

Original Article

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Associations of alcohol and cannabis use with change in posttraumatic stress disorder and depression symptoms over time in recently trauma-exposed individuals

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Abstract

Background. Several hypotheses may explain the association between substance use, post-traumatic stress disorder (PTSD), and depression. However, few studies have utilized a large multisite dataset to understand this complex relationship. Our study assessed the relationship between alcohol and cannabis use trajectories and PTSD and depression symptoms across 3 months in recently trauma-exposed civilians.

Methods. In total, 1618 (1037 female) participants provided self-report data on past 30-day alcohol and cannabis use and PTSD and depression symptoms during their emergency department (baseline) visit. We reassessed participant's substance use and clinical symptoms 2, 8, and 12 weeks posttrauma. Latent class mixture modeling determined alcohol and cannabis use trajectories in the sample. Changes in PTSD and depression symptoms were assessed across alcohol and cannabis use trajectories via a mixed-model repeated-measures analysis of variance.

Results. Three trajectory classes (low, high, increasing use) provided the best model fit for alcohol and cannabis use. The low alcohol use class exhibited lower PTSD symptoms at baseline than the high use class; the low cannabis use class exhibited lower PTSD and depression symptoms at baseline than the high and increasing use classes; these symptoms greatly increased at week 8 and declined at week 12. Participants who already use alcohol and cannabis exhibited greater PTSD and depression symptoms at baseline that increased at week 8 with a decrease in symptoms at week 12.

Conclusions. Our findings suggest that alcohol and cannabis use trajectories are associated with the intensity of posttrauma psychopathology. These findings could potentially inform the timing of therapeutic strategies.

Introduction

Alcohol, drugs, and tobacco are frequently used to cope with posttraumatic sequelae. Indeed, the prevalence of substance use disorders (SUD) among those with posttraumatic stress disorder (PTSD) is high; national estimates indicate that ~46% of people with PTSD are addicted to substances (Pietrzak, Goldstein, Southwick, & Grant, 2011). Likewise, up to ~20% of individuals who have suffered from major depression in their lifetime have had an alcohol or SUD

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(Quello, Brady, & Sonne, 2005). Co-occurring SUD and PTSD predict adverse outcomes, including suicide and unemployment (Allan et al., 2019; Blanco et al., 2013). Substances may be used to ameliorate symptom presence and severity – to avoid painful memories, fall asleep, reduce anxiety, elevate mood, and enhance pleasure in activities.

Several hypotheses attempt to explain the significance of the relationship between PTSD and SUD. The hypothesis with the most empirical evidence is the self-medication hypothesis (Khantzian, 1997). According to this hypothesis, substance use temporarily relieves posttrauma symptoms (Chilcoat & Breslau, 1998). However, this temporary relief reinforces the use of substances, leading to maladaptive use and, ultimately, symptom exacerbation (Stewart, Pihl, Conrod, & Dongier, 1998). Epidemiological studies support this hypothesis in that PTSD and depression develop first, with subsequent onset of SUD (Abraham & Fava, 1999; Chilcoat & Breslau, 1998; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Ouimette, Read, Wade, & Tirone, 2010; Wojciechowski, 2019). Nevertheless, some studies have found the opposite sequence of disorder onset (Croughan, Miller, Wagelin, & Whitman, 1982; Mirin, Weiss, Griffin, & Michael, 1991; Rounsaville, Weissman, Crits-Christoph, Wilber, & Kleber, 1982; Testa, Livingston, & Hoffman, 2007), suggesting a bidirectional relationship. Other hypotheses include the mutual maintenance hypothesis, which suggests that PTSD symptoms lead to substance use, and this use then exacerbates PTSD symptoms (Kaysen et al., 2014; Possemato et al., 2015). Lastly, the shared susceptibility hypothesis suggests that shared factors contribute to the development of co-occurring PTSD and SUD. Such factors include but are not limited to emotion regulation deficits, genetic risk, and behavioral under control (Chilcoat & Breslau, 1998). While correlational studies have shed light on the complex relationship between PTSD, depression, and SUD, longitudinal studies allow for stronger inferences about the causal pathway between these comorbid disorders.

Only a few longitudinal studies have explored the temporal onset of the development of posttraumatic sequelae and substance use. PTSD symptoms predicted greater substance use in trauma-exposed adolescents even after controlling for factors such as pre-trauma family environment, substance use, and demographic variables (Haller & Chassin, 2014). New interpersonal violence exposure was associated with subsequent increases in alcohol and substance use in other longitudinal studies (Berenz et al., 2016; Kaysen, Neighbors, Martell, Fossos, & Larimer, 2006; Kilpatrick, Acierno, Resnick, Saunders, & Best, 1997; Kline et al., 2014). Further, PTSD symptoms and coping motives for using alcohol predicted worse alcohol-related consequences in college students (Read, Griffin, Wardell, & Ouimette, 2014). In a sample of recently trauma-exposed adults recruited from the emergency department (ED), increases in anhedonic symptoms of PTSD corresponded with increases in substance use over 6 months (Fani et al., 2020).

Ecological momentary assessment (EMA) has also been used to measure momentary change and individual-level differences contributing to the relationship between PTSD and substance use. A recent review of EMA studies examining PTSD and alcohol use, in particular, highlighted that collectively, studies showed support for the self-medication hypothesis (Lane, Waters, & Black, 2019). While EMA methods provide greater granular data on daily fluctuations in psychological symptoms and substance use, this method has some limitations including attrition and

compliance rates. Nonetheless, these studies suggest that posttraumatic sequelae lead to increased substance use. However, no large-scale prospective study has measured how posttraumatic sequelae may differ based on substance use trajectories. In the context of the multisite, longitudinal AURORA (Advancing Understanding of Recovery after trauma) study (McLean et al., 2020), we assessed putative relationships between trajectories of alcohol and cannabis use and PTSD and depression symptoms over time among ED patients who had experienced trauma. Alcohol and cannabis use were examined as they are among the most abused substances in trauma-exposed populations (Bhalla, Stefanovics, & Rosenheck, 2017). Given the previous longitudinal data, we hypothesized that escalating alcohol/cannabis use over time, compared to stable or no/minimal alcohol/cannabis use, would be associated with increased PTSD and depression symptoms. We retrospectively examined PTSD and depression symptom changes 30 days before the trauma and subsequent ED admittance 3 months after trauma. This period has been frequently highlighted as a time frame during which PTSD symptom resolution or escalation occurs (Blanchard et al., 1995; Pérez Benítez et al., 2013; Schock, Böttche, Rosner, Wenk-Ansohn, & Knaevelsrud, 2016; Warren et al., 2014).

Materials and methods

Participants

A total of 581 men and 1037 women with a mean age of 35.4 years (*s.d.* = 13) were recruited as part of a multisite study of PTSD conducted in the EDs of level 1 trauma centers (MH094757), as described prior (Harnett et al., 2021; Kessler et al., 2021; McLean et al., 2020; Steuber et al., 2021). Eligible patients were approached in the ED after initial medical evaluation, laboratory testing, and medical clearance. Once informed consent was obtained, trained research assistants collected demographic information and administered assessments on prior trauma, substance abuse, current and past PTSD and depression symptoms, and details concerning the presenting trauma. Patients were queried about past and current medical conditions and medications. Participants who had experienced a DSM-5 criterion A trauma in the past 24 h were eligible for the study but were excluded if they were currently suicidal or had attempted suicide in the last 3 months, were currently intoxicated, or lost consciousness due to the trauma. PTSD and depression symptoms have been examined previously within this sample (see Cakmak et al., 2021; Joormann et al., 2022; Lebois et al., 2022; Ziobrowski et al., 2021).

Clinical assessments

The investigation described in this manuscript used assessments to measure alcohol and cannabis use and PTSD and depression symptoms across four timepoints, baseline, weeks 2, 8, and 12. During the baseline timepoint, participants responded to assessments during their ED visit in reference to the 30 days leading up to the traumatic event. Each subsequent timepoint referenced the past 30 days (or 14 days for week 2). During the ED visit, demographic information, including biological sex, age, education, marital status, and race/ethnicity, was gathered. During the follow-up week 2 visit, demographic information, including body mass index (BMI), employment status, and income, was gathered.

The PTSD checklist for DSM-5 (PCL-5)

The PCL-5 (Blevins, Weathers, Davis, Witte, & Domino, 2015; Weathers et al., 2013) is a 20-item measure that prompts participants to report the frequency of PTSD symptoms over the respective reference periods. Using a Likert scale ranging from 0 ('not at all') to 4 ('extremely'), participants rate the degree a specific symptom disrupts their activities. A severity score is calculated as the total across all 20 items, and a score of 31–33 suggests possible PTSD. For the statistical analyses in this study, we reported the overall PCL-5 score. The PCL-5 has been shown to have strong reliability and validity (Blevins et al., 2015). Cronbach's α values for the PCL-5 at each time point were as follows: ED, 0.94; week 2, 0.95; week 8, 0.96; and month 3, 0.97.

The patient-reported outcomes measurement information system (PROMIS)

For this investigation, we used the PROMIS Depression measure only. The PROMIS Depression item bank (Amtmann et al., 2014; Cella et al., 2007; Pilkonis et al., 2011) is a National Institutes of Health (NIH) measure that assesses self-reported negative mood, views of self, social cognition, and decreased positive affect and engagement. Participants' responses are added to create a raw score and converted to a *T*-score. The *T*-score is a standardized score with a mean of 50 and a standard deviation of 10. The higher the *T*-score, the more severe the depression symptoms. The PROMIS has demonstrated reliability, precision, and construct validity (Cella et al., 2007).

PhenX toolkit

Alcohol and cannabis use were assessed using the PhenX Toolkit Alcohol and PhenX Toolkit Substance Use, respectively (Hamilton et al., 2011). For this investigation, we used the frequency of use as our variable of interest for alcohol and cannabis as we did not have a measure for quantity for alcohol and cannabis use. To assess alcohol use, we asked, 'During the "reference period," how many days did you have at least one drink of any kind of alcohol, not including small tastes or sips?' Our variable of interest was the sum of days the participant consumed alcohol. To assess cannabis use, we similarly asked, 'During the "reference period," how many days did you use marijuana?' Our variable of interest was the sum of days the participant used cannabis.

The childhood trauma questionnaire – short form (CTQ-SF)

The CTQ-SF (Bernstein et al., 2003) is a 28-item scale used to examine exposure to traumatic experiences during childhood. Five types of childhood maltreatment types were measured: emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect. A score for each of the five types of maltreatment is calculated by adding each item within the subtype to create a maltreatment subtype score for a range of 0–12. A total summed score was calculated and used in secondary analyses. Cronbach's α for CTQ-SF was 0.78.

Statistical analyses

A latent class linear mixed model (LCMM) fitted by the maximum likelihood method was used to partition our sample into subgroups based on alcohol or cannabis use. To conduct these analyses, we used the heterogeneous linear mixed model function in the LCMM package in R (v3.6.1), identifying clusters of people with common use patterns. In choosing the appropriate LCMM model fit, we referenced the Bayesian information criteria (BIC)

values and percent class membership. Low BIC values and percentages of no less than 5% in class membership were considered the best fit for the data (Nagin & Odgers, 2010) (online Supplementary Tables S1 and S2). Given that the week 2 time-point assessed alcohol and cannabis use within the past 14 days, for these LCMM analyses only, we divided baseline, week 8, and week 12 timepoints by 2 to achieve a more even distribution of the data. Latent class models included measurements at all four timepoints (baseline, weeks 2, 8, and 12). LCMM analyses revealed that the most optimal model for trajectory classes was a three-class alcohol use model with $n = 1617$ and a three-class cannabis model with $n = 1617$. Participants reporting alcohol use were categorized into three groups, a consistently low use ($n = 1239$, 76.6%) group, a consistently high use ($n = 117$, 7.2%) group, and an increasing use group that demonstrated increased use from week 2 to week 8, and decreased use from week 8 to week 12 ($n = 261$, 16.1%). Participants reporting cannabis use were categorized into groups of consistently low use ($n = 1246$, 77.1%), consistently high use ($n = 262$, 16.2%), and increasing use ($n = 109$, 6.7%). Figure 1a and b present the graphs of individual and mean trajectories of alcohol and cannabis use models, while Fig. 1c and d provides visuals of only the mean trajectories.

For both alcohol and cannabis use, we used a 3 (time: baseline, week 8, and 12) by 3 (trajectory class) mixed-model repeated-measures analysis of variance (ANOVA) to test the effect of trajectory group on PTSD and depression symptom change over time. Where significant time by trajectory class interactions emerged, we conducted post-hoc analyses (univariate ANOVAs) to explicate these interactions. For these ANOVAs, because we were more interested in examining chronic change in PTSD and depression symptoms than short-term (2 week) reactivity, we examined changes in symptoms collected at baseline, week 8, and 12. Mauchly's test was used to determine whether the assumption of sphericity was violated. If violated, degrees of freedom were corrected using either Greenhouse-Geiser ($\epsilon < 0.75$) or Huynh-Feldt ($\epsilon > 0.75$) estimates of sphericity. Pairwise deletion was used for missing data.

Results

Participant characteristics

Sample demographic and clinical characteristics, stratified by alcohol and cannabis use class memberships, are presented in Tables 1 and 2. Given the significant differences found between trajectory classes on demographic and clinical variables, separate follow-up sensitivity analyses, including biological sex as a between-subjects factor, and age, education, CTQ-SF, BMI, marital status, and race/ethnicity as covariates, were conducted, and presented in the results section of the Supplementary material. Participants reported the following traumatic events that brought them to the ED: motor vehicle collision [1135 (70.1%)], physical assault [140 (8.7%)], sexual assault [14 (0.9%)], fall ≥ 10 feet [18 (1.1%)], fall < 10 feet or from unknown height [51 (3.2%)], incident causing traumatic stress exposure to many people [e.g., plane crash, natural disaster; 3 (0.2%)], non-motorized collision [20 (1.2%)], burns [7, (0.4%)], animal-related [29 (1.8%)], other [54 (3.3%)], missing [147 (9.1%)].

Mixed-model repeated-measures ANOVA

Alcohol use trajectories and change in PTSD symptoms

A main effect of time, $F_{(2, 1430)} = 15.37$, $p < 0.001$, $\eta_p^2 = 0.02$, and a significant time by alcohol use trajectory class interaction were

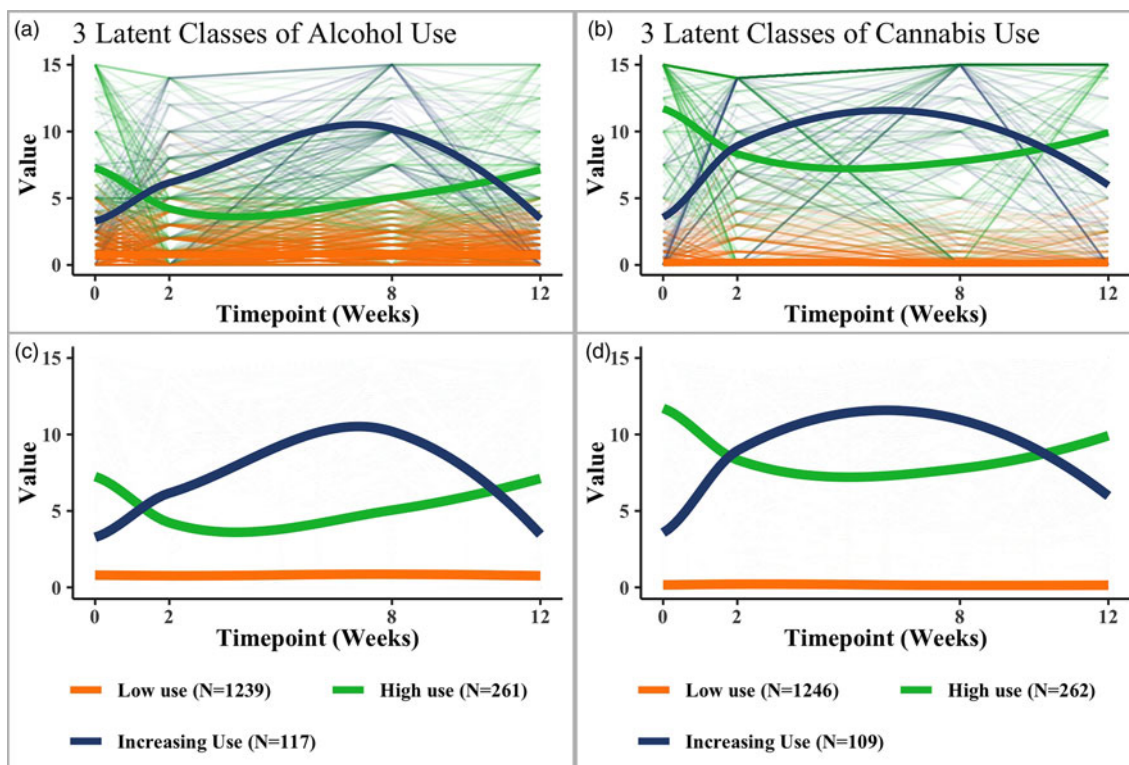


Figure 1. Observed individual (a, b) and mean (c, d) latent trajectories for both alcohol and cannabis use. Individual trajectories determined by measurements at four timepoints are represented by the thin lines, while the thick lines are the average trajectories for each designated group. Each class was identified through the chosen latent growth mixture model, based on Bayesian information criterion (BIC) values and class membership percentages.

observed $F_{(3, 1430)} = 2.83$, $p = 0.04$, $\eta_p^2 = 0.01$ (see Table 3 for means and standard deviations). Analyses revealed the low use alcohol trajectory class had lower PTSD symptoms at baseline than the high use alcohol trajectory class, but not the increasing use trajectory class. There were no significant differences between the trajectory classes across other timepoints. For the low use trajectory class participants, their PTSD symptoms increased from baseline to week 8, reflecting moderate and clinically significant PTSD symptom severity; symptoms also decreased from week 8 to week 12 but remained clinically significant at this time. The increasing use trajectory class showed a similar pattern of change in PTSD symptoms compared to the low use trajectory class; however, no statistically significant differences between timepoints were found for this trajectory class. The high use trajectory class exhibited relatively similar PTSD symptoms at each timepoint, all within the moderate PTSD symptom severity range; no statistically significant mean differences were apparent across timepoints for this trajectory class. Figure 2a illustrates the patterns of PTSD symptom change over time for the three alcohol use trajectory classes.

Alcohol use trajectories and change in depression symptoms

A statistically significant main effect of time was observed, $F_{(2, 1807)} = 53.34$, $p < 0.001$, $\eta_p^2 = 0.05$, all trajectory classes had lower depression symptoms at baseline than at other timepoints after the ED visit (see Table 3 for means and standard deviations). A statistically significant main effect of alcohol trajectory class was found $F_{(2, 1061)} = 4.81$, $p = 0.01$, $\eta_p^2 = 0.01$ whereby the low use alcohol trajectory class had lower depression symptoms than the other two trajectory classes at baseline; the high use and

increasing use trajectory classes did not differ from each other. No statistically significant time by trajectory class interaction was observed $F_{(3, 1807)} = 2.14$, $p = 0.085$. Figure 2c illustrates the patterns of depression symptom change over time for the three alcohol use trajectory classes.

Cannabis use trajectories and change in PTSD symptoms

A statistically significant main effect of time, $F_{(2, 1436)} = 10.72$, $p < 0.001$, $\eta_p^2 = 0.01$, and a time by cannabis use class interaction was observed $F_{(3, 1436)} = 5.45$, $p = 0.001$, $\eta_p^2 = 0.01$ (see Table 3 for means and standard deviations). Analyses revealed the low use cannabis trajectory class had lower PTSD symptoms at baseline than the high use and increasing use trajectory classes; the latter two trajectory classes demonstrated high levels of PTSD symptoms across all timepoints. The low use cannabis trajectory class also exhibited lower PTSD symptoms at week 8 than the high use trajectory class, unlike the increasing use trajectory class. The low use cannabis trajectory class also exhibited lower PTSD symptoms at week 12 than the high use trajectory class, unlike the increasing use trajectory class. No statistically significant differences existed between the high and increasing use trajectory classes across other timepoints. For low use trajectory class participants, PTSD symptoms significantly increased from baseline to week 8, with symptoms reaching the clinical threshold for a PTSD diagnosis at week 8, but then decreasing significantly from week 8 to week 12; however, within this trajectory class, week 12 symptoms were still greater than symptoms reported at the baseline visits and remained clinically significant at week 12. The increasing use trajectory class showed a pattern of PTSD similar to the low use trajectory class across time, with symptoms remaining high

Table 1. Demographics and clinical characteristics for alcohol use trajectory classes

Measure	Low use		High use		Increasing use		<i>p</i> value
	Mean	s.d.	Mean	s.d.	Mean	s.d.	
Age (years)	35.58	13.26	35.13	12.52	33.94	11.72	0.40 ^a
Education (years)	14.87	2.46	15.09	2.57	14.50	2.77	0.10 ^b
CTQ-SF total	9.48	9.86	10.12	9.59	11.66	11.30	0.10 ^c
BMI	30.78	9.02	28.66	7.87	30.11	7.57	0.01 ^d
	Count	%	Count	%	Count	%	
Gender							<0.001 ^e
Male	402	32.45	127	48.66	52	44.44	
Female	837	67.55	134	51.34	65	55.56	
Marital status							0.31 ^f
Married	260	21.14	49	18.92	20	17.09	
Separated	52	4.23	5	1.93	2	1.71	
Divorced	146	11.87	21	9.27	14	11.97	
Annulled	1	0.08	1	0.39	0	0	
Widowed	24	1.95	5	1.93	1	0.85	
Never been married	747	60.73	175	67.57	80	68.38	
Race/ethnicity							0.07 ^g
Hispanic	157	12.73	26	10.00	10	8.55	
Non-Hispanic White	383	31.06	96	36.92	34	29.06	
Non-Hispanic Black	642	52.07	132	50.77	72	61.54	
Non-Hispanic other	51	4.14	6	2.31	1	0.85	
Employment code							0.88 ^h
Employed	809	74.02	179	76.17	76	72.38	
Retired	26	2.38	8	3.40	3	2.86	
Homemaker	22	2.01	3	1.28	2	1.90	
Student	44	4.03	12	5.11	4	3.81	
Unemployed, disabled, or other	192	17.57	33	14.04	20	19.05	
Income code							0.39 ⁱ
<=\$19,000	378	34.97	84	36.05	38	36.19	
\$19,001–\$35,000	342	31.64	67	28.76	29	27.62	
\$35,001–\$50,000	148	13.69	31	13.30	17	16.19	
\$50,001–\$75,000	91	8.42	16	6.87	7	6.67	
\$75,001–\$100,000	57	5.27	16	6.87	11	10.48	
>\$100,000	65	6.01	19	8.15	3	2.86	

Note. Missing data were removed pairwise.

^adf = (2, 1614).

^bdf = (2, 1608).

^cdf = (2, 1249).

^ddf = (2, 1171).

^edf = (2, 1617).

^fdf = (10, 1606).

^gdf = (6, 1610).

^hdf = (8, 1433).

ⁱdf = (10, 1419).

across these timepoints. No statistically significant differences across time were found within this trajectory class. The high use trajectory class exhibited relatively similar (and high) PTSD

symptoms at each timepoint. Figure 2b illustrates the patterns of PTSD symptom change over time for the three cannabis use trajectory classes.

Table 2. Demographics and clinical characteristics for cannabis use trajectory classes

Measure	Low use		High use		Increasing use		<i>p</i> value
	Mean	s.d.	Mean	s.d.	Mean	s.d.	
Age (years)	36.77	13.43	30.60	10.38	31.12	10.22	<0.001 ^a
Education (years)	15.11	2.53	14.08	2.23	14.17	2.32	<0.001 ^b
CTQ-SF total	9.25	9.73	11.42	10.34	11.74	10.93	0.004 ^c
BMI	31.01	8.81	28.54	8.34	27.78	8.08	<0.001 ^d
	Count	%	Count	%	Count	%	
Gender							<0.001 ^e
Male	399	32.02	132	50.38	50	45.87	
Female	847	67.98	130	49.62	59	54.13	
Marital status							<0.001 ^f
Married	290	23.41	25	9.69	14	12.84	
Separated	45	3.63	7	2.71	7	6.42	
Divorced	152	12.27	25	9.69	7	6.42	
Annulled	2	0.16	0	0.0	0	0.0	
Widowed	26	2.10	2	0.78	2	1.83	
Never been married	724	58.43	199	77.13	79	72.48	
Race/ethnicity							0.03 ^g
Hispanic	140	11.26	34	13.13	19	17.59	
Non-Hispanic White	417	33.55	72	27.80	24	22.22	
Non-Hispanic Black	637	51.25	145	55.98	64	59.26	
Non-Hispanic other	49	3.94	8	3.09	1	0.93	
Employment code							0.99 ^h
Employed	816	74.18	178	74.79	70	73.68	
Retired	29	2.64	6	2.52	2	2.11	
Homemaker	22	2.00	4	1.68	1	1.05	
Student	46	4.18	10	4.20	4	4.21	
Unemployed, disabled, or other	187	17.00	40	16.81	18	18.95	
Income code							0.50 ⁱ
<\$19,000	374	34.31	95	40.25	31	33.33	
\$19,001–\$35,000	340	31.19	69	29.24	29	31.18	
\$35,001–\$50,000	156	14.31	26	11.02	14	15.05	
\$59,001–\$75,000	85	7.80	19	8.05	10	10.75	
\$75,001–\$ 100,000	67	6.15	10	4.24	7	7.53	
>\$100,000	68	6.24	17	7.20	2	2.15	

Note. Missing data were removed pairwise.

^adf = (2, 1614).

^bdf = (2, 1608).

^cdf = (2, 1249).

^ddf = (2, 1171).

^edf = (2, 1617).

^fdf = (10, 1606).

^gdf = (6, 1610).

^hdf = (8, 1433).

ⁱdf = (10, 1419).

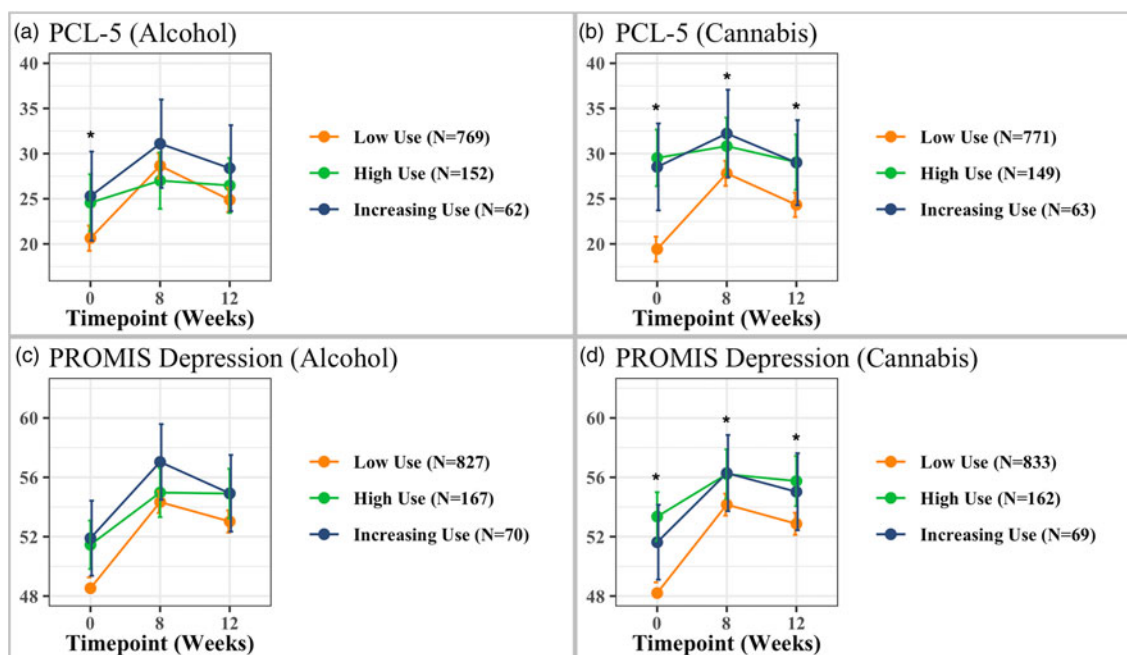
Cannabis use trajectories and change in depression symptoms

A statistically significant main effect of time, $F_{(2, 1811)} = 46.16$, $p < 0.001$, $\eta_p^2 = 0.04$, and a time by cannabis use trajectory class

interaction were observed $F_{(3, 1811)} = 3.68$, $p = 0.01$, $\eta_p^2 = 0.01$ (see Table 3 for means and standard deviations). Analyses revealed that the low use cannabis trajectory class had

Table 3. Means and standard deviation for posttraumatic stress disorder (PTSD) and depression symptoms

Timepoint	Posttraumatic stress symptoms					
	Alcohol use trajectory			Cannabis use trajectory		
	Low use mean (s.d.)	High use mean (s.d.)	Increasing use mean (s.d.)	Low use mean (s.d.)	High use mean (s.d.)	Increasing use mean (s.d.)
Baseline	20.90 (19.63)	24.55 (19.80)	23.69 (21.26)	19.76 (19.69)	28.42 (19.11)	27.56 (18.43)
Week 8	28.83 (20.06)	27.95 (18.13)	31.60 (18.66)	27.93 (19.45)	32.05 (20.06)	32.48 (20.38)
Week 12	25.14 (18.95)	27.36 (19.22)	27.81 (19.70)	24.55 (18.72)	30.28 (19.52)	28.32 (20.22)
Timepoint	Depression symptoms					
	Alcohol use trajectory			Cannabis use trajectory		
	Low use mean (s.d.)	High use mean (s.d.)	Increasing use mean (s.d.)	Low use mean (s.d.)	High use mean (s.d.)	Increasing use mean (s.d.)
Baseline	48.65 (10.89)	51.70 (10.41)	51.17 (11.25)	48.41 (10.51)	52.85 (11.56)	51.40 (11.75)
Week 8	54.41 (11.07)	55.42 (10.37)	57.75 (10.58)	54.20 (10.86)	56.93 (10.64)	56.95 (11.85)
Week 12	53.13(11.17)	53.49 (11.07)	53.27 (11.15)	52.92 (11.07)	56.19 (10.51)	55.18 (11.22)

**Figure 2.** Repeated-measures ANOVA examining interactions between levels of use and measures for PTSD (PCL) and depression (PROMIS). Analyses included three timepoints – baseline, week 8, and 12. Error bars represent 95% confidence interval; *denotes significant interaction.

significantly lower depression symptoms at baseline than the high use and increasing use trajectory classes. The low use cannabis trajectory class also showed lower depression symptoms at week 8 compared to the high use trajectory class and increasing use trajectory class. The low use cannabis trajectory class also showed lower depression symptoms at week 12 than the high use trajectory class and increasing use trajectory class. No statistically significant differences existed between the high and increasing use trajectory classes across timepoints. Within the low use trajectory classes, participants' depression symptoms increased from baseline to week 8 but decreased significantly from week 8 to week 12; however, week 12 symptoms were greater than those reported during the baseline recording. For the high and increasing use trajectory classes participants, depression symptoms significantly

increased from baseline to week 8 but were not statistically significantly different between week 8 and week 12. Figure 2d illustrates the patterns of depression symptom change over time for the three cannabis use trajectory classes.

Discussion

We examined alcohol and cannabis use trajectories among ED patients who recently suffered trauma and whether these trajectories were associated with changes in overall PTSD and depression symptoms over the 3 months following that trauma. We found that alcohol and cannabis use exhibited similar yet functionally different trajectory classes that included low, high, and increasing use trajectory classes. Specifically, the high and

increasing cannabis use trajectory classes exhibited similarly high PTSD and depression symptoms at week 8, unlike the low use group. Conversely, only the increasing alcohol use trajectory class exhibited higher PTSD and depression symptoms at week 8. These findings suggest that increasing cannabis intake after trauma may be linked to increased post-trauma sequelae. They also indicate that high cannabis use at the time of trauma may contribute to a vulnerability for developing post-trauma sequelae.

Contrary to our hypothesis, for both alcohol and cannabis, the increasing use trajectory classes did not show a statistically significant increase in PTSD symptoms over the 3-month posttrauma period. Instead, we observed the following by trajectory class. For the low use alcohol and cannabis classes: (1) PTSD symptoms were lower than the high use trajectory classes measured at the baseline timepoint collected in the ED; (2) PTSD symptoms increased from baseline to week 8, then decreased from week 8 to week 12; and (3) PTSD symptoms increased overall and reached a clinically significant severity threshold by week 12. The increasing cannabis trajectory classes reported higher PTSD symptoms at baseline that increased slightly to week 8 and decreased slightly from week 8 to week 12. In contrast, the high use alcohol and cannabis trajectory classes maintained similar high, clinically significant levels of PTSD symptoms at each timepoint.

Regarding depression symptoms, our results partly support our hypothesis. The low cannabis use trajectory class had lower depression symptoms recorded at baseline than the other two trajectory classes. Furthermore, all cannabis trajectory classes showed similar patterns of increased depression symptoms from baseline to week 8, yet only the low use trajectory class exhibited decreased symptoms from week 8 to week 12. In contrast, for the alcohol use trajectory classes, there was a statistically significant pattern with depression symptoms related to time over the 3-month follow-up period, but no significant interaction. The lack of interaction suggests that the three patterns of alcohol use did not differ in the occurrence of depression symptoms across time.

Our findings reveal two important characteristics of the participants in the low use trajectory classes for alcohol and cannabis use. First, low alcohol and cannabis users exhibited a greater initial increase in clinical symptoms between baseline and week 8 and subsequently a greater decrease from week 8 to week 12. While noteworthy, it is important to highlight that week 12 PTSD and depression symptoms in the alcohol and cannabis low use trajectory classes were greater than at baseline and that these participants' symptoms never returned to baseline levels. This latter finding, in part, provides some evidence that individuals who rarely consume substances could also be at risk for trauma and stress-related psychopathology compared to those who occasionally or frequently use alcohol or cannabis.

Individuals already using alcohol or cannabis exhibited clinically significant PTSD symptoms at baseline that did not significantly change over time. These findings align with other research showing that individuals with substance dependence exhibited greater rates of PTSD than controls (Gielen, Havermans, Tekelenburg, & Jansen, 2012). There could be several explanations for this pattern. The susceptibility hypothesis (Acierno, Resnick, Kilpatrick, Saunders, & Best, 1999; Chilcoat & Breslau, 1998; Cottler, Compton, Mager, Spitznagel, & Janca, 1992) suggests that individuals who use substances might place themselves in more dangerous situations and experience more traumatic events, increasing the likelihood of developing

posttraumatic symptoms after trauma. Indeed, research suggests that being subjected to more traumatic events in one's lifetime could increase PTSD symptoms (Breslau, Peterson, & Schultz, 2008). Such populations show a lifetime prevalence of trauma exposure up to 95% (Dansky, Saladin, Coffey, & Brady, 1997; Farley, Golding, Young, Mulligan, & Minkoff, 2004; Read et al., 2014; Reynolds et al., 2005). Thus, it may be that participants in the alcohol and cannabis high use and increasing groups had been subjected to more traumatic experiences, explaining the high PTSD symptoms reported in the 30 days following the trauma.

Furthermore, alcohol and cannabis use may make an individual more susceptible to developing posttraumatic stress symptoms due to an inability to successfully regulate stress response to a traumatic event. Both alcohol and cannabis use has been associated with dysregulation of hypothalamic-pituitary axis function. Alcohol consumption has been associated with excessive cortisol response (Richardson, Lee, O'Dell, Koob, & Rivier, 2008), whereas cannabis users show blunted cortisol reactivity in response to stress (Cservenka, Lahanas, & Dotson-Bossert, 2018). Heavy cannabis use has been associated with increased sympathetic arousal and fluctuations in heart rate variability [reviewed in (Wemm & Sinha, 2019)]. While we did not include biomarkers, future studies should examine differences in biological functions to determine whether the changes associated with alcohol and substance use affect biological processes that may make an individual susceptible to developing posttrauma psychopathology.

Alcohol consumption might exacerbate PTSD symptoms (Ouimette, Finney, & Moos, 1999; Volpicelli, Balaraman, Hahn, Wallace, & Bux, 1999), and may explain the greater baseline symptoms in the high use trajectory class than the low use trajectory class at baseline. Indeed, alcohol use might exacerbate posttraumatic stress over time by promoting negative coping strategies (Read et al., 2014). Read et al. (2014) used a cross-lagged panel model to test how coping may influence the associations between PTSD symptoms and alcohol use over time in trauma-exposed young adults entering college. Specifically, the authors showed an indirect association between problems caused by alcohol use and PTSD symptoms through negative coping.

Regarding depression symptoms, our study results suggest that for the cannabis trajectory classes, the high and increasing use classes exhibited relatively high symptoms at baseline in the ED that increased by week 8 and remained higher than baseline levels by week 12. One review found a similar association in heavy cannabis use with increasing depression symptoms (Degenhardt, Hall, & Lynskey, 2003). Cannabis use (Hser et al., 2017; Lev-Ran et al., 2014; Moore et al., 2007) and alcohol consumption have been associated with an increased risk for depression (McEachin, Keller, Saunders, & McInnis, 2008; Paljärvi et al., 2009; Sihvola et al., 2008) in some studies, though these findings have not been consistent (Rosenthal et al., 2018).

This study is not without limitations. First, the clinical information acquired was measured on a continuous scale. Therefore, we did not focus on only those who had a clinical diagnosis of PTSD, depression, and alcohol or SUD. Therefore, we cannot generalize the results to samples suffering from the dual clinical diagnosis of PTSD or depression and alcohol or SUD. Though, this also allows the exploration of sub-threshold populations. Second, our clinical measures' assessment was based only on self-report questionnaires and not clinician-based diagnostic assessments. Thus, the data may be a poor representation of the general population. Lastly, for the baseline timepoint, participants

were asked to report symptoms 30 days before the ED visit. Nevertheless, these responses were collected immediately after a traumatic event, potentially leading to inaccurate recall ability.

These limitations do not diminish the many strengths of this study. For one, our findings reveal that, shortly after trauma exposure, there appears to be a window of time wherein frequent substance users or those who increase their substance use may be more sensitive to their effects, potentially leading to the development of PTSD and depression symptoms. This is illustrated by increasing and high use groups having higher PTSD and depression symptoms at baseline, which increased and remained clinically significant over time. This points to the value of interventions or educational materials targeted to these sub-groups of trauma survivors shortly after the event to help prevent an increase in post-trauma sequelae. Furthermore, our data also highlight differences in trajectories and associations between clinical symptoms between substances. For example, while we did not find a significant time by substance use class interaction with depression symptoms for alcohol use, we did for cannabis. This suggests different mechanisms through which substances may negatively affect the development of post-trauma sequelae. Lastly, our data shed light on the importance of assessing PTSD and depression symptoms in substance-using individuals in the aftermath of trauma. Increasingly, substance use clinicals are incorporating trauma-informed care; this study highlights the importance of measuring trauma exposure and substance use in these clinical settings to provide more targeted services to patients. Future studies should examine these associations across even longer periods using more ecologically valid methods such as EMA.

To conclude, three alcohol and cannabis use trajectory classes demonstrated different relationships with changes in PTSD and depression symptoms across 3 months posttrauma. Our results illustrate an interaction between alcohol and cannabis use and change in clinical symptoms soon after trauma exposure. The findings highlight the importance of developing and implementing preventive measures for alcohol and cannabis use in recently trauma-exposed individuals to inhibit the development and continuation of severe post-traumatic sequelae.

Supplementary material. The supplementary material for this article can be found at <https://doi.org/10.1017/S0033291723001642>

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