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## Patterns of co-occurring addictions, PTSD, and MDD in detoxification treatment seekers: Implications for improving detoxification treatment outcomes

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Brief Article:

Patterns of Co-Occurring Addictions, Posttraumatic Stress Disorder, and Major Depressive Disorder in Detoxification Treatment Seekers:  
Implications for Improving Detoxification Treatment Outcomes

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### Abstract:

**Background and Objectives:** Poly-substance use and psychiatric comorbidity are common among individuals receiving substance detoxification services. Posttraumatic stress disorder (PTSD) and major depressive disorder (MDD) are the most common co-occurring psychiatric disorders with substance use disorder (SUD). Current treatment favors a one-size-fits-all approach to treating addiction focusing on one substance or one comorbidity. Research examining patterns of substance use and comorbidities can inform efforts to effectively identify and differentially treat individuals with co-occurring conditions.

**Methods:** Using latent class analysis, the current study identified four patterns of PTSD, MDD, and substance use among 375 addiction treatment seekers receiving medically supervised detoxification.

**Results:** The four identified classes were: 1) a PTSD-MDD-Poly SUD class characterized by PTSD and MDD occurring in the context of opioid, cannabis, and tobacco use disorders; 2) an MDD-Poly SUD class characterized by MDD and alcohol, opioid, tobacco, and cannabis use disorders; 3) an alcohol-tobacco class characterized by alcohol and tobacco use disorders; and 4) an opioid-tobacco use disorder class characterized by opioid and tobacco use disorders. The observed classes differed on gender and clinical characteristics including addiction severity, trauma history, and PTSD/MDD symptom severity.

**Discussion and Conclusions:** The observed classes likely require differing treatment approaches. For example, people in the PTSD-MDD-Poly SUD class would likely benefit from treatment approaches targeting anxiety sensitivity and distress tolerance, while the opioid-tobacco class would benefit from treatments that incorporate motivational interviewing. Appropriate matching of treatment to class could optimize treatment outcomes for polysubstance and comorbid psychiatric treatment seekers. These findings also underscore the importance of well-developed referral networks to optimize outpatient psychotherapy for detoxification treatment-seekers to enhance long-term recovery, particularly those that include transdiagnostic treatment components.

Patterns of Co-Occurring Addictions, PTSD, and MDD in Detoxification Treatment Seekers:  
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## 1. Introduction

Psychiatric comorbidity is highly prevalent in addiction treatment seekers; for instance, 11-41% of people seeking treatment for a substance use disorder (SUD) also meet criteria for posttraumatic stress disorder (PTSD: Read, Brown, & Kahler, 2004). SUD-PTSD comorbidity is especially noteworthy as this comorbidity is associated with more intense cravings and higher rates of relapse following addiction treatment (Brenz & Coffey, 2012) than is SUD alone. Both PTSD and SUD are associated with increased risk for major depressive disorder (MDD: Lai, Cleary, Sitharthan, & Hunt, 2015). Further, PTSD or SUD comorbid with MDD is associated with more severe psychosocial impairment than either PTSD or SUD alone (Erfan, Hashim, Shaheen, & Sabry, 2010). Difficulties in treating SUD comorbidities may be exacerbated in the detoxification setting where treatment seekers may have different motivations and priorities than those in traditional outpatient settings (Freyer-Adam, Gaertner, Rumpf, John, & Hapke, 2010). Indeed, the few differential predictors of SUD treatment outcome identified in Project MATCH are characteristics that are more common in PTSD-SUD samples: more severe psychopathology and anger (Coffey, Schumacher, Brimo, & Brady, 2005). The goal of this study was to identify comorbidity profiles in a special population of people who use substances, detoxification treatment seekers, in order to inform integrative SUD-comorbidity treatment protocols.

Given the prevalence and negative sequelae of psychiatric comorbidity in addiction treatment seekers, current practice guidelines recommend integrative treatments that address both addiction problems and co-occurring psychiatric problems throughout the course of treatment (SAMHSA, 2006). Integrated protocols often consist of cognitive behavioral therapy (CBT) combined with motivational interviewing techniques or a combination of different CBT

protocols. Although integrative treatments are the most efficacious option, many patients still do not respond to these treatments, leaving room for improvement and innovation (Hien et al., 2009). Currently, there is no established standard regarding what components, treatment targets, or number of sessions to include in integrative treatment protocols. Often providers are left to make educated guesses about these important decisions. Research targeted towards better understanding subgroups of detoxification seekers is important to highlight potential differences that can be targeted in treatment. Yet, detoxification seekers have often been excluded from large scale psychotherapy outcome research making it unclear how results from prior patient characteristic/treatment matching research apply to this group (Project MATCH, 1997).

One area of clarity in treatment guidelines is the necessity of delivering treatment for an appropriate duration – a challenge in the detoxification setting given that treatment goals in this context are focused on medically stabilizing patients from extreme use (SAMHSA, 2006). Despite this challenge, detoxification facilities, as the entry point into addiction treatment, are also in a unique position to increase patient success. Detoxification facilities can make long-term treatment recommendations following stabilization that are individualized to the unique needs and problem areas experienced by patients. People seeking treatment at detoxification centers may be more motivated for treatment (Freyer-Adam et al., 2010); yet, people with comorbidities are more likely to drop out of treatment than people without comorbidities, emphasizing the need to match comorbidity profiles to post-detox referral patterns (Tómasson & Vaglum, 1998).

In addition to psychiatric comorbidities, polysubstance use also creates challenges for treatment. Polysubstance use is associated with more severe addiction problems (Moss, Goldstein, Chen, & Yi, 2015), more frequent emergency department admissions (Tait, Hulse, Robertson, & Sprivulis, 2005), greater risk of both non-fatal and fatal overdose (Darke et al.,

2014), greater dropout in detox settings (Tómasson & Vaglum, 1998), and greater risk for relapse following treatment than outcomes for people who use a single substance (Branson, Clemmey, Harrell, Subramaniam, & Fishman, 2012). Furthermore, polysubstance use is associated with increased rates of both MDD and PTSD than rates of these disorders among people who use a single substance (Conway et al., 2013); this is particularly true among those who have experienced interpersonal violence (Ullman & Long, 2008).

Many forms of interpersonal violence disproportionately affect more women than men (Black et al., 2011); which likely contributes to gender-related PTSD-SUD disparities. Women often present with more complex psychiatric symptoms and severe symptoms than men, related to higher rates of interpersonal violence including rape (Najavits, Weiss, & Shaw, 1997). Although women are more likely to have PTSD, men are more likely to seek treatment for SUDs (Najavits, Weiss, & Shaw, 1997; Cohen, Feinn, Arias, Kranzler, 2007). These findings underscore the importance of examining gender differences in studies of psychiatric and SUD comorbidity.

Latent class analysis (LCA) is a person-centered statistical technique that identifies subgroups of individuals who share common values on some set of variables. This feature makes it an ideal tool for examining patterns of polysubstance use and psychiatric comorbidity in people who use substances. Furthermore, in the context of detoxification treatment, it can inform the referral process used to determine appropriate treatment options following medical stabilization by identifying subgroups of patients with common problem areas. Research using LCA in SUD populations has typically identified three classes: a limited involvement class (characterized by alcohol, tobacco, and marijuana use); a moderate involvement class (characterized by substance use including alcohol, tobacco, marijuana, and amphetamine use);

and an extended involvement class (characterized by the use of a large number of substances including alcohol, tobacco, marijuana, amphetamines, non-medical prescription drugs, and other illicit drugs). Members of the extended involvement class tend to have elevated levels of anxiety and depression (Connor et al., 2013). Yet, most research conducting LCAs in people who use substances has not examined PTSD as a comorbid diagnosis. Further, when studies have examined PTSD it was as a covariate, rather than as an indicator variable (a variable used to define classes). This conceptual difference can dramatically impact findings – considering PTSD as an indicator suggests that PTSD is considered to have a possible shared etiology while considering it as a covariate suggests that PTSD is considered more a post-hoc complication. Utilizing PTSD as a covariate is contrary to the tension-reduction model of PTSD-SUD comorbidity which postulates that SUD problems develop after a traumatic event as part of a maladaptive coping process (Berenz & Coffey, 2012).

Despite the growing literature applying LCA to polysubstance use and comorbid psychiatric disorders, limited research has attempted to identify subgroups of people in detoxification treatment-seekers. As described, this is a substantial limitation given that class identification in this unique population can inform treatment and referral approaches which may be especially important in a short-term setting.

### *1.1 Current Study*

The current study used LCA to examine how PTSD, multiple SUDs, and MDD may co-occur in a sample of adults seeking medically supervised detoxification. We specifically chose to focus on MDD as an additional comorbidity given the frequency of MDD diagnoses in relation to both PTSD and SUDs and is (Quello, Brady, Sonne, 2005; Dixon, Resick, & Nishith, 2005). We also sought to examine differences between LCA-identified subgroups on key clinical

characteristics relevant to PTSD, polysubstance use, or MDD including addiction problem severity, trauma history (i.e., sexual/physical assault in childhood vs. adulthood), and PTSD/MDD symptom severity. Finally, given established gender differences in the prevalence of psychiatric disorders, we also considered how the observed subgroups differed according to gender.

*Hypotheses:*

1. *We hypothesized that multiple classes would be identified reflecting the complexity of psychiatric comorbidity and polysubstance use.*
2. *We further hypothesized that classes with greater psychiatric comorbidity (i.e., greater proportion of probable PTSD diagnoses) would experience more severe addiction problems, greater trauma history, higher psychiatric symptom severity, and contain a larger proportion of women than other classes.*

## **2. Materials and Method**

### *2.1 Participants*

Participants were 375 adults seeking medically assisted detoxification at the inpatient unit of the Alcohol, Drug Addiction, and Mental Health Crisis Center in Northeast Ohio. This detoxification center is a private, non-profit organization providing both residential (i.e., inpatient medically assisted detoxification, housing for intoxicated individuals, etc.) and non-residential (i.e., alcohol/drug addiction assessments and treatment referrals, group counseling, 12-step meetings, etc.) services regardless of patients' ability to pay. Participants were recruited within two days of their admission ( $M = 2.02$ ,  $SD = 1.35$ ) and, on average, participants spent 4.5 days receiving treatment at the detoxification facility. Consistent with the detoxification center's demographics (91% Caucasian, 65% male) participants largely identified as Caucasian (93.2%)



with 6.9% identifying as African-American, 0.5% Asian, and 6.9% identifying their ethnicity as Hispanic/Latino. The majority of participants were men (61.3%). The average age was 35.6 years ( $SD = 11.4$ ) and the average education level was 12.2 years ( $SD = 1.9$ ).

## 2.2 Procedure

Participants were approached and consented by research staff. Consenting participants completed a questionnaire battery. Demographic and SUD diagnosis data were collected by medical chart review. After survey completion, participants were provided with a choice of either a \$5.00 gift card or a candy bar to compensate them for their time. Data were collected between February 2013 and April 2014.

## 2.3 Materials

*2.3.1 Trauma history.* Trauma history and Criterion A for the DSM-IV-TR definition of PTSD were assessed using the 21 traumatic event items from the Life Stressor Checklist-Revised (LSC-R: Wolfe, Kimerling, Brown, Chrestman, & Levin, 1996).

*2.3.2 PTSD.* The PTSD Checklist-Civilian (PCL-C: Blanchard, Jones-Alexander, Buckley, & Forneris, 1996) was used to assess PTSD symptoms. The PCL-C is a 17-item measure that asks participants to rate how frequently they have experienced each of the 17 PTSD symptoms corresponding to DSM-IV-TR criteria. Participants were asked to rate how often or how much they had been bothered by each symptom in the past month on a scale ranging from 1 ('Not at all/never') to 5 ('Extremely/daily or almost daily'). In the present study, Cronbach's alpha for the PCL-C was 0.96. Items from the well-validated Posttraumatic Diagnostic Scale (PDS: Foa, Cashman, Jaycox, & Perry, 1997) were included to assess impairment and duration of symptoms; responses to the PCL-C, LSC-R (for items related to criterion A) and PDS were combined to determine probable PTSD diagnostic status. Specifically, participants were

classified as having a probable PTSD diagnosis if they (a) reported experiencing at least one traumatic event meeting Criterion A as assessed by the LSC-R; (b) endorsed at least 1 re-experiencing symptom, 3 avoidance symptoms, and 2 hyperarousal symptoms (symptom endorsement was defined as a rating of 3 or higher) on the PCL-C (NCPTSD, 2014); (c) reported experiencing these symptoms for at least 1 month; and (d) reported functional impairment in at least 1 domain (e.g., home, work, school, etc.) from endorsed symptoms on by the PDS.

*2.3.3 Depression.* The Center for Epidemiologic Studies Depression Scale-Revised (CESD-R: Eaton, Smith, Ybarra, Muntaner, & Tien, 2004) was used to assess depression. In the present study, participants were asked to rate how often they had experienced each symptom in the past month (rather than the past week) on a scale ranging from 0 ('Not at all or less than one day') to 4 ('Nearly every day for the past month'). In the present study, Cronbach's alpha was 0.94. Participants' responses were used to determine both probable diagnostic levels of depression using the algorithmic classification scheme reported by Eaton et al. as well as to assess depression symptom severity.

*2.3.4 SUDs.* Licensed staff clinicians assessed SUDs at intake using the DSM Checklist for SUDs, a semi-structured interview that has demonstrated good reliability and validity (Hudziak et al., 1993). Substance use disorder diagnostic status for each of the following substances (opiates, alcohol, sedatives, amphetamines, cocaine, tobacco, and cannabis) was determined via chart review.

*2.3.5 Problematic substance use.* Problematic substance use was assessed using the Alcohol, Smoking, and Substance Involvement Screening Test (ASSIST: Ali et al., 2002). The ASSIST is a 6-item screening test that assesses difficulties arising from an individual's use of

different psychoactive substances; the six items are assessed for each type of substance endorsed. Cronbach's alpha for each substance subscale ranged from .62 (tobacco) - .95 (opioid).

*2.3.6 Substance use consequences.* Negative consequences related to substance use were assessed using the Shortened Inventory of Problems-Alcohol and Drugs (SIP-AD; Blanchard, Morgenstern, Morgan, Lobouvie, & Bux, 2003). The SIP-AD is a 15-item questionnaire that asks participants to rate how frequently they have experienced different negative consequences resulting from their alcohol or drug use. Items reflect a broad range of domains in which psychosocial impairment may be experienced including psychosocial relationships, financial responsibilities, physical health, etc. Each item is rated on a scale ranging from 0 ('Never') to 3 ('Daily or almost daily'). In the present study, Cronbach's alpha was 0.93.

#### *2.4 Statistical analyses*

Latent class analysis (LCA) was used to characterize the patterns of co-occurring SUDs, PTSD, and MDD in the sample. LCA identifies latent classes or groups of participants based on a given set of indicator variables that are hypothesized to represent one or more latent variables. This analysis used nine indicator variables to determine class composition. Seven of these indicators were dichotomous SUD diagnoses (yes/no) as determined by chart review. Two additional indicator variables were probable PTSD and MDD diagnosis coded dichotomously using the algorithms described above.

The LCA was conducted in an exploratory fashion using Mplus (Version 5.0). Multiple models were examined starting with a two class model and adding additional classes. Model fit was evaluated using a variety of statistical criteria including the Bayesian Information Criterion (BIC), sample size adjusted BIC (SSA-BIC), and Akaike Information Criterion (AIC) where smaller values indicate better fit. The model was also evaluated with the Lo-Mendell-Rubin test

(LMRT) and the bootstrap likelihood ratio test (BLRT) which indicate whether a model with  $k$  classes better fits the data than a model with  $k-1$  classes. In other words, if the  $p$ -value is greater than 0.05 the model with  $k$  classes is not significantly different from the  $k-1$  class and the more parsimonious model is preferred. Finally, model fit was also assessed via the entropy value, where values closer to 1.0 indicate better classification.

Class proportions and conditional item probabilities for each indicator variable by class were then examined to determine the characteristics of observed classes. If 60% or more of the participants in a class had the characteristic, then the characteristic was said to be a distinguishing feature of the class (Galatzer-Levy, Nickerson, Litz, & Marmar, 2013).

Following the LCA, non-indicator variables, or external variables, were considered to evaluate the practical relevance and clinical significance of the best fitting solution. Pearson chi-square analyses were used for dichotomous and categorical non-indicator variables while Tukey's HSD/ Dunnett's T3 post-hoc tests were used following statistically significant one-way ANOVAs for continuous non-indicator variables.

### **3. Results**

#### *3.1 Descriptive statistics*

Trauma history was prevalent in the sample, with 91.8% meeting criteria for at least 1 Criterion A event. On average, participants reported experiencing 4.6 ( $SD = 3.8$ ) types of Criterion A events with the most commonly endorsed events consisting of witnessing a serious accident (48.1%), being in a serious accident (47.4%), and witnessing violence between family members before the age of 16 (38.2%).

Prevalence rates for each diagnosis are listed in the right-hand column of Table 1. The average number of SUD diagnoses was 3.26 ( $SD = 1.32$ ) with the most common diagnoses being

opioid use disorder (76.0%), alcohol use disorder (56.0%), and tobacco use disorder (81.6%). Nearly half of the sample (47.2%) met criteria for probable PTSD, and 64.0% met criteria for probable MDD.

### *3.2 Latent class findings*

Table 2 presents the fit indices for each model tested. While the LMR LRT and the entropy values supported a 2-class model and the BIC supported a 3-class model, the AIC, SSA-BIC, and the BLRT all supported a 4-class model. Given that the greatest support existed for the 4-class solution, this model was selected for further examination. Class proportions are displayed in Table 1. The number of participants in each class was evenly distributed; class 1 consisted of 23.7% of the sample, class 2 made up 25.1% of the sample, class 3 consisted of 22.7% of the sample, and class 4 made up 28.5% of the sample.

Class one was characterized as the PTSD-MDD-Poly SUD class. In this class, nearly 85% of participants met criteria for probable PTSD and all met criteria for probable MDD. Regarding SUDs, 100% met criteria for opioid use disorder, nearly 90% of participants met criteria for tobacco use disorder, and approximately 65% met criteria for cannabis use disorder. Class two was characterized as the MDD-Poly SUD class. In this class, nearly 80% qualified for probable MDD, 100% qualified for alcohol use disorder, over 90% qualified for opioid use disorder, and approximately 80% met tobacco use disorder and cannabis use disorder criteria. Class three was characterized as the alcohol-tobacco SUD class. In this class, 100% had an alcohol use disorder, and nearly 75% had a tobacco use disorder. Finally, class four was characterized as the opioid-tobacco SUD class. In this class, nearly 100% had an opioid use disorder, and 84% had a tobacco use disorder.

### *3.3 Class Differences*

Means, standard deviations, and class differences on external variables are reported by class in Table 3. Analyses of class differences focused on differences between the PTSD-MDD-Poly SUD class compared to the other classes given our hypothesis that subgroups displaying the greatest psychiatric comorbidity would report more severe addiction problems, more extensive psychiatric symptom severity, and would contain a greater proportion of women.

Overall, those in the PTSD-MDD-Poly SUD class reported greater negative consequences resulting from their substance use compared to all other classes observed (MDD-Poly SUD:  $M_{Diff} = 3.82$ ,  $SE = 1.16$ ,  $p = 0.007$ ; alcohol-tobacco SUD:  $M_{Diff} = 7.90$ ,  $SE = 1.35$ ,  $p < 0.001$ ; opioid-tobacco SUD:  $M_{Diff} = 7.63$ ,  $SE = 1.22$ ,  $p < 0.001$ ). In addition, they reported more severe opioid problems than all of the other classes, more severe cannabis, sedative, and cocaine problems than the alcohol-tobacco, and the opioid-tobacco SUD classes and more severe amphetamine problems than the alcohol-tobacco SUD class. However, they reported fewer alcohol problems than either the MDD-Poly SUD or the alcohol-tobacco SUD classes.

In terms of trauma history, a greater proportion of the PTSD-MDD-Poly SUD class reported experiencing physical assault both before and after age 16 relative to the opioid-tobacco SUD class (physical assault <16:  $\chi^2[1] = 5.32$ ,  $p = 0.02$ ; physical assault > 16:  $\chi^2[1] = 9.36$ ,  $p = 0.02$ ); while a greater proportion of participants in PTSD-MDD-Poly SUD class reported experiencing sexual assault both before and after age 16 compared to the alcohol-tobacco (sexual assault < 16:  $\chi^2[1] = 5.49$ ,  $p = 0.02$ ; sexual assault > 16:  $\chi^2[1] = 7.80$ ,  $p = 0.005$ ) and opioid-tobacco classes (sexual assault < 16:  $\chi^2[1] = 13.83$ ,  $p < 0.001$ ; sexual assault > 16:  $\chi^2[1] = 13.25$ ,  $p < 0.001$ ).

The PTSD-MDD-Poly SUD class also reported greater PTSD symptom severity compared to all of the other classes (MDD-Poly SUD:  $M_{Diff} = 9.31$ ,  $SE = 2.43$ ,  $p = 0.001$ ;

alcohol-tobacco SUD:  $M_{Diff} = 17.27$ ,  $SE = 2.59$ ,  $p < 0.001$ ; opioid-tobacco SUD:  $M_{Diff} = 23.63$ ,  $SE = 2.01$ ,  $p < 0.001$ ) and more severe MDD symptom severity relative to the alcohol-tobacco ( $M_{Diff} = 19.67$ ,  $SE = 2.51$ ,  $p < 0.001$ ) and the opioid-tobacco classes ( $M_{Diff} = 19.00$ ,  $SE = 2.11$ ,  $p < 0.001$ ).

Finally, a greater proportion of the PTSD-MDD-Poly SUD class was comprised of females compared to all of the other classes (MDD-Poly SUD:  $\chi^2[1] = 10.97$ ,  $p = 0.001$ ; alcohol-tobacco SUD:  $\chi^2[1] = 18.66$ ,  $p < 0.001$ ; opioid-tobacco SUD:  $\chi^2[1] = 9.57$ ,  $p = 0.002$ ).

#### 4. Discussion

The present results underscore the extent to which psychiatric comorbidity is prevalent among detoxification treatment-seekers; 47.2% of the sample met criteria for probable PTSD, and rates of probable PTSD were over 50% in half of the classes identified. Regarding probable MDD, 64% of the sample met criteria, and the rate of probable MDD ranged in the classes from 40-79%. One difficulty in providing integrative treatment for PTSD-SUD comorbidity is adequately targeting polysubstance use and comorbid psychiatric disorders. This study used LCA to characterize the comorbidity patterns of probable PTSD, MDD, and SUDs and the clinical characteristics associated with those patterns in a sample of medical detoxification treatment-seekers. The challenge of addressing multiple substances and comorbidities is heightened in the detoxification center treatment environment given the emphasis on short-term stabilization to facilitate the longer-term goal of recovery from addiction.

We identified four different and relatively equal sized classes: the PTSD-MDD-Poly SUD group, the MDD-Poly SUD group, the alcohol-tobacco SUD group, and the opioid-tobacco SUD group. The classes not characterized by polysubstance use were primarily differentiated by the presence of alcohol vs. opioid use disorders. Given that a 3-class solution has typically been

found to best describe the patterns of polysubstance use and comorbid psychiatric disorders, it is notable that we found evidence for a 4-class solution (Connor et al., 2013; Tomczyk et al., 2015; Galatzer-Levy et al., 2013). This is likely due to our use of a unique and understudied sample – detoxification treatment-seekers – which may have different characteristics than other samples. Further, we included comorbid psychiatric disorders as key variables (indicators) in the LCA rather than external variables examined post-LCA. In other words, we used probable MDD, PTSD, and multiple SUD diagnoses as variables to define the classes, rather than defining classes by substance and examining how MDD and PTSD varied among the classes post-hoc.

The classes identified have implications for screening and referral processes used in the detoxification treatment setting. The MDD-Poly SUD class was characterized by high rates of both opioid and alcohol use disorders in comparison to the other classes. Given that alcohol use is present in nearly half of all fatal opioid overdoses (Warner-Smith, Darke, Lynskey, & Hall, 2001), this group is at significant risk for overdose, underscoring the importance of addressing opioid use in the context of alcohol use for members of this class. Referrals to outpatient psychotherapy or in-house psychosocial interventions – in conjunction with pharmacotherapy utilizing naltrexone or naloxone – may be important for consolidating treatment gains made in detoxification and may be especially important to minimize the risk of fatal overdose.

The variability of alcohol use disorders between classes is consistent with research suggesting that alcohol use disorders are highly heterogeneous. Following, future treatment research should focus on mechanisms specific to the cycles of alcohol addiction, such as greater emphasis on reducing negative affect during withdrawal early in treatment and tolerating craving later in treatment (Litten, et al., 2015). In addition, both the PTSD-MDD-Poly SUD and the MDD-Poly SUD classes were characterized by concurrent opioid and cannabis use disorders.



This finding is consistent with research implicating the endocannabinoid system in opioid dependence and the potential effectiveness of pharmacotherapies targeting the endocannabinoid system in alleviating opioid withdrawal during detoxification (Bisaga et al., 2015).

Examination of key clinical characteristics indicated that people in the PTSD-MDD-Poly SUD class had more severe addiction problems as well as more severe PTSD/MDD symptom severity than people in other classes. In particular, it is notable that this class had more severe substance use problems even with respect to substances that were used less frequently (i.e., substances not characteristic of that LCA class). Not only were the symptoms of each individual disorder more severe, this class also had a more severe trauma history than other classes. Thus, trauma history characteristics of this class may be contributing factors to the elevated rates of probable PTSD and MDD observed. Notably, this class had more women, and women are more likely to experience interpersonal trauma (Black et al., 2011). Referrals to individual outpatient psychotherapy may be particularly important for long-term recovery for this group, especially women, given the reciprocal relationship between PTSD and SUD symptoms (Read et al., 2004). Women in this class who experience trauma symptoms arising from interpersonal violence may be less comfortable with mixed gender settings.

Interventions that can target specific constructs or processes that are shared across disorders or diagnostic profiles are recommended. Many who seek detoxification continue to struggle one year later (Franken & Hendriks, 1999) suggesting that increasing the services offered at detoxification facilities or expanding referral networks based on baseline assessments of comorbidities may be fruitful for improving long-term recovery. For example, motivational interviews rather than advice regarding ongoing treatment have been associated with less substance use at follow-up (Vederhus, Timko, Kristensen, Hjemdahl, & Clausen, 2014),

illustrating the importance of providing brief interventions as part of the treatment planning process even when services are not provided at the detoxification facility. Motivational interviewing can be easily adapted for specific problems and is one way in which integrated treatment programs can be designed to match diagnostic profiles. For example, people in the PTSD-MDD-Poly SUD class may benefit more from motivational interviewing that discusses anxiety and avoidance symptoms whereas those in the alcohol-tobacco class may benefit from substance use focused motivational interviewing.

Our results also point to transdiagnostic approaches in outpatient care to improve symptoms and reduce distress in a time- and cost-effective manner. Transdiagnostic interventions can be delivered as modules in group formats with each group targeting different processes. The groups could be offered simultaneously, and treatment-seekers could be referred to groups based on their diagnostic profiles. For example, interventions for anxiety sensitivity and nicotine replacement therapy could be offered simultaneously with referrals made based on comorbidity profile. Anxiety sensitivity has been shown to be amenable to a number of treatment approaches in a range of anxiety disorders (Lejuez et al., 2008). Anxiety sensitivity may be a useful target for the PTSD-MDD-Poly SUD class identified here. Another potential target is distress tolerance, which is related to anxiety sensitivity and strongly linked to substance use disorders (Buckner, Keough, & Schmidt, 2007). Newly developed interventions for distress tolerance have been well received by depressed substance use patients (Bornoalova, Gratz, Daughters, Hunt, & Lejuez, 2012). The brief interventions that have been developed for both anxiety sensitivity and distress tolerance have the potential to be easily combined with other treatment components to create integrated, multifaceted interventions that can be provided in short-term focused treatment settings or as transition pieces for longer term care. Distress

tolerance would be relevant for all the classes identified in this study and may be especially relevant for those in the PTSD-MDD-Poly SUD class given the elevated rates of probable PTSD and MDD that characterize members of this subgroup. Distress tolerance may be an especially useful skill to learn early in detoxification settings where treatment seekers may be experiencing acute, painful withdrawal symptoms.

It should be noted that treatment-matching practices such as those proposed above have shown mixed benefits when applied in formal addiction treatment settings (e.g., Project MATCH Research Group, 1997). However, much past research specifically excluded detoxification seekers. It should be noted that the characteristics identified in Project MATCH that were associated with differential treatment outcome (severity of psychopathology, anger, desire for meaning making) are those which are elevated in PTSD-SUD comorbidity samples. Those studies showing success with integrative treatments (e.g., McLellan et al., 1997; Thornton, Gottheil, Weinstein, & Kerachsky, 1998) have demonstrated that integrative services are most appropriate for those patients presenting with the most complex clinical problems. This is consistent with our findings suggesting that those individuals in the PTSD-MDD-Poly SUD class may require additional resources compared to patients in the classes with less severe clinical presentations. For example, women are more likely to be in this class and more likely to experience treatment barriers related to childcare and parenting (Copeland, 1997). Thus referrals which can accommodate childcare needs are necessary; motivational interviewing and structured problem solving around these needs are also recommended. Even so, additional research replicating our findings should be performed to substantiate support for the existence of the classes observed. We also recommend future research examine differences in motivation and post-discharge treatment trajectories.

Self-report measures of PTSD and MDD were used to ascertain probable diagnoses; thus, the findings may be limited by the methodological constraints associated with self-report. Further, the assessment of depression is especially difficult in people who use substances as these symptoms could be caused by substance use and/or detoxification from substances. However, the PCL is highly correlated with clinician interview measures of PTSD ( $r = .93$ ; Blanchard et al., 1996), and people who use substances may be more truthful in disclosing symptoms in self-report than interview formats (Islam et al., 2012). Second, the present study consists of individuals who were seeking medically assisted detoxification; these participants may have more severe symptoms or less social support than other treatment-seeking samples, and results may not generalize to all non-addiction samples. That said, detoxification treatment is an under-researched treatment setting in comparison to typical outpatient treatment, despite the unique features and public health importance of this setting. Finally, future research should examine a broader number of potential diagnostic comorbidities, particularly diagnoses associated with more challenging clinical presentations such as attention deficit-hyperactivity, bipolar, or borderline personality disorders.

#### *4.1 Conclusions*

In conclusion, the current study found evidence for differential patterns of PTSD-SUD-MDD comorbidity in detoxification treatment seekers that indicate the need for tailored referral and treatment programs that can flexibly address specific substances or constructs. Integrative treatment approaches that include different components specialized to target different constructs that are associated with different diagnostic profiles (anxiety sensitivity, distress tolerance, opioid withdrawal, etc.) are recommended as are referral networks which can identify settings and providers that offer these services.

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**Tables**

Table 1

*Class proportions (%) of indicator variables for the 4 class model, N = 375.*

Indicator	PTSD-MDD- Poly SUD (1) <i>n</i> = 89, 23.7%	MDD-Poly SUD (2) <i>n</i> = 94, 25.1%	Alcohol- Tobacco (3) <i>n</i> = 85, 22.7%	Opioid- Tobacco (4) <i>n</i> = 107, 28.5%	Overall Prevalence N = 375
PTSD	<b>84.8</b>	51.0	38.7	20.3	47.2
MDD	<b>100.0</b>	<b>79.0</b>	41.8	40.2	64.0
Opioid	<b>100.0</b>	<b>91.2</b>	0.0	<b>99.0</b>	76.0
Alcohol	24.0	<b>100.0</b>	<b>100.0</b>	20.5	56.0
Sedative	35.5	42.2	2.3	17.2	24.0
Amphetamine	12.6	24.3	0.0	14.7	13.1
Cocaine	34.8	52.2	13.3	10.0	26.1
Tobacco	<b>88.1</b>	<b>77.8</b>	<b>74.4</b>	<b>83.9</b>	81.6
Cannabis	<b>64.7</b>	<b>76.3</b>	27.8	43.4	52.5

*Note.* Table numbers indicate the percentage of participants in the class classified by the diagnosis (indicator variable). Bolded values indicate the diagnoses that were characteristic (60% or greater) for that class.

Table 2

*Fit indices for latent class models*

Latent Class Models	AIC	BIC	SSA-BIC	LMR LRT	BLRT	Entropy
2-class	3771.8	3846.4	3786.2	211.0***	214.5***	0.97
3-class	3724.7	3838.6	3746.6	66.0	67.1***	0.73
4-class	3714.0	3867.1	3743.4	30.2	30.7***	0.74
5-class	3718.1	3910.5	3755.1	15.6	15.9	0.78

*Note.* AIC = Akaike information criterion, BIC = Bayesian information criterion, SSA-BIC = sample size adjusted BIC, LMR LRT =, Lo-Mendell-Rubin likelihood ratio test, BLRT = Bootstrap likelihood ratio test

\*\*  $p < .01$ , \*\*\*  $p < .001$

Table 3

*Means, standard deviations, prevalences, and statistical differences between the PTSD-MDD-Poly SUD class and other classes*

Variables	PTSD-MDD- Poly SUD (1)	MDD-Poly SUD (2)	Alcohol- Tobacco (3)	Opioid- Tobacco (4)	Statistical Test (omnibus)
	23.7%	25.1%	22.7%	28.5%	
Opioid problems ( <i>M,SD</i> )	31.8(5.8) <sup>abc</sup>	27.7(10.0) <sup>a</sup>	4.0(7.8) <sup>b</sup>	28.9(7.4) <sup>c</sup>	$F(3, 370) = 228.5, p < .001$
Alcohol problems ( <i>M,SD</i> )	7.9(10.2) <sup>ab</sup>	19.6(13.4) <sup>a</sup>	32.4(7.1) <sup>b</sup>	6.0(8.0)	$F(3, 371) = 137.0, p < .001$
Cannabis problems ( <i>M,SD</i> )	14.8(12.9) <sup>ab</sup>	13.2(11.2)	5.7(9.7) <sup>a</sup>	8.3(10.5) <sup>b</sup>	$F(3, 370) = 12.9, p < .001$
Sedative problems ( <i>M,SD</i> )	11.5(12.5) <sup>ab</sup>	11.5(11.2)	4.1(8.0) <sup>a</sup>	6.3(8.6) <sup>b</sup>	$F(3, 370) = 12.1, p < .001$
Cocaine problems ( <i>M,SD</i> )	13.1(12.8) <sup>ab</sup>	16.3(13.6)	4.8(9.8) <sup>a</sup>	5.3(8.4) <sup>b</sup>	$F(3, 370) = 24.1, p < .001$
Amphetamine problems ( <i>M,SD</i> )	6.2(9.5) <sup>a</sup>	9.6(11.3)	1.7(5.2) <sup>a</sup>	5.7(9.3)	$F(3, 369) = 11.0, p < .001$
Tobacco problems ( <i>M,SD</i> )	24.5(8.2)	21.7(9.0)	22.3(10.8)	21.7(8.22)	$F(3, 371) = 1.93, p = 0.12$
Negative consequences of use ( <i>M,SD</i> )	40.7(6.2) <sup>abc</sup>	36.8(9.2) <sup>a</sup>	32.8(10.9) <sup>b</sup>	33.0(10.7) <sup>c</sup>	$F(3, 371) = 14.1, p < .001$
Physical assault pre 16 (% within class)	23.6% <sup>a</sup>	27.7%	22.4%	11.2% <sup>a</sup>	$\chi^2(3) = 9.2, p = .03$
Physical assault after 16 (% within class)	36.0% <sup>a</sup>	25.5%	24.7%	27.1% <sup>a</sup>	$\chi^2(3) = 9.4, p = .02$

Sexual Assault pre 16 (% within class)	22.5% <sup>ab</sup>	17.0%	9.4% <sup>a</sup>	4.7% <sup>b</sup>	$\chi^2(3) = 15.9, p = .001$
Sexual Assault after 16 (% within class)	20.2% <sup>ab</sup>	17.0%	5.9% <sup>a</sup>	3.7% <sup>b</sup>	$\chi^2(3) = 18.5, p < .001$
PTSD severity ( <i>M,SD</i> )	60.3(13.5) <sup>abc</sup>	51.0(19.0) <sup>a</sup>	43.0(19.8) <sup>b</sup>	36.6(14.6) <sup>c</sup>	$F(3, 371) = 35.2, p < .001$
MDD severity ( <i>M,SD</i> )	61.6(11.2) <sup>ab</sup>	58.2(15.1)	42.0(20.5) <sup>a</sup>	42.6(18.1) <sup>b</sup>	$F(3, 371) = 35.5, p < .001$
Gender (% women within class)	59.6% <sup>abc</sup>	35.1% <sup>a</sup>	27.1% <sup>b</sup>	37.4% <sup>c</sup>	$\chi^2(3) = 21.39, p < .001$

*Note.* Statistics with the same super script differ at the  $p < 0.05$  significance level.