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Associations of PTSD, chronic pain, and their comorbidity on cannabis use disorder: Results from an American nationally representative study

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Abstract

Background: Cannabis can be prescribed for posttraumatic stress disorder (PTSD) and chronic pain, and comorbid cannabis use disorder (CUD) can occur in both conditions. Research demonstrates that PTSD and chronic pain commonly co-occur.

Methods: Data were acquired from the National Epidemiologic Survey on Alcohol and Related Conditions-III (N = 36,309). Past-year CUD and PTSD were assessed using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-5. Past-year physician-confirmed chronic pain was self-reported and classified as musculoskeletal (e.g., arthritis), digestive (e.g., pancreatitis), and nerve (e.g., reflex sympathetic dystrophy) pain. Weighted cross-tabulations assessed sociodemographic, psychiatric, and chronic pain condition variables among those with PTSD versus no PTSD, among the entire sample and among those with CUD and chronic pain. Multiple logistic regressions examined the relationship between PTSD and chronic pain with CUD. CUD characteristics were also evaluated across PTSD and chronic pain groups.

Results: Rates of CUD were elevated in PTSD (9.4%) compared to those without (2.2%). The odds of CUD were greater for PTSD+digestive pain, PTSD+nerve pain, and PTSD+any chronic pain compared to having neither PTSD nor chronic pain (odds ratio range: 1.88–2.32). PTSD with and without comorbid chronic pain was associated with overall elevated rates of adverse CUD characteristics, including earlier age of onset, greater usage, and greater CUD severity.

Conclusions: PTSD with and without chronic pain is associated with elevated rates and severity of CUD. These results may have implications for prescribing practices and understanding individuals at risk for developing CUD.

KEYWORDS
cannabis use disorder, chronic pain, epidemiology, NESARC-III, posttraumatic stress disorder

1 | INTRODUCTION

Posttraumatic stress disorder (PTSD) is a psychiatric condition that is associated with a number of comorbid physical health conditions (Pietrzak, Goldstein, Southwick, & Grant, 2013; Sareen et al., 2007). Indeed, the relationship between PTSD and chronic pain is well established in the literature (Asmundson & Katz, 2009; Asmundson, Coons, Taylor, & Katz, 2002; El-Gabalawy et al., 2015; Otis, Keane, & Kerns, 2003). The mutual maintenance model suggests that symptoms of PTSD and chronic pain worsen one another (Asmundson & Katz,

2009; Sharp & Harvey, 2001), ultimately resulting in perpetuated distress and maintenance of both conditions. Consequently, health care professionals have become more aware of effective management techniques for this prevalent comorbid relationship.

There has been recent work examining cannabis as a treatment for PTSD (Betthauser, Pilz, & Vollmer, 2015; Bonn-Miller, Babson, & Vandrey, 2014; Yarnell, 2015). Much of this work has focused on the utility of medical cannabis in PTSD populations (Yarnell, 2015); specifically, how cannabis can attenuate PTSD symptomatology (Bonn-Miller et al., 2014; Drost et al., 2017; Greer, Grob, & Halberstadt, 2014). Research has also suggested that using cannabis for therapeutic purposes may increase the likelihood of harmful cannabis use (i.e., frequent and associated with problems) and receiving a diagnosis of a cannabis use disorder (CUD; Metrik et al., 2016; Moitra, Christopher, Anderson, & Stein, 2015; Yarnell, 2015). CUD has been associated with a number of adverse sequela, including mental health, physical health, and psychosocial consequences. For example, CUD has been shown to have high comorbidity with psychiatric conditions, such as anxiety, depression, and other substance use disorders (Hasin et al., 2016; Peters, Schwartz, Wang, O'Grady, & Blanco, 2013) and reduced mental health-related quality of life (Lev-Ran et al., 2012). Research has linked heavy cannabis use and CUD to increased respiratory difficulties (Aldington et al., 2007; Hall & Degenhardt, 2009), cardiovascular dysfunction (Hall & Degenhardt, 2009), poor oral health (Meier et al., 2016), cognitive impairment (Creane, Crane, & Mason, 2011; Hall, 2014), and reproductive complications (Hall & Degenhardt, 2009). Cannabis use is also associated with psychosocial impacts such as poor academic performance (Hall & Degenhardt, 2009), interpersonal and social problems (e.g., greater antisocial and fewer prosocial peers; American Psychiatric Association, 2013; Foster, Arterberry, Iacono, McGue, & Hicks, 2018), decreased quality of life (Goldenberg, IshHak, & Danovitch, 2017), and poorer overall functioning (APA, 2013). Comorbid PTSD can worsen the aforementioned outcomes (Brady & Clary, 2003; Pacella, Hruska, & Delahanty, 2013; Roth, Geisser, & Bates, 2008), and comorbid PTSD and CUD have been associated with elevated rates of co-occurring psychiatric conditions (Kevorkian et al., 2015). Elevated cannabis use among those with PTSD has also been associated with greater PTSD symptom severity and addictive behaviors (Wilkinson, Stefanovics & Rosenheck, 2015), suggesting that the balance of therapeutic versus detrimental outcomes of cannabis use in the context of PTSD is not well understood.

Unlike in the treatment of PTSD, cannabis has been more widely accepted as a treatment strategy for individuals with chronic pain (Hill, 2015; Jensen, Chen, Furnish, & Wallace, 2015; Park & Wu, 2017), albeit not universally across the U.S. (Guttmannova et al., 2016). Interestingly, preliminary research has found that when cannabis is prescribed and used for pain management, the likelihood of experiencing cannabis problems indicative of a CUD are decreased (Cohen, Heinz, Ilgen, & Bonn-Miller, 2016). Moreover, in the context of chronic pain, medical cannabis use is associated with reduced cannabis-related problems (Bonn-Miller, Boden, Bucossi, & Babson, 2014; Cohen et al., 2016). However, individuals with chronic pain may turn to nonmedical cannabis to cope with their pain, as physicians can be hesitant on prescribing cannabis (Carlini, Garrett, & Carter, 2017) and evolving legalization in the U.S. has increased accessibility (Degenhardt et al., 2015; Fleming, Balousek, Klessig, Mundt, & Brown, 2007; Guttmannova et al., 2016; Martel, Shir, & Ware, 2017). For example, 40% of chronic pain patients in an Australian sample reported using cannabis recreationally in their lifetime (Degenhardt et al., 2015) and almost 15% of chronic pain patients in an American sample reported past-month recreational use (Allegretti, Courtwright, Lucci, Korzenik, & Levine, 2013). These proportions are equivalent to estimates in the general population (Substance Abuse and Mental Health Services Administration, 2012), highlighting the accessibility of and engagement with nonmedical cannabis.

To date, no research has comprehensively assessed the influence of comorbid PTSD and chronic pain on the odds of having a CUD or the differences of CUD characteristics (i.e., age of symptom onset, age of most recent symptoms, and number of joints smoked a day) and CUD diagnostic classifications (i.e., mild, moderate, severe) among individuals with PTSD and chronic pain. Considering the varying research about the beneficial and detrimental outcomes of using cannabis to treat various psychiatric and physical health conditions (Bonn-Miller et al., 2014; Cohen et al., 2016; Hill, 2015; Yarnell, 2015) and the high comorbidity between PTSD and chronic pain (Asmundson & Katz, 2009; Asmundson et al., 2002; El-Gabalawy et al., 2015; Otis et al., 2003), research in this area is essential.

Using a nationally representative sample and contemporary diagnostic criteria, this study aimed to (a) examine the relationship between sociodemographic, psychiatric, and pain condition variables among those with PTSD versus no PTSD, among the entire sample and among those with CUD and chronic pain, (b) determine the contributions of PTSD and chronic pain (musculoskeletal, digestive, and nerve pain conditions) on CUD, and (c) assess CUD characteristics and severity across chronic pain conditions and PTSD among those with CUD. We included sociodemographics and comorbid psychiatric conditions as covariates in our analyses as there is research that suggests there are differences in sociodemographic factors, such as age, ethnicity, income, sex, marital status (Hasin et al., 2016), and education (Pacek, Mauro, & Martins, 2015), and psychiatric conditions, such as other substance use, anxiety, and mood disorders between those with and without CUD (Hasin et al., 2016). This allowed us to assess and understand the independent effect of PTSD and its relation to CUD across pain conditions. The results of this work may provide a novel insight into the relationship between PTSD, chronic pain, and CUD and thereby inform the development of cannabis screening and targeted intervention methods for those who may be at a greater risk of having this debilitating substance use disorder.

2 | MATERIALS AND METHODS

2.1 | Sample

Data were acquired from the 2012 to 2013 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III; $N = 36{,}309$,

response rate = 60.1%). The NESARC-III is a cross-sectional, nationally representative survey conducted by the National Institute on Alcohol Abuse and Alcoholism (NIAAA; Grant et al., 2014). The survey was administered to civilian American residents, 18 years or older. Exclusion criteria included addresses that include a post office box or rural route, remote islands in Alaska and Hawaii, being institutionalized, disabled, or an active member of the military. Data were weighted according to the American Community Survey (Bureau of the Census, 2013). This study received ethical approval during the initial data collection by the National Institutes of Health and Westat Institutional Board, and has institution-level approval to utilize these data for the purpose of this project. Participants provided electronic informed consent. Detailed information about the methodology and sampling procedures can be found elsewhere (Grant et al., 2014). This manuscript was prepared using a limited access data set obtained from the NIAAA and does not reflect the opinions or views of the NIAAA or the U.S. Government. Research data are not shared.

2.2 | Measures

2.2.1 | Sociodemographics

We assessed six sociodemographic variables consistent with previous work (e.g., El-Gabalawy, Mackenzie, Pietrzak, & Sareen, 2014; Katz, El-Gabalawy, Keyes, Martins, & Sareen, 2013; Reynolds, Pietrzak, El-Gabalawy, Mackenzie, & Sareen, 2015): age (continuous), sex (female, male), race/ethnicity (White, Black, American Indian/Alaska Native, Asian/Native Hawaiian/Other Pacific Islander, Hispanic), education (less than high school, high school or equivalent, some college or more), marital status (married/common law, widowed/separated/divorced, never married), and household income ($0–$19,999, $20,000–$34,999, $35,000–$59,999, $60,000+).

2.2.2 | Psychiatric conditions

The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-5; Hasin et al., 2015) was used to assess past-year CUD and PTSD. The AUDADIS-5 is a semi-structured clinical interview based on the DSM-5 (APA, 2013), and has good reliability and validity across psychiatric conditions (Grant et al., 2015; Hasin et al., 2015). CUD severity (i.e., mild = 2–3 symptoms; moderate = 4–5 symptoms; severe = 6+ symptoms; APA, 2013; Hasin et al., 2016) was defined in accordance with the DSM-5, using variables from the CUD module of the AUDADIS-5 that most closely aligned with each of the 11 symptoms of CUD. We included additional self-reported cannabis-related variables to assess characteristics of those with CUD, including the age of symptom onset, age of most recent symptoms, and the number of joints smoked a day. We also included other past-year substance use conditions (i.e., alcohol, sedative, cocaine, stimulant, hallucinogen, inhalant/solvent, club drug, heroin, other drug, opioid, tobacco), depressive/bipolar and related conditions (i.e., major depressive disorder, dysthymia, manic episode, hypomanic, bipolar disorder,) and anxiety conditions (i.e., specific phobia, social phobia, panic disorder, agoraphobia, generalized anxiety disorder) as covariates in our analyses. These were coded as "any other substance use," "any depressive," or "any anxiety" conditions.

2.2.3 | Chronic pain

The NESARC-III assessed seven conditions that are associated with chronic pain, which we categorized into three groups in accordance with previous research (El-Gabalawy et al., 2014; Quirk et al., 2015) and clinical recommendations based on the International Statistical Classification of Diseases and Related Health Problems (World Health Organization, 1992). These categories were musculoskeletal pain (fibromyalgia, osteoporosis, arthritis), digestive pain (pancreatitis, irritable bowel syndrome/inflammatory bowel disease), and nerve pain conditions (sympathetic dystrophy/complex regional pain syndrome, other nerve pain in legs, arms, or back). Participants self-reported whether they had a chronic pain condition during the past year and if a physician confirmed the pain condition.

2.3 | Analytic strategy

Weighted prevalence rates of sociodemographics, chronic pain, and CUD among individuals with and without PTSD and among individuals with any chronic pain and CUD with and without PTSD were obtained using cross-tabulations in SPSS (IBM Corp., 2013). Chi-square tests assessed the differences in these variables between those with and without PTSD. Multiple logistic regressions were conducted in STATA 14 (StataCorp., 2015) to examine the contributions of PTSD and chronic pain on the presence of CUD (dependent variable). We created a four-level categorical independent variable (IV) for each chronic pain condition: (a) no PTSD or chronic pain (i.e., no endorsed conditions; reference group), (b) chronic pain only, (c) PTSD only, and (d) PTSD+chronic pain. In addition, we created a four-level categorical IV for the composite "any chronic pain" variable. First, we tested and verified the assumptions of logistic regressions (Tabachnick & Fidell, 2001). We then tested an unadjusted model, followed by a model adjusting for sociodemographics (i.e., age, sex, race/ethnicity, education, marital status, household income), and a final model adjusting for both sociodemographics and psychiatric conditions (i.e., substance use, depressive, and anxiety conditions). Odds ratios (OR) and 95% confidence intervals (CIs) were reported, with a p-value of .05 as our cut-off. In order to maintain the representative sample, appropriate weighting and stratification were applied to these data. We used Taylor series linearization for variance estimation to account for the complex design of the NESARC-III (Levy & Lemeshow, 1999). Finally, to examine characteristics (i.e., age of first use, age of first experienced symptoms, age of most recent symptoms, number of joints smoked a day) and severity of CUD across the groups of interest, cross-tabulations and multiple one-way analyses of variance were run among those with CUD for each IV level across chronic pain condition groups. There were less than 2% of missing data on all primary variables; as such, we treated missing data as pairwise deletions (Schafer, 1999).

3 | RESULTS

Table 1 presents the weighted prevalence rates for sociodemographics, chronic pain, and psychiatric conditions. Among the entire sample, 1,779 (4.7%) had a past-year diagnosis of PTSD. Individuals with PTSD had elevated rates of ever using cannabis (52.0%) compared to those without PTSD (31.2%). Among individuals with PTSD, there was a higher prevalence of CUD (9.4%) and medical cannabis use (3.4%) compared to those without PTSD (2.2% and 1.0%, respectively). However, rates of medical cannabis use were almost equivalent between PTSD (24.4%) and no PTSD (24.3%) among those with any chronic pain and CUD. All conditions were significantly elevated between individuals with PTSD and no PTSD, but only digestive pain was elevated for PTSD (34.6%) among those with chronic pain and CUD compared to those without PTSD (15.7%).

Table 2 reveals the associations between PTSD and chronic pain with CUD. Compared to no endorsed conditions, PTSD alone (adjusted odds ratio [AOR1] range: 1.94–2.07), PTSD+digestive pain (AOR1: 2.32, 95% CI [1.29–4.18]; $p < .01$), PTSD+nerve pain (AOR1:1.88, 95% CI [1.10–3.20]; $p < .05$), and PTSD+any chronic pain (AOR1: 2.22, 95% CI [1.38–3.58]; $p < .01$) were associated with greater odds of CUD. No relationship on CUD was observed for PTSD+musculoskeletal pain (AOR1:1.83, 95% CI [0.99–3.36]; $p > .05$). The effect size for PTSD +digestive pain and PTSD+any chronic pain was larger than the effect for PTSD alone and chronic pain alone (i.e., digestive pain alone and any chronic pain alone), but this trend was not observed for PTSD+nerve pain.

A posthoc analysis was run to examine whether there was an additive relationship of PTSD+digestive pain or PTSD+any chronic pain on CUD. When changing the reference group to PTSD alone in order to make direct comparisons, neither the relationship of PTSD +digestive pain (AOR1: 1.20, 95% CI [0.71–2.03]; $p > .05$) nor PTSD +any chronic pain (AOR1: 1.11, 95% CI [0.66–1.88]; $p > .05$) on CUD was significant.

Table 3 presents the characteristics and severity of CUD according to our IV groups for each chronic pain condition (i.e., no endorsed conditions, chronic pain alone, PTSD alone, PTSD+chronic pain) among individuals with past-year CUD. Across all three chronic pain IVs, severe CUD was the most prevalent among those with PTSD alone, compared to no endorsed conditions, chronic pain alone, or PTSD+chronic pain. Similar trends emerged for the musculoskeletal and nerve pain IVs: groups significantly differed in their age of first cannabis use, with individuals with chronic pain alone having the oldest mean age of first cannabis use. Significant differences also emerged in the number of joints smoked daily: those with PTSD alone within the musculoskeletal pain and nerve pain IVs and those with PTSD+digestive pain reported the highest mean number of joints smoked daily.

4 | DISCUSSION

To the best of our knowledge, this study was the first to assess the relationship between PTSD, chronic pain, and CUD in a nationally representative sample. Consistent with studies that have examined cannabis use in PTSD (Hasin et al., 2016; Yarnell, 2015), we found that the prevalence of CUD was four times greater among those with PTSD compared to those without. This study extends knowledge by examining the contributions of PTSD and chronic pain in the context of CUD. Results suggest that, although the odds of CUD were greater in comorbid PTSD and chronic pain compared to having neither PTSD nor chronic pain, PTSD appears to be driving the relationship with CUD in comorbid relationships and contributes to overall severity.

It is not surprising that PTSD was associated with elevated rates of CUD in this sample as previous work has found a higher prevalence of psychiatric conditions (including PTSD) among patients with CUD (Cornelius et al., 2010; Stinson, Ruan, Pickering, & Grant, 2006). Specifically, the prevalence of CUD in the current study was 9.4% in individuals with past-year PTSD, which is comparable to recently reported rates of 12.3% (Kerridge, Rickering, Chou, Saha, & Hsain, 2018). It is possible that elevated rates of CUD reflect that individuals who suffer from PTSD use cannabis to alleviate their symptoms (Boden, Babson, Vujanovic, Short, & Bonn-Miller, 2013; Colin, Watson, & Robinson, 2013; Cougle, Bonn-Miller, Vujanovic, Zvolensky, & Hawkins, 2011), in line with the self-medication theory (Khantzian, 1997; Potter, Vujanovic, Marshall-Berenz, Bernstein, & Bonn-Miller, 2011). Although initially intended for therapeutic purposes, the use of cannabis for PTSD symptom attenuation can negatively reinforce the continuation of its use (Buckner et al., 2018) and increase the odds of CUD. Thus, despite symptom attenuation, an individual with PTSD may be vulnerable to developing a CUD. This is particularly problematic given that CUD has been associated with various adverse correlates, including increased rates of psychiatric conditions (Hasin et al., 2016; Kedzior & Laeber, 2014; Wittchen et al., 2007), physical health problems (Aldington et al., 2007; Creane et al., 2011; Hall & Degenhardt, 2009), and psychosocial interference (APA, 2013; Foster et al., 2018; Leeies, Pagura, Sareen, & Bolton, 2010), and comorbid PTSD and CUD has been associated with poorer PTSD treatment outcomes, particularly impacting improvements in avoidance and hyperarousal symptoms (Bonn-Miller, Boden, Vujanovic, & Drescher, 2013).

Our results emphasize the importance of PTSD in the relationship between PTSD, chronic pain, and CUD. Specifically, we found that when compared to PTSD alone, PTSD+digestive pain and PTSD+any chronic pain did not increase the odds of CUD. This suggests PTSD may be driving the relationship with CUD when comorbid with digestive or any chronic pain. In the context of comorbid PTSD and chronic pain, this could be problematic because there is greater acceptance by medical professionals and increased rates of prescribing cannabis for chronic pain (Cohen et al., 2016; Hill, 2015) compared to PTSD; the presence of PTSD could elevate risk for CUD for these individuals. This is supported by our finding that those with PTSD, CUD, and chronic pain had a higher prevalence of medical cannabis than those with PTSD only. However, these differential findings and the non-significance between those with and without PTSD among those with CUD and chronic pain may suggest that both medical and nonmedical sources are relevant. There is an industry dedicated to the development of cannabis-derivates for the treatment of health conditions, such as chronic pain

TABLE 1 Summary of primary variables

Variable	*n* weighted (%)			*n* weighted (%) Among those with any chronic pain +CUD		
	PTSD 1,779 (4.7)	No PTSD 34,530 (95.3)	χ^2/t-statistic	PTSD 49 (33.9)	No PTSD 125 (66.1)	χ^2/t-statistic
Sociodemographics						
Sex			154.00**			3.979*
Female	1,255 (67.5)	19,192 (51.1)		29 (49.8)	53 (39.9)	
Male	524 (32.5)	15,338 (48.9)		20 (50.2)	72 (60.1)	
Race/Ethnicity			111.46**			8.43
White	1,003 (68.3)	18,191 (66.1)		25 (65.2)	60 (61.3)	
African American	364 (12.0)	7,402 (11.8)		12 (11.8)	38 (18.9)	
American Indian/Alaska native	65 (4.3)	446 (1.4)		5 (9.6)	2 (2.6)	
Asian/Native Hawaiian/Other Pacific Islander	33 (2.2)	1,768 (5.9)		1 (2.8)	1 (1.1)	
Hispanic	314 (13.2)	6,723 (14.8)		6 (10.7)	24 (16.1)	
Education			6.97*			1.44
Less than high school	307 (16.5)	5,183 (12.8)		11 (17.8)	21(15.9)	
High school or equivalent	478 (25.3)	9,321 (25.8)		11 (22.5)	38 (33.6)	
Some college or more	994 (58.2)	2,0026 (61.4)		27 (59.7)	66 (50.5)	
Marital status			87.37**			2.97
Married/common law	653 (46.2)	16,141 (58.4)		19 (40.1)	52 (47.9)	
Widowed/separated/divorced	609 (28.4)	8,814 (19.2)		9 (20.3)	35 (25.6)	
Never married	517 (25.4)	9,575 (22.4)		21 (39.5)	38 (26.5)	
Past-year household income			174.90**			5.38
$0–$19,999	695 (31.3)	9,238 (20.1)		27 (51.4)	46 (30.3)	
$20,000–$34,999	385 (20.8)	7,387 (18.6)		5 (12.3)	22 (16.4)	
$35,000–$59,999	368 (22.6)	7,348 (21.2)		11 (19.8)	32 (27.2)	
$60,000+	331 (25.3)	10,557 (40.1)		6 (16.5)	25 (26.2)	
Primary dependent variable[a]						
Cannabis use disorder	155 (9.4)	817 (2.2)	261.57**	49 (100)	125 (100)	
Additional cannabis variables						
Ever used cannabis	910 (52.0)	10,362 (31.2)	352.62**	--	--	--
Medical cannabis use	68 (3.4)	377 (1.0)	103.89**	11 (24.4)	28 (24.3)	0
Psychiatric conditions[a]						
Depressive conditions	929 (50.8)	4,171 (11.6)	2257.94**	36 (63.7)	47 (38.1)	18.15**
Anxiety conditions	899 (51.3)	3,802 (11.2)	2344.80**	39 (79.7)	32 (25.5)	42.48**
Substance use conditions	952 (52.4)	9,482 (27.4)	553.90**	44 (86.7)	103 (79.1)	1.47
Chronic pain conditions[a]						
Musculoskeletal pain	564 (31.6)	6,589 (20.2)	172.81**	23 (48.1)	66 (51.6)	0.48
Digestive pain	198 (12.8)	1,163 (3.6)	282.84**	17 (34.6)	22 (15.7)	5.92*
Nerve pain	434 (25.2)	3,160 (9.6)	439.99**	27 (54.7)	61 (52.8)	0.56
Any chronic pain	780 (45.4)	8,365 (25.8)	352.36**	49 (100)	125 (100)	
Continuous variables[b]						
Age	42.19 (0.35)	45.81 (0.09)	43.25**	38.33 (1.70)	41.19 (1.26)	39.41**

Note: n weighted (%), *n*-values are unweighted prevalence rates and weighted % are weighted percentages. -- represents categories that are not applicable (i.e., all individuals with CUD have used cannabis). Musculoskeletal pain includes fibromyalgia, osteoporosis, arthritis; digestive pain includes pancreatitis, irritable bowel syndrome/inflammatory bowel disease; nerve pain includes reflex sympathetic dystrophy/complex regional pain syndrome, other nerve problem in legs, arms, or back.

Abbreviations: CUD, cannabis use disorder; PTSD, posttraumatic stress disorder

[a]Past-year diagnoses.

[b]mean (standard error) and *t*-statistic.

*$p < .05$

**$p < .001$

TABLE 2 Multiple logistic regressions examining the relationship between past-year PTSD and chronic pain conditions on cannabis use disorder

	Cannabis use disorder			
	n (%) Yes	OR (95% CI)	AOR (95% CI)	AOR1 (95% CI)
Musculoskeletal pain				
Reference[a]		1.00	1.00	1.00
Musculoskeletal pain alone	67 (0.8)	0.31 (0.24–0.40)***	1.18 (0.89–1.57)	0.97 (0.71–1.31)
PTSD alone	130 (11.4)	4.90 (3.73–6.43)***	4.63 (3.42–6.27)***	2.03 (1.42–2.90)***
PTSD+musculoskeletal pain	24 (5.1)	2.04 (1.26–3.31)**	4.11 (2.33–7.25)***	1.83 (0.99–3.36)
Digestive pain				
Reference[a]		1.00	1.00	1.00
Digestive pain alone	22 (1.4)	0.60 (0.37–0.97)*	1.15 (0.71–1.87)	0.79 (0.46–1.36)
PTSD alone	136 (9.4)	4.55 (3.52–5.90)***	4.28 (3.20–5.74)***	1.94 (1.38–2.71)***
PTSD+digestive pain	17 (8.8)	4.23 (2.64–6.80)***	6.13 (3.79–9.92)***	2.32 (1.29–4.18)**
Nerve pain				
Reference[a]		1.00	1.00	1.00
Nerve pain alone	61 (1.7)	0.75 (0.54–1.06)	1.48 (1.05–2.10)*	1.09 (0.76–1.57)
PTSD alone	126 (10.1)	4.87 (3.71–6.40)***	4.70 (3.44–6.42)***	2.07 (1.42–2.99)***
PTSD+nerve pain	27 (7.1)	3.30 (2.00–5.44)***	4.21 (2.51–7.07)***	1.88 (1.10–3.20)*
Any chronic pain				
Reference[a]		1.00	1.00	1.00
Any pain alone	125 (1.2)	0.47 (0.37–0.60)***	1.42 (1.10–1.84)**	1.09 (0.82–1.44)
PTSD alone	104 (11.3)	4.83 (3.51–6.64)***	4.56 (3.21–6.48)***	1.94 (1.30–2.92)**
PTSD+any pain	49 (7.3)	2.99 (2.03–4.41)***	5.08 (3.30–7.83)***	2.22 (1.38–3.58)**

Note: *n* (%) represent those with cannabis use disorder in each category of the independent variable, where *n*-values are unweighted and % are weighted percentages. AOR, adjusted odds ratio, adjusted for sex, age, marital status, education, household income, race; AOR1, adjusted for sociodemographics and depressive, anxiety, and other substance use conditions.

Abbreviations: AOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio; PTSD, posttraumatic stress disorder

[a]Reference category, no endorsed conditions.

*$p < .05$.

**$p < .01$.

***$p < .001$.

(Hill, Palastro, Johnson, & Ditre, 2017). Oral cannabinoids (Hill, 2015), cannabidiol (CBD) oil (Blake et al., 2017; Stockings et al., 2018) and topical cannabis (Maida & Corban, 2017) have been associated with both pain relief and a decrease in pain ratings. Cannabis is primarily made up of delta-9-tetrahydrocannabinol (THC) and CBD. THC is associated with psychoactive properties, whereas CBD has been linked to anti-anxiety and antipain effects without the psychoactive properties (Bhattacharyya et al., 2010). It is plausible that there is a differential risk of developing a CUD depending on whether cannabis is prescribed with or without chemical and intoxicating properties. It would be important for future research to examine differences in treatment modality and access to medical versus nonmedical cannabis, particularly for those with comorbid PTSD and chronic pain.

Interestingly, there were differential findings with respect to comorbid PTSD and musculoskeletal pain compared to the other chronic pain conditions. When adjusting for sociodemographics, increased odds of CUD were observed for PTSD+musculoskeletal pain. However, after controlling for other psychiatric conditions, the increased odds of CUD disappeared, suggesting that another psychiatric condition may have been driving the relationship with CUD that is unique to musculoskeletal pain. Research has identified that when depression is experienced in the presence of musculoskeletal pain, it is associated with the highest pain severity and disability compared to those with chronic pain alone (Bair, Wu, Damush, Sutherland, & Kroenke, 2008; Melkevik et al., 2018). It has been argued that, although individuals with depression may use cannabis as a coping mechanism (Walsh et al., 2013), these individuals are the most prone to cannabis misuse (Hyman & Sinha, 2009). Given that there is more stigma associated with using cannabis for mental health difficulties compared to those with chronic pain (Walsh et al., 2013), we speculate that individuals who experience a psychiatric problem, such as depression, may be more likely to use nonmedical cannabis and fall into a cycle of misuse; future research should examine this possibility.

It is important to acknowledge the potentially complex multi-directional relationship between PTSD, chronic pain, and CUD. Although PTSD and chronic pain may be risk factors for CUD, CUD may put an individual at an increased risk of PTSD and chronic pain. CUD has been found to increase risky behaviors, such as increased alcohol consumption and tobacco smoking (Caldeira, Arria, O'Grady, Vincent, & Wish, 2008) and impulsivity (Trull, Wyoff, Lane, Carpenter, & Brown, 2016). These behaviors are associated with risk taking which can be associated with injuries (Kelly, Darke, & Ross, 2004; Hall & Degenhardt, 2009), and may be both traumatic and painful. Risky sexual and driving behaviors, thrill seeking, and firearm possession are also significantly associated with PTSD (Strom et al., 2012). Alternatively, it is possible that PTSD and CUD can develop concurrently following a traumatic accident, and mutually maintain one another. According to

TABLE 3 Summary of cannabis experiences among individuals with CUD across chronic pain, PTSD, and comorbid chronic pain and PTSD

	n (weighted %) or *M* (*SE*)				
	No endorsed conditions	Chronic pain alone	PTSD alone	PTSD+chronic pain	*F*-statistic
Musculoskeletal pain					
Age of first use[a]	15.75 (0.12)	18.03 (0.75)	15.46 (0.39)	15.38 (0.99)	8.07***
Age of first symptoms[a]	20.23 (0.33)	26.58 (2.51)	19.38 (0.67)	21.94 (2.45)	7.69***
Age of most recent symptoms[a]	23.88 (0.49)	21.28 (2.61)	23.78 (1.01)	30.44 (3.87)	6.78***
Number of joints[a,b]	4.35 (0.13)	4.65 (0.55)	6.30 (0.42)	5.95 (1.07)	9.99***
CUD severity					8.07***
Mild (2–3 symptoms)	171 (26.5)	18 (28.2)	14 (12.0)	3 (9.1)	
Moderate (4–5 symptoms)	142 (19.4)	15 (23.1)	11 (7.0)	7 (37.4)	
Severe (6+ symptoms)	376 (48.4)	27 (39.0)	91 (77.8)	13 (53.5)	
Digestive pain					
Age of first use[a]	15.91 (0.13)	16.73 (1.33)	15.53 (0.38)	14.76 (1.26)	1.21
Age of first symptoms[a]	20.59 (0.36)	22.18 (2.49)	19.88 (0.73)	18.78 (1.67)	0.67
Age of most recent symptoms[a]	24.24 (0.50)	28.91 (3.05)	24.91 (1.13)	24.44 (3.80)	0.87
Number of joints[a,b]	4.36 (0.13)	5.23 (0.94)	6.17 (0.42)	6.94 (0.98)	10.36***
CUD severity					6.91***
Mild (2–3 symptoms)	182 (26.5)	6 (28.0)	16 (12.3)	1 (6.3)	
Moderate (4–5 symptoms)	155 (19.9)	2 (10.0)	14 (9.5)	3 (28.0)	
Severe (6+ symptoms)	393 (47.7)	10 (52.0)	93 (75.8)	11 (61.0)	
Nerve pain					
Age of first use[a]	15.82 (0.13)	17.02 (0.72)	15.56 (0.39)	14.89 (0.93)	2.75*
Age of first symptoms[a]	20.47 (0.35)	23.47 (2.55)	19.34 (0.71)	21.68 (1.91)	2.14
Age of most recent symptoms[a]	24.22 (0.49)	27.29 (3.50)	23.47 (1.00)	30.68 (3.45)	3.40*
Number of joints[a,b]	4.45 (0.14)	3.48 (0.33)	6.37 (0.45)	5.64 (0.66)	11.25***
CUD severity					6.99***
Mild (2–3 symptoms)	177 (27.0)	12 (23.3)	14 (12.2)	3 (8.7)	
Moderate (4–5 symptoms)	143 (19.3)	13 (21.8)	14 (10.0)	3 (19.5)	
Severe (6+ symptoms)	370 (47.8)	31 (47.8)	86 (75.8)	18 (66.1)	

Note: n weighted (%), *n*-values are unweighted prevalence rates and weighted % are weighted percentages. No endorsed conditions includes individuals with no PTSD or chronic pain.

Abbreviations: CUD, cannabis use disorder; *M*, mean; PTSD, posttraumatic stress disorder; *SE*, standard error

[a]Mean age (standard error) and *F*-statistic.

[b]Number of joints smoked a day when cannabis was used at the most.

*$p < .05$

***$p < .001$.

the mutual maintenance model (Sharp & Harvey, 2001), when an individual is reminded of a trauma, it can increase arousal and avoidance of the triggering event (Asmundson & Katz, 2009; Asmundson et al., 2002). In line with self-medication theory (Khantzian, 1997; Potter et al., 2011), an individual may use cannabis to aid in the avoidance of affective symptoms (Lazareck et al., 2012) and to lessen intrusive PTSD symptoms, which may inadvertently exacerbate intrusive and hyperarousal symptomatology (Loflin, Earleywine, & Bonn-Miller, 2017) and trigger re-experiencing. Provided that cannabis use may result in short-term alleviation of symptoms (but maintenance of long-term PTSD symptomatology), an individual's drug utilization would be maintained and could increase the likelihood of CUD. However, there are other causal pathways that are possible. Given the complexity of the relationship between these three conditions, it is important for future research to examine all directional possibilities.

To further understand CUD, we assessed group differences in cannabis experiences and CUD severity among those with CUD. We found that among those with CUD, severe CUD was the most prevalent diagnostic classification, which is consistent with work done with an adolescent sample awaiting treatment (Kelly et al., 2014) but contrasts other research with an adult sample of individuals with CUD (Hasin et al., 2016). It is possible that the inconsistency reflects a distinction in assessing a diagnostic severity in a general sample versus, specifically, a CUD sample. Results revealed that PTSD was associated with more severe CUD and risky cannabis experiences, including having the youngest age of first CUD symptoms and the highest number of joints smoked a day among the musculoskeletal and nerve pain conditions; risky cannabis experiences were also elevated when PTSD was combined with chronic pain conditions. However, chronic pain alone was associated with the oldest age of first cannabis use across all chronic pain conditions. Although not directly assessed, perhaps we see an older age of cannabis onset for those with chronic pain because they have exhausted other treatment options first (e.g., opioids). Historically, there have been a greater number of viable and supported nonpharmacologic and pharmacologic treatment options for chronic pain (Chou et al., 2009) than what is available for PTSD specifically (i.e., beyond mood stabilizers or antidepressants; Stein, Ipser, &

Seedat, 2006). This result is in line with the almost equivalent prevalence of medical cannabis use between those with and without PTSD among individuals with any chronic pain or CUD, suggesting that chronic pain, not PTSD, was driving medical cannabis use. We posit that these findings may further support literature that has found that younger age of cannabis onset and experience of CUD symptoms is predictive of future CUD (Caldeira, Arria, O'Grady, Vincent, & Wish, 2008; Rioux et al., 2018; Winters & Lee, 2008). Perhaps the younger onset of cannabis use among those with PTSD may increase the likelihood of self-medicating behavior (Loflin et al., 2017), which could serve to further exacerbate symptoms and contribute to the experience of CUD. Given the known relationship between PTSD and CUD, future research efforts might focus on the implications of targeting PTSD in the treatment of CUD, particularly those with severe CUD, and whether there are subsequent improvements in chronic pain and overall functioning.

Our results highlight the importance of screening individuals for PTSD and informing patients about the potential risks associated with cannabis use, particularly as there is research that has found greater cannabis frequency in individuals with high PTSD symptom scores (Bonn-Miller et al., 2014). In addition, there is research that suggests individuals with PTSD have greater odds of having an alcohol or drug use disorder (Grant et al., 2016; Kevorkian et al., 2015) compared to those without PTSD, suggesting that individuals with PTSD may be more susceptible to drug misuse in general. Interestingly, research has found that PTSD is associated with increased odds of any drug use disorder (comprised of sedative/tranquilizer, cannabis, amphetamine, cocaine, nonheroin opioid, heroin, hallucinogen, club drug, and solvent/inhalant use disorders), whereas there is not increased odds of an alcohol use disorder (Goldstein et al., 2016). Our results also indicated an independent effect of CUD as other comorbid substance use disorders were included as a covariate in the most stringent model. We postulate that there is something unique about drug misuse, particularly cannabis, that may be more strongly related to PTSD. Perhaps it is the recognized short-term symptom improvements associated with cannabis use that draws individuals to use cannabis (Bonn-Miller et al., 2014). More research is needed to tease apart the differential relationships between PTSD and specific substance and drug use disorders to better inform clinicians about unique associations between trauma and substance misuse.

It is important to note the limitations of the current study. First, the NESARC-III is cross-sectional. As indicated, this ultimately inhibits the ability to assess temporal and causal relationships. Second, we limited our data to past-year diagnoses only. This potentially minimized the number of individuals who endorsed conditions; however, we wanted to remain consistent with the chronic pain diagnoses, which had to be present within the past-year, and maintain the same time-frame across conditions. Finally, the NESARC-III did not differentiate between individuals who had CUD, with or without a prescription for cannabis, although we did assess the prevalence of medical cannabis use among CUD and chronic pain. It is important for future research to examine whether there are differential associations with PTSD and chronic pain for prescription cannabis use (vs. without prescription).

5 | CONCLUSIONS

We have demonstrated that the prevalence of CUD and chronic pain are greater among individuals with PTSD compared to those without. The odds of CUD were greater in PTSD alone, PTSD+digestive pain, PTSD+nerve pain, and PTSD+any chronic pain compared to neither PTSD nor chronic pain, with PTSD likely driving this association. It also appears that PTSD has a significant effect on CUD severity both among those with chronic pain conditions and those without. Results may have implications for cannabis prescribing practices for both PTSD and chronic pain (when comorbid with PTSD). This is a critical time for cannabis research in the context of health given many recent changes in legislature increasing access, and the use of this substance for symptom reduction across various conditions. We must better understand who may be at risk of deleterious outcomes of cannabis use, in order to protect the health of Americans. Ultimately, the use of cannabis among those with various conditions including PTSD may require a risk-benefit analysis, and further research should shed light on both therapeutic uses and potential negative health outcomes.

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DATA AVAILABILITY

This manuscript was prepared using a limited access data set obtained from the NIAAA and does not reflect the opinions or views of the NIAAA or the U.S. Government. Research data are not shared.

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