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Prevalence, patterns, and correlates of multiple substance use disorders among adult primary care patients

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ABSTRACT

Background: Addressing multiple substance use disorders (SUDs) in primary care-based screening and intervention may improve SUD treatment access, engagement, and outcomes. To inform such efforts, research is needed on the prevalence and patterns of multiple SUDs among primary care patients.

Methods: Data were analyzed from a sample of 2000 adult (aged ≥ 18) primary care patients recruited for a multisite National Drug Abuse Treatment Clinical Trials Network (CTN) study (CTN-0059). Past-year DSM-5 SUDs (tobacco, alcohol, and drug) were assessed by the modified Composite International Diagnostic Interview. Prevalence and correlates of multiple versus single SUDs were examined. Latent class analysis (LCA) was used to explore patterns of multiple SUDs.

Results: Multiple SUDs were found among the majority of participants with SUD for alcohol, cannabis, prescription opioids, cocaine, and heroin. Participants who were male, ages 26–34, less educated, and unemployed had increased odds of multiple SUDs compared to one SUD. Having multiple SUDs was associated with greater severity of tobacco or alcohol use disorder. LCA of the sample identified three classes: class 1 (83.7%) exhibited low prevalence of all SUDs; class 2 (12.0%) had high-moderate prevalence of SUDs for tobacco, alcohol, and cannabis; class 3 (4.3%) showed high prevalence of SUD for tobacco, opioids, and cocaine. LCA-defined classes were distinguished by sex, age, race, education, and employment status.

Conclusions: Findings suggest that primary care physicians should be aware of multiple SUDs when planning treatment, especially among adults who are male, younger, less educated, or unemployed. Interventions that target multiple SUDs warrant future investigation.

1. Introduction

The gap between the need for and receipt of treatment for substance use disorder (SUD) in the U.S. remains large. The National Survey on Drug Use and Health (NSDUH) estimated that 20.1 million Americans in 2016 had a SUD (alcohol or illicit/nonmedical drugs) in the past-year; however, only 10.6% of those with SUD received treatment (SAMHSA and CBHSQ, 2017). One strategy for increasing treatment access to this underserved population includes the integration of SUD services into primary care settings (Ducharme et al., 2016). To this end, data are needed to inform the specific treatment needs among primary care patients with SUDs in order to guide the development of more targeted and effective screening, assessment, and intervention approaches.

One factor to be taken into consideration when screening for and assessing SUD in primary care is that many individuals may meet criteria for multiple SUDs. For instance, the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) indicated that the majority of adults with past-year DSM-5 SUDs had at least one other co-occurring SUD, ranging from 56.8% for adults with prescription opioid use disorder to 97.5% for adults with hallucinogen use disorder (McCabe et al., 2017). This NESARC analysis also found

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that males, younger adults, African-Americans, and those with concurrent psychiatric disorders had increased odds of having multiple past-year SUDs compared to those with a single SUD. Moreover, studies have found that persons with multiple SUDs have increased odds of overdose, suicide, sexual risk behaviors, infectious disease, and worse treatment outcome (Connor et al., 2014; Petry, 2001). Taken together, individuals with multiple SUDs likely constitute a more severe subset of patients with added barriers to accessing and engaging in SUD treatment services. A better understanding of the prevalence, patterns, and correlates of multiple past-year SUDs among primary care patients may help to more accurately triage patients into risk categories and facilitate linkage to proper care.

The prevalence and correlates of multiple past-year SUDs in patients seen in primary care remain understudied compared to the general population. However, research is needed because findings among samples from the general population may not necessarily translate to primary care samples. For instance, many studies report a higher prevalence of SUDs in primary care compared to national surveys, perhaps due to SUD-related health problems requiring treatment or other distinct correlates (Pilowsky and Wu, 2012). Additionally, prevalence and correlates of multiple SUD data in primary care using DSM-5 dimensional criteria are needed (APA, 2013), which includes modifications from the previously used DSM-4 (APP, 2000), in order to inform future research and provide the most clinically relevant information. For instance, it is unknown whether having multiple SUDs is associated with greater severity (i.e., number of DSM-5 criteria) of substance-specific use disorders, which may have implications for guiding clinical assessment and care.

To further our knowledge on multiple SUDs in primary care, we conducted a secondary data analysis of a multisite clinical trial sponsored by the National Institute on Drug Abuse's National Drug Abuse Treatment Clinical Trials Network (NIDA CTN): The Tobacco, Alcohol, Prescription medications, and other Substance [TAPS] Tool study (McNeely et al., 2016). The TAPS Tool study assessed the performance of a novel brief substance screening and assessment tool among a diverse sample of patients from five primary care practices. Our objectives were to use this study sample to 1) examine the prevalence of multiple SUDs, stratified by substance, and demographic correlates of multiple SUDs, 2) to examine the patterns of single and multiple SUDs by SUD severity level, and 3) to use latent class analysis (LCA) to explore patterns of multiple SUDs by identifying heterogeneous subgroups of patients with SUDs (e.g., Wu et al., 2009a,b, 2011). Analyses were conducted in the total sample as well as among participants who reported substance use in the past 12 months in order to inform screening, brief intervention, and referral to treatment (SBIRT) efforts. Overall, this information may inform early identification or assessment of multiple SUDs among primary care patients, which may lead to more effective treatment strategies among primary care patients screening positive for substance use or SUD.

2. Methods

2.1. Study sample

Methods for the TAPS Tool Study have been published in detail previously (Wu et al., 2016a,b). Briefly, a total of 2000 adult patients were recruited from August 2014 to April 2015 at five primary care clinics for the NIDA CTN TAPS Tool Study (CTN-0059). Eligibility criteria included being an adult aged 18 years or older, having the ability to provide informed consent, and being able to comprehend spoken English. The primary care clinics from which participants were recruited included a Federal Qualified Health Center in Baltimore, MD (n = 589), a public hospital-based clinic in New York, NY (n = 534), a university-based health center in Richmond, VA (n = 211), and two non-academic community-based primary care practices in Kannapolis, NC (n = 287 and 379). Sites were selected on the basis of geographical diversity and to include both academic and non-academic settings.

All study sites conducted recruitment procedures consistently (Wu et al., 2016a,b). Participants were recruited from the waiting area of clinics where research assistants invited them to participate in an anonymous screening for a health study. If interested, participants were brought to a private room and were assessed for eligibility and verbal consent was obtained. Eligible participants completed the TAPS tool (via self-administration and interviewer-administration) and standard reference measures of substance use and substance use-related problems were administered by trained research assistants. Participants were compensated $20 for the completion of all survey assessments. Of 14,171 individuals approached, 12% declined screening, and 88% were assessed for eligibility; 52% were excluded due to ineligibility (not a clinic patient [n = 2884]; language [n = 2142]; previously enrolled [n = 1042], age < 18 [n = 278], or other reason [n = 172]). A total of 2057 adults (35% of eligible adults) were enrolled in the study; 2000 participants completed the study (Wu et al., 2016a,b).

2.2. Study variables

The Composite International Diagnostic Interview (CIDI), Second Edition, Substance Abuse Module has been widely used to assess SUDs (Compton et al., 1996; Cottler, 2000). Using the modified World Mental Health CIDI (WMH-CIDI), the existing CIDI items were mapped onto past-year DSM-5 SUD classifications by omitting the item on legal problems and including the CIDI item on craving (McNeely et al., 2016; Wu et al., 2016a,b). DSM-5 criteria for SUD in the past 12 months was assessed separately for each substance including tobacco, alcohol, cannabis, cocaine/crack, methamphetamine, heroin, prescription opioid, stimulant, sedative, hallucinogen, inhalant, and other nonspecific drug use disorders. Furthermore, all substance-specific criteria for SUD were assessed (i.e., no skip pattern was used when assessing substance-specific criteria). Because the WMH-CIDI does not include many of the DSM-5 tobacco use disorder criteria, the latter was assessed using the language from the drug section. Based on the DSM-5 (APA, 2013), SUD was defined as meeting ≥2 DSM criteria for a given substance, mild SUD was defined as meeting 2–3 criteria, and moderate/severe SUD was defined as meeting ≥4 criteria. Demographic data were also collected via self-report and included age, sex, race, ethnicity, education, marital status, and employment status.

2.3. Data analysis

We first examined the demographic distribution of the sample. Next, we examined the prevalence of single and multiple past-year SUDs in the total sample and among past-year substance users. A single SUD was defined as meeting DSM-5 criteria for a given substance but no other substance. Having multiple SUDs was defined as meeting DSM-5 criteria for SUD of 2 or more substances. The prevalence of single and multiple SUDs was also examined among past-year users of specific substances. Unadjusted and adjusted multinomial logistic regression models were used to estimate the demographic correlates of having only one past-year SUD, 2 past-year SUDs, and 3+ past-year SUDs, all of which were mutually exclusive categories. Logistic regression was also used to examine the association of multiple SUDs with the SUD severity (i.e., number of criteria met). Demographic variables and study site were included as control variables in the adjusted logistic regression models.

LCA was applied to six dichotomous past-year SUD variablesfor tobacco, alcohol, cannabis, cocaine/crack, prescription opioids/heroin, and other drugs (i.e., sedatives, methamphetamine, prescription stimulants/amphetamines, hallucinogens, inhalants, other nonspecific drugs) to empirically determine subgroups of participants with multiple SUDs in the total sample and among those reporting past-year substance use. Model fit was evaluated between 1 and 4 latent classes using information from the likelihood-ratio (G^2) test, Akaike's Information

Criterion (AIC), Bayesian Information Criterion (BIC) statistic, and entropy (Nylund et al., 2007). In general, lower BIC values indicate a better model, and higher entropy values (ranging from 0 to 1) indicate a clearer delineation of classes. Multinomial logistic regression was then used to estimate differences in the demographic correlates between LCA-defined subgroups. All analyses were conducted with Stata 15.0 (StataCorp, 2017).

3. Results

3.1. Sociodemographics

The mean (SD) age of the total sample (n = 2000) was 46.0 (14.7) years (Table S1 in the supplementary material). Females comprised 56.2% of the sample. Over half of the sample was non-Hispanic black/African American (52.9%), 28.9% were non-Hispanic white, 11.7% were Hispanic, and 6.6% were of other or unknown race/ethnicity. Approximately one-third of the sample was employed (35.6%), 45.8% were never married, and 32.5% had attended some college or had an associate's degree.

3.2. Prevalence of multiple SUDs

Among the total sample, over one-third (35.8%) of participants had at least one SUD (tobacco, alcohol, or drug) in the past year, and 22.0% had a single (i.e., non-multiple) SUD (Table 1). Multiple SUDs were reported by 13.8% of participants, of which 7.4% had 2 SUDs and 6.4% had 3 or more SUDs. Multiple SUDs were reported in 45.8% of those meeting SUD criteria for tobacco, 63.6% for alcohol, 73.8% for cannabis, 87.5% for prescription opioids, 90.2% for cocaine/crack, and 93.8% for heroin. A significantly larger proportion of participants with SUD related to the use of all substances except tobacco, methamphetamine, and prescription stimulants/amphetamine met criteria for multiple SUDs than SUD for that substance only.

Among the total sample, 75.4% of participants (n = 1503) reported any substance use in the past 12 months. Among those reporting past-year substance use, almost half (47.5%) met criteria for any SUD (tobacco, alcohol, or drug) in which 29.1% had a single SUD and 18.4% had 2 or more SUDs (Table 2). The prevalence of multiple SUDs (including SUD of the respective substance used) was largest among participants reporting other drug use (90.0%), followed by those reporting heroin use (78.2%) and cocaine/crack use (63.9%).

Tobacco use disorder was the most common comorbid SUD; its prevalence ranged from 53.1% among participants with alcohol use disorder to 72.3% among participants with heroin use disorder (Table S2 in the supplementary material). The prevalence of alcohol use disorder was highest among participants with cocaine use disorder (53.9%), followed by those with cannabis (43.4%), heroin (43.1%), and prescription opioid use disorder (41.7%). Cannabis use disorder was prevalent in approximately a quarter or less of participants with SUD for cocaine (26.5%), alcohol (22.9%), opioids (prescription opioid or heroin; 20.2%), or tobacco (17.3%). Over half of participants with opioid (prescription opioid or heroin) use disorder (56.4%) had an additional comorbid prescription drug (stimulant or sedative) use disorder.

3.3. Correlates of single and multiple past-year SUDs

In unadjusted analyses among the total sample, individuals who were male, white, less educated, disabled, or not married had increased odds of having a single SUD (Table S3 in the supplementary material). With the exception of being white, similar factors were associated with having multiple SUDs (2 or 3+). In addition, individuals who were unemployed had higher odds of multiple SUDs (2 or 3+); ages 26–34 were associated with increased odds of 3 or more SUDs only.

In adjusted analyses among the total sample, the association between having single or multiple SUDs and being male, less educated, or disabled retained statistical significance (Table 3). The association between having 2 SUDs and being unemployed was attenuated in the adjusted model. Additionally, the association between having 3 or more SUDs and being ages 26–34 was attenuated in the adjusted model. Similar factors were associated with single and multiple SUDs among participants reporting past-year substance use (Tables S4 and S5 in the supplementary material).

Compared to having a single SUD, increased odds of having multiple SUDs (2 or more) were associated with being male, less educated, and unemployed (Table 3).

Table 1
Prevalence of single and multiple past-year DSM-5 substance use disorders among adults in primary care (n = 1993[a]).

Past-year SUD, %	Any SUD % (95% CI)	Single SUD- for the substance in row % (95% CI)	Multiple SUDs- including the substance in row % (95% CI)	Proportion with multiple SUDs[b] %
Tobacco	25.3 (23.4–27.2)	13.7 (12.3–15.3)	11.6 (10.3–13.1)	45.8
Alcohol	13.8 (12.4–15.4)	5.0 (4.1–6.1)	**8.8 (7.6–10.1)**	63.6
Cannabis	7.3 (6.2–8.5)	1.9 (1.4–2.6)	**5.4 (4.5–6.4)**	73.8
Cocaine or crack	5.1 (4.2–6.2)	0.5 (0.3–0.9)	**4.6 (3.8–5.6)**	90.2
Methamphetamine	0.5 (0.2–0.9)	0.1 (0.01–0.3)	0.4 (0.2–0.8)	88.9
Rx stimulants/amphetamines	0.4 (0.2–0.8)	0.2 (0.1–0.4)	0.3 (0.1–0.6)	62.5
Hallucinogens	0.5 (0.2–0.9)	0	**0.5 (0.2–0.9)**	100
Inhalants	0.3 (0.1–0.6)	0	**0.3 (0.1–0.6)**	100
Heroin	3.3 (2.6–4.1)	0.2 (0.1–0.5)	**3.1 (2.4–3.9)**	93.8
Rx opioids	2.4 (1.8–3.2)	0.3 (0.1–0.7)	**2.1 (1.6–2.8)**	87.5
Sedatives	1.4 (1.0–2.0)	0.2 (0.1–0.4)	**1.3 (0.9–1.8)**	89.3
Other nonspecific drugs	0.5 (0.2–0.9)	0	**0.5 (0.2–0.9)**	100
Number of SUDs among the sample				
0	64.2 (62.0 – 66.3)	.....	.....	.....
1	22.0 (20.2–23.8)	.....	.....	.....
2	7.4 (6.4–8.7)	.....	.....	.....
3–12	6.4 (5.4–7.6)	.....	.....	.....

Boldface: prevalence significantly differed from prevalence of single SUD ($p < 0.05$).
CI: confidence interval; Rx: prescription; SUD: substance use disorder.
[a] n = 7 participants were excluded due to missing substance use or SUD data.
[b] The proportion of participants with multiple SUDs among those who have a SUD for the substance in that row.

Table 2
Prevalence of single and multiple DSM-5 substance use disorders among adults in primary care who reported substance use in the past year (n = 1503).

Past-year substance users	Sample size n	Any SUD among past-year users % (95% CI)	Single SUD among users – for the substance in row % (95% CI)	Multiple SUDs among users – including the substance in row % (95% CI)
Tobacco	878	57.4 (54.1–60.6)	31.1 (28.1–34.2)	26.3 (23.5–29.3)
Alcohol	1232	22.3 (20.1–24.7)	8.1 (6.7–9.8)	**14.2 (12.4–16.3)**
Cannabis	413	35.1 (30.7–39.8)	9.2 (6.8–12.4)	**25.9 (21.9–30.3)**
Cocaine or crack[a]	144	70.8 (62.9–77.6)	6.9 (3.8–12.3)	**63.9 (55.8–71.3)**
Methamphetamines[a]	14	64.3 (38.8–83.7)	7.1 (1.3–31.5)	**57.1 (32.6–78.6)**
Rx stimulants/amphetamines[a]	23	34.8 (18.8–55.1)	13.0 (4.5–32.1)	21.7 (9.7–41.9)
Hallucinogens[a]	37	24.3 (13.4–40.1)	0	**24.3 (13.4–40.1)**
Inhalants[a]	29	17.2 (7.6–34.5)	0	**17.2 (7.6–34.5)**
Heroin[a]	78	83.3 (73.5–90.0)	5.1 (2.0–12.5)	**78.2 (67.8–85.9)**
Rx opioids[a]	96	50.0 (40.2–59.8)	6.3 (2.9–13.0)	**43.8 (34.3–53.7)**
Sedatives[a]	82	34.1 (24.8–44.9)	3.7 (1.3–10.2)	**30.5 (21.6–41.1)**
Other nonspecific drugs[a]	10	90.0 (59.6–98.2)	0	**90.0 (59.6–98.2)**
Number of SUDs among participants reporting past-year substance use	1503			
0	.....	52.5 (50.0–55.0)	.....	.....
1	.....	29.1 (26.9–31.5)	.....	.....
2	.....	9.8 (8.4–11.5)	.....	.....
3–12	.....	8.5 (7.2–10.0)	.....	.....

Boldface: prevalence significantly differed from prevalence of single SUD ($p < 0.05$).
CI: confidence interval; Rx: prescription; SUD: substance use disorder.
[a] The estimates are based on a small sample size and should be interpreted with caution.

3.4. Pattern and adjusted odds ratios of multiple past-year SUDs by severity level

Among participants reporting multiple SUDs, a higher proportion met criteria for moderate/severe vs. mild SUD for tobacco (62.3% vs. 37.7%), alcohol (61.1% vs. 38.9%), cannabis (58.9% vs. 41.1%), cocaine (87.0% vs. 13.0%), heroin (88.5% vs. 11.5%), and prescription opioids (71.4% vs. 28.6%; Table 4). A higher proportion of participants with a single SUD for tobacco, alcohol, and cannabis use met mild SUD criteria. Adjusted logistic regression indicated that multiple SUDs were associated with greater odds of moderate/severe (vs. mild) tobacco or alcohol use disorder.

Table 3
Adjusted odds ratios of single and multiple past-year DSM-5 substance use disorders in the total sample (n = 1989).

Past-year SUD Adjusted odds ratio (AOR)	n	1 SUD vs. none AOR (95% CI)	2 SUDs vs. none AOR (95% CI)	3+ SUDs vs. none AOR (95% CI)	> 1 SUDs vs. 1 SUD AOR (95% CI)
Sex					
Male	872	1.00	1.00	1.00	1.00
Female	1117	**0.57 (0.45–0.72)**	**0.44 (0.30–0.63)**	**0.31 (0.21–0.48)**	**0.66 (0.48–0.93)**
Age in years					
18–25	222	1.00	1.00	1.00	1.00
26–34	297	0.85 (0.54–1.33)	1.68 (0.77–3.65)	1.69 (0.78–3.63)	**2.02 (1.06–3.83)**
35–49	526	0.72 (0.47–1.10)	1.16 (0.54–2.49)	0.78 (0.36–1.69)	1.35 (0.72 − 2.54)
50 +	944	**0.59 (0.38–0.91)**	0.92 (0.43–1.98)	**0.37 (0.17–0.84)**	1.05 (0.55 − 1.99)
Race/ethnicity					
White, non-Hispanic	574	1.00	1.00	1.00	1.00
Black/African American, non-Hispanic	1055	**0.65 (0.50–0.85)**	0.82 (0.52–1.30)	0.62 (0.37–1.02)	1.11 (0.75–1.64)
Hispanic	230	**0.52 (0.33–0.81)**	0.68 (0.34–1.36)	0.76 (0.38–1.54)	1.42 (0.78–2.59)
Other/unknown	130	**0.29 (0.16–0.53)**	0.68 (0.30–1.52)	0.41 (0.16–1.05)	1.90 (0.85–4.22)
Education					
Less than high school	379	1.00	1.00	1.00	1.00
High school/GED	577	0.87 (0.62–1.22)	0.65 (0.41–1.03)	0.91 (0.55–1.51)	0.88 (0.58–1.34)
Some college/associate degree	647	1.06 (0.76–1.47)	**0.58 (0.35–0.94)**	0.67 (0.39–1.17)	**0.58 (0.38–0.91)**
Bachelor/graduate degree	386	**0.50 (0.33–0.76)**	**0.28 (0.15–0.54)**	**0.20 (0.09–0.44)**	**0.49 (0.27–0.89)**
Employment					
Employed	707	1.00	1.00	1.00	1.00
Unemployed	418	1.18 (0.85–1.63)	1.44 (0.86–2.41)	**3.37 (1.92–5.92)**	**1.84 (1.18–2.89)**
Disabled	470	**1.72 (1.25–2.37)**	**2.18 (1.31–3.62)**	**3.11 (1.68–5.77)**	1.47 (0.93–2.32)
Other[a]	394	0.91 (0.65–1.28)	1.35 (0.77–2.36)	1.79 (0.90–3.56)	1.67 (1.00–2.78)
Marital Status					
Married/cohabited	522	1.00	1.00	1.00	1.00
Separated/divorced/widowed	557	1.35 (0.98–1.86)	1.28 (0.74–2.23)	1.08 (0.57–2.06)	0.89 (0.55–1.44)
Never married	910	1.23 (0.91–1.67)	**1.80 (1.09–2.96)**	**1.79 (1.02–3.12)**	1.45 (0.94–2.26)

Note: The multinomial logistic regression model included all variables listed in the first column and controlled for study site (state); n = 4 participants were excluded due to missing demographic information.
Boldface: AOR significantly differed from reference category ($p < 0.05$).
AOR: adjusted odds ratio; CI: confidence interval; GED: general educational development; SUD: substance use disorder.
[a] Other employment included retired, student, keeping house, or other/not specified.

Table 4
Pattern of past-year DSM-5 substance use disorders by severity level and adjusted odds ratios of moderate/severe SUD: stratified by substance.

Past-year SUD	Single SUD			Multiple SUDs			Moderate/Severe vs. Mild[a]
	Overall	Mild[c]	Moderate/Severe[c]	Overall	Mild[c]	Moderate/Severe[c]	
Adults with SUD	n	Row% (95% CI)	Row% (95% CI)	n	Row% (95% CI)	Row% (95% CI)	AOR (95% CI)
Tobacco use disorder	273	51.6 (45.7–57.5)	48.4 (42.5–54.3)	231	37.7 (31.7–44.1)	62.3 (55.9–68.3)	**1.59 (1.10–2.31)**
Alcohol use disorder	100	67.0 (57.3–75.4)	33.0 (24.6–42.7)	175	38.9 (31.9–46.2)	61.1 (53.8–68.1)	**3.70 (2.13–6.42)**
Cannabis use disorder[b]	38	52.6 (37.3–67.5)	47.4 (32.5–62.7)	107	41.1 (32.3–50.6)	58.9 (49.4–67.7)	1.56 (0.73–3.34)
Cocaine use disorder[b]	10	30.0 (10.8–60.3)	70.0 (39.7–89.2)	92	13.0 (7.6–21.4)	87.0 (78.6–92.4)	2.36 (0.50–11.04)
Heroin use disorder[b]	4	25.0 (4.6–69.9)	75.0 (30.1–95.4)	61	11.5 (5.7–21.8)	88.5 (78.2–94.3)	.....
Rx opioid use disorder[b]	6	33.3 (9.7–70.0)	66.7 (30.0–90.3)	42	28.6 (17.2–43.6)	71.4 (56.4–82.8)	.....

Note: Estimates for sedative, methamphetamine, Rx stimulant, hallucinogen, inhalant, or other nonspecific drug use disorders were not included due to small sample size.
AOR: adjusted odds ratio; CI: confidence interval; Rx: prescription; SUD: substance use disorder.
[a] Adjusted odds ratios of substance use disorder severity (for the substance in that row) and multiple SUDs; each logistic regression model was controlled for sex, age groups, and race/ethnicity.
[b] The estimates are based on a small sample size and should be interpreted with caution.
[c] Mild: 2–3 DSM-5 SUD criteria; Moderate/Severe: ≥4 DSM-5 SUD criteria.

3.5. Latent class analysis

LCA model fit indices suggested that the better fitting model was one consisting of three classes. That is, the three-class model had the highest entropy estimate and generally lower AIC and BIC values (Table S6 in the supplementary material).

The three classes were differentiated by participants' different patterns in the prevalence of SUDs (Fig. 1A and B, Table S7 in the supplementary material). Class 1 (Low SUD; 83.7% of the total sample; 81.6% of past-year substance users) specified a group with a low prevalence of all SUDs (0.4–15.9% in the total sample; 0.7–24.4% among substance users). Class 2 (Medium SUD; 12.0% of the total sample; 12.9% of past-year substance users) exhibited a high prevalence of tobacco use disorder (72.7% in the sample; 73.7% among substance users), a moderate prevalence of alcohol (55.8% in the sample; 59.2% among substance users), cannabis (36.1% in the sample; 40.0% among substance users), and cocaine (20.1% in the sample; 22.9% among substance users) use disorder, and a low prevalence of opioid (< 1% in total sample/substance users) and other drug use disorder (9.7% in the total sample; 11.3% among substance users). Class 3 (High SUD; 4.3% of the total sample; 5.6% of past-year substance users) was characterized by a high prevalence of SUD for opioids (96.0% in total sample/substance users), tobacco (75.3% in total sample/substance users), and cocaine (51.9% in the total sample; 53.3% among substance users) and a moderate prevalence of other SUDs (23.0–45.3% in the total sample; 23.6–46.2% among substance users).

In the total sample, being male, younger (18–34 years), having lower education (less than high school), and indicating unemployment, disability, and other employment were associated with increased odds of being in the Medium SUD class compared to the Low SUD class (Table 5). Similar factors were associated with the High SUD class, including white race. Overall, correlates of LCA-defined classes were similar when considering the subsample of participants who reported past-year substance use (Table 5).

4. Discussion

To our knowledge, this study represents the first comprehensive examination of the prevalence and correlates of multiple SUDs based on DSM-5 criteria in a primary care sample. The main overall finding from this study was that the majority of primary care patients who had a past-year SUD for most substances in this sample also met DSM-5 criteria for one or more additional SUDs. Results from this study also provide information on the pattern of multiple SUDs in the sample and suggest the presence of heterogeneous subgroups of primary care patients with SUDs. Given the critical opportunity of primary care settings to identify individuals with SUDs, these data shed light on the treatment needs and potential barriers to successful screening, brief intervention, and referral to treatment outcomes for this patient population.

Our findings are consistent with national survey data showing that the majority of adults who met criteria for a drug use disorder also met criteria for additional SUDs based on DSM-4 (Grant and Pickering, 1996; Stinson et al., 2005) or DSM-5 criteria (McCabe et al., 2017). Our study, however, compared to data from the NESARC (McCabe et al., 2017), found a relatively higher prevalence of multiple SUDs among adults meeting SUD criteria for several drug classes including cannabis (73.8% vs. 63.5%), prescription opioids (87.5% vs. 56.8%), sedatives (89.3% vs. 73.7%), cocaine (90.2% vs. 86.0%), and heroin (93.8% vs. 77.1%). The prevalence of additional SUDs among those with alcohol use disorder, especially, was higher in our study (63.6%) compared to the NESARC (15.0%; McCabe et al., 2017). One important difference is that our study included tobacco use disorder, which was the most prevalent comorbid SUD and may have accounted for the relatively higher prevalence of multiple SUDs. However, other studies assessing the prevalence of SUDs in primary care samples generally report higher rates than those reported from national samples (Pilowsky and Wu, 2012; Wu et al., 2017). It should be noted that methodological differences including setting, interview mode, and contextual effects make comparisons difficult between national surveys and clinical trials. Further, our sample size of various drug users was relatively small, which affects the estimate of prevalence and generalizability. Nevertheless, the high prevalence of substance use and SUD in primary care settings highlights the need to better integrate screening and intervention within this setting as an approach to reduce unmet treatment need.

Our study found that being younger, being white, less education, unemployment, and disability were associated with increased odds of having multiple past-year SUDs among the total sample or past-year substance users. Despite a relatively larger distribution of females, older adults, and blacks in our sample, these findings are largely consistent with correlates of multiple SUDs in national samples of adults (McCabe and West, 2017; McCabe et al., 2017; Redonnet et al., 2012). Early alcohol and drug prevention programs are needed among these demographic subgroups to reduce the morbidity and mortality associated with multiple substance use and SUDs. Future research should investigate the causal mechanisms underlying multiple SUDs among these subgroups in order to develop more targeted prevention efforts and to understand potential barriers to treatment. Previous work has also shown that the odds of polysubstance use/multiple SUDs are greater among those with comorbid psychiatric disorders including anxiety and mood disorders (Connor et al., 2014; McCabe and West, 2017; McCabe et al., 2017; Midanik et al., 2007). Although our sample is limited by

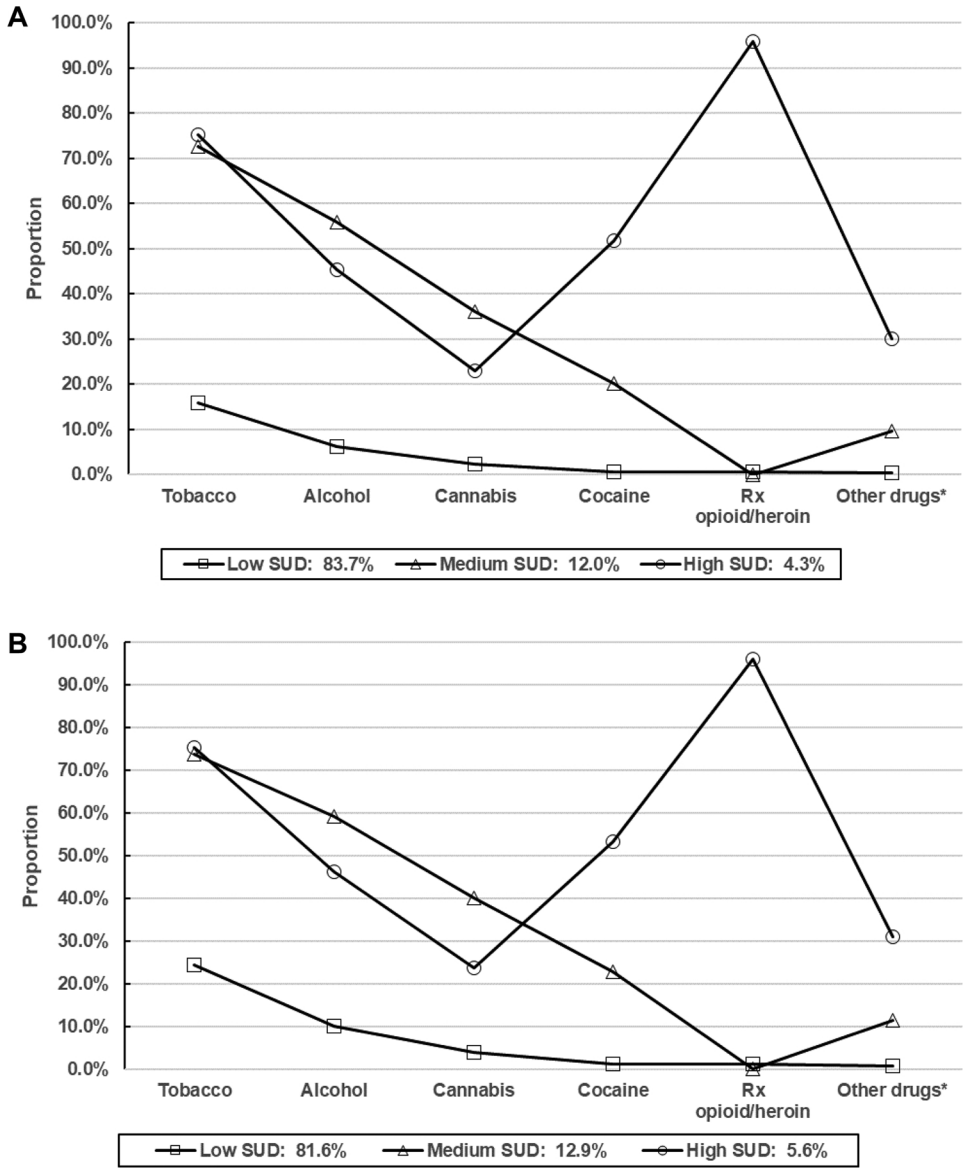

Fig. 1. Patterns of substance use disorders (SUDs) by LCA-defined class in the total sample (A; n = 1993) and among participants reporting past-year substance use (B; n = 1503). * Other drugs included sedatives, methamphetamine, Rx stimulants/amphetamines, hallucinogens, inhalants, and other nonspecific drugs.

the lack of mental health disorder data, comorbid SUDs and mental health disorders have been shown to be associated with greater SUD severity and worse treatment outcome (Compton et al., 2003; Fenton et al., 2012; Grant et al., 2016). As a result, more research is needed on how to better integrate mental health and substance use screening, especially in primary care settings. A more comprehensive assessment may be useful to guide the most effective behavioral and pharmacological treatment approaches.

Greater severity of tobacco or alcohol use disorder was associated with greater odds of meeting criteria for another (non-tobacco, non-alcohol) SUD. These findings provide evidence via DSM-5 criteria to support previous work suggesting that multiple SUDs are associated with more substance-specific related problems (Midanik et al., 2007). Underlying mechanisms may include a bidirectional association between use of one substance and another due to cross reinforcement, cross tolerance, or management of withdrawal and craving symptoms (Magee et al., 2016). Primary care settings may already screen for tobacco use and/or problem alcohol use based on recommendations from the U.S. Preventive Services Task Force (USPSTF) supporting the efficacy of such screening (Moyer, 2013; Siu and U.S. Preventive Services Task Force, 2015). However, screening for illicit or nonmedical drug use has yet to meet the bar of evidence for efficacy in primary care and thus has not been recommended by the USPSTF (Tai et al., 2012; USPSTF, 2014). Therefore, a useful first step to identify other SUDs in primary care based on this study's findings would be to recommend subsequent screening/assessment for illicit/nonmedical drug use among patients who screen positive for tobacco or alcohol use.

The LCA-defined classes of multiple SUDs reported here are in line with prior research in the general population (Connor et al., 2014) and suggest important differences in the patterns of SUD comorbidity which carry clinical implications. Notably, the High SUD class (4.3% of the total sample; 5.6% among patients reporting past-year substance use), who exhibited a high prevalence of past-year opioid use disorder, also had a relatively high prevalence of SUD for cocaine and other illicit drugs. This pattern of comorbid SUDs is particularly concerning given the high prevalence and increased trend of opioid overdose deaths involving other substances, especially cocaine (Kandel et al., 2017; McCall Jones et al., 2017). Hence, compared to the LCA-defined class characterized by SUDs predominantly for tobacco, alcohol, and cannabis, the short-term harms of the High SUD class are likely to be more

Table 5
Adjusted odds ratios of LCA-defined subtypes of substance use disorders in the total sample and among past-year substance users.

	Model 1: Total sample (n = 1989)		Model 2: Past-year substance users (n = 1501)	
LCA-defined classes Adjusted odds ratio (AOR)	Medium SUD vs. low SUD AOR (95% CI)	High SUD vs. low SUD AOR (95% CI)	Medium SUD vs. low SUD AOR (95% CI)	High SUD vs. low SUD
Sex				
Male	1.00	1.00	1.00	1.00
Female	**0.45 (0.32–0.63)**	**0.37 (0.22–0.62)**	**0.52 (0.37–0.73)**	**0.43 (0.26–0.72)**
Age in years				
18–34	1.00	1.00	1.00	1.00
35–49	**0.58 (0.37–0.91)**	1.27 (0.62–2.57)	0.65 (0.41–1.03)	1.40 (0.69–2.86)
50 +	**0.40 (0.25–0.63)**	0.76 (0.36–1.60)	**0.50 (0.31–0.80)**	0.93 (0.44–1.97)
Race/ethnicity				
White, non-Hispanic	1.00	1.00	1.00	1.00
Black/African American, non-Hispanic	1.15 (0.77–1.72)	**0.50 (0.28–0.89)**	1.29 (0.86–1.93)	**0.53 (0.29–0.95)**
Hispanic	0.90 (0.49–1.63)	0.98 (0.43–2.19)	1.00 (0.55–1.83)	1.03 (0.46–2.34)
Other/unknown	0.85 (0.41–1.75)	0.65 (0.23–1.83)	1.06 (0.51–2.24)	0.83 (0.29–2.40)
Education				
Less than high school	1.00	1.00	1.00	1.00
High school/GED	0.69 (0.46–1.05)	0.96 (0.55–1.68)	0.68 (0.44–1.05)	0.93 (0.53–1.63)
Some college/associate degree/bachelor/graduate degree[a]	**0.56 (0.38–0.85)**	**0.32 (0.16–0.61)**	**0.55 (0.36–0.83)**	**0.30 (0.15–0.59)**
Employment				
Employed	1.00	1.00	1.00	1.00
Unemployed	**1.81 (1.16–2.84)**	**2.87 (1.47–5.61)**	**1.84 (1.16–2.90)**	**2.85 (1.44–5.62)**
Disabled	**2.29 (1.45–3.63)**	**2.08 (1.01–4.29)**	**2.38 (1.49–3.81)**	**2.20 (1.06–4.57)**
Other[b]	**1.67 (1.03–2.71)**	1.08 (0.42–2.80)	**1.85 (1.13–3.02)**	1.17 (0.45–3.06)
Marital Status				
Married/cohabited	1.00	1.00	1.00	1.00
Separated/divorced/widowed	0.94 (0.57–1.56)	1.50 (0.70–3.21)	0.85 (0.51–1.42)	1.39 (0.64–3.00)
Never married	1.51 (0.98–2.33)	1.71 (0.84–3.49)	1.37 (0.88–2.13)	1.63 (0.79–3.33)

Note: Both multinomial logistic regression models included all variables listed in the first column and controlled for study site (state); n = 4 participants in the total sample and n = 2 participants among past-year substance users were excluded due to missing demographic information.
Boldface: AOR significantly differed from reference category ($p < 0.05$).
AOR: adjusted odds ratio; CI: confidence interval; GED: general educational development; LCA: latent class analysis; SUD: substance use disorder.
[a] The groups of some college/associate degree and bachelor/graduate degree were combined due to small sample size.
[b] Other employment included retired, student, keeping house, or other/not specified.

acute and would suggest a different treatment approach from the primary care physician. Demographic characteristics were also associated with LCA-defined class membership. Specifically, male sex and lower education were positively associated with both multiple SUD classes, which is consistent with prior studies of polysubstance use (Bohnert et al., 2014; Midanik et al., 2007). Moreover, blacks were less likely than whites to be in the High SUD class, which is consistent with findings for opioid use disorder among the general population (Saha et al., 2016).

Going forward, research on how to best integrate multiple substance components into primary care-based screening assessments and interventions for problem substance use is needed. Research is also needed to develop more effective intervention strategies for primary care patients screening positive for multiple SUDs. One remaining question is whether multiple SUDs are most effectively treated concurrently or individually and sequentially. For instance, some studies demonstrate that concurrent treatment for nicotine dependence may enhance treatment outcomes for drug or alcohol use (Bobo et al., 1998; Tsoh et al., 2011; Winhusen et al., 2014); however, some evidence suggests that drinking outcomes among alcohol dependent patients may be adversely affected by concurrent compared to delayed smoking intervention (Fu et al., 2008; Joseph et al., 2004). Additional prospective randomized trials are needed to determine the optimal timing and prioritization of treatment for multiple SUDs. Moreover, it also remains to be determined whether certain behavioral and pharmacological treatments are more effective for some combinations of co-occurring SUDs vs. others.

The findings from this study should be considered in the context of a few methodological limitations. First, the cross-sectional nature of this study precludes determinations of causality and temporality. There is a need, however, to better understand the temporal nature of polysubstance behaviors given that trajectories and adverse consequences have been shown to differ as a function of whether polysubstance use occurs concurrently or simultaneously (McCabe et al., 2006; SAMHSA, 2014). Second, the study used self-report to measure substance use in the past year, which could have been subject to recall bias and/or underreporting. Despite these concerns, previous research has demonstrated good accuracy of self-report measures of alcohol and drug use (Del Boca and Darkes, 2003; Hser, 1997). Third, the sample size for some SUDs was small despite the overall large sample size of the study. Thus, these results should be interpreted with caution, and future studies should consider incorporating multiple SUD subgroups into the study design. Fourth, like all existing clinical trials of substance use, the study sample was not representative of the population from which the sample was drawn (i.e., adult primary care patients). The sample was based on participants' voluntary participation, and it was constrained by the locations and the number of participating sites (i.e., five primary care clinics in the Eastern U.S). Thus, selection bias may have affected the generalizability. Nevertheless, the study contained a relatively large sample with high patient diversity that was recruited from multiple regions. Finally, patients were not asked to identify the substance(s) they were concerned or most concerned about. In terms of guiding treatment approaches for multiple SUDs, this information could be important for better engaging patients in committing to behavior change or for assisting providers with sequencing interventions.

In conclusion, the present study suggests that multiple SUDs are the norm rather than the exception among primary care patients with SUD. As a result, multiple SUDs are a treatment need that should be screened and assessed for in order to better direct intervention strategies to potentially increase treatment access, engagement, and improve outcomes. However, it should be noted that the treatment and management of multiple SUDs and other associated comorbidities may be out

of the scope of expertise for many primary care physicians. This argues for the need of additional approaches to address SUD in primary care, such as the development of coordinated care models and linkage services to improve access to specialty care and follow-up of clinical outcomes.

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Contributors

William S. John and Li-Tzy Wu contributed to the study design and analysis. William S. John conducted the literature review and drafted the manuscripts. He Zhu conducted data analyses under the supervision and guidance of Li-Tzy Wu. All authors contributed to revisions and interpretations of the findings that resulted in the final manuscript. All authors have contributed to and approved of the final manuscript submission.

Conflicts of interest

Li-Tzy Wu has received research funding from Alkermes Inc. Paolo Mannelli has received consultation fees from Guidepoint Global and research funding from The Laura and John Arnold Foundation, Orexo, and Alkermes Inc., and served on Scientific Advisory Boards for Alkermes. The other authors have no conflicts of interest to disclose.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.drugalcdep.2018.01.035.

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