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Longitudinal Associations Between Negative Urgency, Symptoms of Depression, Cannabis and Alcohol Use in Veterans

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## Longitudinal associations between negative urgency, symptoms of depression, cannabis and alcohol use in veterans

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### Abstract

There is a high comorbidity between symptoms of depression and cannabis and alcohol use in civilian and veteran populations. Prospective studies attempting to clarify the directionality of these comorbidities have yielded mixed results. Further, the relations between these constructs and impulsive personality, particularly negative urgency (NU, the tendency to act rashly when experiencing emotional distress) warrants further attention, as NU relates to symptoms of depression and alcohol and cannabis use. Importantly, NU partially accounts for the association between symptoms of depression and cannabis and alcohol problems in cross-sectional studies. This study examined alternative theories of directionality in order to better understand the longitudinal associations between symptoms of depression, NU, and cannabis or alcohol use. Three semi-annual waves of data (baseline, 6-month, and 12-month) were collected in parallel assessments from a sample of OEF/OIF/OND veterans ( $N=361$ ). Autoregressive cross-lagged panel models were used to test four alternative theory-driven models about the longitudinal associations between the interaction of symptoms of depression and NU and cannabis or alcohol use. Models revealed unique direction of effects specific to each substance, such that the interaction between symptoms of depression and NU at 6-months post-baseline predicted more alcohol use at 12-months post-baseline, whereas more cannabis use at 6-months post-baseline predicted more severe symptoms of depression at 12-months post-baseline. Results suggests alternate directions of effect for cannabis and alcohol use. Future research should examine these patterns over wider assessment periods in order to see more variability and change over time.

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## Keywords

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## Introduction

Aside from tobacco, cannabis and alcohol are the most commonly used substances nationwide (Substance Abuse and Mental Health Services Administration, 2019). Both alcohol and cannabis are often used to cope with the negative affect experienced with depression (Holahan, Holahan, Moos, Cronkite, & Randall, 2003; Simons, Gaher, Correia, Hansen, & Christopher, 2005). However, the use of substances such as cannabis and alcohol also predicts increased symptoms of depression and poorer clinical and health care outcomes (Lev-Ran et al., 2014; Sullivan, Fiellin, & O'Connor, 2005; Sullivan, Goulet, Justice, & Fiellin, 2011). These independent directional findings suggest that these constructs may be reciprocally related over time (i.e., bi-directionally associated). Consistent with this bi-directional association, individuals with cannabis and alcohol use disorders (CUD/AUD) have higher rates of major depressive disorder (MDD), relative to those without CUD or AUD (Chen, Wagner, & Anthony, 2002; Grant et al., 2016; Metrik et al., 2016). Rates of comorbidity between substance use disorders and mood disorders are also common among military veterans (Seal et al., 2009; Teeters, Lancaster, Brown, & Back, 2017). By testing parallel models of cannabis and alcohol use, we were able to examine whether or not similar patterns of associations with symptoms of depression exist across cannabis use and alcohol use.

Although little research has compared the association between depression symptoms and cannabis versus alcohol use within the same sample, extant cross-sectional and prospective studies have independently suggested use of both substances is strongly linked with depression symptoms. Cross-sectional research has shown that the link between symptoms of depression and cannabis use or CUD is robust both in the general population (Chen et al., 2002; Degenhardt, Hall, & Lynskey, 2003; Dierker, Selya, Lanza, Li, & Rose, 2018; Farris, Metrik, Bonn-Miller, Kahler, & Zvolensky, 2016; Feingold, Fox, Rehm, & Lev-Ran, 2015; Grant, 2004) and among veteran samples (Goldman et al., 2010; Metrik et al., 2016). A similar pattern has emerged for alcohol use. Numerous cross-sectional studies have found a link between AUD or alcohol use and symptoms of depression in the general population (e.g. Buckner, Keough, & Schmidt, 2007; Grant et al., 2015) and among veterans (Brooks Holliday, Pedersen, & Leventhal, 2016; Seal et al., 2011; Yoon, Petrakis, & Rosenheck, 2015).

The affective-motivational theory sheds light on the comorbidity among substance use and negative emotionality, positing that substances are used to regulate negative emotions. This theory underscores the central role of negative affect in motivating substance use (Baker, Piper, McCarthy, Majeskie, & Fiore, 2004; Cox & Klinger, 1988; Simons et al., 2005). Consistent with this theory, both cross-sectional (Bonn-Miller, Boden, Bucossi, & Babson, 2014; Brooks Holliday et al., 2016; Gonzalez, Reynolds, & Skewes, 2011; Metrik et al., 2016) and prospective (Swendsen et al., 2000) data suggest that greater intensity of negative

affect leads to increased cannabis use or alcohol use as a short-term means of coping with negative emotions. Importantly, this pattern of negative reinforcement from substances becomes increasingly salient with greater progression to alcohol or drug dependence when long-term neuroadaptation occurs in the withdrawal/negative affect stage of the addiction cycle (Koob & Volkow, 2010). Thus, coping-oriented use of substances can lead to increased depression symptoms over time (Martens et al., 2008; Swendsen & Merikangas, 2000), suggesting a bi-directional association among the constructs.

However, longitudinal studies of directions of effects specific to depression symptoms and MDD and cannabis use and CUD yield mixed findings. In both adolescent girls (Patton et al., 2002) and adults (Bovasso, 2001), increased cannabis use predicted increased symptoms of depression, but increased depression symptoms did not predict increased use of cannabis. When cannabis use and symptoms of depression were evaluated simultaneously to examine bi-directional effects from adolescence to adulthood, reciprocal associations were found, suggesting that they mutually exacerbate each other over time (Womack, Shaw, Weaver, & Forbes, 2016). In one systematic review, Lev-Ran and colleagues (2014) found that, controlling for baseline depression, cannabis use (and especially heavy use) was associated with increased risk for developing MDD. However, large epidemiological studies have found stronger evidence that MDD predicts CUD, rather than the reverse (Agosti, Nunes, & Levin, 2002; Blanco et al., 2016; Conway, Compton, Stinson, & Grant, 2006).

The prospective literature on alcohol use and depression yields a similarly mixed set of findings. Studies have found evidence that MDD precedes AUD (Kuo, Gardner, Kendler, & Prescott, 2006; McCarty et al., 2009), that AUD precedes MDD (Fergusson, Boden, & Horwood, 2009; Rohde, Lewinsohn, Kahler, Seeley, & Brown, 2001), as well as bi-directional associations (Bulloch, Lavorato, Williams, & Patten, 2012; Gilman & Abraham, 2001). Further, one large prospective study found that within the transition to adulthood (compared to other developmental transitions), MDD was more likely to precede AUD than the converse (Brière, Rohde, Seeley, Klein, & Lewinsohn, 2014). Similarly, a prospective study of individuals transitioning from adolescence to young adulthood found that symptoms of depression predicted persistence of alcohol problems (Copeland et al., 2012). Finally, veterans with depression pre-deployment were at increased risk of alcohol-related problems post-deployment (Jacobson et al., 2008). These mixed findings signal the associations between depression symptoms and cannabis or alcohol use may differ at the trait level, such as individual responses to the experience of negative affect.

Impulsive personality is trait that contributes significantly to the etiology of alcohol and cannabis use (Coskunpinar, Dir, & Cyders, 2013; Dawe & Loxton, 2004; De Wit, 2009; Gunn, Finn, Endres, Gerst, & Spinola, 2013; Settles et al., 2012; Verdejo-García, Lawrence, & Clark, 2008). Impulsivity is a multi-faceted trait, for which multiple models and conceptualizations exist. All facets of impulsivity have been linked to both alcohol and cannabis use in various populations (Coskunpinar et al., 2013; De Wit, 2009; Stamatou & Lau-Barraco, 2017). One model of impulsivity classifies impulsivity into five unique domains: negative urgency (NU), positive urgency, sensation seeking, lack of perseverance, and lack of premeditation (Lynam, Smith, Whiteside, & Cyders, 2006; Smith et al., 2007; Whiteside & Lynam, 2001). When examined together, each of these constructs are related to

specific risky behaviors (Adams, Kaiser, Lynam, Charnigo, & Milich, 2012; Birthrong & Latzman, 2014; Cyders, Flory, Rainer, & Smith, 2009; Derefinko, Dewall, Metze, Walsh, & Lynam, 2011; Smith et al., 2007). Specifically, trait negative urgency (NU), which is characterized as the tendency to engage in rash action while experiencing emotional distress (Whiteside & Lynam, 2001), may be particularly relevant to the comorbidity between symptoms of depression and cannabis or alcohol use (Dvorak & Day, 2014; Kaiser, Milich, Lynam, & Charnigo, 2012; Simons et al., 2005; Smith & Cyders, 2016).

In the context of the affective-motivational theory (Cox & Klinger, 1988; Simons & Carey, 2006), those who are high in trait NU and who also experience increased negative affect associated with symptoms of depression may be more likely to drink or use cannabis relative to individuals with low NU traits. This may be due to the reduced ability to inhibit substance use when experiencing negative affect. In fact, the link between symptoms of depression and increased NU has been observed in cross-sectional studies of undergraduate college students (Anestis, Selby, & Joiner, 2007), community samples (Novak, Novak, Lynam, & Foti, 2016), and this sample of veterans (Gunn et al., 2018). In line with this theory, NU partially accounted for high rates of comorbid depression and alcohol problems in a cross-sectional study of college students (Gonzalez et al., 2011). Another cross-sectional study found that higher levels of NU partially accounted for the positive association between symptoms of depression and alcohol use initiation in adolescents (Pang, Farrahi, Glazier, Sussman, & Leventhal, 2014). However, no studies to date have tested competing theories of directionality between symptoms of depression and cannabis or alcohol use while also considering individual differences in NU as a moderator of these associations longitudinally. This is particularly relevant among veterans, who experience higher levels of negative affect and symptoms of depression, compared to civilian samples (Kessler, Chiu, Demler, & Walters, 2005; Kessler et al., 2014). It may be that NU is an additional critical factor that could help to explain mixed findings regarding the directionality between depression and cannabis or alcohol use.

### **The Current Study**

The purpose of this longitudinal study is to examine temporal relationships by probing alternative directions of effects between symptoms of depression and substance use (cannabis and alcohol use), while considering whether NU interacts with symptoms of depression. We utilized three semi-annual waves of observational data from a sample of veterans deployed post-9/11/2001. Our primary aim was to determine the direction of effects among depression symptoms and cannabis use and alcohol use (independently) over time by comparing the fit of alternative models. Additionally, based on prior research and theory (Anestis et al., 2007; Gonzalez et al., 2011; Guillot, Pang, & Leventhal, 2014; Gunn, Jackson, Borsari, & Metrik, 2018; Smith & Cyders, 2016), we hypothesized that higher trait NU paired with more severe symptoms of depression would lead to more frequent cannabis and alcohol use at later assessment points.

## Methods

### Sample and Procedure

Participants ( $N=361$ ) completed a prospective study examining cannabis use and affective disorders in returning Operation Enduring Freedom, Operation Iraqi Freedom, and Operation New Dawn (OEF/OIF/OND) veterans who were deployed post 9/11/2001 and who used cannabis at least once in their lifetime. Participants were recruited from a Veteran's Health Administration (VHA) facility in the Northeast region of the United States by utilizing the VHA OEF/OIF/OND Roster, an accruing database of combat veterans who recently returned from military service in Iraq and Afghanistan and were enrolled in VHA (see Metrik et al., 2016, for details of recruitment procedures). Veterans were screened for eligibility by telephone and were invited for a baseline visit, at which time they signed informed consent and completed a battery of interview and self-report assessments. The baseline visit was followed by two additional visits with parallel assessments at 6-months ( $N=312$ ; 86.4% retention) and 12 months ( $N=310$ ; 85.9% retention). The study was approved by the university and local VHA Institutional Review Boards. Participants were compensated \$50 per visit and an additional \$50 bonus payment for completing all three visits.

### Measures

**Time-Line Follow-Back**—The Time-Line Follow-Back Interview (TLFB; (Dennis, Funk, Harrington Godley, Godley, & Waldron, 2004; Sobell & Sobell, 1992)) was used to assess past-six-month patterns of cannabis and alcohol use. The percent of cannabis and alcohol use days in the 30 days prior to each assessment was used in the present analyses to ensure that the variable captured cannabis and alcohol use across a time period that more closely matched our assessment of depression symptoms.

**UPPS-P Impulsive Behavior Scale**—Negative urgency was assessed using the Short UPPS-P Impulsive Behavior Scale (Cyders, Littlefield, Coffey, & Karyadi, 2014). The UPPS-P is a 20-item self-report inventory which uses a 4-point Likert scale to assesses five subscales of impulsive personality (negative urgency, positive urgency, sensation seeking, lack of premeditation, and lack of perseverance), each demonstrating high levels of internal consistency in previous studies (Cyders et al., 2014). The NU subscale demonstrated good internal consistency (baseline  $\alpha = .77$ , 6-months  $\alpha = .77$ , 12-months  $\alpha = .80$ ).

**Depression Symptoms**—Depressive symptoms over the past week were assessed at each study wave via the Center for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1997), which is a 20-item self-report inventory using a 4-point Likert scale. The CES-D demonstrated good internal consistency (baseline  $\alpha = .87$ , 6-months  $\alpha = .84$ , 12-months  $\alpha = .86$ ).

### Data Analytic Strategy

All analyses were conducted in Mplus version 8.2 using maximum likelihood estimation for missing data (Muthén & Muthén, 1998–2018). Missing data were minimal and largely due to attrition in the study, with 49 (14%) and 51(14%) data points missing at 6- and 12-

months, respectively, for CES-D and 47 (13%) and 49 (14%) data points at 6- and 12-months for cannabis and alcohol use. The present study utilized cross-lagged panel modeling (CLPM) which is well-suited for testing prospective associations with regard to directionality. We estimated four alternative models that systematically evaluate directional effects to inform hypotheses about the prospective association between the interaction of depression symptoms and NU (i.e., depression X NU) with cannabis and alcohol use, separately, over time (see Figure 1; Arnett et al., 2012). For example, in cannabis use models these prospective associations may include: (1) bi-directional effects of depression symptoms X NU on cannabis use and cannabis use on depression symptoms; (2) cannabis-driven effects, such that cannabis use results in more depression symptoms over time (cannabis use → depression symptoms) but depression X NU does not predict later cannabis use; (3) depression X NU driven effects, such that the interaction between depression symptoms and NU may result in more cannabis use over time (depression X NU → cannabis use) but cannabis use does not predict depression symptoms; or (4) no cross-lagged effects between depression X NU and cannabis use. All models examined time over and above autoregressive (i.e., stability) parameters. Parallel models were run for alcohol use. As outlined in the introduction, a theory-driven approach was taken to only examine the interaction between depression symptoms and NU on cannabis or alcohol use, as opposed to also examining the interaction between cannabis or alcohol use and NU on depression symptoms.

We first tested a saturated bi-directional model where all autoregressive and cross-lagged parameters were freely estimated for depression X NU and cannabis or alcohol use (Model 1, reference model). In Models 2–4, we systematically constrained cross-lagged parameters to zero (i.e., *c* and/or *d* cross-lagged parameters; see Figure 1) and compared these constrained models to the unconstrained model (Model 1) using a chi-square difference test. A statistically nonsignificant change in chi-square ( $p < .05$ ) between the unconstrained (Model 1) and constrained models (Models 2–4) indicates the paths constrained to zero can be removed from the model without a significant decrement in model fit. For models where the depression-NU interaction was significant, we proceeded with that model. When this interaction was not statistically significant, we then tested a model with only main effects (e.g., depression → cannabis use vs. cannabis use → depression). The most parsimonious model that did not result in a significant decrement in model fit when compared to Model 1 was selected.

Model fit was evaluated using chi-square ( $\chi^2$ ), comparative fit index (CFI), and root mean square error of approximation (RMSEA), with CFI values above .90 indicating good model fit (Hu & Bentler, 1999) and with RMSEA values of .06 (or below) suggesting a closer fit to the data and values of .08 and .10 values representing fair and marginal fit, respectively (Browne & Cudeck, 1993). Akaike's Information Criteria (AIC) and Bayesian Information Criterion (BIC) were also inspected to guide model selection, where lower values indicate closer fit to the data (Vrieze, 2012). All variables were centered and all models adjusted for age and percent cannabis use days (for alcohol models) and percent alcohol use days (for cannabis models) at each assessment point. Race, ethnicity, sex, and marital status were also considered as covariates but these were not statistically significant and were subsequently removed from all analyses.



## Results

Demographic and descriptive statistics are presented in Table 1.

### Cannabis Model 1: Bi-directional model

Fit statistics for all models are presented in Table 2. Model 1 examined the most-saturated model by estimating the bi-directional associations between depression symptoms X NU on cannabis use and cannabis use on depression symptoms (see Figure 1) across three time points. Less than adequate model fit was obtained (CFI=.897; RMSEA=.115 [90% CI=.097-.135];  $\chi^2 = 138.25(28)$ ,  $p < .001$ ). Regarding cross-lagged paths, more cannabis use at 6-months post baseline significantly predicted increased depressive symptoms at 12-months post baseline ( $\beta = .11$ ; 95% CI=.01, .21). However, there were no significant cross-lagged paths for depression X NU on later cannabis use at either time point. We subsequently examined a model without the interaction between depression and NU. Model fit indices were suboptimal (CFI=.85; RMSEA=.124 [90% CI=.11, .14];  $\chi^2 = 207.73(37)$ ,  $p < .001$ ). This model served as the reference model for all nested comparisons; all model fit statistics are presented in Table 2, panel A. All autoregressive paths for cannabis use and depression symptoms were positive and significant. The cross-lagged path from cannabis use at 6-months to depressive symptoms at 12-months remained significant ( $\beta = .11$ ; 95% CI=.01, .21), whereas the reverse effect was not statistically significant (see Table 3).

### Cannabis Model 2–4: Test of direction of effects

Next, we compared Models 2–4 to Model 1. Models 2, 3, and 4 also revealed marginally acceptable fit. Whereas there was a significant chi-square difference test for Model 3 versus Model 1 (Table 2, panel A), the chi-square difference test for Model 2 (i.e., cannabis-driven effects) versus Model 1 ( $\chi^2(2) = 2.03$ ,  $p = .36$ ) and Model 4 (i.e., no cross-lagged effects) versus Model 1 ( $\chi^2(4) = 8.72$ ,  $p = .07$ ) were not significant, indicating that constraining these parameters did not result in significantly worse model fit. To examine comparative model fit between these two models (2 and 4), we conducted another chi-square difference test (i.e., Model 2 versus Model 4 because Model 4 is nested under Model 2) and found that Model 4 differed significantly from Model 2 ( $\chi^2(2) = 6.70$ ,  $p = .04$ ), indicating that Model 2 retained the best fit to the data; thus, it was selected. Results from this model again revealed the cross-lagged effect from cannabis use at 6-months post baseline to depression symptoms at 12-months post baseline ( $\beta = .11$ ; 95% CI=.01, .21; see Figure 2, Panel A), but not baseline cannabis use to depression symptoms at 6-months post baseline. Therefore, evidence from the comparative analytic models supports the prospective association between more frequent cannabis use at 6-months post baseline and subsequent increase in severity of depression symptoms 12-months post baseline.

### Alcohol Model 1: Bi-directional model

Model fit statistics are presented in Table 1, panel B. Good model fit was obtained in Model 1 (CFI=.877; RMSEA=.105 [90% CI=.09-.125];  $\chi^2 = 154.51(36)$ ,  $p = .00$ ). Autoregressive and cross-lagged path standardized estimates are reported in Table 4. All autoregressive paths for alcohol use and depression symptoms were positive and significant. Regarding cross-lagged paths, the interaction between depression symptoms and NU at 6-months



significantly predicted alcohol use at 12-months ( $\beta=.12$ ; 95% CI=.04, .19; see Figure 1) but not between baseline and 6-months post baseline. There were no significant cross-lagged paths for alcohol use to later depression symptoms at either time point. The covariances (baseline) and residual covariances between alcohol use and depression symptoms were not significant at any time point.

#### Alcohol Models 2–4: Test of direction of effects

Models 2, 3, and 4 also fit the data well. Comparisons between these models and Model 1 showed that the chi-square difference test for comparing Models 2 and 4 were significant (Table 2, panel B), suggesting worse fit for these models relative to Model 1. The chi-square difference test for Model 3 versus Model 1 ( $\chi^2(2) = 1.23, p = .54$ ) was not significant, indicating that constraining cross-lagged parameters from symptoms of depression to cannabis and alcohol use to zero did not result in significantly worse model fit; thus, Model 3 was selected. Results revealed a significant cross-lagged effect from the interaction of depression symptoms and NU at 6-months predicting alcohol use at 12-months ( $\beta=.11$ ; 95% CI=.04, .19; see Figure 3). Simple slope analyses revealed unstandardized estimates of  $-3.75$  ( $p = .30$ ) those 1 SD below the mean of NU,  $3.42$  ( $p = .09$ ) at the mean, and  $10.59$  ( $p < .001$ ) for 1 SD above the mean. In other words, veterans with higher symptoms depression and higher NU at 6-months reported more alcohol use one year later. This path was not significant from baseline depression symptoms X NU to alcohol use at 6-months. Therefore, results from the comparative analytic models support prospective associations between greater severity of depression symptoms in combination with higher levels of NU 6-months post baseline with subsequent alcohol use 12-months post baseline.

## Discussion

This study examined directions of effects between symptoms of depression alone and in conjunction with NU and cannabis or alcohol use in a sample of OEF/OIF/OND veterans. Directions of effects was tested rigorously and systematically using a series of nested autoregressive cross-lagged panel models, adjusting for age and cannabis or alcohol use (in respective models) at each time point. There was an interaction between symptoms of depression and NU at 6-months post baseline that predicted more frequent alcohol use 12-months post baseline, whereas cannabis use at 6-months post baseline predicted greater severity of depression symptoms 12-months post baseline. All other cross-lagged paths (from baseline to 6-months post baseline) were non-significant. As expected, autoregressive paths for symptoms of depression, alcohol use, and cannabis use were all highly significant and positive, suggesting stability over time.

As hypothesized, and consistent with prior studies of alcohol problems (Anestis et al., 2007; Gonzalez et al., 2011; Pang et al., 2014), there was a significant interaction between symptoms of depression and NU predicting more frequent alcohol use. This is the first study to find an association between depression symptoms and NU in the prediction of alcohol use, and the first study to examine these processes in veterans. These findings are consistent with an affective-motivational model which posits that symptoms of depression predict more frequent alcohol use. Further, the association between depression symptoms and alcohol use

may be exacerbated by high levels of NU. In other words, veterans with difficulty inhibiting appetitive behaviors who experience more severe symptoms of depression may be even more likely to drink in order to regulate frequent negative affect, leading to more frequent alcohol consumption. Consistent with other studies (e.g. Brière et al., 2014; Copeland et al., 2012), results did not suggest a bi-directional association (from alcohol use to increased symptoms of depression) in this sample.

However, it is important to note that some studies have found bi-directional associations (Bulloch et al., 2012). Heterogeneity in populations, controls, measures, and severity of depression symptoms may explain these associations. For example, this population of veterans who were predominately male may yield a different set of results compared to a population with a greater proportion of females (see Limitations). Taken together with this prior literature, results suggest that the longitudinal association between depression symptoms (especially when coupled with high levels of NU) and increased alcohol use is strong, but in some samples, alcohol use may also relate to increased symptoms of depression over time.

In contrast to the alcohol use findings, more cannabis use at 6-months post baseline predicted more severe symptoms of depression 12-months post baseline. These results are consistent with other studies suggesting cannabis use may be a risk factor for increased symptoms of depression (Bovasso, 2001; Degenhardt et al., 2003; Lev-Ran et al., 2014; Patton et al., 2002). Although it was hypothesized that the interaction between depression and NU would predict cannabis use, it may be that this moderator plays a greater role in accounting for the association with affect-related alcohol use, rather than cannabis use, over time. Consistent with this, a study of young adults found that anxiety symptoms, but not depression symptoms, were associated with frequency of cannabis use (Johnson, Bonn-Miller, Leyro, & Zvolensky, 2009), suggesting cannabis may not be used as frequently to manage depressive symptoms. Rather, use of cannabis may exacerbate symptoms of depression. This possible link between cannabis use and increased symptoms of depression has important implications for the use of cannabis to self-medicate mental health symptoms, particularly as use of medicinal cannabis is increasing in the general population and in veteran samples (Metrik, Bassett, Aston, Jackson, & Borsari, 2018) who also perceive cannabis as a low-risk substance (Wilkinson, van Schalkwyk, Davidson, & D'Souza, 2016).

Additionally, cross-sectional analysis from our group in this same sample found that NU partially accounted for the association between MDD and cannabis problems, but not cannabis use (Gunn et al., 2018). It is possible that the effect of NU is more consequential when the relationship between depression and cannabis involvement is amplified to higher levels of impairment—that of a major psychiatric disorder in relation to clear negative consequences from cannabis use. Although this and prior studies suggest that cannabis use may lead to later increased symptoms of depression, there is also robust evidence for the opposite direction of effects (Agosti et al., 2002; Conway et al., 2006) as well as absence of a longitudinal relationship between cannabis use and depression (Blanco et al., 2016). Furthermore, there is evidence of shared genetic risk for depression and cannabis use, suggesting that there may be an underlying propensity to experience both (Reviewed in Hasin, 2018). Future research should examine within- and between-person variability over

time between symptoms of depression and cannabis use while also considering the role of NU.

Contrasting patterns of effects between cannabis versus alcohol use which may suggest unique etiology of cannabis versus alcohol use with depression symptoms and NU. For alcohol, the only significant directional cross-lagged effect observed was from the interaction between depression symptoms and NU predicting subsequent alcohol use, whereas for cannabis, increased use predicted greater severity of depression six months later. These associations were both limited to the 6-month to 12-month timepoints, however, with no significant effects from baseline to 6-months post baseline. Given the observational nature of the study, it is difficult to interpret potential explanations for these differences between time points, as we would have expected the effects observed to be consistent across time periods. Future research should consider examining these patterns across a longer study window to potentially capture more variability within the constructs, as well as possibly changes in the associations across constructs over time. Although we did not explore additional mechanisms (i.e., mediators) of the effects observed here, these findings suggest that coping-related alcohol use may be particularly prevalent among veterans high in NU. The relationship between cannabis and depression is complex and may vary by the severity of cannabis use and depression, other substance use, and situational factors that may drive these effects (Troup, Andrzejewski, Braunwalder, & Torrence, 2016). It is also possible that an alternative mechanism, such as social avoidance or isolation resulting from cannabis use leads to increased depression symptoms over time (Buckner, Heimberg, & Schmidt, 2011).

### Strength and Limitations

To our knowledge, this is the first study to examine competing models of directionality between depression symptoms in conjunction with NU and cannabis or alcohol use. We used a statistically robust approach to examine these associations prospectively. A few limitations should be considered when interpreting the results of this study. First, the cannabis models revealed poorer fit to the data compared to alcohol models, therefore these findings require replication and should be considered preliminary. Second, this sample had relatively low levels of depression symptoms overall. Although we had a relatively high proportion of individuals with a current major depressive disorder (15%) relative to the general population (Kessler et al., 2005). Future research should examine clinical samples with higher rates of depression symptoms in order to fully characterize these associations. The sample also had relatively low proportion of current cannabis users relative to alcohol users (45 and 94%, respectively). Although including a range of cannabis use in the sample strengthens the test of its association with depression symptoms, a sample of more regular cannabis users may have impacted the strength of the relationship between depression symptoms, negative urgency, and frequency of cannabis use. Third, similar to many studies of veterans who are disproportionately male, a small number of females limit the generalizability of findings to both sexes. Gender difference is particularly important to examine in future research given higher prevalence rates of depression in women (Substance Abuse and Mental Health Services Administration., 2018). Finally, the current study focused on substance use frequency (rather than AUD and/or CUD) and depression symptoms rather than MDD. Although the use of categorical diagnoses is crucial for prioritizing individuals most in need

of intervention, the utility of symptom counts vs. categorical diagnoses have been demonstrated for dimensional behaviors (Micalizzi, Brick, Marraccini, Benca-Bachman, Palmer, & Knopik, under review). Levels of both depression and substance use are variable within the population and it is important to understand how those varying levels interrelate. In light of this, different patterns of effects may emerge across dimensional and clinical characterization of variables, and this fact should be considered carefully and evaluated empirically in future studies.

## Conclusions

The present study utilized data from a sample of veterans assessed across a period of 12-months to evaluate how depression symptoms and NU are related to cannabis or alcohol use over time. For alcohol, the only significant cross-lagged effect observed was from the interaction between depression symptoms and NU at 6-months post baseline predicting alcohol use at 12-months post baseline. Whereas for cannabis, increased use at 6-months post baseline predicted greater severity of depression symptoms 12-months post baseline. These findings suggest unique etiology of cannabis versus alcohol use with depression in that veterans high in depression symptoms and NU are at increased risk for more alcohol use; whereas veterans with higher levels of cannabis use are at increased risk for depression symptoms over time.

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**Public Significance Statement**

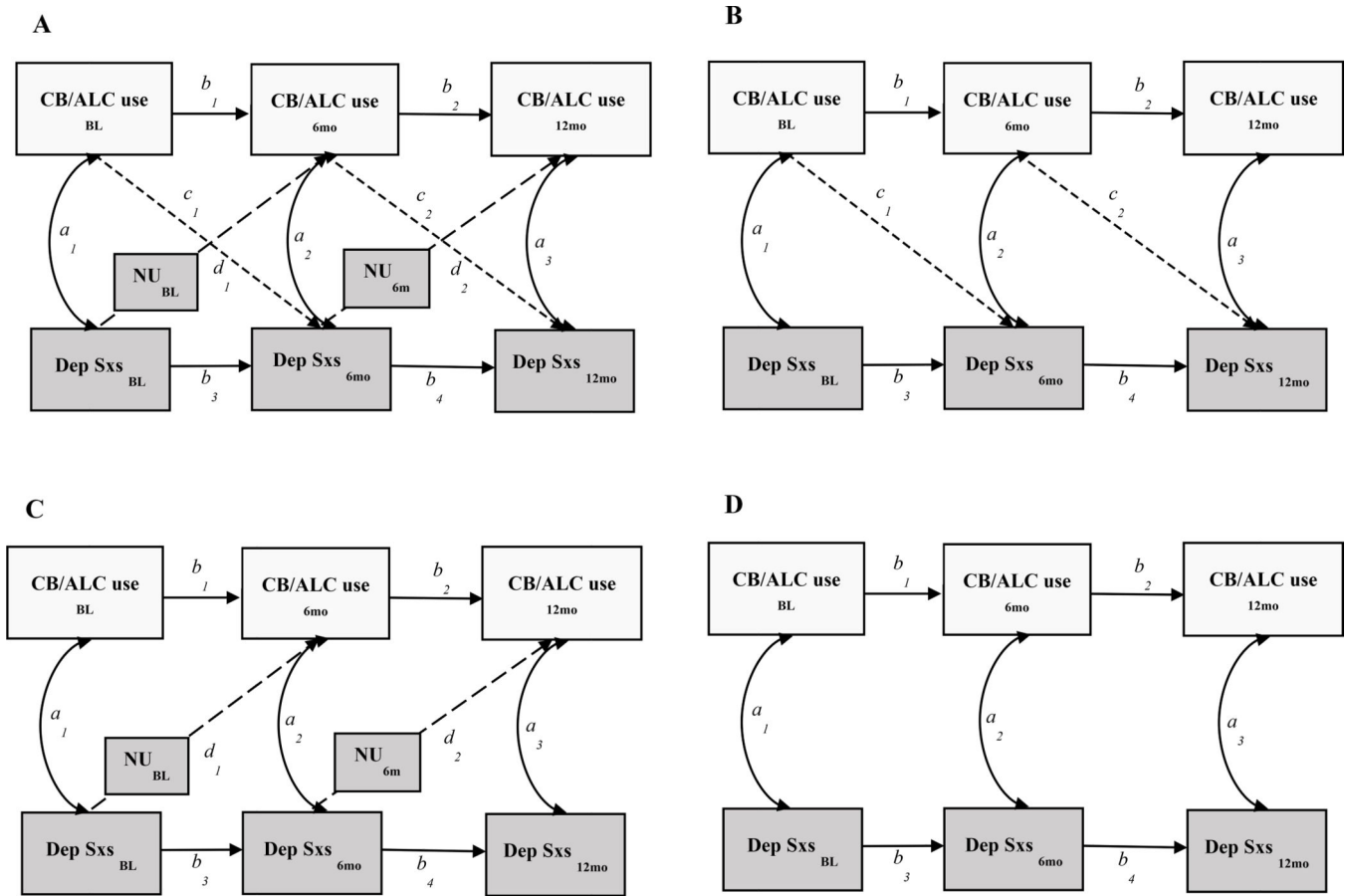
Depression, cannabis use, and alcohol use are significant problems among the general public and military veterans. Results from this study suggest that symptoms of depression are related to cannabis use and alcohol use in different ways among veterans. Veterans with more severe symptoms of depression and high trait negative urgency use alcohol more frequently over time.

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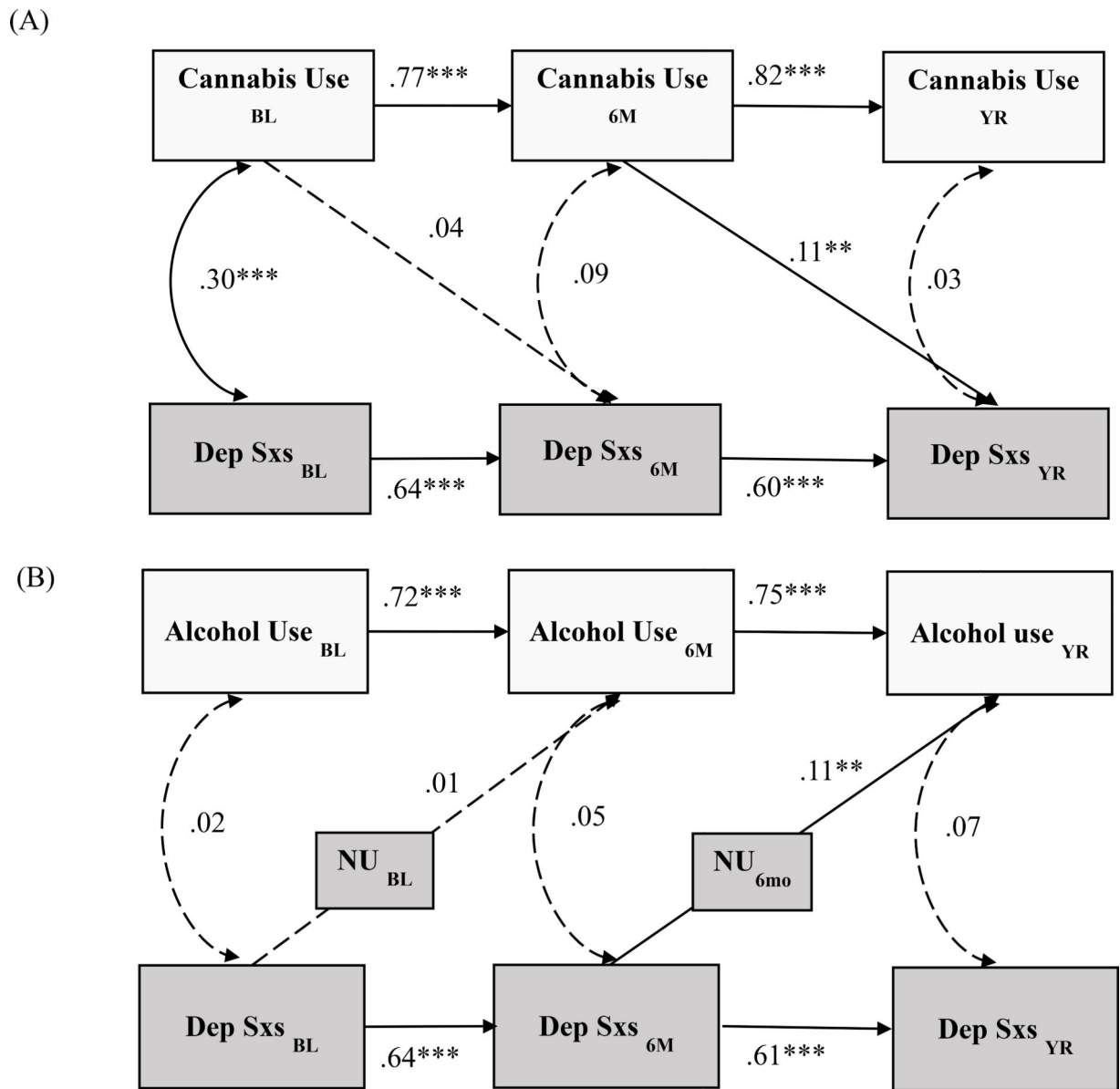
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**Figure 1. Analytic approach of alternative autoregressive cross-lagged panel path models.** Autoregressive cross-lagged panel path model depicting associations between cannabis use, alcohol use, symptoms of depression, and the interaction with NU across three time points. Curved, double-headed arrows represent correlations among the variables, diagonal arrows represent cross-lagged paths, straight arrows represent autoregressive paths. NU box represents path with interaction of depression symptoms and NU. (A) Bidirectional effects of depression symptoms X NU on cannabis/alcohol use and cannabis/alcohol use on depression symptoms; (B) Cannabis/alcohol-driven effects, such that cannabis/alcohol use results in more depression symptoms over time (d paths dropped); (C) Depression symptoms X NU driven effects, such that the interaction between depression symptoms and NU may result in more cannabis/alcohol use over time (c paths dropped); or (D) No cross-lagged effects between depression symptoms X NU and cannabis/alcohol use over time (c and d paths dropped).



**Figure 2. Results from the best fitting cross-lagged panel model for cannabis use (panel A) and alcohol use (panel B)**

\*\*\* $p < .001$ ; \*\* $p < .01$ . Cannabis use = past month % cannabis use days from TLFB; Alcohol use = past month % alcohol use days from TLFB; Dep sxs = CES-D depression symptoms.

Curved, double-headed arrows represent correlations among the variables that they connect.

Dashed paths were not significant. All variables centered.

**Table 1.**

## Sample Demographics and descriptive statistics

Variable	<i>n</i>	%
Gender <sup>a</sup>		
Male	337	93
Race <sup>a</sup>		
White	289	80
Black/African American	16	4
Asian	6	2
Native Hawaiian/Pacific Islander	2	.8
American Indian/Alaska Native	2	2.8
Multiracial	17	4
Other	29	8
Ethnicity <sup>a</sup>		
Hispanic/Latino(a)	43	27
Marital Status <sup>a</sup>		
Single/Never married	116	32
Married/Living with partner	173	48
Divorced/Separated	72	20
Employment Status <sup>b</sup>		
Employed	283	78
Unemployed/Homemaker	67	19
Student	87	24
Military Service	101	28
Combat Operation (s) served in <sup>ab</sup>		
Operation Enduring Freedom (OEF)	269	75
Operation Iraqi Freedom (OIF)	191	53
Operation New Dawn (OND)	71	20
<b>Most recent branch of service</b>		
<b>Army</b>	<b>249</b>	<b>69</b>
<b>Marines</b>	<b>30</b>	<b>8</b>
<b>Air Force</b>	<b>32</b>	<b>9</b>
<b>Navy</b>	<b>46</b>	<b>13</b>
<b>Coast Guard/Other</b>	<b>4</b>	<b>1</b>
Current Cannabis Use Disorder (BI)	53	15
Current Alcohol Use Disorder (BI)	113	31
Current Major Depressive Disorder (BI)	53	15
<b>Any alcohol use<sup>c</sup></b>	<b>340</b>	<b>94</b>
<b>Any cannabis use<sup>c</sup></b>	<b>163</b>	<b>45</b>
	<i>M</i>	<i>SD</i>

Variable	<i>n</i>	%
Age <sup>a</sup>	33.56	9.44
<b>Years since last deployment</b>	<b>3.93</b>	<b>2.80</b>
<b>Number of deployments</b>	<b>1.87</b>	<b>1.15</b>
BI CES-D	.72	.73
6mo CES-D	.65	.65
12mo CES-D	.60	.64
BI NU	2.16	.72
6mo NU	2.12	.71
BI % Alcohol use <b>days</b>	25.90	29.87
6mo % Alcohol use <b>days</b>	27.82	31.39
12mo % Alcohol use <b>days</b>	26.46	31.45
BI % Cannabis use <b>days</b>	16.81	34.93
6mo % Cannabis use <b>days</b>	16.49	33.61
12mo % Cannabis use <b>days</b>	16.31	33.72

*Note.* *N*=361, BL=baseline assessment, 6mo= 6-month follow-up; 12mo=12-month follow-up assessment, NU = **Negative urgency**, CES-D = **symptoms of depression from the Center for Epidemiological Studies-Depression Scale**

<sup>a</sup>Baseline assessment reported

<sup>b</sup>Multiple responses permitted

<sup>c</sup>Defined as reporting use on at least one day on the Timeline Follow-back across all three time points.



**Table 2.**

Model fit statistics for four alternative models

Model	$\chi^2$	df	CFI	RMSEA	BIC	AIC	$\chi^2$	df	<i>p</i>
A. Cannabis Use Models									
1	207.73	37	.850	.124	10829.58	10685.39			
2	209.75	39	.850	.121	10820.21	10683.42	2.03	2	.36
3	214.35	39	.846	.123	10824.80	10688.01	6.62	2	.04
4	216.44	41	.845	.120	10815.51	10686.12	8.72	4	.07
B. Alcohol Use Models									
1	154.51	36	.877	.105	9794.56	9650.63			
2	169.18	42	.868	.101	9775.08	9653.30	14.67	6	.03
3	155.75	38	.878	.102	9784.41	9647.87	1.23	2	.54
4	170.41	44	.869	.099	9764.93	9650.53	15.90	8	.04

*Note.* CFI = comparative fit index; RMSEA = root mean square error of approximation; BIC = Bayesian Information Criteria; AIC = Akaike's Information Criteria. Model 1 (comparison for all nested models): Bidirectional associations (i.e., depression X NU ↔ cannabis/alcohol use); Model 2: cannabis/alcohol use to depression symptoms; Model 3: depression symptoms x NU to cannabis/alcohol use; Model 4: no reciprocal transactions modeled. Model comparisons reflect a chi-square difference test comparing Models 2–4 to Model 1 for both outcomes. A *p*-value <.05 reflects a statistically significant difference in model fit.

**Table 3.**

Standardized parameter estimates (standard errors) from the traditional and nested cross-lagged panel models examining cannabis use

	Model 1	Model 2	Model 3	Model 4
<b>Autoregressive</b>				
<b>Cannabis Use</b>				
BI → 6mo	0.75 (0.03)***	0.77 (0.03)***	0.75 (0.03)***	0.77 (0.03)***
6mo → 12mo	0.82 (0.02)***	0.82 (0.02)***	0.82 (0.02)***	0.82 (0.02)***
<b>Depression Symptoms</b>				
BI → 6mo	0.64 (0.04)***	0.64 (0.04)***	0.66 (0.03)***	0.65 (0.03)***
6mo → 12mo	0.60 (0.04)***	0.60 (0.04)***	0.63 (0.04)***	0.63 (0.04)***
<b>Cross-lagged</b>				
<b>Cannabis Use → Depression Symptoms</b>				
BI → 6mo	0.04 (0.05)	0.04 (0.05)	—	—
6mo → 12mo	0.11 (0.05)**	0.11 (0.05)**	—	—
<b>Depression Symptoms → Cannabis Use</b>				
BI → 6mo	0.06 (0.04)	—	0.06 (0.04)	—
6mo → 12mo	0.01 (0.03)	—	0.01 (0.03)	—
<b>Covariance</b>				
<b>Cannabis Use/ Depression Symptoms</b>				
BI	0.30 (0.05)***	0.30 (0.05)***	0.30 (0.05)***	0.30 (0.05)***
6mo	0.10 (0.06)	0.09 (0.06)	0.09 (0.06)	0.09 (0.06)
12mo	0.03 (0.06)	0.03 (0.06)	0.03 (0.06)	0.03 (0.06)

Note. Model 1: Bidirectional associations from depression symptoms to cannabis use vs. cannabis use to depression symptoms; Model 2: cannabis use to depression symptoms; Model 3: depression symptoms to cannabis use; Model 4: no cross-lagged parameters modeled. Assessments: BI=baseline; 6mo=6 months post-baseline; 12mo=12 months post-baseline.

Standardized parameter estimates (standard errors) from the traditional and nested cross-lagged panel models examining alcohol use

**Table 4.**

	Model 1	Model 2	Model 3	Model 4
<b>Autoregressive</b>				
<b>Alcohol Use</b>				
BI → 6mo	0.72 (0.03)***	0.72 (0.03)***	0.72 (0.03)***	0.72 (0.03)***
6mo → 12mo	0.75 (0.03)***	0.75 (0.03)***	0.75 (0.03)***	0.75 (0.03)***
<b>Depression Symptoms</b>				
BI → 6mo	0.64 (0.04)***	0.64 (0.04)***	0.64 (0.04)***	0.64 (0.04)***
6mo → 12mo	0.61 (0.04)***	0.61 (0.04)***	0.61 (0.04)***	0.61 (0.04)***
<b>Cross-lagged</b>				
<b>Alcohol Use → Depression Symptoms</b>				
BI → 6mo	0.05 (0.05)	0.05 (0.05)	—	—
6mo → 12mo	-0.02 (0.05)	-0.02 (0.05)	—	—
<b>Depression symptoms (Dep) X NU → Alcohol Use</b>				
BI Dep x NU → 6mo	0.01 (0.04)	—	0.01 (0.04)	—
BI Dep	-0.00 (0.04)	—	-0.00 (0.04)	—
BI NU	0.03 (0.04)	—	0.03 (0.04)	—
6mo Dep x NU → 12mo	0.11 (0.04)*	—	0.11 (0.04)*	—
6mo Dep	0.07 (0.04)	—	0.07 (0.04)	—
6mo NU	-0.07 (0.04)	—	-0.07 (0.04)	—
<b>Residual Covariance</b>				
<b>Alcohol Use/ Depression Symptoms</b>				
BI	0.02 (0.06)	0.02 (0.06)	0.02 (0.06)	0.02 (0.06)
6mo	0.05 (0.06)	0.05 (0.06)	0.05 (0.06)	0.05 (0.06)
12mo	0.09 (0.06)	0.07 (0.06)	0.09 (0.06)	0.07 (0.06)

*Note.* Model 1: Bidirectional from depression symptoms X NU to alcohol use vs. alcohol use to depression symptoms; Model 2: alcohol use to depression symptoms; Model 3: depression symptoms x NU to alcohol use; Model 4: no cross-lagged parameters modeled. Assessments: BI=baseline; 6mo=6 months post-baseline; 12mo=12 months post-baseline.

$p < .001$   
\*\*\*  
 $p < .01$   
\*\*  
 $p > .05$   
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