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Comorbidity of Generalized Anxiety Disorder and Substance Use Disorders: Results from the National Epidemiologic Survey on Alcohol and Related Conditions

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Abstract

Objective—Prior research has consistently documented a strong association between generalized anxiety disorder (GAD) and substance use disorder (SUD). GAD and SUD comorbidity (GAD-SUD) represents clinical challenges as the patients' symptoms are often more severe and are frequently prolonged making their management more complex when compared with individuals with GAD only. The purpose of this study was to examine whether individuals with GAD-SUD differ meaningfully from individuals with GAD and no SUD comorbidity (GAD-NSUD) in terms of demographic characteristics, risk factors, psychiatric comorbidity and clinical correlates.

Methods—Data were derived from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (N=43,093). Diagnoses were made using the Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV version.

Results—We found that the lifetime prevalence rate of GAD-SUD is about 2.04% while that of GAD-NSUD is of 2.10%. Individuals with GAD-SUD showed higher psychiatric comorbidity rates than those with GAD-NSUD. Treatment seeking rates for GAD are equally low in GAD-SUD and GAD-NSUD. Both groups were as likely to receive pharmacological treatment for anxiety.

Conclusion—The findings of our study indicate that individuals of GAD-SUD constitutes half of the lifetime prevalence of GAD and that GAD-SUD is associated with high overall vulnerability for additional psychopathology, particularly in the externalizing spectrum, higher disability and higher use of alcohol and drugs to relieve anxiety symptoms.

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Keywords

Comorbidity; Generalized anxiety disorder; Substance use disorders; epidemiology

INTRODUCTION

Generalized anxiety disorder (GAD) is characterized by excessive anxiety of at least 6 months' duration that is hard to control, not focused on a specific situation or objects, and not triggered by recent stressing events. Associated symptoms include restlessness, fatigue, concentration difficulties, irritability, muscle tension, and sleep disorders. GAD has a 12-month prevalence of 1% – 2.1% and a lifetime prevalence of 2.8% – 4.1% in Europe and in the US,[1,2] is chronic and disabling, and is associated with high rates of psychiatric comorbidity[1–3] and substantial personal, societal and economic costs.[4–6]

Prior research has consistently documented a strong association between GAD and substance use disorder (SUD).[7–9] High rates of comorbidity of GAD and SUD have been frequently reported in clinical[10–14] and community samples[8,15–22] and have been associated with worse outcomes than their single diagnosis counterparts. Among individuals with alcohol use disorders, those with comorbid anxiety are more disabled,[1] drink more heavily[23,24] have worse social adjustment and outcome,[8,25] greater number of hospitalizations, and a greater severity of psychiatric illness as compared with those with alcohol use disorders only. A long-term follow-up study[26] found that comorbid SUD among individuals with GAD significantly decreased the likelihood of recovery from GAD and significantly increased the risk of recurrence of this disorder. Thus, GAD and SUD comorbidity (GAD-SUD) represents clinical challenges as the patients' symptoms are often more severe and are frequently prolonged making their management more complex.

Despite the obvious differences in symptom presentation, course and treatment response across different anxiety disorders, a number of research studies examining the correlates of comorbid SUD and anxiety has considered anxiety disorders as a single, unitary entity[23,24,27,28] whereas only few have studies have looked at the association of SUD and GAD as a specific type of anxiety disorder.[25, 29–31] Furthermore, prior studies of the comorbidity of SUD and GAD often relied upon treatment-seeking samples and focused almost exclusively on alcohol use disorders.[25, 29–31]

In view of the limitations of prior research, we sought to fill this gap in knowledge examining whether individuals with GAD-SUD differ meaningfully from individuals with GAD and no SUD comorbidity (GAD-NSUD) in terms of demographic characteristics, risk factors, psychiatric comorbidity and clinical correlates in a nationally representative sample of individuals of the United States, as assessed in the National Institute on Alcohol Abuse and Alcoholism's (NIAAA) 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). Specifically, we sought to: 1) Examine prevalence of GAD-SUD and GAD-NSUD and their sociodemographic correlates; 2) Estimate the prevalence of risk factors for anxiety disorders in individuals in those two groups; 3) Compare the lifetime prevalence of psychiatric disorders in both groups of individuals; and, 4) Estimate rates and patterns of treatment-seeking in individuals with GAD-SUD and GAD-NSUD.

METHOD

NESARC Sample

The 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) is a survey of a representative sample of the USA conducted by NIAAA, as

described elsewhere.[16,32] The NESARC target population was individuals aged 18 years and over in the civilian non-institutional population residing in households and group quarters. The survey included those residing in the continental United States, District of Columbia, Alaska and Hawaii. A total of 43,093 participants completed face-to-face personal interviews. Data were weighted to reflect design characteristics of the NESARC survey and to account for oversampling and non-response.

DSM-IV diagnostic assessment

The diagnostic interview used to generate diagnoses was the Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (AUDADIS-IV) from the National Institute on Alcohol Abuse and Alcoholism.[33] This structured diagnostic interview designed for lay interviewers was developed to advance measurement of substance use and mental disorders in large-scale surveys. The test-test reliability and validity of AUDADIS-IV measures of DSM-IV disorders has been reported elsewhere.

Generalized Anxiety Disorder (GAD)

DSM-IV GAD was diagnosed when excessive anxiety and worry were present more days than not for at least 6 months, about a number of events or activities, accompanied by difficulty controlling the worry and at least three of the six DSM-IV GAD symptoms. Lifetime GAD was defined as having at least one episode of GAD over the life course. Diagnoses of GAD also required that the DSM-IV clinical significance criterion be met, that is, symptoms of the disorder must have caused clinically significant distress or impairment. The DSM-IV GAD diagnosis excludes substance-induced episodes or due to a medical condition. In differentiating substance-induced from independent disorders AUDADIS used specific questions about the chronological relationship between intoxication or withdrawal and the full anxiety syndrome.[34] Specific questions about chronology improve the reliability and validity of GAD diagnoses in individuals who use psychoactive substances.[35–37] As reported in detail elsewhere[38–42] test–retest reliability for GAD was fair (k= 0.42). We subdivided the sample of individuals with GAD between those with lifetime SUD comorbidity (GAD-SUD) and those with no lifetime SUD comorbidity (GAD-NSUD).

Mood and anxiety disorders

Other mood (depression dysthymia, bipolar I, bipolar II) and anxiety (panic disorder with and without agoraphobia, social phobia, and specific phobia) diagnoses in this report are DSM-IV primary diagnoses. In DSM-IV, ‘primary’ excludes mental disorders that are substance-induced or due to a medical condition.

All mood and anxiety disorders satisfied the DSM-IV clinical significance criterion. Test-retest reliabilities of AUDADIS –IV measures of DSM-IV mood and anxiety disorders were fair to good, ranging from k=0.42 for specific phobia to k=0.62 for major depression.[32,43]

Substance use disorders (SUD)

The questions of AUDADIS-IV operationalize DSM-IV criteria for alcohol and drug-specific abuse and dependence for 10 drug classes(aggregated in this report).[16] Consistent with the DSM-IV, lifetime AUDADIS-IV diagnoses of alcohol abuse required at least 1 of the 4 criteria for abuse either in the 12-month period preceding the interview or previously. The AUDADIS-IV alcohol dependence diagnoses required at least 3 of the 7 DSM-IV criteria for dependence during the past year or prior. For prior diagnoses of alcohol dependence, at least 3 criteria must have occurred within a 1-year period, following DSM-IV. Drug abuse and dependence and nicotine dependence diagnoses used the same algorithms.[31] The test re-test reliabilities of AUDADIS-IV alcohol and drug disorders measures were excellent, exceeding k=0.74 for

alcohol diagnoses and k=0.79 for drug diagnoses.[38–44] The discriminant and convergent,[38,39,42,44,46] concurrent,[48,49] construct,[42,50] and population validity of the AUDADIS alcohol and drug use disorder diagnoses also have been well documented.

Personality disorders (PD)

The AUDADIS-IV assessments of DSM-IV PDs have been presented previously.[51,52] They include avoidant, dependent, obsessive-compulsive, paranoid, schizoid, and antisocial PDs. The DSM-IV PD diagnoses require evaluating long-term patterns of functioning. The AUDADIS-IVPD diagnoses were made accordingly. To receive a DSM-IV PD diagnosis, respondents needed to endorse the required number of DSM-IV symptom items for the specific PD, with at least 1 symptom causing distress or social or occupational dysfunction. The reliability of AUDADIS-IV categorical diagnoses and dimensional scales of each personality disorder was assessed in a test re-test study as part of the NESARC survey proper.[32] The reliability of the personality disorders in the community samples ranged from fair to good, from k=0.40 for histrionic personality disorder to k=0.67 for antisocial personality disorder.

Lifetime risk factors

Consistent with previous research,[53] this study included variables that addressed the etiologic complexity of internalizing disorders and are known risk factors for anxiety. The risk constructs specified were as follows: predisposing genetic influences[54] such as (1) family history of depression, (2) family history of alcohol or drug problems and (3) family history of problem behavior; childhood risk factors such as (1) parental loss due to death before age 18 years, (2) early-onset anxiety, operationalized as onset of any anxiety disorder before age 18 years; and (3) conduct disorder, operationalized as childhood conduct problems. We also examined 3 adult risk measures that have featured prominently in the literature on anxiety:[55,56] (1) being divorced, measured by a self-report of history of a divorce, (2) stressful life events, measured with 12 items from the Social Readjustment Rating Scale (e.g., fired from a job, forced to move)[57] and (3) history of trauma and victimization in the past 12 months, assessed by self-report of having personally been the victim of a crime or attempted crime, such as: being beat up, mugged, or attacked by a stranger or someone the person knew.

Other measures

Age of onset, number of episodes, duration of only or longest (if applicable) episode, use of alcohol or drugs to help relieve symptoms of GAD, treatment utilization, and age at first treatment were ascertained among respondents with lifetime GAD. Additional questions queried about overall health status assessed by self-report. Twelve-month disability was assessed using the Mental Health Physical Social Functioning, Role Emotional Functioning, and Component Summary scores of the Short Form-12 version 2 (SF-12v2), a reliable and valid impairment measure commonly used in population surveys. Respondents were classified as receiving treatment for GAD or SUD if, they ever: (1) visited a counselor, therapist, physician, or psychologist; (2) were a patient in a hospital for at least one night; (3) visited an emergency room; or (4) were prescribed medications.

Statistical Analyses

Weighted percentages and means were computed to derive prevalence, sociodemographic and clinical characteristics and risk factors of respondents with GAD with and without comorbid SUD. A set of logistic regressions analyses yielded odds ratios (ORs) indicating measures of association between GAD-NSUD, GAD-SUD and lifetime comorbid psychiatric disorders, risk factors and clinical characteristics. ORs were further adjusted (AOR) for those sociodemographic characteristics of the sample that were significantly different between the groups at a univariate level of analysis. Analyses were estimated using SUDAAN,[58] a software

package that uses Taylor series linearization to adjust for the design effects of complex sample surveys like the NESARC.

RESULTS

Prevalence and sociodemographic correlates

Table 1 shows the prevalence and sociodemographic correlates of individuals with lifetime GAD-NSUD and GAD-SUD. Individuals with GAD-SUD were significantly more likely than individuals with GAD-NSUD to be male, US-born, to be in the 2 highest income groups and to have a family income of $20,000–34,000. Individuals with GAD-SUD were significantly less likely to be Black, be 45 years and older and to live in the South than individuals with GAD-SUD.

Lifetime risk factors

Lifetime prevalence of risk factors among individuals with GAD-SUD and GAD-NSUD are shown in Table 2. In the unadjusted models, Individuals with GAD-SUD were more likely than those with GAD-NSUD to have a higher prevalence of family history of AUD/SUD and family history of problem behavior as shown by unadjusted ORs. Individuals with GAD-SUD also had significantly higher prevalence of being ever divorced and history of victimization than those with GAD-NSUD.

When the ORs were adjusted for sociodemographic characteristics, individuals with GAD-SUD continued to be more likely than those with GAD-NSUD to have a higher prevalence of family history of AUD/SUD, family history of problem behavior, vulnerable family environment and being ever divorced while differences on the prevalence of history of victimization lost significance. Furthermore individuals with GAD-SUD showed significantly lower prevalence of early onset-anxiety than those with GAD-NSUD.

Psychiatric comorbidity

Table 3 shows the lifetime prevalence of axis I and II disorders among individuals with GAD-SUD and with GAD-NSUD. In the unadjusted models, individuals with GAD-SUD were significantly more likely than those individuals with GAD-NSUD to have a lifetime history of any psychiatric disorder, any axis I disorder, nicotine dependence, bipolar I and II disorder, any anxiety disorder, panic disorder, social anxiety disorder, pathological gambling, any personality disorder, paranoid, histrionic and antisocial personality disorder. Individuals with GAD-SUD were less likely than those with GAD-NSUD to have a lifetime history of MDD.

When the ORs were adjusted for sociodemographic characteristics, individuals with GAD-SUD continued to be more likely than those with GAD-NSUD to have a lifetime history of any psychiatric disorder, any axis I disorder, nicotine dependence, bipolar I and II disorder, any anxiety disorder, panic disorder, pathological gambling and antisocial personality disorder but differences on the prevalence of social phobia, any personality disorder, paranoid and histrionic personality disorder failed to reach significance. Individuals with GAD-SUD continued to be less likely than those with GAD-NSUD to have a lifetime history of MDD.

Clinical characteristics of GAD

Table 4 shows the differences in clinical characteristics among individuals with GAD-NSUD and with GAD-SUD. Individuals with GAD-SUD were more likely than those with GAD-NSUD to present difficulty concentrating, have arguments with friends or relatives, and difficulty completing daily tasks.

When adjusted for sociodemographic characteristics, individuals with GAD-SUD continued to be significantly more likely to report difficulty concentrating than those with GAD-SUD, and the prevalence of associated cardiovascular and respiratory symptoms became significantly higher among those with GAD-SUD than those with GAD-NSUD whereas differences in the prevalence of arguments with friends or relatives and difficulty completing daily tasks lost significance. In these adjusted models, individuals with GAD-SUD were more likely to have lower scores on the mental component summary, social functioning and mental health scales of the SF-12 than those with GAD-NSUD.

Age of onset, course and treatment-seeking and self-medication

Age of onset, course, treatment and self-medication characteristics among individuals with GAD-SUD and GAD-NSUD are shown in Table 5. Individuals with GAD-SUD had a mean age of onset for GAD of 30.45 years old with a mean age of first treatment of 32.47 whereas individuals with GAD-NSUD had a mean age of onset of 34.9 years old with a mean age of first treatment of 36.99. In the unadjusted models, individuals with GAD-SUD were more likely to have an earlier age of onset of GAD and an earlier age at first treatment of GAD and to use of alcohol and drugs to relieve GAD symptoms.

In models adjusted for sociodemographic characteristics, age of onset of GAD and age of first treatment for GAD did not differ significantly between individuals with GAD-SUD and those with GAD-NSUD. Individuals with GAD-SUD continued to be significantly more likely than individuals with GAD-NSUD to use alcohol and drugs to relieve GAD symptoms. GAD treatment-seeking rates in the two groups were low and did not differ significantly.

Age of onset and treatment patterns of SUD among individuals with GAD-SUD were also obtained. Individuals with GAD-SUD had a mean age of onset for SUD of 21.25 years old with a mean age of first treatment of 28.24 years old. Among individuals with GAD-SUD, 18.20% were treated for SUD as an outpatient, 16% as inpatient and 8.55% reported emergency room admittance.

DISCUSSION

This is the first epidemiological study to report the prevalence of the joint comorbidity of GAD with SUD, and to compare the prevalence and sociodemographic and clinical characteristics among individuals with GAD with and without comorbid SUD (i.e., GAD-SUD and GAD-NSUD) in a nationally representative sample of the general population. We found that 1) the lifetime prevalence of GAD-SUD is about 2.04% while that of GAD-NSUD is of 2.10%, 2) individuals with GAD-SUD showed higher psychiatric comorbidity rates than those with GAD-NSUD; and, 3) treatment seeking rates for GAD are equally low in GAD-SUD and GAD-NSUD groups.

Our study found that GAD-SUD has a higher prevalence (2.04%) than other anxiety disorders widely recognized as important and disabling such as obsessive-compulsive disorder (1.6%) [59] and other Axis I disorders such as schizophrenia. Consistent with the strong association between these two disorders previously described,[7,8] almost 50% of individuals with lifetime GAD in the NESARC had a comorbid lifetime SUD. Three converging set of factors may partially help explain this high rate of comorbidity. First, our study found significantly higher prevalence of vulnerable family environment, family history of antisocial behavior and family history of alcohol and drug use disorders among those with GAD-SUD, suggesting that risk factors for psychopathology may play a stronger role in the onset of GAD-SUD than in GAD-NSUD. Second, the onset of SUD preceded the onset of GAD among those with GAD-SUD, suggesting that SUD, at least in some cases, may facilitate the initiation of GAD. Third, individuals with GAD-SUD had significantly higher rates of use of alcohol and drugs to relieve

symptoms of anxiety among those with GAD-NSUD, a behavior that may provide temporary relief for the anxiety symptoms, but often leads to their long-term maintenance. Taken together, these findings suggest a stronger predisposition for psychopathology among individuals with GAD-SUD that is further exacerbated by the use of substances. From the treatment point of view, these findings suggest caution in the use of benzodiazepine in individuals with GAD-SUD due to the increased risk for dependence of prescription drugs among individuals with SUD.[60] Antidepressant (e.g, SSRIs), many of which are effective for GAD, may preferable as first-line treatment for most individuals with GAD-SUD.[61]

An alternative explanation for the high comorbidity between GAD and SUD would be to postulate the existence of an underlying (i.e., latent) process that can cause both disorders, but which sometimes manifests only one disorder, depending on the genetic and environmental factors of each individual. Future studies investigating the existence of genetic, neuroimaging, longitudinal course or treatment response differences between GAD-SUD and GAD-NSUD may help discriminate between these two competing explanations.

Our study found a higher prevalence of psychiatric comorbidity (other than SUD) in individuals with GAD-SUD than in those with GAD-NSUD, further suggesting that the former is associated with a general vulnerability to psychopathology and to its exacerbation, especially to externalizing spectrum disorders.[62] In this line, we found a considerably high rate (30%) of lifetime bipolar disorder among those with GAD-SUD, a finding that extends those reported in epidemiological studies regarding the strong association between bipolar, substance use and anxiety disorders.[63, 64] This subgroup of bipolar individuals is likely to suffer from a more severe psychopathology and burden since the comorbidity of anxiety disorders and SUD in bipolar individuals have been consistently associated with worse prognosis and higher rates of suicide attempts.[65–68] A recent study investigating use of self-medication among individuals with mood disorders found that the highest prevalence of self-medication was seen in bipolar I disorder (41.0%) and that, after adjusting for the effects of substance use disorders, self-medication was associated with higher odds of comorbid anxiety.[69] This suggests that in a considerable number of cases of bipolar disorder, the comorbidity with anxiety and substance use disorders may be explained by the self-medication hypothesis.

The lower prevalence of MDD in the GAD-SUD group than in the GAD-NSUD group appears to be a direct result of the high prevalence of bipolar disorder in the GAD-SUD group. Because a diagnosis of bipolar disorder precludes a diagnosis of MDD, only 70.04% of individuals of GAD-SUD (i.e., those without bipolar disorder) could meet a DSM-IV diagnosis of MDD, whereas 84.73% in the GAD-NSUD could. Recalculation of the prevalence of MDD in these restricted groups yielded a prevalence of 62.28% (95% CI 58.27%–66.29%) in the GAD-SUD group exclusive of bipolar disorder and 61.18% (95% 56.11–66.25%) in the GAD-NSUD after excluding bipolar disorders from that group, yielding an OR= 0.95 (95% CI=0.72–1.27). Thus, after excluding individuals with bipolar disorder the prevalence, of MDD was similar in both groups. In individuals with GAD, comorbidity with SUD seems to increase the burden of mood disorders, mainly through an increase in the co-occurrence of bipolar disorder.

In addition, although we found that SUD was a marker of greater severity and disability in individuals with GAD as assessed by statistically significant lower SF-12 scores in the mental health scale, social functioning scale and mental component summary, the difference between mean scores are somewhat small. The lack of differences between GAD individuals with and without comorbid SUD may be partially explained by a somewhat successful decrease in anxiety levels through self-medication, at the least in the short term[1]. Longitudinal studies are necessary to investigate the long-term impact of SUD on quality of life in individuals with GAD.

Our study found no differences in the rates of treatment seeking for GAD between those with GAD-SUD and GAD-NSUD across a broad range of service settings. Regardless of the presence of SUD, nearly 50% of individuals with GAD received no treatment, with an approximate 2-year lag between onset and first treatment among those that received treatment for GAD. Similarly, we also found no difference in the time lapsed from onset of GAD to first treatment despite the increased severity and additional psychiatric comorbidity present in the GAD-SUD group. This is consistent with prior studies showing that, although psychiatric comorbidity and mental health-related disability are generally strong predictors of mental health service use,[70, 71] comorbidity with SUD may not significantly increase rates of treatment for mood and anxiety disorders.[72]

Among those that sought treatment, individuals with GAD-SUD were as likely as those with GAD-NSUD to receive pharmacological treatment for anxiety. This practice is consistent with evidence [62, 73,74] that medication for anxiety symptoms in individuals with comorbid SUD are efficacious, but in contrast with previous findings in mayor depressive disorder (MDD) by our group showing that individuals with MDD-SUD were considerably less likely to be treated with antidepressants than those with MDD-NSUD.

The findings of this study should be interpreted in light of several limitations. First, because the NESARC sample only included civilian households and group quarters populations 18 years and older, information was unavailable on adolescents or individuals in prison, groups that may be at increased risk for GAD and SUD. Second, the cross-sectional design of the NESARC limits elucidation of the impact of the risk of chronicity and disability in GAD and comorbid conditions conferred by diagnostic group. Third, the reliability of the diagnosis GAD was only fair, which may have attenuated the relationship between GAD diagnosis and other variables in the study. Thus, our results are conservative. Fourth, although our study included a broad range of risk factors, it is not fully comprehensive.

Despite these limitations, this study provides the most comprehensive information to date on the prevalence, risk factors, psychiatric comorbidity, clinical correlates, and treatment patterns among individuals suffering from GAD with and without comorbid SUD. Our findings indicate that individuals of GAD-SUD constitutes half of the lifetime prevalence of GAD and is associated with high overall vulnerability for additional psychopathology, particularly in the externalizing spectrum, higher disability and higher use of alcohol and drugs to relieve anxiety symptoms. Future studies should investigate the existence genetic, neuroimaging differences between GAD-SUD and GAD-NSUD and the impact of SUD in the longitudinal course and treatment patterns of GAD.

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Table 1

Sociodemographic correlates of individuals with GAD-SUD and GAD-NSUD

Characteristics	GAD-NSUD[1] N=918		GAD-SUD N=839		OR (95%CI)
	%	S.E.	%	S.E.	
Sex					
Male	19.90	1.68	45.81	2.17	3.40 (2.59–4.47)
Female	80.10	1.68	54.19	2.17	1.00 (1.00–1.00)
Race/Ethnicity					
White	76.21	1.96	81.80	1.81	1.00 (1.00–1.00)
Black	9.86	1.06	6.30	0.91	0.60 (0.41–0.86)
Asian	2.38	0.62	4.08	0.97	1.60 (0.81–3.15)
Native American	2.69	0.74	1.36	0.58	0.47 (0.17–1.32)
Hispanic	8.88	1.39	6.46	1.15	0.68 (0.44–1.05)
US Born					
Yes	88.01	1.63	96.33	0.81	3.57 (2.26–5.63)
No	11.99	1.63	3.67	0.81	1.00 (1.00–1.00)
Age					
18–29	15.02	1.41	18.64	1.79	1.00 (1.00–1.00)
30–44	28.02	2.01	40.38	2.18	1.16 (0.81–1.67)
45–64	41.04	2.01	36.77	1.98	0.72 (0.53–0.99)
65+	15.92	1.24	4.22	0.79	0.21 (0.13–0.34)
Education					
< High School	14.81	1.34	13.13	1.44	0.82 (0.59–1.16)
High School	31.50	2.06	29.16	2.04	0.86 (0.65–1.15)
College	53.69	2.16	57.71	2.17	1.00 (1.00–1.00)
Individual Income					
0–19K	57.08	2.16	47.38	2.08	1.00 (1.00–1.00)
20–34K	20.48	1.65	22.12	1.59	1.30 (0.96–1.76)
35–64K	17.99	1.74	23.43	1.66	1.57 (1.17–2.10)
>70K	4.45	0.95	7.07	1.05	1.91 (1.13–3.25)
Family Income					
0–19K	28.92	1.73	26.01	1.93	1.00 (1.00–1.00)

Characteristics	GAD-NSUD[1] N=918		GAD-SUD N=839		OR (95%CI)
	%	S.E.	%	S.E.	
20–34K	17.58	1.34	22.40	1.76	1.42 (1.02–1.96)
35–69K	31.93	2.04	31.99	2.28	1.11 (0.80–1.54)
>70K	21.56	2.13	19.61	1.73	1.01 (0.71–1.43)
Marital Status					
Married	56.61	1.92	53.16	2.09	1.00 (1.00–1.00)
Widowed/Separated/Divorced	28.30	1.58	28.75	1.78	1.08 (0.83–1.40)
Never Married	15.09	1.31	18.09	1.67	1.28 (0.95–1.72)
Urbanicity					
Urban	78.71	2.12	77.84	2.52	1.00 (1.00–1.00)
Rural	21.29	2.12	22.16	2.52	1.05 (0.80–1.39)
Region					
Northeast	17.57	3.71	15.80	2.62	0.72 (0.48–1.09)
Midwest	26.15	3.23	29.90	3.61	0.92 (0.68–1.25)
South	34.86	3.41	27.66	3.06	0.64 (0.47–0.87)
West	21.42	3.27	26.65	3.92	1.00 (1.00-- 1.00)
Insurance					
Private	53.47	1.85	56.45	2.11	1.00 (1.00–1.00)
Public	28.52	1.65	23.80	1.81	0.79 (0.61–1.02)
No insurance	18.02	1.56	19.75	1.66	1.04 (0.78–1.39)

[1]Reference group

Table 2

Prevalence of GAD risk factors among individuals with GAD-NSUD and GAD-SUD

Risk Factors	GAD-NSUD[1] N=918		GAD-SUD N=839		OR (95%CI)	AOR[2] (95%CI)
	%	S.E.	%	S.E.		
Family history of Depression	68.25	1.84	70.45	1.91	1.11 (0.87–1.42)	1.09 (0.83–1.43)
Family history of AUD/SUD	52.33	1.86	66.61	1.87	1.82 (1.47–2.25)	2.06 (1.59–2.67)
Family history of problem behavior	35.88	1.82	47.22	1.95	1.60 (1.29–1.98)	1.65 (1.30–2.08)
Parental loss before 18 y	11.13	1.19	10.40	1.44	0.93 (0.62–1.39)	0.98 (0.62–1.53)
Early onset of anxiety	64.83	1.88	61.73	1.96	0.88 (0.71–1.08)	0.75 (0.58–0.96)
Conduct Disorder before 15y	1.46	0.57	1.69	0.46	1.16 (0.44–3.07)	0.87 (0.33–2.31)
Ever divorced	28.45	2.02	44.28	2.20	2.00 (1.53–2.61)	2.32 (1.71–3.15)
Low self-esteem	31.31	1.95	33.27	2.22	1.09 (0.84–1.42)	1.02 (0.75–1.37)
History of victimization	5.64	1.03	9.38	1.11	1.73 (1.09–2.75)	1.56 (0.92–2.63)

[1] Reference group

[2] AOR is adjusted for sex, race, US born, age, individual income, family income, and region.

Table 3

Lifetime prevalence of axis I and axis II disorders in individuals with GAD-NSUD and GAD-SUD

Psychiatric Comorbidity	GAD-NSUD[1] N=918		GAD-SUD N=839		OR (95%CI)	AOR[4] (95%CI)
	%	S.E.	%	S.E.		
Any Psychiatric Disorder[2]	89.99	1.14	94.29	1.14	1.84 (1.13–3.00)	1.64 (1.04–2.58)
Any Axis I Disorder	85.58	1.26	92.94	1.20	2.22 (1.44–3.41)	2.10 (1.39–3.18)
Alcohol Use Disorder	0.00	0.00	92.68	1.19		
Alcohol Abuse	0.00	0.00	38.55	1.99		
Alcohol Dependence	0.00	0.00	54.13	1.91		
Drug Use Disorder	0.00	0.00	46.59	2.30		
Drug Abuse	0.00	0.00	24.15	1.81		
Drug Dependence	0.00	0.00	22.44	2.09		
Nicotine Dependence	18.71	1.52	54.04	2.42	5.11 (3.86–6.75)	4.83 (3.68–6.36)
Mood Disorder	70.63	1.74	74.47	2.02	1.21 (0.92–1.59)	1.24 (0.93–1.65)
Major Depressive Disorder	52.77	1.98	42.85	2.10	0.67 (0.53–0.85)	0.68 (0.53–0.88)
Bipolar I	11.91	1.21	23.19	1.88	2.23 (1.65–3.03)	2.11 (1.51–2.96)
Bipolar II	3.36	0.76	6.77	1.11	2.09 (1.19–3.65)	2.19 (1.27–3.77)
Dysthymia	19.59	1.70	18.55	1.58	0.93 (0.69–1.26)	1.01 (0.73–1.40)
Any Anxiety Disorder[3]	53.87	2.02	61.44	2.12	1.36 (1.08–1.72)	1.34 (1.04–1.72)
Panic Disorder	23.45	1.70	34.61	1.94	1.73 (1.34–2.23)	1.80 (1.35–2.40)
Social Anxiety Disorder	25.19	1.83	30.83	1.96	1.32 (1.02–1.71)	1.17 (0.87–1.57)
Specific Phobia	33.63	2.11	38.02	1.92	1.21 (0.94–1.55)	1.25 (0.95–1.64)
Conduct Disorder	1.46	0.57	1.69	0.46	1.16 (0.44–3.07)	0.87 (0.33–2.31)
Pathological Gambling	0.40	0.20	1.91	0.56	4.84 (1.51–15.51)	5.42 (1.49–19.63)
Psychotic Disorder	1.33	0.33	1.91	0.54	1.44 (0.68–3.05)	1.06 (0.46–2.45)
Any Personality Disorder	47.15	1.97	57.54	2.26	1.52 (1.21–1.90)	1.19 (0.92–1.55)
Avoidant	15.09	1.58	19.12	1.92	1.33 (0.94–1.88)	1.00 (0.66–1.50)
Dependent	3.48	0.72	5.58	1.24	1.64 (0.90–2.98)	1.82 (0.96–3.44)
Obsessive-Compulsive	27.66	1.95	30.75	2.06	1.16 (0.90–1.50)	0.94 (0.70–1.25)
Paranoid	21.45	1.74	27.85	1.89	1.41 (1.06–1.89)	1.38 (0.98–1.95)
Schizoid	14.09	1.40	17.42	1.71	1.29 (0.92–1.79)	1.26 (0.88–1.79)

Psychiatric Comorbidity	GAD-NSUD[1] N=918		GAD-SUD N=839		OR (95%CI)	AOR[4] (95%CI)
	%	S.E.	%	S.E.		
Histrionic	6.55	0.96	10.36	1.47	1.65 (1.09–2.48)	1.47 (0.93–2.30)
Antisocial	3.07	0.74	19.36	1.62	7.58 (4.45–12.91)	5.62 (3.25–9.72)

[1]Reference group

[2]Any psychiatric Disorder doesn't include AUD, DUD, and GAD

[3]Any Anxiety disorder doesn't include GAD.

[4]AOR is adjusted for sex, race, US born, Age, individual in come, family income, and region.

Table 4

Prevalence of criteria and clinical characteristics of individuals with GAD-NSUD and GAD-SUD

GAD clinical symptoms and correlates	GAD-NSUD[1] N=918		GAD-SUD N=839		Wald F	p value	Wald F	p value
	Mean	S.E.	Mean	S.E.				
Number of criteria	4.94	0.04	4.94	0.04	0.00	0.9966	0.33	0.5684
Diagnostic Criteria	%	S.E.	%	S.E.	OR	95% CI	AOR[2]	95% CI
Restlessness or feeling keyed up or on edge	92.45	1.20	92.42	1.07	1.00	(0.61–1.63)	0.97	(0.59–1.59)
Being easily fatigued	84.18	1.41	80.93	1.51	0.80	(0.60–1.05)	0.92	(0.67–1.26)
Difficulty concentrating or mind going blank	90.05	1.22	93.28	0.99	1.53	(1.01–2.33)	1.75	(1.11–2.77)
Irritability	83.49	1.54	86.85	1.59	1.31	(0.92–1.86)	1.27	(0.87–1.85)
Muscle tension	63.73	2.14	61.74	1.99	0.92	(0.71–1.19)	1.04	(0.79–1.35)
Sleep disturbance	80.46	1.47	79.21	1.90	0.93	(0.70–1.23)	0.87	(0.65–1.18)
Associated Clinical Characteristics								
Associated Autonomic symptoms	68.42	2.02	70.31	1.85	1.09	(0.85–1.40)	1.30	(0.98–1.72)
Associated cardiovascular symptoms	42.61	1.99	47.89	2.00	1.24	(0.99–1.55)	1.33	(1.04–1.71)
Associated Respiratory symptoms	40.94	2.10	44.84	2.01	1.17	(0.93–1.47)	1.34	(1.04–1.74)
Associated gastrointestinal symptoms	55.34	2.07	55.12	2.03	0.99	(0.78–1.26)	1.10	(0.83–1.45)
Urinary symptoms	30.34	1.67	30.29	2.06	1.00	(0.78–1.28)	1.20	(0.90–1.58)
Arguments or friction with relatives or friends	57.82	1.93	64.53	2.21	1.33	(1.04–1.69)	1.03	(0.80–1.32)
Difficulty or inability to complete daily tasks	73.91	1.78	78.76	1.74	1.31	(1.00–1.72)	1.30	(0.98–1.73)
Restrict usual activities	53.73	2.11	56.76	2.25	1.13	(0.88–1.45)	1.14	(0.87–1.48)
	Mean	S.E.	Mean	S.E.	Wald F	P value	Wald F	P value
Number of stressful situations in last 12 months	7.07	0.24	7.38	0.24	0.95	0.3472	0.06	0.8126
SF-12v2 Scores								
Physical component summary	47.21	0.53	48.33	0.57	1.45	0.1532	1.16	0.2850
General health scale	44.70	0.55	45.35	0.60	0.81	0.4200	1.22	0.2738
Physical functioning scale	47.97	0.53	46.89	0.50	1.51	0.1350	2.39	0.1271
Role physical scale	46.27	0.50	47.38	0.51	1.61	0.1111	1.07	0.3045
Bodily pain	44.41	0.59	44.66	0.51	−0.33	0.7425	3.87	0.0534
Mental component summary	43.29	0.49	42.22	0.56	1.38	0.1734	5.41	0.0231
Social function scale	44.66	0.56	43.78	0.58	1.09	0.2786	5.51	0.0220

GAD clinical symptoms and correlates	GAD-NSUD[1] N=918		GAD-SUD N=839		Wald F	p value	Wald F	p value
	Mean	S.E.	Mean	S.E.				
Role emotional scale	43.20	0.51	43.07	0.65	0.15	0.8838	3.55	0.0641
Mental health scale	42.83	0.47	42.06	0.55	1.05	0.2965	5.17	0.0263
	%	S.E.	%	S.E.	OR	95% CI	AOR[2]	95% CI
Overall Health excellent to good	70.19	1.72	72.31	1.91	1.11	(0.87–1.42)	0.89	(0.66–1.21)
Overall health fair to poor	29.81	1.72	27.69	1.91	1.00	(1.00–1.00)	1.00	(1.00–1.00)

[1] Reference group

[2] AOR is adjusted for sex, race, US born, Age, individual in come, family income, and region.

Table 5

Age of Onset, Course and Treatment patterns of individuals with GAD-NSUD and GAD-SUD

Characteristics of GAD	GAD-NSUD[1] N=918		GAD-SUD N=839		Wald F	p value	Wald F	p value
	Mean	S.E.	Mean	S.E.				
Age at onset (y.o.)	34.90	0.66	30.45	0.55	5.53	<0.0001	0.55	0.4616
Number of GAD episodes	3.12	0.27	3.73	0.48	1.10	0.2755	0.88	0.3523
Duration of longest episode (median)	11.53	0.01	11.76	0.02				
Age at first treatment	36.99	0.79	32.47	0.69	4.39	<0.0001	1.58	0.2132
Time from onset to 1st treatment,	2.16	0.32	2.45	0.37	0.58	0.5622	0.37	0.5459
	%	S.E.	%	S.E.	OR	(CI 95%)	AOR[2]	(CI 95%)
Treated as outpatient	39.22	1.89	41.28	2.03	1.09	(0.86 1.37)	1.18	(0.91 1.53)
Treated as inpatient	6.05	0.93	8.36	1.22	1.42	(0.90 2.22)	1.37	(0.88 2.12)
Use of prescribed medication	34.79	1.94	37.50	2.16	1.12	(0.88 1.43)	1.18	(0.90 1.56)
Emergency room admittance	5.42	0.89	8.03	1.19	1.52	(0.94 2.48)	1.78	(1.06 3.00)
Use of alcohol to help relieve GAD	6.89	1.03	31.56	1.99	6.23	(4.34 8.94)	5.57	(3.76 8.24)
Substance-use to help relieve GAD	0.91	0.33	13.58	1.48	17.06	(8.05 36.1)	14.35	(6.48 31.76)
Characteristics of AUD/SUD			Mean	S.E.				
Age of onset, years old	-	-	21.25	0.33				
Age at first treatment	-	-	28.24	0.84				
			%	S.E.				
Treated as outpatient	-	-	18.20	1.61				
Treated as inpatient	-	-	16.00	1.58				
Emergency room admittance	-	-	8.55	1.17				

[1] Reference group

[2] AOR is adjusted for sex, race, nativity, age, individual in come, family income, region, and insurance.