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RESEARCH ARTICLE

Medical Cannabis for Chronic Posttraumatic Stress Disorder in Dutch Veterans: A Health Care Evaluation

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ABSTRACT

Introduction: Medical cannabis has emerged as a promising treatment for Posttraumatic Stress Disorder (PTSD), particularly among veterans. Given the high prevalence of PTSD in this population and the limited availability of effective therapeutic options, medical cannabis has garnered increased interest. However, evidence remains scarce endorsing its efficacy and patients' experiences with this treatment.

Method: To gain more insight into patients' experiences with medical cannabis, we interviewed 18 Dutch veterans diagnosed with chronic PTSD who were prescribed off-label medical cannabis for symptom relief at an outpatient clinic in the Dutch Military Mental Health Service. The interviews were recorded and transcribed verbatim, followed by a framework analysis with thematic coding.

Results: A group of 18 patients turned to medical cannabis as an alternative to traditional treatments due to persistent symptoms of PTSD. Of these, 15 continued using the Bediol strain, primarily before bedtime to aid sleep. They reported significant improvements, including increased peace of mind and reduced irritability. Although patients expressed satisfaction, they often asked assistance in dosage and reimbursement. Despite initial reservations from some family members, there was notable support, signaling a changing perception of medical cannabis through increased education. However, a few patients still faced lingering stigma. Through the analysis, five overarching themes were identified: (1) assessment phase, (2) intervention phase, (3) termination phase, (4) access and availability, and (5) social support.

Conclusion: Based on the data collected, we advocate for the continued prescription of medical cannabis, as most of the interviewed patients reported positive effects, including alleviation of core symptoms like sleep disturbances, irritability, and hyperarousal. Secondly, we recommend the continued reimbursement of medical cannabis due to its positive impacts, as many patients expressed potential financial hardship if this reimbursement were halted. Furthermore, we propose the appointment of a cannabis coach to provide patient-centered care. Reliable information on cannabis use is often challenging for patients to access, and proper use, including dosage, strain, cannabidiol (CBD) to Tetrahydrocannabinol (THC) ratio, and timing of administration, is essential to ensure optimal benefits and minimize risks. Lastly, we emphasize the necessity for further research, including longitudinal studies and randomized controlled trials, to explore individualized treatment approaches that work best under specific conditions. Greater clarity on dosages and product selection is also essential to minimize confusion and potential over- or under-consumption risks. Overall, these recommendations can guide the advancement of medical cannabis treatment for chronic PTSD in veterans, enhancing patient outcomes and paving the way for evidence-based practices.

Keywords: PTSD, Cannabis, Veterans, Health Care Evaluation.

Introduction

Posttraumatic Stress Disorder (PTSD) is a psychiatric condition that can arise following exposure to a traumatic event. Its clinical manifestations include re-experiencing the trauma, avoidance, emotional numbing, and hyperarousal.¹ Many patients experience a profound decline in their quality of life due to these symptoms.² The prevalence of PTSD is notably high in the general population and even more pronounced among military veterans (up to 34.84%).^{3,4} While there is considerable knowledge about the neurobiological alterations associated with PTSD, the evidence about effective treatment options remains limited. Cognitive Behavioral Therapy (CBT) is widely recommended as the primary therapeutic approach, with support from Brief Eclectic Psychotherapy (BEP), Eye Movement Desensitization and Reprocessing (EMDR), or Narrative Exposure Therapy (NET).⁵ However, the efficacy of these psychotherapy modalities is modest, with only 67% of patients achieving full recovery.^{6,7,8} Psychopharmacology is often used in conjunction with psychotherapy to augment treatment outcomes. Sertraline, paroxetine, fluoxetine, and venlafaxine are the commonly recommended medications for PTSD. Nonetheless, these medications have not demonstrated sufficient efficacy, highlighting the need for alternative therapeutic options.^{9,10,11}

In recent years, there has been growing interest in exploring cannabinoids as a potential treatment avenue for PTSD. This emerging field of research holds promise and may offer new possibilities for enhancing therapeutic outcomes for individuals living with PTSD.^{12,13} Since 2003, the Netherlands has had a program for medical cannabis. The supply of medical cannabis in The Netherlands is subject to stringent regulation and oversight by the Office for Medical Cannabis, an established government department responsible for compliance with the Opium Law by the United Nations Treaty and ensuring the quality of medical cannabis. Permits are granted to selected growers, with the entire harvest purchased and retained by the Office of Medical Cannabis. Subsequently, the cannabis undergoes gamma radiation irradiation at a designated company to eliminate any potential microbes, parasites, and fungi. Before distribution to pharmacies, the cannabis undergoes rigorous laboratory testing to ensure its safety and quality. Bedrocan, a single designated company, grows all medical cannabis in the Netherlands.¹⁴ It adheres to the Good Manufacturing Practice (GMP) standards set by the European Medicines Agency, ensuring that crops produced for medical use are safe and consistently contain desired levels of cannabinoids and terpenes. Through strict protocols and hygiene

measures, Bedrocan provides that its cannabis is free from pesticides, heavy metals, bacteria, and fungi.

A key advantage of Bedrocan's standardized cultivation process is that each plant receives the same amount of water, light, and nutrition and is harvested, cut, and dried at precisely the same time. As a result, the medical cannabis grown by Bedrocan exhibits chemical and genetic consistency over time, allowing patients to anticipate similar effects with each use and researchers to study the substance without concern for inter-dose variability. Overall, the regulated and standardized supply of medical cannabis in The Netherlands, spearheaded by Bedrocan, may serve as a model for ensuring the safety, quality, and predictability of medical cannabis products for patients and researchers alike.

Previous research has yielded mixed findings regarding the efficacy of cannabis as a treatment for PTSD. Several studies have reported improvements in PTSD symptoms among patients who use cannabis.^{15, 16, 17} However, it is crucial to acknowledge the limitations of these studies. For instance, Greer et al.'s study only included participants who had already experienced symptom improvement with cannabis use.¹⁵ Conversely, specific reviews have been unable to verify the efficacy of cannabis for PTSD conclusively.^{18,19}

Despite the inconclusive evidence, some doctors resort to off-label prescriptions of cannabis for patients with chronic PTSD who struggle with nightmares and sleep disturbances. It is essential to exercise caution in this practice, given the need for more robust research to establish the therapeutic benefits and potential risks associated with cannabis use for PTSD.

Several countries are piloting medical cannabis for PTSD. In Canada, medical cannabis has been widely prescribed to patients with PTSD, with Nabilone, a synthetic cannabinoid, initially named based on research showing significant relief for patients.²⁰ Subsequently, medical cannabis was also prescribed, leading to a substantial increase in prescriptions for military veterans. In 2021-2022, one in forty veterans (n=17,495) received medical cannabis prescriptions, amounting to 1453 kilograms reimbursed, marking an eightfold increase compared to five years prior.²¹ This rapid surge in medical cannabis prescriptions in Canada raises important considerations. On the one hand, it could suggest that medical cannabis is highly effective in treating PTSD, reflecting its increasing acceptance and success. On the other hand, it could

also raise concerns, given that current evidence on its efficacy may not be sufficiently robust.

In the Netherlands, the prevalence of medical cannabis use for veterans with PTSD is relatively modest. A single psychiatrist (EV) within the Dutch Military Mental Health Service began prescribing medical cannabis in 2016. The exact number of prescribing psychiatrists and veterans using medical cannabis remains unclear, necessitating further research. During the time of this study period, cannabis was reimbursed. Although currently, approximately one in 3500 military veterans in the Netherlands receive medical cannabis for PTSD treatment, there is a possibility that use may increase, mirroring the Canadian experience. Additionally, unregulated cannabis use is prevalent among veterans in the Netherlands due to its availability in dispensaries.

To ensure proper monitoring and a comprehensive understanding of medical cannabis experiences among veterans with PTSD, further research is crucial. Addressing potential concerns and gathering more data will be essential in assessing the long-term impact and effectiveness of medical cannabis as a treatment option for PTSD in veterans. Based on anecdotal evidence, this study aims to provide insights into patient experiences using medical cannabis for symptom relief for PTSD in Dutch veterans. Previous research by Krediet et al. explored cannabis use in military veterans with PTSD, revealing a positive overall experience-based theme.²² However, this study involved a focus group with only seven participants. In contrast, our research sought to enhance the breadth of understanding by recruiting a larger sample size of long-term cannabis users (n=18) among Dutch veterans. To capture comprehensive information, we conducted semi-structured interviews for this study, allowing participants to share their unique experiences of using cannabis for PTSD treatment in-depth. By delving into the patient perspective, this study sheds light on the potential benefits and challenges associated with medical cannabis use in managing PTSD symptoms among Dutch veterans.

Method

STUDY SAMPLE

Before considering a prescription of cannabis, patients must meet specific criteria, including having an ineffective response to at least one trauma-based psychotherapy (e.g., EMDR or exposure therapy) and pharmacological treatment (e.g., sertraline and paroxetine) for PTSD. Additionally, patients must be 25 or older and experience nightmares and sleep problems related to chronic PTSD.

Exclusion criteria for medical cannabis use encompass severe comorbid medical conditions, current or previous moderate to severe substance abuse, or impulse control problems in the context of personality disorder. Patients with comorbid or previous psychotic disorder, dissociative disorder, or manic/hypomanic episode, as well as those predisposed to psychotic disorders or at high risk of suicide, are also excluded. Furthermore, pregnant or breastfeeding individuals or those expecting to have a child within the next three months are not eligible for medical cannabis use.

Patients who meet these criteria receive medical cannabis according to the hospital's protocol, starting with the cannabis strain, Bediol, in oil form (sublingual) and transitioning to the strain, Bedrocan, if the initial effect is insufficient.

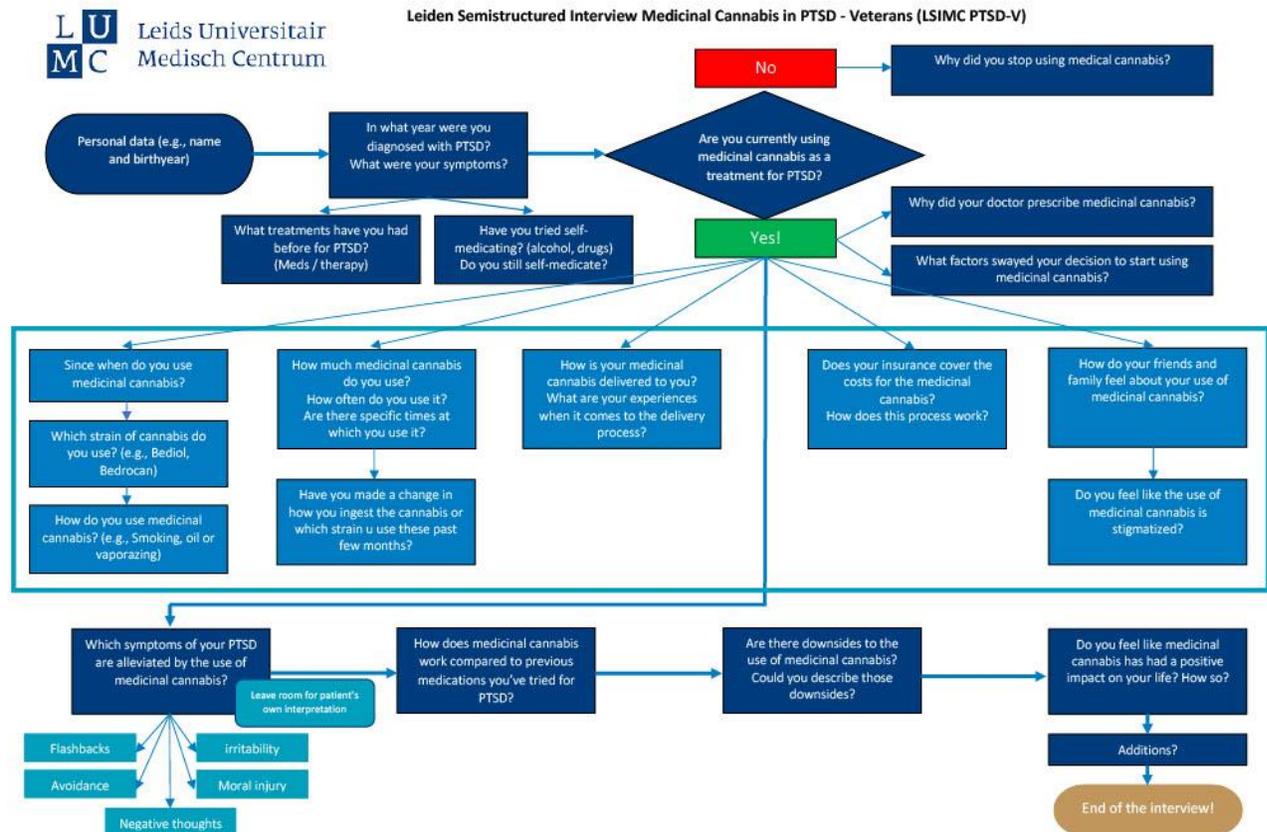
This study was conducted at the Leiden University Medical Centre in collaboration with the Central Military Hospital. Initially, approximately 30 military veterans in the Netherlands were using medical cannabis prescribed by a doctor for their PTSD, and this study sought to explore the experiences and outcomes of medical cannabis use in this specific population.

Data collection

Participants in this qualitative study on patient experiences using medical cannabis among Dutch veterans were invited via email by their respective psychiatrists. After obtaining informed consent, an independent researcher conducted semi-structured interviews with the participants. While two interviews occurred at an outpatient clinic, the rest were conducted remotely. Recruitment continued until data saturation was achieved, indicated by the absence of new information emerging from the data (n=18). The semi-structured interview guide, presented in Figure 1, was designed collaboratively by the research team (JDW, EV) and served as a flexible framework for guiding the conversation. It drew on common themes identified in Krediet et al.'s focus group research, providing an insightful foundation for the interview process.²²

On average, each interview lasted approximately 30 minutes and was audio-recorded to ensure accurate transcription. Subsequently, the interviews were transcribed verbatim to preserve the integrity of the data. The study received ethical approval from the Medical Research Ethics Committee of the University Medical Centre Utrecht. The committee confirmed that the Medical Research Involving Human Subject Act did not apply to this study (WAG/mb/19/013711), ensuring that all ethical considerations were met during the research process.

Figure 1. The Leiden Semistructured Interview for Medicinal Cannabis in PTSD - Veterans (LSIMC PTSD)



Analysis

Approximately 540 minutes of audio data transcribed from the interviews were processed and analyzed using MAXQDA 22 software. A framework analysis with thematic coding methodology was employed to examine the transcribed data systematically. The data was thoroughly reviewed multiple times to understand the content comprehensively. This process allowed for the developing of meaningful themes and subthemes, employing inductive and deductive analysis approaches.

Following the thematic coding, the identified themes were thoroughly discussed among all authors, engaging in collaborative deliberation until a consensus was achieved. This rigorous analytical process ensured the robustness and validity of the findings, contributing to the reliability of the study's conclusions.

Results

The study included 18 participants aged between 37 and 68 years, with only one female participant (5.6%). Among the participants, 14 were still using medical cannabis (77.8%), three had discontinued its use (16.7%), and one individual grew their own cannabis (5.6%). The participants reported using different cannabis strains with varying Tetrahydrocannabinol (THC) and Cannabidiol (CBD) percentages. The administration routes differed, with 13 participants (72.2%) using sublingual methods and five (27.8%) employing inhalation through smoking or vaporizing. Most patients used medical cannabis before sleep, while others used it during the day. Further details on patient characteristics are presented in Figure 2.

Figure 2. Patient characteristics listed by age, sex, year of diagnosis, current medical cannabis use, duration of medical cannabis use, cannabis train, CBD% and THC%, route of administration, dose, and dose schedule.

	Age (years)	Sex	Diagnosed (year)	Current military employed	Current MC use	Duration of MC use	Cannabis strain*	Percent of medical content (%)		Route of administration	Dose (per day)	Dose schedule
								CBD	THC			
1	68	Male	2016	No	Yes	2 y	Bediol	2.0	1.3	Sublingual	20 drops	Before sleep and when necessary
2	49	Male	1996 /2000	No	Yes	1 y	Bedrocan	<1.0	22	Inhalation (smoking)	0.7 gr	In the evening
3	40	Male	2010	Yes	Yes	1,5 y	Bedrocan	<1.0	2	Sublingual	18 - 20 drops 12 - 14 drops	In the morning Before sleep
4	52	Male	2015	No	Yes	3 y	Bediol	2.0	1.3	Sublingual	56 drops	Three times a day
						Bedrocan /Bedrolite	5.0	10	6.5 drops**		Before sleep	
5	54	Male	2011	No	Yes	3 y	Bediol	2.0	1.3	Sublingual	7 drops	Before sleep
6	46	Male	2004	No	Yes	3 y	Bediol	8	6.3	Inhalation (smoking)	0.7 gr	During the day
						Bedrocan	<1.0	22	0.36 gr		At night	
						Bedrolite	7.5	<1.0	0.57 gr		At night	
						Bedica	<1.0	14	0.18 gr		During the day	
7	55	Male	2004	No	Yes	1 y	Bediol	2.0	1.3	Sublingual	6 - 7 drops***	Before sleep and during the day when necessary
						Bedrolite	2.0	<1.0				
8	53	Male	2016	Yes	Yes	5 mo	Bediol	2.0	1.3	Sublingual	5 - 8 drops	Three times a day
9	37	Female	2016	Yes	No	2 wks	Bediol	2.0	1.3	Sublingual	3 - 6 drops	Before sleep
10	47	Male	2012	No	Yes	2.5 y	Bedrocan	<1.0	22	Inhalation (smoking)	0.5 gr	Before sleep
11	51	Male	2014	No	Yes	4 y	Bedrocan	<1.0	2	Sublingual	3 drops	Before sleep
12	66	Male	2011	No	No	3 y	Bediol	2.0	1.3	Sublingual	10 drops	Before sleep
13	61	Male	2009	No	Yes	1 y	Bediol	2.0	1.3	Sublingual	8 drops	Before sleep
									6 drops		In the morning when necessary	
14	42	Male	2017	No	No	2 mo	Bediol	2.0	1.3	Sublingual	Variable amounts	In the afternoon and before sleep
						Bedrocan	<1.0	2				
15	47	Male	2010	No	Yes	10 y	Home-grown	Unknown		Inhalation (smoking, vaporizing)	3 - 4 gr	During the entire day
16	52	Male	2012	No	Yes	3 y	Bediol	2	1.3	Sublingual	16 drops	Before sleep
17	55	Male	2015	No	Yes	7 mo	Bedrocan	<1.0	2	Sublingual	4 drops	Before sleep
18	61	Male	2001	No	Yes	2 y	Bedrocan	<1.0	22	Inhalation (smoking)	0.14 - 0.18gr	In the evening
						Bedica	<1.0	14	0.14 - 0.18gr			

*Bediol: Cannabis sativa L. Elida.; Bedrocan: Cannabis sativa L. Afina.; Bedica: Cannabis sativa L. Talea.; Bedrolite: Cannabis sativa L. Rensina

**Tapering of

*** Strain depending on need to drive

The semi-structured interviews yielded five overarching themes based on patients' responses, which align with themes identified in Krediet et al.'s study (22). Three themes focused on distinct phases of medical cannabis use, (1) the assessment phase, (2) intervention period, and (3) termination phase.

The other two themes centered around general aspects of medical cannabis, including (4) access and availability and (5) social support. Subthemes for these overarching themes are detailed below and can be found in Figure 3.

Figure 3. Identified themes and subthemes

ASSESSMENT PHASE	INTERVENTION PHASE	TERMINATION PHASE
<p>PTSD Symptoms</p> <p>Experiences with previous medication</p> <p>Assessment factors</p> <ul style="list-style-type: none"> • Alternative medication • Natural product • Suffer from symptoms • Better something than nothing • Previous experience with cannabis • Barrier to drugs 	<p>Administration of medical cannabis</p> <ul style="list-style-type: none"> • Cannabis strains • Doses • Route of administration <p>The search for proper use</p> <ul style="list-style-type: none"> • Need for information <p>Efficacy of medical cannabis</p> <ul style="list-style-type: none"> • Therapeutic effects • Ineffective in treating some symptoms <p>Comparison with other medications</p> <p>Negative consequences</p>	<p>Permanent termination</p> <p>Temporary termination</p>
<p>AVAILABILITY</p> <ul style="list-style-type: none"> • Access and delivery of medical cannabis • Reimbursement for medical cannabis 		
<p>SOCIAL SUPPORT</p> <ul style="list-style-type: none"> • Reaction from friends and family • Stigma 		

1 Assessment phase

Before the patients started using medical cannabis, they considered other options and advantages and disadvantages of using medical cannabis. During this time, patients often suffered from PTSD symptoms, even though they were using prescription drugs.

1.1 PTSD SYMPTOMS

The patients suffered considerably from their symptoms, even using pharmaceutical medicines. Those symptoms described by the patients can be divided into three groups; aggression and irritability, sleep and nightmares, and hyperarousal and fear. Every patient mentioned difficulty with sleep, specifically that they only slept a few hours per night or suffered from nightmares. "I slept about three hours a night, and I did that for years." (cc07). This was the main reason medical cannabis was considered and prescribed to the patients.

In addition, many patients felt more irritable or showed aggression toward their surroundings. "I was heavily aggressive, paranoia to placing booby traps in my home." (cc03)

Another common symptom was hyperarousal. Many patients experienced hypervigilant awareness of their surroundings and difficulty relaxing. "The

battle mindset and the hyperarousal never went away." (cc03)

1.2 EXPERIENCES WITH PREVIOUS MEDICATION

Before the patients began with medical cannabis, they had tried a variety of pharmaceuticals and therapies. Almost every patient experienced substantial side effects from previous medications. As previously mentioned, this was one consideration in using medical cannabis. Patients reported not feeling like themselves while using prescription medications. "I felt that everything had leveled off, no more lows but also no more highs. Just like a kind of zombie."(cc02). "I just lived in a kind of cloud; I was foggy all day." (cc12)

In addition, several patients suffered from physical side effects. "The side effects from Citalopram, like the gastrointestinal complaints, were terrible."(cc11). "I tried it [other medication] for a few months, and I believed that I could fly."(cc12)

Furthermore, some patients mentioned that the doses had to be increased to maintain therapeutic effects. "At a certain point, you get used to it, and then it has a lesser function."(cc13) These and other reasons made the patients look for a different type of medication.

1.3 ASSESSMENT FACTORS

Patients in the interviews mentioned multiple assessment factors. Most patients said they wanted an alternative to their current medication. “For me, it was straightforward; I wanted to get rid of the Zopiclon, the sleeping medication. Because that is just chemical crap and my body is just tired.”(cc11)

Four more patients (22.2%) expressed that they appreciated the natural state of medical cannabis compared to chemical medication. “If I can replace the chemical product with a natural product, that would be nice.”(cc11). “Because the cannabis oil is on a natural basis. I was in favor of that.” (cc09)

As previously mentioned, many patients mentioned they experienced side effects from previous medication and wanted to try something different. “I had quite a lot of side effects from the medication, dizziness and stuff like that. I thought, well, it is good if I get off the medication”. (cc07)

Eight patients did not experience improved PTSD symptoms from their previous medication, which made them consider medical cannabis. “Well, because the regular medicines helped a little bit but not enough.” (cc01)

For some patients, the PTSD symptoms were so intense that they were willing to try anything. “The symptoms you experience dominate your life in such

a way that you feel like you have to do something.” (cc03)

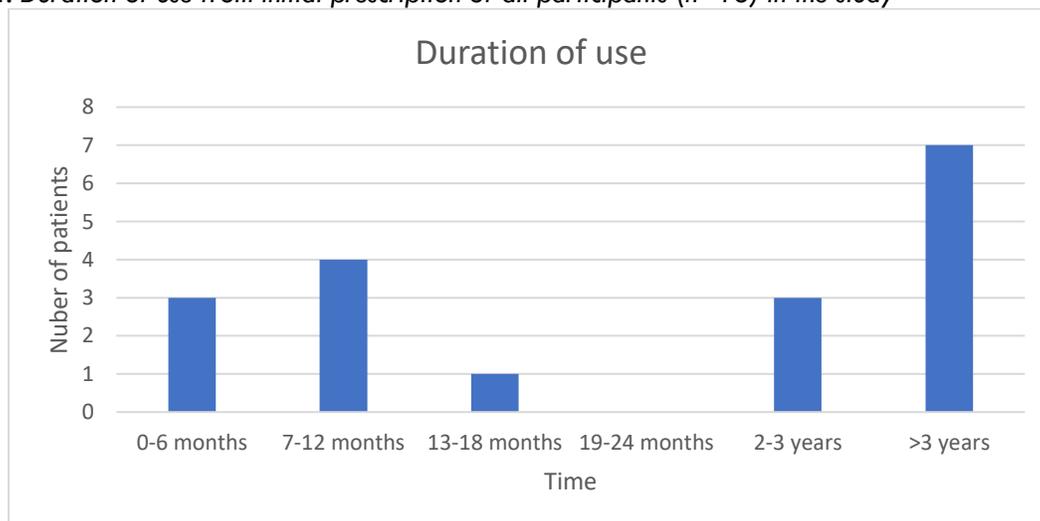
Three patients (16.7%) mentioned that they had previous experience with cannabis, which made them more likely to try medical cannabis. “Because I was already familiar with, let us say, self-medication. So I already had experience with MDMA [3,4-Methylenedioxyamphetamine] and cannabis.” (cc04)

In addition to the positive consideration factors, four patients (22.2%) mentioned a barrier to using drugs. All patients worked for the military, where there is a no-tolerance policy when it comes to drug use, and some even helped to stop drug trafficking, which made them uncomfortable using drugs. “In my career, I have worked against drugs; it was a bit weird to use it myself.” (cc16)

2 Intervention phase

The patients can be divided into two groups; short-term users (<1.5 years) and long-term users (>1.5 years), as shown in Figure 4. The duration of the intervention or application phase depends on the following variables: the timing of the use for the treatment of PTSD, the variety of cannabis strains and dosage, the length of their struggle to find relief, the extent of relief they achieve, and how it compares to the conventional prescription medication treatments.

Figure 4. Duration of use from initial prescription of all participants (n=18) in the study



2.1 ADMINISTRATION OF MEDICAL CANNABIS

The administration of medical cannabis can differ widely. Patients use different cannabis strains (i.e., Bediol, Bedrocan, Bedrolite, Bedica, and homegrown) with varying CBD and THC levels, routes of administration, and doses. All patients had started with Bediol and switched to Bedrocan, which

contains higher THC levels if they were not experiencing enough reduction of symptoms. Most patients still use Bediol; 7 patients (38.8%) switched or added Bedrocan, as shown in Figure 5. Only two patients (11.1%) tried different strains like Bedrolite, which does not contain THC, or Bedica, which contains exceptionally high levels of THC.

The two routes of administration used by the patients are sublingual (using oil) and inhalation (smoking and vaporizing). Of the 18 patients, 13 use medical cannabis sublingually (73.8%), as shown in Figure 5. They expressed that they did not like the smell, taste, or side effects of smoking. There are five patients (27.8%) who smoke medical cannabis and one patient who also vaped (5.6%) medical cannabis. For two patients, the oil did not have the desired effect. In contrast, another patient mentioned that it takes at least a half hour before the oil works, and they notice an immediate impact when they administer the cannabis by smoking. Two patients also mentioned that they appreciate the ritual of smoking medical cannabis. "With the oil, you do not take the moment of rest that you do have with smoking." (cc02). "The oil did not work at all.

And now there are some rituals in the evening. Maybe that also helps, that it is just in your head, the ritual." (cc18)

Most patients who use medical cannabis sublingually started with three drops a day and increased until the desired effect was achieved. When they felt "stoned," they were instructed to lower the dose. Most patients currently use a little under ten drops a day. The patients who smoked medical cannabis all started at different amounts and then raised the doses until the desired effect was achieved. As well as differing doses, patients differ in the time of day they administer the cannabis. One patient used it all day, whereas the other only used it before bed. For more information on dosing data, see Figure 1.

Figure 5. Population distribution of cannabis strain and route of administration

Cannabis strain	Number of patients
Bediol	11
Bedrocan	7
Bedrolite	2
Bedica	2
Homegrown	1
Route of administration	
Sublingual (oil)	13
Smoking	5
Vaporizing	1

2.2 THE SEARCH FOR PROPER USE

With so many options for consuming medical cannabis, it is tough for each individual to find an effective product. Many patients struggled to find the right strain and dose of medical cannabis. They mentioned that it required a lot of perseverance and energy to get to the right dose, which not all patients possess. "Of course, finding out which strain fits well was quite a puzzle, and you must have some perseverance. However, you will see progression when the right chord is struck, and you use the right strain at some point." (cc04)

However, finding the correct dose for one patient was too tricky. It led to too many moments where the patient did not experience the desired effects of the cannabis and as many moments where the patient experienced a stoned feeling. "Yes, I have tried, but I feel like it is a search, and I did not finish that search." (cc09)

Multiple patients mentioned that they felt they would have benefited from more guidance and explanations from their healthcare provider during the search for proper use. Because research regarding precision medicine for medical cannabis is in its infancy, patients were allowed to experiment with dosing. The patients expressed that they experienced difficulty with the lack of

information they received about dosing. One patient mentioned using different strains mixed with high doses while searching for the correct strain and dose. This led to a "greening out," a phenomenon that causes hyperemesis in users of cannabis. "It was when I was trying to find out what I should take and what amount. I had four or five different bottles, and I was trying everything, which resulted in too much cannabis and nicotine intake. Moreover, I think I threw up every morning for a week or two." (cc18) He mentioned that starting with low doses and taking more every other day instead of immediately using high doses is important.

Furthermore, it was mentioned by some patients that it is difficult to determine the dose because they experience different stress levels each day. This means that the amount required to suppress their symptoms varies daily. "You cannot take one pill; you are a different person every day. Tomorrow you will not feel like today; that is not possible and not possible for a military with PTSD" (cc06)

2.3 EFFICACY OF MEDICAL CANNABIS

Of the 18 patients, 15 (83.3%) reported that medical cannabis improved their sleep. While some patients experienced fewer nightmares, others felt they could fall asleep more easily. The patients

slept longer and felt more peaceful during sleep. This resulted in patients feeling more relaxed and less irritable during the day. "It gave me, for the first time, more than 4 hours of sleep. I sleep now almost 7 hours every night, and I am not very aware of the nightmares I have had." (cc16)

"If I have a good night's sleep, I wake up well. With standard medicine, I woke up angry in the morning. So I could not have anyone near me, which lasted all day. Moreover, that is no longer the case with medical cannabis." (cc01)

In addition to sleeping better, 11 patients (61.1%) also reported that medical cannabis reduced their feelings of anger and irritability. "If I have a trigger during the day, then there is a certain anger that also arises, and if I take it [medical cannabis], then it just disappears. So then I am also more pleasant for my environment." (cc01) In general, patients felt calmer and less irritated. "I found myself more tolerant. I could react more calmly to certain things, whereby I sometimes bent out of shape or could go on a rampage. That became calmer. (cc12)

Furthermore, almost every patient mentioned they felt less distress and hyperarousal. When they took cannabis, they felt a calmness come over them and experienced greater peace of mind. "It feels like a warm blanket surrounding you" (cc04). "It takes the edge off alertness for me. It gives me a kind of stable feeling, a calm feeling. Moreover, the moment I, for whatever reason, feel more alertness or arousal coming on, those drops work pretty quickly, and I notice that I am showing some normal behavior again. So I feel more calm and, as a result, more balanced." (cc08) "It is purely that hyperarousal, the speed of my brain is slowed down so that I do not hear those sounds increase in the evening and at night. That I have that peace of mind, that I am not overstimulated with those sounds." (cc10)

As well as the previously mentioned reduction in symptoms, in some patients, the use of medical cannabis led to a decrease in their use of other psychotherapeutic medications. When all patients were asked if medical cannabis positively affected their lives, 13 patients (72.2%) agreed. "I smile again, I sing again. Yes, for me, medical cannabis is just right." (cc18)

2.4 COMPARISON WITH OTHER MEDICATIONS

When the patients were asked to compare medical cannabis to other medications, almost all stated that cannabis was a much better product. Where other drugs flattened all emotions, medical cannabis did not. "It [medical cannabis] dampens my symptoms,

but you still feel like yourself and not completely zombie-like from that chemical junk." (cc03)

With medical cannabis, patients also suffered fewer side effects. Most patients experienced side effects from other medications, such as loss of libido, headache, stomach ache, and dizziness, which they did not experience with medical cannabis. "I do not have stomach cramps anymore; I do not have diarrhea anymore; my muscles are no longer in revolt. Of course, I used my body well, but with Citalopram, you are a zombie. You cannot ride a bike for 100m because all your muscles blow up." (cc11)

Some patients mentioned that medical cannabis worked much better or was the only medication that helped reduce their symptoms. Furthermore, they expressed that it did not feel like taking medication. It felt more natural, and they did not feel the same level of physical dependency they felt with other medications. Another advantage compared to other medications mentioned by the patients was that they could quickly stop the medication when they wanted to. Citalopram, for example, takes a month to taper off gradually. They felt more addicted to their pharmaceutical medication and expressed that it was more challenging to stop taking it. Last, they liked that they could adjust their dose of medical cannabis when they felt they needed it, for example, if they had a bad night or a stressful day. "With medical cannabis, you can see for yourself. If I am more restless, I take an extra drop. So you can adjust a little yourself. And of course, you don't have that with those tablets; you have to take them" (cc13)

2.5 NEGATIVE CONSEQUENCES

Seven patients (38.9%) did not experience negative consequences from medical cannabis; other patients experienced an adverse reaction. Four patients (22.2%) mentioned they felt stoned when they took, intentionally or unintentionally, too much medical cannabis. Further adverse effects that some patients mentioned were feeling anxious, depressed, or drowsy at times. One patient noticed that he was starving after using medical cannabis. Another disadvantage mentioned by three patients (16.7%) was the inconsistency of the effect of medical cannabis. Sometimes they noticed more of an impact and a sluggish or stoned feeling, while others experienced little to no effect. "Now and then, the medical cannabis hits a little harder than another day. Sometimes you are exhausted and a bit sluggish, well, I get through that." (cc03)

The five patients (27.8%) who only noticed relief when they smoked the medical cannabis mentioned

they did not like inhaling the smoke with all the health consequences. Furthermore, they said that they did not like the taste and the smell. Also, some family members said they do not like the smell and do not want their partner to smoke inside the house. This means those patients must remove themselves from family life and step outside, which they experience as a disadvantage. In addition, one patient mentioned that he did not feel comfortable smoking his joints everywhere because of the current stigma associated with cannabis. "Well, sometimes you do worry about smoking. And when you smoke in the house, the house stinks, that is one of the downsides." (cc02)

"A downside, for example, is that it's difficult to use publicly. I would not stand in a busy street and light a joint for myself and others. Some people are disturbed by that, and I do not want to stir that up, so that is why. So I do it secretly; I will sit in my car or something similar". (cc06)

Another disadvantage of medical cannabis is the cost. Currently, medical cannabis is being reimbursed for veterans by their healthcare organizations. However, there is concern about reimbursement since this situation is unstable. Some patients reported failing to get reimbursed (n=4), while the reimbursement went smoothly with others. Some patients who are not receiving a refund for the medical cannabis and have to pay the total amount themselves mentioned that they wanted to try a higher dose but could not afford the accompanying cost. "I was under pressure because of the costs. I do not want to use it a lot because it costs me a lot. Maybe I will have a wonderful life if I double my dose, but I do not dare to try it with my financial position yet." (cc16). More patients mentioned that if reimbursement were to stop, they would not be able to afford medical cannabis.

The last disadvantage patients mentioned was concern about the product's legality in other countries. While one patient already had to pay multiple fines for the possession of cannabis and for driving while using cannabis, another patient reported he was terrified that he would be caught. "I am terrified that I will be tested at customs or the police abroad when I am in an accident, and I will be THC positive. That frightens me." (cc16)

3 Termination phase

While most patients still used medical cannabis at the start of this research, three patients (16.7%) had discontinued their use for different reasons. In addition, some patients temporarily suspended using medical cannabis for various reasons.

3.1 PERMANENT TERMINATION

Three patients (16.7%) decided to discontinue medical cannabis. The first patient discontinued because she felt the effect of the medical cannabis was inconsistent. Some nights she did not experience any relief, while other nights, she felt stoned. "Sometimes it worked nicely, and then I had that morning where I felt stoned, and then I had nights where I felt paranoid. For me, it was not stable." (cc09)

The second patient decided to quit because he experienced some relief. However, it was not enough for him. He hoped it would do more and felt that medical cannabis did not meet his expectations. At the time, he used a lot of medication and decided he wanted to quit all medication. The last patient did not experience any relief. He increased his dosage until he experienced a stoned feeling, indicating that too much was taken. Unfortunately, he still did not experience any comfort at this dose. "I just did not notice the effect, and I felt like I was stoned, and I did not like that feeling" (cc14)

3.2 TEMPORARY TERMINATION

Two patients (11.1%) mentioned that they temporarily discontinued their use of medical cannabis during specific times. One patient stopped using it when he went on vacation to avoid complications at the border. The other patient mentioned that when the effects began to wear off, he stopped using and restarted later to experience relief once again. Many patients said discontinuing their medical cannabis is much easier than discontinuing other medications. They found it less addictive and appreciated that they did not have to reduce their dose slowly.

4 Availability of medical cannabis

In the Netherlands medical cannabis is delivered by one supplier and delivered by number of pharmacies. The patients can get medical cannabis by a prescription from their psychiatrist. At the time of this research, medical cannabis was reimbursed by the Health Insurance System for veterans.

4.1 ACCESS AND DELIVERY OF MEDICAL CANNABIS

Of the 15 patients who still use medical cannabis, 2 (13.3%) patients pick up their medication at the pharmacy, and 13 (86.7%) patients have it delivered to their residences. All patients reported that they had good experiences with delivery. "I am continuously informed of what time they will bring it and who will bring it. I think it is great." (cc07). The patients choose when they want their medication delivered and are constantly informed if there are any changes to their delivery. "It is a severe

pharmacy, and the courier service that they have is perfect.” (cc18)

However, sometimes things went wrong with the payment or prescription during the ordering process, which caused delivery delays. This meant that patients had to order early to avoid extra stress. “I cannot say I need medical cannabis next week; I will order it today because too often it goes wrong, so I need to order a month ahead.” (cc04)

4.2 REIMBURSEMENT FOR MEDICAL CANNABIS

The costs per patient in this project range between €12,- and €500,-, depending on the cannabis strain and the dose. The average costs are €105,- per patient per month. One patient who grew his cannabis was not included; however, his costs would be around €1000,- per month if he obtained the cannabis through the pharmacy. The average chronic PTSD patient uses an antidepressant, like an SSRI, a benzodiazepine, and an atypical antipsychotic. The average cost per patient for these medications is €36,- per month, significantly lower than the cost for medical cannabis.^{23, 24, 25} During this research medical cannabis was reimbursed for most of the participating veterans as part of the Health Insurance (reimbursement from agency Algemeen Burgelijk Pensioenfonds ABP [General Civil Pension Fund]) for veterans with PTSD. However, only 12 of the 18 patients received compensation. One patient grew his cannabis, and one patient, a British veteran, was rendered ineligible for compensation based on his citizenship. The reasons why the four remaining patients did not receive reimbursement are unknown. Furthermore, most patients did not receive compensation from the start. Receiving compensation was described as complex and stressful for some patients. “At the beginning with ABP [the reimbursement agency], the care coordinator reacted weirdly. That it would not be reimbursed and that it was only a money matter.” (cc02)

Patients pay for their medication when they order it, submit their receipts to the reimbursement agency (ABP), and, if approved, receive their reimbursement. Delays in reimbursement occur, creating additional stress for patients who need financial support. When patients do not receive their refund, they must contact the reimbursement agency (ABP) to inquire, which causes unnecessary stress. “So in the entire story, my only comment is that this process should not go through me but directly through The Ministry of Defence and that I only get the cannabis sent.” (cc04)

5 Social support

Patients experienced positive as well as negative

social interactions while using medical cannabis. Most patients told their family and friends about their medical cannabis use, and the reactions they received differed between patients. There were also various responses to medical cannabis use in their daily social lives, where some patients were stigmatized, and their medical cannabis was perceived as a recreational street drug.

5.1 REACTIONS FROM FRIENDS AND FAMILY

On average, most patients' family members and friends accepted the idea of them trying medical cannabis for their ailment. “They have just seen me struggling all this time. And to try something which is also legal, let me put that first, to see if that helps, everyone was open to that, of course. If it helps, it helps.” (cc14) Once they noticed that their loved one had found a medicine which helped them with their symptoms, family and friends were even more pleased with the medical cannabis. “They are all pleased, everyone. Everyone who knows me. Anyone who knows me from before and now. They see the difference between the past and the present from the look in my eyes.”(cc04)

The spouses of two patients even suggested that medical cannabis could work for them and wanted to try it themselves. By experiencing relief from taking medical cannabis, some patients have increased the interest of relatives and friends, who wonder if they, too, could benefit from CBD oil. Where most family members and friends reacted positively to medical cannabis, a few patients' family members had to get used to the idea. They were not happy that their loved one started using, in their eyes, a form of street drug. However, once it was better understood, family members were more accepting of it. “Well, his psychiatrist already mentioned it a few years ago, and then I was like, that is drugs. It would be best if you did not start with that. Then we often discussed it with his psychiatrist, and he convinced me too.”(cc wife of 18)

Notably, several patients chose not to tell their friends or family members due to a lack of interest in sharing with others or in others' opinions. One patient decided not to share that they were taking medical cannabis for fear of being disciplined at work.

5.2 STIGMA

Of the 18 patients, 8 (44.4%) feel like the use of medical cannabis is stigmatized. They mentioned that many people associate medical cannabis with recreational/street drugs and perceive it as bad. “Many people do not know what it is about. They hear the word drugs, and they have heard

something about that, and then the indoctrination starts, ooh, that is drugs that's bad for you. Yes, of course, that is not true." (cc06)

Some patients also experience judgment in their personal lives because they use cannabis. They mentioned that people avoid them or criticize them for using what is, in their view, drugs. "You only have to stand somewhere and smoke; then you already have people who look at you stupidly or criticize you." (cc10)

Patients experienced differences in people's opinions about smoking cannabis versus using cannabis oil. Where almost every patient who smokes cannabis experienced stigma, only 30% of the oil users felt stigmatized. Furthermore, some patients mentioned that medical cannabis is far less stigmatized than recreational cannabis, and what you call it influences people's opinions. "Not medical cannabis but cannabis as a product, yes. As you name it differently, it turns into a bigger deal. If you call it weed, it becomes synonymous with criminal activity and drug trafficking, and all the shows you see on television, all Netflix shows, are linked to it." (cc11)

Patients also expressed that when they explained to people where they get their medical cannabis from, its effect on their symptoms, and how they still function with medical cannabis, people are more inclined to see it as a medicine and not as street drugs. This reduced some stigma. "When you say I am on cannabis, people immediately think you smoke it. However, I also add that I do not get it in the store because you do not know what is in the oil. I get it prescribed, and then people react differently, more positively." (cc13)

In addition, some patients felt like stigma decreased over time. They reported that more people have started to use CBD oil and are more familiar with using cannabis as a therapy option.

Discussion

The use of medical cannabis as a potential treatment for PTSD has gained increased attention in recent years. Several studies have explored the effects of cannabinoids, such as cannabidiol (CBD) and tetrahydrocannabinol (THC), in alleviating the symptoms associated with PTSD, including intrusive thoughts, anxiety, and sleep disturbances. The findings suggest that medical cannabis may offer a novel approach to managing these symptoms, offering potential relief to individuals who have not responded well to conventional treatments.

This is the first study to evaluate veterans' experiences of medical cannabis through in-depth

interviews revealing five distinct phases and themes: (1) assessment phase, considering PTSD symptoms, experience with previous medication, and assessment factors (2) intervention phase, with administration of cannabis, and search for proper use, efficacy of cannabis, comparison with other medications, negative consequences (3) termination phase, with permanent termination, temporary discontinuation (4) access and availability, with access and delivery theme, reimbursement and (5) social support, with reactions from friends and family and stigma as nodes and subnodes. Patients sought medical cannabis as an alternative to conventional medications to address persistent symptoms despite traditional treatments. Among the 18 patients initially included, 15 continued using medical cannabis, primarily the Bediol strain, the first step in the dosing schedule. Most patients took Bediol before bedtime to aid sleep and reported significant improvements in various symptoms, such as increased peace of mind and reduced irritability. While patients expressed overall satisfaction with medical cannabis, they faced challenges in determining the appropriate dosage and navigating the reimbursement process. Despite some family members' initial reservations, many were supportive, and patients noted a shift in the stigma surrounding medical cannabis with hopes for positive change through increased education. However, a few patients still encountered the stigma associated with its use. This study highlights the need for enhanced guidance on dosing and reimbursement processes while underscoring the potential of medical cannabis as a valuable treatment option for veterans, fostering improved well-being and symptom relief.

As the introduction mentions, recent research has shown promising results with medical cannabis for PTSD. Importantly, cannabis interacts with the endocannabinoid system, which plays a crucial role in regulating stress responses and emotional memory. This interaction provides a biological basis for understanding how cannabinoids may modulate the hyperarousal and fear responses commonly seen in PTSD. By addressing these underlying neurobiological mechanisms, medical cannabis could offer a unique avenue for treating the root causes of PTSD rather than merely managing symptoms.

Recent literature has provided growing evidence supporting this use. Several studies have indicated that the cannabinoids found in cannabis, such as cannabidiol (CBD) and tetrahydrocannabinol (THC), may have therapeutic properties that can help alleviate PTSD symptoms, including intrusive thoughts, anxiety, and sleep disturbances. These

cannabinoids interact with the endocannabinoid system, which plays a crucial role in regulating stress responses and emotional memory^{12,13}. Some studies have shown that medical cannabis can help reduce the severity and frequency of nightmares, a particularly distressing symptom for many veterans with PTSD. For individuals with PTSD, nightmares can be especially disruptive, leading to heightened anxiety and sleep deprivation. While the exact mechanisms are not fully understood, it is believed that cannabinoids interact with the body's endocannabinoid system, which plays a role in regulating sleep cycles and emotional responses. However, it is important to note that individual responses to medical cannabis can vary, and the potential for side effects and long-term use should be carefully considered in consultation with healthcare professionals when exploring cannabis as a sleep aid for PTSD. For instance, Greer et al. reported a remarkable 75% reduction in CAPS score, a measure of PTSD symptoms, in patients using medical cannabis.¹⁵ Similarly, Reznik demonstrated a decrease in CAPS score and reduced usage of painkillers and sedative pharmacological agents.¹⁷ Forsythe et al. and Orsolini also found that cannabinoids improved various PTSD symptoms, including sleep quality, hyperarousal, and treatment-resistant nightmares, which aligns with the findings in this study.^{23,24} There is a difference in veterans who use cannabis for recreational purposes with those that use it for medicinal purposes. Browne et al. showed that the latter group reported significantly lower other drug use, alcohol or drug-related problems, or alcohol or drug use disorders.²⁵ Furthermore Metrik reported that veterans who use cannabis for medicinal purposes did better in sleep, physical, and mental health functioning than those who use it for recreational purposes.²⁶

However, it is important to note that some studies, like Black et al., did not find sufficient evidence to suggest that cannabinoids improve PTSD symptoms.¹⁸ Nevertheless, their review included low-quality studies, focusing not solely on PTSD symptoms. Additionally, Steenkamp et al. found that cannabis increases the risk of developing depression, anxiety, psychosis, and substance use disorder, commonly comorbid with PTSD.¹⁹ While good counseling can help minimize the risk of a substance use disorder, it is crucial to remain aware of this possibility.

While the patients observed in our study did not exhibit signs of depression, anxiety, or psychosis resulting from cannabis use, it remains crucial to undertake longitudinal research to evaluate potential associated risks comprehensively. Recent

findings by Turna and MacKillop underscore the importance of directly studying the therapeutic effectiveness of cannabis-based therapies among veterans, a perspective that aligns with their review of cannabis use.²⁷ Yet, it is being argued by Wolfgang and Hoge that the favorable outcomes that patients report with medical cannabis for both pain and PTSD currently are better explained by expectancy biases than by a treatment effect.²⁸ Engaging in further research will provide a better understanding of the safety and efficacy of medical cannabis in addressing PTSD, enabling more precise conclusions to be drawn on its potential benefits. It should also be studied in light of the administrative burdens veterans face accessing legal, medical cannabis and how they may be compounded as medical uses are being legalized in different countries.²⁹

Krediet et al. previously explored patients' experiences with medical cannabis in focus group sessions, with 6 out of 7 patients expressing high satisfaction, consistent with our study findings.²² However, utilizing personal interviews, our study revealed patients' challenges in finding the proper dose and strain and their need for accurate information about medical cannabis. Notably, our study sample was double that of Krediet et al., and it needs to be marked that an independent researcher conducted interviews to mitigate bias.

The significance of these findings lies in the potential for medical cannabis to fill a treatment gap for individuals with treatment-resistant PTSD. Traditional therapies like cognitive-behavioral therapy (CBT) and selective serotonin reuptake inhibitors (SSRIs) do not work for everyone, leaving many patients with limited options⁶. Recent emerging evidence supporting the efficacy of medical cannabis suggests that it could be a valuable addition to the therapeutic toolkit for mental health professionals^{30,31,32}.

However, it is essential to emphasize that while the findings are promising, there are several caveats to consider. The long-term safety of medical cannabis, potential side effects, and the risk of dependence or misuse require careful evaluation. Additionally, individual responses to cannabis can vary widely, necessitating personalized treatment plans and close monitoring by healthcare providers.

This sample size in this study was small due to the limited number of veterans using medical cannabis in the Netherlands, with only one female participant. Additionally, most patients were under the care of the same prescribing psychiatrist, as few psychiatrists currently incorporate medical cannabis

in PTSD treatment. Moreover, only three patients discontinued medical cannabis, which may have affected the study's outcomes.

Our study provides valuable insights into veterans' experiences with medical cannabis. However, further research is essential to explore the efficacy of medical cannabis and compare outcomes with different cannabis strains to understand its potential benefits for PTSD treatment better.

Conclusion and recommendations

This study sheds light on veterans' experiences with chronic PTSD using medical cannabis, utilizing interviews to gain unique insights. Based on the gathered data, we propose the following recommendations:

1. **Continued Prescription of Medical Cannabis:** The study reveals that medical cannabis positively impacted 15 out of 18 patients, reducing core symptoms such as lack of sleep, restlessness, irritability, and hyperarousal. Patients preferred medical cannabis over other medications due to its effectiveness and minimal side effects, improving overall quality of life. Hence, we advocate for the continued prescription of medical cannabis to patients with chronic PTSD.
2. **Continued Reimbursement of Medical Cannabis:** Despite the relatively higher costs compared to conventional treatments, we recommend the continuation of medical cannabis reimbursement. Several patients expressed financial hardships if the reimbursement were to cease, potentially leading to discontinuing medical cannabis use. Quality of life should not be compromised based on financial limitations.
3. **Introduction of a "Cannabis Coach":** To provide patient-centered care, we suggest incorporating a "cannabis coach" in the treatment team. This certified health practitioner can offer personalized guidance on strain selection, administration methods, and dosing, ensuring optimal outcomes. A social psychiatric nurse could fulfill this role, preventing unnecessary cost escalation.
4. **Clarity on Doses and Products:** We advocate for increased transparency regarding product information and dosing to enhance user-friendliness. Inconsistencies in THC and CBD

percentages between different sources were identified, leading to confusion and potential dosing errors. Standardizing and clarifying dosing measurements are essential to prevent overconsumption or underconsumption.

Further Research on Effectiveness and Risks: Although medical cannabis shows promise, there remains a need for extensive research to understand its risks and determine the most effective dose schedules and strains. Longitudinal studies and randomized controlled trials (RCTs) should explore optimal treatment protocols for specific patient profiles, considering factors such as age, gender, and diagnoses.

Finally, the research on the medical use of cannabis for the treatment of PTSD offers new insights into alternative therapies for this complex and debilitating condition. While the findings are significant and suggest a potential breakthrough in symptom management and addressing the underlying neurobiology of PTSD, further research is needed to fully understand the nuances of dosing, safety, and long-term effects³³. By adopting the recommendations in this paper, we can optimize the use of medical cannabis for veterans with chronic PTSD, ensuring better treatment outcomes and improved quality of life. The evolving landscape of medical cannabis as a treatment for PTSD underscores the importance of continued investigation, clinical trials, and collaboration between researchers and healthcare professionals to advance our understanding and provide the best care for individuals living with PTSD.

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References

1. Burbach, L., Brémault-Phillips, S., Nijdam, M. J., McFarlane, A., & Vermetten, E. (2023). Treatment of Posttraumatic Stress Disorder: A State-of-the-art Review. *Curr. Neuropharmacol.*
2. Rapaport MH, Clary C, Fayyad R, Endicott J. Quality-of-life impairment in depressive and anxiety disorders. *The American Journal of Psychiatry.* 2005; 162(6): 1171-8. <https://doi.org/10.1176/appi.ajp.162.6.1171>
3. Xue C, Ge Y, Tang B, et al. A Meta-Analysis of Risk Factors for Combat-Related PTSD among Military Personnel and Veterans. *PLoS One.* 2015; 10(3). <https://doi.org/10.1371/journal.pone.0120270>
4. Lyk-Jensen SV, Weatherall CD, Jepsen PW. The effect of military deployment on mental health. *Economics and Human Biology.* 2016; 23: 193-208. <https://doi.org/10.1016/j.ehb.2016.09.005>
5. American Psychological Association. Clinical Practice Guideline for the Treatment of Posttraumatic Stress Disorder. [Internet]. Available from: <https://www.apa.org/ptsd-guideline/treatments>. [Accessed 13 August 2023].
6. Kitchiner NJ, Lewis C, Roberts NP, et al. Active duty and ex-serving military personnel with post-traumatic stress disorder treated with psychological therapies: systematic review and meta-analysis. *European Journal of Psychotraumatology.* 2019; 10(1)
7. Steenkamp MM, Litz BT, Hoge CW, et al. Psychotherapy for Military-Related PTSD, A Review of Randomized Clinical Trials. *Journal of the American Medical Association.* 2015; 314(5): 489-500. DOI: 10.1001/jama.2015.8370
8. Bradley R, Greene J, Russ E, et al. A multidimensional meta-analysis of psychotherapy for PTSD. *The American Journal of Psychiatry.* 2005; 162(2): 214-227 <https://doi.org/10.1176/appi.ajp.162.2.214>
9. Cipriani A, Williams T, Nikolakopoulou A, et al. Comparative efficacy and acceptability of pharmacological treatments for post-traumatic stress disorder in adults: a network meta-analysis. *Psychological Medicine.* 2018; 48(12): 1975 – 1984. <https://doi.org/10.1017/S003329171700349X>
10. Hoskins MD, Bridges J, Sinnerton R, et al. Pharmacological therapy for post-traumatic stress disorder: a systematic review and meta-analysis of monotherapy, augmentation, and head-to-head approaches. *European Journal of Psychotraumatology.* 2021; 12(1). <https://doi.org/10.1080/20008198.2020.1802920>.
11. Hoskins M, Pearce J, Bethell A, et al. Pharmacotherapy for post-traumatic stress disorder: Systematic review and meta-analysis. *The British Journal of Psychiatry.* 2015; 206(2): 93-100. Doi: 10.1192/bjp.bp.114.148551
12. Ney LJ, Matthew A, Bruno R, et al. Cannabinoid interventions for PTSD: Where to next? *Progress in Neuro-Psychopharmacology and Biological Psychiatry.* 2019; 93: 124-140. <https://doi.org/10.1016/j.pnpb.2019.03.017>.
13. Hill MN, Campolongo P, Yehuda R, et al. Integrating Endocannabinoid Signaling and Cannabinoids into the Biology and Treatment of Posttraumatic Stress Disorder. *Neuropsychopharmacology.* 2018; 43(1): 80-102. DOI: 10.1038/npp.2017.162
14. Bedrocan. Over Bedrocan – Onze methode. [Internet]. Available from: <https://bedrocan.com/nl/over-bedrocan/onze-methode/>. [Accessed 20 October 2021].
15. Greer GR, Grob CS, Hakberstadt AL. PTSD Symptom Reports of Patients Evaluated for the New Mexico Medical Cannabis Program. *Journal of Psychoactive Drugs.* 2014; 46(1): 73-77. <https://doi.org/10.1080/02791072.2013.873843>.
16. Passie T, Emrich HM, Karts M, et al. Mitigation of post-traumatic stress symptoms by Cannabis resin: A review of the clinical and neurobiological evidence. 2012; 4(7-8): 649-59. <https://doi.org/10.1002/dta.1377>
17. Reznik I. P.4.a.011 Post-traumatic stress disorder and medical cannabis use: a naturalistic observational study. *Drug testing and analysis.* 2012; 22(2): 363-364. [https://doi.org/10.1016/S0924-977X\(12\)70563-1](https://doi.org/10.1016/S0924-977X(12)70563-1)
18. Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *The Lancet Psychiatry.* 2019; 6(12): 995-1010. [https://doi.org/10.1016/S2215-0366\(19\)30401-8](https://doi.org/10.1016/S2215-0366(19)30401-8)
19. Steenkamp MM, Blessing EM, Galatzer-Levy IR, et al. Marijuana and other cannabinoids as a treatment for posttraumatic stress disorder: A literature review. *Depression and Anxiety.* 2017; 34(3): 207-216. <https://doi.org.ezproxy.leidenuniv.nl/10.1002/da.22596>
20. Jetly R, Heber A, Fraser G, et al. The efficacy of nabilone, a synthetic cannabinoid, in the treatment of PTSD-associated nightmares: A

- preliminary randomized, double-blind, placebo-controlled cross-over design study. *Psychoneuroendocrinology*. 2015; 51: 585-588. <https://doi.org/10.1016/j.psyneuen.2014.11.002>
21. Government of Canada. Cannabis for Medical Purposes. [Internet]. Available from: <https://www.veterans.gc.ca/eng/about-vac/research/research-directorate/publications/reports/cmp#statistics>. [Accessed 27 January 2022]
 22. Krediet E, Jansen DGA, Heerdink ER, et al. Experiences with medical cannabis in the treatment of veterans with PTSD: Results from a focus group discussion. *European Neuropsychopharmacology*. 2020; 36: 244-254. <https://doi.org/10.1016/j.euro-neuro.2020.04.009>.
 23. Forsythe ML, Boileau AJ. Use of cannabinoids for the treatment of patients with post-traumatic stress disorder. *Journal of Basic and Clinical Physiology and Pharmacology*. 2021. <https://doi.org/10.1515/jbcpp-2020-0279>
 24. Orsolini L, Chiappini S, Volpe U, et al. Use of Medicinal Cannabis and Synthetic Cannabinoids in Post-Traumatic Stress Disorder (PTSD): A Systematic Review. *Medicina*. 2019; 55(9): 525. <https://doi.org/10.3390/medicina55090525>
 25. Browne K, Leyva Y, Malte CA, Lapham GT, Tiet QQ (2022). Prevalence of medical and non-medical cannabis use among veterans in primary care. *Psychology of Addictive Behaviors*, 36(2), 121–130. <https://doi.org/10.1037/adb0000725>
 26. Metrik J, Bassett SS, Aston ER, Jackson KM, Borsari B. Medicinal versus recreational cannabis use among returning veterans. *Transl Issues Psychol Sci*. 2018 Mar;4(1):6-20. doi: 10.1037/tps0000133.
 27. Turna J, MacKillop J. Cannabis use among military veterans: A great deal to gain or lose? *Clin Psychol Rev*. 2021 Jan 11;84:101958. doi: 10.1016/j.cpr.2021.101958
 28. Wolfgang AS, Hoge CW. Cannabis and Cannabinoids for Pain and Posttraumatic Stress Disorder in Military Personnel and Veterans. *JAMA Psychiatry*. 2023 Sep 1;80(9):869-870. doi: 10.1001/jamapsychiatry.2023.1685.
 29. Mallinson DJ, Puello F. Veterans and Medical Cannabis: A Perfect Federalism Storm. *Public Administration Quarterly*. 2023;47(3): 347-373
 30. Metrik, J., Stevens, A. K., Gunn, R. L., Borsari, B., & Jackson, K. M. (2022). Cannabis use and posttraumatic stress disorder: prospective evidence from a longitudinal study of veterans. *Psychological medicine*, 52(3), 446-456.
 31. Walsh, Z., Mitchell, I., Crosby, K., St Pierre, M., DeClerck, D., Ong, K., & Lucas, P. (2023). A small clinical trial of vaporized cannabis for PTSD: suggestive results and directions for future study. *Trials*, 24(1), 1-4.
 32. Bonn-Miller, M. O., Brunstetter, M., Simonian, A., Loflin, M. J., Vandrey, R., Babson, K. A., & Wortzel, H. (2022). The long-term, prospective, therapeutic impact of cannabis on post-traumatic stress disorder. *Cannabis and cannabinoid research*, 7(2), 214-223.
 33. Coelho, M. P., Duarte, P., Calado, M., Almeida, A. J., Reis, C. P., & Gaspar, M. M. (2023). The current role of cannabis and cannabinoids in health: A comprehensive review of their therapeutic potential. *Life Sciences*, 121838.