The 3-Year Course of Multiple Substance Use Disorders in the United States:
A National Longitudinal Study

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ABSTRACT

Objective: To examine the 3-year course of multiple co-occurring substance use disorders (SUDs) based on longitudinal survey data from a large, nationally representative sample.

Methods: National estimates of the prevalence of *DSM-IV* SUDs were derived by analyzing data from structured, face-to-face diagnostic interviews as part of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), which collected data from a large, nationally representative sample of noninstitutionalized US adults at 2 waves (2001–2002 and 2004–2005; N = 34,653).

Results: US adults with multiple past-year SUDs at Wave 1 were substantially more likely than those with an individual past-year SUD or no SUD at Wave 1 to report at least 1 past-year SUD at Wave 2 (66.3% vs 46.0% vs 6.9%, respectively). There were several sociodemographic characteristics and psychiatric disorders (ie, male, younger age, never married, sexual minority identity, nicotine dependence, mood disorder, and personality disorder) associated with increased odds of developing multiple SUDs and having 3-year persistence of multiple SUDs. The majority of adults with multiple past-year SUDs had a lifetime personality disorder and did not utilize substance abuse treatment or other help-seeking.

Conclusions: Multiple SUDs are associated with a more persistent 3-year course of disease over time relative to individual SUDs. Despite a more severe 3-year course and higher rates of comorbidity with other psychiatric disorders, the majority of US adults with multiple SUDs do not utilize substance abuse treatment or other help-seeking. Clinical assessments and the substance abuse literature tend to focus on drug-specific individual SUDs rather than considering the more complex multiple SUDs, which can be more challenging to treat.

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Recent epidemiologic studies have documented high rates of polysubstance use behaviors in several countries worldwide.[1–7] Historically, large-scale epidemiologic studies have found substantial comorbidity between substance use disorders (SUDs) and other psychiatric disorders in the United States.[8–21] A few of these studies examined the prevalence of multiple co-occurring SUDs involving non-alcohol drug use disorders and other SUDs.[8–10,17] Indeed, some experts have encouraged future practice and research to move beyond binary measures of substance-specific use to polysubstance use profiles that incorporate measures of severity and multiple SUDs.[3,22,23]

With the release of the *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition (*DSM-5*), there have been some important diagnostic changes. Prior to the *DSM-5*, "polysubstance dependence" was diagnosed by the use of 3 or more substances (excluding caffeine and nicotine), with no single substance dominating. In the *DSM-5*, the diagnosis of "polysubstance dependence" has been removed, and there is no diagnosis involving multiple SUDs, despite the high rates of polysubstance use behaviors. Prior work has not investigated whether multiple SUDs are more persistent than individual SUDs over time. In order to fill these important gaps in knowledge, the present study examined the prevalence and 3-year course associated with multiple SUDs based on a large, nationally representative sample of noninstitutionalized US adults, which was surveyed in 2001–2002 and had a longitudinal follow-up in 2004–2005.

METHODS

Design and Sample

Data collected from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) across 2 waves (2001–2002, or Wave 1, and 2004–2005, or Wave 2) were used as the primary sources of information regarding SUDs among the general adult population in the United States. Waves 1 and 2 of the NESARC included the National Institute on Alcohol Abuse and Alcoholism (NIAAA) Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS-IV), a fully structured diagnostic interview conducted in households. The sample for NESARC Wave 1 was representative of the civilian noninstitutionalized US population, aged 18 years and older. More details about the NESARC sample design and data collection methods for both Waves 1 and 2 are available elsewhere.[24,25] The United States Census Bureau and the United States Office of Budget and Management approved the NESARC research protocol. The University of Michigan Institutional Review Board approved the current study.

The overall response rate for Wave 1 of the NESARC was 81%; the household response rate was 89%, and the person response rate was 93%. The response rate among those eligible for Wave 2 was 86.7%, resulting

Clinical Points

- Prior research has not investigated whether multiple co-occurring substance use disorders (SUDs) are more persistent than individual SUDs over time.
- Health professionals should move beyond a binary drug-specific approach to diagnosing, studying, and treating SUDs toward one that takes into account multiple SUDs and comorbidity with other psychiatric disorders.
- If a patient presents with multiple SUDs, clinicians should assess for other psychiatric disorders (eg, anxiety, mood, and personality disorders) and plan treatment accordingly.

in a cumulative response rate of 70.2% (the product of the response rates from Waves 1 and 2). The Wave 1 NESARC sample consisted of 43,093 adults aged 18 years or older and represented a population that was 52% women, 71% white, 12% Hispanic, 11% African American, 4% Asian, and 2% Native American or other racial category. Nonresponse at Wave 2 differed as a function of prior-to-past-year (PPY) SUDs, as recorded at Wave 1—an estimated 20.1% of individuals with no PPY SUDs would be expected to not respond at Wave 2, as opposed to 14.9% of individuals with an individual SUD and 15.1% of individuals with multiple SUDs in their lifetime (Rao-Scott $F_{2.0,129.7} = 48.4$, $P < .001$). Potential biases in Wave 2 due to this nonresponse were minimized via NESARC's weight adjustment procedures.

Measures

The NESARC measures assessed sociodemographic characteristics including sex, race/ethnicity, age, marital status, educational attainment, personal annual income, sexual identity, and geographical region based on the US Census (Northeast, South, Midwest, and West). SUDs and other psychiatric disorders were also assessed including *DSM-IV* anxiety, mood, and personality disorders; more details regarding these measures are available elsewhere.[13,26]

Substance use disorders were assessed at both waves of the NESARC according to the criteria of the *DSM-IV* using the AUDADIS-IV. Substance-specific diagnoses were determined for 10 substances, including alcohol, marijuana, cocaine, heroin, hallucinogens, inhalants, prescription opioids, sedatives, stimulants, and tranquilizers. A past-year diagnosis of substance abuse required at least 1 positive response to 4 criteria defined for abuse in the 12-month period preceding the interview and the absence of a dependence diagnosis. A past-year diagnosis of substance dependence was defined as a positive response to at least 3 of the 7 dependence criteria. Nicotine dependence was also assessed and included as a covariate in our models due to the differences between the nicotine dependence measure and the other 10 SUD measures that included both abuse and dependence, consistent with prior work.[9–11] Reliability and validity of the *DSM-IV* AUDADIS-IV SUD diagnoses have been documented in numerous psychometric studies, with test-retest reliability ranging from good to excellent (0.70 to 0.91).[27–34]

Substance abuse treatment utilization or other help-seeking was assessed for all respondents who had a history of alcohol and/or other drug use. Alcohol treatment and other help-seeking included self-help (eg, Alcoholics Anonymous), social services (eg, family services, employee assistance program, clergy), alcohol services (eg, alcohol/drug detoxification, inpatient ward, outpatient clinic, alcohol/drug rehabilitation program, halfway house, private physician, psychiatrist, psychologist, social worker or other professional), and emergency room or crisis center. The response scale for all items was dichotomous (yes/no). Respondents were also asked a separate series of questions related to drug treatment or other help-seeking that paralleled the questions related to alcohol.

Data Analysis

All analyses presented in this study were design-based, in that (1) NESARC sampling weights adjusted for nonresponse and calibrated to population control totals based on the US Census (either for Wave 1 or Wave 2 respondents, depending on the variables being analyzed) were used to compute weighted population estimates and (2) the stratified multistage cluster sample design of the NESARC was accounted for when computing linearized estimates of sampling variance for the weighted estimates. Design-adjusted Rao-Scott tests of bivariate associations between categorical measures were used to examine population associations between (1) PPY SUDs at Wave 1 and past-year SUDs at Waves 1 and 2, (2) past-year SUDs at Wave 1 and past-year SUDs at Wave 2, (3) past-year substance dependence at Wave 1 and past-year substance dependence at Wave 2, and (4) past-year SUDs and substance abuse treatment utilization or other help-seeking at either wave. Finally, pseudo–maximum likelihood estimation methods (accounting for the NESARC sample design features) were used to fit multivariate logistic regression models to various past-year SUD and help-seeking outcomes as a function of sociodemographic characteristics, prior SUDs, and the various psychiatric disorders, enabling assessment of significant correlates of these outcomes at the population level.

RESULTS

Among individuals with any PPY SUDs at Wave 1, an estimated 73.5% (SE = 0.5%) had an individual PPY SUD and 26.5% (SE = 0.5%) had multiple PPY SUDs. The 3-year course of PPY SUDs was examined based on Waves 1 and 2 (Table 1). Among individuals without any PPY SUD at Wave 1, the vast majority did not meet criteria for any past-year SUDs at Wave 1 (98.5%) or Wave 2 (94.7%). In contrast, past-year SUDs at Waves 1 and 2 were more prevalent among those with any PPY SUDs at Wave 1, especially those with multiple PPY SUDs.

US adults with multiple past-year SUDs at Wave 1 were more likely than those with an individual past-year SUD or no past-year SUD at Wave 1 to report at least 1 past-year SUD at Wave 2 (Table 2). An estimated 66.3% (SE = 3.1%) of those with multiple past-year SUDs at Wave

Table 1. Three-Year Course of Lifetime Substance Use Disorders[a] Based on NESARC Wave 1 (2001–2002) and NESARC Wave 2 (2004–2005)

2001–2002 NESARC Wave 1 Prior-to-Past-Year (n = 43,093 Wave 1) (n = 34,653 Waves 1 and 2)	2001–2002 NESARC Wave 1 Past-Year (n = 43,093)	2004–2005 NESARC Wave 2 Past-Year (n = 34,653)
0 SUDs (n = 30,797 Wave 1) (n = 24,318 Waves 1 and 2)	0 SUDs: 98.5% (n = 30,387) 1 SUD: 1.4% (n = 383) 2+ SUDs: 0.1% (n = 27)	0 SUDs: 94.7% (n = 23,115) 1 SUD: 4.7% (n = 1,077) 2+ SUDs: 0.6% (n = 126)
1 SUD (n = 9,061 Wave 1) (n = 7,607 Waves 1 and 2)	0 SUDs: 77.4% (n = 7,016) 1 SUD: 22.0% (n = 1,989) 2+ SUDs: 0.6% (n = 56)	0 SUDs: 81.2% (n = 6,205) 1 SUD: 17.1% (n = 1,286) 2+ SUDs: 1.7% (n = 116)
2+ SUDs (n = 3,235 Wave 1) (n = 2,728 Waves 1 and 2)	0 SUDs: 62.2% (n = 2,011) 1 SUD: 25.9% (n = 845) 2+ SUDs: 11.9% (n = 379)	0 SUDs: 67.1% (n = 1,853) 1 SUD: 25.1% (n = 664) 2+ SUDs: 7.8% (n = 211)

[a]All estimates are weighted. Design-adjusted Rao-Scott tests of the association between Wave 1 prior-to-past-year disorder and past-year disorder status at each wave were significant at the $P < .0001$ level, suggesting substantial differences in the distribution of past-year disorder status as a function of prior-to-past-year disorder status at Wave 1.

Abbreviations: NESARC = National Epidemiologic Survey on Alcohol and Related Conditions, SUD = substance use disorder.

Table 2. Three-Year Course of Past-Year SUDs and Comorbid SUDs[a] Based on NESARC Wave 1 (2001–2002) and NESARC Wave 2 (2004–2005)

2001–2002 NESARC Wave 1 Past-Year (n = 34,653)	2004–2005 NESARC Wave 2 Past-Year (n = 34,653)
0 SUDs (n = 31,678)	0 SUDs: 93.1% (n = 29,601) 1 SUD: 6.1% (n = 1,873) 2+ SUDs: 0.8% (n = 204)
1 SUD (n = 2,620)	0 SUDs: 54.0% (n = 1,446) 1 SUD: 40.1% (n = 1,026) 2+ SUDs: 5.9% (n = 148)
2+ SUDs (n = 355)	0 SUDs: 33.7% (n = 126) 1 SUD: 38.7% (n = 128) 2+ SUDs: 27.6% (n = 101)

[a]All estimates are weighted. Design-adjusted Rao-Scott test of the association between Wave 1 past-year disorder status and Wave 2 past-year disorder status was significant at the $P < .0001$ level, suggesting substantial differences in the distribution of Wave 2 past-year disorder status as a function of past-year disorder status at Wave 1.

Abbreviations: NESARC = National Epidemiologic Survey on Alcohol and Related Conditions, SUD = substance use disorder.

1 still met criteria for at least 1 SUD at Wave 2, as compared to 46.0% (SE = 1.3%) of those with an individual past-year SUD and only 6.9% (SE = 0.2%) of individuals with no past-year SUD ($P < .0001$). Similarly, individuals with multiple past-year substance dependence diagnoses at Wave 1 were more likely to report past-year dependence on at least 1 substance at Wave 2 than those with 1 or no past-year substance dependence at Wave 1 (results not shown). An estimated 55.7% (SE = 6.4%) of individuals with multiple past-year substance dependence diagnoses at Wave 1 still met past-year dependence criteria for at least 1 substance at Wave 2 as compared to 36.1% (SE = 1.7%) of those with an individual past-year substance dependence and only 3.5% (SE = 0.1%) of individuals with no past-year substance dependence ($P < .0001$).

We examined the sociodemographic characteristics associated with having various types of past-year SUDs at Waves 1 and 2 using both design-adjusted Rao-Scott tests of bivariate associations and multiple logistic regression models. Notably, an estimated 63.9% (SE = 3.3%) of individuals with multiple past-year SUDs at Wave 1 were aged 18–29 years, and roughly half of these individuals (54.3%, SE = 3.3%) had at least 1 lifetime personality disorder (see Table 3). The results in Table 3 suggest that there are substantial differences in the sociodemographic profiles of individuals with and without multiple past-year SUDs. With the exception of education ($P < .05$), past-year SUD status has very strong associations with all other sociodemographic characteristics. In particular, those with multiple past-year SUDs tend to be younger, white, male, never married, of lower income, nicotine dependent, and more prone to anxiety, mood, and personality disorders.

As illustrated in Table 4, the estimated multivariate models indicate that multiple SUDs are significantly more prevalent among males; younger individuals; divorced or never married adults; those who live in the West; those who self-identify as lesbian, gay, or bisexual; nicotine-dependent adults; those with any past-year mood disorders; and especially those with any lifetime personality disorders. Individuals falling into several of these subgroups are at significantly increased risk of experiencing multiple SUDs.

Similarly, persistent multiple SUDs across the 3-year period were significantly more prevalent among males, younger individuals, never married adults, those identifying as lesbian or gay, nicotine-dependent adults, those with multiple past-year anxiety disorders, those with multiple past-year mood disorders, and those with multiple lifetime personality disorders (see Table 4). Individuals falling into several of these subgroups are at increased risk of having multiple SUDs persist across a 3-year period.

We found that the majority of adults with multiple SUDs did not utilize substance abuse treatment or other help-seeking in either 2001–2002 or 2004–2005. An estimated 67.6% (SE = 3.0%) of US adults with multiple past-year SUDs in 2001–2002 and 72.5% (SE = 2.0%) of those with multiple past-year SUDs in 2001–2002 or 2004–2005 did not utilize substance abuse treatment or other help-seeking at either wave, respectively. We found a significant association between Wave 1 past-year SUD status and any substance abuse treatment utilization or other help-seeking behaviors at either Wave 1 or Wave 2 (Rao-Scott $P < .001$). Specifically, an estimated 32.4% (SE = 3.0%) of those with multiple SUDs at Wave 1 utilized substance abuse treatment or sought other help at either wave, compared to 9.7% (SE = 0.7%) of those with an individual past-year SUD. As illustrated in Table 5, we fitted a multivariate logistic regression model of treatment utilization or other

Table 3. Estimated Distributions of Sociodemographic Characteristics and Other Psychiatric Disorders as a Function of Past-Year SUD Status (NESARC Wave 1) (Wave 1 Measures; Case Base = Respondents at Both Waves 1 and 2[a])

Sociodemographic and Psychiatric Variables[a]	No Past-Year SUDs (n = 31,678) % (SE %)	1 Past-Year SUD (n = 2,620) % (SE %)	2+ Past-Year SUDs (n = 355) % (SE %)	Design-Adjusted Rao-Scott Test of Association		
				F	*df*	*P*
Sex						
Female	54.2 (0.4)	31.2 (1.1)	28.0 (2.8)	214.5	2.0, 129.8	<.0001
Male	45.8 (0.4)	68.9 (1.1)	72.0 (2.8)			
Race/ethnicity						
White	70.7 (1.6)	74.1 (1.9)	69.6 (3.4)	5.4	6.8, 439.3	<.0001
Black	11.2 (0.7)	9.6 (0.8)	9.6 (1.8)			
Native American	2.1 (0.2)	2.5 (0.4)	7.3 (2.0)			
Asian	4.5 (0.6)	2.4 (0.6)	2.3 (1.2)			
Hispanic	11.6 (1.2)	11.6 (1.7)	11.2 (2.0)			
Age, y						
45 and older	49.8 (0.5)	23.9 (1.1)	9.1 (2.0)	187.5	3.9, 250.6	<.0001
30–44	30.4 (0.4)	36.8 (1.2)	26.9 (2.9)			
18–29	19.7 (0.4)	39.4 (1.2)	63.9 (3.3)			
Marital status						
Married/partnered	64.8 (0.5)	48.7 (1.1)	24.8 (2.6)	104.8	5.1, 329.8	<.0001
Divorced/separated	10.1 (0.2)	13.9 (0.8)	12.8 (2.0)			
Widowed	6.5 (0.2)	1.7 (0.3)	2.0 (1.2)			
Never married	18.6 (0.5)	35.7 (1.2)	60.4 (3.1)			
Education						
Some college	56.2 (0.6)	58.7 (1.3)	47.6 (3.4)	3.4	3.9, 253.3	<.0104
High school/GED	29.0 (0.6)	28.9 (1.2)	33.2 (3.2)			
Less than high school	14.8 (0.5)	12.5 (1.0)	19.2 (2.9)			
Personal income						
$70,000 or more	8.5 (0.4)	8.6 (0.7)	2.1 (0.8)	12.5	5.8, 377.9	<.0001
$35,000–$69,999	22.4 (0.4)	25.3 (1.1)	11.0 (1.9)			
$20,000–$34,999	22.6 (0.4)	25.6 (1.2)	22.5 (2.8)			
$19,999 or less	46.5 (0.6)	40.5 (1.3)	64.5 (3.2)			
Geographical region						
South	35.8 (3.2)	30.7 (3.0)	23.9 (3.6)	6.3	5.3, 344.8	<.0001
Northeast	19.8 (3.4)	18.2 (3.0)	20.2 (4.3)			
Midwest	22.6 (3.1)	28.6 (3.2)	26.6 (4.1)			
West	21.8 (3.4)	22.5 (3.3)	29.3 (4.3)			
Sexual identity[a]						
Heterosexual	97.4 (0.2)	96.2 (0.5)	92.5 (1.7)	11.7	5.8, 379.0	<.0001
Lesbian/gay	0.7 (<0.1)	1.5 (0.3)	4.4 (1.5)			
Bisexual	0.5 (<0.1)	1.3 (0.3)	1.9 (0.9)			
Not sure/unknown	1.3 (0.1)	0.9 (0.3)	1.2 (0.7)			
Past-year nicotine dependence						
No	89.8 (0.4)	69.0 (1.3)	39.6 (3.4)	475.3	2.0, 129.8	<.0001
Yes	10.2 (0.4)	31.0 (1.3)	60.4 (3.4)			
Past-year anxiety disorders						
None	89.6 (0.3)	83.1 (0.9)	69.3 (3.2)	49.1	3.9, 251.7	<.0001
1	8.3 (0.3)	13.2 (0.8)	18.8 (2.9)			
2+	2.1 (0.1)	3.6 (0.4)	12.0 (2.0)			
Past-year mood disorders						
None	91.8 (0.2)	82.4 (0.8)	60.5 (3.3)	127.0	4.0, 257.2	<.0001
1	6.3 (0.2)	13.0 (0.8)	23.0 (2.7)			
2+	1.9 (0.1)	4.7 (0.5)	16.5 (2.4)			
Lifetime personality disorders						
None	86.6 (0.3)	73.0 (1.1)	45.7 (3.3)	149.8	3.8, 248.1	<.0001
1	8.9 (0.2)	15.9 (0.9)	25.1 (3.1)			
2+	4.4 (0.2)	11.2 (0.7)	29.3 (3.3)			

[a]All sociodemographic characteristics and other psychiatric disorders are based on Wave 1 with the exception of sexual identity, which is based on Wave 2. This is the reason that the case base was defined by respondents at both Wave 1 and Wave 2.

Abbreviations: GED = General Educational Development test, NESARC = National Epidemiologic Survey on Alcohol and Related Conditions, SUD = substance use disorder.

help-seeking at either wave to data from those respondents with a past-year SUD at Wave 1 (n = 2,974) and found that individuals with multiple SUDs had significantly greater odds of utilizing substance abuse treatment or other help-seeking than those with an individual SUD (adjusted odds ratio = 3.21; 95% CI, 2.25–4.58).

DISCUSSION

This study represents the first examination of the prevalence, 3-year course, and correlates associated with multiple co-occurring SUDs among US adults based on a nationally representative longitudinal survey. The findings of

Table 4. AORs and 95% CIs in Logistic Regression Models Predicting 4 Wave-Specific Indicators of SUD Status

Sociodemographic or Psychiatric Variable[a]	Model 1[b] No Past-Year SUDs Wave 1 AOR (95% CI)	Model 2 1 Past-Year SUD Wave 1 AOR (95% CI)	Model 3 Multiple Past-Year SUDs Wave 1 AOR (95% CI)	Model 4 Multiple Past-Year SUDs Wave 2 AOR (95% CI)
Sex				
Male	0.37 (0.33–0.41)***	2.46 (2.20–2.75)***	3.36 (2.48–4.55)***	2.60 (1.96–3.45)***
Race/ethnicity				
Black	1.19 (1.04–1.37)*	0.84 (0.72–0.97)*	1.02 (0.68–1.54)	0.96 (0.69–1.33)
Native American	0.83 (0.59–1.18)	0.96 (0.66–1.39)	2.62 (1.27–5.37)*	0.79 (0.39–1.62)
Asian	2.07 (1.38–3.10)**	0.50 (0.31–0.79)**	0.53 (0.16–1.73)	0.51 (0.22–1.16)
Hispanic	1.09 (0.88–1.34)	0.94 (0.75–1.18)	0.81 (0.51–1.29)	0.61 (0.43–0.85)**
Age, y				
30–44	0.44 (0.39–0.51)***	2.15 (1.87–2.47)***	3.84 (2.34–6.28)***	2.45 (1.69–3.56)***
18–29	0.27 (0.23–0.31)***	3.27 (2.81–3.81)***	7.83 (4.75–12.91)***	4.69 (3.17–6.93)***
Marital status				
Divorced/separated	0.53 (0.46–0.61)***	1.82 (1.57–2.10)***	2.40 (1.55–3.73)***	1.90 (1.31–2.74)**
Widowed	0.95 (0.70–1.29)	0.90 (0.66–1.24)	3.73 (1.12–12.44)*	0.23 (0.06–0.85)*
Never married	0.59 (0.52–0.66)***	1.54 (1.35–1.75)***	2.68 (1.93–3.70)***	1.83 (1.39–2.41)***
Personal income				
$35,000–$69,999	1.00 (0.83–1.19)	1.01 (0.84–1.21)	1.30 (0.54–3.16)	1.31 (0.68–2.55)
$20,000–$34,999	1.08 (0.89–1.30)	0.90 (0.75–1.09)	1.79 (0.77–4.13)	1.46 (0.77–2.78)
$19,999 or less	1.31 (1.08–1.59)**	0.71 (0.58–0.86)**	2.09 (0.92–4.73)	1.93 (1.03–3.60)*
Geographical region				
Northeast	0.86 (0.72–1.05)	1.08 (0.89–1.32)	1.78 (1.15–2.74)*	1.09 (0.76–1.56)
Midwest	0.72 (0.61–0.84)***	1.36 (1.15–1.61)**	1.40 (1.00–1.97)	0.82 (0.55–1.22)
West	0.76 (0.65–0.90)**	1.20 (1.02–1.41)*	2.26 (1.52–3.34)***	1.57 (1.11–2.20)*
Sexual identity[a]				
Lesbian/gay	0.67 (0.43–1.05)	1.17 (0.73–1.87)	2.56 (1.30–5.01)**	4.63 (2.30–9.31)***
Bisexual	0.57 (0.35–0.92)*	1.78 (1.10–2.87)*	1.25 (0.32–4.84)	4.24 (2.14–8.41)***
Not sure/unknown	1.18 (0.72–1.94)	0.85 (0.48–1.50)	0.99 (0.32–3.01)	1.10 (0.35–3.50)
Past-year nicotine dependence				
Yes	0.30 (0.26–0.33)***	2.76 (2.41–3.16)***	5.94 (4.24–8.32)***	2.66 (2.08–3.40)***
Past-year anxiety disorders				
1	0.72 (0.62–0.85)***	1.36 (1.16–1.60)***	1.45 (0.96–2.20)	0.99 (0.69–1.44)
2+	0.90 (0.69–1.17)	0.96 (0.72–1.29)	1.77 (1.07–2.95)*	1.33 (0.68–2.61)
Past-year mood disorders				
1	0.63 (0.53–0.74)***	1.47 (1.23–1.76)***	1.86 (1.28–2.69)**	1.56 (1.09–2.22)*
2+	0.60 (0.47–0.77)***	1.28 (0.96–1.72)	2.56 (1.60–4.09)***	1.17 (0.67–2.04)
Lifetime personality disorders				
1	0.64 (0.55–0.75)***	1.41 (1.20–1.66)***	2.34 (1.60–3.42)***	1.69 (1.21–2.34)**
2+	0.53 (0.45–0.64)***	1.56 (1.27–1.90)***	2.94 (1.98–4.36)***	2.06 (1.45–2.91)***

*$P < .05$.
**$P < .01$.
***$P < .001$.
[a]Sociodemographic and psychiatric variables are based on Wave 1 with the exception of sexual identity, which is based on Wave 2. Reference categories for these variables were female, white, 45 years and older, married/partnered, $70,000 or more, South, heterosexual, no, 0, 0, and 0. Sample size is n = 34,653 for all models. Education was not a significant predictor in any model.
[b]Each column represents a separate model, and odds ratios were adjusted for all the sociodemographic and psychiatric variables in each column.
Abbreviations: AOR = adjusted odds ratio, SUD = substance use disorder.

the present study revealed important distinctions related to multiple SUDs that have critical implications for diagnosis, research, and treatment. The present study found a more persistent 3-year course associated with multiple SUDs as compared to individual SUDs over time. US adults with multiple SUDs at Wave 1 of the NESARC were more likely than those with individual SUDs to report subsequent SUDs at Wave 2. Indeed, the majority of US adults with a past-year individual SUD at Wave 1 no longer met criteria for a past-year SUD 3 years later, while the majority of those with multiple past-year SUDs at Wave 1 still met criteria for at least 1 SUD 3 years later. Notably, the same pattern held true for past-year dependence on multiple substances.

There were several subgroups of US adults with increased odds of having multiple SUDs and persistent multiple SUDs, including males, younger adults, never married individuals, sexual minorities, those residing in the Western US Census region, and those with past-year nicotine dependence, past-year anxiety disorders, past-year mood disorders, or lifetime personality disorders. Other cross-sectional national studies have found that similar subgroups of US adults have increased risk of alcohol use disorders and other drug use disorders.[12–16,35] Although prior national longitudinal studies have not examined sociodemographic characteristics and other psychiatric disorders associated with persistent multiple SUDs, there is some evidence that polysubstance use is more prevalent among individuals with higher levels of psychological distress, men who have sex with men, and younger age groups including adolescents and young adults.[4,5,23,36]

We found that the majority of US adults with multiple SUDs had nicotine dependence and that persistent multiple SUDs were associated with nicotine dependence. Prior research has found evidence of a similar association between nicotine dependence and symptomatic other drug use and speculated that this could be the result of analogous effects

Table 5. AORs in Logistic Regression Models Predicting Persistence in SUDs Across Waves (Models 5 and 6) and Substance Abuse Treatment/Help-Seeking at Either Wave Among Individuals With a Past-Year SUD at Wave 1 (Model 7)

Sociodemographic and Psychiatric Variables[a]	Model 5 Multiple Past-Year SUDs at Wave 1 and Wave 2 (n = 31,597) AOR (95% CI)[b]	Model 6 Wave 1 Prior-to-Past-Year SUDs and Multiple Past-Year SUDs at Wave 1 and Wave 2 (n = 31,597) AOR (95% CI)[b]	Model 7 Substance Abuse Treatment or Help-Seeking at Wave 1 or Wave 2 (n = 2,974) AOR (95% CI)[b]
Sex			
Male	5.34 (2.90–9.86)***	5.16 (2.82–9.43)***	1.77 (1.26–2.50)**
Age, y			
30–44	2.96 (1.08–8.08)*	2.88 (1.06–7.84)*	1.25 (0.86–1.81)
18–29	5.62 (2.27–13.89)***	5.48 (2.19–13.73)***	0.53 (0.33–0.87)*
Marital status			
Divorced/separated	2.05 (0.77–5.47)	2.04 (0.76–5.47)	1.35 (0.91–2.02)
Widowed	N/A (all zeroes)[c]	N/A (all zeroes)[c]	1.51 (0.71–3.22)
Never married	2.28 (1.30–4.01)***	2.12 (1.20–3.76)*	1.26 (0.84–1.89)
Geographical region			
Northeast	1.94 (0.96–3.94)	2.17 (1.06–4.42)*	1.00 (0.66–1.50)
Midwest	1.88 (0.97–3.64)	1.87 (0.95–3.67)	1.14 (0.82–1.59)
West	2.05 (1.01–4.13)*	2.19 (1.06–4.54)*	1.29 (0.86–1.93)
Sexual identity[a]			
Lesbian/gay	8.31 (3.22–21.46)***	8.60 (3.32–22.25)***	1.19 (0.53–2.67)
Bisexual	4.08 (0.79–20.94)	4.63 (0.92–23.28)	2.13 (0.84–5.37)
Not sure/unknown	1.98 (0.38–10.27)	2.03 (0.41–10.16)	0.41 (0.07–2.39)
Past-year nicotine dependence			
Yes	4.74 (2.85–7.88)***	4.50 (2.69–7.54)***	1.39 (1.01–1.92)*
Past-year substance use disorders (Wave 1)			
2+	NA	NA	3.21 (2.25–4.58)***
Past-year anxiety disorders			
1	1.76 (0.92–3.37)	1.89 (0.99–3.63)	1.66 (1.11–2.49)*
2+	3.05 (1.31–7.11)*	3.57 (1.51–8.43)**	1.79 (1.07–3.00)*
Past-year mood disorders			
1	1.63 (0.91–2.92)	1.49 (0.82–2.69)	1.75 (1.26–2.43)**
2+	2.90 (1.24–6.76)*	2.62 (1.06–6.48)*	2.22 (1.42–3.45)**
Lifetime personality disorders			
1	1.94 (0.98–3.86)	1.90 (0.95–3.80)	1.03 (0.68–1.56)
2+	1.99 (1.09–3.64)*	1.74 (0.91–3.31)	1.20 (0.80–1.79)

*$P < .05$.
**$P < .01$.
***$P < .001$.
[a]Sociodemographic and psychiatric variables are based on Wave 1 with the exception of sexual identity, which is based on Wave 2. Reference categories for these variables were female, white, 45 years and older, married/partnered, $70,000 or more, South, heterosexual, no, 0, 0, and 0. Race/ethnicity, education, and personal income were not significant predictors in any model.
[b]Each column represents a separate model, and AORs were adjusted for all the sociodemographic and psychiatric variables in each column.
[c]This odds ratio could not be estimated because no individuals in this category had a value of 1 for the dependent variable.
Abbreviations: AOR = adjusted odds ratio, NA = not applicable.

on the reward pathway, shared delivery mechanisms, or common genetic liability.[10] Notably, we found that the majority of US adults with multiple SUDs had a lifetime personality disorder. The finding that multiple SUDs were more prevalent among adults with multiple anxiety, mood, or personality disorders was consistent with previous work identifying a small subset of adults with high rates of psychiatric comorbidity.[15] In addition, several past studies have shown that sexual minorities have higher rates of SUDs relative to heterosexual-identified adults,[37,38] and the current study is the first national study to show that lesbian and gay adults have greater odds of multiple SUDs over time. Despite evidence suggesting major substance-related health disparities among sexual minorities, very little research has examined why such health disparities exist between sexual minority and heterosexual adults.

Prior work indicates that there could be a need to distinguish individual and multiple SUDs because the adverse consequences appear to differ between polysubstance use behaviors and other types of substance use behaviors.[36,39] Despite evidence indicating high rates of polysubstance use behaviors and a more severe 3-year course associated with multiple SUDs, there is no current *DSM-5* diagnosis involving multiple SUDs. Taken together, these findings reinforce the notion that the substance abuse field should move beyond a binary individual drug-specific approach toward diagnosing, studying, and treating individual SUDs to one that takes into greater account multiple SUDs and comorbidity with other psychiatric disorders.[3,22,23]

The findings of the present study raise some important questions about how to best conceptualize, diagnose, and treat individuals with multiple co-occurring SUDs. Although multiple SUDs had a more severe 3-year course and higher degree of comorbidity with other psychiatric disorders, the majority of US adults with multiple SUDs do not utilize substance abuse treatment or seek other help. Although personality disorders were significantly associated with multiple SUDs and persistent multiple

SUDs, personality disorders did not predict substance abuse treatment or help-seeking behaviors. Prior work found similar strong associations between persistence of drug use disorders and antisocial, borderline, or schizotypal personality disorders and noted that treating these types of comorbid disorders poses unique challenges because these individuals might be unable to recognize their disorders and/or reflect that their symptoms merit change.[11] In contrast, we found that both anxiety and mood disorders increased the probability of substance abuse treatment or other help-seeking. At least 2 studies[40,41] have found that patients with comorbid bipolar disorder and substance dependence had fewer days of substance use following integrated group therapy, which addressed the 2 disorders simultaneously, than group drug counseling alone. Future research should examine whether treating multiple SUDs and comorbid psychiatric disorders simultaneously is more effective than treating each disorder individually and sequentially based on severity.

There were several strengths that are noteworthy based on the objectives of the present study. Both waves of the NESARC used similar methodology and survey wording, which allowed for valid comparisons of estimates based on data collected over time, including identical criteria to assess SUDs at both waves. The large, nationally representative sample of the NESARC allowed for calculation of national prevalence estimates for sociodemographic characteristics, SUDs, other psychiatric disorders, substance abuse treatment, and other help-seeking behaviors. Notably, attrition was higher among individuals with no SUDs, which is consistent with recent studies of this phenomenon.[42,43]

There were also some limitations that should be taken into account while considering implications of the findings. First, the NESARC only sampled individuals aged 18 years and older, and patterns of multiple SUDs may differ for adolescents. Future studies are needed that examine potential differences in the course of multiple SUDs among adolescents and adults, including those that incorporate nicotine use disorder. Second, the NESARC was limited to 2 waves only 3 years apart; future longitudinal studies are needed to examine the long-term developmental course of multiple SUDs over a more extensive time period that includes childhood and adolescence, including studies with more than 2 waves that would enable assessment of any causal relationships of the sociodemographic factors and other predictors with persistence of multiple SUDs. Finally, the NESARC was interviewer-administered, so caution should be exercised when comparing results from these studies and other sources of data based on different modes of data collection; the survey methodology literature suggests that our estimates may be biased on the low side, given the ability of self-administered modes to generate more frequent reports of sensitive behaviors like drug use.[44]

In conclusion, the present study extends prior work by demonstrating a more persistent 3-year course associated with multiple SUDs as compared to individual SUDs over time among US adults. There were important differences in the 3-year course of individual SUDs versus multiple SUDs. We hope that these findings will enhance the diagnosis and treatment of multiple SUDs and lead to more focused research regarding the long-term developmental course, trends, and remission and relapse rates associated with multiple SUDs.

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REFERENCES

1. Armour C, Shorter GW, Elhai JD, et al. Polydrug use typologies and childhood maltreatment in a nationally representative survey of Danish young adults. *J Stud Alcohol Drugs*. 2014;75(1):170–178.
2. Oliveira LG, Alberghini DG, dos Santos B, et al. Polydrug use among college students in Brazil: a nationwide survey. *Rev Bras Psiquiatr*. 2013;35(3):221–230.
3. Moss HB, Chen CM, Yi HY. Early adolescent patterns of alcohol, cigarettes, and marijuana polysubstance use and young adult substance use outcomes in a nationally representative sample. *Drug Alcohol Depend*. 2014;136:51–62.
4. Olthuis JV, Darredeau C, Barrett SP. Substance use initiation: the role of simultaneous polysubstance use. *Drug Alcohol Rev*. 2013;32(1):67–71.
5. Quek L-H, Chan GCK, White A, et al. Concurrent and simultaneous polydrug use: latent class analysis of an Australian nationally representative sample of young adults. *Front Public Health*. 2013;1:61.
6. Reyes CR, Perez CM, Colon HM, et al. Prevalence and patterns of polydrug use in Latin America: analysis of population-based surveys in six countries. *Review of European Studies*. 2013;5(1):10–18.
7. Smith GW, Farrell M, Bunting BP, et al. Patterns of polydrug use in Great Britain: findings from a national household population survey. *Drug Alcohol Depend*. 2011;113(2–3):222–228.
8. Huang B, Dawson DA, Stinson FS, et al. Prevalence, correlates, and comorbidity of nonmedical prescription drug use and drug use disorders in the United States: results of the National Epidemiologic Survey on Alcohol and Related Conditions. *J Clin Psychiatry*. 2006;67(7):1062–1073.
9. Compton WM, Thomas YF, Stinson FS, et al. Prevalence, correlates, disability, and comorbidity of *DSM-IV* drug abuse and dependence in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2007;64(5):566–576.
10. Compton WM, Dawson DA, Conway KP, et al. Transitions in illicit drug use status over 3 years: a prospective analysis of a general population sample. *Am J Psychiatry*. 2013;170(6):660–670.
11. Fenton MC, Keyes K, Geier T, et al. Psychiatric comorbidity and the persistence of drug use disorders in the United States. *Addiction*. 2012;107(3):599–609.
12. Grant BF, Saha TD, Ruan WJ, et al. Epidemiology of *DSM-5* drug use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions-III. *JAMA Psychiatry*. 2016;73(1):39–47.
13. Grant BF, Stinson FS, Dawson DA, et al. Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry*. 2004;61(8):807–816.
14. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of

DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):593–602.
15. Kessler RC, Chiu WT, Demler O, et al. Prevalence, severity, and comorbidity of 12-month *DSM-IV* disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005;62(6):617–627.
16. Lasser K, Boyd JW, Woolhandler S, et al. Smoking and mental illness: a population-based prevalence study. *JAMA*. 2000;284(20):2606–2610.
17. McCabe SE, Cranford JA, West BT. Trends in prescription drug abuse and dependence, co-occurrence with other substance use disorders, and treatment utilization: results from two national surveys. *Addict Behav*. 2008;33(10):1297–1305.
18. Regier DA, Farmer ME, Rae DS, et al. Comorbidity of mental disorders with alcohol and other drug abuse: results from the Epidemiologic Catchment Area (ECA) Study. *JAMA*. 1990;264(19):2511–2518.
19. Lipari RN, Hedden SL, Hughes A. Substance Use and Mental Health Estimates from the 2013 National Survey on Drug Use and Health: Overview of Findings. In: *The CBHSQ Report*. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2014.
20. Swendsen J, Conway KP, Degenhardt L, et al. Mental disorders as risk factors for substance use, abuse and dependence: results from the 10-year follow-up of the National Comorbidity Survey. *Addiction*. 2010;105(6):1117–1128.
21. Warner LA, Kessler RC, Hughes M, et al. Prevalence and correlates of drug use and dependence in the United States: results from the National Comorbidity Survey. *Arch Gen Psychiatry*. 1995;52(3):219–229.
22. Compton WM, Thomas YF, Conway KP, et al. Developments in the epidemiology of drug use and drug use disorders. *Am J Psychiatry*. 2005;162(8):1494–1502.
23. Connor JP, Gullo MJ, White A, et al. Polysubstance use: diagnostic challenges, patterns of use and health. *Curr Opin Psychiatry*. 2014;27(4):269–275.
24. Grant BF, Kaplan K, Shepard K, et al. *Source and Accuracy Statement for Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*. Bethesda, MD: National Institute on Alcohol Abuse and Alcoholism; 2003.
25. Grant BF, Kaplan KD. *Source and Accuracy Statement for the Wave 2 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)*. Rockville, MD: National Institute on Alcohol Abuse and Alcoholism; 2005.
26. Grant BF, Hasin DS, Stinson FS, et al. Co-occurrence of 12-month mood and anxiety disorders and personality disorders in the US: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *J Psychiatr Res*. 2005;39(1):1–9.
27. Grant BF. *DSM-IV*, *DSM-III-R*, and *ICD-10* alcohol and drug abuse/harmful use and dependence, United States, 1992: a nosological comparison. *Alcohol Clin Exp Res*. 1996;20(8):1481–1488.
28. Grant BF, Dawson DA, Stinson FS, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule-IV (AUDADIS-IV): reliability of alcohol consumption, tobacco use, family history of depression and psychiatric diagnostic modules in a general population sample. *Drug Alcohol Depend*. 2003;71(1):7–16.
29. Grant BF, Harford TC, Dawson DA, et al. The Alcohol Use Disorder and Associated Disabilities Interview schedule (AUDADIS): reliability of alcohol and drug modules in a general population sample. *Drug Alcohol Depend*. 1995;39(1):37–44.
30. Hasin D, Carpenter KM, McCloud S, et al. The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS): reliability of alcohol and drug modules in a clinical sample. *Drug Alcohol Depend*. 1997;44(2–3):133–141.
31. Hasin D, Grant BF, Cottler L, et al. Nosological comparisons of alcohol and drug diagnoses: a multisite, multi-instrument international study. *Drug Alcohol Depend*. 1997;47(3):217–226.
32. Hasin D, Li Q, Mccloud S, et al. Agreement between *DSM-III*, *DSM-III-R*, *DSM-IV* and *ICD-10* alcohol diagnoses in US community-sample heavy drinkers. *Addiction*. 1996;91(10):1517–1527.
33. Nelson CB, Rehm J, Usten B, et al. Factor structure for *DSM-IV* substance disorder criteria endorsed by alcohol, cannabis, cocaine and opiate users: results from the WHO Reliability and Validity Study. *Addiction*. 1999;94:843–855.
34. Pull CB, Saunders JB, Mavreas V, et al. Concordance between *ICD-10* alcohol and drug use disorder criteria and diagnoses as measured by the AUDADIS-ADR, CIDI and SCAN: results of a cross-national study. *Drug Alcohol Depend*. 1997;47(3):207–216.
35. Stinson FS, Grant BF, Dawson DA, et al. Comorbidity between *DSM-IV* alcohol and specific drug use disorders in the United States: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Drug Alcohol Depend*. 2005;80(1):105–116.
36. McCabe SE, Cranford JA, Morales M, et al. Simultaneous and concurrent polydrug use of alcohol and prescription drugs: prevalence, correlates, and consequences. *J Stud Alcohol*. 2006;67(4):529–537.
37. Hughes T, McCabe SE, Wilsnack SC, et al. Victimization and substance use disorders in a national sample of heterosexual and sexual minority women and men. *Addiction*. 2010;105(12):2130–2140.
38. McCabe SE, West BT, Hughes TL, et al. Sexual orientation and substance abuse treatment utilization in the United States: results from a national survey. *J Subst Abuse Treat*. 2013;44(1):4–12.
39. Abé C, Mon A, Durazzo TC, et al. Polysubstance and alcohol dependence: unique abnormalities of magnetic resonance-derived brain metabolite levels. *Drug Alcohol Depend*. 2013;130(1-3):30–37.
40. Weiss RD, Griffin ML, Jaffee WB, et al. A "community-friendly" version of integrated group therapy for patients with bipolar disorder and substance dependence: a randomized controlled trial. *Drug Alcohol Depend*. 2009;104(3):212–219.
41. Weiss RD, Griffin ML, Kolodziej ME, et al. A randomized trial of integrated group therapy versus group drug counseling for patients with bipolar disorder and substance dependence. *Am J Psychiatry*. 2007;164(1):100–107.
42. Dawson DA, Goldstein RB, Pickering RP, et al. Nonresponse bias in survey estimates of alcohol consumption and its association with harm. *J Stud Alcohol Drugs*. 2014;75(4):695–703.
43. McCabe SE, West BT. Selective nonresponse bias in population-based survey estimates of drug use behaviors in the United States. *Soc Psychiatry Psychiatr Epidemiol*. 2016;51(1):141–153.
44. Turner CF, Villarroel MA, Rogers SM, et al. Reducing bias in telephone survey estimates of the prevalence of drug use: a randomized trial of telephone audio-CASI. *Addiction*. 2005;100(10):1432–1444.