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## Personality Disorders and the 3-Year Course of Alcohol, Drug, and Nicotine Use Disorders

Deborah Hasin, Ph.D.<sup>1,2,3</sup>, Miriam C. Fenton, M.P.H.<sup>2,3</sup>, Andrew Skodol, M.D.<sup>1,4</sup>, Robert Krueger, Ph.D.<sup>5</sup>, Katherine Keyes, Ph.D.<sup>2,3</sup>, Timothy Geier, B.A.<sup>3</sup>, Eliana Greenstein, M.A.<sup>3</sup>, Carlos Blanco, M.D., Ph.D.<sup>1,3</sup>, and Bridget Grant, Ph.D., Ph.D.<sup>6</sup>

<sup>1</sup>College of Physicians and Surgeons, Department of Psychiatry, Columbia University, New York, NY 10032

<sup>2</sup>Mailman School of Public Health, Department of Epidemiology, Columbia University, New York, NY 10032

<sup>3</sup>New York State Psychiatric Institute, New York, NY 10032

<sup>4</sup>University of Arizona College of Medicine, Tucson, Arizona 85724

<sup>5</sup>University of Minnesota, Department of Psychology

<sup>6</sup>Intramural Laboratory of Epidemiology and Biometry, National Institute on Alcohol Abuse and Alcoholism, Rockville MD 20849

### Abstract

**Context**—Little is known about the role of a broad range of personality disorders in the course of substance use disorder (SUD), and whether these differ by substance. The existing literature focuses mostly on antisocial personality disorder and does not come to clear conclusions.

**Objective**—To determine the association between the ten DSM-IV personality disorders and the persistence of common SUDs in a 3-year prospective study of a national sample.

**Design**—Data were drawn from participants in the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) who had alcohol dependence (N=1,172), cannabis use disorder (N=454) or nicotine dependence (N=4,017) at baseline and who were re-interviewed three years later. Control variables included demographic characteristics, family history of substance disorders, baseline Axis I disorders and treatment status, and prior SUD duration.

**Main outcome measure**—Persistent SUD, defined as meeting full criteria for the relevant SUD throughout the 3-year follow-up period.

**Results**—Persistent SUD was found among 30.1% of participants with alcohol dependence, 30.8% with cannabis use disorder, and 56.6% with nicotine dependence at baseline. Axis I disorders did not have strong or consistent associations with persistent SUD. In contrast, antisocial personality disorder was significantly associated with persistent alcohol, cannabis and nicotine use disorders (adjusted odds ratios: 2.46-3.51), as was borderline personality disorder (adjusted odds ratios: 2.04-2.78) and schizotypal personality disorder (adjusted odds ratios: 1.65-5.90). Narcissistic, schizoid, and obsessive-compulsive personality disorders were less consistently associated with SUD persistence.

**Conclusions**—The consistent findings on the association of antisocial, borderline and schizotypal personality disorders with persistent SUD indicates the importance of these

personality disorders in understanding the course of SUD. Future studies should examine dimensional representations of personality disorders and the role of specific components of these disorders, biological and environmental contributors to these relationships, and potential applications of these findings to treatment development.

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## Introduction

Alcohol, nicotine and drug use disorders are highly prevalent<sup>1-3</sup>, comorbid with other mental disorders<sup>1, 2, 4, 5</sup>, and associated with considerable health, economic and social burdens. The chronic nature of substance use disorders (SUD) seen in alcohol and drug treatment settings<sup>6, 7</sup> continues to present challenges to clinicians and researchers. Identifying consistent predictors of chronic SUDs in prospective studies has been difficult. Some factors suggested in the literature include family history of substance use disorders<sup>8, 9</sup> and Axis I disorders such as major depression<sup>10-15</sup> and anxiety disorders<sup>11, 12, 16, 17</sup>. However, not all studies have had consistent findings on these relationships<sup>5, 17-19</sup>

The association of antisocial personality disorder and its childhood antecedent, conduct disorder, with the *risk* for occurrence of substance use disorders is well known. However, regarding *course*, in clinical and school samples, antisocial personality disorder predicts poor outcome of SUD in some studies<sup>20-23</sup>, but not in others<sup>17, 24, 25</sup>. The inconsistencies could have been due to methodological variation, different substance disorder profiles among participants, and non-representative samples, suggesting a need to investigate this issue in a substance-specific manner, using standardized methods in representative samples.

In cross-sectional general population research, all ten DSM-IV personality disorders were shown to have strong associations with alcohol and nicotine dependence, and with drug disorders (abuse and dependence).<sup>1, 2, 4, 26-29</sup> Further, personality disorders, by definition characterized by extended duration, are associated with considerable additional impairment in functioning among those with alcohol and nicotine dependence compared to those without personality disorders<sup>30</sup>. However, the relationship of personality disorders other than antisocial to the persistence of SUDs has been far less studied, despite a suggestion made several years ago to expand the scope of substance abuse research to include a broader range of personality disorders<sup>31</sup>. Recent prospective studies suggested worse course of SUDs among patients with borderline personality disorder<sup>32-34</sup>, supporting the need for expanded investigation of this area.

Practical considerations may have limited research on the full range of personality disorders and the course of substance use disorders, since structured diagnostic interviews for Axis I disorders ordinarily include only one Axis II disorder, antisocial personality disorder<sup>31</sup>. However, symptoms and impaired functioning across multiple life domains characterize not only antisocial personality disorder but the other personality disorders as well. Given these considerations, the association of a broader range of personality disorders with the persistence of the most common SUDs appeared to represent a relatively unexplored area of high potential importance. Our aim was therefore to investigate the relationship between the ten DSM-IV personality disorders and the persistence of alcohol, cannabis and nicotine use disorders. For this, we used data from a large, nationally representative sample that included measurement of all ten DSM-IV personality disorders and a three-year follow-up with an excellent response rate. These data present a unique opportunity to investigate our research question. In conducting the analyses, we used statistical methods that enabled us to control for a wide variety of potential demographic and clinical confounders, including other psychiatric disorders.

## Methods

### Sample and procedures

The National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)<sup>35, 36</sup> was the source of data. The NESARC target population at Wave 1 was the civilian non-institutionalized population 18 years and older residing in households and group quarters. Blacks, Hispanics, and adults 18-24 were oversampled, with data adjusted for oversampling, household- and person-level non-response. Interviews were conducted with 43,093 participants by experienced lay interviewers with extensive training and supervision<sup>35, 36</sup>. All procedures, including informed consent, received full ethical review and approval from the U.S. Census Bureau and U.S. Office of Management and Budget. The Wave 2 interview was conducted approximately 3 years later (mean interval: 36.6 (s.e. 2.6) months. Excluding ineligible respondents (e.g., deceased), the Wave 2 response rate was 86.7%, reflecting 34,653 completed interviews<sup>36</sup>. Wave 2 NESARC weights include a component that adjusts for non-response, demographic factors and psychiatric diagnoses, to ensure that the Wave 2 sample approximated the target population, that is, the original sample minus attrition between the two waves. As described previously<sup>36</sup>, adjustment for non-response was successful, as the Wave 2 respondents and the original target population did not differ on age, race-ethnicity, sex, socioeconomic status or the presence of any substance, mood, anxiety or personality disorder<sup>36</sup>. Participants included in this analysis were those with Wave 1 diagnoses of current (last 12 month) DSM-IV alcohol dependence (N=1,172), cannabis abuse or dependence (N=454) and nicotine dependence (N=4,017). Demographic and clinical characteristics of the three groups (including the prevalence of other disorders) are shown in Table 1.

### Measures

The NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV)<sup>37-39</sup>, a structured diagnostic interview, was developed to advance measurement of substance use and mental disorders in large-scale surveys. Computer algorithms produced DSM-IV diagnoses based on AUDADIS-IV data.

### Substance disorder outcomes

We investigated the course of SUD using three substance-specific variables. We assessed alcohol and nicotine dependence as outcomes without a corresponding abuse diagnosis; for alcohol, abuse has little relationship with personality disorders<sup>1, 27, 29</sup>, and for nicotine, no abuse diagnosis exists in DSM-IV. We assessed cannabis use disorders because cannabis is the most widely used illicit drug, and because drug abuse and dependence are both associated with personality disorders in the NESARC<sup>4, 28-30</sup>. We focused on these three substances because they are the most common in the general population.

In the AUDADIS, all users of alcohol, cannabis and nicotine are assessed for the DSM-IV criteria for these substance use disorders. Alcohol and nicotine dependence were assessed using multiple items covering all seven DSM-IV criteria, with 3 or more required within a 12-month period for a diagnosis. In DSM-IV, cannabis dependence criteria do not include withdrawal. However, cannabis withdrawal has been demonstrated in clinical and laboratory studies<sup>40, 41</sup> and in the NESARC<sup>42</sup> and will be included in DSM-5.<sup>43</sup> We therefore based the cannabis dependence diagnosis on all seven dependence criteria in this analysis. Cannabis abuse was assessed with items covering the four DSM-IV abuse criteria, of which at least one is required to meet criteria. A cannabis abuse diagnosis was given to respondents who met criteria for cannabis abuse but never for cannabis dependence. The good to excellent ( $k = 0.70-0.91$ ) test-retest reliability of AUDADIS-IV substance use disorder diagnoses is documented in clinical and general population samples<sup>37-39, 44-46</sup>. Convergent, discriminant

and construct validity of AUDADIS-IV substance use disorder criteria and diagnoses were good to excellent<sup>47-51</sup>, including international studies<sup>52-57</sup>, and agreement with clinical reappraisals<sup>44, 52</sup>.

At Wave 1, the substance disorder criteria were assessed in two timeframes: (a) current, last 12 months (1 year); and (b) past, i.e., any time prior to last 12 months. At Wave 2, three years later, the criteria were also assessed in two timeframes: (a) current, last 12 months (1 year); and (b) past, i.e., any time prior to last 12 months but since Wave 1 (2 years), covering the three years between Waves 1 and 2. Persistent alcohol or nicotine dependence were defined as meeting full criteria for current dependence at Wave 1, and evidencing at least three criteria for dependence in both Wave 2 timeframes, i.e., continuing to meet full criteria for the disorder throughout the entire three-year follow-up. Persistent cannabis disorder was defined as meeting current abuse or dependence criteria at Wave 1, and evidencing at least three dependence criteria or one abuse criterion in both Wave 2 timeframes, i.e., continuing to meet full criteria for the disorder throughout the entire three-year follow-up.

### Personality disorders

Antisocial, avoidant, borderline, dependent, histrionic, narcissistic, obsessive-compulsive, paranoid, schizoid and schizotypal personality disorders were all assessed. As defined in DSM-IV, these diagnoses require evidence of long-term maladaptive patterns of cognition, emotion and functioning. The AUDADIS-IV was designed to diagnose the disorders accordingly<sup>27-29, 58, 59</sup>. Except for antisocial, all personality disorders were assessed with an introduction and repeated reminders asking respondents to answer about how they felt or acted “most of the time, throughout your life, regardless of the situation or whom you were with”, excluding symptoms occurring only when depressed, manic, anxious, drinking heavily, using drugs, recovering from the effects of alcohol or drugs, or physically ill. All positive responses were followed by a question on distress, social or occupational dysfunction. Diagnoses were made if the required number of DSM-IV personality symptoms were positive, and at least one of these caused distress, social or occupational dysfunction. Antisocial personality disorder was assessed with questions about conduct disorder before age 15 and adult antisocial symptoms at or after age 15, similar to other standardized interviews<sup>60-64</sup>. Consistent with DSM-IV, we required conduct disorder before age 15 and at least three adult antisocial symptoms for a diagnosis of antisocial personality disorder. Because antisocial was the only personality disorder in the NESARC with adult symptoms assessed at both waves, we also required that adult antisocial symptoms be reported at both waves to be considered positive.

The symptom items, worded in non-technical language to avoid the need for insight or judgment, were adapted to be fully structured from items in the Structured Clinical Interview for DSM-IV Personality Disorders<sup>65</sup>, International Personality Disorder Examination<sup>66</sup>, and Diagnostic Interview for DSM-IV Personality Disorders<sup>62</sup>. AUDADIS-IV reliability, assessed in test-retest studies of NESARC participants<sup>37, 38</sup>, ranged from fair (paranoid, histrionic, avoidant  $\kappa=0.40-0.45$ ) to very good (schizotypal, antisocial, narcissistic, borderline  $\kappa=0.67-0.71$ )<sup>37, 38</sup>, comparing favorably with semi-structured interviews in clinical samples<sup>67</sup>. Convergent validity ranges from good to excellent<sup>27-29, 58, 59, 68</sup>. Analysis of the personality disorders in the NESARC<sup>69</sup> indicated that avoidant and dependent personality disorders were so highly associated that they could be considered alternative representations of the same disorder. Accordingly, we analyzed variables indicating 9 DSM-IV personality disorders; each disorder was defined by the DSM-IV, except for a variable representing avoidant and dependent personality disorders that was positive if 1 or both disorders were diagnosed.

## Control covariates

Demographic covariates included gender, race/ethnicity (White, Hispanic, Black, Asian, Native American), Wave 1 age (18-29, 30-39, 40-49, 50+), and education (any college vs. others). Family history of alcohol or drug problems was defined as positive if experienced by parents or siblings; NESARC family history methodology is described in detail elsewhere<sup>70</sup>. Since treatment in naturalistic, non-randomized studies may indicate more severe or persistent disorders<sup>7</sup>, we also controlled for treatment status at baseline for alcohol or drug problems (treatment for nicotine dependence was not ascertained). As detailed elsewhere, the binary treatment variable was defined as positive if respondents participated in any of twelve types of inpatient or outpatient treatment<sup>1</sup>, or a 12-step program group. Duration of the alcohol, cannabis or nicotine disorder was defined as the number of months of the current or longest episode, with a minimum of 12 months (required to meet diagnostic criteria). Axis I disorders were also controlled, including DSM-IV primary affective and anxiety disorders, and substance disorders other than the disorder that was the outcome in a particular analysis. DSM-IV-defined mood disorders included bipolar I, bipolar II, major depressive and dysthymic disorders. Anxiety disorders included panic, social anxiety, specific phobia, and generalized anxiety disorders. In addition to alcohol, nicotine dependence and cannabis use disorders, substance disorders included stimulant, hallucinogen, inhalant/solvent, opioid, sedative/tranquilizer, or cocaine dependence or abuse. The timeframe for all Axis I disorder control variables was current (last 12 months) at baseline. AUDADIS-IV methods to diagnose these DSM-IV disorders are described elsewhere, including AUDADIS-IV methods of differentiating primary and substance-induced disorders<sup>71, 72</sup>. As previously reported, test-retest reliability was good for major depression, and fair to good for other mood and anxiety disorders<sup>37, 72</sup>. Validity of mood and anxiety disorders was supported via highly significant associations with impairment using the *Short Form 12 Health Survey*, version 2 (SF-12v2)<sup>73</sup>, a reliable, valid measure of current impaired functioning used in large population surveys. The prevalence of these control covariates is shown in Table 1.

## Statistical Analyses

Separate analyses were conducted for each of the three substance disorder outcomes, using multiple logistic regression models to produce adjusted odds ratios (AOR) and 95% confidence intervals (95% CI). Standard errors and confidence intervals were estimated with SUDAAN to adjust for non-response and the sample design. All models included the demographic covariates listed above. For each substance disorder outcome, we first tested individual effects of Wave 1 current (last 12 months) Axis I disorders, controlling for the demographic covariates. Then, to determine the impact of personality disorders, we tested individual models for each personality disorder, controlling for Axis I disorders, family history, treatment status, the duration of the substance disorder at the baseline interview and the variables representing other personality disorder comorbidity. In these models, to guard against collinearity, we created combined-disorder variables. This included a variable coded positive for affective or anxiety disorders, including unipolar affective disorders (major depressive disorder and dysthymia); bipolar disorders (bipolar I or bipolar II disorders); and anxiety disorders (panic, generalized anxiety, social anxiety and/or specific phobia disorder). In analysis of the persistence of each separate substance disorder, we also controlled for other substance disorders. For each of the three substance outcomes, we controlled for the other two, and we also controlled for any other substance use disorders with a combined variable. For alcohol and nicotine alcohol dependence, this variable included all substance disorders listed above. For cannabis abuse/dependence, the control variable included all substance disorders listed above except cannabis abuse/dependence. To determine the specific effect of each personality disorder controlling for other personality disorder

comorbidity<sup>27-29, 69</sup> while minimizing collinearity, we created variables coded positive if any personality disorder other than the one of focus in the model was present.

## Results

### Alcohol Dependence

Among the 1,172 respondents with 12-month alcohol dependence at Wave 1, 30.1% evidenced persistent alcohol dependence throughout the 3-year follow-up. No baseline Axis I disorder was significantly associated with persistent alcohol dependence. As shown in Table 2, four personality disorders were associated with persistent alcohol dependence: antisocial (AOR=3.51), borderline (AOR=2.52), narcissistic (AOR=1.96), and schizotypal (AOR=3.36).

### Cannabis Use Disorder

Among the 454 respondents with 12-month cannabis use disorders at Wave 1, 30.8% evidenced persistent cannabis use disorders throughout the 3-year follow-up. Adjusting for demographic characteristics, the only Axis I variable significantly associated with persistent cannabis use disorder was the combined “other DSM-IV substance abuse/dependence” variable defined in footnote, Table 1; AOR, 1.45, 95% CI, 1.01-2.08). Three personality disorders predicted persistent cannabis use disorder (Table 2): antisocial (AOR= 2.46), borderline (AOR= 2.78), and schizotypal (AOR= 5.90).

### Nicotine Dependence

Among the 4,017 respondents with 12-month nicotine dependence at Wave 1, 56.6% evidenced persistent nicotine dependence throughout the 3-year follow-up. Adjusting for demographic characteristics, Axis I categories significantly associated with persistent nicotine dependence included unipolar affective disorders (AOR, 1.30, 95% CI, 1.03-1.64), anxiety disorders (AOR, 1.44, 95% CI, 1.15-1.79), alcohol dependence (AOR, 1.29, 95% CI, 1.01-1.66), and drug abuse/dependence (AOR, 1.47, 95% CI, 1.11-1.95). Personality disorders associated with persistent nicotine dependence (Table 2) included antisocial (AOR=3.19), borderline (AOR=2.04), obsessive-compulsive (AOR=1.40), schizoid (AOR=1.47), and schizotypal (AOR=1.65).

## Discussion

This study provides a rigorous test of the impact of personality disorder on the course of substance-specific substance use disorders in a nationally representative sample assessed with a well-established instrument. A large number of participants with substance use disorders were ascertained independently of treatment status and were re-evaluated three years later with excellent retention. This study tested the prognostic significance of PDs while controlling for demographic factors, Axis I disorders, other personality disorder comorbidity, duration of the substance use disorders, family history, and treatment status at baseline. The sample sizes and covariates controlled allowed for multivariate tests of the association of the DSM-IV personality disorders with the persistence of substance use disorders in a manner not possible in previous studies. Our primary finding was that three personality disorders, antisocial, borderline and schizotypal, significantly and robustly predicted the persistence of the substance use disorders, even after controlling for many other potentially negative prognostic indicators. Other personality disorders were also significantly associated with persistent SUD, but in a less consistent manner.

The likelihood of persistent SUD across the three years was similar for alcohol dependence and cannabis use disorders, approximately 30%. The likelihood of persistent nicotine



dependence was higher (56.6%), highlighting the difficulty of achieving a good outcome for this substance. We defined our outcome variables in terms of persistence rather than remission for two reasons. First, the field lacks consensus on the conceptualization and measurement of remission from SUD. Second, we wished to focus this study on the respondents who manifested active symptoms of their disorders throughout the follow-up period, arguably the most important in terms of need, public health and clinical significance.

While some of the earlier studies did not find an association between antisocial personality disorder and poor course of SUD, our findings on the association between antisocial personality disorder and the persistence of alcohol, cannabis and nicotine disorders are consistent with most previous studies of patients and students<sup>20-23</sup>, suggesting that the relationship is generalizable. These results are also consistent with studies suggesting that substance use disorders and antisocial personality disorder form part of a unidimensional domain of psychopathology often referred to as the externalizing domain<sup>74, 75</sup>. While the externalizing domain is usually conceptualized in terms of risk for the disorders (i.e., as different manifestations of a single underlying condition explaining comorbidity risk), our results suggest that this framework could be broadened to include examination of persistence as well. In addition, while an extensive literature focuses on the relationship between alcohol and drug disorders and antisocial personality disorder, far less attention has been paid to the relationship of antisocial personality disorder and the course of nicotine dependence or smoking cessation. The strength of the finding, even after controlling for multiple other potential confounders, suggests further investigation of this relationship, e.g., identification of mechanisms.

Borderline personality disorder is recognized as a serious form of psychopathology associated with distress, suicide, impaired functioning, and healthcare costs<sup>76-79</sup>. When studied, this personality disorder is also associated with substance use disorders in clinical<sup>33, 80</sup> and general population samples<sup>29, 79</sup>. Using structural modeling techniques, we recently showed that borderline personality disorder is located on both the internalizing and externalizing domains of psychopathology<sup>79</sup>. In prospective research, we have also shown that borderline personality disorder is a robust predictor of poor course of major depression in both clinical<sup>81, 82</sup> and general population<sup>83</sup> samples. While borderline personality disorder has received less attention than antisocial personality disorder in its relationship to substance use disorders, several criteria for borderline personality disorder (e.g., unstable interpersonal relationships, impulsivity, anger) are common problems among substance abusers. Therefore, borderline personality disorder was of particular interest as we undertook this study. Recent clinical studies also suggests poor substance outcomes among patients with comorbid borderline personality disorder<sup>32-34</sup>. Our finding that borderline personality disorder is a robust predictor of the persistence of alcohol, cannabis and nicotine use disorders even after controlling for many other potential confounders suggests the need for greater research and clinical focus on the conjunction of these disorders, such as work on dialectical behavior therapy for patients with comorbid substance abuse and borderline personality disorder<sup>84-86</sup>.

Schizotypal personality disorder was present in about 10% of the participants in our study. In a Norwegian study of substance abuse treatment retention several years ago, schizotypal traits predicted treatment dropout<sup>87</sup>, but we have not found more recent studies of schizotypal personality disorder and SUD treatment outcome. However, the strong cross-sectional relationship between schizotypal personality disorder and substance use disorders<sup>22, 27, 88</sup> is drawing increased attention<sup>88</sup>. Given the interest in cannabis use as a risk factor for schizophrenia and the connection of schizotypal personality disorder to schizophrenia in the schizophrenia-spectrum domain, several cross-sectional studies examined the association between cannabis use and schizotypal symptoms, finding positive

associations<sup>89-95</sup>. The only study among these to address time order found that the schizotypal symptoms preceded cannabis use<sup>91</sup>, suggesting that this association is not an artifact of cannabis effects. We were unable to find studies on schizotypal personality disorder as a predictor of the course of cannabis use disorder, so in this regard, the strong present study findings are novel and invite further investigation.

The relationship between schizotypal personality disorder and nicotine is also receiving increasing attention, given the high prevalence of smoking among individuals with schizophrenia and the hypothesized links between schizotypal personality disorder and schizophrenia. Several studies have found a positive relationship between levels of schizotypal symptoms and levels of smoking<sup>95-99</sup>. A prior study that examined the relationship between sub-factors within schizotypal symptoms found associations between smoking and eccentric behavior and odd speech, but not other domains<sup>95</sup>. The present results suggest the need for further fine-grained investigation of the specific symptoms of schizotypal personality disorder that predict persistent nicotine dependence. This type of symptom-based research has recently begun, focused on a SUD persistence outcome consisting of a global category of drug use disorders<sup>88</sup>. More work of this type may be informative in terms of phenotypes for etiologic study, and in identifying targets of new treatments. Substance abuse treatment specialists may not necessarily be attuned to schizotypal symptoms in their patients. Greater awareness of the potential for odd or eccentric thoughts or behavior to signal poor substance abuse outcomes could lead to greater treatment attention to these symptoms, and may lead to better substance abuse outcomes.

Persistent alcohol dependence was also predicted by narcissistic personality disorder. The only related prospective study we found suggested that narcissistic personality traits predicted problem drinking during medical training<sup>100</sup>. These findings suggest merit in replication and further investigation of this relationship.

Baseline unipolar affective disorders, anxiety disorders and other substance disorders predicted persistent nicotine dependence, although the low ORs (1.29-1.47) are consistent with a previously mixed literature<sup>5, 101-103</sup>. Speaking generally, a set of weak or inconsistent relationships can sometimes be explained by identifying previously undetected moderators of the associations. Improving smoking cessation treatment for patients with comorbid disorders is an active, important area<sup>104-106</sup>. Research that can identify moderators of the relationship between comorbid disorders and smoking outcomes may offer information that would help in developing more targeted and therefore more effective smoking cessation treatments.

Obsessive-compulsive and schizoid personality disorders were not associated with persistent alcohol or cannabis disorders, but did predict persistent nicotine dependence. Given the public health importance of smoking cessation, further investigation in this and other datasets of whether particular elements of these two personality disorders predict persistent nicotine dependence could identify potential targets for more effective smoking cessation interventions.

Many treated substance abusers with antisocial personality disorder have other personality disorders, and aspects of substance outcomes may differ between antisocial substance abuse patients with and without other personality disorders<sup>107</sup>. Accordingly, we explored whether borderline or schizotypal personality disorders modified the effects of antisocial personality disorder on substance outcomes by adding interaction terms to the logistic regression models. None of these interactions were statistically significant, suggesting that the influence of antisocial personality did not differ by the co-occurrence of these other two personality disorders. Note that as was previously shown for the full sample<sup>27-29, 69</sup>,



comorbidity among personality disorders within the alcohol, cannabis and nicotine subsamples was common. Among those with alcohol dependence, cannabis use disorder and nicotine dependence, 27.6%, 32.4% and 20.3%, respectively, had more than one personality disorder. Further, within these three subgroups, over 95% of pairwise associations between personality disorders were significant, as indicated by adjusted odds ratios. This comorbidity was the reason we controlled for potential confounding by other personality disorders when analyzing the effects of each one.

Study limitations are noted. Information on substance use disorders was based on self-report. Future studies should include biomarkers when these are sufficiently developed to be practical and valid. The sample did not include individuals permanently institutionalized or under age 18, so results cannot be generalized to these groups. Lower reliability of some personality disorders (e.g., paranoid, histrionic, avoidant) may limit the ability to detect associations with persistent substance use disorders. This study assessed psychiatric disorders categorically, consistent with DSM-IV. Dimensional approaches could also be undertaken in future studies, e.g. number (count) of personality disorders or their criteria, or use of the Five-Factor Model of Personality as measured, for example, by the NEO Personality Inventory<sup>108-110</sup>. Disorders were assessed with structured interviews by lay interviewers, not trained clinicians. When done reliably, clinician assessment is desirable, but is generally not possible in studies of the size of the NESARC. Information on personality disorder symptoms during periods of heavy substance use and other periods would be better ascertained by many repeated assessments across the lifecourse, which would also be desirable when feasible. Finally, diagnostic interviews covering antisocial personality disorder, including the AUDADIS, do not include instructions to report only symptoms persisting across different situations and time periods. This may be because diagnostic assessment of antisocial personality disorder was standardized many years ago<sup>111</sup> in longitudinal studies of delinquents and prisoners, or because the requirement of childhood as well as adult symptoms made instructions on symptom persistence appear unnecessary. Future studies could investigate whether such instructions improve the validity of the antisocial personality diagnosis in clinical and general population settings. These limitations are considered relative to the fact that the test-retest reliability of the personality disorder assessments compared favorably with semi-structured interviews in clinical samples, the personality disorder diagnoses have been shown to be associated with significant functional impairment in this sample, and the use of lay interviewers enabled ascertainment of a large sample and a breadth of covariates that enabled us to control for confounding in a manner not possible in smaller studies that relied on clinician evaluation. Additional study strengths include a representative, general population sample, a good follow-up response rate, and an analytic strategy allowing control for multiple factors.

Previously, the NESARC has shown that alcohol, cannabis and nicotine use disorders are prevalent among U.S. adults. These disorders are largely untreated and associated with considerable comorbidity and disability. Our results showed that a substantial minority of those with alcohol dependence and cannabis use disorders manifested symptoms throughout a three-year period, and in addition, that a majority of those with nicotine dependence remained fully symptomatic throughout this period. Three personality disorders were associated with persistent course of the substance disorders, antisocial, borderline and schizotypal. Other personality disorders were associated with poor course, but less consistently across the substance use disorders. While the findings for antisocial personality disorder may not be surprising, far less attention in the substance abuse field has been paid to borderline and schizotypal personality disorders. The findings suggest the importance of extending research and clinical attention to a broader range of personality psychopathology when investigating and treating substance use disorders, and of gaining a better understanding of the environmental and biological causes of these relationships.

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**Table 1**

Demographic and clinical characteristics at Wave 1

	Alcohol Dependence (N=1,172)		Cannabis Abuse/Dependence (N=454)		Nicotine Dependence (N=4,017)	
	%	SE	%	SE	%	SE
<b>Demographic characteristics</b>						
Male	68.02	1.6	71.19	2.4	52.88	0.9
<b>Age</b>						
18 – 29	53.52	1.8	66.40	3.0	28.43	1.0
30 – 39	21.64	1.5	17.00	2.2	23.00	0.8
40 – 49	17.52	1.2	12.66	1.9	24.87	0.9
50+	7.32	0.8	3.94	1.2	23.71	0.8
Completed High School	83.43	1.4	80.54	2.4	85.35	0.5
<b>Race/ Ethnicity</b>						
White, non-Latino	69.92	2.4	68.70	2.9	79.58	1.0
Black, non-Latino	10.84	1.2	11.61	1.9	8.27	0.7
Native American	3.26	0.8	4.83	1.3	4.06	0.5
Asian/Pacific Islander	2.33	0.6	3.70	1.5	2.02	0.4
Hispanic	13.64	2.0	11.16	1.9	6.07	0.6
<b>Axis I categories</b>						
<b>Affective/anxiety</b>						
Unipolar affective	11.91	1.2	11.21	1.6	11.10	0.6
Bipolar affective	10.64	1.2	13.16	2.1	5.90	0.5
Anxiety disorder	20.79	1.5	20.17	2.4	19.31	0.8
<b>Substance disorders</b>						
Alcohol dependence	--	--	41.99	3.0	13.15	0.7
Cannabis abuse/dependence	16.95	1.5	--	--	6.44	0.5
Nicotine dependence	44.70	2.1	54.26	2.6	--	--
Other DSM-IV substance abuse/dependence <sup>1</sup>	21.76	1.7	23.67	2.5	8.14	0.5
<b>Personality disorders</b>						
Narcissistic	15.99	1.2	20.89	2.6	9.78	0.6

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	Alcohol Dependence (N=1,172)		Cannabis Abuse/Dependence (N=454)		Nicotine Dependence (N=4,017)	
	%	SE	%	SE	%	SE
Schizotypal	9.27	1.0	12.96	1.9	8.51	0.6
Borderline	19.31	1.5	22.04	2.4	14.12	0.7
Histrionic	10.75	1.1	13.07	2.1	5.55	0.5
Schizoid	8.41	1.0	10.70	1.7	7.40	0.5
Paranoid	15.98	1.3	18.92	2.3	11.05	0.7
Obsessive-compulsive disorder	15.59	1.2	19.59	2.2	14.62	0.8
Avoidant / Dependent	8.95	1.0	10.75	1.7	6.11	0.5
Antisocial	4.95	0.8	11.60	2.0	2.55	0.4
<b>Other clinical characteristics</b>						
Family history alcohol/drug	53.31	2.0	61.42	2.6	54.11	1.0
Current substance treatment	12.63	1.1	14.32	2.1	5.76	0.4
Alcohol Dependence Duration <sup>2</sup> (Mean [S.E.])	34.62	1.9	--	--	--	--
Cannabis Abuse/Dependence Duration <sup>2</sup> (Mean [S.E.])	--	--	51.61	4.8	--	--
Nicotine Dependence Duration <sup>2</sup> (Mean [S.E.])	--	--	--	--	25.55	1.3

<sup>1</sup>For the alcohol and nicotine dependence groups, these include DSM-IV stimulant, hallucinogen, inhalant/solvent, opioid, sedative/tranquilizer, cannabis or cocaine dependence or abuse. For the cannabis abuse/dependence group, this variable includes all these disorders except cannabis abuse/dependence.

<sup>2</sup>Number of months of the current or longest episode



**Table 2**

Relationship of Axis II disorders to 3-year persistence of substance use disorders \*

	Alcohol dependence (N=1,172)		Cannabis Abuse/Dependence (N=454)		Nicotine dependence (N=4,017)	
	OR	CI	OR	CI	OR	CI
Antisocial	<b>3.51</b> ***	<b>1.74-7.08</b>	<b>2.46</b> *	<b>1.05-5.73</b>	<b>3.19</b> ***	<b>1.64-6.18</b>
Avoidant / Dependent	0.92	0.49-1.74	0.73	0.29-1.83	1.02	0.69-1.51
Borderline	<b>2.52</b> ***	<b>1.64-3.85</b>	<b>2.78</b> **	<b>1.40-5.50</b>	<b>2.04</b> ***	<b>1.56-2.68</b>
Histrionic	0.96	0.57-1.60	1.10	0.46-2.65	1.10	0.76-1.59
Narcissistic	<b>1.96</b> **	<b>1.32-2.91</b>	1.32	0.63-2.74	1.22	0.92-1.61
Obsessive-compulsive disorder	0.89	0.57-1.38	0.91	0.44-1.87	<b>1.40</b> *	<b>1.06-1.85</b>
Paranoid	1.18	0.72-1.95	0.83	0.40-1.73	0.99	0.73-1.35
Schizoid	1.10	0.59-2.06	0.80	0.33-1.97	<b>1.47</b> *	<b>1.08-2.01</b>
Schizotypal	<b>3.36</b> ***	<b>1.98-5.72</b>	<b>5.90</b> ***	<b>2.68-13.00</b>	<b>1.65</b> **	<b>1.19-2.28</b>

\* controlling for demographics, Axis I categories shown in Table 1 and the other personality disorders, family history of alcohol/drug problems, current alcohol/drug treatment at baseline, and baseline duration (months) of longest/only use disorder

\* p<0.05

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p<0.01

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p<0.0001