Polysubstance Use by Stimulant Users: Health Outcomes Over Three Years

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ABSTRACT. Objective: Studies show that stimulant users have varied substance use patterns and that polysubstance use is associated with poorer past or concurrent medical, mental health, and substance use outcomes. This study examined outcomes of substance use patterns prospectively. **Method:** A latent class analysis was conducted to examine substance use patterns among adults using stimulants ($n = 710$; 38.6% women) at baseline, and the health and treatment utilization outcomes of different use patterns over the subsequent 3 years. To examine associations between latent class membership and outcomes, generalized estimating equation modeling was conducted. **Results:** Four classes of substance use patterns at baseline were identified, involving high use of (a) methamphetamine and marijuana (23%); (b) crack cocaine and alcohol (25%); (c) powder cocaine, alcohol, and marijuana (23%); and

(d) nonprescribed opioids, alcohol, marijuana, crack cocaine, and powder cocaine (i.e., polysubstance [29%]). Polysubstance class members had poorer physical health and mental health status, and more severe substance use, over the subsequent 3-year period, than other class members. Regarding treatment utilization, polysubstance class members had more medical care utilization than crack cocaine class members, and more substance use treatment utilization than powder cocaine class members. The methamphetamine, crack cocaine, and powder cocaine classes did not differ from each other on any health or treatment utilization outcome. **Conclusions:** People using stimulants commonly use other substances, and those whose polysubstance use includes nonprescribed opioids have especially poor health outcomes. (*J. Stud. Alcohol Drugs*, 79, 799–807, 2018)

POLYSUBSTANCE USE is the consumption of more than one substance over a defined period, simultaneously or at different times (Connor et al., 2014). It is common and associated with psychiatric and medical problems, engagement in health risk behaviors, and cognitive functioning deficits that increase the chances of poor treatment adherence and outcomes (Booth et al., 2010; Brecht et al., 2008; Connor et al., 2014). Operationalizations of polysubstance use have typically been based on lifetime prevalence, 1–12 month prevalence, or simultaneous substance use, which has been assessed mainly in small studies of high-risk populations because it is impractical to routinely ask about all combinations of substance pairs (Connor et al., 2014). Polysubstance use is associated with the demographic characteristics of being male, young adult, African American, not married or partnered, having less education, living in an urban area, and be-

ing employed (Connor et al., 2014; Kedia et al., 2007). The purpose of this study was to examine substance use patterns, that is, the use of alcohol and drugs in the past month, and the outcomes of different patterns over time, among adults using stimulants at baseline.

Although some studies have assessed polysubstance use as a count of substances used during the observation period (Booth et al., 2010), more recently the approach to describing polysubstance use has employed latent class analysis (LCA; Connor et al., 2014). LCA is a person-centered approach to identifying latent classes or common profiles of substance use that reflect relatively distinct subgroups (Chung et al., 2013). For example, LCA was used to determine patterns of past-year illegal drug use in a U.S. national sample of alcohol-dependent respondents (Hedden et al., 2010). Results demonstrated a five-class solution, with the largest class being an almost-zero probability of illegal drug use (65% of the sample), and the second largest being high marijuana plus medium cocaine use (21% of the sample). Alcohol-marijuana-cocaine class members were more likely to have a history of sexually transmitted infection, incarceration, and behaviors consistent with conduct disorder than those in the alcohol-only class (Hedden et al., 2010). Another LCA conducted on past-month drug use among

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treatment-referred cannabis users found a three-class solution: cannabis plus tobacco (22%); cannabis, tobacco, and alcohol (62%); and wide-ranging substance use (16%) (Connor et al., 2013). Wide-ranging substance users had more severe substance use and mental health symptoms (Connor et al., 2013). Findings of Hedden et al. (2010) and Connor et al. (2013) suggest that people engaged in wider-ranging substance use need more intensive service resources.

Substance use patterns and outcomes among stimulant users

It is important to examine polysubstance use among stimulant users because there are additional risks associated with using stimulants in combination with other substances. According to the Substance Abuse and Mental Health Services Administration (SAMHSA; see Hedden et al., 2015), 2,069,000 Americans were past-month users of stimulants (cocaine and/or methamphetamine). Emergency department visits related to use of stimulants have risen recently, and about two thirds (62%) of these visits involved the use of stimulants with at least one other substance (SAMHSA, 2014). To compare, among all emergency department visits involving the use of any substance, less than one half (49%) of visits involved multiple substances (SAMHSA, 2014). Increasing the risk of harm, current methods are producing purer and more potent formulations of methamphetamine and cocaine as their prices are decreasing (SAMHSA, 2014; Werb et al., 2013).

In addition to being harmful, polysubstance use is common among stimulant users. Among 350 adults treated for methamphetamine use disorders, a majority reported using alcohol, marijuana, and cocaine, and a substantial minority reported use of heroin and tranquilizers. Even when substances used by all or almost all participants were excluded (i.e., methamphetamine, alcohol, marijuana), the mean number of substances used was 5.0 of 10 types (Brecht et al., 2004). Among 1,016 methamphetamine-dependent outpatients, concurrent use of other substances was 63% for alcohol, 59% for marijuana, 10% for prescription opioids, 9% for tranquilizers, and 6% for heroin (Christian et al., 2007). Use of other substances in addition to methamphetamine significantly increased the odds of a history of physical and/or sexual abuse, suicidal ideation and other mental health symptoms, and suicide attempt. Because of the cross-sectional design, these results could be interpreted as either a need for more substances to self-medicate psychiatric symptoms or as clinical pathology stemming from polysubstance use (Christian et al., 2007). A subsequent study of adults with previous, long histories of methamphetamine use found varied patterns of past-year substance use: methamphetamine only (7%), marijuana only (16%), methamphetamine plus marijuana (19%), heroin plus cocaine (20%), or had not used any substances (38%). Polysubstance users, compared with

single-substance or non-users, had more symptoms of mental health disorders (Herbeck et al., 2013).

More recent studies of stimulant users employed LCA. In examining patterns of past-year substance use disorders in a U.S. national sample of adults reporting past-year nonmedical use of attention-deficit/hyperactivity disorder stimulants (Chen et al., 2014), a four-class model identified low probability of any substance use disorder (53%), high probability of alcohol and marijuana use disorders (29%), use of prescription drugs (13%), and high probability of multiple drugs and alcohol use (5%). Those in the multiple drugs plus alcohol class were more likely to report mental health and behavioral problems as well as past-year use of mental health treatment and of addiction treatment. Among treated patients who were past-year injectors of amphetamine, LCA identified three substance use patterns: low polydrug (low use of all substances; 59%), opiates polydrug (heroin or other opioids plus alcohol and cannabis; 15%), and alcohol polydrug (only alcohol plus cannabis; 26%). The low-polydrug class demonstrated somewhat better functioning and safer injecting practices than the other classes (Kelly et al., 2017).

Present study

The studies reviewed suggest that stimulant users have varied substance use patterns and that polysubstance use is associated with poorer past or concurrent medical, mental health, and substance use outcomes. However, all of the reviewed studies were retrospective or cross-sectional, such that associations of substance use patterns with subsequent outcomes could not be examined. The present study used LCA to characterize patterns of substance use at baseline among adults who were using stimulants, and outcomes of the identified classes over the subsequent 3 years. Research on the identification and consequences of polysubstance use may be beneficial for informing the targeting of specific profiles in treatment settings (Connor et al., 2014). That is, a better understanding of outcomes associated with substance use profiles could shed light on recovery processes and ensure that services address the needs of each identified group (Hagen et al., 2017).

Method

Participants

Study participants were 710 stimulant users living in Arkansas, Kentucky, and Ohio counties. The study was approved by the institutional review boards at the investigators' universities, and a Certificate of Confidentiality was obtained from the National Institute on Drug Abuse. Participant eligibility criteria were use of stimulants (methamphetamine, cocaine) within the past 30 days, no treatment or mutual-help group attendance within the past 30 days, being at least

TABLE 1. Baseline sociodemographic characteristics of the sample ($n = 710$) and comparison of substance use pattern classes on baseline sociodemographic characteristics

Variable	Full sample	Meth-amphetamine	Crack cocaine	Powder cocaine	Poly-substance	χ^2 (df)	p
Male, % (n)	61.4 (426)	58.2 (95)	53.3 (95)	69.3 (113)	61.6 (127)	6.3 (3)	.099
White , % (n)	67.9 (482)	98.2 (160)	25.2 (45)	57.6 (94)	86.4 (178)	236.4 (3)	<.001
Age , M (SD)	32.5 (10.4)	31.3 (9.9)	39.6 (8.8)	30.9 (9.6)	29.2 (9.8)	106.7 (3)	<.001
Not married , % (n)	48.5 (344)	41.1 (67)	41.0 (73)	55.8 (91)	52.9 (109)	12.8 (3)	.005
High school graduate, % (n)	41.3 (293)	34.9 (57)	44.9 (80)	50.3 (82)	27.6 (57)	22.7 (3)	<.001
Employed, % (n)	32.2 (229)	41.7 (68)	25.2 (45)	32.5 (53)	29.6 (61)	6.5 (3)	.090
Insured, % (n)	27.5 (195)	34.9 (57)	23.0 (41)	25.7 (42)	23.7 (49)	4.8 (3)	.189

Note: **Bold** indicates significant differences among the four classes on that characteristic.

18 years old, and having a verifiable address within one of the study counties. Participants' baseline sociodemographic characteristics are provided in Table 1.

Procedure

Participants were recruited using respondent-driven sampling, a type of snowball sampling (Heckathorn, 1997; Wang et al., 2005). Study seeds completed a baseline interview and handed out information about the study to up to three people they knew who used drugs. Each seed received \$10 for up to three referred individuals who contacted the study coordinator and were eligible for, and enrolled in, the study. Participants received \$50 for each completed study session.

Participants completed informed consent before the baseline interview. Follow-up interviews were conducted every 6 months for a total of 36 months. Interviews were conducted in person by trained study staff using computer-assisted interview software on laptop computers. Retention rates were 85%, 82%, 81%, 79%, 79%, and 73% for the 6-, 12-, 18-, 24-, 30-, and 36-month interviews, respectively; 73% of the initial sample completed all interviews.

Measures

Baseline substance use. At baseline, participants stated how many days in the past 30 days they had used each of the following 10 substances: alcohol, amphetamines, crack cocaine, heroin, marijuana, methamphetamine, nonprescribed opioid pain medications, nonprescribed tranquilizers, powder cocaine, and prescribed opioid pain medications.

Health outcomes. To assess medical status at baseline and each follow-up, four variables were combined to create an index, as follows: (a) the number (0–29) of medical conditions (past 6 months) that participants had been told by a doctor that they had; (b) the number (0–5) of diagnosed physical ailments (past 6 months); (c) the seriousness of the diagnosed physical ailments (past 6 months; 0 = *not serious at all* to 4 = *extremely serious*); and (d) the medical severity score from the Addiction Severity Index (ASI; McLellan et al., 1980), which ranged on a continuous scale from 0 to 1, with higher scores indicating greater severity. Mental health

status was the composite of the following four variables: (a) the Patient Health Questionnaire (PHQ-9; Kroenke et al., 2001) score (0–27, with higher scores indicating greater depression symptom severity); (b) the number (0–5) of emotional problems (past 6 months); (c) the seriousness of the emotional problems (past 6 months; 0 = *not at all* to 4 = *extremely*); and (d) the psychiatric subscale of the ASI (McLellan et al. 1980), which ranged on a continuous scale from 0 to 1 with higher scores indicating greater severity. Substance use severity combined four variables: how many days in the past 30 days the participant had (a) used alcohol and (b) drugs; (c) whether the participant met criteria for an alcohol use disorder (yes/no); and (d) the count of how many other substances the participant met criteria for disorders. Each outcome was computed by converting the variables it included to z scores and then taking the mean of the z scores (Blonigen et al., 2005, 2016; for additional detail, see Woodhead et al., 2018).

Treatment utilization. Three types of treatment utilization with regard to the past 6 months were examined. The medical care index combined three variables: (a) number of hospitalizations (0–5); (b) number of days for each hospitalization; and (c) number of outpatient visits (0–6); again, this dependent variable was computed by converting the variables it included to z scores and then taking the mean of the z scores (Woodhead et al., 2018). Substance use treatment was assessed with one question (yes/no) that asked participants whether they had been in a substance use treatment program (residential, intensive outpatient, outpatient, methadone, or other). Mental health treatment was assessed with one question that asked participants whether they had been treated for psychological or emotional problems by a professional such as a psychologist, social worker, psychiatrist, or therapist.

Analysis plan

SAS PROC LCA was used for the LCA analysis, that is, to identify use patterns of the 10 substances (alcohol, amphetamines, crack cocaine, heroin, marijuana, methamphetamine, nonprescribed opioid pain medications, nonprescribed tranquilizers, powder cocaine, and prescribed

opioid pain medications) during the past 30 days. We used the timeframe of the past 30 days to more accurately examine recent substance use patterns (Connor et al., 2013; Kelly et al., 2017); zero days was coded as no use, and one or more days as use. To examine the assumption of conditional independence that must be met in LCA, we conducted bivariate correlations among the substance use variables and examined the tolerances or VIFs among variables (i.e., we regressed each variable assessing substance use on all of the other substance use variables). Results of these analyses indicated that the assumption of conditional independence was met; that is, correlations were small to moderate, and tolerances and VIFs did not raise concerns about non-independence.

Model fit was assessed using three indices including the Akaike information criterion (AIC), the Bayesian information criterion (BIC), and G^2 (likelihood-ratio statistic). The optimal number of classes was selected based on these indices. Model fitting started with a one-class solution and proceeded up to a five-class solution. Comparisons were made among the latent classes with Bonferroni adjusted confidence intervals.

To examine associations between latent class membership and outcomes, because of the repeated structure of the data, we used generalized estimating equation (GEE) models for all outcomes. For each dependent variable, we first checked the distribution. If the normal assumption was satisfied, a normal distribution with an identity link was specified; this held for the outcomes of medical status, mental health status, and substance use severity. For skewed dependent variables, a gamma distribution with log link was specified; this held for the outcome of medical care utilization. For dichotomized outcomes, a binominal distribution with logit link was specified; this held for mental health and substance use treatment. Robust standard errors were used in all models with an AR(1) correlation matrix specified. Demographic covariates were included in all models, that is, gender (male vs. female), race (White vs. not White), age, marital status (not married vs. married), education (high school education or more vs. less), employment status (employed vs. unemployed), health insurance status (insured vs. uninsured), and state of residence (Arkansas and Kentucky vs. Ohio), as well as time indicating each interview.

Results

Model fit statistics for 1 to 5 class solutions are presented in Table 2. The value of the information criteria decreased as the number of classes increased, indicating successively better-fitting models. The 4-class solution was selected as the most parsimonious representing the data.

Figure 1 shows the probability of past-30-day use for each substance by class. For brevity, we refer to the high, moderate, or low probability of having used a substance at least

once in the past 30 days as “high, moderate, or low use,” respectively. Class 1 (23%, $n = 163$) was characterized by high use of methamphetamine and marijuana, moderate use of alcohol and nonprescribed opioid pain medications, and low use of crack cocaine, powder cocaine, heroin, prescribed opioid pain medications, amphetamines, and nonprescribed tranquilizers. Class 2 (25%, $n = 178$) was characterized by high use of crack cocaine and alcohol, moderate use of marijuana, and low use of powder cocaine, heroin, prescribed opioids, nonprescribed opioids, methamphetamine, amphetamine, and nonprescribed tranquilizers. Class 3 (23%, $n = 163$) was characterized by high use of powder cocaine, alcohol, and marijuana; moderate use of crack cocaine; and low use of heroin, prescribed opioids, nonprescribed opioids, methamphetamines, amphetamines, and nonprescribed tranquilizers. Class 4 (29%, $n = 206$) was characterized by high use of nonprescribed opioids, alcohol, marijuana, crack cocaine, and powder cocaine; moderate use of prescribed opioids, methamphetamine, and nonprescribed tranquilizers; and low use of heroin and amphetamine. While recognizing that each class characterizes the use of multiple substances, for conciseness, we refer to Class 1 as the Methamphetamine class, Class 2 as the Crack Cocaine class, Class 3 as the Powder Cocaine class, and Class 4 as the Polysubstance class.

Table 1 compares the four classes on baseline sociodemographic characteristics. Most members of the Methamphetamine, Polysubstance, and Powder Cocaine classes were White, compared with only 25% of Crack Cocaine class members; Crack Cocaine class members were also older than other class members. Most Polysubstance and Powder Cocaine class members were not married, whereas most Methamphetamine and Crack Cocaine class members were married. About one half of Crack and of Powder Cocaine class participants had at least a high school education, compared to roughly one third of Methamphetamine and of Polysubstance class members. Classes did not differ on gender or employment or insurance status.

Analyses initially used GEE to compare each class to each other class, considering time and demographics, on each outcome. These analyses found differences only between the Polysubstance class and other classes. Therefore, for parsimony in reporting, Table 3 shows results of GEE models comparing the Methamphetamine, Crack Cocaine, and Powder Cocaine classes to the Polysubstance class on physical and mental health status, and substance use severity. Polysubstance class members had poorer physical health and mental health status, and more severe substance use, than other class members.

Table 4 shows results of GEE models comparing the Methamphetamine, Crack Cocaine, and Powder Cocaine classes to the Polysubstance class on medical, mental health, and substance use treatment use. Regarding medical care, Polysubstance class members had more utilization than

FIGURE 1. Latent classes of substance use patterns among adults using stimulants

TABLE 2. Fit statistics of the latent class analysis

Class	AIC	BIC	G ²
1 Class	1,334.90	1,380.44	1,314.90
2 Classes	884.02	979.65	842.02
3 Classes	693.25	838.97	629.25
4 Classes	544.02	739.84	458.02
5 Classes	530.70	776.61	422.70

Notes: AIC = Akaike information criterion; BIC = Bayesian information criterion.

Crack Cocaine class members. Classes did not differ on mental health care utilization. Regarding substance use treatment, Polysubstance class members were more likely to have received treatment than Powder Cocaine class members.

Discussion

This study accomplished two aims. The first was to identify classes of substance use patterns among people using stimulants by conducting LCA. The second was to extend previous retrospective and cross-sectional studies of the

outcomes of different substance use patterns by prospectively examining outcomes over the 3-year postbaseline period. The findings are useful to substance use treatment practitioners and researchers because they highlight the particularly poor health associated with polysubstance use over time, despite more use of medical and substance use treatment by Polysubstance class members, and thus the need for more effective interventions for people using particular combinations of substances.

The identified four classes indicate that substance use patterns are diverse among people using stimulants. Classes were differentiated by (a) high use of methamphetamine and marijuana, and moderate use of alcohol and nonprescribed opioid pain medications (Methamphetamine class); (b) high use of crack cocaine and alcohol, and moderate use of marijuana (Crack Cocaine class); (c) high use of powder cocaine, alcohol, and marijuana, and moderate use of crack cocaine (Powder Cocaine class); and high use of nonprescribed opioids, alcohol, marijuana, crack cocaine, and powder cocaine, and moderate use of prescribed opioids, methamphetamine, and nonprescribed tranquilizers (Polysubstance class). Each

TABLE 3. Parameter estimates from GEE models for medical, mental health, and substance use status

Variable	Medical	Mental health	Substance use severity
Intercept	-0.22 (-0.42, -0.02)	0.22 (-0.06, 0.50)	0.76 (0.53, 0.98)
Latent class			
Methamphetamine	-0.18 (-0.28, -0.07)	-0.24 (-0.39, -0.10)	-0.70 (-0.85, -0.55)
Crack cocaine	-0.23 (-0.35, -0.10)	-0.34 (-0.50, -0.18)	-0.64 (-0.80, -0.48)
Powder cocaine	-0.16 (-0.26, -0.05)	-0.34 (-0.48, -0.20)	-0.62 (-0.75, -0.48)
Time			
Month 6	0.00 (-0.05, 0.05)	-0.02 (-0.07, 0.03)	-0.30 (-0.41, -0.19)
Month 12	0.01 (-0.05, 0.07)	-0.01 (-0.07, 0.05)	-0.27 (-0.41, -0.13)
Month 18	0.00 (-0.06, 0.06)	-0.02 (-0.08, 0.04)	-0.39 (-0.53, -0.24)
Month 24	0.01 (-0.05, 0.07)	-0.01 (-0.08, 0.05)	-0.36 (-0.51, -0.22)
Month 30	0.01 (-0.05, 0.07)	-0.01 (-0.07, 0.05)	-0.33 (-0.48, -0.18)
Month 36	0.00 (-0.06, 0.07)	0.00 (-0.06, 0.07)	-0.29 (-0.43, -0.15)
Demographics			
Male	-0.21 (-0.28, -0.14)	-0.26 (-0.35, -0.17)	0.09 (0.01, 0.17)
White	0.05 (-0.05, 0.15)	0.05 (-0.09, 0.18)	-0.07 (-0.19, 0.05)
Age	0.02 (0.01, 0.02)	0.01 (0.00, 0.02)	-0.00 (-0.01, 0.00)
Not married	-0.05 (-0.13, 0.02)	-0.11 (-0.21, -0.01)	-0.01 (-0.10, 0.08)
High school graduate	-0.04 (-0.11, 0.03)	-0.09 (-0.19, 0.00)	-0.09 (-0.16, -0.02)
Employed	-0.12 (-0.19, -0.05)	-0.11 (-0.21, -0.01)	-0.05 (-0.13, 0.03)
Insured	0.19 (0.11, 0.27)	0.22 (0.11, 0.33)	-0.03 (-0.11, 0.05)
State			
Arkansas	-0.25 (-0.36, -0.15)	-0.38 (-0.52, -0.24)	-0.06 (-0.18, 0.06)
Kentucky	-0.09 (-0.18, 0.00)	-0.06 (-0.19, 0.06)	-0.16 (-0.26, -0.05)

Notes: Parameter estimates that are in **bold** indicate statistical significance. Medical status refers to number of medical conditions and physical ailments and their severity; mental health status refers to depression symptoms, emotional problems, and psychiatric distress severity; substance use severity refers to frequency of alcohol and drug use and meeting criteria for substance use disorders. Referent groups are Polysubstance class for latent class, baseline for time, and Ohio for state. GEE = generalized estimating equation.

class represented about one quarter of the sample of stimulant users at baseline.

Two commonalities across the first three classes may help to explain why they did not differ on outcomes related to health and health care utilization. One was that in each of those classes a high probability of use occurred for only two or three substances, in contrast to the polysubstance use class, which had a high probability of use of five substances. The number as well as the type of multiple substances used may be associated with health (Bhalla et al., 2017). Another commonality across the first three classes was the use of stimulants with alcohol and marijuana, despite known dangers of such use. Marijuana is often used to decrease side effects of “coming down” from stimulants (Compton & Volkow, 2006; Oliére et al., 2013), but its use increases risk of severe paranoia and psychosis (Hanna et al., 2017). Alcohol is often used with stimulants because its sedative properties counteract some of the stimulant’s effects, such as sleep disturbances (Compton & Volkow, 2006). However, whereas methamphetamine use elevates the risk of cardiac pathology, mixing alcohol with methamphetamine increases this risk (Kaye et al., 2007). Further, methamphetamine use masks the effects of drinking such that drinking-impaired persons do not perceive themselves as so and are more likely to engage in dangerous behaviors such as drinking and driving (Compton & Volkow, 2006). In addition, the specific combination of cocaine and alcohol produces cocaethylene, a metabolite that is more toxic than either cocaine or alco-

hol alone, in the liver (Compton & Volkow, 2006). Finally, whereas methamphetamine use increases the likelihood of psychotic symptoms, additional frequent cannabis or marijuana use increases the likelihood even more (McKetin et al., 2013).

Our findings on the common use of stimulants with other substances, combined with the dangers of this practice, serve to underscore the importance of screening for and targeting treatment to ongoing multiple substances use among stimulant users presenting for treatment, as do findings from Wang et al. (2017). Wang et al. (2017) found that secondary substance use consistently moderated associations between treatment and primary drug use. During months without any secondary substance use, treatment was strongly associated with decreased odds of primary drug use, but during months of secondary use, the association was weaker. However, clinical guidelines provide minimal guidance on the management of polydrug use (Wang et al., 2017); they suggest only that multiple substance use disorders be managed according to recommendations made for individual disorders (e.g., National Institute on Drug Abuse, 2012).

In our examination of demographic characteristics, Crack Cocaine class members were more likely to be Black and older than other class members. Similarly, in U.S. national samples, older and Black respondents were at increased risk for crack cocaine use in unconditional models (Palamar et al., 2015). However, because the association with race no longer held when socioeconomic variables were controlled,

TABLE 4. Parameter estimates from GEE models for medical, mental health, and substance use treatment utilization

Variable	Medical	Mental health	Substance use treatment
Intercept	-0.28 (-0.54, -0.03)	-3.80 (-6.00, -1.60)	-1.93 (-3.71, -0.16)
Latent class			
Methamphetamine	0.20 (-0.00, 0.40)	0.05 (-0.40, 0.51)	-0.44 (-1.66, 0.77)
Crack cocaine	-0.23 (-0.42, -0.05)	-0.40 (-0.91, 0.11)	-1.78 (-3.61, 0.05)
Powder cocaine	0.05 (-0.13, 0.24)	-0.42 (-0.93, 0.08)	-2.45 (-3.93, -0.97)
Time			
Month 6	0.07 (-0.01, 0.14)	-0.50 (-0.79, -0.21)	-1.23 (-1.59, -0.87)
Month 12	0.09 (0.01, 0.17)	-0.40 (-0.69, -0.11)	-1.04 (-1.39, -0.70)
Month 18	0.07 (-0.02, 0.15)	-0.44 (-0.73, -0.16)	-0.93 (-1.28, -0.58)
Month 24	0.10 (0.01, 0.19)	-0.40 (-0.69, -0.12)	-0.72 (-1.05, -0.40)
Month 30	0.09 (0.00, 0.18)	-0.47 (-0.76, -0.17)	-0.89 (-1.24, -0.54)
Month 36	0.06 (-0.03, 0.15)	-0.67 (-0.98, -0.35)	-0.92 (-1.28, -0.55)
Demographics			
Male	-0.21 (-0.29, -0.12)	-0.49 (-0.81, -0.17)	0.14 (-0.33, 0.60)
White	0.11 (-0.04, 0.25)	0.58 (0.05, 1.11)	0.06 (-0.42, 0.53)
Age	0.01 (0.00, 0.01)	0.14 (0.02, 0.26)	0.12 (0.01, 0.23)
Not married	-0.08 (-0.17, 0.01)	-0.33 (-0.73, 0.08)	-0.13 (-0.43, 0.18)
High school graduate	0.02 (-0.06, 0.10)	0.05 (-0.29, 0.39)	-0.06 (-0.35, 0.23)
Employed	-0.09 (-0.18, -0.00)	-0.56 (-0.93, -0.20)	-0.26 (-0.56, 0.05)
Insured	0.30 (0.21, 0.38)	0.69 (0.35, 1.02)	-0.12 (-0.42, 0.18)
State			
Arkansas	-0.12 (-0.41, 0.17)	-0.72 (-1.26, -0.18)	-1.23 (-1.71, -0.76)
Kentucky	0.14 (-0.06, 0.34)	-0.20 (-0.61, 0.20)	-1.03 (-1.41, -0.65)

Notes: Medical care refers to numbers of hospitalizations, hospital days, and outpatient visits; mental health treatment refers to having been treated for psychological or emotional problems by a professional; substance use treatment refers to having been in a substance use treatment program. Referent groups are polysubstance class for latent class, baseline for time, and Ohio for state. GEE = generalized estimating equation.

the higher risk for crack cocaine use among racial minorities may be driven by socioeconomic factors (Palamar et al., 2015). More generally, our sample was notably uneducated (40% with <12 years of schooling), uninsured (73%), and unemployed (50%), supporting the notion that socioeconomic factors are contributing determinants of substance use. We found that Crack and Powder Cocaine class members were more likely to have completed high school than Methamphetamine and Polysubstance class members, whereas previous studies found noncompletion of high school associated with more use of tobacco, alcohol, marijuana, and illicit drugs (Tice et al., 2013).

Our prospective findings that Polysubstance class members had poorer physical, mental, and substance-related health status, and a greater likelihood of use of medical and substance use care, than other stimulant users over the follow-up period are consistent with and extend previous studies relying on retrospective or cross-sectional data; these studies also found polysubstance use to be associated with poorer functioning (Kelly et al., 2017). In our study, only the Polysubstance class had members with high use of nonprescribed opioids, which may help to explain members' poor outcomes. Opioid use is associated with poorer health and quality of life and more health care use among noncancer pain patients (Eriksen et al., 2006). Specifically, opioids cause adverse events in several organ systems through a variety of mechanisms, such that longer-term opioid use is associated with gastrointestinal problems (constipation and

nausea), hyperalgesia, sleep-related breathing problems, increased risk of fractures (due to dizziness and reduced alertness causing falls), cardiovascular problems (myocardial infarction and heart failure), hormone problems, and depression (Baldini et al., 2012; Benyamin et al., 2008). Accordingly, adults who used opioids or multiple drugs had higher health care utilization than adults who used only stimulants (Calcaterra et al., 2015).

Despite this study's strengths, including successfully following a large sample of stimulant users over a relatively long time, it also had limitations. We relied on participants' self-reports, which may have been influenced by social desirability and other response biases. Although studies have found substance-using individuals to provide accurate self-reports of use (Napper et al., 2010; SAMHSA, 2010), biological tests and/or collateral reports would provide corroboration. In this study, we used the time frame of the past 30 days (zero or any days of use) to characterize substance use patterns. This fits with the current definition of polysubstance use as use of at least two different substances (no or yes) either simultaneously or separately in a defined period of time, including lifetime or the past year, 6 months, month, or 2 weeks (Tomczyk et al., 2016). However, we did not differentiate simultaneous (co-ingestion of different substances at the same time) from concurrent (use of different substances on the same or separate occasions within the same period) polysubstance use. Studies examining both simultaneous and concurrent use in the same samples have found

that most polysubstance use is simultaneous (Baggio et al., 2014; McCabe et al., 2006; Quek et al., 2013; Subbaraman & Kerr, 2015). Reliable and valid measures are essential for describing substance use patterns, evaluating effectiveness of interventions, and enacting harm-prevention policies. Another limitation was that substance use and mental health treatment were each analyzed as only one dichotomous item. A better understanding of substance use patterns and treatment would be achieved with more comprehensive differentiation of types and amounts of help obtained.

Conclusion

This study's findings that people using stimulants commonly also use other substances, and that people whose polysubstance use includes nonprescribed opioids have especially poor health outcomes, suggest that intervention is needed at multiple levels. This includes increasing public awareness of the dangers of polysubstance use through effective educational efforts that provide clear communication about harms of mixing substances (SAMHSA, 2014). Raising awareness among first responders, such as emergency medical technicians and emergency department staff, about the likelihood and negative effects of polysubstance use can also help reduce the harmful consequences of mixing stimulants and other substances on patients' health and well-being.

Treatment providers are typically trained to diagnose and treat disorders separately even though there is growing awareness that multimorbidity, such as polysubstance use with co-occurring mental health conditions, is the norm in clinical practice and represents more than a simple occurrence of simultaneous problems. However, treating each substance use problem and its medical and mental health correlates in isolation may fail to adequately address these challenging clinical situations in their full complexity. Studies support the adoption of gradually stepped-up treatments, such that polysubstance use patients are first stabilized to achieve abstinence, and then interventions for comorbid problems are offered later (Hagen et al., 2017). These same studies found that patients treated for polysubstance use showed improved life satisfaction, executive functioning, and psychological distress following 1 year of abstinence (Hagan et al., 2017). This knowledge may provide hope for patients (thereby reducing treatment dropout) and treatment providers in that it highlights the benefits of sustained abstinence.

Our findings on harms of using nonprescribed opioids in combination with stimulants and other substances are consistent with findings that more than 90% of opioid overdose deaths also involve non-opioid drugs. The near ubiquity of multiple drugs in opioid overdose deaths is also true of deaths caused by drugs other than opioids (DuPont, 2018). DuPont observes that sustained recovery from polysubstance use can be achieved in treatments such as state physician health programs, which involve comprehensive evaluation,

high-quality initial treatment, and extensive recovery support, such as 12-step groups, including Al-Anon for family members (McLellan et al., 2008; Merlo et al., 2016). Clinical research is critically needed to further inform targeted treatments for polysubstance use to prevent harm, promote recovery, and lessen incurred treatment burdens and costs for individuals and society.

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