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After studying this article, you should be able to:

- Encourage cessation or prevention of the use of marijuana by patients with posttraumatic stress disorder

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Marijuana Use Is Associated With Worse Outcomes in Symptom Severity and Violent Behavior in Patients With Posttraumatic Stress Disorder

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ABSTRACT

Objective: An increasing number of states have approved posttraumatic stress disorder (PTSD) as a qualifying condition for medical marijuana, although little evidence exists evaluating the effect of marijuana use in PTSD. We examined the association between marijuana use and PTSD symptom severity in a longitudinal, observational study.

Method: From 1992 to 2011, veterans with *DSM-III/IV* PTSD (N=2,276) were admitted to specialized Veterans Affairs treatment programs, with assessments conducted at intake and 4 months after discharge. Subjects were classified into 4 groups according to marijuana use: those with no use at admission or after discharge ("never-users"), those who used at admission but not after discharge ("stoppers"), those who used at admission and after discharge ("continuing users"), and those using after discharge but not at admission ("starters"). Analyses of variance compared baseline characteristics and identified relevant covariates. Analyses of covariance then compared groups on follow-up measures of PTSD symptoms, drug and alcohol use, violent behavior, and employment.

Results: After we adjusted for relevant baseline covariates, marijuana use was significantly associated with worse outcomes in PTSD symptom severity ($P < .01$), violent behavior ($P < .01$), and measures of alcohol and drug use ($P < .01$) when compared with stoppers and never-users. At follow-up, stoppers and never-users had the lowest levels of PTSD symptoms ($P < .0001$), and starters had the highest levels of violent behavior ($P < .0001$). After adjusting for covariates and using never-users as a reference, starting marijuana use had an effect size on PTSD symptoms of +0.34 (Cohen $d = \text{change}/\text{SD}$), and stopping marijuana use had an effect size of -0.18.

Conclusions: In this observational study, initiating marijuana use after treatment was associated with worse PTSD symptoms, more violent behavior, and alcohol use. Marijuana may actually worsen PTSD symptoms or nullify the benefits of specialized, intensive treatment. Cessation or prevention of use may be an important goal of treatment.

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Considerable interest and controversy have arisen regarding the clinical benefits and risks of marijuana for the treatment of various medical conditions.¹ Medical marijuana is now legal in at least 23 states,² although it remains illegal under federal law. Approval has come through state legislative processes or by direct

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popular vote, and thus medical marijuana has not met scientific standards typically required by the US Food and Drug Administration.³ Posttraumatic stress disorder (PTSD) has been approved in at least 9 states as a qualifying condition for use of medical marijuana.² However, thus far, little is known about the effect of marijuana on PTSD; there have been no randomized controlled trials evaluating its efficacy or safety.

Preclinical studies suggest that specific cannabinoids (cannabidiol) may show therapeutic promise in treating PTSD.^{4,5} Survey studies suggest that PTSD patients report feeling better subjectively as a result of marijuana use⁶ and that patients who use marijuana are more likely to report doing so to help them cope with their symptoms than for reasons such as social motives, conformity, or enjoyment.⁷⁻⁹ Other studies suggest, to the contrary, that PTSD contributes to the development of cannabis use disorder.^{10,11} At best, the most rigorous studies merely show a noncausal association between PTSD and marijuana use.¹² The only longitudinal studies thus far involve a Veterans Affairs (VA) inpatient treatment program; these show that less improvement in PTSD during treatment was associated with greater risk of marijuana use at follow-up¹³ and that the presence of a marijuana use disorder at admission is associated with less improvement in PTSD symptoms.¹⁴ These studies, however, did not exclude veterans with other forms of substance use or alcohol misuse and did not directly compare outcomes for veterans who initiated cannabis use with outcomes for veterans who stopped using or never used marijuana. All other studies to date have been cross-sectional in nature and thus have failed to address any longitudinal relationship between symptom severity in PTSD and subsequent marijuana use.

In 1992, the Veterans Health Administration system implemented a national data collection system that monitored outcomes of over 47,000 veterans treated in specialized intensive PTSD programs through 2011.¹⁵ Here, we present data from all sites participating in this national program evaluation effort over a 20-year period. None of the veterans were prescribed medical marijuana. However, as part of the program evaluation, data were collected on voluntary use of marijuana in the 30 days prior to program entry and again in the prior 30 days, 4 months after discharge. Because of the large sample size, we were able to identify subsamples who reported marijuana use but no other use of drugs or use of alcohol to intoxication at the time of admission as well as veterans who reported no drug use at all. We have thus been able to examine the relationship between change in marijuana use (in the absence of other initial drug or alcohol misuse) and change in PTSD symptoms and other outcomes (violent behavior, employment, and alcohol use), which we chose on the basis of their important association with PTSD.¹⁶⁻¹⁹ On the basis of previous literature showing that substance use is associated with worse PTSD symptom outcomes,²⁰ we hypothesized that marijuana use would likewise be associated with greater symptom severity.

- Medical marijuana has been approved for treatment of posttraumatic stress disorder (PTSD) in several states, despite an absence of clinical trials evaluating efficacy and safety.
- Psychiatrists are frequently asked whether they would recommend marijuana for PTSD.
- This study shows that starting marijuana use may be associated with worse outcomes in PTSD.

METHOD

The study was approved by the Institutional Review Board of the West Haven Center of the VA Connecticut Healthcare System and was given a waiver of informed consent.

Participants

Data were drawn from the national evaluation of specialized intensive PTSD programs implemented by the Northeast Program Evaluation Center of the Veterans Health Administration from 1992 to 2011. All patients entering these programs were evaluated at baseline and 4 months after discharge using a standardized set of sociodemographic and clinical measures. The sample from which the subjects were selected included 47,310 veterans with a diagnosis of PTSD (*DSM-III* criteria until 1994; *DSM-IV* criteria thereafter). To minimize confounding from the effects of substances other than marijuana, we excluded subjects with problematic alcohol use (more than 2 drinks on 1 occasion), those with any drug use other than marijuana in the 30 days prior to admission, and those who entered treatment on transfer from an inpatient or residential program that would have restricted their access to alcohol or drugs. Any drug use was defined as having reported use of any other substances (cocaine, amphetamines, crack cocaine, heroin, “downers,” or hallucinogens) besides cannabis. From the initial sample of 47,310 patients, 12,770 were found to meet inclusion criteria, according to the following groups: (1) those reporting no marijuana use prior to admission or after discharge ($n = 11,344$)—“never-users”; (2) those reporting marijuana use at admission but not at 4 months after discharge ($n = 299$)—“stoppers”; (3) those reporting use at admission and 4 months after discharge ($n = 296$)—“continuing users”; and (4) those reporting no use at admission but reporting use 4 months after discharge ($n = 831$)—“starters.” We considered the last group (starters) to be a rough proxy for those who might have used medical marijuana for PTSD. To provide more balanced samples, 850 subjects were randomly selected from the never-user group, yielding a total analytic sample of 2,276 veterans.

Measures

Measures available from the dataset included sociodemographic characteristics, clinical data (PTSD symptom severity, other comorbid psychiatric diagnoses, history of psychiatric hospitalization, drug and alcohol use severity measures, chronic medical problems), community adjustment variables, and treatment program characteristics. Outcomes included

4-month follow-up assessments of PTSD symptom severity, employment status, violent behavior, and composite measures of alcohol and drug use from the Addiction Severity Index (ASI).²¹

Clinical data. PTSD symptom severity was measured by the Short Form of the Mississippi Scale for Combat-Related PTSD (range, 11–55), which has been described and validated elsewhere.²² Other measures addressed the participation in or witnessing of atrocities by self-report, history of war-zone service, and receipt of service-connected disability benefits related to PTSD.

Treatment program characteristics. Characteristics of treatment program included discharge status, length of stay, year of admission to program, and whether the veteran had been on a waiting list prior to admission to the program. Discharge status reflected the conditions under which the veteran left the program, using the following classifications: successful completion of the program, departure associated with unacceptable behavior or violation of program rules, choosing to leave prematurely (without staff concurrence), being assessed as too sick to continue in the program, or being transferred to another program.

Community adjustment variables. Variables assessing a veteran's community adjustment included employment status, violent behavior, history of incarceration, and whether the veteran was planning on attending military reunions after discharge. Employment status was assessed as the average number of days a veteran had worked for pay in the previous 30 days using items from the ASI.²¹ Violent behavior was assessed using a 4-item self-report questionnaire from the National Vietnam Veterans' Readjustment Study.²³

Data Analysis

First, analysis of variance was used to compare baseline characteristics of the 4 marijuana use groups (never-users, starters, stoppers, or continuing users). These characteristics (sociodemographic features, baseline clinical variables, community adjustment variables, and characteristics of program participation) could potentially confound comparison of postdischarge outcomes between the groups. Because 5 outcome measures were examined and the sample size was substantial, an α level of .01 was used to test for statistical significance.

Variables that were found to be significant on the bivariate analysis were used as covariates in a subsequent analysis of covariance (ANCOVA) that compared the groups at follow-up on PTSD symptoms and other outcomes controlling for potential baseline confounders. If the overall ANCOVA was significant at $P < .01$, t tests were used to compare adjusted means. Subsequently, a linear multiple regression analysis including all marijuana users (whether at baseline or follow-up) was conducted to examine the association of change in days of marijuana use from before to after program entry and change in PTSD symptoms, violent behavior, days of employment, and the ASI alcohol and drug use composite scores, again controlling for potential baseline confounders, including the baseline values of the change

variables (to adjust for regression to the mean). Standardized regression coefficients were used to evaluate the strength of association between change in days of marijuana use and change in other outcomes.

RESULTS

General Sample Characteristics

The sample consisted of 2,276 veterans with a mean age of 51.7 years ($SD = 8.6$); the majority (96.7%) were male. Most were white (72.7%), while 21.2% were African American, and 6.1% were reported as "other." Married veterans comprised 40.7% of the sample, while an equivalent portion (40.7%) were separated/divorced, and 1.9% were widowed. The mean education level of the sample was 12.9 years ($SD = 1.9$). A slight majority (51.4%) had a history of incarceration. Comorbid psychiatric diagnoses included affective disorder (28.4%), anxiety disorder (12.2%), personality disorder (8.2%), bipolar disorder (4.3%), psychosis other than schizophrenia (1.9%), and schizophrenia (0.8%). Most (86.2%) had been prescribed psychotropic medications in the past 30 days, and most (63.6%) entered the treatment program from waiting list status. The mean length of stay was 42.5 days ($SD = 22.8$).

Bivariate Analysis

Participants who never used marijuana were slightly older (53.2 years) than other groups and more likely to be married than continuing users and starters (46.5% vs 37.2% and 36.3%, respectively) (Table 1). They also had the lowest baseline ASI composite scores for both alcohol and (unsurprisingly) drugs. Generally, this group (never-users) had better measures of community adjustment, with lower rates of incarceration (compared to starters and continuing users) and lower measures of violent behavior (compared to stoppers and starters), and they were more likely to plan to attend reunions after discharge (compared to stoppers and continuing users). Veterans who were using marijuana at admission (continuing users and stoppers) had higher measures of violent behavior prior to admission than those who never used before or after the program. In measures of treatment process, continuing users had shorter lengths of stay compared to never-users and starters (38.2 vs 44.8 and 42.8 days, respectively) and were less likely to be on a waiting list than never-users and starters (53.9% vs 68.2% and 64.9%, respectively). Other than history of war-zone service, groups did not differ in measures of PTSD or other psychiatric disorders. Other variables that had a statistically significant association with marijuana use groups ($P < .01$) included race, chronic medical problems, employment status at admission, and number expelled from the program. All variables that had significant ($P < .01$) interaction with marijuana use groups were included as covariates in subsequent examination of clinical variables at follow-up.

Clinical and Community Adjustment Outcomes

After adjusting for relevant covariates, ANCOVAs revealed significant differences among marijuana use

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Table 1. Demographic, Clinical, Community, and Treatment Characteristics^a

	Never-Users [1] (n=850)	Stoppers [2] (n=299)	Continuing Users [3] (n=296)	Starters [4] (n=831)	F	P	Paired Comparisons*
Demographic variables							
Male, n (%)	568 (96.1)	210 (95.5)	223 (97.0)	573 (97.8)	1.32	.2669	
Age, mean (SD), y	53.15 (8.13)	49.28 (9.64)	49.77 (10.02)	51.76 (7.97)	21.00	<.0001	1 > 4 > 2, 3
Highest level of school, mean (SD), y	12.83 (2.05)	12.94 (1.87)	13.09 (1.73)	12.86 (1.89)	1.54	.2024	
Marital status, n (%)							
Married	395 (46.5)	119 (39.8)	110 (37.2)	302 (36.3)	6.68	.0002	1 > 3, 4
Separated/divorced	308 (36.2)	117 (39.1)	129 (43.6)	373 (44.9)	4.81	.0024	4 > 1
Widowed	16 (1.9)	10 (3.3)	6 (2.0)	13 (1.6)	1.22	.3012	
Race, n (%)							
White	597 (70.2)	215 (72.4)	243 (82.1)	597 (71.9)	5.37	.0011	3 > 1, 2, 4
African American	212 (24.9)	61 (20.5)	36 (12.2)	173 (20.8)	7.30	<.0001	1, 4 > 3
Other	41 (4.8)	21 (7.1)	16 (5.4)	60 (7.2)	1.67	.1704	
Clinical variables							
Baseline PTSD measures							
Symptom severity (SF-MISS), baseline, mean (SD) ^b	39.63 (6.00)	39.87 (5.40)	39.73 (5.59)	40.20 (5.72)	1.42	.2347	
Witnessed atrocities, n (%)	202 (23.8)	69 (23.1)	72 (24.3)	213 (25.7)	0.39	.7613	
Participated in atrocities, n (%)	138 (16.2)	45 (15.1)	51 (17.2)	165 (19.9)	1.80	.1458	
Service-connected PTSD, n (%)	468 (55.3)	155 (52.2)	161 (54.4)	452 (54.4)	0.29	.8326	
War zone service, n (%)	795 (93.6)	275 (92.3)	259 (87.5)	783 (94.2)	5.40	.0011	1, 4 > 3
Other psychiatric disease, n (%)							
Anxiety disorder	119 (14.0)	29 (9.7)	43 (14.5)	86 (10.4)	2.82	.0378	
Affective disorder	254 (29.9)	87 (29.2)	86 (29.3)	219 (26.4)	0.92	.4290	
Bipolar disorder	32 (3.8)	19 (6.4)	12 (4.1)	34 (4.1)	1.29	.2777	
Schizophrenia	8 (0.9)	2 (0.7)	3 (1.0)	7 (0.8)	0.09	.9678	
Psychosis, other than schizophrenia	19 (2.2)	7 (2.4)	4 (1.4)	14 (1.7)	0.49	.6912	
Personality disorder	62 (7.3)	23 (7.7)	28 (9.5)	74 (8.9)	0.74	.5269	
Other psychiatric disorder	34 (4.0)	14 (4.7)	14 (4.8)	38 (4.6)	0.17	.9190	
Ever hospitalized (psychiatric)	677 (79.7)	278 (93.0)	265 (89.5)	735 (88.6)	2.22	.0838	
Prescribed psychotropic medication in last 30 days, n (%)	738 (86.8)	247 (82.6)	258 (87.2)	720 (86.6)	1.30	.2735	
Drug, alcohol use							
Drug abuse at admission (ASI), mean (SD) ^b	0.0259 (0.039)	0.1027 (0.100)	0.1139 (0.097)	0.0394 (0.061)	195.17	<.0001	2, 3 > 4 > 1
Alcohol abuse at admission (ASI), mean (SD) ^b	0.0634 (0.098)	0.0984 (0.116)	0.0863 (0.086)	0.0804 (0.119)	9.62	<.0001	2, 3, 4 > 1
Chronic medical problems, n (%)	631 (74.4)	192 (64.2)	203 (68.6)	578 (69.6)	4.28	.0050	1 > 2
Community adjustment variables							
Employment status at admission (ASI), mean (SD) ^b	0.589 (0.258)	0.536 (0.273)	0.592 (0.242)	0.560 (0.259)	4.33	.0048	1, 3 > 2
Days worked in the past 30 days, mean (SD)	3.39 (8.13)	2.43 (6.57)	3.14 (7.52)	2.58 (7.01)	1.96	.1174	
Violence at admission, mean (SD) rating ^b	1.37 (1.36)	1.63 (1.32)	1.48 (1.28)	1.68 (1.42)	7.57	<.0001	2, 4 > 1
History of incarceration, n (%)	366 (43.2)	153 (51.2)	165 (55.7)	485 (58.4)	14.14	<.0001	3, 4 > 1
Willing to attend reunions, n (%)	599 (70.9)	168 (56.8)	151 (51.7)	534 (65.4)	15.05	<.0001	1, 4 > 2, 3
Treatment characteristics							
Length of stay in program, mean (SD), d	44.8 (22.4)	39.3 (23.9)	38.2 (25.2)	42.8 (22.0)	8.10	<.0001	1 > 2, 3; 4 > 3
Year of program admission	2002.7 (4.5)	2003.0 (5.0)	2003.5 (5.1)	2002.6 (4.7)	2.68	.0454	
Expelled from program, n (%)	16 (1.9)	24 (8.1)	9 (3.1)	24 (2.9)	9.18	<.0001	2 > 1, 3, 4
Transferred from program, n (%)	10 (1.2)	7 (2.4)	2 (0.7)	9 (1.1)	1.30	.2730	
Left program without staff concurrence, n (%)	30 (3.6)	13 (4.4)	21 (7.2)	25 (3.1)	3.39	.0173	
Too sick for program, n (%)	4 (0.5)	0 (0)	2 (0.7)	3 (0.4)	0.64	.5900	
Was on waiting list, n (%)	578 (68.2)	166 (56.3)	158 (53.9)	535 (64.9)	9.07	<.0001	1, 4 > 2, 3

^aData are incomplete for gender (28.5%) and days worked in the past 30 days (9.9%) and for < 1.2% of the sample for the following variables: age, education, race, PTSD symptom severity, witnessing atrocities, PTSD service connection, other psychiatric diseases, drug and alcohol abuse at admission, chronic medical problems, and community adjustment and treatment characteristic variables.

^bSF-MISS range, 11–55; ASI range, 0–1; violence rating range, 0–4.

*P < .01.

Abbreviations: ASI = Addiction Severity Index; PTSD = posttraumatic stress disorder; SF-MISS = Mississippi Scale for Combat-Related PTSD, Short Form; SD = standard deviation.

groups in several outcome measures (Table 2), including PTSD symptom severity. Starters and continuing users had significantly higher measures of PTSD symptom severity at follow-up compared to never-users and stoppers. Starters showed significantly higher measures of violent behavior at follow-up than all other groups. In measures of alcohol problems at follow-up, starters had the highest measures, while stoppers had lower measures than continuing users but did not differ from never-users. Stoppers and never-users had

lower composite scores of drug abuse (ASI) than continuing users and starters at follow-up. After adjusting for covariates and using never-users as a comparison, starting marijuana had an effect size on PTSD symptoms at follow-up of +0.34 (Cohen *d* = group difference/SD), and stopping marijuana had an effect size of –0.18. There was no difference at follow-up among the groups in employment status. Additional multivariate regression analyses, controlling for covariates identified previously, yielded similar results,

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Table 2. Relationship Between Marijuana Use and Clinical Outcomes at 4-Month Follow-Up

Outcome Variable ^a	Never-Users [1] (n = 767)	Stoppers [2] (n = 263)	Continuing Users [3] (n = 268)	Starters [4] (n = 738)	F	P	Paired Comparisons*
PTSD symptom severity (SF-MISS)	37.71 (0.228)	36.64 (0.385)	38.92 (0.383)	39.67 (0.226)	21.47	<.0001	3, 4 > 1, 2
Violence	0.87 (0.041)	0.76 (0.068)	0.93 (0.068)	1.25 (0.040)	21.28	<.0001	4 > 1, 2, 3
Alcohol abuse (ASI)	0.096 (0.007)	0.079 (0.011)	0.129 (0.011)	0.229 (0.006)	88.51	<.0001	4 > 1, 2, 3; 3 > 2
Drug abuse (ASI)	0.037 (0.0033)	0.034 (0.0056)	0.128 (0.0056)	0.130 (0.0033)	176.26	<.0001	3, 4 > 1, 2
Employment status (ASI)	0.578 (0.007)	0.575 (0.011)	0.594 (0.011)	0.577 (0.007)	0.66	.5752	

^aData presented as least-squares mean (SE), covarying for marital status, age, race, history of incarceration, waiting list status, psychosis, chronic medical problems, war zone service, length of stay, expulsion from treatment, and baseline measures of violence, PTSD, drug and alcohol abuse, and employment.

*P < .01.

Abbreviations: ASI = Addiction Severity Index; PTSD = posttraumatic stress disorder; SF-MISS = Mississippi Scale for Combat-Related PTSD, Short Form; SE = standard error.

with significant associations as measured by standardized regression coefficients between change in days of marijuana used and change in PTSD symptoms ($\beta = 0.17, t = 4.08, P < .0001$), severity of violent behavior ($\beta = 0.10, t = 2.79, P = .0054$), the ASI alcohol index ($\beta = 0.24, t = 5.60, P < .0001$), and the ASI drug abuse index ($\beta = 0.65, t = 21.62, P < .0001$).

DISCUSSION

This is the first longitudinal study of the association of marijuana use with PTSD symptom severity and other outcomes that excluded the potentially confounding effect of baseline use of other drugs or problematic alcohol use. These data show that initiating marijuana use was associated with higher measures of PTSD symptoms at follow up, with a modest effect size ($d = 0.34$) compared to never-users. Stopping marijuana use during treatment, in contrast, was associated with the greatest improvement in PTSD. Regression analyses showed statistically significant positive associations between increased days of marijuana use and more severe PTSD symptoms, violent behavior, and alcohol use, but not days of employment. This study cannot exclude the possibility that PTSD patients refractory to treatment are more likely to use marijuana in an attempt to self-medicate.

Our findings are consistent with previous longitudinal studies of the relationship between marijuana use and PTSD^{13,14} and with a previous study of substance use more generally in PTSD.²⁰ However, this study extends previous literature by directly comparing outcomes among those who begin marijuana use following treatment, those who stop use during treatment, those who continued to use before and after treatment, and those who never used. Further, our larger sample size and refined exclusion criteria (ie, recent use of other drugs and intoxication with alcohol) provide a purer sample more capable of isolating the association of initiating marijuana use among veterans with PTSD and subsequent symptom severity. Although our use of the starter group as a rough proxy for medical marijuana use is imperfect and does not take into account the frequency or quantity (ie, dosing) of recommended use for medical marijuana, it should be noted that the concept of a prescribed dose in the medical marijuana literature has not been specified, and most clinical trials of medical marijuana allow patients to self-titrate based on symptoms and tolerability.

These findings can be contextualized within existing literature suggesting that patients feel that marijuana use is helpful in the treatment of PTSD.^{6,24} The data are associational and allow for the possibility that patients with PTSD refractory to specialized, intensive treatment begin marijuana use in an effort to self-medicate. This is highlighted by the fact that among all “pure” marijuana users in this study (n = 1,426), over half (n = 831, 58%) began use after treatment. Previous research also suggests that patients feel that other substances (alcohol, heroin, benzodiazepines) may alleviate PTSD symptoms,⁶ but more objective assessments indicate that these substances are generally associated with worse outcomes.^{20,25} Our findings do not suggest, however, that marijuana is associated with improvement in PTSD. Previous evidence suggesting that marijuana improves PTSD symptoms come from isolated case reports²⁴ or studies methodologically weakened by recall bias and/or post hoc subjective assessment of symptom severity.^{6,26} Such biases are minimized in the current longitudinal study based on standard psychometric data. Another possible interpretation of these data is that marijuana use in patients with PTSD provides transient relief but that subsequent periods of withdrawal contribute to a worsening of baseline symptoms. Hence, while patients may feel that marijuana improves their PTSD, it may contribute to an overall worsening of the disorder. This is consistent with previous literature characterizing marijuana use in PTSD as a “pernicious feedback loop”⁸ and is consistent with existing theories explaining the high comorbidity of PTSD and substance abuse generally.²⁷

An unanticipated finding was the robust association of the initiation of marijuana use with higher follow-up measures of violent behavior. Previous literature regarding the association between cannabis use and violence is inconsistent.²⁸⁻³¹ Despite its popular reputation as a drug that does not induce violence, cannabis has been shown in some populations (adolescents, inner-city youth) to be associated with violent behavior.^{32,33} The only study to date examining an association between marijuana use and violence in a population diagnosed with PTSD found that patients with a recent history of violence were more likely to report recent marijuana use.³⁴ Our finding that those who started using marijuana in the months after completing treatment had higher overall rates of violent behavior could

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be partially explained by the fact that starters also had higher rates of alcohol use at follow-up (which is associated with violence^{35,36}) and that marijuana withdrawal symptoms include irritability and aggression.³⁷ Another possible interpretation is that the association between marijuana use and violence represents a selection effect or “general deviance syndrome,”³² whereby individuals who are more impulsive or prone to breaking rules or laws resort to violence as well as marijuana in the face of stress or problem situations; however, these interpretations cannot explain why starters had higher rates of violence at follow-up compared to continuing users.

Strengths of the current study include exclusion of subjects who recently used drugs other than marijuana or experienced alcohol intoxication, a large sample size, adjustment for multiple potentially confounding factors, and the longitudinal nature of the study, albeit with a relatively short follow-up period. Despite the robust statistical findings of this study, several limitations require comment. First, patients were not randomized to receive marijuana or placebo, and thus the groups cannot be considered to have been equivalent at the time of program entry. Hence, these data are associational in nature and cannot be taken as demonstrating causal relationships. Unmeasured differences between the groups at the time of program entry in areas such as impulsivity or antisocial behavior may explain both worsening symptoms and marijuana use. Second, drug use was assessed by self-report and not verified by toxicologic testing. Third, we could not assess or control for the varying

levels of cannabinoids in the marijuana used. This point is significant because Δ_9 -tetrahydrocannabinol, which is responsible for the euphoria associated with the drug, has been shown to exacerbate anxiety,³⁸ while cannabidiol has anxiolytic properties.^{39–41} Fourth, our sample was limited to older, mostly male veterans suffering from long-standing PTSD. The generalizability of our study to other populations is unknown. Finally, our assessments were conducted when veterans were presumably not under the immediate influence of marijuana. It does not address the possibility that some veterans do receive transient symptomatic relief while intoxicated.

The above limitations notwithstanding, our study has suggestive implications for clinical practice and public policy. The results of our study provide no support for the hypothesis that marijuana is associated with general improvement in PTSD symptoms, and the observed associations suggest that it may actually worsen PTSD symptoms or nullify the benefits of specialized, intensive treatment. Especially in light of the adverse health effects of marijuana use,¹ these data indicate that providers should be cautious or even avoidant in using this agent to treat PTSD. Given that our study shows only associations and not causation, it remains possible that more severe PTSD symptoms drive people to seek marijuana to transiently self-medicate symptoms. Prospective randomized clinical trials would be needed to establish a more definitive understanding of the impact of marijuana use on individuals with PTSD.

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Additional information: The Intensive PTSD VA Treatment database is managed by the VA New England Mental Illness Research and Education Center, West Haven, Connecticut. The data are on secure VA servers and are not available to the public. Queries can be directed to Dr Rosenheck (robert.rosenheck@yale.edu).

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POSTTEST

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1. **Randomized controlled trials (RCTs) evaluating the efficacy and safety of marijuana for the treatment of posttraumatic stress disorder (PTSD) suggest which of the following findings?**
 - a. Marijuana is clearly related to a reduction in PTSD symptoms and improved functioning
 - b. RCTs of marijuana have shown mixed results in this clinical context
 - c. No RCTs of marijuana for use in PTSD have been completed at this time
 - d. Marijuana has been shown to lead to worsening of symptoms in PTSD patients in RCTs
2. **Mr M has PTSD resulting from his military service in Iraq. As you discuss how his specialized treatment has gone, he requests a prescription for medical marijuana, which has been legalized in your state. He says he has never used the drug before—only alcohol—but he believes that marijuana must be safe and effective since it is legal. According to data in this longitudinal, observational study, which outcome should you expect if Mr M starts using marijuana following intensive PTSD treatment?**
 - a. A reduction in PTSD symptom severity
 - b. An increase in PTSD symptom severity
 - c. Loss of employment
 - d. A decrease in alcohol use