outcome variables and conducted repeated measures ANOVAs or Friedman tests (for variables that did not meet the normality assumption) using SAS PROC GLM to compare scores on the following outcomes of pre- and post-MMJ treatment: (1) PTSD symptoms: PTSD severity (PCL-5 total score) and nightmare frequency as measured by PCL-5, (2) sleep: Global PSQI score and sleep quality, duration, and efficiency derived from the PSQI, (3) affect: PANAS, and (4) physical and mental health (PROMIS Global Health). For variables with significant p values from the omnibus test, post hoc analyses were carried out to examine the changes between baseline and 30-day follow-up, 30- and 70-day follow-ups, and baseline and 70-day follow-up.

Results

The average age of the participants in the study was 44 years (SD 11.9). The majority (80%) of the participants were white, 60% were women, 27% were never married/single, 33% were married, 64% were employed, and a majority (73%) had some form of health insurance in the past 12 months. Concerning substance use, 73% smoked cigarettes, 67% used alcohol, and 53% used other drugs in the past 12 months. Only one participant reported ever using injection drugs (Table 1).

Traumatic experiences (not shown in table) that happened directly to participants include physical assault (87%), unwanted/uncomfortable sexual experiences not including sexual assault (67%), sexual assault (60%), witnessing/learning about sudden accidental death (60%), transportation accident (60%), assault with a weapon (53%), natural disaster (53%), sudden violent death – homicide/suicide (53%), serious accident at work, home, or during recreational activity (40%), fire explosion (33%), life-threatening illness or injury (27%), severe human suffering (27%), captivity – being kidnapped, abducted, held hostage, or prisoner of war (20%), exposure to toxic substances such as dangerous chemicals or radiation (13%), and combat or exposure to a war-zone (13%).

The means and standard deviations were examined for the variables of interest at baseline to provide descriptive information (Table 1). The baseline PTSD symptoms' total score in this sample was 49.6 (SD 13.2), which is above the clinical cut-off of 33 [32, 33]. Likewise, the PSQI total score of 13.7 (SD 3.5) exceeded the clinical cut-off of 5 [31]. The average sleep efficiency at baseline in the current sample was 47.2% (SD 25.8), which is in the very bad range, while the average sleep duration was 5.03 h corresponding to the fairly bad range. The sleep quality score of 2.27 was in the fairly to very bad range. The baseline global physical health and mental health scores in this sample were 12.87 (SD 3.3) and 8.73 (SD 2.8), respectively. The baseline positive affect score in this sample was 28.8 (SD 9.3), which is lower than the standard score of 33.3, and the negative affect score was 31.6 (SD 8.1), which is over the standard score of 17.4 (31). Although not shown, PTSD total score was positively correlated with the negative mood. Physical well-being was correlated positively with the positive mood. Participants reporting low PTSD score reportedly had better physical well-being. Likewise, mental well-being was correlated with the positive mood, low PTSD score, and physical well-being. All these correlations were significant at $p < 0.05$.

Changes in the Use of MMJ

The use of up to three MMJ products was reported at both 30- and 70-day assessments. We reviewed the MMJ products, THC/CBD ratio, route of use, and frequency of use at both individual and product levels (Table 2). At the individual level, about the same proportion of participants reported using one (35.7%), two (35.7%), or three (28.6%) marijuana products at the 30-day assessment. In comparison, almost half (46.7%) of the participants reported using only one marijuana product at the 70-day assessment. At the product level, most of the MMJ products (88.9% at 30-day and 74.1% at 70-day) used had more THC than CBD. Inhalation appeared to be the most preferred route of use, with 74.1% of MMJ products used this way at both 30- and 70-day assessments.

Changes in the Outcomes of Interest

Changes in the total scores of the main outcome variables at 30 and 70 days post-initiation of MMJ are summarized in Table 3. PTSD symptom severity as

Table 1. Demographic characteristics of the sample and means and standard deviations for baseline variables (N = 15)

Variable	N (%)
Race	
White	12 (80.0)
Other	3 (20.0)
Gender	
Male	6 (40.0)
Female	9 (60.0)
Education	
Some college, associate's degree, or technical degree	7 (46.0)
Bachelor's degree	4 (27.0)
Master's degree	4 (27.0)
Marital status	
Never married/single	4 (27.0)
Living with long-term partner	1 (6.7)
Married	5 (33.3)
Divorced	4 (26.7)
Widowed	1 (6.7)
Currently employed	
Yes	9 (64.0)
No	5 (36.0)
Ever without insurance in the past 12 months	
Yes	4 (27.0)
No	11 (73.0)
Cigarette smoking in the past 12 months	11 (73.0)
Alcohol use in the past 12 months	10 (67.0)
Ever injected drugs	
Yes, not in the past 12 months	1 (7.0)
Never	14 (93.0)
Ever used other drugs	
Yes, in the past 12 months	8 (53.0)
Yes, not in the past 12 months	3 (20.0)
Never	4 (27.0)

	Mean	SD
Age, years	44	11.9
PANAS-GEN positive affect	28.86	9.3
PANAS-GEN negative affect	31.64	8.1
PCL-5 total score	49.60	13.2
PSQI total score	13.79	3.5
Sleep efficiency	47.2	25.8
Overall sleep quality	2.27	0.5
Sleep duration hours	5.03	1.0
Global health physical score	12.87	3.3
Global health mental score	8.73	2.8
Nightmares (PCL-5)	2.00	1.1

measured by the total PCL-5 score improved significantly at 30- and 70-day follow-ups (49.6 vs. 30.3 vs. 29.0, $F = 13.25$, $p = 0.0001$). At both 30- and 70-day follow-up, PCL-5 total scores were lower than the standard clinical cutoff score (33.0). Significant reductions in nightmares, as assessed by item 2 on the PCL-5, were reported at 30- and 70-day follow-ups (2.00 vs. 1.57 vs. 0.87, $\chi^2 = 7.54$, $p = 0.023$). Corresponding improvements in sleep were noticed with participants reporting increased duration of sleep hours (5.03 h vs. 6.64 h vs. 6.83 h, $F = 8.83$, $p = 0.0015$), sleep quality (2.27 vs. 1.21. vs. 1.07, $\chi^2 = 19.48$, $p < 0.0001$), sleep efficiency (47.20 vs. 52.26 vs. 49.79, $\chi^2 = 6.53$, $p = 0.0381$), and total PSQI score (13.79 vs. 10.62 vs. 9.13,

Table 2. MMJ use characteristics at individual and product levels at 30- and 70-day follow-ups

	30-day (T2)	70-day (T3)
Individual level	*n* = 14[a]	*n* = 15[a]
Number of MMJ products		
1	5 (35.7)	7 (46.7)
2	5 (35.7)	4 (26.7)
3	4 (28.6)	4 (26.7)
THC-CBD ratio[b]		
More THC than CBD	12 (85.7)	13 (86.7)
1:1	0	2 (13.3)
More CBD than THC	2 (14.3)	0
Route of use[b]		
Oral	1 (7.1)	2 (13.3)
Inhale/vaping	12 (85.7)	11 (73.3)
Sublingual	1 (7.1)	2 (13.3)
Use frequency (times/day)[b]		
1	2 (14.3)	5 (33.3)
2	5 (35.7)	6 (40.0)
3	1 (7.1)	2 (13.3)
4	4 (28.6)	2 (13.3)
5	1 (7.1)	0
6	1 (7.1)	0
Product level	*n* = 27	*n* = 27
THC-CBD ratio		
More THC than CBD	24 (88.9)	20 (74.1)
1:1	0	4 (14.8)
More CBD than THC	3 (11.1)	3 (11.1)
Route of use		
Oral	2 (7.4)	2 (7.4)
Inhale/vaping	20 (74.1)	20 (74.1)
Sublingual	5 (18.5)	5 (18.5)
Use frequency (times/day)		
1	9 (33.3)	9 (33.3)
2	9 (33.3)	8 (29.6)
3	2 (7.4)	6 (22.2)
4	4 (14.8)	3 (11.1)
5	1 (3.7)	1 (3.7)
6	1 (3.7)	0
Missing	1 (3.7)	0

[a]Three people have missing data at T2 and two people have missing data at T3. [b]For the first MMJ product.

$F = 16.54$, $p < 0.0001$). Negative affect scores improved significantly after MMJ initiation (31.64 vs. 24.14 vs. 22.93, $F = 9.92$, $p = 0.0007$). Likewise, global mental health scores improved significantly at follow-up (8.73 vs. 10.36 vs. 12.13, $F = 8.44$, $p = 0.0014$). According to the post hoc analyses, the most statistically significant changes occurred between baseline and 30-day follow-up. The exception to this pattern was nightmares, which did not show significant improvement until day 70.

Discussion

In recent years, cannabinoids have been increasingly used to treat psychiatric disorders, including PTSD, despite the evidence on their therapeutic potential being underdeveloped and mixed [29, 36]. The current pilot study aimed to contribute to our understanding of the effects of MMJ on PTSD symptoms and associated sleep disturbances using a prospective study design. Our primary findings were that individuals with PTSD reported improvements in overall PTSD symptom severity 30 and 70 days after initiating MMJ. Post hoc analyses revealed that most participants experienced a significant improvement in PTSD severity by the 30-day timepoint and that these improvements were maintained through day 70. In addition to improvements in overall PTSD symptom severity, participants reported improvements in sleep quality and duration, as well as reduced nightmare frequency. Moreover, they reported reductions in negative affect and improvements in overall well-being. These findings suggest that MMJ use may be associated with clinical benefits in people with PTSD.

Our findings are in line with previous open-label studies and randomized controlled trials showing that cannabis or cannabinoid products (e.g., nabilone, THC, and whole plant cannabis preparations) are associated with improvements in PTSD symptoms, including nightmares and sleep disturbances [15, 17, 19, 27]. In addition, our findings are consistent with observational evidence from community MMJ users who self-report that it reduces their PTSD symptoms and improves their sleep quality [22]. Cannabis products may produce these beneficial effects by acting on the endocannabinoid system (eCBS), a neuromodulatory system that regulates neurotransmitter release [37–39]. The eCBS is closely involved in stress and fear regulation [40, 41], as well as in learning and memory processes [42, 43], both of which play a critical role in PTSD pathophysiology. In adults with PTSD, alterations to the eCBS have been observed, including decreased levels of endocannabinoid ligands and increased levels of endocannabinoid receptors [44]. THC directly activates cannabinoid type 1 receptors (CB1Rs) as a partial agonist, which may help to normalize eCBS activity in patients with PTSD, at least in low doses, given the biphasic effect of THC [45]. CBD exerts an anxiolytic effect by indirectly activating CB1Rs by inhibiting the uptake or enzymatic breakdown of their endogenous ligands [46–48]. When taken together with THC, CBD has been shown to offset some of the negative effects that come with higher THC doses [49]. Through these mechanisms, MMJ products may be able to alter

Table 3. Repeated measure ANOVA/Friedman test for main variables of interest ($N = 15$)

Variables	Mean (SD)			df	Error	F/χ^2	p value	Post-hoc p value**
	baseline (T1)	30-day (T2)	70-day (T3)					
PCL-5 total	49.60 (13.2)	30.33 (13.2)	29.0 (15.2)	2	24	13.25	0.0001	ac
Nightmares (PCL-5)*	2.00 (1.1)	1.57 (1.2)	0.87 (1.2)	2	26	7.54	0.023	c
Sleep duration (h)	5.03 (1.0)	6.64 (1.7)	6.83 (1.9)	2	27	8.33	0.0015	ac
Sleep quality*	2.27 (0.5)	1.21 (0.5)	1.07 (0.8)	2	27	19.48	<0.0001	ac
Sleep efficiency*	47.2 (25.8)	52.26 (22.2)	49.79 (18.0)	2	27	6.53	0.0381	a
PSQI total	13.79 (3.5)	10.62 (4.8)	9.13 (2.9)	2	25	16.54	<0.0001	ac
PANAS negative affect	31.64 (8.1)	24.14 (10.6)	22.93 (9.0)	2	26	9.82	0.0007	ac
PANAS positive affect	28.86 (9.3)	29.64 (12.4)	32.53 (8.6)	2	26	0.80	0.4618	NA
Global health-physical health	12.87 (3.3)	13.00 (3.4)	14.40 (3.0)	2	27	2.40	0.1097	NA
Global health-mental health	8.73 (2.8)	10.36 (3.9)	12.13 (2.47)	2	27	8.44	0.0014	c

*Friedman's test was used since the normality assumption for ANOVA was not met. **Post hoc p value: a indicates a significant change between baseline (T1) and 30-day (T2); b indicates a significant change between 30-day (T2) and 70-day (T3); c indicates a significant change between baseline (T1) and 70-day (T3). NA, Not applicable since the omnibus test was not statistically significant.

processes underlying PTSD maintenance and facilitate recovery, although it is important to note that negative outcomes have been associated with MMJ use as well [25, 50].

The present study was a nonrandomized, single-arm pilot study and therefore lacked a control group. As such, improvements observed in PTSD symptoms and sleep disturbances could be due to placebo effects. In fact, in a recent randomized controlled trial examining the effect of different cannabis preparations on PTSD symptoms, participants in both the active and placebo groups showed improvements in PTSD symptoms, and the magnitude of improvement did not differ between groups [27]. The authors suggest that the lack of differentiation between the active and control conditions could be due to many factors, including the fact that most participants had a history of cannabis use that may have biased their expectations upon entering the study. It is possible that expectancy effects could have also affected the findings in the present study. However, regardless of whether the effects were due to MMJ, placebo, or other unmeasured factors, the improvements reported by our participants may be clinically meaningful and warrant further exploration. This is especially true given our finding of improvements in nightmares and sleep quality, as sleep disturbances are among the most difficult-to-treat symptoms of PTSD and there is a need for new treatment approaches [11].

In addition to our primary findings, the current investigation also collected valuable data on the number of MMJ products that patients used, their THC:CBD content, frequency of use, and route of administration. We found a modest shift toward participants using fewer MMJ products at the 70-day versus 30-day follow-up. Similarly, there was a modest shift in their use frequency such that some participants reported using MMJ products fewer times per day at the 70-day follow-up. These findings may suggest that participants are still experimenting with various MMJ products and use patterns 1 month after initiation of MMJ, but that they may consolidate or stabilize their products and use frequency by the 70-day timepoint. With regard to THC: CBD ratios, we found that most participants reported using products with higher THC than CBD content at both timepoints, consistent with the preferences observed in other studies [27]. Finally, we also found that inhalation was the most common route of use at both timepoints.

Limitations to the present pilot study include small sample size and use of self-report. In particular, the use of self-report methods for tracking THC and CBD doses posed a challenge as participants had difficulty accessing and accurately recording this information. In future trials partnering with MMJ clinics, it may be beneficial to verify THC and CBD doses directly with the prescribing physicians. It would also be beneficial to track PTSD and sleep outcomes using more objective measures, such as clinician-rated assessments of PTSD symptoms and polysomnograpy or actigraphy for sleep metrics. The lack of a control group limited our ability to determine the effects of MMJ above and beyond placebo, and future randomized controlled trials are greatly needed to clarify this issue. In addition, we had a limited follow-up period of 70 days and were unable to determine with our current study design and analytic approach the order in which symptom change occurred (e.g., if improvement in sleep symptoms preceded or followed an improvement in daytime PTSD symptoms). It would be beneficial for future studies to examine and compare these trajectories

of change and also explore how patient-level factors may influence them to determine which patients may benefit most from MMJ use.

Despite these weaknesses, our study also had several strengths. Individuals with confirmed PTSD were included in the study and prospectively assessed, reducing the potential for recall bias, which was present in many prior studies in this area. In addition, we were able to obtain baseline data before participants initiated MMJ and while they were abstaining from any recreational marijuana use. We tracked and reported descriptive statistics regarding MMJ use patterns and preferences of our participants, which may help inform future clinical and research considerations. 94% of participants were successfully retained across the two follow-up timepoints, suggesting positive feasibility and study engagement.

Conclusions

The current pilot study adds to the growing literature evaluating the therapeutic potential of MMJ for patients with psychiatric conditions. While our findings showed improvements in PTSD symptom severity and sleep disturbances among MMJ users, they occurred in the context of a small, nonrandomized, single-arm pilot study and will require future replication and clarification. Nonetheless, these results highlight the potential of MMJ in improving patient outcomes for those with PTSD, particularly concerning sleep disturbances, which often do not respond to currently available treatments. Future randomized controlled trials are needed to further this line of research and inform public policy and clinical decision-making.

Acknowledgments

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Statement of Ethics

This study protocol was reviewed and approved by the Institutional Review Board of the University of Florida, approval number IRB201903193. Written informed consent was obtained from all study participants.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Krishna Vaddiparti: conceptualization, methodology, funding acquisition, and writing-original draft; Yiyang Liu: formal analysis (Table 2) and writing-review and editing; Sarah Bottari: writing-review and editing and visualization; Carly Crump Boullosa: investigation and collection of data; Zhi Zhou: data curation, formal analysis, and writing-review and editing; Yan Wang: resources and writing-review and editing; John Williamson: validation and writing-review and editing; and Robert L. Cook: resources and writing-review and editing.

Data Availability Statement

Data cannot be shared publicly because of sensitive information on the use of medical marijuana. Data are available from the University of Florida's Ethics Committee's approval for researchers who meet the criteria for access to confidential data. Further inquiries can be directed to the corresponding author.

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