



Associations between prescription stimulant use as prescribed, nonmedical use, and illicit stimulant use among adults evaluated for substance use treatment, 2017-2021

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ABSTRACT

Background: Limited data exist on risk factors for illicit stimulant use, including associations between prescription stimulant use/nonmedical use (NMU) and illicit stimulant use.

Methods: We used 2017–2021 data from adults assessed for substance use disorder (SUD) treatment using the National Addictions Vigilance Intervention and Prevention Program Addiction Severity Index-Multimedia Version® tool. Multivariable Poisson regression models analyzed associations between past 30-day prescription stimulant use as prescribed or NMU and past 30-day illicit stimulant use. Separate models examined past 30-day illicit stimulant, methamphetamine, and cocaine use. We explored problem severity across seven biopsychosocial domains (e.g., drug, psychiatric, family) by past 30-day prescription stimulant use/NMU and illicit stimulant use.

Results: Among 218,981 assessments, 1.8% reported prescription stimulant NMU; 1.6% reported use as prescribed. Past 30-day prescription stimulant NMU (vs. no use) was associated with past 30-day illicit stimulant use (adjusted prevalence ratio [aPR] [95% CI]: 2.67 [2.59, 2.75]), methamphetamine use (aPR: 2.81 [2.71, 2.92]), and cocaine use (aPR: 3.53 [3.33, 3.74]). Prescription stimulant use as prescribed (vs. no use) was associated with lower prevalence of past 30-day illicit stimulant use. Assessments reporting prescription stimulant NMU (vs. no use, or use as prescribed) appeared more likely to have moderate-to-extreme problem scores across biopsychosocial domains, indicating greater need for treatment or assistance. Assessments reporting prescription stimulant use as prescribed or NMU frequently reported opioids, alcohol, or other substances as their primary substance problem.

Conclusions: Adults using illicit stimulants/nonmedically using prescription stimulants may benefit from care addressing polysubstance use, mental health, social, and recovery support services.

1. Introduction

Cocaine and amphetamine-type stimulants such as methamphetamine are highly addictive and potent central nervous system stimulants (Ciccarone, 2011). Use of these substances is associated with a range of physical and psychological harms, including mental disorders, cognitive and neurologic deficits, cardiovascular and renal dysfunction, infectious disease transmission, fatal and nonfatal overdose, and increased mortality (Barr et al., 2006; Butler et al., 2017;

Cheng et al., 2010; Cunningham et al., 2015; Darke et al., 2017a, 2017b; Hedegaard et al., 2021; Hoots et al., 2020; Liu et al., 2020; Strathdee and Stockman, 2010; Vivolo-Kantor et al., 2020; Wang et al., 2017). Prescription stimulants, prescribed for conditions such as Attention-Deficit/Hyperactivity Disorder (ADHD), may also be used nonmedically, which is associated with negative health consequences (Benson et al., 2015; Compton et al., 2018; Han et al., 2017b; Hedegaard et al., 2021; Holt et al., 2022).

Abbreviations: ADHD, Attention-Deficit/Hyperactivity Disorders; aPR, adjusted prevalence ratio; ASI-MV, Addiction Severity Index-Multimedia Version; CI, confidence interval; GEE, generalized estimating equations; NAVIPPRO, National Addictions Vigilance Intervention and Prevention Program; NMU, nonmedical use; NSDUH, National Survey on Drug Use and Health; PROSPER, Promoting School-Community-University Partnerships to Enhance Resilience; SUD, substance use disorder; FDA, U.S. Food and Drug Administration.

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Globally, the prevalence of stimulant use, in particular cocaine and methamphetamine, has increased in the past decade. An estimated 21.5 million people aged 15–64 years used cocaine in 2020 globally, with the highest prevalences in Oceania (2.7%; Australia and New Zealand: 3.6%), North and South America (2.0% and 1.6%, respectively), and Western/Central Europe (1.4%). North America had the largest absolute number of people using cocaine in the past year in 2020 (6.4 million). An estimated thirty-four million people aged 15–64 years used amphetamines (amphetamine, methamphetamine, or pharmaceutical stimulants used nonmedically) in 2020 globally. Past-year amphetamine use prevalence among people aged 15–64 years in 2020 was highest in North America (3.9% [increasing from 1.3% in 2010], or 12.5 million individuals), followed by Australia/New Zealand (1.3%) (UNODC, 2022).

In the U.S., stimulants are increasingly contributing to the drug overdose crisis. U.S. stimulant-involved overdose deaths increased sharply from 2012 to 2020; cocaine-involved overdose death rates more than quadrupled, and psychostimulant-involved (primarily methamphetamine) overdose death rates increased even faster (Hedegaard et al., 2021). The increases continued in 2021 (Spencer et al., 2022). Additionally, nonfatal psychostimulant-involved overdoses have increased in the U.S. (Hoots et al., 2020; Liu et al., 2020; Vivolo-Kantor et al., 2020). Importantly, these increases in morbidity and mortality occurred concurrently with increasing availability of illicit stimulants. In recent years, seizures of amphetamine-type stimulants, particularly methamphetamine, have increased in the U.S. (DEA, 2021) and globally, with the U.S. being the top country for methamphetamine seizures in 2020 (UNODC, 2022). Cocaine seizures have also grown globally, including large increases in North American cocaine seizures from 2015–2020 (UNODC, 2022). U.S. prescription stimulant dispensing has also risen (Board et al., 2020), offering more potential opportunities for diversion and nonmedical use (NMU) (DEA, 2021).

As prescription stimulant dispensing grows against the backdrop of high availability of illicit stimulants and rising health harms from stimulants, it is increasingly important to understand the relationship between prescription stimulant use or NMU and illicit stimulant use. Research indicates that illicit stimulant use is associated with NMU of prescription stimulants. U.S. adults reporting prescription stimulant NMU in the past year had nearly twice the odds of past-year methamphetamine use (Jones et al., 2020b), and more than four times the odds of past-year cocaine use (Mustaquim et al., 2021), compared to adults reporting no NMU of prescription stimulants. Thus, identifying predictors of illicit stimulant use, especially modifiable risk factors such as prescription stimulant use or NMU, is vital to inform prevention and response efforts aimed at addressing stimulant overdoses. In addition, because polysubstance use is common among people who use drugs, and most stimulant-involved overdose deaths involve multiple substances (CDC, 2023; UNODC, 2022)—particularly opioids (Kariisa et al., 2021)—it is important to evaluate use of other substances, in addition to illicit stimulant use, among people who use prescription stimulants.

Limited research has examined these associations among U.S. adults seeking treatment for substance use disorders (SUDs), as most existing research comes from U.S. population-based community surveys. Adults being evaluated for SUD treatment represent an important population for tailored interventions to reduce overdose morbidity and mortality. As this population has a touchpoint with the health system, understanding their needs, especially polysubstance, mental health, and social services needs, can help strengthen the care and services provided to these populations. Additionally, people evaluated for SUD treatment may have progressed further in their substance use trajectory and have higher risks of negative health outcomes (e.g., overdose, death, infectious disease complications) compared to individuals earlier in their substance use trajectory.

Using data from U.S. adults evaluated for SUD treatment between 2017 and 2021, this paper first examines the association between prescription stimulant use as prescribed/NMU and illicit stimulant use; second, explores the severity of challenges across seven biopsychosocial

domains (medical, employment, legal, family, psychiatric, alcohol, and drug) by prescription and illicit stimulant use history; and third, examines primary substance use problem by prescription stimulant use history.

2. Methods

This cross-sectional study uses real-world data from adults evaluated for SUD treatment at facilities that use the Addiction Severity Index-Multimedia Version (ASI-MV) assessment tool; all adults (aged ≥ 18 years) who completed the ASI-MV at these facilities between January 2017 and December 2021 were included. Data are from the National Addictions Vigilance Intervention and Prevention Program (NAVIPP) dataset (Butler et al., 2008; Kacha-Ochana et al., 2022). Data contained clinical assessments from 699 sites in 44 states and the District of Columbia. The ASI-MV network is comprised of sites receiving public or private funding (or both); it represents a smaller network of sites compared to the National Survey of Substance Abuse Treatment Services (site-level data on all known U.S. public and private substance use treatment facilities) and fewer annual assessments than the Treatment Episode Data Set Admissions (assessment-level data on substance use treatment admissions from state agency [primarily publicly funded] data systems). Analyses were restricted to assessments with complete information on the exposure variable, all model covariates, and at least one outcome variable. We included all assessments in analyses (14.2% were repeat assessments); thus, most analyses are interpreted at the ‘assessment’ level. In contrast, the ‘individual’ was the unit of analysis for prevalence ratio analyses, which accounted for repeat assessments using Poisson models. The main exposure variable in this analysis, prescription stimulant use in the past 30 days, had three mutually exclusive categories: no use (referent), use as prescribed, and NMU. Prescription stimulant NMU was any use not considered “use as prescribed.” “Use as prescribed” was defined as obtaining the stimulant medication only from one’s own prescription, no use of the medication via an alternate route of administration, and no reported days of use in a manner not as prescribed.

The ASI-MV is a validated self-administered, computerized, structured clinical assessment tool which collects information on substance use patterns and demographic information among individuals assessed for SUD treatment (Butler et al., 2001). The ASI-MV collects detailed information on lifetime and past 30-day use of tobacco, alcohol, illicit drugs, and use and NMU of prescription drugs. The ASI-MV also assesses seven biopsychosocial domains (medical, employment, legal, family, psychiatric, alcohol, and drug). The ASI-MV domains cover a broad range of areas related to substance use (two domains assess substance use directly; the others may affect, or, alternatively, be affected by, substance use) (McLellan et al., 1992, 1980). The domains are described further in the Supplementary Table (Butler et al., 2001). A rating for each domain indicates the severity of the problem and the need for treatment or assistance. Moderate to extreme problem is defined as a score of 4–9 on a scale of 0–9, suggesting the individual probably needs treatment or assistance in that area. While these designations (i.e., categorization of scores in each domain) are part of the validated clinical assessment, a ‘moderate to extreme problem’ is not a diagnosis of a specific condition; rather, the responses reflect a probable need for more support in that area, which the health care provider can follow up on using clinical judgment for each patient.

We first calculated trends in past 30-day illicit stimulant use (any use; includes methamphetamine, crack/cocaine, ecstasy, and/or bath salts), methamphetamine use, and crack/cocaine (hereafter, ‘cocaine’) use over the study period using Cochran-Armitage Trend Tests. Next, we calculated frequencies and column percentages of sociodemographic and other risk factors by prescription stimulant use status (no use, use as prescribed, or NMU in the past 30 days) and used χ^2 tests to assess statistically significant differences. We repeated these analyses for three categories of past 30-day illicit stimulant use: any illicit stimulant use,

methamphetamine use, and cocaine use. These outcome categories were not mutually exclusive; therefore, χ^2 tests were not conducted.

Subsequently, we calculated the percentage of assessments reporting past 30-day illicit stimulant use, methamphetamine use, and cocaine use by past 30-day prescription stimulant use status, using χ^2 tests to assess differences. In addition, we calculated frequencies of the substance reported as the primary substance use problem by past 30-day prescription stimulant use status, restricting to responses with $\geq 1\%$ frequency. Primary substance use problem is defined as the primary or most serious problem individuals reported among the substances they used in their lifetime. Next, we evaluated the percent of assessments with moderate to extreme scores in each biopsychosocial domain by past 30-day prescription and illicit stimulant use categories. Differences by prescription stimulant use status were assessed using χ^2 tests.

Finally, we calculated crude and adjusted prevalence ratios (PRs) and 95% confidence intervals (CIs) for the associations between past 30-day prescription stimulant NMU or use as prescribed (vs. no use) and past 30-day use of illicit stimulants using Poisson regression models without an offset (Poisson regression models were chosen given convergence problems with log-binomial regression models). We applied generalized estimating equations (GEE) with an exchangeable correlation matrix to account for repeated assessments at the individual level. The unit of analysis for GEE modeling results is 'unique adult' instead of unique assessments. Covariates (potential confounding variables) were selected *a priori* and included sex, age, race and ethnicity, education, employment status, urban/rural status of assessment site (CDC, 2017), insurance type, past 30 days in controlled environment (e.g., jail, inpatient treatment), and assessment year. We repeated these analyses for two additional outcomes: past 30-day methamphetamine use and past 30-day cocaine use. No collinearity was detected in adjusted models.

Analyses were conducted in SAS 9.4 (Cary, NC). Statistical significance was considered $p < 0.05$. The CDC determined human subject regulations and IRB approval were not applicable because deidentified secondary data were used.

3. Results

3.1. Sample characteristics

Of 245,133 assessments between 2017 and 2021, 218,981 assessments (89.3%) from 187,989 individuals had complete information on the exposure variable, model covariates, and at least one study outcome. Of these, 1.8% ($n = 3947$) of assessments reported NMU of prescription stimulants, 1.6% ($n = 3510$) used them as prescribed, and 96.6% ($n = 211,524$) did not use prescription stimulants in the past 30 days. In addition, 43,586 (19.9%) used any illicit stimulant, 14.0% used methamphetamine, and 7.7% used cocaine in the past 30 days. The percentage of assessments reporting past 30-day illicit stimulant use increased slightly from 20.0% to 21.0% between 2017 and 2021 ($p = 0.0002$), while the percentage reporting methamphetamine use increased from 13.2% to 16.0% ($p < 0.0001$). In contrast, the percentage of assessments reporting past 30-day cocaine use declined from 8.4% to 7.0% ($p < 0.0001$) (Supplementary Fig. 1).

All sociodemographic characteristics examined varied by prescription stimulant use status (Table 1; all comparisons $p < 0.0001$). There were more males (62.5%) than females (37.5%) in the "no prescription stimulant use" category. However, the sex distribution was more even for the other prescription stimulant categories (use as prescribed: 51.2% male; NMU: 51.7% male). Adults aged 25–34 years were the most common age group, ranging from 38.4% among the no prescription stimulant use category to 45.0% among the prescription stimulant NMU category. More than four in five assessments reporting prescription stimulant use as prescribed or NMU identified their race and ethnicity as non-Hispanic White; the percentage was lower among assessments reporting no prescription stimulant use. Additionally, the majority of assessments across all three prescription stimulant use categories were conducted

in metropolitan ASI-MV sites; this was highest among the prescription stimulant use as prescribed category. Almost three-fourths of assessments that reported prescription stimulant NMU indicated having health insurance; the percentages appeared slightly less among those that reported using prescription stimulants as prescribed or not using them at all. Finally, over ten percent of assessments reporting prescription stimulant NMU spent the past 30 days in inpatient medical/psychiatric treatment; percentages were smaller in other groups.

We also observed some differences in sociodemographic characteristics by illicit stimulant use status, although these were not tested for statistical significance (Table 1). While most respondents reporting all three types of illicit stimulant use were male, the frequency of males appeared slightly higher in those who used cocaine, compared to methamphetamine or any illicit stimulant. In addition, the most common racial and ethnic group reported for all three illicit stimulant categories was non-Hispanic White, but this appeared highest in those reporting methamphetamine use. The frequency of past 30-day inpatient alcohol/drug-related treatment ranged from 11.0% to 15.8%.

3.2. Illicit stimulant use by prescription stimulant use status

The percentage of assessments reporting illicit stimulant use varied by prescription stimulant use status (Fig. 1; all p -values < 0.0001). The majority (59.6%) of assessments reporting prescription stimulant NMU also reported past 30-day illicit stimulant use; illicit stimulant use appeared lower in assessments reporting prescription stimulant use as prescribed (12.8%) or no prescription stimulant use (19.3%). This pattern held when examining prevalence of past 30-day use of methamphetamine and cocaine.

3.3. Primary substance use problem by prescription stimulant use status

Primary substance use problem differed by prescription stimulant use status (Supplementary Fig. 2a–c). The most frequently reported primary substance use problem among assessments reporting prescription stimulant NMU in the past 30 days was any opioid (38.0%), followed by psychostimulants (which includes prescription stimulants) (22.2%), prescription opioids (20.1%), and alcohol (17.0%); 4.2% reported cocaine as the primary problem. The most frequently reported primary substance use problem for the other two groups was alcohol (22.8% for both), followed by any opioid (among prescription stimulant use as prescribed: 19.0%; among no prescription stimulant use: 20.9%); smaller percentages reported psychostimulants (among prescription stimulant use as prescribed: 6.0%; among no prescription stimulant use: 14.9%) or cocaine (prescription stimulant use as prescribed: 1.9%; no prescription stimulant use: 4.1%) as their primary substance use problem.

3.4. Biopsychosocial domains by prescription and illicit stimulant use categories

The frequency of moderate to extreme scores in all seven biopsychosocial domains varied by prescription stimulant use status (Fig. 2a; all p -values < 0.0001). We observed that a larger percentage of assessments reporting past 30-day prescription stimulant NMU had moderate to extreme ratings in the seven biopsychosocial domains—suggesting a probable need for treatment/assistance in that area—compared to those reporting prescription stimulant use as prescribed or those not using prescription stimulants (Fig. 2a). Strikingly, 85.8% of assessments reporting prescription stimulant NMU had moderate to extreme scores in the drug domain compared to 48.9% of assessments reporting no use of prescription stimulants and 38.8% of those reporting use as prescribed. Assessments reporting use of prescription stimulants as prescribed were qualitatively similar across most domains compared to assessments reporting no use of prescription stimulants. However, 48.6% of assessments reporting use of prescription stimulants as prescribed had moderate to extreme problem scores in the psychiatric domain compared

Table 1
Sociodemographic and Health Characteristics by Past 30-Day Prescription and Illicit Stimulant Use, 2017–2021.¹

Unit of Analysis: Adult treatment assessment	Prescription stimulant use in past 30 days (study exposure) ^{1,2}			Illicit stimulant use in past 30 days (study outcomes) ³		
	No prescription stimulant use N = 211,524	Prescription stimulant use as prescribed N = 3,510	Prescription stimulant NMU N = 3,947	Any illicit stimulant ⁴ N = 43,586	Methamphetamine N = 30,680	Cocaine ⁵ N = 16,851
Sex						
Male	132,185 (62.5%)	1796 (51.2%)	2041 (51.7%)	24,413 (56.0%)	16,302 (53.1%)	10,187 (60.5%)
Female	79,339 (37.5%)	1714 (48.8%)	1906 (48.3%)	19,173 (44.0%)	14,378 (46.9%)	6664 (39.5%)
Age						
18–24 years	32,609 (15.4%)	618 (17.6%)	691 (17.5%)	5496 (12.6%)	4024 (13.1%)	2109 (12.5%)
25–34 years	81,169 (38.4%)	1421 (40.5%)	1778 (45.0%)	18,359 (42.1%)	13,847 (45.1%)	6388 (37.9%)
35–44 years	53,605 (25.3%)	958 (27.3%)	1050 (26.6%)	12,046 (27.6%)	8803 (28.7%)	4241 (25.2%)
45 years or older	44,141 (20.9%)	513 (14.6%)	428 (10.8%)	7685 (17.6%)	4006 (13.1%)	4113 (24.4%)
Race and Ethnicity						
Non-Hispanic White	137,583 (65.0%)	2882 (82.1%)	3181 (80.6%)	30,092 (69.0%)	23,617 (77.0%)	9677 (57.4%)
Non-Hispanic Black	28,955 (13.7%)	82 (2.3%)	187 (4.7%)	5715 (13.1%)	1160 (3.8%)	4581 (27.2%)
Non-Hispanic Other race	18,745 (8.9%)	231 (6.6%)	298 (7.6%)	3552 (8.1%)	2855 (9.3%)	1020 (6.1%)
Hispanic	26,241 (12.4%)	315 (9.0%)	281 (7.1%)	4227 (9.7%)	3048 (9.9%)	1573 (9.3%)
Education Level						
Less than high school	46,174 (21.8%)	287 (8.2%)	748 (19.0%)	11,223 (25.7%)	7661 (25.0%)	4424 (26.3%)
High school/GED	93,617 (44.3%)	980 (27.9%)	1523 (38.6%)	20,337 (46.7%)	14,777 (48.2%)	7428 (44.1%)
Some college or more	71,733 (33.9%)	2243 (63.9%)	1676 (42.5%)	12,026 (27.6%)	8242 (26.9%)	4999 (29.7%)
Employment Status						
Full-time	103,655 (49.0%)	1808 (51.5%)	1654 (41.9%)	16,293 (37.4%)	11,109 (36.2%)	6706 (39.8%)
Part-time	40,320 (19.1%)	644 (18.3%)	983 (24.9%)	9465 (21.7%)	6778 (22.1%)	3592 (21.3%)
Other ⁶	38,457 (18.2%)	758 (21.6%)	748 (19.0%)	8260 (19.0%)	5769 (18.8%)	3088 (18.3%)
Unemployed	29,092 (13.8%)	300 (8.5%)	562 (14.2%)	9568 (22.0%)	7024 (22.9%)	3465 (20.6%)
Urban-Rural Status of ASI-MV Site						
Micropolitan	40,690 (19.2%)	665 (18.9%)	789 (20.0%)	6568 (15.1%)	5427 (17.7%)	1733 (10.3%)
Noncore (rural)	25,855 (12.2%)	313 (8.9%)	645 (16.3%)	6688 (15.3%)	5179 (16.9%)	2153 (12.8%)
Metropolitan	144,979 (68.5%)	2532 (72.1%)	2513 (63.7%)	30,330 (69.6%)	20,074 (65.4%)	12,965 (76.9%)
Insurance type						
Commercial payer, Medicare and/or Medicaid, or other	132,409 (62.6%)	1857 (52.9%)	2927 (74.2%)	33,438 (76.7%)	23,316 (76.0%)	13,376 (79.4%)
Uninsured/exhausted benefits or self-pay	79,115 (37.4%)	1653 (47.1%)	1020 (25.8%)	10,148 (23.3%)	7364 (24.0%)	3475 (20.6%)
Past 30 days in controlled environment						
None	133,243 (63.0%)	2487 (70.9%)	2389 (60.5%)	25,942 (59.5%)	18,054 (58.8%)	10,111 (60.0%)
Jail/prison	45,059 (21.3%)	600 (17.1%)	690 (17.5%)	8880 (20.4%)	7114 (23.2%)	2449 (14.5%)
Inpatient alcohol or drug-related treatment	25,172 (11.9%)	272 (7.7%)	456 (11.6%)	5424 (12.4%)	3374 (11.0%)	2658 (15.8%)
Inpatient medical/psychiatric treatment	8050 (3.8%)	151 (4.3%)	412 (10.4%)	3340 (7.7%)	2138 (7.0%)	1633 (9.7%)
Year of assessment						
2017	53,919 (25.5%)	938 (26.7%)	1118 (28.3%)	11,204 (25.7%)	7409 (24.1%)	4726 (28.0%)
2018	49,412 (23.4%)	735 (20.9%)	1049 (26.6%)	9916 (22.8%)	6633 (21.6%)	4117 (24.4%)
2019	42,512 (20.1%)	708 (20.2%)	754 (19.1%)	8521 (19.5%)	6113 (19.9%)	3199 (19.0%)
2020	31,265 (14.8%)	553 (15.8%)	556 (14.1%)	6511 (14.9%)	4855 (15.8%)	2312 (13.7%)
2021	34,416 (16.3%)	576 (16.4%)	470 (11.9%)	7434 (17.1%)	5670 (18.5%)	2497 (14.8%)

Footnotes:

NMU, nonmedical use.

¹ Prescription stimulant NMU is any use that is not considered “use as prescribed.” “Use as prescribed” is defined as obtaining the stimulant medication only from one’s own prescription, no use of the medication via an alternate route of administration, and no days of use in a manner not as prescribed.

² For each sociodemographic or health characteristic, we conducted a χ^2 test comparing the frequencies of each characteristic by prescription stimulant exposure category; all *p*-values were <0.0001.

³ Categories of past 30-day stimulant use are not mutually exclusive (e.g., a person could have used both methamphetamine and cocaine in the past 30 days). Of the 43,586 assessments reporting illicit stimulant use (including methamphetamine, cocaine, ecstasy, and/or bath salts), 57.7% reported using methamphetamine but no other illicit stimulants in the past 30 days, 26.6% reported using cocaine but no other illicit stimulants in the past 30 days, 8.9% reported using both methamphetamine and cocaine in the past 30 days, 1.6% used ecstasy but no other illicit stimulants, 1.5% used methamphetamine, cocaine, and ecstasy, 1.5% used methamphetamine and ecstasy, 1.2% used cocaine and ecstasy, and 0.1% used bath salts but no other illicit stimulants. The percentage of all other illicit stimulant drug combinations (among the 43,586 assessments reporting illicit stimulant use) was <0.5% (e.g., 0.4% used methamphetamine and bath salts, and 0.1% used all four illicit stimulants).

⁴ Composite variable including any use of methamphetamine, cocaine, ecstasy, and/or bath salts.

⁵ Includes crack.

⁶ Includes people who were students, homemakers, retired, had a disability, were in a prison or hospital, or were in military service.

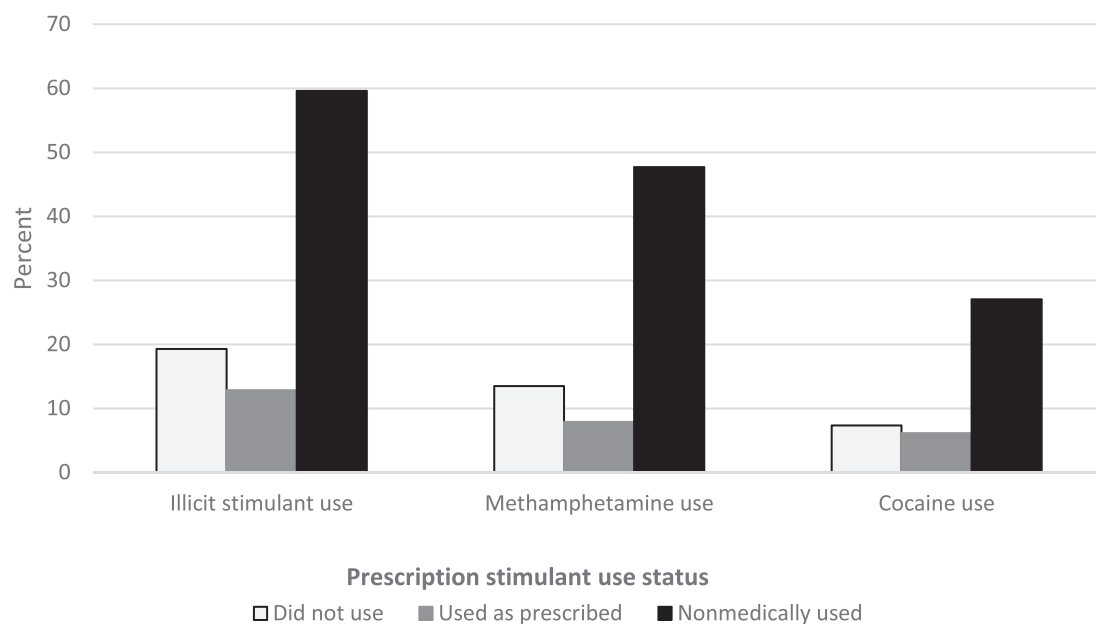


Fig. 1. Illicit stimulant use,¹ methamphetamine use, or cocaine² use in the past 30 days by prescription stimulant use status³ among adult assessments for substance use treatment, 2017–2021.⁴

Fig. 1 caption. This figure shows the percentages of assessments reporting illicit stimulant use, methamphetamine use, and cocaine use in the past 30 days by prescription stimulant use status (did not use, used as prescribed, or nonmedically used during the past 30 days) among adults evaluated for substance use treatment in 2017–2021.

Footnotes: NMU, nonmedical use.

¹Composite variable including any use of methamphetamine, cocaine/crack, ecstasy, and/or bath salts.

²Includes crack.

³Prescription stimulant NMU is any use that is not considered “use as prescribed.” “Use as prescribed” is defined as obtaining the stimulant medication only from one’s own prescription, no use of the medication via an alternate route of administration, and no days of use in a manner not as prescribed. Exposure categories (nonmedically used prescription stimulants in the past 30 days, used prescription stimulants as prescribed in the past 30 days, or did not use prescription stimulants in the past 30 days) were mutually exclusive.

⁴All p -values were <0.0001 (from χ^2 tests with 2 degrees of freedom comparing frequency of each outcome by prescription stimulant use status).

to 36.8% of assessments reporting no prescription stimulant use. Problem scores indicating the need for treatment or assistance across most biopsychosocial domains were qualitatively similar by *illicit* stimulant use status (Fig. 2b). More assessments reporting methamphetamine use in the past 30 days (43.5%) had moderate to extreme problem scores for the legal domain compared to those reporting cocaine use (33.1%), although illicit stimulant categories were not mutually exclusive. Additionally, it appeared that more assessments reporting cocaine compared to methamphetamine use had moderate to extreme problem scores in the alcohol domain (38.8% vs. 21.6%, respectively). More than 90% of assessments reporting illicit stimulant use had problem scores in the drug domain indicating a probable need for drug treatment.

3.5. Prevalence ratios for associations between prescription stimulant use/NMU and illicit stimulant use

After adjusting for covariates, adults who nonmedically used prescription stimulants in the past 30 days were 2.67 (95% CI 2.59, 2.75) times as likely to have used illicit stimulants in the past 30 days as those who did not use prescription stimulants (Fig. 3a). Adults who used prescription stimulants as prescribed were 25% less likely to have used illicit stimulants (adjusted PR [aPR]: 0.75 [0.69, 0.81]). The association between prescription stimulant use and past 30-day methamphetamine use was similar to that for illicit stimulant use overall. Compared to adults who did not use prescription stimulants, those who nonmedically used prescription stimulants had a higher prevalence of methamphetamine use (aPR: 2.81 [2.71, 2.92]), while those who used prescription stimulants as prescribed had a lower prevalence (aPR: 0.61 [0.55, 0.68]) (Fig. 3b). Similar to findings for illicit stimulant use and metham-

phetamine use, adults who nonmedically used prescription stimulants had a higher prevalence of past 30-day cocaine use (aPR: 3.53 [3.33, 3.74]) compared to adults who did not use prescription stimulants (Fig. 3c). However, in the adjusted models, using prescription stimulants as prescribed was not associated with past 30-day cocaine use (aPR: 1.06 [0.93, 1.21]).

4. Discussion

This study is the first to examine in-depth the associations between prescription stimulant use as prescribed and NMU with illicit stimulant use among U.S. adults screened for SUD treatment. Past 30-day prescription stimulant NMU was associated with increased use of any illicit stimulant, methamphetamine, and cocaine in the past 30 days. Our findings for cocaine and methamphetamine are consistent with several prior studies among community samples of U.S. individuals not being evaluated for treatment (Compton et al., 2018; Han et al., 2017b; Jones et al., 2020b; Mustaquim et al., 2021; Shearer et al., 2022). Also consistent with U.S. national trends, we found that the frequency of treatment assessments reporting recent methamphetamine use increased (Jones et al., 2023), whereas those for cocaine declined (Substance Abuse and Mental Health Services Administration, 2021), underscoring the increasing role methamphetamine is playing in the U.S. overdose crisis. Increasing U.S. methamphetamine treatment admissions are consistent with trends in other countries such as Australia and Mexico; however, declining U.S. cocaine treatment admissions differ from increasing cocaine treatment admissions seen in Western/Central Europe and Australia (UNODC, 2022).

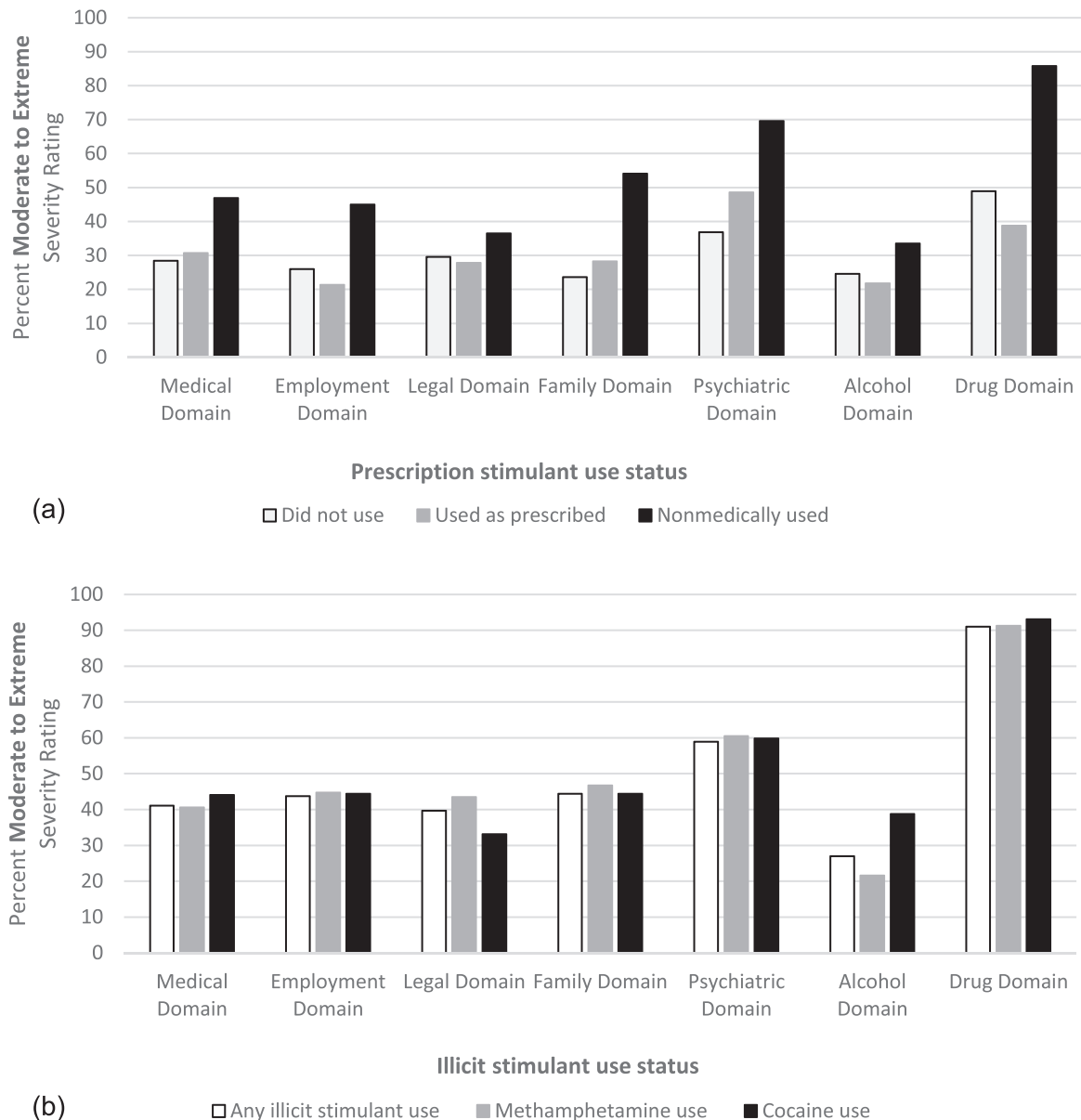


Fig. 2. Percent of assessments with moderate to extreme scores in each biopsychosocial domain, by drug use status, among adult assessments for substance use treatment, 2017–2021.

2a. By prescription stimulant use status¹

2b. By illicit stimulant use status: illicit stimulant use,² methamphetamine use, and cocaine³ use

Fig. 2 caption. This figure shows the percentage of assessments reporting moderate to extreme scores in seven biopsychosocial domains, by prescription stimulant use status (Fig. 2a) and illicit stimulant use status (Fig. 2b). The ASI-MV assesses seven biopsychosocial domains (medical, employment, legal, family, psychiatric, alcohol, drug) related to a respondent’s substance use. A rating is calculated for each domain, indicating the severity of the problem and the need for treatment or assistance in that area. Interpretation of the biopsychosocial domain problem severity ratings was as follows: 0–1, no problem; 2–3, slight problem; 4–5, moderate problem; 6–7, severe problem; and 8–9, extreme problem. Moderate to extreme problem was defined as a score of 4–9 on a scale of 0–9, suggesting that the individual probably needs treatment or assistance in that area. Higher scores indicate a greater need for treatment or assistance in that area. For each domain in Fig. 2a, we conducted χ^2 tests (2 df) comparing the frequency of moderate to extreme scores by prescription stimulant use status; all p -values were <0.0001. We could not conduct statistical tests for Fig. 2b because illicit stimulant categories were not mutually exclusive.

Footnotes: NMU, nonmedical use.

¹Prescription stimulant NMU is any use that is not considered “use as prescribed.” “Use as prescribed” is defined as obtaining the stimulant medication only from one’s own prescription, no use of the medication via an alternate route of administration, and no days of use in a manner not as prescribed. Exposure categories (nonmedically used prescription stimulants in the past 30 days, used prescription stimulants as prescribed in the past 30 days, or did not use prescription stimulants in the past 30 days) were mutually exclusive.

²Illicit stimulant use is a composite variable including any use of methamphetamine, cocaine/crack, ecstasy, and/or bath salts. Illicit stimulant use categories in Fig. 2b (any illicit stimulant use, methamphetamine use, cocaine use) were not mutually exclusive, so statistical tests comparing the differences were not conducted.

³Includes crack.

In contrast with prescription stimulant NMU, we found that use of prescription stimulants as prescribed (vs. no use) was associated with a lower prevalence of past 30-day use of illicit stimulants and methamphetamine, and was not associated with cocaine use. These findings differ from those in a recent U.S. community sample using National Survey of Drug Use and Health (NSDUH) data, which found that past-year prescription stimulant use as prescribed (vs. no use) was associated with higher past-year prevalence of cocaine and methamphetamine use (Shearer et al., 2022). Differences likely stem primarily from differences in the populations sampled. Adults in the NAVIPPRO dataset likely have a generally raised risk for substance use since this group is being assessed for SUD treatment; in contrast, the NSDUH samples the general, noninstitutionalized U.S. population, where most people do not use substances or have SUDs. Similarly, people with SUD also have higher prevalence of mental health conditions (Center for Behavioral Health Statistics and Quality, 2022), which may drive some differences in why people in our

study sample might be prescribed stimulants differently than in the general U.S. population. Another potential reason for discrepancies is the difference in outcomes examined (i.e., past 30-day use in our study vs. past-year use in NSDUH). In our study, those using prescription stimulants as prescribed may have been receiving SUD treatment evaluation for a different type of drug problem: adult assessments reporting prescription stimulant use as prescribed were the least likely out of the three prescription stimulant use categories to report psychostimulants or cocaine as their primary substance problem. This group (use as prescribed) was also the least likely to have moderate to extreme domain scores in the drug domain, suggesting lesser need for drug treatment, whereas those reporting prescription stimulant NMU had scores indicating the greatest probable need for drug treatment.

Findings related to biopsychosocial domains are also informative for prevention, treatment, and response. Assessments reporting prescription stimulant NMU appeared more likely to have moderate to extreme

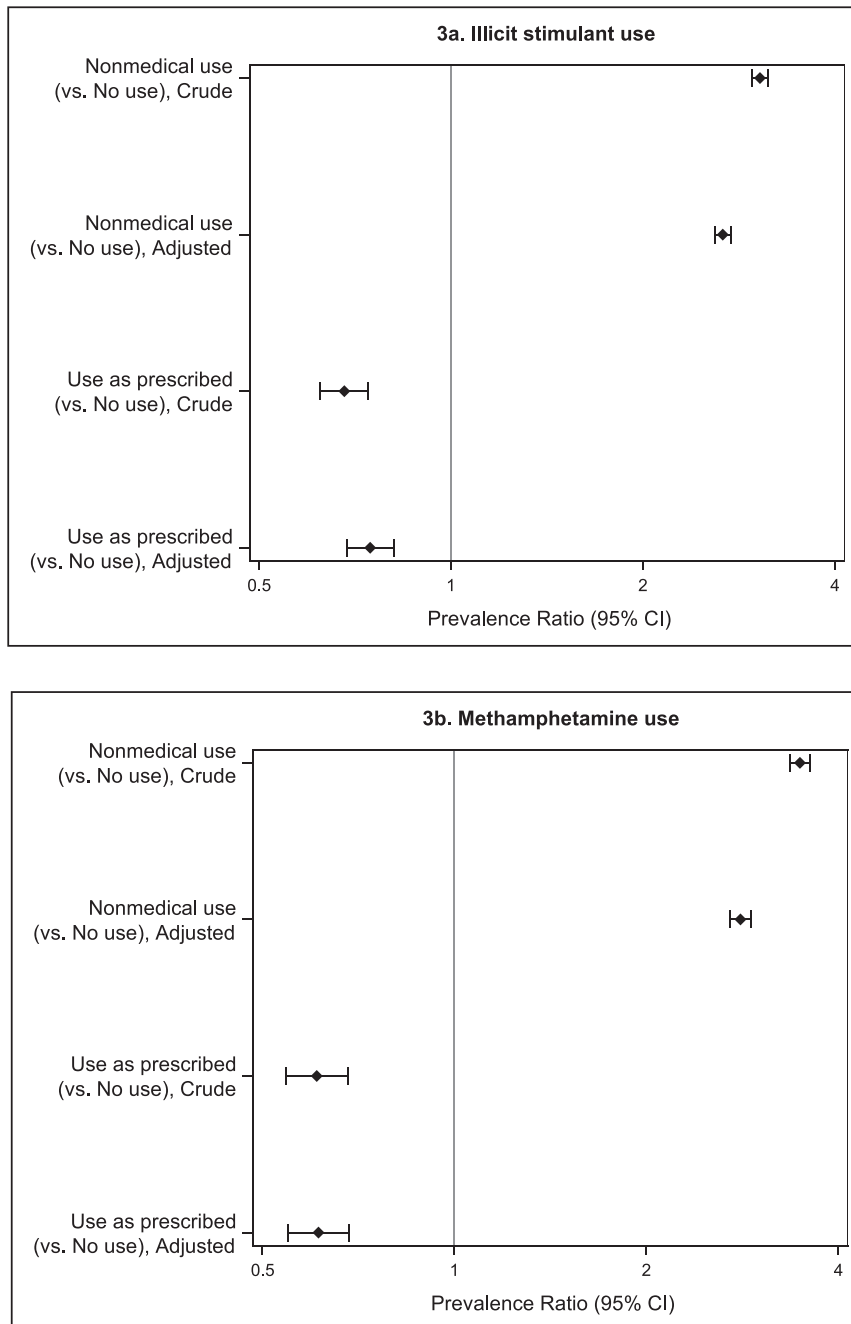


Fig. 3. Associations between prescription stimulant use as prescribed or nonmedical use¹ and illicit stimulant use,² methamphetamine use,³ and cocaine use⁴ in the past 30 days among 187,989 adults assessed for substance use treatment, 2017–2021.

a. Prevalence ratios for associations between prescription stimulant use as prescribed or nonmedical use (vs. no use) and illicit stimulant use

b. Prevalence ratios for associations between prescription stimulant use as prescribed or nonmedical use (vs. no use) and methamphetamine use

c. Prevalence ratios for associations between prescription stimulant use as prescribed or nonmedical use (vs. no use) and cocaine use

Fig. 3 caption. This figure shows unadjusted (crude) and adjusted prevalence ratios for associations between past 30-day prescription stimulant use as prescribed/nonmedical use and three different outcomes—1) past 30-day illicit stimulant use (3a), 2) past 30-day methamphetamine use (3b), and 3) past 30-day cocaine use (3c)—among 187,989 adults evaluated for substance use treatment in 2017–2021. Adjusted prevalence ratios include adjustment for the following covariates: sex, age, race and ethnicity, education, employment status, urban/rural status of assessment site, insurance type, past 30 days in controlled environment (e.g., jail, inpatient treatment), and assessment year. We used generalized estimating equations (GEE) models with an exchangeable correlation matrix to account for the 14.2% of repeat assessments; hence, the unit of analysis for GEE models is ‘adult.’

Footnotes: PR, prevalence ratio. CI, confidence interval. This analysis was restricted to assessments with complete data on all demographic characteristics in Table 1.

¹Prescription stimulant nonmedical use is any use that is not considered “use as prescribed.” “Use as prescribed” is defined as obtaining the stimulant medication only from one’s own prescription, no use of the medication via an alternate route of administration, and no days of use in a manner not as prescribed. Exposure categories (nonmedically used prescription stimulants in the past 30 days, used prescription stimulants as prescribed in the past 30 days, or did not use prescription stimulants in the past 30 days) were mutually exclusive.

²Composite variable including any use of methamphetamine, cocaine, ecstasy, and/or bath salts. 218,792 assessments were included in the analysis (Fig. 3a).

³218,836 assessments were included in the analysis of past 30-day methamphetamine use (Fig. 3b).

⁴218,979 assessments were included in the analysis of past 30-day cocaine (includes crack) use (Fig. 3c).

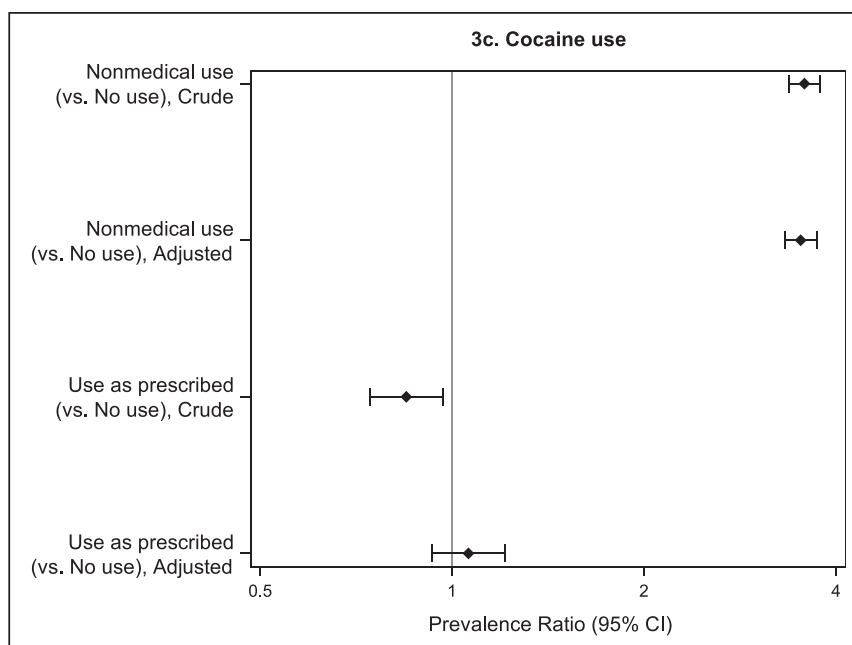


Fig. 3. (Continued).

scores in the employment, legal, and family domains, indicating a probable need for assistance in these areas, compared to those reporting no prescription stimulant use or use as prescribed. Additionally, many assessments reporting *illicit* stimulant use had moderate to extreme scores in the employment, legal, or family assistance domains, indicating a probable need for assistance in these areas. This highlights the potential benefit of comprehensive treatment and social and recovery support services. Interventions for those using illicit or nonmedically using prescription stimulants can focus on the root causes of illicit stimulant use/prescription stimulant NMU, including social determinants of health and preventing and responding to adverse childhood experiences (Delcher et al., 2022; Marshall et al., 2011; Scheidell et al., 2018; Schimmenti et al., 2022; Tang et al., 2021). Additionally, it is important to examine how policies related to employment support services and job skills training affect people who use illicit stimulants or nonmedically use prescription stimulants.

The need for psychiatric care was common among individuals illicitly using stimulants. For example, 59% of those using illicit stimulants and nearly 70% of those nonmedically using prescription stimulants had assessment scores indicating a probable need for psychiatric care. These findings are consistent with earlier U.S. studies, which found that 33.6% of adults who used cocaine in the last year reported serious psychological distress (Mustaquim et al., 2021), while 57.7% of people who used methamphetamine in the past year had mental illness (Jones et al., 2020a). These findings suggest that adults who illicitly use stimulants may benefit from evaluation for and referral to mental health treatment in addition to substance use treatment, as many U.S. adults with co-occurring diagnoses have unmet treatment needs (Han et al., 2017a).

In addition, approximately half of those reporting prescription stimulant use as prescribed had moderate to extreme scores in the psychiatric domain. This may reflect the therapeutic use of some stimulants in the treatment of psychiatric conditions such as ADHD, narcolepsy, depression, and eating disorders (Bahji and Mesbah-Oskui, 2021; Chamakalayil et al., 2020; Faraone et al., 2021; Monteleone et al., 2022). To optimize the use of these medications in patients at risk for misuse and diversion, clinicians can counsel patients about the potential benefits and risks of these medications, implement more intense monitoring of patients during treatment, and utilize resources such as prescription drug monitoring programs to identify other controlled substances being prescribed to patients (Chamakalayil et al., 2020).

Our findings, coupled with evidence that stimulant availability, use, and harms are intertwined with the ongoing U.S. opioid overdose crisis (Jones et al., 2020a, 2022), suggest the value of prevention, treatment, and response efforts that are comprehensive and broad-based. Universal preventive interventions such as Promoting School-Community-University Partnerships to Enhance Resilience (PROSPER) have resulted in lasting protective effects on preventing substance use generally, and for stimulants and opioids specifically (Spoth et al., 2017). Physicians can screen for prescription stimulant NMU and SUDs, check prescription drug monitoring programs, and follow prescribing guidelines to support the safe and appropriate use of medications while reducing risk for diversion (Compton et al., 2018; Han et al., 2017b). Those who prescribe stimulants can also discuss the risks of prescription stimulant NMU and diversion with their patients (Board et al., 2020; Compton et al., 2018).

Currently no medications are U.S. FDA-approved for the treatment of stimulant use disorders; thus, treatment strategies involve evidence-based psychosocial approaches (e.g., community reinforcement or cognitive-behavioral therapy) combined with contingency management, where rewards are provided to reinforce positive behavior (De Crescenzo et al., 2018). Recent studies found that less than one-third of U.S. adults with past-year methamphetamine or cocaine use disorders received past-year SUD treatment (Jones et al., 2020b; Mustaquim et al., 2021). These low treatment rates are concerning given that our study and another U.S. publication using January 2013–March 2016 ASI-MV data indicate that most adults assessed for SUD treatment who report NMU of prescription stimulants had a probable need for drug treatment (Burtner et al., 2018). In addition, a large proportion of people with stimulant use disorder may benefit from treatment for co-occurring opioid or other substance use disorders. The need for treatment to address polysubstance use is underscored by our finding that many assessments reporting prescription stimulant use as prescribed/NMU indicated that opioids, alcohol, or other non-stimulant substances were their primary substance problem, as well as by high rates of polysubstance use and use disorders found in other U.S. publications (Burtner et al., 2018; Compton et al., 2018; Han et al., 2017b; Jones et al., 2020b, 2020c; Mustaquim et al., 2021). Efforts to reduce overdose risk among those who use both stimulants and opioids include access to medications for opioid use disorder and harm reduction services such as fentanyl test strips and naloxone (Carroll et al., 2018).

This study is subject to limitations. First, although NAVIPPRO collects data from a geographically diverse set of states and treatment programs, it is a convenience sample; hence, results may not be representative of or generalizable to all U.S. adults assessed for SUD. Second, substance use is self-reported and is subject to social desirability and recall biases. Third, the cross-sectional nature of the sample limits the ability to make causal inferences. Fourth, the sample includes repeat assessments from some individuals; however, we used GEE to account for repeat assessments in our Poisson models. Finally, we only included individuals with complete data in our analyses. Despite these limitations, this study has several important strengths and provides recent, timely data collected via a validated clinical tool among adults assessed for SUD treatment (Butler et al., 2001). The ASI-MV captures experiences from a unique population of individuals evaluated for SUD treatment and who thus may be more severely affected by substance use; these data may include those traditionally excluded from U.S. household surveys such as NSDUH (e.g., institutionalized individuals, court ordered treatment) and are able to differentiate between therapeutic use and NMU of prescription stimulants.

5. Conclusions

Among U.S. adults evaluated for substance use treatment between 2017 and 2021, past 30-day prescription stimulant NMU was associated with increased prevalence of past 30-day use of illicit stimulants, methamphetamine, and cocaine. Most adult assessments reporting prescription stimulant NMU or illicit stimulant use had moderate to extreme problem scores in the drug domain, indicating a probable need for drug-related treatment. Adult assessments reporting prescription stimulant use as prescribed or NMU frequently reported opioids, alcohol, or other substances as their primary substance problem. In addition, assessments reporting prescription stimulant NMU (vs. no use, or use as prescribed) appeared more likely to have moderate to extreme problem scores in the alcohol, psychiatric, medical, family, employment, and legal domains, indicating a probable need for treatment or assistance in these areas. Adults who use illicit stimulants or nonmedically use prescription stimulants may benefit from care that is comprehensive, addresses polysubstance use (e.g., co-use of opioids and stimulants), incorporates harm-reduction resources, and includes mental health treatment, as well as social and recovery support services.

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CDC disclaimer

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Declaration of Competing Interest

Taryn Dailey Govoni and Jody L. Green are employees of Inflexxion, a division of Uprise Health. Inflexxion contracts with FDA and companies with interests in prescription stimulant products, which are evaluated as a class in this article. The authors have no other conflicts of interest or relevant financial relationships to disclose.

CRedit authorship contribution statement

Cassandra M. Pickens: Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Christopher M. Jones:** Conceptualization, Supervision, Writing – original draft, Writing – review & editing. **Gery P. Guy Jr.:** Conceptualization, Supervision, Writing –

original draft, Writing – review & editing. **Taryn Dailey Govoni:** Validation, Writing – original draft, Writing – review & editing. **Jody L. Green:** Investigation, Writing – original draft, Writing – review & editing.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2023.100153.

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