Cigarette Smoking Is Associated With Increased Risk of Substance Use Disorder Relapse:

A Nationally Representative, Prospective Longitudinal Investigation

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ABSTRACT

Objective: Little is known about the relationship between cigarette smoking and long-term outcomes for substance use disorder (SUD). The current study examined the association between smoking and SUD relapse among adults with remitted SUDs.

Methods: Analyses were conducted on respondents who completed Waves 1 and 2 of the National Epidemiologic Survey on Alcohol and Related Conditions and met *DSM-IV* criteria for substance abuse and dependence prior to but not during the year before the Wave 1 interview (n = 5,515). Relationships between smoking status (Wave 2 smoking vs nonsmoking among Wave 1 smokers; Wave 2 smoking vs nonsmoking among Wave 1 nonsmokers) and Wave 2 substance use and SUD relapse were examined using logistic regression analyses. Analyses were adjusted for demographics, psychiatric and alcohol use disorders, nicotine dependence, and SUD severity.

Results: In the fully adjusted models, continued smoking at Wave 2 among Wave 1 smokers was associated with significantly greater odds of substance use (OR = 1.56, 95% CI, 1.10–2.20) and SUD relapse (OR = 2.02, 95% CI, 1.65–2.47) compared to Wave 2 nonsmoking. In the fully adjusted model, smoking at Wave 2 among Wave 1 nonsmokers was associated with significantly greater odds of SUD relapse compared to Wave 2 nonsmoking (OR = 4.86, 95% CI, 3.11–7.58).

Conclusions: Continued smoking among smokers and smoking initiation among nonsmokers were associated with greater odds of SUD relapse. More research is needed to examine the timing of SUD relapse in relation to smoking behaviors. Incorporating smoking cessation and prevention efforts into substance abuse treatment may improve long-term substance use outcomes for adult smokers with SUDs.

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Illicit substance use and substance use disorders (SUDs) are growing public health concerns in the United States. In 2011, an estimated 22.5 million Americans, roughly 8.7% of the population aged 12 years or older, were current or past-month users of illicit drugs, including marijuana/hash, cocaine (including crack), heroin, hallucinogens, inhalants, or prescription medicine used non-therapeutically.[1] One hundred thirteen people die from drug overdose every day in the United States, and over 6,700 people are treated daily in emergency departments for drug misuse or abuse.[1] In the United States, opioid abuse accounts for nearly $55.7 billion divided up among attributable workplace costs, health care costs, and criminal justice costs.[2,3] Further, illicit drug abuse is growing in popularity as demonstrated by a 118% increase from 1992 to 2011.[1]

While the use of illicit drugs is increasing, the use of cigarettes in the United States has been declining. The prevalence of smoking among US adults has declined from 42% in 1964, the year of the Surgeon General's first report about the health consequences of smoking, to 18% in 2012, although the decline has slowed in recent years.[4] Cigarette smoking causes more than 480,000 deaths each year in the United States,[4,5] roughly 20% of all yearly deaths,[4] and leads to an increased number of deaths when combined with illicit substance abuse.[6–8]

Illicit substance use and smoking behaviors are highly comorbid. Cross-sectional epidemiologic data from the US adult population suggest that more than half (53.6%) of adults with a lifetime SUD diagnosis and two-thirds (66.7%) of adults with a past-year SUD diagnosis are current smokers.[9] Rates of lifetime smoking among adults with lifetime or past-year SUDs reach three-quarters or more (75.4% and 77.6%, respectively[9]). Further, clinical data consistently report smoking prevalences ranging from 77% to 88% among patients in treatment for substance use problems.[10–12]

While smoking is common among the vast majority of people who enter treatment for SUD, and nicotine dependence itself is an SUD, smoking cessation therapy is neither a standard part of care nor required as a component of SUD treatment. Tobacco use disorder is the sole SUD for which treatment is not consistently integrated into treatment programs for other SUDs. Further, required abstinence from cigarettes may not be actively encouraged or theoretically linked with recovery or with the notion of becoming "drug-free" in many cases. Clinical lore has been that quitting both illicit substances and cigarettes may be "too difficult," all at once, yet data are beginning to suggest that not doing so may lead to poorer outcomes. For example,

Clinical Points

- Historically in clinical settings, it has been suggested that quitting cigarette smoking while also addressing drug treatment would be too difficult and that continued smoking has no impact on long-term outcomes of substance use treatment or abstinence. While a majority of persons in treatment for substance use disorders also use cigarettes, smoking cessation treatments are not routinely offered in the same treatment setting.
- The authors found that, among adults with remitted substance use disorders, those who were smokers and reported continued smoking 3 years later had increased odds of substance use and relapsing to substance use disorders compared to those who were no longer smoking. Those who were nonsmokers and reported smoking 3 years later had increased odds of relapsing to substance use disorders compared to those who continued to be nonsmokers.
- Future research should examine how the inclusion of smoking prevention and cessation programs in substance use treatment impacts long-term abstinence from illicit substance use.

data from clinical samples of adults in treatment for SUDs suggest that quitting smoking does not harm SUD treatment outcomes,[13,14] whereas continued use of cigarettes after cannabis treatment was associated with relapse to cannabis use in adolescents.[15] Cross-sectional epidemiologic data have suggested that nicotine dependence is associated with an increased likelihood of cocaine dependence remission.[16] While many people with SUDs will quit using substances for varying lengths of time, a primary feature of substance use disorders is that attempts to cut down or stop using substances are unsuccessful,[17] so it is critical that research on SUDs examines not just quit attempts but also long-term success at avoiding relapse. To our knowledge, no prior epidemiologic study has prospectively examined the relationship between cigarette smoking over time and the risk of relapse to SUDs among adults in remission from an SUD.

The current study used longitudinal data from a representative sample of US adults who completed 2 assessments that occurred 3 years apart in order to compare the risk of SUD relapse among respondents with remitted SUDs by smoking status using data on smoking from both assessment timepoints. The first aim of the study was to examine the risk of (1) substance use and (2) SUD relapse among adults with remitted SUDs at the end of the 3-year study period for 2 distinct populations: those who initiated smoking compared to those who reported never smoking among respondents who were not smoking at Wave 1, and those who continued smoking compared to those who quit smoking among respondents who were smoking at Wave 1. The second aim of the study was to examine the relationships between smoking status and risk of substance use and SUD relapse after controlling for demographics; mood, anxiety, and personality disorders; alcohol use disorders; nicotine dependence; and severity of remitted SUD.

METHODS

Data Source and Study Population

Study data were taken from a subsample of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), an assessment of substance use, SUDs, and related physical and psychiatric conditions in a representative sample of the US population of civilian non-institutionalized adults. The study had a 2-wave multistage stratified design in which primary sampling units, housing units, and group-quarter units were stratified to collect data on certain underrepresented sociodemographic criteria. Specifically, non-Hispanic black, Hispanic, and young adult (ages 18–24 years) units were selected at higher rates than other housing units. The final data were weighted according to the demographic distribution of the US population based on the 2000 census. Experienced lay interviewers completed Wave 1 interviews of 43,093 respondents in 2001–2002. Wave 2 interviews occurred 3 years later with 34,653 (80%) of the Wave 1 respondents. Study design and administration details have been described elsewhere.[18,19] The original data sets for the NESARC were obtained from the National Institute on Alcohol Abuse and Alcoholism (NIAAA, http://www.niaaa.nih.gov), and researchers can currently request specific analyses of the data sets through the NIAAA. Our subsample included respondents who completed both waves of data collection and reported a history of any substance use, abuse, or dependence prior to but not during the year before Wave 1 interview (N = 5,515; 12.8% of the original Wave 1 sample).

Measures

Substance use status. The 2 primary outcomes under investigation were substance use and SUD relapse (ie, diagnoses of substance abuse or dependence) as measured at the Wave 2 follow-up assessment. The SUD diagnoses assessed in Wave 2 of NESARC included *DSM-IV* substance-specific abuse and dependence for 10 substance types: sedatives, tranquilizers, opioids, heroin, amphetamines, cannabis, cocaine, hallucinogens, inhalants/solvents, and other drug categories.[20] Disorder diagnosis was determined by using the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule—*Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition (*DSM-IV*) Version (AUDADIS-IV), a fully structured diagnostic interview instrument.[21] The reliability of the AUDADIS has been shown to be good to excellent for the assessment of SUDs in the general population ($\kappa = 0.63–0.99$)[22] and in a clinical sample of adults in outpatient and inpatient treatment for SUDs ($\kappa = 0.57–0.83$).[23] A respondent who endorsed any type of substance use, abuse, or dependence was classified as having a positive outcome. Those with no reported substance use behaviors were classified as having no substance use. Participants who endorsed the use of any substance and did not meet criteria for abuse or dependence for any substance were classified as positive for substance use at Wave 2. Participants who met criteria for abuse or dependence for at least 1 substance at Wave 2 were classified

as positive for SUD relapse at Wave 2. The relapse of substance abuse and substance dependence was each modeled as a separate outcome, but because the reported prevalence of substance dependence was low, the SUD relapse outcome included participants who met criteria for either substance abuse or substance dependence (or both). The categories of substance use and SUD relapse were mutually exclusive and were compared to the reference group of respondents who reported no substance use at Wave 2. To accurately capture the temporality of the relapse, the baseline study sample was limited to respondents with a lifetime history of SUD but who reported no substance use or SUD remission for at least 1 year prior to Wave 1. We also considered 3 measures of SUD severity—the duration of the longest episode of substance abuse (in months), the number of episodes of abuse, and the age at onset of abuse—to investigate if our association of interest was due solely to a smaller subpopulation of the most severe cases of SUDs.

Tobacco use and nicotine dependence. Tobacco use was assessed for 5 tobacco products: cigarettes, cigars, pipe tobacco, snuff, and chewing tobacco. Smoking status was classified using data on cigarette smoking from both the Wave 1 and Wave 2 assessments and was defined as 2 dichotomous variables based on definitions used by the US Department of Health and Human Services' Centers for Disease Control and Prevention.[24] Wave 2 nonsmoking was defined as smoking fewer than 100 lifetime cigarettes at Wave 1 (ie, did not meet criteria for lifetime smoking) and no past-year smoking at Wave 2. Wave 2 initiated smoking included those who reported smoking fewer than 100 lifetime cigarettes at Wave 1 and past-year use of cigarettes at Wave 2. Wave 2 quit smoking was defined as a report of lifetime smoking of 100 or more cigarettes at Wave 1 and a report of no past-year smoking at the Wave 2 follow-up. Wave 2 continued smoking was defined as a report of lifetime smoking of 100 or more cigarettes at Wave 1 and past-year cigarette smoking at Wave 2. To accurately measure the association of cigarette use and substance use relapse, participants who reported use of other forms of tobacco (eg, cigars, pipes, snuff, chewing tobacco) were included in the sample only if respondents also reported cigarette use. Lifetime nicotine dependence diagnosis was based on meeting 4 criteria from the AUDADIS module on nicotine dependence disorder: experiencing withdrawal, giving up activities in favor of nicotine use, spending a great deal of time using nicotine, and using nicotine more than intended.[25] The AUDADIS has been shown to have good reliability in the general population for the assessment of smoking behavior (intraclass coefficients = 0.60–0.92) and nicotine dependence ($\kappa = 0.60–0.63$).[26]

Sociodemographic covariates and other potential confounders. Sociodemographic covariates were considered in the analysis and added to a series of multivariable-adjusted models. Variables included sex, age, education, race/ethnicity groups (Asian/Pacific Islander, non-Hispanic black, Hispanic, Native American/Alaskan, and non-Hispanic white), marital status (married/living with someone as married, widowed, divorced/separated, single), and income. Sex, race/ethnicity, and marital status were added as discrete variables, while age, education, and income were continuous.

A summary dichotomous variable was also created to adjust for a range of lifetime psychiatric disorders reported at Wave 2, including *DSM-IV* major depression, bipolar disorder, dysthymia, hypomania, panic disorder with or without agoraphobia, agoraphobia, social and specific phobia, generalized anxiety disorder, posttraumatic stress disorder, attention-deficit/hyperactivity disorder, antisocial personality disorder, borderline personality disorder, schizotypal personality disorder, and narcissistic personality disorder. Two binary alcohol use covariates were also considered in our models: one adjusted for any lifetime alcohol abuse or dependence as reported at Wave 2 and one adjusted for nondisordered alcohol use (ie, participants who reported alcohol use but did not meet criteria to receive a diagnosis of either abuse or dependence). In addition, covariates related to the severity of the outcome were considered, including the disorder duration, frequency, and age at onset.

Statistical Analysis

Sample frequencies. The Rao-Scott χ^2 test, which accounts for the complex survey design, was used to test if the demographics were statistically significant among smoking status groups. The Rao-Scott χ^2 test was also used to test for significant differences between the Wave 2 smoking statuses (Wave 2 smoking vs nonsmoking among Wave 1 smokers; Wave 2 smoking vs nonsmoking among Wave 1 nonsmokers) and the 3 possible Wave 2 substance use outcome groups (no substance use, substance use, SUD relapse).

Regression modeling. Two separate sets of logistic regression models were created to address the second study aim. The first set of models included a sample of only nonsmokers at Wave 1. In this population, we examined the association between past-year smoking at Wave 2 (ie, initiated smoking) vs no past-year smoking (ie, nonsmoking) at Wave 2 and (1) Wave 2 substance use and (2) Wave 2 SUD relapse. The second set of models included a sample of those who reported current smoking at Wave 1. In this population, we examined the association between no past-year smoking (ie, quit smoking) at Wave 2 vs past-year smoking at Wave 2 (ie, continued smoking) and (1) Wave 2 substance use and (2) Wave 2 SUD relapse. Outcomes were analyzed as a 3-level categorical variable using those with no substance use as the reference group. Models were run to determine the unadjusted odds ratio of (1) substance use and (2) SUD relapse by the smoking status groups (Wave 1 smokers: Wave 2 continued smoking vs quit smoking; Wave 1 nonsmokers: Wave 2 initiated smoking vs nonsmoking). Then, 4 additional models were run for each of the 2 outcome variables (substance use, SUD relapse) to adjust for the potential confounders and covariates. The first of these models adjusted for sociodemographic covariates. A second model adjusted for lifetime history of psychiatric disorders. The third model adjusted for nondisordered

Table 1. Sample Frequencies of Demographic Categories by Smoking Status in Waves 1 and 2

	Wave 1 Nonsmoking				Wave 1 Current Smoking			
Demographic Category[a]	Total (n = 3,458)	Wave 2 Nonsmoker[b]	Wave 2 Initiated Smoking[c]	*P*	Total (n = 2,057)	Wave 2 Quit Smoking[d]	Wave 2 Continued Smoking[e]	*P*
Total, n (%)	…	3,291 (95.2)	167 (4.8)		…	397 (19.3)	1,660 (80.7)	
Sex								
Men	51.5	50.9	64.4	<.0001	57.6	56.6	57.8	.489
Women	48.5	49.1	35.6		42.4	43.4	42.2	
Age, y								
18–29	11.7	11.2	22.2	<.0001	19.1	22.3	18.4	<.0001
30–44	40.0	39.8	44.3		41.9	45.7	41.0	
45–64	43.1	43.7	31.8		37.4	29.8	39.1	
65+	5.1	5.3	1.6		1.6	2.2	1.5	
Race/ethnicity								
Non-Hispanic white	77.4	77.4	78.5	.115	79.2	74.0	80.3	<.0001
Non-Hispanic black	9.5	9.6	9.0		8.6	8.5	8.6	
Non-Hispanic Native American/Alaska native	2.4	2.4	3.3		3.7	2.5	4.0	
Non-Hispanic Asian/Pacific Islander	2.0	1.9	2.9		1.6	1.4	1.7	
Hispanic	8.6	8.8	6.3		6.9	13.6	5.4	
Marital status								
Current	71.7	71.8	70.3	.033	59.8	61.6	59.4	<.0001
Previous	14.4	14.5	13.0		22.2	17.5	23.2	
Never	13.9	13.7	16.7		18.0	20.8	17.4	
Personal income, $								
0–19,999	29.8	29.7	31.5	.010	36.7	34.0	37.3	<.0001
20,000–34,999	19.9	19.7	24.5		25.5	23.1	26.0	
35,000–69,999	32.1	32.3	27.5		29.2	29.1	29.3	
70,000+	18.2	18.3	16.6		8.6	13.8	7.5	
Education								
Less than high school degree	6.1	6.0	7.6	.001	13.4	10.0	14.2	<.0001
High school degree	41.7	41.3	48.9		56.6	49.3	58.2	
More than high school	52.2	52.7	43.5		30.0	40.6	27.6	
Current use of each tobacco product at Wave 1[f]								
Cigarettes	0.0	0.0	0.0	…[g]	100.0	100.0	100.0	…[g]
Cigars	0.0	0.0	0.0	…[g]	7.1	6.4	7.3	.356
Pipe	0.0	0.0	0.0	…[g]	1.1	1.1	1.1	.821
Snuff	0.0	0.0	0.0	…[g]	5.6	4.8	5.8	.455
Chewing tobacco	0.0	0.0	0.0	…[g]	1.9	1.3	2.0	.349
Lifetime nicotine dependence[h]	1.33	0.0	27.4	<.0001	65.6	52.6	68.5	…[g]

[a]Values shown as percentages unless otherwise specified.
[b]A report of smoking fewer than 100 lifetime cigarettes at Wave 1 and no past-year smoking at Wave 2.
[c]A report of smoking fewer than 100 lifetime cigarettes at Wave 1 and past-year smoking at Wave 2.
[d]A report of lifetime smoking of 100 or more cigarettes at Wave 1 and no past-year smoking at Wave 2.
[e]A report of lifetime smoking of 100 or more cigarettes at Wave 1 and past-year smoking at Wave 2.
[f]Smoker sample includes those who reported smoking cigarettes, with or without other tobacco use; percentages are the number of respondents reporting use of the product out of the full analytic sample.
[g]*P* values could not be calculated due to 0 frequency cells.
[h]Assessed at Wave 2.
Symbol: … = not applicable.

alcohol use, lifetime history of alcohol abuse or dependence, and nicotine dependence. The fourth model adjusted for all covariates in models 1–3 and the 3 measures of SUD severity (duration, frequency, age at onset). Results from all 5 models are presented with unadjusted odds ratios (ORs), adjusted ORs (AORs), and 95% confidence intervals (CIs).

Sensitivity analyses. To further examine the specificity and robustness of our study associations, several sensitivity analyses were completed. To examine any dose-response effect of smoking on the study outcomes, a supplementary set of models tested the association between the quantity of cigarettes reported by Wave 1 smokers who reported smoking at Wave 2 and Wave 1 nonsmokers who reported smoking at Wave 2 and the odds of substance use or SUD at Wave 2. A second sensitivity analysis limited the outcome variable to only those who reported substance dependence at Wave 2 (ie, excluding respondents who reported substance abuse) to test the specificity of our results to the respondents with the most clinically problematic use of substances.

All tests were completed in STATA using weighted analysis (StataCorp, 2011) to account for residual differences between the sample and the population profile, according to the 2000 United States Population Census, as well as to account for nonresponse and sample attrition. The weighted Wave 2 data represent the same baseline population as represented in Wave 1.

RESULTS

Demographic Characteristics

Among the analytic sample of Wave 1 nonsmokers (n = 3,458), 4.9% reported initiating smoking at Wave 2.

Table 2. Wave 2 Substance Use and SUD Relapse by Smoking Status Between Waves 1 and 2, Among Individuals With a History of Illicit Substance Use, Abuse, or Dependence Prior to Wave 1

	Total		Wave 2 Nonsmoking[a]		Wave 2 Initiated Smoking[b]		
Wave 2 Substance Use Status	n	%	n	%	n	%	*P*
Wave 1 nonsmoking: Wave 2 nonsmoking vs initiated smoking (n = 3,458)							
Wave 2 no substance use	3,167	91.2	3,033	91.7	134	80.3	<.0001
Wave 2 substance use	226	6.7	210	6.6	16	8.8	
Wave 2 SUD relapse[c]	65	2.1	48	1.7	17	10.9	
	Total		Wave 2 Quit Smoking[d]		Wave 2 Continued Smoking[e]		
	n	%	n	%	n	%	*P*
Wave 1 smoking: Wave 2 quit smoking vs continued smoking (n = 2,057)							
Wave 2 no substance use	1,765	85.5	357	90.3	1,408	84.5	<.0001
Wave 2 substance use	210	10.4	32	7.5	178	11.0	
Wave 2 SUD relapse[c]	82	4.1	8	2.2	74	4.5	

[a]A report of smoking fewer than 100 lifetime cigarettes at Wave 1 and no past-year smoking at Wave 2.
[b]A report of smoking fewer than 100 lifetime cigarettes at Wave 1 and past-year smoking at Wave 2.
[c]Met criteria for abuse or dependence of at least 1 substance at Wave 2.
[d]A report of lifetime smoking of 100 or more cigarettes at Wave 1 and no past-year smoking at Wave 2.
[e]A report of lifetime smoking of 100 or more cigarettes at Wave 1 and past-year smoking at Wave 2.
Abbreviation: SUD = substance use disorder.

Among the sample of Wave 1 smokers (n = 2,057), 81.7% reported continued smoking at Wave 2. The analytic sample identified primarily as non-Hispanic white and currently married. Approximately half of the sample was female, and the majority of the sample had a high school degree or more. Table 1 lists the complete demographic frequencies by Wave 2 smoking status (Wave 1 nonsmoker, Wave 1 smoker) and by Wave 2 smoking classification.

Substance Use and SUD Relapse at Wave 2

Table 2 presents the prevalences of no substance use, substance use, and SUD relapse at Wave 2 by smoking status. Among Wave 1 nonsmokers, prevalences of Wave 2 substance use and SUD relapse were significantly higher for Wave 1 nonsmokers who initiated smoking at Wave 2 compared to Wave 1 nonsmokers who were also Wave 2 nonsmokers. Among Wave 1 smokers, the prevalences of Wave 2 substance use and SUD relapse were significantly higher for Wave 1 smokers who had continued smoking at Wave 2 compared to Wave 1 smokers who had quit smoking at Wave 2. The highest prevalence of Wave 2 SUD relapse was found for adults who were lifetime nonsmokers at Wave 1 and had engaged in past-year smoking by Wave 2 (10.9%).

Wave 2 Substance Use and SUD Relapse by Smoking Status

In the fully adjusted model (labeled AOR[8]), Wave 1 nonsmokers who had initiated smoking at Wave 2 had 4.86 times the odds of reporting Wave 2 SUD relapse (95% CI, 3.11–7.58) compared to Wave 2 nonsmokers. Wave 1 nonsmokers who had initiated smoking at Wave 2 reported no greater odds of reporting substance use (OR = 0.92; 95% CI, 0.75–1.12) compared to Wave 2 nonsmokers. Among Wave 1 smokers, those who continued smoking at Wave 2 reported 1.56 times greater odds of substance use (95% CI, 1.10–2.20) and 2.02 times greater odds of SUD relapse (95% CI, 1.65–2.47) compared to smokers who did not report smoking at Wave 2 in the fully adjusted models. Unadjusted odds ratios were slightly larger, but the resulting changes to the model parameters were slight after adjusting for demographics; lifetime mood, anxiety, or personality disorders; lifetime alcohol use disorder; nicotine use disorder; and severity of substance use. Complete model results are presented in Table 3.

Sensitivity Analyses

The fully adjusted models were also re-run with an additional covariate for the number of daily cigarettes smoked in a sensitivity analysis to examine if the quantity of cigarettes smoked was associated with an increase in the odds of substance use or SUD at Wave 2. Those who reported smoking at Wave 1 smoked a mean of 17.7 (SE = 0.19) cigarettes per day, while those who initiated smoking at Wave 2 smoked a mean of 13.1 (SE = 0.15) cigarettes per day. The odds of Wave 2 SUD relapse increased by 2.4% with each additional daily cigarette smoked by nonsmokers at Wave 1 who reported smoking at Wave 2 (95% CI, 1.8%–2.9%), while the odds of Wave 2 SUD relapse increased by 0.7% with each additional daily cigarette smoked by smokers at Wave 1 who also reported smoking at Wave 2 (95% CI, 0.2%–1.1%). The odds of Wave 2 substance use did not significantly increase with the number of daily cigarettes smoked in either group.

Table 3. Odds of Wave 2 Substance Use and SUD Relapse by Smoking Status Between Waves 1 and 2 Among Individuals With a History of Illicit Substance Use or Abuse/Dependence Prior to Wave 1

W2 substance use status	OR	95% CI	AOR[a]	95% CI	AOR[b]	95% CI	AOR[c]	95% CI	AOR[d]	95% CI
Wave 2 initiated smoking vs Wave 2 nonsmoking (n = 3,458)[e]										
Wave 2 no substance use	1.0	…	1.0	…	1.0	…	1.0	…	1.0	…
Wave 2 substance use[c]	1.36	1.16 –1.60	1.09	0.96–1.25	1.28	1.10–1.49	1.28	1.08–1.51	0.92	0.75–1.12
Wave 2 SUD relapse[d]	7.17	5.50–9.35	5.30	3.70–7.58	5.97	4.51–7.89	6.90	5.28–9.01	4.86	3.11–7.58
Wave 2 continued smoking vs Wave 2 quit smoking (n = 2,057)[f]										
Wave 2 no substance use	1.0	…	1.0	…	1.0	…	1.0	…	1.0	…
Wave 2 substance use[g]	1.52	1.14–2.03	2.03	1.76–2.34	1.48	1.11–1.97	1.55	1.15–2.10	1.56	1.10–2.20
Wave 2 SUD relapse[h]	2.11	1.87–2.37	1.40	1.04–1.90	1.91	1.69–2.15	2.17	1.93–2.45	2.02	1.65–2.47

[a]Adjusted for age, sex, income, race, education, and marital status.
[b]Adjusted for any lifetime mood, anxiety, or personality disorders.
[c]Adjusted for non-disordered alcohol use, any lifetime alcohol use disorders, and nicotine dependence.
[d]Adjusted for all previous model covariates, duration of the longest episode of substance abuse, number of episodes of substance abuse, and the age at onset of substance abuse.
[e]Comparing past-year smoking at Wave 2 to no past-year smoking at Wave 2, among those who reported smoking fewer than 100 lifetime cigarettes at Wave 1.
[f]Comparing past-year smoking at Wave 2 to no past-year smoking at Wave 2, among those who reported smoking 100 or more lifetime cigarettes at Wave 1.
[g]Reported substance use below the threshold for abuse or dependence status at Wave 2.
[h]Met criteria for abuse of or dependence on at least 1 substance at Wave 2.
Abbreviations: AOR = adjusted odds ratio, SUD = substance use disorder.
Symbol: … = not applicable.

To examine whether the results would change when "SUD relapse" was defined as substance dependence alone rather than report of substance abuse and dependence, models were re-run limiting the outcome to relapse to substance dependence. Effect estimates were slightly larger but were similar to the models combining substance abuse and dependence disorders (data not shown).

DISCUSSION

This study examined the association between smoking and relapse to substance use and SUD 3 years later among adults in the United States with remitted SUDs. Among respondents who were smoking at Wave 1, those who were smoking at Wave 2 were significantly more likely to report substance use and relapse to SUDs 3 years later compared with respondents who did not report smoking at Wave 2. Among respondents who were not smoking at Wave 1, those who were smoking at Wave 2 were significantly more likely to relapse to SUDs 3 years later compared with respondents who did not report smoking at Wave 2. These relationships remained significant after controlling for demographics; mood, anxiety, and personality disorders; alcohol use disorders; nicotine dependence; and severity of past SUD. These relationships were also significant when SUD relapse was defined by the more severe category of substance dependence rather than a variable that combined both substance dependence and abuse. Further, after these adjustments, sensitivity analyses suggested that a higher number of cigarettes consumed by Wave 1 smokers who smoked at Wave 2 and Wave 1 nonsmokers who smoked at Wave 2 was associated with a greater likelihood of SUD relapse. To our knowledge, no prior study has shown that cigarette smoking—both continued smoking and new-onset smoking—is associated with an increase the likelihood of relapse to SUD among adults with past SUDs. More research is needed to clarify whether quitting smoking (for smokers) or not initiating smoking (for nonsmokers) would reduce relapse to SUDs and lead to better long-term abstinence outcomes.

There are several reasons that smoking may increase the likelihood of relapse to SUDs. Smoking often occurs in combination with the use of other drugs, and cigarettes may become a cue for use of illicit drugs. Preclinical and laboratory research has shown a link between nicotine and increased cravings for and administration of stimulants and opiates.[27–29] Also, combined use of nicotine with other substances (eg, cannabis) is associated with greater psychiatric and personality disorders,[30,31] which are associated with difficulty quitting smoking[32] and dropping out of substance abuse treatment.[33] Research on the reasons why adults who smoke are more likely to relapse to SUDs can provide important information that can be incorporated into SUD treatment programs.

It has been suggested that addressing smoking among adults with SUDs is important for treating SUDs.[34] The majority of adults with SUDs are interested in quitting smoking and motivated to quit at rates consistent with the general population.[35] While there are concerns about whether quitting smoking would make it difficult to remain abstinent from illicit drugs, studies in clinical treatment settings have found that smoking abstinence does not appear to lead to a compensatory increase in other drug use and may even improve drug abstinence.[13,14,36–41] The conversation about providing smoking services for adults with SUDs has typically focused on smoking cessation services; however, our results suggest that efforts related to preventing smoking initiation could be beneficial as well, since adults with past SUDs who initiated smoking demonstrated the greatest odds of SUD relapse.

If research continues to show a relationship between smoking and SUD relapse, then incorporating smoking

prevention efforts and smoking cessation treatments into substance abuse treatment may be important services to provide to adults with SUDs to help sustain long-term substance treatment outcomes. The balance of research suggests that providing smoking treatment concurrently with treatment for other drugs improves smoking outcomes in the short term and does not appear to harm drug treatment outcomes.[35,40,42] Relapse to smoking is common among smokers attempting to quit,[43] including adults with SUDs.[40] Few studies have tested effective smoking treatments for adults with SUDs,[29] but there are promising preliminary results with pharmacotherapies for nicotine dependence.[29,44,45] More research is needed to determine what treatments will best help the greatest number of adults with SUDs to achieve abstinence from both cigarettes and illicit drugs over the long term. In addition, little is known about smoking initiation among adults with past SUDs. It would be useful for future studies to examine factors that have been shown to play a role in smoking initiation for younger or older adults (eg, demographics, stress, psychiatric symptoms and disorders, temperament, environment[46–50]) to determine which factors may play a significant role in the smoking initiation of adults with SUDs. Additional research on the timing of and reasons for cigarette smoking initiation would aid in determining which prevention efforts could help adults with SUDs to avoid smoking initiation.

It should also be noted that more information is needed to determine how to aid SUD treatment programs in developing and incorporating smoking-related services. A minority of treatment centers report that they have a designated leader or formalized procedures related to smoking cessation services, the ability to prescribe smoking cessation pharmacotherapies, the financial capacity to provide medication or counseling, and staff training on smoking treatments.[51] Further, an absence of barriers (eg, being hospital-based, having a lower number of clinicians who smoked) and the availabilities of incentives (eg, reimbursement for smoking services) are associated with incorporating pharmacotherapies,[52] while support from administrators and building staff expertise have been found to be important for continued success of active smoking cessation services within SUD treatment sites.[53] While more information is needed to build on the research related to SUD treatment programs providing smoking services, research on all aspects of smoking prevention efforts is needed (eg, the degree to which efforts to prevent smoking initiation are already included in SUD treatment programs, how administrators and staff can develop or build prevention efforts, the most useful content or form of prevention efforts). Improving the ability of SUD treatment programs to provide patients who smoke with treatment access and support and to provide patients who do not smoke with support to remain smoke-free may lead to not just better smoking outcomes but also better outcomes related to illicit drug use.

A number of limitations to this study must be noted. These results may have limited generalizability to those who were not part of the NESARC sample, such as adults outside of the United States and persons under the age of 18 years. Also, the survey excluded institutionalized and incarcerated populations, who may exhibit unique or elevated patterns of risk for SUD relapse. It should also be noted that the reliability for some modules of the AUDADIS (eg, smoking behavior) was determined using the full NESARC participant sample, which differs from the analytic sample for the current analyses. Smoking and drug use were documented by self-report without biochemical confirmation and therefore may have been underreported. In addition, due to sample sizes and power issues, it was not possible to determine whether the SUD relapse reported by participants at Wave 2 was the same substance for which they had initially reported use or abuse/dependence at Wave 1. Similarly, the sample sizes were small for several groups (ie, those who quit smoking and reported SUD relapse and those who began smoking and reported substance use or SUD relapse), which may have affected the precision of our effect estimates.

It was also not possible to determine the timing of SUD relapse in relation to the timing of smoking initiation or smoking cessation, which limits the ability to determine causality and the sequence of events in the relationship between smoking and SUD relapse. Studies of clinical samples would be useful to more closely examine the timing, context, and details of changes in drug behavior in association with smoking, as would longitudinal data sets with multiple follow-up periods that would allow for an investigation into this association using methods to account for time-varying variables and correlated measures (eg, cross-lagged structural equation modeling). While outside the scope of the current investigation, it would also be important for future studies to examine potential mechanisms (eg, mediators, effect modifiers) through which cigarette smoking is associated with SUD relapse. Additionally, it would be useful for future investigations to examine potential moderators of the relationship between smoking and SUD relapse (eg, sex, race, psychiatric disorders).

Finally, it must be noted that cigarette smoking is just one potential factor associated with SUD relapse. Our data suggest that continued smoking and smoking initiation are related to statistically significant increases in the odds of SUD relapse compared to those who quit smoking; however, more data are needed to determine the clinical significance of these relationships. The treatment of SUDs is extremely challenging, and even if not smoking is just modestly associated with improvements in sustained abstinence, this association may be useful in treatment programs. Smoking is modifiable and is relatively easily evaluated. Attention to smoking in illicit drug treatment programs would also be in line with the Clinical Practice Guideline Treating Tobacco Use and Dependence,[54] which recommends that all patients in various clinical settings be assessed for smoking and given aid with regard to smoking cessation treatments. In addition to the impact that smoking cessation could have

on SUD treatment outcomes, smoking is causally associated with a wide range of illnesses,[4] and therefore both smoking cessation and the avoidance of smoking initiation would potentially be associated with improved overall health.

Relapse is common among the majority of people with past illicit substance use disorders, and identifying factors associated with relapse to SUDs after stopping the use of illicit drugs may improve long-term outcomes of individuals with SUDs. Continuing or initiating cigarette use after stopping the use of illicit drugs was associated with an increased likelihood of relapse to SUDs. Incorporating smoking cessation treatments and smoking prevention efforts into substance abuse treatment may be one way to improve long-term substance use outcomes for adult smokers with SUDs.

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