Prevalence and Burden of General Medical Conditions Among Adults With Bipolar I Disorder: Results From the National Epidemiologic Survey on Alcohol and Related Conditions

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Objective: To examine the prevalence and burden of general medical conditions (GMCs) among a nationally representative sample of adults with bipolar I disorder.

Method: Data for this study were derived from the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (N = 43,093), which included US adults aged 18 years and older. This study focused on the subsample of adults with *DSM-IV*–diagnosed bipolar I disorder (n = 1,548). The past-year prevalence of 11 GMCs was examined. Associations between GMCs, bipolar I disorder, and disability measures (12-Item Short-Form Health Survey) were tested using multivariate regression analyses.

Results: Approximately 32.4% of adults with bipolar I disorder had 1 or more GMCs. In the general population, diagnosis with bipolar I disorder was a significant risk factor for 7 of 11 GMCs in adjusted analyses. Among adults with bipolar I disorder, those with 1 or more GMCs evidenced significantly greater disability across all disability measures compared to those without a GMC. Individual GMCs were significantly associated with physical, mental, and psychosocial disability in adjusted analyses and predicted specific patterns of disability.

Conclusions: GMCs were found disproportionately among persons with bipolar I disorder and associated with significant impairments in health and psychosocial functioning. Health care providers should screen for and treat GMCs in service populations including persons with bipolar disorder, given the heightened rates of morbidity, mortality, and disability that attend untreated GMCs in this client group. Integrated and collaborative treatment approaches could significantly improve overall functioning and quality of life for persons with this treatable disorder.

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Bipolar disorder is a generally chronic mental disorder with significant individual and social consequences. It has been associated with lower levels of educational attainment,[1] unemployment,[2] criminal involvement,[3] and extensive utilization of health care services.[4] In addition to facing a wide range of psychosocial problems, persons with bipolar disorder are at increased risk for a wide range of clinical comorbidities. Recent research has revealed that persons with bipolar disorder are also at increased risk for having a general medical condition (GMC).[5–9] Such conditions include cardiovascular disease,[5] pulmonary conditions and diabetes mellitus,[10–13] hepatitis C,[14] liver problems,[11] and thyroid disease.[15,16] GMCs among this population are significant, given their contribution to increased rates of mortality,[17] decreased health-related quality of life,[18] and poorer treatment outcomes.[19]

Although causal associations are not clearly established, prior research suggests that bipolar symptoms, especially mania, may contribute to the development of or exacerbate medical conditions. More specifically, persons with bipolar disorder frequently exhibit high-risk behaviors,[14,20] poor diet and limited exercise,[21] decreased awareness of health needs,[22] and circadian rhythm abnormalities.[23] Previous research links the use of psychotropic medication, particularly mood stabilizers and atypical antipsychotics, and unhealthy lifestyle practices to the development of medical conditions in this population.[24] Many pharmacologic treatments contribute to obesity,[25] and only about half of patients report receiving appropriate laboratory monitoring of serum drug levels, blood toxicity, and other cardiovascular disease–related risk factors.[26]

While significant attention has focused on substance use and other psychiatric comorbidities in persons with bipolar disorder,[15,27–30] less research has examined comorbid GMCs,[5,9,18,19,31,32] with much of the research focusing on a single medical comorbidity.[7,20] Despite the recent attention

For Clinical Use

- Medical disorders are common among persons with bipolar disorder.
- Persons with bipolar disorder who have co-occurring medical conditions tend to have greater functional impairments compared to those without co-occurring medical conditions.
- Medical conditions can alter the course and outcomes for persons with bipolar disorder.

to medical conditions afflicting persons with bipolar disorder, it remains unclear which GMCs are most prevalent and the extent to which individual GMCs are associated with specific forms of disability across a wide range of measures. Further, we are aware of no studies that have investigated this issue in a nationally representative sample (as opposed to a clinical sample). Therefore, we investigated the prevalence and correlates of GMCs in individuals with bipolar disorder who participated in the 2001–2002 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) (N = 43,093), which included US adults aged 18 and older. Data for this study were derived from a nationally representative survey that utilized psychometrically sound diagnostic assessments and measures of disability, in addition to screening for 11 GMCs. This study provides an important community-based perspective on the critical issues of physical health, mental health, functional status, and overall quality of life for persons with this disabling and costly psychiatric condition.

Bipolar I and bipolar II disorders are characterized by important differences in diagnostic features and course of illness.[33] A core defining feature of bipolar I disorder—1 or more lifetime episodes of mania—is also associated with a variety of adverse health consequences, including (but not limited to) problems with diet, hygiene, substance use, and risky sexual practices. Whereas mania can be associated with psychotic symptoms and significant functional impairment, including hospitalization, it can be difficult to distinguish hypomania, which is a feature of bipolar II disorder,[33] from other psychiatric syndromes, such as euthymia following a depressive episode, personality disorders, and hyperthymic temperament. Therefore, similar to prior studies of bipolar disorders, this study separates these disorders and focuses exclusively on bipolar I disorder.[10,21,23,25,34]

METHOD

Survey Description

Study findings are based on data from the 2001–2002 NESARC. The population studied by NESARC is a nationally representative sample of 43,093 noninstitutionalized US residents aged 18 years and older.[35] The survey gathered information on alcohol use and comorbid conditions from individuals living in households and group settings such as shelters, college dormitories, and group homes.

NESARC utilized a multistage cluster sampling design, oversampling young adults, Hispanics, and African Americans in the interest of obtaining reliable statistical estimation in these subpopulations and to ensure appropriate representation of racial/ethnic subgroups. The overall response rate was 81%. Data were weighted at the individual and household levels and to adjust for oversampling and nonresponse on demographic variables (ie, age, race/ethnicity, sex, region, place of residence). Data were also adjusted to be representative (based on region, age, race, and ethnicity) of the US adult population as assessed during the 2000 Census.

Data were collected through face-to-face interviews conducted by US Census Bureau workers trained by the National Institute on Alcohol Abuse and Alcoholism and the US Census Bureau. Interviewers administered the Alcohol Use Disorder and Associated Disabilities Interview Schedule-*DSM-IV* version (AUDADIS-IV), which has been shown to have good-to-excellent reliability in assessing substance use and psychiatric disorders in the general population.[36,37]

Measures

Bipolar I disorder. Subjects were identified as having lifetime bipolar I disorder if they ever met criteria for a *DSM-IV*–diagnosed manic episode. The reliability of the AUDADIS-IV diagnosis of bipolar disorder is moderate ($\kappa = .59$).[34,38,39] It should be noted that bipolar I disorder does not have a diagnostic requirement for a major depressive episode.[33] However, given that major depressive episodes are a common feature of bipolar I disorder, this investigation includes major depressive episodes as a key variable in study analyses. Bipolar I diagnoses were assigned consistent with *DSM-IV* criteria and guidelines. Additional information about the course of bipolar I disorder was included in the analysis, including age at first manic episode, lifetime number of manic episodes, and duration of longest manic episode.

Major depressive episode. Subjects were identified as having a lifetime major depressive episode if they had met all *DSM-IV* criteria for such an episode, as assessed by the AUDADIS-IV. The reliability of the AUDADIS-IV diagnosis for major depressive episode was $\kappa = .65$.[38] Age at onset and lifetime number of major depressive episodes were also assessed.

Table 1. Characteristics of Adults With and Without Bipolar I Disorder and With and Without General Medical Conditions (GMCs) in NESARC

Variable	Adults Without Bipolar Disorder		Adults With Bipolar Disorder		
	A. Without Any GMC (n = 25,170), % (SE)	B. With Any GMC (n = 16,375) % (SE)	C. Without Any GMC (n = 644), % (SE)	D. With Any GMC (n = 904), % (SE)	Overall χ^{2a}
Race					54.33*
White (non-Hispanic)	68.3 (1.85)	75.2 (1.20)	69.1 (2.66)	72.4 (2.17)	B = D, C = D
Black (non-Hispanic)	10.9 (0.69)	11.2 (0.64)	12.4 (1.55)	11.1 (1.28)	
Asian/Native Hawaiian/Pacific Islander	5.3 (0.64)	3.0 (0.48)	2.7 (1.11)	2.4 (0.93)	
American Indian/Alaskan Native	1.8 (0.16)	2.5 (0.21)	4.4 (1.08)	3.8 (0.75)	
Hispanic/Latino	13.8 (1.45)	8.0 (0.89)	11.4 (1.64)	10.2 (1.58)	
Education					126.47*
Less than high school	12.9 (0.59)	19.8 (0.56)	14.8 (1.52)	23.7 (1.90)	A = C, B = D
High school or equivalent	27.4 (0.60)	32.5 (0.62)	29.6 (2.23)	31.2 (1.73)	
More than high school	59.8 (0.69)	47.7 (0.75)	55.6 (2.41)	45.2 (2.25)	
Marital status					170.70*
Married/cohabitating	60.6 (0.54)	64.4 (0.55)	45.8 (2.16)	55.0 (2.02)	
Widowed/divorced/separated	12.5 (0.24)	25.4 (0.40)	14.8 (1.54)	24.7 (1.63)	
Never married	26.9 (0.54)	10.3 (0.37)	39.5 (2.24)	20.3 (1.68)	
Income					118.15*
< $19,999	20.8 (0.55)	27.4 (0.55)	28.9 (2.26)	37.5 (2.19)	B = C
$20,000–$34,999	19.0 (0.39)	21.7 (0.45)	24.6 (1.95)	20.7 (1.57)	
$35,000–$69,999	32.9 (0.42)	31.2 (0.51)	30.5 (2.21)	29.2 (2.21)	
≥ $70,000	27.4 (0.85)	19.8 (0.61)	16.0 (1.93)	12.6 (1.48)	
Age					201.33*
18–34	42.6 (0.48)	12.0 (0.38)	59.1 (2.35)	32.8 (2.09)	
35–54	43.0 (0.46)	34.9 (0.49)	36.3 (2.32)	44.6 (2.07)	
≥ 55	14.4 (0.30)	53.1 (0.57)	4.6 (0.91)	22.6 (1.73)	
Gender					62.52*
Male	50.4 (0.43)	44.0 (0.50)	49.5 (2.34)	44.1 (2.26)	A = B, B = D, C = D
Female	49.6 (0.43)	56.0 (0.50)	50.5 (2.34)	56.0 (2.26)	
Lifetime substance use disorder	31.3 (0.88)	31.0 (0.75)	64.0 (2.38)	63.2 (2.06)	113.93* C = D
Lifetime personality disorder	9.7 (0.31)	15.4 (0.39)	53.3 (2.29)	65.6 (2.14)	171.14*
Lifetime major depressive episode	13.1 (0.38)	21.4 (0.45)	65.7 (2.58)	75.2 (1.70)	171.07*
Lifetime anxiety disorder	12.6 (0.45)	22.3 (0.51)	45.6 (2.45)	65.5 (1.94)	151.21*

[a]Post hoc pairwise comparisons of each group were conducted using χ^2 tests. Note that all pairwise comparisons were statistically significant ($P < .05$) unless null findings for group contrasts are reported (eg, A = C). Letters for group differences correspond to groups presented in each column.
*$P < .001$.
Abbreviations: GMC = general medical condition, NESARC = National Epidemiologic Survey on Alcohol and Related Conditions.

Disability. Disability was measured using scales from the 12-Item Short-Form Health Survey, version 2 (SF-12v2).[40] These scales measure physical, mental, and psychosocial domains of disability. Each score is presented as a continuous measure, ranging from 0–100 points. Lower scores indicate a greater level of disability. A mean value of 50 represents the expected value in the general population. Scales from this instrument serve as indicators of quality of life in a substantial body of mental health services research[41–43] and have demonstrated good psychometric properties.[40]

General medical conditions. Subjects were asked to self-report whether they experienced any of 11 different GMCs in the past 12 months at the time of the survey. These conditions included arthritis, hypertension, gastritis, angina, tachycardia, other forms of heart disease, stomach ulcer, arteriosclerosis, myocardial infarction, cirrhosis of the liver, and other forms of liver disease. When administered the survey, subjects were provided with nontechnical examples of the medical conditions (eg, tachycardia was also described as "rapid heartbeat").

Covariates. Four additional sets of clinical diagnoses were included in this study, which were assigned in accordance with *DSM-IV* specifications. These included lifetime substance use disorders, defined as either abuse or dependence on alcohol or drugs (ie, heroin, hallucinogens, cocaine/crack, marijuana, stimulants, painkillers, tranquilizers, sedatives, inhalants). Age at onset of first substance use disorder and total number of lifetime substance use disorders were included in this study. Other psychiatric disorders included were lifetime anxiety disorders (ie, social phobia, panic disorder with or without agoraphobia, generalized anxiety disorder) and lifetime personality disorders (ie, antisocial, avoidant, dependent, obsessive-compulsive, paranoid, schizoid, histrionic). Response categories for race, gender, age, marital status, educational level, and annual family income are listed in the first column of Table 1.

Analytic Procedures

All analyses were computed using SUDAAN Version 9.0 (Research Triangle Institute, Raleigh, North Carolina, 2004). This system implements a Taylor series linearization to adjust standard errors of estimates for complex survey sampling design effects including clustered data. The study sample, including sociodemographic, psychiatric, and

medical characteristics, was described with weighted prevalence estimates and standard errors. Disability scores were compared for persons with bipolar I disorder, both with and without GMCs. Multiple logistic regression analyses were used to examine the association between bipolar I disorder and GMCs, and multiple linear regression analyses were used to examine the association between bipolar I disorder and measures of disability. All multiple regression analyses controlled for potentially confounding variables.

RESULTS

Sample Characteristics

Table 1 provides a summary of the NESARC sample characteristics, comparing adults with and without bipolar I disorder and with and without GMCs. Based on the overall NESARC sample, 3.6% met criteria for bipolar I disorder. Among persons with bipolar I disorder, 46.4% were male, and almost half had some education beyond high school (49.6%). Thirty percent had a high school or equivalent education, and 20% had less than a high school education. The largest racial/ethnic group was white (71.6%), followed by black (11.7%) and Hispanic/Latino (10.7%). Only 6.0% of the sample was classified as another race or ethnicity. Slightly more than half were married or cohabitating (51.0%), 20.4% were separated or divorced, and 28.6% had never married.

Among persons with bipolar I disorder, 32.4% had at least 1 GMC. Within this group of persons with both bipolar I disorder and a GMC, 43.1% had 1 GMC, 25.2% had 2, 13.6% had 3, 8.5% had 4, and 9.6% had 5 or more conditions.

Persons with bipolar I disorder and GMCs tended to be female and older, with lower levels of education and income. While statistically significant, race-related differences were small. Persons with bipolar I disorder, including those with and without GMCs, exhibited significantly higher rates of substance use disorders, anxiety disorders, major depressive episodes, and personality disorders.

Course of Bipolar I Disorder and General Medical Conditions

The mean age of bipolar I onset was 25.4 (SE = 0.40) years. Approximately 67.2% (SE = 2.09) reported a lifetime history of 1 manic episode, 21.5% (SE = 1.75) reported 2 episodes, and 11.3% reported 3 or more episodes (1.29%, SE = 0.17). Approximately 25.2% (SE = 1.15) reported that the longest (or only) manic episode lasted 1 week or less; 27.8% (SE = 1.00) reported a duration of 2–4 weeks; and 47.0% (SE = 1.26) reported a duration of more than 4 weeks. Persons with a GMC, in comparison to those without a GMC, were more likely to have a later age at onset of bipolar I disorder (mean = 27.6 vs 22.5 years, respectively, $t = 6.44$, $P < .001$), report 2 or more manic episodes in a lifetime (89.6% vs 86.8%, $\chi^2_1 = 4.6$, $P < .001$), and report manic episodes lasting more than 4 weeks (51.6% vs 42.5%, $\chi^2_2 = 7.8$, $P < .001$).

Seventy-one percent (SE = 1.50) of persons with bipolar I disorder met lifetime criteria for a major depressive episode. Among these persons, approximately 34.5% (SE = 1.73) reported 1 lifetime depressive episode, 15.8% (SE = 1.34) reported 2 such episodes, and 49.6% (SE = 1.83) reported 3 or more episodes. Having a GMC was not associated with a greater number of major depressive episodes ($\chi^2_2 = 2.0$, $P = .138$). However, persons with a GMC had a later age at onset of depressive episodes compared to those without a GMC (mean = 26.5 vs 22.3, $t = 5.13$, $P < .001$).

Approximately 63.5% of persons with bipolar I disorder met criteria for lifetime substance use disorder. Among these persons, approximately 47.6% (SE = 2.05) reported 1 lifetime substance use disorder, 24.6% (SE = 1.34) reported 2 disorders, and 27.8% (SE = 1.75) reported 3 or more disorders. Having a GMC was associated with a greater number of substance use disorders ($\chi^2_2 = 7.8$, $P < .001$). Specifically, 30.7% of persons with a GMC reported 3 or more substance use disorders compared to 24.1% of persons without a GMC. The mean age at onset of the first substance use disorder was 20.2 years. Persons with a GMC had a slightly later age at onset for the first substance use disorder compared to those without a GMC (mean = 20.7 vs 19.5, $t = 2.06$, $P = .044$).

Prevalence of Specific General Medical Conditions

Table 2 provides annual GMC prevalence rates for adults with and without bipolar I disorder. Separate comparisons were also made for persons with and without a major depressive episode (described below). Regarding the overall sample, the 5 most common conditions were arthritis, hypertension, gastritis, angina, and tachycardia. Adults with bipolar I disorder exhibited significantly higher rates for 8 of the 11 GMCs, with the largest differences occurring for the most common medical conditions. The largest observed differences in annual prevalence rates between persons without and with bipolar I disorder, based on χ^2 values, were observed for tachycardia (5.7% vs 17.9%), angina (5.7% vs 17.9%), and stomach ulcers (2.5% vs 9.1%).

A lifetime history of major depressive episode was associated with a higher rate of 4 different GMCs among persons with bipolar I disorder compared to those without a history of major depressive episode (see Table 2). The most notable differences were in rates of arthritis (34.3% vs 21.9%) and tachycardia (20.4% vs 11.6%). Small but significant differences were also observed for angina (19.8% vs 13.3%) and stomach ulcers (10.3% vs 6.3%).

Associations Between Bipolar I Disorder and Medical Comorbidities

Table 3 shows the association between bipolar I disorder and GMCs. Findings are based on a series of logistic regression models, with diagnosis with bipolar I disorder (yes or no) serving as the primary independent variable. Each

Table 2. Annual Prevalence Rates of GMCs Among Adults With and Without Bipolar I Disorder and Lifetime History of a Major Depressive Episode

	Overall Sample Comparison			Subsample Comparison		
Variable	Adults Without Bipolar I Disorder (n = 41,545), % (SE)	Adults With Bipolar I Disorder (n = 1,548), % (SE)	χ^2	Adults With Bipolar I Disorder Without Major Depressive Episode (n = 451), % (SE)	Adults With Bipolar I Disorder and Major Depressive Episode (n = 1,097), % (SE)	χ^2
Arthritis	20.92 (0.52)	30.73 (1.54)	34.14***	21.89 (2.38)	34.32 (1.80)	16.91***
Hypertension	18.99 (0.39)	24.34 (1.50)	11.37**	21.25 (2.60)	25.60 (1.80)	1.87
Gastritis	5.93 (0.17)	14.99 (1.07)	45.83***	12.45 (2.12)	16.02 (1.28)	1.92
Angina	5.73 (0.17)	17.94 (1.32)	50.43***	13.34 (1.89)	19.81 (1.63)	6.84*
Tachycardia	5.70 (0.17)	17.88 (1.34)	57.79***	11.61 (1.84)	20.43 (1.73)	10.72**
Other forms of heart disease[a]	2.80 (0.12)	4.24 (0.62)	5.40*	3.24 (1.09)	4.64 (0.73)	1.17
Stomach ulcer	2.50 (0.10)	9.11 (0.87)	48.33***	6.29 (1.55)	10.25 (1.04)	4.32*
Arteriosclerosis	1.89 (0.09)	2.68 (0.48)	2.74	2.48 (0.95)	2.77 (0.57)	0.06
Myocardial infarction	.93 (0.06)	1.19 (0.28)	0.83	1.00 (0.44)	1.27 (0.34)	0.25
Other forms of liver disease[a]	.53 (0.04)	1.95 (0.41)	11.81***	1.40 (0.61)	2.18 (0.53)	0.89
Cirrhosis of the liver	.21 (0.03)	.91 (0.38)	3.20	0.55 (0.39)	1.06 (0.50)	0.65

[a]Refers to generic categories included in the original NESARC survey and includes all forms of heart and liver disease other than those specifically assessed.
*$P < .05$.
**$P < .01$.
***$P < .001$.
Abbreviation: GMC = general medical condition.

Table 3. Multivariate Logistic Regression Analysis of Associations Between Bipolar I Disorder and General Medical Conditions

Medical Condition	AOR[a]	95% CI
Arthritis	1.40	1.16–1.70
Hypertension	1.42	1.16–1.73
Gastritis	1.49	1.21–1.85
Angina	1.61	1.30–1.99
Tachycardia	1.68	1.64–2.16
Other forms of heart disease	1.26	0.88–1.81
Stomach ulcer	1.66	1.31–2.11
Arteriosclerosis	1.43	0.94–2.16
Myocardial infarction	1.22	0.69–2.15
Other forms of liver disease	1.69	1.04–2.75
Cirrhosis of the liver	1.72	0.70–4.23

[a]AOR represents the odds of an adult with bipolar I disorder having each condition compared to persons without bipolar I disorder, while controlling for race, education, marital status, age, income, lifetime history of major depressive episode, anxiety disorder, alcohol or drug use disorder, and personality disorder.
Abbreviation: AOR = adjusted odds ratio.

Table 4. Comparisons of Adults With Bipolar I Disorder Across SF-12v2 Measures of Disability, by Presence Versus Absence of One or More Past-Year GMCs

Disability Measure	Bipolar I With a GMC Mean (95% CI)	Bipolar I Without a GMC Mean (95% CI)	F[a]
Physical disability	44.1 (43.0–45.2)	53.7 (52.9–54.4)	221.36
Mental disability	40.7 (39.5–41.9)	46.6 (45.6–47.7)	54.63
Physical functioning	44.8 (43.8–45.8)	53.4 (52.7–54.1)	195.19
Role physical functioning	43.0 (41.8–44.1)	52.1 (51.4–52.8)	180.44
Bodily pain	41.4 (40.3–42.5)	50.2 (49.0–51.4)	110.59
General health	39.8 (38.6–41.0)	51.0 (50.0–52.0)	200.63
Vitality	46.3 (45.3–47.3)	52.5 (51.5–53.6)	74.68
Social functioning	41.4 (40.1–42.6)	48.3 (47.1–49.4)	67.62
Role emotional functioning	39.5 (38.2–40.8)	48.0 (47.0–49.1)	101.95
Mental health	40.6 (39.5–41.7)	46.8 (45.8–47.8)	71.61

[a]All F values are statistically significant ($P < .001$). Expected overall population mean value for each disability score is 50.
Abbreviations: GMC = general medical condition, SF-12v2 = 12-Item Short-Form Health Survey, version 2.

regression model adjusted for sociodemographic factors (ie, race, education, marital status, age, income) and lifetime psychiatric syndromes (ie, major depressive episode, anxiety disorder, alcohol or drug use disorder, and 1 or more personality disorders). Bipolar I disorder was significantly associated with 7 of the 11 GMCs examined, with adjusted odds ratios (AORs) ranging from 1.40–1.69. The strongest effect sizes were for noncirrhotic forms of liver disease (AOR = 1.69, 95% CI = 1.04–2.75).

Levels of Disability

Levels of disability, as measured by subscales of the SF-12v2, are presented in Table 4. Across all measures of disability, adults with bipolar I disorder and a GMC had significantly lower scores (ie, greater disability) on all measures of disability, as compared to adults with bipolar I disorder without a GMC. Moreover, these scores were consistently lower than the expected mean value for the general population (mean = 50). Adults with bipolar I disorder but without a GMC scored close to the expected population mean value on all measures, with the exception of scores in mental disability and mental health, which were about 10% below the expected mean (means = 46.6 and 46.8, respectively).

The largest differences between adults with and without GMCs were seen in physical measures, including physical disability, physical functioning, bodily pain, and general health. Persons with GMCs also exhibited significantly lower scores on measures related to mental and psychosocial functioning. For example, adults with a GMC had role emotional functioning scores that were, on average,

Table 5. Multivariate Linear Regression Analysis of Associations Between GMCs and Levels of Functioning/Disability Among Adults With Bipolar I Disorder[a]

	Measures of Functioning									
Variable	Physical Disability	Mental Disability	Physical Functioning	Role Physical Functioning	Bodily Pain	General Health	Vitality	Social Functioning	Role Emotional Functioning	Mental Health
Intercept	61.48 (1.39)***	54.16 (1.72)***	60.19 (1.39)***	61.02 (1.42)***	59.45 (1.77)***	59.09 (2.03)***	60.30 (1.45)***	55.64 (1.93)***	57.52 (1.89)***	53.53 (1.67)***
Hypertension	−4.22 (0.85)***	−1.98 (1.01)	−3.52 (0.88)***	−4.11 (0.92)***	−2.89 (1.04)**	−4.55 (0.92)***	−3.41 (0.87)***	−3.61 (1.10)**	−2.96 (1.09)**	−1.20 (0.92)
Tachycardia	−0.85 (0.93)	−5.19 (1.24)***	−0.40 (1.00)	−3.27 (0.98)**	−2.09 (1.09)	−2.70 (1.17)*	−2.63 (0.95)**	−4.36 (1.32)**	−5.35 (1.15)***	−3.74 (1.29)**
Chest pain	−2.88 (1.02)**	−0.99 (1.26)	−2.96 (1.06)**	−1.28 (1.08)	−2.69 (1.30)*	−3.79 (1.21)**	−0.51 (0.96)	−2.44 (1.27)	−1.77 (1.27)	−1.25 (1.27)
Gastritis	−3.62 (0.88)***	−2.03 (1.13)	−2.93 (1.00)**	−4.05 (1.00)***	−3.25 (1.12)**	−3.84 (1.22)**	−3.60 (0.98)***	−0.73 (1.28)	−3.82 (1.34)**	−1.82 (0.98)
Arthritis	−6.45 (0.85)***	0.85 (0.93)	−5.38 (0.89)***	−4.13 (0.91)***	−5.05 (1.00)***	−5.32 (0.77)***	−2.36 (0.85)**	−1.20 (1.01)	−0.56 (1.00)	−0.73 (0.83)
Lifetime major depressive episode	−0.76 (0.64)	−5.51 (0.85)***	−0.78 (0.60)	−2.45 (0.69)**	−2.45 (0.90)**	−2.46 (0.87)**	−3.91 (0.77)***	−4.06 (0.93)***	−4.87 (0.87)***	−4.41 (0.80)***
Lifetime substance use disorder	−1.25 (0.65)	0.01 (0.76)	−1.48 (0.63)*	−0.27 (0.67)	−1.36 (0.72)	−.56 (0.86)	−1.18 (0.64)	−.22 (0.83)	−0.41 (0.80)	0.03 (0.70)
Lifetime personality disorder	−0.15 (0.58)	−3.08 (0.72)***	−0.76 (0.64)	−1.58 (0.62)*	−0.47 (0.75)	−1.13 (0.76)	−1.21 (0.66)	−2.26 (0.75)**	−2.91 (0.78)***	−2.79 (0.70)***
Lifetime anxiety disorder	0.08 (0.64)	−1.74 (0.76)*	-0.05 (0.61)	0.88 (0.70)	−2.38 (0.85)**	−0.08 (0.85)	−0.57 (0.68)	−1.74 (0.85)*	−0.30 (0.81)	−2.35 (0.79)**

[a]Values are unstandardized regression coefficients (standard errors). All models were adjusted for race, education, income, age, and gender.
*$P < .05$.
**$P < .01$.
***$P < .001$.
Abbreviation: GMC = general medical condition.

approximately 20% lower than scores of persons without a GMC (mean scores = 39.5 and 48.0, respectively). Scores on mental health and vitality were also approximately 15% lower for persons with GMCs.

Multivariate Associations Between Level of Functioning and Specific GMCs

Table 5 summarizes the multivariate associations between the 5 most common GMCs and levels of functioning, while controlling for other sociodemographic and psychiatric characteristics. Each GMC was significantly associated with multiple measures of functioning. The strongest effect observed was for arthritis, which had consistently strong associations with physical measures of health, but no mental or psychosocial measures. The effects were particularly notable for measures of physical disability (b = −6.45, $P < .001$) and physical functioning (b = −5.38, $P < .001$). In comparison to arthritis, tachycardia had weaker or nonsignificant associations with physical health, but consistent associations with mental and psychosocial functioning. More specifically, persons with tachycardia had, on average, scores approximately 5 points lower on measures of mental disability (b = −5.19, $P < .001$) and emotional functioning (b = −5.35, $P < .001$) and 4 points lower on social functioning (b = −4.36, $P < .01$), compared to persons without this condition. Hypertension exhibited the strongest and most consistent relationship to measures of physical functioning, especially general health (b = −4.55, $P < .001$) and physical disability (b = −4.22, $P < .001$). Hypertension was not associated with mental health or mental disability, but exhibited moderate associations with social functioning (b = −3.61, $P < .01$), vitality (−3.41, $P < .001$), and role emotional functioning (b = −2.96, $P < .01$). Gastritis and chest pain were limited measures of physical functioning, with the exception of gastritis having a significant association with role emotional functioning (b = −3.82, $P < .01$).

Similar to many GMCs, lifetime major depressive episodes exhibited significant and consistent associations with measures of mental and psychosocial measures of functioning. The strongest associations were observed on the mental disability (b = −5.51, $P < .001$) and role emotional functioning (b = −4.87, $P < .001$) scales, which were almost equal to those of tachycardia on the same measures (b = −5.19, $P < .001$ and b = −5.35, $P < .001$, respectively). Lifetime major depressive episodes were not significantly associated with physical disability or physical functioning.

In comparison to other psychiatric conditions and GMCs, lifetime substance use disorders exhibited only a weak relationship with physical functioning (b = −1.48, $P < .05$). Lifetime personality disorder was associated with only mental and psychosocial measures of functioning, although these effect sizes were generally weaker than the effect sizes observed for GMCs. Lifetime anxiety disorder also exhibited weak or nonsignificant relationships across all measures of functioning.

DISCUSSION

This study documented elevated rates of GMCs among a nationally representative sample of persons with bipolar I disorder. The most prevalent conditions included arthritis, hypertension, angina, and tachycardia. The literature remains unclear whether bipolar patients are at higher risk for medical conditions.[19] For example, literature on mood disorders has considered depressive symptoms to account for negative health behaviors that lead to medical comorbidities.[7,44] As argued by Frank and colleagues,[45] however, the instability and chronic symptomatology may be part of a common diathesis that increases risk for both psychiatric and medical conditions. Using nationally representative data, the current study provides evidence that persons with bipolar I disorder are at increased risk of GMCs after controlling for other psychiatric conditions, including major depressive episode and substance use disorders. While an increased risk was observed, it is important to note that certain conditions, such as tachycardia, angina, and hypertension, could be symptoms of anxiety, somatization, and other nonorganic conditions afflicting patients with bipolar I disorder. Elevated rates of liver diseases could be attributable to infection with hepatitis C or hepatitis B virus or to alcoholic hepatitis, all of which are potentially indicative of greater substance use in persons with bipolar I disorder.

Based on a review of clinic-based studies, Bauer and colleagues[8] demonstrated that few characteristics of persons with bipolar disorder were significantly associated with functional outcomes. The most consistent correlate identified by Bauer et al[8] was depressive symptoms, which exhibited effect sizes close to those of specific medical conditions. The current study, using a nationally representative sample of adults, exhibited similar findings. Specifically, a history of major depressive episodes was significantly associated with physical, emotional, and psychosocial impairments. In addition to having significant associations with physical functioning, specific medical conditions were also associated with lower levels of functioning on emotional and psychosocial measures, with effect sizes being on par with major depressive episodes. This was particularly true for tachycardia and hypertension. Such findings provide further support that medical conditions can alter the course of illness and outcomes for persons with bipolar disorder. Thus, if left untreated, these conditions could lead to further functional decline and premature mortality.

It is interesting to note that for patients with bipolar I disorder who did not have a GMC, level of disability was relatively similar to the entire NESARC population except in mental disability and mental health. Because most data on disability and health-related quality of life in persons with bipolar disorder are from clinical settings, they tend to exhibit greater levels of dysfunction. Because this is among the first studies with community-based data, we are unable to consider the consistency of results. However, in the absence of serious medical conditions, persons with bipolar I disorder may tend to overestimate their current level of health and underestimate disability and functional impairment. Age and gender were also key factors associated with GMCs and should be the focus of future investigations. This finding is particularly important given the recent evidence showing gender differences in health-related quality of life among persons with serious mental illness.[46]

This study has a number of important features to consider. In particular, the large sample provided the opportunity to conduct subgroup analyses while maintaining sufficient statistical power. All psychiatric disorders, substance use disorders, and disability measures were based on standardized instruments with good psychometric properties, an important feature that overcomes the major limitations of claims-data research.

Despite the comprehensiveness and strengths of this study, it is important to consider study findings in the context of its limitations. In particular, this study relied on self-report of medical conditions, which could not be corroborated against clinical documentation or physician reports. Persons with bipolar disorder could have overreported as a result of anxiety or somatization, or underreported due to lack of knowledge of their medical conditions and limited receipt of health care. These problems may be evidenced in the moderate level of reliability of the AUDADIS-IV in the assessment of bipolar disorder ($\kappa = .0.59$).

Prior research based on the National Comorbidity Survey Replication revealed a lifetime prevalence of 1.0% for bipolar I disorder, which was lower than the estimates observed in this study.[47] However, as described by Merikangas et al,[47] a large discrepancy in rates of bipolar disorder are found in both large-scale community surveys and prospective longitudinal studies. The findings from this study may have underestimated the rates of medical comorbidities and association between comorbidity and disability, given that the sample included only noninstitutionalized adults. Associations across all domains may be stronger in clinical populations. The rates and associations may also be biased if bipolar disorder was underdiagnosed among groups who are at risk for medical conditions (eg, older persons, persons with substance use disorders). At the same time, this nationally representative sample serves as a useful indicator of the prevalence of comorbidity, while further work can be done to improve the reliability and validity of methods for estimating comorbidity at the population level. Finally, because these data are observational and cross-sectional, it is important to emphasize that causality between GMCs, levels of disability, and bipolar disorder cannot be established. However, follow-up data on approximately 80% of the entire NESARC sample will soon become available, which can help address this problem.

With the foregoing limitations in mind, this study has important service implications. Most importantly, it provides a useful analysis of the medical comorbidities that

outpatient clinicians might observe in their patients and how these comorbidities are related to global functioning. As suggested by Kilbourne and colleagues,[5] providers need to consider the role of GMCs as they relate to regimen tolerability and treatment adherence. Study findings also underscore the importance of integration of care, targeting the deep division between mental health and medical services.[48]

Detection of GMCs is dependent on the primary location of care.[49] As the majority of clinical services for persons with bipolar disorder are provided in mental health settings, further work is necessary to encourage integration of medical and mental health services. A significant body of research has focused on serious mental illness and co-occurring substance use disorders,[50–52] but few studies have addressed the challenges of integrating care for psychiatric and medical conditions.[20,53] Given the high prevalence and associated functional impairments, medical and psychiatric comorbidities should be considered a priority area of quality improvement.

This study may serve as a point of departure for future research. Given the large sample of NESARC, future research should explore gender-specific and age-specific analyses. This line of research would provide for tailored intervention and assessment approaches as medical and mental health services become integrated.[18] Additional research is needed to better understand a wider range of medical conditions over a longer period of time, especially issues of obesity and diabetes, using multiple measures of known reliability and validity. This is important given the evidence associating second-generation antipsychotics with such medical problems.[54]

Further research is needed to better understand the extent of unmet needs within this population. This is particularly important, as Redelmeier and colleagues[49] found an inverse relationship between the presence of a chronic disease and the likelihood of treatment of an unrelated disorder. Bipolar disorder may be perceived as the most pressing and severe condition among others, overshadowing other conditions that may not be as severe although these other conditions could have significantly deleterious effects on multiple domains of functioning over time. Additional data derived through survey methods regarding where patients with bipolar disorder receive care, especially those with medical comorbidities, could be useful for the purposes of targeting additional resources needed to improve care. Finally, as this study was limited to only persons with bipolar I disorder, future research should examine a continuum of effects of GMCs with regard to bipolar II disorder and cyclothymia.

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