Increased Risk for Suicidal Behavior in Comorbid Bipolar Disorder and Alcohol Use Disorders: Results From the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)

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Objective: Bipolar disorder is associated with a high rate of suicide attempt, and alcohol use disorders have also been associated with elevated risk for suicidal behavior. Whether risk for suicidal behavior is elevated when these conditions are comorbid has not been addressed in epidemiologic studies.

Method: 1,643 individuals with a *DSM-IV* lifetime diagnosis of bipolar disorder were identified from 43,093 general-population respondents who were interviewed in the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions. Assessments were made using the National Institute on Alcohol Abuse and Alcoholism Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM-IV* Version (AUDADIS-IV). Lifetime prevalence of reported history of suicide attempt and suicidal thoughts among bipolar disorder respondents with and without *DSM-IV* lifetime alcohol use disorders (abuse or dependence) was assessed using χ^2 and adjusted odds ratios with confidence intervals. Logistic regression was used to test the relevance of other comorbid clinical conditions to suicide risk in bipolar respondents with and without comorbid alcohol use disorders.

Results: More than half of the respondents (54%) who met criteria for bipolar disorder also reported alcohol use disorder. Bipolar individuals with comorbid alcohol use disorder were at greater risk for suicide attempt than those individuals without alcohol use disorder (adjusted odds ratio = 2.25; 95% CI, 1.61–3.14) and were more likely to have comorbid nicotine dependence and drug use disorders. Nicotine dependence and drug use disorders did not increase risk for suicidal behavior among those with bipolar disorder, nor did they confer additional risk among bipolar respondents who also reported alcohol use disorder. Despite greater psychopathological burden, individuals with comorbid bipolar disorder and alcohol use disorder did not receive more treatment or more intensive treatment.

Conclusions: Suicidal behavior is more likely to occur in bipolar respondents who also suffer from alcohol use disorder. Interventions to reduce suicide risk in bipolar disorder need to address the common and high-risk comorbidity with alcohol use disorders.

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Bipolar disorders I and II are estimated to manifest in 2.1% of the US population, and, if subthreshold cases are included, the lifetime rate may be as high as 4.5%.[1] Alcohol use disorders, including both abuse and dependence, are estimated to affect between 13.5% and 30.3% of the adult US population.[2,3] Bipolar disorder is commonly associated with alcohol use disorder. Epidemiologic samples report that lifetime alcohol use disorder is present in 46%–58% of those who meet criteria for bipolar I disorder and in 19%–39% of those with bipolar II disorder,[1,2,4] and, in clinical studies, lifetime estimates range between 10%–40% (see Bauer et al[5] for a review). This co-occurrence has significant negative consequences for the individual. For example, in a clinical sample, work disability rates for bipolar disorder comorbid with alcohol use disorders are about 46.5%, compared to 25.8% for those with bipolar disorder alone.[6]

Perhaps the most worrisome sequela associated with both conditions is suicidal behavior. In a population sample, 29% of all respondents who met criteria for bipolar disorder also acknowledged at least 1 suicide attempt in their lifetime,[7] and rates of suicide completion for bipolar disorder samples are among the highest for any psychiatric disorder, with an estimated range between 8%–15%.[8] Rates of suicidal behavior in alcohol use disorders are also high, with 16%–29% of individuals seeking treatment for alcohol use disorders reporting at least 1 lifetime suicide attempt,[9–12] with rates of suicide completion ranging between 2.4% and 7%.[13,14]

Studies examining the co-occurrence of bipolar disorder and alcohol use disorders with respect to risk for suicidal acts in clinical samples report increased probability of suicidal behavior in bipolar individuals with comorbid lifetime alcohol use disorder compared to bipolar individuals with no alcohol use disorder comorbidity.[15–18] From a different vantage point, bipolar suicide attempters are reported to be more likely to meet criteria for comorbid alcohol use disorder (ORs: 2.44–3.25) compared to bipolar nonattempters.[19,20]

Use of substances other than alcohol has also been associated with elevated risk for suicidal behavior in both clinical and population studies. For example, cigarette smoking has been shown to be associated with elevated risk for suicidal behavior among mood-disordered individuals both cross-sectionally[21,22] and prospectively.[23,24] As well, drug use disorders have long been observed to be a factor

For Clinical Use

- Bipolar disorder is often comorbid with alcohol use disorder.
- The presence of both bipolar disorder and alcohol use disorder significantly increases the risk of suicidal behavior.

in suicide attempt and death.[25,26] Given that patients with bipolar disorder have a propensity toward drug use disorders, the impact of these disorders on suicidal behavior in bipolar disorder warrants investigation. To date, epidemiologic studies have not examined the effect of alcohol use disorders on suicidal behavior in bipolar disorder—or any additional effects of nicotine dependence or other drug use disorders.

We analyzed data from respondents who met criteria for lifetime bipolar I or II disorder in the National Epidemiologic Study of Alcohol Related Conditions (NESARC) to test 3 hypotheses. First, we hypothesized that bipolar respondents with comorbid lifetime alcohol use disorder (abuse or dependence) would be more likely to report a lifetime suicide attempt than those without alcohol use disorder. The second hypothesis was that the contribution of alcohol use disorder comorbidity to suicide attempt risk is independent of any contribution that lifetime drug use disorder (abuse or dependence) or nicotine dependence may make to suicide attempt risk. Third, we hypothesized that comorbid drug use disorder and/or nicotine dependence would further increase risk for suicidal behavior in bipolar respondents with alcohol use disorder. We also examined whether treatment rates among bipolar respondents with alcohol use disorder were lower than for those without alcohol use disorder, as we have observed in our clinical samples.[27]

METHOD

The methods utilized to collect and adjust NESARC data have been published elsewhere.[4] Briefly, data were collected from 43,093 adult respondents not residing in institutions between 2001 and 2002. The response rate was 81%. African Americans and Hispanics were oversampled. Data were weighted and adjusted to be representative of the US population for variables such as age, sex, region, ethnicity, and race based on the 2000 Decennial Census. *DSM-IV* Axis I and Axis II disorders were assessed using the National Institute on Alcohol Abuse and Alcoholism Alcohol Use Disorder and Associated Disabilities Interview Schedule–*DSM-IV* Version (AUDADIS-IV),[28] a structured diagnostic interview designed for use by lay interviewers. 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.[4] Lifetime bipolar II disorder was defined as having at least 1 hypomanic episode with or without 1 or more major depressive or hypomanic episodes. Lifetime diagnoses of alcohol abuse required 1 or more of the 4 abuse criteria in the 12 months prior to the interview or previously, and lifetime alcohol dependence diagnoses required 3 or more of the 7 *DSM-IV* dependence criteria in the prior 12 months or during any previous 12-month period.[3] Professional interviewers from the US Census Bureau conducted interviews, and test-retest reliability of the instrument was assessed. Kappas for alcohol use disorders and drug use disorders were excellent ($\kappa = 0.74$ and $\kappa = 0.79$, respectively) and were good for bipolar disorder and other mood and anxiety disorders ($\kappa = 0.59$ and $\kappa = 0.40–0.65$, respectively) (for more details, see Grant et al[4]). Individuals who screened into the major depressive episode section in the NESARC survey were asked the following questions: "During that time when your mood was at its lowest/you enjoyed or cared the least about things, did you (1) have thoughts of death? (2) think about committing suicide? (3) attempt suicide?" We used the second question to assess a lifetime history of suicidal ideation, while the third question was used to assess a lifetime history of suicide attempt. A total of 1,643 lifetime bipolar respondents completed the suicide questions. Wave I of NESARC, used for the present analyses, also assessed the following personality disorders: avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic, and antisocial.

Statistical Analysis

Demographic and clinical variables were compared between the group with bipolar disorder without alcohol use disorder and the group with bipolar disorder with alcohol use disorder using χ^2 or *t* tests as appropriate. Odds ratios and confidence intervals were calculated, and, for comparisons of clinical and suicide-related variables, ORs and confidence intervals were adjusted for demographic characteristics that differed between the 2 groups. To test hypothesis 1, we compared suicidal thoughts and attempts between the group with bipolar disorder with alcohol use disorder and the group with bipolar disorder without alcohol use disorder using χ^2, and we calculated odds ratios and confidence intervals, adjusted for demographic differences between the 2 groups. Logistic regression was used to test hypothesis 2. Suicide attempt was the response variable, while alcohol use disorder, drug use disorder, and nicotine dependence were the independent variables of interest, and additional clinical factors associated with suicide attempts, specifically age at onset of bipolar disorder,[29] number of depressive episodes,[30–32] comorbid antisocial personality disorder,[33] and comorbid panic disorder,[34] were included to examine their possible effect. The model also controlled for clinical and demographic variables that differed between the group with bipolar disorder with alcohol use disorder and the group with bipolar disorder without alcohol use disorder. To test hypothesis 3, logistic regression models were constructed only for respondents

with bipolar disorder with alcohol use disorder, with suicide attempt as the dependent variable and drug use disorder, nicotine dependence, age at onset of bipolar disorder, number of depressive episodes, comorbid antisocial personality disorder, comorbid panic disorder, use of alcohol to self-medicate,[35] and demographic variables described above as independent variables.

RESULTS

Demographic and Clinical Characteristics of Bipolar Disorder Respondents With and Without Comorbid Alcohol Use Disorder

Among NESARC respondents, 1,643 individuals met criteria for lifetime bipolar disorder and completed the major depressive episode module. Over half of those meeting criteria for bipolar disorder (54% [n = 881]) also met *DSM-IV* criteria for lifetime alcohol use disorder. Compared to respondents with bipolar disorder without alcohol use disorder, respondents with bipolar disorder with alcohol use disorder were more likely to be male, have a middle income, and be US-born and were less likely to be over age 65, African American or Hispanic, or from the southern United States (Table 1). Regarding clinical characteristics, respondents with bipolar disorder with alcohol use disorder were more likely than respondents with bipolar disorder without alcohol use disorder to report an earlier age at onset of mania or hypomania; to have other lifetime comorbid conditions including nicotine dependence, drug use disorder, antisocial personality disorder, and panic disorder; and to endorse use of alcohol and other drugs to self-medicate (Table 2).

Table 1. Demographic Characteristics of Bipolar Disorder Respondents With and Without Alcohol Use Disorders

Characteristic	Bipolar Disorder With Alcohol Use Disorders (N = 881)		Bipolar Disorder Without Alcohol Use Disorders (N = 762)		Adjusted Odds Ratio[a]	
	%	95% CI	%	95% CI		95% CI
Age, y						
18–29	33.74	29.53–38.23	35.44	31.00–40.15	1.00	1.00–1.00
30–44	37.71	33.76–41.84	31.15	27.03–35.59	1.27	0.92–1.76
45–64	26.25	23.03–29.76	27.24	23.81–30.96	1.01	0.75–1.37
≥65	2.29	1.47–3.56	6.17	4.57–8.28	0.39	0.22–0.70
Sex, male	51.11	47.29–54.92	28.21	24.16–32.65	2.66	2.07–3.42
Race/ethnicity						
White, non-Hispanic	76.08	72.09–79.66	66.97	61.35–72.15	1.00	1.00–1.00
Black, non-Hispanic	9.53	7.39–12.21	14.78	12.07–17.97	0.57	0.41–0.79
Native American or Asian/ Pacific Islander	6.96	4.87–9.86	6.16	4.03–9.32	0.99	0.55–1.81
Hispanic	7.43	5.53–9.91	12.09	8.99–16.06	0.54	0.37–0.79
Place of birth, United States	93.92	90.87–96.00	86.72	81.69–90.54	2.37	1.40–4.00
Marital status						
Married/cohabiting	47.06	43.04–51.12	50.16	45.95–54.36	1.00	1.00–1.00
Widowed/separated/divorced	22.39	19.70–25.34	19.63	16.80–22.80	1.22	0.92–1.61
Never married	30.55	27.09–34.24	30.22	26.24–34.51	1.08	0.82–1.42
Education						
Less than high school	18.15	15.31–21.38	18.83	15.80–22.27	0.96	0.70–1.33
High school graduate	30.64	26.77–34.79	30.08	26.50–33.91	1.02	0.77–1.34
Some college or higher	51.21	46.73–55.68	51.10	46.97–55.21	1.00	1.00–1.00
Personal income, $						
0–19,999	55.80	51.46–60.04	68.21	64.13–72.03	1.00	1.00–1.00
20,000–34,999	24.07	20.73–27.76	16.25	13.35–19.64	1.81	1.33–2.46
35,000–69,999	16.78	14.02–19.95	12.42	10.05–15.25	1.65	1.18–2.31
≥70,000	3.36	2.13–5.26	3.12	1.93–4.99	1.32	0.68–2.54
Urbanicity						
Urban	77.98	72.37–82.72	79.18	73.87–83.65	1.00	1.00–1.00
Rural	22.02	17.28–27.63	20.82	16.35–26.13	1.07	0.80–1.44
Region of the United States						
Northeast	17.20	11.63–24.68	19.77	13.27–28.41	0.69	0.43–1.11
Midwest	27.44	20.87–35.17	21.19	15.45–28.36	1.03	0.74–1.42
South	27.57	21.93–34.04	37.04	29.91–44.78	0.59	0.43–0.80
West	27.79	20.56–36.39	22.00	15.30–30.58	1.00	1.00–1.00

[a]Adjusted for age, sex, race, US-born, individual income, and region.

Despite their more frequent history of suicidal behavior and higher rates of comorbid conditions, respondents with bipolar disorder with alcohol use disorder had almost identical lifetime rates of mental health treatment, emergency department visits, psychiatric hospitalization, and prescription of medication as did respondents with bipolar disorder without alcohol use disorder (Table 3).

Suicidal Behavior in Bipolar Disorder With and Without Comorbid Alcohol Use Disorders

Confirming the first hypothesis, respondents with bipolar disorder with alcohol use disorders were more likely to report thoughts of death, suicidal ideation, and suicide attempts, compared to respondents with bipolar disorder without alcohol use disorders (Table 4), despite no difference in the frequency of depressive episodes. Among individuals with bipolar disorder with alcohol use disorders, there was no difference between those with comorbid alcohol abuse and those with comorbid alcohol dependence in reported prevalence of suicidal ideation or suicide attempts (adjusted OR [AOR]: 0.76; 95% CI, 0.51–1.14; and AOR: 0.82; 95% CI, 0.51–1.3, respectively).

Supporting the second hypothesis, in logistic regression controlling for demographic differences between groups, alcohol use disorder remained independently associated with lifetime history of suicide attempt (AOR: 1.63; 95% CI, 1.04–2.55; $P = .033$), while drug use disorders and nicotine dependence were not (AOR: 1.16; 95% CI, 0.77–1.74; $P = .47$; and AOR: 1.21; 95% CI, 0.85–1.72; $P = .28$, respectively). In the sample as a whole, a greater number of depressive episodes increased the probability of a past suicide attempt, with each depressive episode increasing risk by approximately 2% (AOR: 1.02; 95% CI, 1.01–1.03; $P < .001$). Similarly, presence of lifetime antisocial personality disorder and panic disorder also independently increased the probability of suicide attempt (AOR: 1.56; 95% CI, 1.04–2.35; $P = .03$; and AOR: 2.13; 95% CI, 1.52–2.99; $P \leq .001$, respectively), but age at onset of bipolar disorder did not (AOR: 0.98; 95% CI, 0.96–1.00; $P = .089$).

Table 2. Clinical Characteristics of Bipolar Disorder Respondents With and Without Alcohol Use Disorders

Characteristic	Bipolar Disorder With Alcohol Use Disorders (N = 881) %	95% CI	Bipolar Disorder Without Alcohol Use Disorders (N = 762) %	95% CI	Adjusted Odds Ratio[a]	95% CI
Nicotine dependence	61.69	57.26–65.94	23.99	20.46–27.91	5.14	3.83–6.89
Any drug use disorder	53.59	49.31–57.83	11.46	8.92–14.62	9.39	6.60–13.37
Prescription drug use disorder	42.37	38.25–46.60	11.74	9.20–14.86	5.08	3.63–7.11
Antisocial personality disorder	29.52	25.81–33.52	7.89	5.88–10.52	4.52	3.03–6.73
Panic disorder	29.32	25.99–32.89	24.77	21.55–28.29	1.39	1.05–1.84
Self-medication						
Reports alcohol use to self-medicate	28.94	25.13–33.08	4.67	3.13–6.92	7.66	4.87–12.05
Any medicine or drug use as self-medication	14.02	11.17–17.45	2.39	1.53–3.73	5.92	3.46–10.13
Course of illness	Mean	95% CI	Mean	95% CI	*t* Test	*P* Value
Number of depressive episodes	8.21	6.84–9.59	6.76	5.51–8.01	1.45	.1519
Number of manic episodes	7.65	6.23–9.07	6.36	5.18–7.55	1.35	.1807
Age at first depressive episode, y	23.59	22.75–24.43	24.45	23.33–25.58	−1.27	.2092
Age at first manic or hypomanic episode, y	24.09	23.21–24.98	25.62	24.49–26.76	−2.29	.0255
Age at first mood episode, y	20.88	20.15–21.60	21.94	20.89–22.98	−1.72	.0899

[a]Adjusted for age, sex, race, US-born, individual income, and region.

Table 3. Treatment Received by Bipolar Disorder Respondents With and Without Alcohol Use Disorders

Treatment Variable	Bipolar Disorder With Alcohol Use Disorders (N = 881) %	95% CI	Bipolar Disorder Without Alcohol Use Disorders (N = 762) %	95% CI	Adjusted Odds Ratio[a]	95% CI
Any mental health treatment	34.12	30.48–37.96	33.37	29.55–37.42	1.05	0.80–1.39
Any psychiatric hospitalization	11.52	9.20–14.33	8.70	6.56–11.46	1.43	0.93–2.20
Any emergency room visit	8.67	6.79–11.01	7.45	5.62–9.82	1.25	0.81–1.91
Any prescribed psychotropic medication	25.77	22.11–29.81	26.79	23.20–30.72	0.98	0.71–1.35
	Mean	95% CI	Mean	95% CI	*t* Test	*P* Value
Age at first treatment for depression, y	28.13	26.76–29.50	29.09	27.73–30.46	−1.03	.3090

[a]Adjusted for age, sex, race, US-born, individual income, and region.

Table 4. Suicide-Related Characteristics of Bipolar Disorder Respondents With and Without Alcohol Use Disorders

Characteristic	Bipolar Disorder With Alcohol Use Disorders (N = 881) %	95% CI	Bipolar Disorder Without Alcohol Use Disorders (N = 762) %	95% CI	Adjusted Odds Ratio[a]	95% CI
Thoughts about death	71.26	67.42–74.82	58.19	53.37–62.86	1.90	1.45–2.49
Suicidal ideation	56.90	52.73–60.97	41.80	37.33–46.42	1.81	1.42–2.30
Suicide attempt	25.29	21.82–29.10	14.78	12.19–17.80	2.25	1.61–3.14

[a]Adjusted for age, sex, race, US-born, individual income, and region.

The third hypothesis was not confirmed. Among respondents with bipolar disorder with alcohol use disorder, the presence of other lifetime drug use disorders (AOR: 0.98; 95% CI, 0.60–1.60; $P = .93$) or nicotine dependence (AOR: 1.08; 95% CI, 0.66–1.77; $P = .76$) had no effect on risk for suicide attempt, controlling for number of depressive episodes, age, sex, race, nativity, personal income, and region. However, use of alcohol to self-medicate was independently associated with suicide attempt (AOR: 1.71; 95% CI, 1.06–2.75; $P = .029$), as were comorbid lifetime panic disorder (AOR: 1.91; 95% CI, 1.25–2.93; $P = .003$) and number of depressive episodes (AOR: 1.02; 95% CI, 1.01–1.03, $P = .003$), with the same approximate 2% increase in risk for suicide attempt per episode observed in the sample as a whole. Lifetime antisocial personality disorder did not increase the likelihood of suicide attempt in this model (AOR: 1.40; 95% CI, 0.88–2.21; $P = .152$).

DISCUSSION

In this community sample of individuals who met lifetime criteria for bipolar disorder, those who reported having an alcohol use disorder were substantially more likely to report a lifetime history of suicide attempts. This effect was independent of the number of major depressive episodes, presence of earlier age at onset of bipolar disorder, comorbidity with drug use disorders or nicotine dependence, and endorsement of alcohol use as self-medication. Disturbingly, despite the presence of comorbid alcohol use disorders and suicidal behavior, these individuals did not report receiving more psychiatric treatment. This was the case even though bipolar respondents with alcohol use disorder had considerably higher rates of drug use disorders and were more often afflicted with character pathology.

Alcohol Use Disorder and Bipolar Disorder

That 54% of respondents meeting criteria for bipolar disorder also acknowledged alcohol use disorder is in line with reports from other US epidemiologic studies. Several reports note lifetime alcohol use disorder comorbidity ranging from 38% to 56% among those with bipolar I disorder,[1,2,4] although lower rates (39% in men and 7.9% in women) were reported in a smaller Australian epidemiologic study.[36] Of interest, rates among community respondents with bipolar disorder are higher than the 10%–40% reported in clinical samples.[5,17,37–40] This may reflect a reported tendency for bipolar patients with alcohol use disorder to be less likely to seek, or stay in, clinical treatment.[41,42] Whether difficulties with treatment adherence in this population relate to difficulties in recognizing the need for treatment or to additional barriers to accessing clinical care, such as trouble

keeping appointments, is not known. Alternatively, it may be that individuals with comorbid bipolar disorder and alcohol use disorder seek help in alcohol treatment facilities and therefore are not present in clinics focusing on mood disorders. This possibility is supported by the work of Albanese and colleagues,[43] who reported that, among men who met criteria for bipolar disorder and were being cared for in a substance abuse treatment program, 49% had not been identified as bipolar. Instead, most carried a diagnosis of unipolar depression. Nonetheless, the similar rate of treatment observed in the NESARC sample for bipolar respondents with and without alcohol use disorder suggests that, regardless of where they obtain treatment, those with bipolar disorder with alcohol use disorders are seriously undertreated, an observation we have seen in our clinical samples as well.[27]

Alcohol Use Disorders and Bipolar Disorder: A Comorbidity That Increases Risk for Suicide Attempt?

The prevalence of lifetime suicide attempt in this sample (21%) was somewhat lower than that reported in other epidemiologic studies (29%).[7] However, it is within the range reported in clinical studies (21%–42%).[15,19,37,38] As hypothesized, we found that among those with bipolar disorder with alcohol use disorders, 25% acknowledged a suicide attempt, compared to 15% among those with bipolar disorder without alcohol use disorders. This finding is consistent with most clinical studies of bipolar disorder.[15,17,19,20] Clinical studies that do not find a relationship between alcohol use disorder and suicidal behavior in bipolar disorder have included mostly or exclusively subjects suffering manic or mixed episodes.[44,45] Given that suicide attempts in bipolar disorder are more likely to occur in the context of depression,[30–32] use of a manic or mixed sample may select for individuals with fewer depressive episodes and thus make it difficult to identify variables key to risk for suicidal behavior.

It is worth noting that, among respondents with bipolar disorder without alcohol use disorders, the rate of suicide attempt (15%) is close to that cited for unipolar depression: 15.9% in the Epidemiologic Catchment Area study[7] and 16.9% in the NESARC data itself.[33] An intriguing possibility is that bipolar disorder has the highest rate of suicide attempt and completion among all psychiatric diagnoses due to the staggering rate of alcohol use disorder comorbidity among individuals with this disorder. However, Bolton et al[33] report that, although rates of any alcohol use disorder were high among major depressive disorder respondents (55%), the odds of being a suicide attempter were not related to the presence of alcohol use disorder (AOR: 1.11; 95% CI, 0.72–1.73). Thus, simply suffering from alcohol use disorder comorbid with a mood disorder does not lead to increased risk for suicidal behavior. Whether the increased risk for suicide attempts observed among respondents with bipolar disorder with alcohol use disorders is related to an interaction between the impulsivity reported among bipolar subjects[46] and the disinhibiting effects of alcohol intoxication is an area for further study.

Alcohol Use Disorder, Drug Use Disorder, and Nicotine Dependence and Risk for Suicidal Behavior in Bipolar Disorder

Drug use disorders are associated with suicidal behavior and are frequently comorbid with bipolar disorder. In the community, 36%–41% of bipolar individuals also report drug use disorders,[2,4] and in clinical samples, lifetime rates of drug abuse or dependence range from 14%–65%.[47] The prevalence of nicotine dependence in bipolar disorder is also elevated, with a 12-month prevalence of 35% and 33% in bipolar I and II disorders, respectively, compared to 13% in the general population.[48] In this sample, 56.0% of bipolar respondents had a lifetime drug use disorder and 42.8% had nicotine dependence. Given the association of drug use disorders and nicotine dependence with increased risk for suicidal behavior, and given the frequent comorbidity of drug use disorder and alcohol use disorder,[3] one might expect cumulative effects of multiple comorbidities on risk. However, our data did not support this hypothesis, as neither drug use disorders nor nicotine dependence independently increased the risk for suicide attempt among bipolar individuals, over and above that associated with alcohol use disorder. These findings stand in contrast to most clinical studies focused on this question, possibly due to methodological issues such as differences in sampling or differences in ascertainment. For example, clinical studies linking nicotine dependence to suicide attempt in mood disorders generally exclude individuals who are currently alcohol or drug dependent,[21,23,24] and a study of the association between drug use disorders and suicidal behavior in bipolar disorder included patients with schizoaffective disorder,[49] making comparisons with the current data problematic. As well, postmortem studies of suicide victims with drug use disorder do not address the presence of affective disorders.[50]

Thus, although clinical studies report a relationship between drug use disorders and/or nicotine dependence and suicide attempts,[22,51] we could find no study that examined additive risk for suicidal behavior with abuse of or dependence on multiple substances. Whether the lack of additive effects observed in the current study would also hold in clinical samples using a similar design requires further inquiry.

Other Psychiatric Comorbidities: Panic Disorder and Antisocial Personality Disorder

Panic disorder is common (20.8%) in epidemiologic samples of bipolar disorder[52] and is associated with suicidal behavior independent of the presence of other psychiatric disorders.[53] A similar association is reported in clinical populations,[54–56] although not all studies, including ours, agree.[57,58] In this sample, the group with bipolar disorder with alcohol use disorders had a higher lifetime prevalence of panic disorder than the group with bipolar disorder without alcohol use disorders. As well, panic disorder was independently associated with increased risk for suicide attempt. It has been suggested that comorbidity of alcohol use disorders and anxiety disorders may reflect an attempt to self-medicate anxiety. National epidemiologic studies have

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shown that 3%–23% of panic disorder respondents endorse the use of substances to ease anxiety symptoms.[35,59] Moreover, anxiety-disordered respondents who use substances to self-medicate tend to have higher rates of comorbid bipolar disorder than non–self-medicators (12.6% vs 2.8%), and higher rates of suicide attempt (21.7% vs 6.2%),[35] suggesting that panic disorder, use of substances to self-medicate, and suicidal behavior are closely linked.

Although we found higher rates of comorbid antisocial personality disorder among the group with bipolar disorder with alcohol use disorders compared to the group with bipolar disorder without alcohol use disorders, antisocial personality disorder independently increased risk for suicide attempt in the bipolar group as a whole, but not within the subgroup with bipolar disorder with alcohol use disorders. This counterintuitive finding raises the question of whether the increased risk for suicidal behavior conferred by antisocial personality disorder in bipolar disorder is due to the heightened aggression and impulsivity, a hallmark of antisocial personality disorder and shown in clinical samples to be closely related to suicidal acts.[23,46] Perhaps there is a ceiling effect in terms of aggression and impulsivity, such that, once the individual meets criteria for alcohol use disorder, the presence of antisocial personality disorder does not confer additional risk because of the already high level of aggression and impulsivity in the subpopulation with bipolar disorder with alcohol use disorders. The current data cannot address this question. However, the findings suggest there may be related underlying mechanisms driving these associations, rather than a simple additive effect from disease burden.

Self-Medication With Alcohol and Other Drugs

We found that reported use of alcohol to self-medicate was associated with a further increased risk for suicide attempt among bipolar respondents with alcohol use disorder. A small number of studies examining reasons given for substance use in bipolar disorder samples found that the majority of bipolar patients with substance use disorders (including alcohol) report using substances to self-medicate.[60–63] None of these studies examined alcohol use separately from other drugs, nor did they focus on risk for suicidal behavior. One possible mechanism for this association could be that suicide attempters have cognitive difficulties that impair decision-making.[64,65] This impaired decision-making may lead such individuals to use suicidal behavior or alcohol as a maladaptive way of managing painful feelings. Alternatively, use of alcohol to self-medicate feelings of distress may lead to disinhibition resulting in more suicidal behavior. We do not have data to address these possibilities, but neuropsychological studies of this population would be instructive.

Mental Health Care Utilization

The rates of mental health care received by bipolar participants for their mood disorder were generally low. Only 27% of respondents had received any kind of treatment, and fewer than 25% had received pharmacotherapy, which is considered the cornerstone of treatment for bipolar disorder. That the presence of alcohol use disorder was not associated with higher rates of treatment in this sample is of concern for 2 reasons: (1) increased morbidity and mortality is well documented when these conditions co-occur and (2) there is greater frequency of personality, anxiety, and other substance use disorders among those with bipolar disorder with alcohol use disorder. Two potential reasons for the observed undertreatment include the low overall treatment rate for alcohol use disorder,[3] possibly creating a floor effect in terms of additional treatment received when comorbid with bipolar disorder, and/or that bipolar disorder with alcohol use disorder is more common in men, who are less likely to seek treatment for all disorders.[66] These findings are consistent with those of an Australian epidemiologic study,[36] which found that impaired functioning was not associated with more care utilization. Clearly, interventions to improve adherence and venues to make care more accessible for this population with high disease burden would be of utility.

Limitations

Concerns have been raised about the use of lifetime diagnoses from epidemiologic studies to determine rates of comorbidity because of the possibility that such associations may be spurious.[67] However, both bipolar disorder and alcohol use disorder are diagnoses that are considered enduring. That is, once a diagnosis of bipolar disorder or alcohol use disorder is established, the diagnosis stands even though episodes may remit. When diagnoses are considered part of an ongoing diathesis rather than being constituted of discrete, unrelated episodes, the concern regarding pseudocomorbidity is obviated. Moreover, NESARC data regarding 12-month prevalence showed a strong association between bipolar disorder and alcohol use disorder, further supporting the notion that the relationship between the 2 disorders is real.[3]

The proportion of bipolar individuals reporting a past suicide attempt was somewhat lower than in other epidemiologic studies. It is possible that the NESARC did not identify all suicidal behavior because the question for suicide attempts was posed only to those who screened into the major depressive episode module. Thus, individuals who had not experienced at least 2 weeks of low mood or anhedonia but had made a suicide attempt would not be included in our sample. However, as suicidal behavior is overwhelmingly associated with depression in bipolar disorder,[30–32] it is likely that the bulk of attempters are identified with this strategy. Moreover, in the National Longitudinal Alcohol Epidemiologic Survey (NLAES), which examined a representative sample of the US household population (1991–1992), the number of individuals who did not screen into the major depressive module but reported a suicide attempt was very low: less than 0.1% of the NLAES sample. This finding suggests that, had we been able to include those who did not screen into the major depressive episode module, the results would have most likely remained unchanged.[68] Data on suicide attempt were limited to presence or absence, with no data available on frequency or medical sequelae of suicide attempts, which would have been informative on the

relationship of comorbid alcohol use disorder to severity of suicidal behavior.

The AUDADIS-IV structured interview has demonstrated good diagnostic validity and reliability. Nevertheless, there may be differences in terms of illness course and characteristics between bipolar individuals identified by this method and those who come to clinical attention. Such differences may, in part, explain the low levels of treatment reported in the community, even among bipolar individuals with multiple comorbidities and suicidal behavior. Further research is needed to examine differences between bipolar individuals in the community and those seen in clinical settings.

CONCLUSION

In summary, data from this study suggest that the presence of alcohol use disorder in the context of bipolar disorder is a risk factor for suicidal behavior. This effect is independent of that of earlier onset of bipolar disorder, frequency of depressive episodes, presence of panic disorder and antisocial personality disorder, and the use of alcohol to self-medicate bipolar disorder symptoms. Moreover, drug use disorders and nicotine dependence were not independently related to suicide attempts in bipolar disorder in the community and did not increase risk further in those with bipolar disorder and comorbid alcohol use disorder. Given the high disease burden suffered by these individuals and the increased risk for morbidity and mortality when bipolar disorder and alcohol use disorder are comorbid, targeting them for treatment is a public health imperative.

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents that is outside US Food and Drug Administration–approved labeling has been presented in this article.

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