

## Original Article

## The burden of obesity among adults with bipolar disorder in the United States

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**Objectives:** Previous studies of clinical samples of adults with bipolar disorder (BD) suggest that there is increased prevalence of obesity and that obesity is associated with greater BD severity. We therefore examined this topic in a representative epidemiologic sample.

**Methods:** The 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions was used to determine whether the prevalence of obesity is elevated among subjects with lifetime BD, and whether obesity is associated with greater severity of BD.

**Results:** The age-, race-, and sex-adjusted prevalence of obesity was significantly greater among subjects with BD versus controls [odds ratio (OR) = 1.65, 95% confidence interval (CI): 1.45–1.89,  $p < 0.001$ ]. Obesity among subjects with BD was significantly positively associated with greater age, female sex, comorbid anxiety and medical conditions, and depression-related treatment utilization, and significantly negatively associated with past-year substance use disorder (SUD). In multivariable analyses, obesity among adults with BD was positively associated with age, comorbid anxiety disorders, duration of depressive episodes, and history of hospitalization for depression, and negatively associated with past-year SUD.

**Conclusions:** The increased prevalence of obesity in BD and its association with illness severity, particularly in relation to depression, cannot be attributed to biases inherent in treatment-seeking samples. Future studies are needed to examine the direction of the observed associations and to develop preventive and treatment strategies seeking to mitigate the burden of obesity in BD.

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The prevalence of overweight and obesity (henceforth obesity) continues to rise in the United States (1). Adults with bipolar disorder (BD) comprise a group for whom obesity may be a particularly concerning condition because the leading cause of mortality in BD is premature cardiovascular

disease (CVD) (2), and CVD among adults with BD is evident up to 14 years before adults without BD (3). Treatment with medications associated with weight gain is a leading explanation for the increased prevalence of obesity in BD (4, 5), however increased prevalence of obesity has also been reported among medication-naïve patients with BD (6). Other explanations have been invoked for the association between obesity and BD, including excessive carbohydrate consumption, low rate and intensity of exercise, reduced fat oxidation, substance misuse, and maladaptive efforts at self-modulation of mood by over-eating (4, 5, 7–11). Taken together, these findings indicate

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that adults with BD are at increased risk of obesity due to a multitude of factors.

In addition to concerns regarding the medical consequences of obesity among adults with BD, there is substantial evidence demonstrating that obesity is associated with a number of proxies for the burden of BD including increased number of manic and depressive episodes, increased depressive symptom severity, treatment-resistance, suicidality, and treatment use (12–19). Due to the association of obesity with increased BD severity, the morbidity of obesity may be greater among individuals with, as compared to without, BD. However, to date, only clinical studies have examined for correlates of obesity among subjects with BD. Previous representative epidemiologic studies have examined the prevalence of BD based on obesity (rather than the converse), have not examined BD separately from other mood disorders, or have not examined broadly for correlates of obesity among persons with BD (20–24). This study seeks to extend our understanding of obesity in BD by examining the relative prevalence of obesity among persons with BD, and by examining for correlates of obesity in BD which may inform prevention and treatment strategies.

We set out to examine the following hypotheses: (i) subjects with BD will have significantly greater prevalence of obesity compared to subjects without BD; and (ii) among subjects with BD, obesity will be associated with increased illness burden as determined by presence of past-year episodes, lifetime number of episodes, duration of longest episode, history of suicide attempts, mixed manic episodes, comorbid conditions, and rates of treatment utilization. We also set out to examine in exploratory fashion the prevalence of obesity among subjects with BD versus those with major depressive disorder (MDD), which has also been associated with increased prevalence of obesity (25, 26). Finally, because of previous contradictory reports among adults and youth with BD (23, 27), we examined whether comorbid substance use disorders (SUD) are associated with obesity among adults with BD.

## Methods

### Sample

Subjects were identified from among the respondents of the cross-sectional 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (28). The NESARC is a representative sample of the United States conducted by the National Institute on Alcoholism

and Alcohol Abuse (NIAAA). A detailed description of the NESARC can be found elsewhere (28). Briefly, a total of 43,093 noninstitutionalized civilian respondents, 18 years and older, completed brief face-to-face computer-assisted personal interviews. The overall survey response rate was 81% (28). Blacks, Hispanics, and young adults (ages 18–24 years) were over-sampled with data adjusted for oversampling and nonresponse. The weighted data were then adjusted to represent the U.S. civilian population based on the 2000 census.

### Assessment

*Psychiatric diagnoses.* The NIAAA Alcohol Use Disorder and Associated Disabilities Interview Schedule-DSM-IV Version (AUDADIS-IV) was used to generate the diagnoses presented in this report. The AUDADIS-IV diagnoses of SUD and of mood and anxiety disorders have demonstrated adequate reliability and validity (28–30). Subjects were considered to have BD if they had a lifetime manic or mixed episode that was not secondary to substance use or a medical condition (bipolar I disorder), or lifetime history of at least one hypomanic episode and at least one major depressive episode (bipolar II disorder) (28). This study examined subjects with a *lifetime* diagnosis of BD because each of the putative links between BD and obesity (including medications, dietary intake, and sedentary lifestyle) would be hypothesized to cumulatively assert their influence through the entire course of BD irrespective of whether the individual experienced a manic or mixed episode in the past year.

The anxiety disorders included in the present study were social anxiety disorder, panic disorder, and generalized anxiety disorder. The NESARC provides information regarding daily nicotine use and abuse and dependence of alcohol and illicit drugs. For the purpose of this report, a combined category of abuse or dependence was computed. Subjects with a lifetime prevalence of abuse or dependence of alcohol or any illicit drugs were considered to have *lifetime SUD*. In light of previous findings regarding past-year SUD and obesity in BD (23), we also examined *past-year SUD*. For analyses, subjects were divided into three groups: subjects with lifetime BD ( $n = 1,905$ ), subjects with lifetime MDD ( $n = 5,695$ ), and a comparison group with neither of these conditions ( $n = 35,493$ ) who could have non-MDD, non-BD diagnoses, including anxiety disorders and SUD. We excluded subjects who had a history of hypomania in the absence of a history of major depressive episode(s) ( $n = 514$ ).

*Obesity.* Self-reported height and weight were systematically obtained in NESARC. Obesity was defined as having a body mass index [(BMI): weight in kilograms divided by the square of height in meters] of  $\geq 30 \text{ kg/m}^2$ . In addition, overweight was defined as a BMI  $\geq 25 \text{ kg/m}^2$ , and extreme obesity was defined as a BMI  $\geq 40 \text{ kg/m}^2$ .

*Medical diagnoses.* NESARC respondents were asked about the presence of 11 medical conditions within the past year. For illnesses that included lay terminology in addition to medical terminology, the lay terminology is indicated in parentheses: arthritis, hypertension (high blood pressure), gastritis, stomach ulcer, liver cirrhosis, other liver disease, angina (chest pain), arteriosclerosis (hardening of the arteries), myocardial infarction (heart attack), tachycardia (rapid heartbeat), and other heart disease. Only diagnoses made by physicians or health professionals (“Did a doctor or other health professional tell you that you had \_\_\_?”) were considered present for the purpose of this study.

*Functioning.* The NESARC also includes among its measures the Short-Form 12 version 2 (SF-12), a reliable and valid measure of generic quality of life used in large population surveys that yields component and profile scores assessing various dimensions of physical and mental disability and impairment, with lower scores demonstrating greater disability and impairment (31, 32).

#### Statistical analyses

Chi-square tests for contingency tables were computed to compare the distribution of the proportions across groups and regression analyses was used to compare these groups on dimensional measures. Demographic variables with between-group differences in bivariate analyses ( $p < 0.2$ ) were included in a logistic regression analysis to examine the independent contribution of BD to the variance in obesity. To examine our second hypothesis, that obesity is associated with increased illness severity among adults with BD, clinical variables with between-group differences in bivariate analyses ( $p < 0.2$ ) were included in a logistic regression analysis to examine their independent contribution to the variance in obesity. We examined lifetime variables, and in addition examined past-year SUD which has previously been negatively associated with obesity (23). Results of univariate analyses are reported using odds ratios (OR) whereas multivariable analyses

are reported using adjusted ORs (AOR), along with 95% confidence intervals (CI). Because of the large number of comparisons, statistical significance for univariate analyses was set at  $p < 0.01$ . All analyses were conducted using SUDAAN to adjust for the design effects of the NESARC.

#### Results

Hypothesis 1: Controlling for demographic variables, subjects with BD will have higher risk of obesity versus subjects without mood disorders

Table 1 contains information regarding between-group differences in demographic and clinical variables among subjects with BD, subjects with MDD, and controls. There were significant between-group differences in the BMI categories. In post-hoc pairwise comparisons, the prevalence of obesity was significantly greater among subjects with BD (28.9%) as compared to controls (21.2%), but not significantly different from subjects with MDD (28.3%). Controlling for age, sex, and race, the prevalence of obesity was significantly greater among subjects with BD versus controls (AOR = 1.65, 95% CI: 1.45–1.89), and the prevalence among subjects with MDD was significantly greater than among controls (AOR = 1.58, 95% CI: 1.46–1.71).

Hypothesis 2: Among subjects with BD, obesity will be associated with increased clinical burden as determined by episode number and duration, comorbid conditions, and treatment utilization

Tables 2 and 3 compare obese and non-obese BD subjects with regard to demographic and clinical characteristics, respectively. Obese BD subjects were significantly older and more likely to be female compared to non-obese BD subjects. Obese BD subjects reported significantly greater duration of lifetime longest major depressive episodes, higher lifetime prevalence of anxiety disorders, and lower past-year prevalence of SUD. Moreover, there were consistent differences related to depression treatment variables. Obese BD subjects were significantly more likely to receive medications for depression, to seek treatment from a professional for depression, to be hospitalized for depression, and to attend the emergency department due to depression. In multivariable analyses, the most robust positive predictors of obesity among BD subjects were older age (AOR = 1.01, 95% CI: 1.00–1.02), greater duration of longest depressive episode (AOR = 1.02, 95% CI: 1.00–1.05), presence of comorbid anxiety disorders (AOR = 1.41,

Table 1. Weight categories and demographic variables among adults with bipolar disorder, major depressive disorder (MDD), and controls

	Bipolar disorder (n = 1,905)	MDD <sup>a</sup> (n = 5,695)	Controls (n = 35,493)	$\chi^2$ or <i>F</i>	df	p-value
Weight				15.93	6	< 0.0001
Normal (BMI < 25)	39.12	41.91	42.19			
Overweight (BMI 25.0–29.9)	32.02	29.78	36.62			
Obese (BMI 30.0–39.9)	23.66	24.12	18.92			
Extremely obese (BMI 40+)	5.20	4.19	2.27			
Age, mean (SE)	37.15 (0.41)	43.97 (0.26)	45.87 (0.21)	195.88	2	< 0.0001
Female	55.15	67.34	49.46	83.79	2	< 0.0001
Caucasian	71.12	78.13	69.72	21.21	2	< 0.0001
Married	48.79	56.23	63.18	44.82	2	< 0.0001
Completed high school or greater	81.56	86.61	84.14	10.97	2	0.0001
Currently employed	62.39	66.00	64.95	2.54	2	0.0866
Personal income				15.48	6	< 0.0001
\$0–19,999	60.07	50.09	46.11			
\$20,000–34,999	21.43	22.57	22.73			
\$35,000–69,999	15.11	20.41	22.57			
\$70,000+	3.39	6.93	8.59			
Anxiety disorders <sup>b</sup>	51.64	37.62	8.53	96.15	2	< 0.0001
Alcohol abuse or dependence	56.99	40.33	27.23	63.25	2	< 0.0001
Drug abuse or dependence	34.85	17.21	7.90	66.58	2	< 0.0001
Daily cigarette smoker	50.20	43.53	34.46	48.50	2	< 0.0001

Values indicated as percent except where noted otherwise. BMI = body mass index.

<sup>a</sup>The MDD sample excluded those patients with a history of mixed, manic, or hypomanic episodes.

<sup>b</sup>Generalized anxiety disorder, panic disorder, and/or social anxiety disorder.

Table 2. Demographic variables among bipolar disorder subjects with obesity versus without obesity

	Obese (n = 568)	Not obese (n = 1,337)	$\chi^2$ or <i>t</i>	df	p-value
Age, mean (SE)	39.71 (0.63)	36.14 (0.48)	4.86	1	< 0.0001
Female	62.03	52.43	11.35	1	0.0013
Caucasian	70.01	71.57	0.47	1	0.4950
Married	51.88	47.57	2.15	1	0.1476
Completed high school or greater	83.86	80.65	1.91	1	0.1720
Currently employed	57.23	64.43	5.43	1	0.0229
Personal income			1.44	3	0.2396
\$0–19,999	63.89	58.56			
\$20,000–34,999	20.06	21.97			
\$35,000–69,999	13.30	15.83			
\$70,000+	2.75	3.64			
Daily cigarette smoker	46.65	51.60	2.49	1	0.1194

Values indicated as percent except where noted otherwise.

95% CI: 1.03–1.94), and history of hospitalization for depression (AOR = 1.46, 95% CI: 1.01–2.10). Past-year SUD was a significant negative predictor of obesity (AOR = 0.60, 95% CI: 0.42–0.85).

Comorbid medical conditions and functioning

Exploratory analyses examined the association of obesity among BD subjects with the ten medical conditions assessed in the NESARC as well as with physical and emotional-psychological functioning. As indicated in Table 4, obese BD subjects had significantly worse functioning on all but one SF-12

subscales, and had significantly greater prevalence of arthritis, hypertension, and tachycardia, as well as a significantly greater number of total medical conditions.

Of note, the analyses were repeated including subjects with hypomania but not depression (n = 514), and the overall findings were unchanged.

## Discussion

In a large, nationally representative sample, we found a nearly two-fold age-, race-, and sex-adjusted

Table 3. Clinical characteristics, comorbidities, and treatment among bipolar disorder (BD) subjects with obesity versus without obesity

	Obese (n = 568)	Not obese (n = 1,337)	$\chi^2$ or <i>t</i>	p-value
<b>Clinical characteristics</b>				
Past-year mania/hypomania, %	57.88	59.34	0.22	0.6395
Past-year depression, %	32.05	30.94	0.15	0.7008
Age of BD onset, mean (SE) <sup>a</sup>	26.32 (0.60)	23.96 (0.40)	3.49	0.0009
Duration of BD, mean (SE) <sup>b</sup>	13.22 (0.60)	11.85 (0.45)	1.85	0.0684
Number of manic episodes, mean (SE)	6.78 (0.78)	6.87 (0.52)	-0.09	0.9285
Number of depressive episodes, mean (SE)	8.66 (0.99)	7.14 (0.49)	1.32	0.1899
Mixed episodes, %	41.27	43.55	0.54	0.4661
Non-remitting symptoms, %	80.13	77.59	0.88	0.3530
Longest depressive episode, weeks, mean (SE)	155.04 (15.68)	94.49 (7.95)	3.42	0.0011
Longest hypo/manic/mixed episode, weeks, mean (SE)	79.59 (11.15)	85.94 (8.75)	-0.46	0.6506
Suicide attempt, %	24.21	19.32	3.32	0.0730
<b>Comorbidities (%)</b>				
Lifetime anxiety disorder <sup>c</sup>	59.54	48.51	12.27	0.0008
Lifetime alcohol abuse or dependence	54.23	58.08	2.06	0.1558
Lifetime drug abuse or dependence	31.05	36.35	3.17	0.0795
Lifetime gambling	3.58	2.10	1.51	0.2233
Lifetime substance use disorder <sup>d</sup>	59.80	62.36	0.99	0.3243
Past-year substance use disorder <sup>d</sup>	16.93	27.98	17.89	0.0001
<b>Treatment variables (%)</b>				
Professional: mania/hypomania	24.30	19.65	3.90	0.0526
Professional: depression	50.73	41.66	9.37	0.0032
Medication: mania/hypomania	23.96	17.67	5.68	0.0201
Medication: depression	47.51	33.73	20.51	< 0.0001
ER visit: mania/hypomania	8.82	5.10	6.22	0.0152
ER visit: depression	19.63	10.85	12.10	0.0009
Hospitalization: mania/hypomania	9.61	6.69	3.22	0.0773
Hospitalization: depression	20.05	12.54	9.15	0.0036

Degrees of freedom = 1 for all categories.

<sup>a</sup>Age of onset of mania/hypomania.

<sup>b</sup>Current age minus age of BD onset.

<sup>c</sup>Generalized anxiety disorder, panic disorder, and/or social anxiety disorder.

<sup>d</sup>Substance use disorder category includes abuse or dependence of alcohol or drugs.

increased risk of obesity among adults with BD versus controls, whereas the difference between adults with BD and MDD was not significant. These findings suggest that the excessive prevalence of obesity cannot be attributed to the biases of treatment-seeking samples, but rather that there is elevated prevalence of obesity in a representative sample of adults with BD. Furthermore, our hypothesis regarding the association of obesity with increased BD severity was partially supported. Obese subjects with BD had more comorbid anxiety disorders, longer depressive episodes, and a pattern of increased mood-related treatment utilization. Obese subjects with BD also had more physician-diagnosed medical conditions and significantly poorer physical and mental health functioning versus non-obese BD subjects.

These findings must be considered in the context of the methodologic limitations of this study. First, obesity was determined by self-report. The determination of obesity based on self-reported height and weight has excellent specificity but only fair to good sensitivity, suggesting that present findings

may under-estimate the prevalence of obesity (33–35). Indeed, whereas the prevalence of obesity among controls in the NESARC was 21.3%, the prevalence of obesity in the general population in 2001–2002, contemporaneously with the NESARC, was 27.8% for men and 33.3% for women (1). Second, this study employed a cross-sectional retrospective methodology; therefore, the direction of the associations between the variables cannot be determined. Moreover, many of the variables examined were lifetime variables and lack of information regarding current mood symptoms precluded an examination of obesity with respect to contemporaneous mood. Third, the NESARC study did not include information regarding specific medications. Ways in which this may have affected study findings are elaborated in greater detail below. Fourth, this study cannot address specific putative pathophysiological or behavioral underpinnings of these associations, because information regarding physical activity, dietary intake, glucose, lipids, and other biological factors was not collected in the NESARC. Fifth, this study

Table 4. Medical conditions and 12-item Short-Form Health Survey functioning among bipolar disorder subjects with obesity versus without obesity

	Obese (n = 568)	Not obese (n = 1,337)	$\chi^2$ or <i>t</i>	p-value
<b>Medical conditions (past year), %</b>				
Arthritis	36.93	23.94	14.30	0.0003
Hypertension	33.19	16.91	27.34	< 0.0001
Gastritis	16.39	12.63	2.86	0.0954
Angina	19.10	16.18	1.56	0.2163
Tachycardia	20.89	14.72	7.09	0.0097
Other forms of heart disease	3.61	4.04	0.15	0.7002
Stomach ulcer	6.42	7.80	1.02	0.3155
Arteriosclerosis	3.11	2.31	0.64	0.4249
Myocardial infarction	1.26	0.85	0.62	0.4348
Cirrhosis of the liver	0.86	0.60	0.19	0.6647
Other forms of liver disease	1.84	1.23	0.69	0.4079
Total medical conditions, mean (SE)	1.41 (0.07)	0.99 (0.05)	4.96	< 0.0001
<b>Functioning, mean (SE)</b>				
Physical disability	46.64 (0.59)	50.68 (0.35)	-6.11	< 0.0001
Mental disability	42.46 (0.74)	44.28 (0.40)	-2.28	0.0257
Physical functioning	46.68 (0.62)	50.68 (0.34)	-5.52	< 0.0001
Role physical	45.79 (0.60)	49.22 (0.39)	-4.87	< 0.0001
Bodily pain	44.38 (0.67)	47.04 (0.45)	-3.59	0.0006
General health	42.92 (0.70)	47.32 (0.43)	-5.56	< 0.0001
Vitality	47.10 (0.60)	50.35 (0.37)	-4.72	< 0.0001
Social functioning	43.14 (0.73)	45.94 (0.45)	-3.37	0.0013
Emotional health	42.08 (0.72)	45.13 (0.45)	-3.93	0.0002
Mental health	42.76 (0.69)	44.11 (0.42)	-1.70	0.0936

Degrees of freedom = 1 for all categories.

examined bipolar I and II disorder specifically and not other subtypes of BD. Therefore, present findings may not generalize to cyclothymia, or to bipolar disorder not otherwise specified; however, findings were unchanged when subjects with hypomania but not depression were included. Finally, as with any large-scale epidemiologic study, this study is limited by its reliance on lay interviewer-administered structured interviews to determine psychiatric diagnoses.

The present findings support our first hypothesis, that obesity is more prevalent in a representative sample of adults with BD versus adults without mood disorders. A total of 29.8% of BD subjects were obese based on self-reported height and weight. Previous estimates for obesity prevalence are generally 25–45%, although higher (36) and lower (37) rates have been reported as well. Thus, our estimates are within the range of previous studies.

Our hypothesis regarding obesity being associated with proxies for increased severity of BD was only partially supported. Treatment-seeking in various forms was consistently associated with obesity, and previous research suggests that this is a valid proxy for illness severity (38). Obese adults with BD had longer depressive episodes, and treatment-seeking for bipolar depression in particular was strongly associated with obesity among

adults with BD. In addition to the mechanisms linking BD and obesity described above, it is also possible that hyperphagia, hypersomnia, anergia, and carbohydrate craving associated with atypical depressive episodes during the course of BD confer increased risk of weight gain (20, 39). The finding that treatment-seeking for BD depression is associated with obesity converges with previous findings regarding the association between obesity and increased BD depression severity (6, 15, 16). In summary, it appears that much of the association between BD and obesity is explained by the burden of depression. This could be expected based on the known substantial burden of depression in BD (40–42) together with the known association between depression and obesity (25, 43).

Our findings replicate previous Canadian epidemiologic data suggesting that obesity and past-year SUD are negatively associated among adults with BD (23). In contrast, previous findings from children and adolescents with BD suggest that the presence of lifetime SUD is associated with increased prevalence of obesity (27). Further investigations are required in order to determine whether there are developmental differences in the association between SUD and obesity in BD. The finding that female sex was associated with obesity in BD is consistent with previous epidemiologic and clinical studies (10, 22). Present

findings regarding significant associations of obesity with increasing age, functional impairment, and comorbid anxiety, hypertension, and arthritis also converge with and extend previous clinical findings (12, 44, 45).

Past-year depression or mania, lifetime number of depressive or manic episodes, history of suicide attempt, and history of mixed mania were not significantly associated with obesity among BD subjects. The lack of an association with suicide attempts in particular is unexpected (13, 14, 18, 19), and may be due to the fact that the AUDADIS-IV only ascertains suicide attempts that occur in the most recent and/or severe depressive episode. It is possible that undetected suicide attempts may have occurred during other depressive episodes or outside of the context of depressive episodes. The lack of an association between treatments for mania/hypomania and obesity was also unexpected. However, the absence of data regarding specific medications constrains conclusions regarding the implications of present findings. Data regarding specific medications would have allowed us to examine the contribution to obesity of medications with varying propensity for weight gain (4, 10, 46, 47).

Despite its limitations, this study confirms and extends previous findings on this subject. The prevalence of obesity, taking into account multiple potential confounding variables, is nearly two-fold greater in a representative epidemiologic sample of adults with BD. Moreover, the prevalence of obesity in BD may increase with age, and may be more pronounced among women with BD, and among those who seek treatment for BD. Given the increased risk of cardiovascular disease, diabetes, and hypertension in BD (3, 48, 49), these findings underscore the excessive medical morbidity to which obese adults with BD may be exposed. Strategies are needed that mitigate weight gain in the course of BD. One such approach may be integration of lifestyle and weight-management counseling into the long-term management of BD. Preliminary findings from studies of such interventions suggest possible physical and psychological benefits (50, 51). Counseling regarding nutrition and exercise for patients with BD is feasible, however strategies for retaining patients with BD in lifestyle management-related services are needed (52). Prospective studies examining predictors of weight gain in BD may inform the design of these interventions as well. Prevention and management of obesity has yet to take a significant role in training of psychiatrists. In light of major disparities in the medical care of adults with BD and other forms of

severe and persistent mental illness (53–55), there are important opportunities for psychiatrists to effect change in medical outcomes among patients suffering from BD.

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