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Article

Patterns and Correlates of Polysubstance Use Among Individuals With Severe Alcohol Use Disorder

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Abstract

Aim: The present study examined patterns and correlates of polysubstance use among individuals with severe alcohol use disorder (AUD).

Methods: Participants were 2785 individuals (63% female; mean age = 43 years, range = 18–78 years) from the Genes, Addiction and Personality Study. All participants met lifetime criteria for severe AUD (6+ symptoms). We used latent class analysis to identify patterns of frequency of lifetime use for cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens. A variety of demographic and behavioral correlates of latent class membership were tested in univariable and multivariable models.

Results: A five-class solution was selected: extended range polysubstance use (24.5%); cigarette and marijuana use (18.8%); 'testers,' characterized by high probabilities of smoking 100 or more cigarettes, using marijuana 6+ times, and trying the remaining substances 1–5 times (12.3%); moderate range polysubstance use (17.1%) and minimal use (reference class; 27.3%). In univariable analyses, all potential correlates were related to latent class membership. In the multivariable model, associations with gender, race/ethnicity, age of onset for alcohol problems, dimensions of impulsivity, depressive symptoms, antisocial behavior and family history density of alcohol problems remained significant, though the pattern and strength of associations differed across classes. For instance, sensation-seeking, lack of premeditation and family history were uniquely associated with membership in the extended range polysubstance use class.

Conclusion: Patterns of polysubstance use are differentially related to demographic and behavioral factors among individuals with severe AUD. Assessing use across multiple substances may inform the selection of targets for treatment and prevention.

INTRODUCTION

Concurrent use of multiple substances is common among individuals affected by AUD: 13% of individuals with AUD have met criteria for a drug use disorder in the past year (Stinson *et al*., 2005) and 65% have met criteria in their lifetime (Staines *et al*., 2001). Patterns of wide-ranging polysubstance use are associated with a persistent course of AUD (Moss *et al*., 2015), underscoring the importance of investigating patterns and correlates of polysubstance use among AUD-affected individuals.

A number of studies have examined correlates of polysubstance use, defined as the consumption of more than one drug within a defined period, simultaneously, or at different times (Connor *et al*., 2014). Consistent with work examining the etiology of alcohol and drug use disorders' comorbidity (Chassin *et al*., 2004; Sintov *et al*., 2009), using a higher number of substances concurrently has been linked to a range of demographic and psychosocial factors, including gender, racial/ethnic identity, parental substance problems, depression and conduct problems (Hakansson *et al*., 2011; Pacek *et al*., 2012; Morley *et al*., 2015; Votaw *et al*., 2020). Person-centered approaches, which identify subgroups of individuals with similar constellations of use across substance types, have offered further insight into patterns and predictors of polysubstance use. For example, Hedden *et al*. (2010) used LCA to, first, identify groups of individuals with similar substance use patterns and, second, investigate predictors of group membership among individuals meeting DSM-IV criteria for alcohol dependence. When examining binary indicators of past-year use across eight substances, LCA yielded a five-class solution, wherein classes ranged from near-zero probabilities of illegal drug use to high probabilities of using all six classes of drugs. Membership in classes with more extended patterns of polysubstance use was associated with generalized anxiety disorder, major depressive disorder, deviant behavior, meeting five or more criteria for DSM-IV alcohol dependence and participating in substance use treatment (Hedden *et al*., 2010).

Previous person-centered analyses of polysubstance use among individuals with AUD have been limited to binary indicators of illicit drug use (Hedden *et al*., 2010; Moss *et al*., 2015), and the patterns and correlates of polysubstance use among individuals with severe DSM-5 AUD (defined as meeting 6+ criteria) (American Psychiatric Association, 2013) have not been examined. Importantly, polysubstance use may be particularly prevalent within the population of individuals with severe AUD, since individuals who use multiple substances tend to report more AUD symptoms than individuals who experience problems with alcohol

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only (Sintov *et al*., 2009; Hedden *et al*., 2010; Moss *et al*., 2015). In addition, individuals affected by severe AUD are more likely to seek treatment than those with mild AUD (Tuithof *et al*., 2016). Therefore, characterizing patterns and risk factors for polysubstance use among individuals with severe AUD may inform efforts to better address individuals' additional substance use behavior and broader psychosocial needs during inpatient or outpatient treatment for alcohol problems (AP).

In the present study, we characterized patterns of lifetime use for cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens among individuals meeting DSM-5 criteria for severe AUD. We differentiated between experimental use and more regular use by asking participants to report if they had used each substance and, if yes, whether they had used between 1 and 5 times or 6+ times. LCAs were applied to derive subgroups of individuals with similar substance use behaviors. In addition, we investigated whether previously identified predictors of AP or polysubstance use, including gender, race/ethnicity, family history of AP, response to alcohol, age of onset for AP, neuroticism, impulsivity, depressive symptoms and antisocial behavior, were associated with latent class membership.

Our hypotheses and analytic plan were pre-registered using the Open Science Framework (https://osf.io/y9eck). Given the relatively limited work on patterns of polysubstance use among individuals with AUD, we did not specify hypotheses regarding the number and nature of polysubstance use classes. However, we did expect that male gender, identifying as non-Hispanic White, earlier age of onset of AP, and higher levels of familial risk for AP, neuroticism, impulsivity, depressive symptoms and antisocial behavior would be associated with increased likelihood of belonging to a class with more extended polysubstance use. Because prior work had not examined sensitivity to the effects of alcohol as a predictor of polysubstance use, we considered analyses involving low response to alcohol to be exploratory.

MATERIALS AND METHODS

Sample

Participants were from the Genes, Addiction and Personality Study, a cross-sectional study initiated in 2018 to investigate genetic and environmental influences on severe AUD. Participants were recruited either in person through substance abuse treatment facilities (22.7%) or online through recovery community organizations and Facebook advertisements (77.3%). Both groups completed a 15–20-min survey including questions on demographics, symptoms of AUD, family history of AP, other substance use, personality, depressive symptoms, impulsivity and antisocial behavior. In-person participants completed the survey using a custom-designed app (Ondersma *et al*., 2011), while participants recruited online completed the survey via REDCap (Harris *et al*., 2009, 2019). The current analyses were limited to 2785 individuals (63% female; mean age = 43 years, range = 18–78 years) who met lifetime criteria for severe AUD (6+ symptoms). Participants self-reported their race/ethnicity as American Indian or Alaskan Native (1.1%), Asian (1.3%), Black or African American (9.0%), Native Hawaiian or Pacific Islander (0.3%), White or Caucasian (84.6%), or Other (3.8%); 6.2% of participants also identified as Hispanic. Participants provided written consent, and a university institutional review board approved all study procedures.

Measures

Lifetime substance use

Indicators for the LCA included lifetime use for cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens. Participants identified which statement best described their lifetime smoking behavior: 'I have never smoked cigarettes' (coded as 0), 'I have smoked less than 100 cigarettes' (coded as 1) and 'I have smoked 100 or more cigarettes' (coded as 2). For marijuana, cocaine, stimulants, sedatives and hallucinogens, participants were asked, 'how many times in your life have you ever used [drug]?' Participants were provided with a list of examples for stimulants (e.g. speed and crystal meth), sedatives (e.g. benzodiazepines and Xanax) and hallucinogens (e.g. phencyclidine (PCP) and lysergic acid diethylamide (LSD)). For prescription medications, participants were asked to think about times that they used the drug without a doctor's permission or in a way other than prescribed. Response options included 0 = 'never,' 1 = '1–5 times' and 2 = '6+ times' (Spitzer *et al*., 1992), which were selected to align with substance use items from the Clinical Trials Network Common Assessment Battery (Svikis *et al*., 2012). Finally, participants reported on how many times in their life they had used opioids (e.g. heroin, OxyContin); response options included 'never,' 'once or twice,' 'monthly,' 'weekly' and 'daily or almost daily' (NIDA, 2012). Individuals who selected 'never' were coded as 0, individuals who selected 'once or twice' were coded as 1 and individuals who selected any other response option were coded as 2.

Correlates of polysubstance use

Potential predictors of class membership included gender, race/ethnicity, family history of AP, sensitivity to the effects of alcohol, age of onset for AP, neuroticism, impulsivity, depressive symptoms and antisocial behavior.

Demographic correlates

Participants indicated whether they identified as female (coded as 0) or male (coded as 1). In addition, individuals reported on their race (White or Caucasian, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander, Other) and ethnicity (Hispanic, Not Hispanic). Race/ethnicity was aggregated into the following classifications: Non-Hispanic White, Hispanic White, non-Hispanic Black or African American, Hispanic Black or African American and Other. A set of dummy-coded variables was created, with non-Hispanic White serving as the reference group.

Family history of AP

To construct a family history risk score, we calculated a weighted sum of the number of family members with a history of AP (with fathers, mothers, full siblings, sons and daughters weighted 0.50 and half-siblings, grandfathers, grandmothers, aunts and uncles weighted 0.25) divided by the total family size. We then computed a standardized score.

Low response to alcohol

Sensitivity to the effects of alcohol was measured using the Self-Report of the Effects of Alcohol (SRE) questionnaire, which asks participants to report the number of drinks needed

during the first five drinking occasions to feel tipsy, feel dizzy or slur speech, stumble and pass out. We summed the number of drinks reported for each effect and divided by the number of effects reported (Schuckit *et al*., 2008).

Age of onset for AP

After participants reported on DSM-5 criteria for AUD, they were asked, 'how old were you when you first began to experience any of these problems?' Participants entered their age in years.

Neuroticism

Neuroticism was assessed using six items from the Big Five Inventory (John and Srivastava, 1999). Response options ranged from 1 = 'disagree strongly' to 5 = 'agree strongly.' We averaged responses across items, with higher scores reflecting greater neuroticism.

Impulsivity

Impulsivity was measured using 15 items from the short version of the Urgency, Premeditation (lack of), Perseverance (lack of), Sensation seeking, Positive urgency (UPPS-P) impulsive behavior scale (Cyders *et al*., 2014). This instrument included three items for each dimension of impulsivity proposed by the UPPS-P model: (a) negative urgency, the tendency to act rashly in response to negative affect, (b) lack of premeditation, the tendency to act without careful thought and planning, (c) lack of perseverance, defined by one's likelihood to complete a task, (d) sensation-seeking, the tendency to seek excitement and (e) positive urgency, the tendency to act rashly in response to positive affect (Whiteside and Lynam, 2001). Responses were recorded on a 4-point Likert scale, with 1 = 'disagree strongly' and 4 = 'agree strongly.' We created a mean score for each subscale such that higher scores reflect greater impulsivity.

Depressive symptoms

Depressive symptoms were measured as a lifetime clinical criterion count for DSM-5 major depressive disorder (American Psychiatric Association, 2013).

Antisocial behavior

Seventeen items were used to assess the lifetime occurrence of antisocial behaviors (Supplementary Table S1). Response options included 0 = 'never,' 1 = '1–2 times,' 2 = '3–5 times' and 3 = 'more than 5 times.'

Statistical methods

Preliminary analyses

We performed a series of factor analyses to investigate the latent structure of antisocial behavior. One-, two-, three- and four-factor models were compared using SAS 9.4 (©2002-2012 SAS Institute Inc., Cary, NC, USA). Next, we conducted confirmatory factor analyses (CFA), allowing for correlated factors and constraining each indicator to load on only one latent factor. We selected the appropriate factor structure based on the Comparative Fit Index, Tucker-Lewis Index and Root Mean Square Error of Approximation, as well as model interpretability. Antisocial behavior factor scores were carried forward for the remaining analyses.

Because many participants chose not to report their age (275 missing values), we imputed the age variable using a *k*-Nearest Neighbors (kNN) imputation algorithm (Beretta and Santaniello, 2016). kNN imputation was conducted using the R {VIM} package (Kowarik and Templ, 2016). We used age of onset for AP, marital status, household composition, employment status, educational attainment and gender to identify participants that were most similar to the missing observation. The median value calculated from five nearest neighbors was then imputed as the value for age.

Latent class analyses

To identify patterns and correlates of polysubstance use among individuals with severe AUD, we implemented the maximum likelihood three-step approach (Vermunt, 2010), which accounts for classification error when estimating associations with latent class membership. LCAs were conducted using Mplus 8.4 (Muthén and Muthén, 2017). We first estimated a series of unconditional latent class models with ordered three-category variables for lifetime use of cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens as indicators. We selected the number of latent classes based on the Bayesian Information Criterion (BIC), Sample-Size Adjusted BIC (SSABIC) and Akaike Information Criterion (AIC). We also considered entropy, an index of the quality of assignment of individuals to latent classes. We used TECH11 and TECH14 in Mplus 8.4 to perform the Lo–Mendell–Rubin likelihood ratio test and the bootstrapped likelihood ratio test, which evaluate whether adding a latent class leads to a statistically significant improvement in model fit. Finally, we considered parsimony and latent class interpretability when deciding on a final model.

After selecting a model based on statistical fit information and interpretability of the latent classes, we used posterior classification probabilities, defined as the probability of being assigned to a latent class given true latent class membership, to calculate the probability of classification error (Vermunt, 2010). We constructed a latent class model with assigned class membership as a single nominal indicator of true class membership with known classification error probabilities. We performed a series of univariable analyses, with each potential correlate entered into a separate model, then carried forward significant predictors into a multivariable model. Mplus employs listwise deletion of missing values on the predictor variables and covariates. Thus, for univariable analyses, the number of missing values on the correlate of interest (Table 1) determined the number of observations included in the analysis. For the multivariable model, 304 individuals had at least one missing value and were excluded from the analysis (yielding $N = 2481$). Age and ascertainment method were included as covariates in both univariable and multivariable analyses.

RESULTS

Preliminary analyses

Item frequencies and factor loadings from one-, two-, three- and four-factor models of antisocial behavior are shown in Supplementary Tables S1 and S2, respectively. Based on model fit indices and interpretability, we performed CFA with three latent factors, hereafter referred to as unreliable behavior, aggressive behavior and criminal behavior. Model fit indices and factor loadings used to derive factor scores are shown in Supplementary Table S3.

Frequencies of use for each substance are shown in Figure 1, descriptive statistics for each potential correlate of latent class

Table 1. Descriptive statistics for potential correlates of latent class membership

Correlate	*M* (SD)	Range	Missing values, *N*
Family history density for AP	0.15 (0.09)	0.00–0.50	34
Sensitivity to the effects of alcohol	5.18 (2.55)	0.00–16.50	0
Age of onset for AP	24.94 (10.15)	0–66	59
Neuroticism	3.53 (0.86)	1–5	89
Negative urgency	2.69 (0.80)	1–4	60
Lack of premeditation	2.08 (0.71)	1–4	75
Lack of perseverance	1.87 (0.65)	1–4	55
Sensation-seeking	2.57 (0.79)	1–4	58
Positive urgency	2.14 (0.81)	1–4	68
Depressive symptoms	7.42 (2.78)	0–9	3
Unreliable behavior	0.05 (0.88)	−1.73–3.03	26
Aggressive behavior	0.08 (0.81)	−1.31–2.88	26
Criminal behavior	0.11 (0.79)	−1.25–2.43	26

Notes. Descriptive statistics were computed for each study variable prior to standardization. *Abbreviations*. *M*, mean; SD, standard deviation.

membership are shown in Table 1 and inter-item correlations are shown in Supplementary Table S4.

Latent class analyses

We conducted LCA on ordered three-category item indicator variables for lifetime use of cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens. We evaluated models extracting from 1 through 6 latent classes. Model fit statistics and results from the likelihood ratio tests are shown in Table 2. The Lo–Mendell–Rubin likelihood ratio test was not significant for the six-class model, suggesting that adding a sixth class did not lead to a statistically significant improvement in model fit. Furthermore, the BIC was lowest for the five-class solution and the six-class solution showed a low convergence rate; with 50,000 initial starts and 5000 final starts, 93.2% of iterations failed to converge. Guided by the high failure rate within the six-class model and class interpretability, we selected the more parsimonious five-class solution. Supplementary material provides additional information on the four- and six-class solutions (Supplementary Figs S1 and S2).

Based on conditional probabilities, defined as the probability of reporting a substance use category given membership in a latent class, we applied the following descriptions to the five-class model: (a) the 'extended range polysubstance use' class (24.5% of the sample), characterized by high probabilities of using all substances 6+ times; (b) the 'cigarette and marijuana use' class (18.8%), characterized by high probabilities of using cigarettes and marijuana 6+ times; (c) the 'tester' class (12.3%), characterized by high probabilities of using cigarettes and marijuana 6+ times and moderate-to-high probabilities of trying the remaining substances 1–5 times; (d) the 'moderate range polysubstance use' class (17.1%), characterized by high probabilities of using cigarettes, marijuana and opioids 6+ times and moderate probabilities of using sedatives 6+ times and (e) the 'minimal use' class (27.3%). Figure 2 displays the conditional probabilities for each of the use categories across all seven substances. Supplementary Figure S3 shows the distribution of alcohol-related outcomes within each class.

Identifying associations with latent class membership

In the univariable models, each predictor was nominally associated with latent class membership ($P < 0.05$); see the Supplementary Material for parameter estimates (Supplementary Table S5 and Fig. S4). Table 3 and Supplementary Figure S4 present odds ratios (ORs) for multivariable unique direct effects on latent class membership, and Supplementary Table S6 shows derived multivariable unique direct effects when using alternative reference groups. Below, we review statistically significant findings from the multivariable model. Age and ascertainment method were included as covariates, and the minimal use class was designated as the reference class.

Extended range polysubstance use versus minimal use

Individuals who reported lower levels of positive and negative urgency, younger age of onset for AP, and higher levels of sensation-seeking, lack of premeditation, depressive symptoms, unreliable behavior, criminal behavior and family history density of AP were more likely to be members of the extended range polysubstance use class when compared to the minimal use class. Individuals who identified as male, Black and non-Hispanic, or other race/ethnicity were less likely to be classified in the extended range polysubstance use class.

Cigarette and marijuana use versus minimal use

Individuals who endorsed greater depressive symptoms were more likely to be members of the cigarette and marijuana use class than the minimal use class, whereas individuals who identified as Black and non-Hispanic were less likely to be assigned to the cigarette and marijuana use class.

Tester versus minimal use

Individuals who reported lower levels of negative urgency, younger age of onset for AP and more depressive symptoms and unreliable behavior were more likely to be members of the tester class when compared to the minimal use class. In addition, individuals who identified as Black and non-Hispanic were less likely to be grouped in the tester class.

Moderate range polysubstance use versus minimal use

Individuals who reported female gender, lower levels of positive urgency, younger age of onset for AP and higher levels of depressive symptoms, unreliable behavior and criminal behavior were more likely to be members of the moderate range polysubstance use class than the minimal use class.

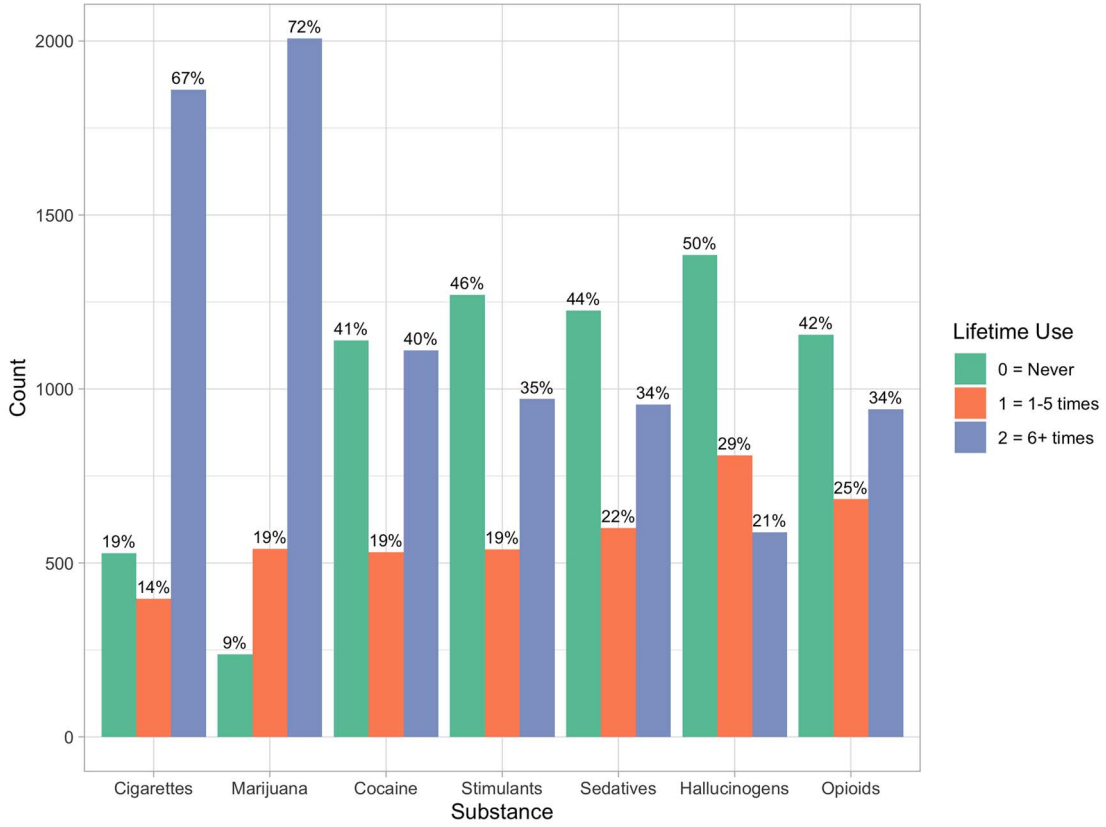

Figure 1. Frequencies for lifetime substance use measures. Response options for marijuana, cocaine, stimulants, sedatives and hallucinogens were 'never,' '1–5 times' and '6+ times.' For cigarettes, participants who had never smoked cigarettes were coded as 0, participants who had smoked fewer than 100 cigarettes were coded as 1 and participants who smoked 100 or more cigarettes were coded as 2. For opioids, participants who had never used opioids were coded as 0, participants who reported using opioids once or twice were coded as 1 and all others were coded as 2. The majority of participants reported smoking 100+ cigarettes and using marijuana 6+ times. For the remaining substances, 'never' was the most commonly endorsed response category.

Table 2. Latent class analysis fit statistics

Classes	Log-likelihood	AIC	BIC	SSABIC	Entropy	AvePP	Lo–Mendell–Rubin LRT	Bootstrapped LRT
1	−19,163.67	38,355.34	38,438.39	38,393.91	—	1.000	—	—
2	−16,815.14	33,688.27	33,860.30	33,768.16	0.823	0.948	4657.92 ($P < 0.001$)	4697.07 ($P < 0.001$)
3	−16,435.36	32,958.73	33,219.73	33,079.93	0.750	0.884	759.54 ($P < 0.001$)	753.21 ($P < 0.001$)
4	−16,267.57	32,653.14	33,003.13	32,815.67	0.760	0.866	332.79 ($P < 0.001$)	335.59 ($P < 0.001$)
5	−16,168.18	32,484.35	32,923.32	32,688.20	0.733	0.832	197.13 ($P = 0.027$)	198.79 ($P < 0.001$)
6	−16,111.25	32,400.51	32,928.45	32,645.67	0.722	0.804	112.90 ($P = 0.129$)	113.85 ($P < 0.001$)

Notes. Lower values for the AIC, BIC and SSABIC indicate better model fit, entropy values closer to 1 suggest greater precision in latent class assignment, and AvePP values greater than 0.70 provide evidence for well-separated classes. The Lo–Mendell–Rubin likelihood ratio test and bootstrapped likelihood ratio test show whether adding a latent class leads to a statistically significant improvement in model fit. *Abbreviations*. AvePP, average posterior probability; LRT, likelihood ratio test.

DISCUSSION

The present study investigated patterns and correlates of lifetime use for cigarettes, marijuana, cocaine, stimulants, sedatives, opioids and hallucinogens among individuals meeting DSM-5 criteria for severe AUD. LCA model fitting suggested five qualitatively distinct classes based on patterns of polysubstance use: an extended range polysubstance use class, characterized by high probabilities of using all substances 6+ times; a cigarette and marijuana use class; a tester class, characterized by high probabilities of using cigarettes and marijuana 6+ times and trying the remaining substances 1–5 times; a moderate range polysubstance use class, described by high probabilities of using cigarettes, marijuana, sedatives and opioids 6+ times; and a minimal use class. These findings indicate that polysubstance use varies considerably, even within a high-risk population—namely, individuals with severe AUD.

Interestingly, Hedden *et al*. (2010) also extracted five latent classes when investigating patterns of illicit drug use among individuals with DSM-IV AUD, including a class with

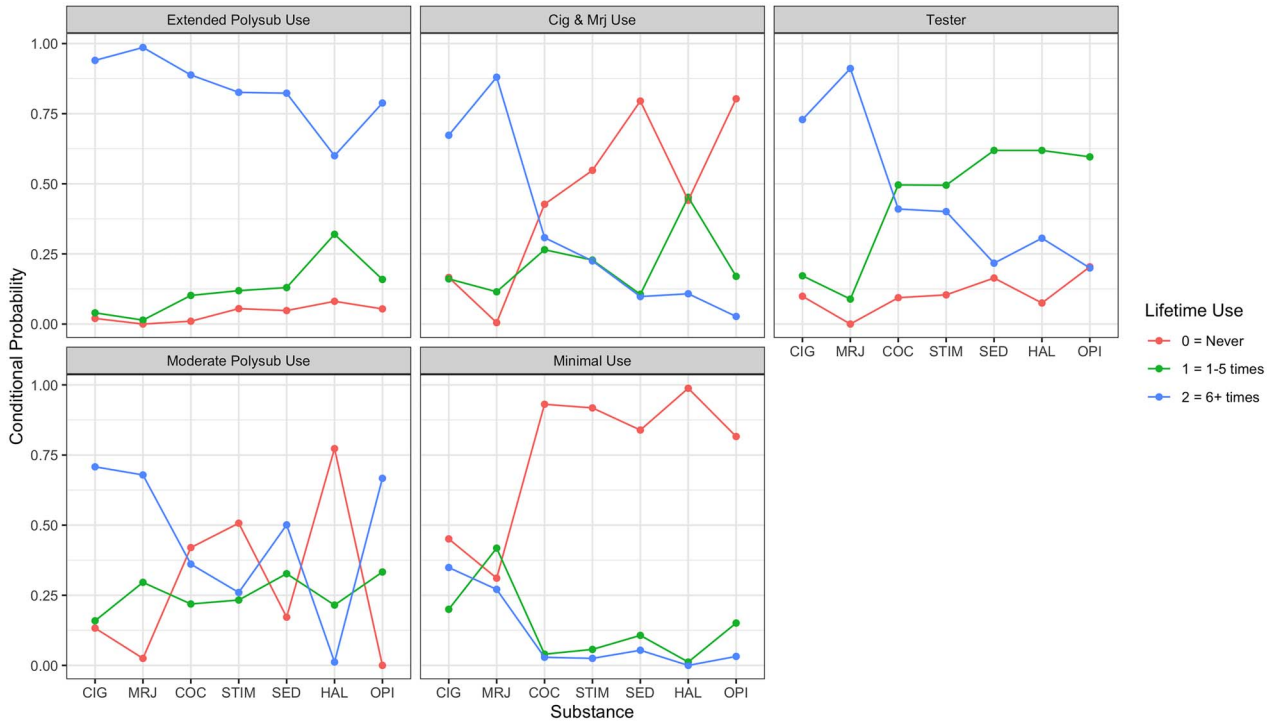

Figure 2. Conditional probabilities of lifetime substance use given latent class membership across three levels of usage for seven substances. It should be noted that response options for lifetime cigarette use (0 = never, 1 = fewer than 100 cigarettes, 2 = 100 or more cigarettes) and opioid use (0 = never, 1 = once or twice, 2 = monthly or more) differed from the remaining substances. As an example of how to interpret this figure, consider individuals classified in the moderate range polysubstance use class (shown in the bottom left panel). For each substance, the conditional probabilities of selecting options 'never,' '1–5 times' and '6+ times' sum to 1 (e.g. the probabilities of using hallucinogens 0, 1–5 times and 6+ times are ∼0.75, ∼0.25 and ∼0, respectively). Thus, among individuals assigned to the moderate range polysubstance use class, the most probable response options were '6+ times' for cigarettes, marijuana, sedatives and opioids and 'never' for cocaine, stimulants and hallucinogens. *Abbreviations*. Polysub, polysubstance; CIG, cigarettes; MRJ, marijuana; COC, cocaine; STIM, stimulants; SED, sedatives; HAL, hallucinogens; OPI, opioids.

Table 3. Odds ratios and 95% confidence intervals for multivariable associations with latent class membership

	Extended range polysubstance use (vs. minimal use)	Cigarette and marijuana use (vs. minimal use)	Testers (vs. minimal use)	Moderate range polysubstance use (vs. minimal use)
Gender (1 = male)	**0.54 [0.31, 0.77]**	1.03 [0.62, 1.45]	0.95 [0.52, 1.38]	**0.44 [0.21, 0.66]**
White, Hispanic	1.19 [0.00, 2.37]	1.09 [0.01, 2.17]	1.93 [0.24, 3.63]	0.92 [−0.25, 2.09]
Black, non-Hispanic	**0.08 [0.01, 0.14]**	**0.31 [0.08, 0.54]**	**0.09 [−0.05, 0.23]**	0.91 [0.39, 1.43]
Black, Hispanic	—	—	—	0.09 [−0.85, 1.02]
Other race	**0.48 [0.11, 0.85]**	0.74 [0.21, 1.26]	0.87 [0.22, 1.51]	1.44 [0.37, 2.51]
SRE score	1.00 [0.93, 1.08]	0.97 [0.89, 1.04]	1.00 [0.91, 1.09]	0.94 [0.86, 1.01]
Neuroticism	0.89 [0.66, 1.11]	0.86 [0.66, 1.07]	0.89 [0.65, 1.13]	1.08 [0.75, 1.41]
Negative urgency	**0.73 [0.49, 0.96]**	0.87 [0.61, 1.13]	**0.64 [0.41, 0.87]**	1.01 [0.64, 1.37]
Lack of perseverance	0.98 [0.68, 1.29]	0.87 [0.60, 1.14]	1.34 [0.92, 1.76]	0.87 [0.58, 1.16]
Sensation-seeking	**1.75 [1.33, 2.18]**	1.14 [0.87, 1.41]	1.14 [0.85, 1.43]	1.03 [0.77, 1.30]
Lack of premeditation	**1.58 [1.08, 2.09]**	1.02 [0.70, 1.34]	1.43 [0.92, 1.93]	1.36 [0.91, 1.80]
Positive urgency	**0.67 [0.47, 0.87]**	0.77 [0.53, 1.01]	0.94 [0.64, 1.24]	**0.72 [0.49, 0.94]**
Depressive symptoms	**1.12 [1.04, 1.21]**	**1.06 [1.00, 1.12]**	**1.09 [1.01, 1.16]**	**1.15 [1.05, 1.25]**
Age of first AP	**0.93 [0.91, 0.95]**	0.99 [0.97, 1.01]	**0.97 [0.94, 0.99]**	**0.97 [0.95, 0.98]**
Unreliable behavior	**4.81 [2.94, 6.67]**	1.34 [0.79, 1.89]	**2.05 [1.15, 2.94]**	**3.36 [1.91, 4.80]**
Aggressive behavior	1.64 [0.99, 2.29]	1.21 [0.67, 1.74]	1.41 [0.80, 2.02]	0.80 [0.44, 1.16]
Criminal behavior	**2.15 [1.26, 3.05]**	1.70 [0.94, 2.46]	1.78 [0.91, 2.65]	**1.91 [1.03, 2.79]**
Family history Index	**1.36 [1.12, 1.61]**	1.21 [0.98, 1.44]	1.18 [0.95, 1.41]	1.18 [0.96, 1.39]
Ascertainment method (1 = in-person)	**5.65 [2.86, 8.44]**	1.75 [0.83, 2.66]	1.67 [0.62, 2.72]	**4.48 [2.20, 6.76]**
Age	1.02 [1.00, 1.03]	1.00 [0.98, 1.01]	1.00 [0.98, 1.02]	1.02 [1.00, 1.03]

Notes. Age and ascertainment method were included as covariates, and Class 5 (the minimal use class) was the reference class. Statistically significant odds ratios are shown in bold font. Because very few participants identified as Black and Hispanic, some parameters were not estimable (shown as '—').

near-zero probabilities of illicit drug use, a class characterized by moderate probabilities of using marijuana, sedatives and analgesics (comparable to the moderate range polysubstance use class), and a class with high probabilities of use across all substances. However, our findings deviate from those of Hedden *et al.* (2010) in two notable ways. First, the present analysis utilized ordinal (rather than binary) substance use indicators, allowing us to identify a novel class of 'testers,' who sample a wide range of substances but do not progress to more regular use. Second, 54% of participants, compared to ~14% in Hedden *et al.* (2010), belonged to latent classes with extended patterns of polysubstance use, which highlights the prevalence of polysubstance use among individuals with severe DSM-5 AUD.

We subsequently evaluated a variety of demographic and behavioral factors as putative correlates of latent class membership. Consistent with our pre-registered hypotheses, earlier age of onset for AP and higher levels of sensation-seeking, lack of premeditation, depressive symptoms, antisocial behavior and familial risk for AP were associated with increased likelihood of belonging to a class with more extensive polysubstance use in the multivariable model. Unexpectedly, higher levels of positive and negative urgency were associated with decreased likelihood of belonging to a class with more extensive polysubstance use.

We also found that women were more likely to be classified in the moderate or extended range polysubstance use classes than men, which was unanticipated. However, there is evidence to suggest that women with severe AUD may be a unique population (Polak *et al.*, 2015). For instance, when comparing men and women in treatment for severe substance use problems, women are more likely to demonstrate a 'telescoping' course, progressing rapidly from initiation to regular use to problems. When examining a wider range of substance use severity, however, women and men are similar in their progression to problems (McHugh *et al.*, 2018). In parallel, findings from the present study suggest that women with severe AUD are at elevated risk for extended polysubstance use, though prior analyses did not identify a significant relationship between sex and patterns of polysubstance use among individuals with alcohol dependence (Hedden *et al.*, 2010). It should be noted, however, that 63% of participants in the present study were female, though men are at two times higher risk for severe AUD (Grant *et al.*, 2015). Accordingly, further work is needed to replicate this pattern of effects in other samples.

These results should be considered in light of several limitations. First, because we assessed lifetime use for each substance, it was not possible to determine whether participants used multiple substances within the same time period, at different times, or simultaneously. There is evidence to suggest that concurrent polysubstance use (defined as the use of multiple drugs within the same time period) and simultaneous polysubstance use (defined as the co-ingestion of multiple drugs at the same time) are different constructs with overlapping but distinct correlates (McCabe *et al.*, 2006; Midanik *et al.*, 2007). Thus, it will be important for future research to separately examine patterns and correlates of concurrent and simultaneous polysubstance use among individuals with severe AUD. Second, given that our measures were cross-sectional, we cannot evaluate whether behavioral and psychosocial correlates preceded participants' use of multiple substances, or vice versa. Third, though participants remained anonymous while responding to the substance use items, self-reported substance use is subject to underreporting bias (Khalili *et al.*, 2021), which may have implications for the pattern of results. Fourth, substance use items combined substances by class and did not distinguish between prescription medication misuse and illicit drug use. In view of evidence to support different risk factors for prescription medication misuse and use of an illicit drug within the same class (McHugh *et al.*, 2015), replication of the present work with substance-specific measures may be warranted.

CONCLUSION

In summary, we found evidence for five qualitatively different patterns of polysubstance use among individuals with severe DSM-5 AUD. We highlight three key takeaways from our findings. First, DSM-5 depressive symptoms were consistently associated with more extended patterns of polysubstance use, underscoring the need to evaluate and address comorbid depression in substance use treatment. Second, participants ascertained from treatment facilities were more likely to be members of the moderate or extended range polysubstance use classes than individuals who were ascertained online, which supports prior evidence that treatment-seeking individuals may not be representative of the broader population of individuals with AUD (Ray *et al.*, 2017). Third, patterns of polysubstance use were differentially related to a number of demographic and behavioral factors. Thus, identifying individuals with specific patterns of polysubstance use is important, both to detect individuals at particularly heightened risk for negative health outcomes (Connor *et al.*, 2014) and to inform the selection of additional treatment targets among individuals with severe AUD. For example, membership in the extended range polysubstance use class was related to higher levels of sensation-seeking, lack of premeditation, depressive symptoms, unreliable behavior and criminal behavior. Prior evidence suggests that impulsivity, depressive symptoms and lower social support are associated with lower alcohol-related self-efficacy, a robust predictor of remission and recovery from substance use disorders (McKellar *et al.*, 2008). Therefore, members of the extended range polysubstance use class may particularly benefit from addressing concurrent depression, impulsivity and antisocial behavior during substance use treatment, which in turn bolsters self-efficacy and improves the likelihood of recovery.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *Alcohol and Alcoholism* online.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data presented in this article cannot be shared publicly to protect the privacy of individuals that participated in the study. The data will be shared on reasonable request to the corresponding author.

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