Prevalence, Correlates, and Comorbidity of Bipolar I Disorder and Axis I and II Disorders: Results From the National Epidemiologic Survey on Alcohol and Related Conditions

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Objective: To present nationally representative data on 12-month and lifetime prevalence, correlates, and comorbidity of bipolar I disorder.

Method: The data were derived from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (N = 43,093). Prevalences and associations of bipolar I disorder with sociodemographic correlates and Axis I and II disorders were determined.

Results: Prevalences of 12-month and lifetime DSM-IV bipolar I disorder were 2.0% (95% CI = 1.82 to 2.18) and 3.3% (95% CI = 2.76 to 3.84), respectively, and no sex differences were observed. The odds of bipolar I disorder were significantly greater among Native Americans, younger adults, and respondents who were widowed/separated/divorced and of lower socioeconomic status and significantly lower among Asians and Hispanics ($p < .05$). Men were significantly ($p < .05$) more likely to have unipolar mania and earlier onset and longer duration of manic episodes, while women were more likely to have mixed and major depressive episodes and to be treated for manic, mixed, and major depressive episodes. Bipolar I disorder was found to be highly and significantly related ($p < .05$) to substance use, anxiety, and personality disorders, but not to alcohol abuse.

Conclusion: Bipolar I disorder is more prevalent in the U.S. population than previously estimated, highlighting the underestimation of the economic costs associated with this illness. Associations between bipolar I disorder and Axis I and II disorders were all significant, underscoring the need for systematic assessment of comorbidity among bipolar I patients.

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The essential feature of bipolar I disorder is a clinical course that is characterized by the occurrence of 1 or more manic or mixed episodes. Individuals with bipolar I disorder often have had 1 or more major depressive episodes.[1] Bipolar I disorder can be a debilitating illness with a significantly increased risk for suicide, frequent hospitalizations, and high treatment costs.[2,3] Several studies have shown the deleterious consequences of bipolar I disorder on occupational functioning.[4,5] Furthermore, epidemiologic[6–10] and clinical[11–17] data indicate that substance use and anxiety, personality, and eating disorders are highly comorbid with bipolar I disorder. Axis I and II comorbidity with bipolar I disorder has been associated with increased severity, disability, earlier age at onset of bipolar I disorder, higher rates of suicidality, resistance to pharmacologic treatment, poorer overall outcome, and lower probability of recovery.[12,17–26]

Despite the seriousness and recurrent nature of bipolar I disorder, very little is known about its prevalence, corre-

lates, and comorbidity in general population samples. Although numerous epidemiologic surveys worldwide have estimated the lifetime prevalence of bipolar I disorder to be between 0.2% and 1.9%,[7,8,10,27–36] these surveys had several limitations. First, most of these surveys had sample sizes that were not large enough to provide stable estimates for rare disorders, such as bipolar I, particularly across important subgroups of the population. Second, none of these surveys used the most recent classification of the American Psychiatric Association, the DSM-IV,[1] but relied on the DSM-III[37] or the DSM-III-R.[38] The diagnostic criteria for bipolar disorders in these earlier nomenclatures were less clear than the current nomenclature. For example, in the DSM-III and DSM-III-R, there were no explicit diagnostic criteria for mixed episode, which plays a larger role in DSM-IV definitions of bipolar I disorder. Third, none of these surveys assessed DSM-IV definitions of independent and substance-induced disorders to determine if bipolar I disorder is related to substance use disorders even when substance-induced disorders are ruled out. Fourth, the response rates in many of these surveys were low (often < 60%), precluding both reliable and precise estimates of the disorder. Fifth, very few epidemiologic studies[7–10,34–36] have examined the comorbidity of bipolar I disorder with anxiety disorders and antisocial personality disorder, and in each of these surveys, the number of individuals with bipolar I disorder was small (N = 1–168). Sixth, in contrast to the clinical literature,[11–13] no epidemiologic survey has examined the co-occurrence of bipolar I disorder with Axis II personality disorders, other than antisocial personality disorder.

The lack of accurate information about the prevalence, correlates, and co-occurrence of bipolar I disorder represents a gap in our knowledge in terms of prevention, intervention, treatment need, and economic costs. Accordingly, the present study was designed, in part, to address this gap. This article presents data from a major national survey designed, in part, to overcome the limitations of previous epidemiologic surveys on bipolar I disorder. This survey, the National Institute on Alcohol Abuse and Alcoholism (NIAAA) National Epidemiologic Survey on Alcohol and Related Conditions (NESARC),[39,40] covers the prevalence and comorbidity of major DSM-IV substance use, mood and anxiety disorders, and 7 of the 10 personality disorders in a nationally representative U.S. sample of 43,093 respondents. The sample size and excellent response rate of the NESARC allow for the accurate estimation of the rates of rare conditions, the examination of rates of disorder by important sociodemographic correlates, and accurate analysis of the comorbidity of bipolar I disorder with other disorders. This study also provides information on the age at onset, course, and treatment-seeking patterns among individuals with bipolar I disorder.

METHOD

NESARC Sample

Wave 1 of the NESARC was a nationally representative face-to-face survey of 43,093 respondents, 18 years and older, conducted by the NIAAA in 2001–2002.[39,40] The target population of the NESARC is the civilian noninstitutionalized population residing in the United States, including Alaska and Hawaii. The housing unit sampling frame of the NESARC was the U.S. Bureau of the Census Supplementary Survey. The NESARC also included a group quarters sampling frame derived from the Census 2000 Group Quarters Inventory. The group quarters sampling frame captures important subgroups of the population with heavy substance use patterns not often included in general population surveys. These subgroups of the population included the military living off base as well as those living in boarding houses, rooming houses, nontransient hotels and motels, shelters, facilities for housing workers, college quarters, and group homes. Hospitals, jails, and prisons were not among the group quarters sampled. The overall survey response rate was 81.0%, substantially higher than that of other surveys of this kind.

Black and Hispanic households were oversampled. The oversampling procedure increased the percentage of non-Hispanic black households in the sample from 12.3% to 19.1% (N = 8245) and the percentage of Hispanic households from 12.5% to 19.3% (N = 8308). Black and Hispanic persons were oversampled because these subgroups have been underrepresented in previous comorbidity surveys. One sample person from each household or group quarters unit was randomly selected for interview, and young adults, aged 18 to 24 years, were oversampled at a rate of 2.25 times that of other members in the household.

The NESARC sample was weighted to adjust for the probabilities of selection of a sample housing unit or housing unit equivalent from the group quarters sampling frame, nonresponse at the household and person levels, selection of 1 person per household, and oversampling of young adults. Once weighted, the data were adjusted to be representative of the U.S. population for various sociodemographic variables, including region, age, sex, race, and ethnicity, based on the 2000 Decennial Census.

Interviewer Training and Field Quality Control

Approximately 1800 professional interviewers from the U.S. Census Bureau administered the NESARC using laptop computer-assisted software that included built-in skip, logic, and consistency checks. On average, the interviewers had 5 years' experience working on Census and other health-related national surveys. Regional supervisors recontacted a random 10% of all respondents for quality-control purposes and to verify the accuracy of the interviewer's performance. In addition, 2657 respondents were randomly selected to participate in a reinterview

study after completion of their NESARC interview that served as a check on survey data quality and formed the basis of an additional test-retest reliability study of Wave 1 NESARC measures.[41]

DSM-IV Psychiatric Disorder Assessment

The NESARC diagnostic interview used to generate diagnoses is the NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (AUDADIS-IV), a state-of-the-art structured diagnostic interview designed for use by lay interviewers.[42] Lifetime bipolar I disorder was defined as having at least 1 manic or mixed episode with or without 1 or more major depressive or hypomanic episodes on a lifetime basis. Among respondents with a lifetime diagnosis of bipolar I disorder, respondents who had at least 1 manic, mixed, hypomanic, or major depressive episode in the year preceding the interview were classified with 12-month bipolar I disorder. Mixed episodes were defined as a period of time, lasting at least 1 week, in which the criteria were met both for a manic episode and for a major depressive episode accompanied by rapidly alternating moods (e.g., depression, euphoria). DSM-IV anxiety diagnoses included in the AUDADIS-IV and the focus of comorbidity analysis presented here were panic disorder (with and without agoraphobia), social phobia, specific phobia, and generalized anxiety disorder.

As discussed in detail elsewhere,[43] 12-month and lifetime mood and anxiety diagnoses presented in this article are defined in the DSM-IV as primary or independent diagnoses. In the DSM-IV, the term *primary* is used as shorthand to indicate those mental disorders that are not substance-induced and that are not due to a general medical condition.[1(p192)] Respondents classified with disorders that were only substance-induced and/or due to a general medical condition were not included in the analyses presented here. Major depressive episodes entirely accounted for by bereavement were also excluded. All mood and anxiety disorders satisfied the clinical significance criteria of the DSM-IV.

The AUDADIS-IV included an extensive list of symptom questions that separately operationalized DSM-IV criteria for alcohol and drug-specific abuse and dependence for 10 classes of drugs, including sedatives, tranquilizers, opiates (other than heroin or methadone), stimulants, hallucinogens, cannabis, cocaine (including crack cocaine), inhalants/solvents, heroin, and other drugs.

Consistent with the DSM-IV, lifetime AUDADIS-IV diagnoses of alcohol abuse required a respondent to meet at least 1 of the 4 criteria defined for abuse either in the 12-month period preceding the interview or before that 12-month period. AUDADIS-IV alcohol dependence diagnoses required the respondent to satisfy at least 3 of the 7 DSM-IV criteria for dependence either during the past year or within any 1-year period prior to the past year. The drug-specific diagnoses of abuse and dependence were derived using the same algorithm described for alcohol use disorders.

Rather than assessing nicotine dependence in the same modules as alcohol or drugs, nicotine dependence was assessed in a separate AUDADIS-IV module, as described in detail elsewhere.[44] This was done to closely adhere to the DSM-IV guidelines,[1(p243)] indicating that generic drug dependence criteria do not apply or need to be modified to assess nicotine dependence. Past 12-month and lifetime measures of nicotine dependence were derived using the same algorithm described for alcohol and drug-specific diagnoses of dependence.[44]

The AUDADIS-IV also assessed 7 of the 10 Axis II personality disorders appearing in the DSM-IV: avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial. The diagnosis of personality disorders requires an evaluation of the individual's long-term patterns of functioning.[1(p630)] To receive a DSM-IV diagnosis, respondents needed to endorse the requisite number of DSM-IV symptom items for the particular personality disorder, and at least 1 of the positive symptom items must have caused social and/or occupational dysfunction. DSM-IV conduct disorder (without antisocial adult behaviors) also was assessed in the NESARC. Because of time and space constraints, not all DSM-IV personality disorders were assessed in the Wave 1 NESARC. However, in the follow-up Wave 2 of the NESARC, personality disorders that require many more symptom items to operationalize (e.g., borderline, schizotypal, and narcissistic) will be assessed.

The test-retest reliabilities of AUDADIS-IV alcohol and drug disorder measures were excellent, exceeding $\kappa = 0.74$ for alcohol diagnoses and $\kappa = 0.79$ for drug diagnoses.[41,45–48] The discriminant and convergent,[49–60] concurrent,[61,62] construct,[63–65] and population[66] validity of the AUDADIS-IV alcohol and drug use disorder diagnoses also have been well documented, including in the World Health Organization/National Institutes of Health Reliability and Validity Study.[57,60,62,67–69]

The test-retest reliability of bipolar I disorder was good ($\kappa = 0.59$), and reliability was fair to excellent for other mood and anxiety disorders ($\kappa = 0.40$–0.65) and personality disorders ($\kappa = 0.40$–0.67).[41,45,48] In addition, the validity of both 12-month and lifetime bipolar I disorder was assessed in a series of linear regression analyses, using the NESARC data, that examined the associations between bipolar I disorder and Short Form-12v2[70] mental disability scores, controlling for age, conduct disorder, and all substance use, anxiety, personality, and other mood disorders. In the present analyses, the focus was on 4 Short Form-12v2 mental disability scores: the mental component summary score, the social functioning score, the role emotional function score, and the mental health score, reflecting general mental health functioning. Regardless of

time period, bipolar I disorder was shown to be a highly significant ($p < .0001$) predictor of all 4 scores. Respondents with bipolar I disorder had significantly greater disability and social/occupational dysfunction than respondents who did not have the disorder. Interestingly, the results of parallel linear regression analyses showed that respondents with bipolar I disorder had significantly ($p < .0001$) greater disability and social/occupational dysfunction compared to respondents with lifetime major depressive disorder as assessed with all 4 Short Form-12v2 scores. With few exceptions, analyses show similar relationships between DSM-IV mood, anxiety, and personality disorders and SF-12v2 disability scores.[40,43,71–74]

Other Measures

Treatment utilization, age at first treatment, number of episodes, and duration of only or longest (if applicable) episode were ascertained separately for manic, mixed, and major depressive episodes among respondents with lifetime bipolar I disorder. Respondents were classified as receiving treatment if they (1) visited a counselor, therapist, doctor, psychologist, or other health professional to get help for an episode; (2) were a patient in a hospital for at least 1 night related to an episode; (3) visited an emergency room to get help for an episode; or (4) were prescribed medications for an episode. Ages at onset of manic, mixed, and major depressive episodes among bipolar I respondents were measured as the first age at which the requisite number of symptoms for each diagnosis clustered in time.

Statistical Analyses

Most of the analyses presented in this study were carried out with simple computations of means, medians, or cross-tabulations. A logistic regression analysis was used to examine the multivariate associations between bipolar I disorder and all sociodemographic correlates entered into the same model. Odds ratios (ORs) were used to examine the associations between 12-month and lifetime bipolar I disorder and other psychiatric disorders, both unadjusted and adjusted for sociodemographic factors. Hazard rates, reflecting the risk of onset of bipolar I disorder at specific ages among the population at risk for the disorder at those ages, were calculated using standard life table methods.[75,76] Standard errors and 95% confidence intervals for all analyses were estimated using Survey for Data Analysis (SUDAAN),[77] a software package that adjusts for design characteristics of complex sample surveys.

RESULTS

Prevalence and Sociodemographic Correlates

The lifetime and 12-month estimates of DSM-IV bipolar I disorder were 3.3% (95% CI = 2.76 to 3.84) (N = 1411) and 2.0% (95% CI = 1.82 to 2.18) (N = 883), respectively (Table 1). For both time periods, Native Americans and respondents who were younger, never married, or widowed/separated/divorced and those with lower educational and income levels were more likely to have bipolar I disorder. The prevalences of bipolar I disorder were similar among men and women.

Table 1. Prevalence of 12-Month and Lifetime DSM-IV Bipolar I Disorder by Sociodemographic Characteristics

	12-Month (N = 883)		Lifetime (N = 1411)	
Characteristic	%[a]	SE	%[a]	SE
Total	2.0	0.09	3.3	0.13
Sex				
Men	1.8	0.11	3.2	0.16
Women	2.2	0.13	3.4	0.18
Race-ethnicity				
White	2.1	0.12	3.3	0.16
Black	2.1	0.23	3.5	0.32
Native American	3.3	0.76	6.2	1.06
Asian/Pacific Islander	1.0	0.29	2.0	0.44
Hispanic	1.9	0.20	3.1	0.25
Age, y				
12–29	3.4	0.25	5.0	0.32
30–44	2.2	0.16	3.7	0.23
45–64	1.8	0.15	3.0	0.19
65+	0.4	0.07	0.9	0.12
Marital status				
Married/living with someone as if married	1.5	0.10	2.7	0.14
Widowed/separated/divorced	2.5	0.21	3.8	0.26
Never married	3.2	0.23	4.7	0.26
Education				
Less than high school	2.6	0.25	4.0	0.31
High school	2.1	0.16	3.5	0.22
Some college or higher	1.8	0.10	3.0	0.15
Personal income, $				
0–19,999	2.8	0.16	4.4	0.20
20,000–34,999	1.8	0.16	3.0	0.21
35,000–69,999	1.1	0.14	2.1	0.20
70,000+	0.6	0.13	1.3	0.20
Urbanicity				
Urban	1.9	0.10	3.3	0.14
Rural	2.4	0.24	3.6	0.31
Region				
Northeast	1.9	0.25	3.3	0.37
Midwest	2.4	0.20	3.4	0.27
South	1.8	0.14	2.9	0.18
West	2.1	0.18	3.9	0.25

[a]Based on weighted data.

When associations between bipolar I disorder and sociodemographic characteristics were examined in the multivariate logistic analysis, no sex difference was found (Table 2). The odds of bipolar I disorder were significantly greater among Native Americans (OR = 1.5) and significantly lower among Asians (OR = 0.5) and Hispanics (OR = 0.6) compared with whites ($p < .05$). The odds of bipolar I disorder also were significantly greater for 18- to 29-year-olds (OR = 7.1), 30- to 44-year-olds (OR = 6.3), and 45- to 64-year-olds (OR = 4.7) compared with the oldest age group and significantly greater among respondents who were widowed/separated/divorced (OR = 1.8) relative to those who were married or cohabiting ($p < .05$).

Table 2. Odds Ratios of DSM-IV Lifetime Bipolar I Disorder and Sociodemographic Characteristics[a]

Characteristic	Odds Ratio (95% CI)
Sex	
Men	1.0
Women	1.1 (1.0 to 1.3)
Race-ethnicity	
White	1.0
Black	0.9 (0.7 to 1.1)
Native American	1.5 (1.1 to 2.2)
Asian/Pacific Islander	0.5 (0.3 to 0.8)
Hispanic	0.6 (0.5 to 0.7)
Age, y	
18–29	7.1 (5.1 to 10.1)
30–44	6.3 (4.7 to 8.7)
45–64	4.7 (3.5 to 6.3)
65+	1.0
Marital status	
Married/living with someone as if married	1.0
Widowed/separated/divorced	1.8 (1.5 to 2.1)
Never married	1.1 (0.9 to 1.4)
Education	
Less than high school	1.3 (1.1 to 1.6)
High school	1.0 (0.9 to 1.2)
Some college or higher	1.0
Personal income, $	
0–19,999	3.7 (2.6 to 5.4)
20,000–34,999	2.3 (1.6 to 3.4)
35,000–69,999	1.6 (1.2 to 2.3)
70,000+	1.0
Urbanicity	
Urban	1.0
Rural	1.0 (0.9 to 1.3)
Region	
Northeast	0.8 (0.7 to 1.1)
Midwest	0.8 (0.6 to 0.9)
South	0.7 (0.5 to 0.8)
West	1.0

[a]Results of a multivariate logistical regression analysis in which all sociodemographic characteristics are input into the same model simultaneously.

With regard to socioeconomic correlates, respondents in the 3 lowest income groups ($0–19,999, OR = 3.7; $20,000–34,999, OR = 2.3; $35,000–69,999, OR = 1.6) had greater odds of bipolar I disorder than respondents in the highest income group as did respondents with less than a high school education (OR = 1.3) compared with those with at least a 4-year college degree ($p < .05$). Furthermore, respondents residing in the South (OR = 0.7) and Midwest (OR = 0.8) had lower odds of bipolar I disorder than respondents living in the West.

Age at Onset and Course

Overall, the mean age at onset of bipolar I disorder was 22.3 years (Table 3). The median age at onset was 18.9 years (95% CI = 18.1 to 20.4). As shown in Figure 1, age at onset for bipolar I disorder peaked between 16 and 18 years and declined steadily over the next 5 decades of life. Among respondents with lifetime bipolar I disorder, 29.9% had manic and major depressive episodes, 32.1% had mixed and major depressive episodes, while 22.2% and 10.2% had only manic or mixed episodes, respectively. Very few respondents reported manic and mixed episodes (1.2%) or manic, mixed, and major depressive episodes (4.3%) at some time in their lives.

The mean age at onset of a major depressive episode (23.6) was younger, but not significantly younger, than the corresponding ages at onset for manic (24.9) or mixed (25.1) episodes. The median numbers of lifetime major depressive (2.3) and mixed (2.0) episodes were significantly greater ($p < .05$) than for manic episodes (1.3). Similarly, the median duration of major depressive episodes (25.4 weeks) was significantly greater than the durations of both mixed (8.2 weeks) and manic episodes (5.5 weeks), with the duration of mixed episodes significantly ($p < .05$) exceeding that of manic episodes.

With regard to sex, men were significantly more likely than women to have unipolar mania (30.4% vs. 15.3%), and women were significantly more likely than men to have mixed episodes in addition to major depressive episodes. The relationship between the number of years since onset of mania and probability of ever having a major depressive episode was weak (point-biserial correlation = 0.025, $p < .251$). The age at onset of a manic episode also was significantly earlier among men compared with women (22.8 vs. 26.9 years). In addition, the duration of manic episodes among men (6.0 weeks) was greater than among women (4.7 weeks).

12-Month and Lifetime Prevalence of DSM-IV Axis I and II Disorders Among Respondents With Bipolar I Disorder

As indicated in Table 4, 23.6% of the respondents with bipolar I disorder in the 12 months preceding the interview had at least 1 alcohol use disorder during that same 12-month period. Corresponding prevalences of any drug use disorder, predominantly dependence, and nicotine dependence were 12.9% and 37.0%, respectively. Furthermore, 48.5% of respondents with 12-month bipolar I disorder had at least 1 anxiety disorder. Prevalences of specific phobia (25.6%) and generalized anxiety disorder (21.8%) were especially high among respondents with bipolar I disorder. The prevalence of any personality disorder among respondents with bipolar I disorder was also quite high (70.8%), with prevalence of specific personality disorder ranging from 7.8% for dependent to 39.5% for obsessive-compulsive personality disorder. In general, the pattern of rates of other DSM-IV psychiatric disorders among respondents with lifetime bipolar I disorder mirrored those of respondents with 12-month bipolar I disorder, but were much higher except for Axis II personality disorders.

12-Month and Lifetime ORs of DSM-IV Bipolar I Disorder and Other Psychiatric Disorders

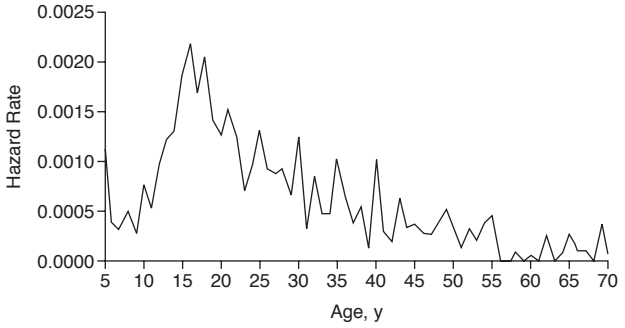
As a preliminary to presenting associations between bipolar I disorder and other specific psychiatric disorders among all individuals with bipolar I disorder, separate

Table 3. Age at Onset and Course of Bipolar I Disorder

Characteristic	Men	Women	Total
Age at onset of bipolar I disorder, mean (SE), y	22.1 (0.60)	22.4 (0.46)	22.3 (0.36)
Only manic episodes, % (SE)	30.4 (2.47)	15.3 (1.46)	22.2 (1.37)[a]
Only mixed episodes, % (SE)	10.7 (1.36)	9.7 (1.31)	10.2 (0.98)
Manic and major depressive episodes, % (SE)	27.3 (2.32)	32.1 (2.03)	29.9 (1.50)
Mixed and major depressive episodes, % (SE)	27.0 (2.38)	36.5 (2.02)	32.1 (1.60)[b]
Manic and mixed episodes, % (SE)	1.3 (0.49)	1.1 (0.39)	1.2 (0.31)
Manic, mixed, and major depressive episodes, % (SE)	3.3 (0.80)	5.2 (0.97)	4.3 (0.65)
Age at onset of manic episode, mean (SE), y	22.8 (0.74)	26.9 (0.82)	24.9 (0.60)[b]
Age at onset of major depressive episode, mean (SE), y	23.7 (0.76)	23.5 (0.54)	23.6 (0.40)
Age at onset of mixed episode, mean (SE), y	23.5 (0.92)	26.2 (0.70)	25.1 (0.56)[c]
No. of lifetime manic episodes, median (SE)	1.3 (0.12)	1.4 (0.18)	1.3 (0.12)
No. of lifetime major depressive episodes, median (SE)	1.9 (0.36)	2.4 (0.16)	2.3 (0.16)
No. of lifetime mixed episodes, median (SE)	1.9 (0.58)	2.1 (0.24)	2.0 (0.24)
Duration of only/longest manic episode, median (SE), wk	6.0 (0.93)	4.7 (1.39)	5.5 (1.38)[c]
Duration of only/longest major depressive episode, median (SE), wk	25.7 (5.92)	25.3 (4.10)	25.4 (3.02)
Duration of only/longest mixed episode, median (SE), wk	7.7 (2.12)	8.1 (1.24)	8.2 (1.07)

[a]Sex difference significant at $p < .0001$.
[b]Sex difference significant at $p < .0030$.
[c]Sex difference significant at $p < .0500$.

Figure 1. Hazard Rates for Age at Onset of Bipolar I Disorder



logistic regressions were conducted among respondents with bipolar I disorder who were in full remission (i.e., reported at least 2 months with no symptoms) during the year preceding the interview and among those respondents who remained symptomatic. There were no differences observed in the magnitude of the ORs between bipolar I disorder and other psychiatric disorders between these 2 groups of bipolar I respondents. Thus, Table 5 presents the 12-month and lifetime associations between bipolar I disorder and other psychiatric disorders among all individuals with bipolar I disorder during each time period. These associations are presented for unadjusted bivariate models and for models in which the ORs are adjusted for sociodemographic factors. The pattern of 12-month and lifetime ORs is overwhelmingly positive (i.e., > 1.0) and statistically significant for all disorders except alcohol abuse. Although the associations between bipolar I disorder and other psychiatric disorders were somewhat lower when adjusted for important covariates, the relationships remained strong and statistically significant. In general, ORs were greater for the 12-month period compared to lifetime disorders.

Table 4. Twelve-Month and Lifetime Prevalence of DSM-IV Psychiatric Disorders Among Survey Respondents With 12-Month and Lifetime Bipolar I Disorder

	Bipolar I Disorder			
	12-Month		Lifetime	
Comorbid Psychiatric Disorder	%	SE	%	SE
Any alcohol use disorder	23.6	1.87	58.0	1.64
Alcohol abuse	5.8	0.90	17.4	1.32
Alcohol dependence	17.8	1.83	40.5	1.78
Any drug use disorder	12.9	1.65	37.5	1.73
Any drug abuse	5.1	0.95	19.4	1.35
Any drug dependence	7.8	1.37	18.1	1.40
Nicotine dependence	37.0	2.26	44.4	1.92
Any anxiety disorder	48.5	2.07	56.3	1.73
Panic disorder with agoraphobia	6.8	0.96	8.3	0.90
Panic disorder without agoraphobia	12.3	1.41	17.2	1.12
Social phobia	18.0	1.60	23.7	1.62
Specific phobia	25.6	1.76	29.7	1.47
Generalized anxiety	21.8	1.83	25.0	1.52
Any personality disorder[a]	70.8	1.85	64.7	1.63
Avoidant	24.8	1.81	19.6	1.37
Dependent	7.8	1.18	5.9	0.78
Obsessive-compulsive	39.5	2.05	35.5	1.67
Paranoid	36.4	2.04	32.3	1.52
Schizoid	24.4	1.79	19.9	1.24
Histrionic	17.5	1.52	14.4	1.10
Antisocial	21.7	1.73	21.6	1.34
Conduct disorder	3.3	0.96	3.1	0.64

[a]Personality disorders assessed on a lifetime basis only.

With regard to the adjusted models, the 12-month and lifetime associations between bipolar I disorder and alcohol and drug dependence were strong (ORs = 4.1–10.6), while the corresponding relationships with drug abuse (ORs = 2.5 and 2.5, respectively) and nicotine dependence (ORs = 3.1 and 3.4, respectively) were weaker. Bipolar I disorder also was strongly associated with all anxiety disorders regardless of time frame (ORs = 4.0–13.5), with associations being strongest among bipolar I dis-

Table 5. Twelve-Month and Lifetime Odds Ratios (ORs) of DSM-IV Bipolar I Disorder and Other Psychiatric Disorders[a]

	12-Month		Lifetime	
Comorbid Psychiatric Disorder	Unadjusted[b] OR (95% CI)	Adjusted[c] OR (95% CI)	Unadjusted[b] OR (95% CI)	Adjusted[c] OR (95% CI)
Any alcohol use disorder	3.5 (2.8 to 4.3)	2.8 (2.2 to 3.5)	3.3 (2.9 to 3.8)	3.5 (3.0 to 4.1)
Alcohol abuse	1.3 (0.9 to 1.8)	1.1 (0.8 to 1.6)	1.0 (0.8 to 1.2)	1.0 (0.8 to 1.3)
Alcohol dependence	5.9 (4.6 to 7.7)	4.1 (3.1 to 5.6)	5.2 (4.5 to 6.1)	4.5 (3.9 to 5.3)
Any drug use disorder	8.2 (6.0 to 11.1)	5.4 (3.9 to 7.4)	5.8 (5.0 to 6.7)	4.8 (4.1 to 5.6)
Any drug abuse	4.0 (2.7 to 6.0)	2.5 (1.6 to 3.9)	3.0 (2.5 to 3.7)	2.5 (2.0 to 3.0)
Any drug dependence	17.8 (11.5 to 27.4)	10.6 (6.8 to 16.6)	10.5 (8.6 to 12.8)	7.7 (6.3 to 9.5)
Nicotine dependence	4.2 (3.5 to 5.1)	3.1 (2.6 to 3.8)	4.0 (3.4 to 4.6)	3.4 (2.9 to 4.0)
Any anxiety disorder	8.2 (7.0 to 9.7)	7.1 (6.0 to 8.4)	6.9 (6.0 to 7.9)	6.6 (5.7 to 7.6)
Panic with agoraphobia	16.8 (11.9 to 23.7)	12.5 (8.7 to 18.1)	10.8 (8.3 to 14.1)	8.7 (6.6 to 11.3)
Panic without agoraphobia	10.4 (8.0 to 13.7)	8.0 (6.0 to 10.8)	5.6 (4.8 to 6.7)	5.1 (4.3 to 6.1)
Social phobia	8.8 (7.0 to 11.0)	7.3 (5.8 to 9.1)	6.9 (5.7 to 8.3)	6.0 (5.0 to 7.3)
Specific phobia	4.8 (4.0 to 5.8)	4.1 (3.3 to 5.0)	4.4 (3.8 to 5.1)	4.0 (3.5 to 4.7)
Generalized anxiety	16.7 (13.3 to 20.9)	13.5 (10.5 to 17.3)	9.4 (8.0 to 11.0)	8.9 (7.5 to 10.6)
Any personality disorder[d]	15.4 (12.9 to 18.2)	13.2 (11.1 to 15.7)	12.2 (10.6 to 14.0)	10.6 (9.2 to 12.3)
Avoidant	17.1 (13.9 to 21.1)	12.5 (10.1 to 15.5)	13.5 (11.2 to 16.4)	10.4 (8.5 to 12.8)
Dependent	24.8 (16.1 to 38.0)	15.6 (10.3 to 23.7)	20.1 (13.3 to 30.5)	13.6 (9.0 to 20.6)
Obsessive-compulsive	8.4 (7.0 to 9.9)	8.1 (6.8 to 9.7)	7.4 (6.4 to 8.6)	7.2 (6.2 to 8.4)
Paranoid	14.7 (12.3 to 17.5)	11.3 (9.3 to 13.6)	13.3 (11.4 to 15.5)	10.7 (9.1 to 12.6)
Schizoid	11.4 (9.6 to 14.3)	9.8 (8.0 to 12.0)	9.5 (8.0 to 11.1)	8.1 (6.8 to 9.6)
Histrionic	13.7 (10.8 to 17.3)	10.2 (8.0 to 13.1)	11.7 (9.4 to 14.7)	9.1 (7.1 to 11.7)
Antisocial	8.2 (6.6 to 10.1)	6.8 (5.5 to 8.4)	8.9 (7.5 to 10.5)	7.3 (6.1 to 8.6)

[a]The ORs represent the odds of having a specific comorbid disorder among individuals with bipolar I disorder relative to the odds of having a specific comorbid disorder among individuals who do not have bipolar I disorder.
[b]Unadjusted bivariate odds ratios.
[c]Odds ratios adjusted for age, sex, race-ethnicity, marital status, education, income, urbanicity, and geographic region.
[d]Personality disorders assessed on a lifetime basis only.

order and panic disorder with agoraphobia (ORs = 8.7 for lifetime and 12.5 for 12-month) and generalized anxiety disorder (ORs = 8.9 for lifetime and 13.5 for 12-month).

With respect to any personality disorder, the associations (in adjusted models) with bipolar I disorder were large on a 12-month (OR = 13.2) and lifetime (OR = 10.6) basis. Avoidant (ORs = 12.5 and 10.4), dependent (ORs = 15.6 and 13.6), and paranoid (ORs = 11.3 and 10.7) personality disorders were more strongly related to 12-month and lifetime bipolar I disorder, respectively, than other personality disorders assessed in this study.

Treatment for Bipolar I Disorder

Among respondents with lifetime bipolar I disorder, 60.0% had been treated at some time in their lives. Among respondents with lifetime bipolar I disorder who had at least 1 major depressive episode, 74.0% had received treatment. Furthermore, among respondents with at least 1 manic or 1 mixed episode, 51.7% and 68.5% had received treatment, respectively. The mean ages at first treatment for a manic, mixed, or major depressive episode were 33.2, 30.4, and 28.4 years, respectively.

Women were significantly more likely than men to be treated for major depressive ($p < .02$; 77.7% vs. 68.4%), manic ($p < .0001$; 61.3% vs. 42.1%), and mixed episodes ($p < .0316$; 72.9% vs. 62.1%). Women also received treatment for a manic episode significantly earlier than men ($p < .04$; 28.3 vs. 31.3 years).

CONCLUSION

The prevalences of 12-month and lifetime DSM-IV bipolar I disorder in this general population sample were 2.0% (representing 4.2 million American adults) and 3.3% (representing 6.9 million American adults), respectively. The 12-month rate slightly exceeded the upper end of the range of 12-month prevalence estimates (1.6%) found in previous epidemiologic studies,[6–10,27–36] while the lifetime prevalence rate exceeded the upper end of the range of lifetime estimates (1.9%) found in these other studies. These discrepancies highlight the refinement and broadening of the diagnostic definition of bipolar I disorder introduced in the DSM-IV and the relatively small sample sizes of previous surveys that precluded precise and reliable estimates of rare disorders like bipolar I. Moreover, the most recent prior epidemiologic survey[7] was conducted in the United States over 10 years ago, and the increase in the rates of bipolar I disorder found in this study may simply reflect the mere passage of time.

With regard to sociodemographic correlates, bipolar I disorder was equally prevalent among men and women as has been consistently found in all national and cross-national surveys conducted to date.[6–10,27–36] With respect to race-ethnicity, Native Americans had a significantly greater odds, whereas Asians and Hispanics had significantly lower odds of bipolar I disorder relative to whites. These results were consistent with the few studies[78–80] that

have presented data for whites and blacks, in which rates of bipolar I disorder were not found to differ between these 2 race-ethnic groups. Although none of the previous surveys presented data on Native Americans, Hispanics, or Asians in the United States, it is interesting that rates of bipolar I disorder in Asian samples were lower, but not significantly lower, than in mostly white samples.[34] That Hispanics were less likely to have bipolar I disorder is consistent with a recent study[74] that found rates of most psychiatric disorders were lower among foreign-born and U.S.-born Mexican Americans than their non-Hispanic white counterparts. That traditional cultural retention may serve as a protective factor of bipolar I disorder among Hispanics is worthy of further study. However, that Hispanics and Asians were less likely to have bipolar I disorder than whites suggests that cultural factors, language, and/or reporting biases may be responsible for the lower rates observed among these 2 race-ethnic groups. Further research is critically needed to ascertain the degree to which cultural factors, language bias, and differential response patterns influence the rates of bipolar I disorder.

The odds of bipolar I disorder also were significantly greater among the 3 youngest age groups. This age effect may indicate a birth cohort effect, since age at onset significantly increased in this study with each successively older age group ($p < .05$). However, the consistency of this finding across several surveys[7,8,36,81–85] does not suggest that the increased lifetime prevalence of bipolar I disorder among younger cohorts is real. The appearance of an elevated rate of bipolar I disorder in more recent cohorts might occur if this and the other studies systematically undercounted the disorder in older cohorts who have poorer recall of remote events. Longitudinal or repeated cross-sectional surveys are needed to more definitively address this issue. Moreover, even if a birth cohort effect were to be demonstrated, it would not rule out genetic vulnerability to bipolar I disorder. Most complex psychiatric disorders are characterized by an interaction of biological vulnerabilities and environmental factors.

Consistent with previous epidemiologic research,[7,8,35,86] the odds of bipolar I disorder were higher among widowed/separated/divorced individuals. However, the early onset of bipolar I disorder can negatively impact the maintenance of intimate relationships.[80] The finding that low socioeconomic status increases the likelihood of bipolar I disorder also has been found in other epidemiologic surveys,[7,8,80,86] but contrasts with the earlier clinical literature[87–89] that found strong associations between bipolar I disorder and upper social class. This discrepancy may be due to more socially advantaged individuals having a higher probability of obtaining treatment since the earlier studies were based on treated samples of patients. Furthermore, this study found lower odds of bipolar I disorder among individuals living in the South and Midwest regions of the United States. It may be the case that environmental factors that must operate to make manifest a genetic vulnerability to bipolar I disorder are less common in the South and Midwest relative to other regions of the country. Future research on geographic variation in the rates of bipolar I disorder is warranted.

The mean age at onset for bipolar I disorder was 22 years, consistent with onset ages in the late teens and early 20s found in other epidemiologic surveys[7,8,27–36] and in treatment samples of bipolar I patients.[3] Interestingly, 22.2% of individuals with bipolar I disorder had unipolar mania, which was much more prevalent among men (30.4%) than women (15.3%). The rate of unipolar mania in this study is much higher than rates reported in the earlier clinical literature (< 5%),[88,90,91] but more similar to the rates reported in more recent epidemiologic (20%)[7] and clinical (16%–28%) studies.[92–94] The weak relationship found in this study between number of years since onset of mania and probability of ever having a major depressive episode, together with the absence of differences in the ages at onset of manic, mixed, and depressive episodes among individuals with bipolar I disorder, suggests that few individuals with unipolar mania will have a subsequent depressive episode in view of the potential for recall bias. This finding, of course, cannot be addressed fully in this cross-sectional survey. However, the longitudinal Wave 2 of the NESARC, currently in the field, will allow use of the Wave 1 results on unipolar mania as a platform for investigation of this critical prospective question.

A major finding of this study documents the extremely high rates of DSM-IV Axis I and II disorders among individuals with bipolar I disorder and confirms the strength of associations between them. Associations between drug dependence, panic disorder with agoraphobia, and generalized anxiety disorder and bipolar I disorder were particularly strong as documented in previous epidemiologic research[7–9] and the clinical literature.[11–17] Although epidemiologic surveys[95] have found high rates of smoking among individuals with bipolar I disorder, the finding that nicotine dependence is highly comorbid with bipolar I disorder, occurring in over 40% of all cases, is a new finding worthy of replication.

With the exception of antisocial personality disorder, this study was the first to examine comorbidity between 6 other DSM-IV personality disorders and bipolar I disorder in a large representative sample of the U.S. population. The strongest associations were found for avoidant and dependent personality disorders (both cluster C personality disorders) and paranoid personality disorder (a cluster A personality disorder). Most clinical studies[11–13,96–100] have found cluster B and C personality disorders to be more prevalent than cluster A personality disorders among bipolar I patients. In view of the strong associations found between bipolar I disorder and Axis I and II disorders in this study, future research would benefit greatly by addressing risk factors of comorbidity itself.

Some clinical studies have found a predominance of major depressive[101–103] and mixed[104,105] episodes among women and a predominance of manic episodes among men,[101–103] whereas others have not.[106–108] In this study, there were no sex differences in the number of episodes of manic, mixed, or major depressive episodes. Furthermore, women were more likely to receive treatment for mania, mixed, and major depressive episodes than men, despite the findings that men had an earlier onset of mania and longer durations of manic episodes than women. The age at first treatment for a manic episode also was significantly younger among women than men. Taken together, these results suggest that women may have more severe manic episodes than men. The need to examine factors, such as the greater prevalence of mixed and major depressive episodes among women compared to men found in this study, that might lead to increased severity of manic episodes among women is an important line of research currently being pursued using the NESARC data.

The major findings of this study have several public health, economic, and clinical implications. With regard to public health, this study has determined the magnitude of bipolar I disorder confronting the nation and identified important subgroups of the population at risk for the disorder. This information is critical to the planning of local and national mental health services and the design of prevention and intervention programs. The more precise estimates of bipolar I disorder afforded by the NESARC's large sample size also have major economic implications. The 1-year economic costs of bipolar I disorder in 1991 were estimated at $45 billion based on a lifetime prevalence rate of 1.3%, and the lifetime costs of 1998 incident cases based on a lifetime prevalence rate of 1.6% were $24 billion.[109,110] Logic dictates that if the prevalence of bipolar I disorder used in these econometric studies have been underestimated, then so too are the economic costs of the disorder. The 2-fold increase in the rate of bipolar I disorder found in this study underscores the urgent need for prevention and the importance of achieving stable outcome among individuals with bipolar I disorder not only to limit the economic consequences of the disorder but also to decrease the devastating toll on the quality of life of those afflicted with the disorder and among those around them.

With regard to clinical implications, the results of this study are clear in showing that conduct, substance use, anxiety, and personality disorders are highly comorbid with bipolar I disorder ($p < .05$). Comprehensive evaluation of patients with bipolar I disorder should include a systematic assessment of these and other comorbid disorders. Longitudinal epidemiologic studies that attempt to elucidate the temporal relationship between the onsets of manic, mixed, and depressive episodes among individuals with bipolar I disorder and between the onset of bipolar I disorder and other comorbid disorders also promise to increase our understanding of comorbid etiology and to delay and even prevent the onset of bipolar I disorder. The Wave 2 NESARC, which seeks to reinterview all Wave 1 respondents, is nearing completion and, along with Wave 1 data, will serve as a platform for investigation of these important prospective questions underlying the course and comorbidity of bipolar I disorder.

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