Screening for Bipolar Disorder in the Community

Robert M. A. Hirschfeld, M.D.; Joseph R. Calabrese, M.D.; Myrna M. Weissman, Ph.D.; Michael Reed, Ph.D.; Marilyn A. Davies, Ph.D.; Mark A. Frye, M.D.; Paul E. Keck, Jr., M.D.; Lydia Lewis, B.A.; Susan L. McElroy, M.D.; James P. McNulty, Sc.B./A.B.; and Karen D. Wagner, M.D., Ph.D.

Background: Our goal was to estimate the rate of positive screens for bipolar I and bipolar II disorders in the general population of the United States

Method: The Mood Disorder Questionnaire (MDQ), a validated screening instrument for bipolar I and II disorders, was sent to a sample of 127,800 people selected to represent the U.S. adult population by demographic variables, 85,358 subjects (66.8% response rate) that were 18 years of age or above returned the survey and had usable data. Of the nonrespondents, 3404 subjects matched demographically to the 2000 U.S. Census data completed a telephone interview to estimate nonresponse bias.

Results: The overall positive screen rate for bipolar I and II disorders, weighted to match the 2000 U.S. Census demographics, was 3.4%. When adjusted for the nonresponse bias, the rate rose to 3.7%. Only 19.8% of the individuals with positive screens for bipolar I or II disorders reported that they had previously received a diagnosis of bipolar disorder from a physician, whereas 31.2% reported receiving a diagnosis of unipolar depression. An additional 49.0% reported receiving no diagnosis of either bipolar disorder or unipolar depression. Positive screens were more frequent in young adults and low income households. The rates of migraine, allergies, asthma, and alcohol and drug abuse were substantially higher among those with positive screens.

Conclusion: The positive MDQ screen rate of 3.7% suggests that nearly 4% of American adults may suffer from bipolar I and II disorders. Young adults and individuals with lower income are at greater risk for this largely underdiagnosed disorder.

(J Clin Psychiatry 2003;64:53–59)

Received June 6, 2002; accepted Nov. 7, 2002. From the Department of Psychiatry & Behavioral Sciences, University of Texas Medical Branch, Galveston (Drs. Hirschfeld and Wagner); the Department of Psychiatry, Case Western Reserve University, Cleveland, Ohio (Drs. Calabrese and Davies); the College of Physicians & Surgeons, Columbia University and the New York Psychiatric Institute, New York, N.Y. (Dr. Weissman); Vedanta Associates Inc., Chapel Hill, N.C. (Dr. Reed); the Department of Psychiatry & Biobehavioral Sciences, University of California at Los Angeles, Los Angeles (Dr. Frye); the Department of Psychiatry, University of Cincinnati College of Medicine, Cincinnati, Ohio (Drs. Keck and McElroy); the Depression and Bipolar Support Alliance, Chicago, Ill. (Ms. Lewis); and the National Alliance for the Mentally Ill, Alexandria, Va. (Dr. McNulty).

(Dr. McNutty).

This study was supported by GlaxoSmithKline, Inc.
Financial disclosure appears at the end of the article.
The authors thank Paul Crits-Christoph, Ph.D., and Lana A. Vornik, M.Sc., for their assistance in the preparation and writing of this article.
Corresponding author and reprints: Robert M. A. Hirschfeld, M.D., Department of Psychiatry & Behavioral Sciences, 1.302 Rebecca Sealy, 301 University Blvd., Galveston, TX 77555-0188 (e-mail: rohirsch@utmb.edu).

Bipolar disorder is a serious, recurrent, and sometimes chronic psychiatric illness. It is characterized by a dysregulation of mood, and associated impulsivity, risky behavior (e.g., alcohol abuse, sexual indiscretion, excessive spending), and interpersonal problems. Because of these problems, individuals with bipolar disorder experience increased mortality from suicide, natural causes (e.g., cardiovascular disease), homicide, and accidents. ¹⁻⁴ Recent data suggest that bipolar disorder is third only to depression and schizophrenia in the loss of healthy life due to premature death or disability. ⁵

Bipolar I disorder has been the focus of most research on bipolar disorder. A diagnosis of bipolar I requires at least 1 episode of mania, defined as a week or longer period of abnormally elevated or irritable mood with associated symptoms such as decreased need for sleep, being more talkative than usual, racing thoughts, and excessive involvement in high-risk activities. A manic episode causes a marked impairment in social or occupational functioning and often requires hospitalization.

The lifetime prevalence rate of DSM-III bipolar I disorder is approximately 1%.⁷ In the United States, the lifetime prevalence rates for bipolar I disorder were reported to be 0.8% in the Epidemiological Catchment Area (ECA) study⁸ and 1.6% in the National Comorbidity Study (NCS).⁹

Bipolar disorder, however, encompasses a much broader range of illness than bipolar I disorder. This range of illness is often referred to as bipolar spectrum disorder (BSD)^{10–12} and includes bipolar I disorder, bipolar II disorder, and other forms of bipolar disorder.

Many authorities 10,11,13 have suggested that these milder forms of bipolar disorder are more frequent than bipolar I disorder. Lifetime prevalence rates for BSD have been reported to range from 3.0% to 6.5% across 7 studies. However, most of these studies were small and used varying definitions of bipolar spectrum disorder. No prospective large-scale epidemiologic study has yet examined the prevalence of BSD in adults using DSM-IV criteria.

The problem of misdiagnosis and underdiagnosis of bipolar spectrum disorder has recently been highlighted. 11,12 Correct diagnosis is essential, since the treatment of bipolar disorder differs from the treatment for major depressive disorder. Controlled data indicate that there is a risk for inducing mania in patients with bipolar spectrum disorder who are treated solely with antidepressant agents. 14-16

The goal of the current study was to estimate the life-time prevalence of DSM-IV bipolar I and bipolar II disorders among adults in the United States using data from a nationwide sample of over 80,000 respondents that represent a broad age range and all geographic regions of the country. We sought to estimate the overall lifetime prevalence of bipolar I and II disorders by using a validated screening instrument and then to estimate their prevalence by gender, age, household size, and geographic region. The magnitude of the public health issues created by bipolar I and II disorders is further examined by estimating the proportion of the population that is reported to be undiagnosed or incorrectly diagnosed.

METHOD

Sample

Subjects for this study were sampled from the list of nationwide households maintained by National Family Opinion Inc. (NFO), a market research firm that maintains a panel of over 600,000 continental U.S. households for marketing and survey purposes. The NFO panel of households has previously been used to determine the general population prevalence of several general health problems, including migraine. 17-20 Potential households are initially selected for the NFO panel as part of a stratified probability sample constructed to be representative of the U.S. population in terms of urban versus rural residence, age of the head of the household, and household income and size. Very high and very low income groups are underrepresented in the overall panel. Selected households are then recruited by volunteer response to an initial mailing, with demographic information obtained from a

second mailing to households agreeing to participate in the panel. Updated demographics are obtained every 2 years. New members are solicited from the general population with an average response rate of 6%.

Samples were selected from the full panel of households using a balancing system that provides a sample with the same proportions from various demographic groups that match demographic characteristics of the population based on the 2000 U.S. Census data.²¹

Survey Procedures

The Mood Disorder Questionnaire (MDQ) was then mailed to heads of households from 100,000 demographically representative U.S. households, with a supplemental mailing of 27,800 individuals selected to improve the representativeness of the combined samples for matching adults (18 years of age or older) from the U.S. population. The household sample was balanced to match census data for U.S. households for the 9 geographic census regions, household size and income, and age of head of household within each census region for market size. The household survey was addressed to the NFO member in each household or his or her spouse (if applicable) to create a proper male-female balance. The individual-based sample was sent to specific household members selected to balance the sample and represent non-heads of household. Sixty percent of the surveys were targeted toward males and 40% toward females to offset a female bias in the NFO panel membership.

The supplemental individual sample was balanced such that the combined household and individual samples would approximately match the 2000 U.S. Census data for the same variables.

The MDQ was mailed in January 2001 to both the household- and individual-based samples. Nearly 72% (71,836) of the household questionnaires were returned within 6 weeks and 17,973 (64.7%) questionnaires from the individual-based sample were returned within 5 weeks. Some questionnaires were excluded as unusable because they were incomplete, age and gender data were missing, or the respondent was under 18 years of age. The final data set included 85,358 (66.8%) usable returns for analysis.

Telephone Survey of Non-Returners

A telephone survey of non-returners was conducted to determine whether a bias existed in responses between those panelists who did and did not return the survey. Since the total sample (N = 127,800) was not entirely representative of the U.S. population aged 18 and older, a subsample of these original individuals was created to provide benchmark demographics for the non-returner survey. The resultant subsample included 55,000 individuals balanced for geographic region, market size, household size, household income, age and gender according to

the 2000 Current U.S. Population Survey. A maximum of 1 percentage point variation was allowed between the target census quota for each category and the demographic variable balanced.

The returned surveys from this constructed sample (N=34,913) were used to establish demographic quotas for selecting individuals for the non-responder interviews. To eliminate the effect of demographic characteristics on prevalence estimates, these quotas were used to select a sample and complete interviews with individuals from among the nonresponders to the original survey. A total of 4766 individuals were contacted, and 3404 (71%) agreed to participate in the interview.

Measures

A positive screen for bipolar I and bipolar II disorders was assessed using the MDQ, a validated self-report instrument that screens for the presence of a lifetime history of bipolar disorder.²² The questionnaire consists of 13 ves/no items derived from both DSM-IV criteria and clinical experience. Items ask about mood, self-confidence, energy, sociability, interest in sex, loquaciousness, distractibility, and other behaviors. In addition to the symptom items, there are 2 additional questions, 1 asking if the symptoms ever co-occurred during the same period of time (yes/no) and 1 asking about the degree of functioning impairment caused by the symptoms (4-point scale from "no problem" to "serious problem"). An individual case is "positive" for bipolar disorder if 7 or more of the 13 symptom items, plus the co-occurrence item, are endorsed and a moderate or serious degree of functional impairment is reported on the final item. In addition, subjects were queried about whether a health professional had ever told them that they had alcohol or drug abuse problems, allergies, asthma, bipolar disorder, depression, diabetes, emphysema or chronic obstructive pulmonary disease (COPD), epilepsy, hypertension, manic depression, migraine, or seizure disorder.

Using a sample of 198 psychiatric outpatients, the initial validation study of the MDQ obtained good sensitivity (0.73) and very good specificity (0.90) against clinician diagnosis of bipolar I and II disorders.²³ In addition, an internal consistency reliability (Cronbach alpha) of 0.90 was reported for the total of the items. A second validation study was conducted as part of the current project to determine the operative qualities of the MDQ within this general population sample. Briefly, a stratified random sample of 695 subjects was drawn from the sample who returned the MDQ. These people received a research diagnostic interview conducted over the telephone, the Structured Clinical Interview for DSM-IV (SCID),²³ from a research interviewer who was blind to MDQ scores. A sensitivity of 0.281 and a specificity of 0.972, weighted to the sample of 85,358 general population respondents, were found for the MDQ against interview-based diagnosis of bipolar I and II disorders. The details of this validation study are described in a separate report.²⁴

Statistical Analysis

Lifetime prevalence rates for returners compared with non-returners of the MDQ were compared using chisquare statistics.

In addition to the obtained (unweighted) lifetime prevalence rates, we calculated weighted lifetime prevalence rates to correct biases in the returns toward older, female respondents and to reflect proportions for U.S. adult individuals from the 2000 Current Population Survey. Data were weighted for individual age, gender, household income, household size, geographic region, and market size.

The relationship of demographic factors to bipolar I and II disorders was examined by entering 6 variables (age, household income, gender, race, geographic region, and market size) as predictors of presence/absence of BSD in a logistic regression analysis.

RESULTS

Survey Return Rates and Demographic Characteristics

Overall there was a 66.8% (85,358 of 127,800) usable return rate in the combined sample of household and individual-targeted surveys. The demographic characteristics and geographic distribution of the total target sample (all those households and individuals mailed a survey) and the respondent sample are given in Table 1.

Rates of Positive Screens

The rate of positive screens in the responder sample of 85,358 adults (unweighted) was 2.5% (Table 2). The unweighted sample (N = 85,358) was disproportionately more female, older, and from smaller household size than the 2000 U.S. Census sample. When corrected for the demographic deviations of the sample from the U.S. Census, the weighted overall positive screen rate was 3.4%. The unweighted positive screen rate among the non-returners was 4.3%, higher than among the returners. When the weighted overall positive screen rate was corrected for this nonresponse bias, the weighted and adjusted overall positive screen rate became 3.7%.

Health Care Professional Diagnosis of Bipolar Disorder

Of the individuals with positive screens for the MDQ, only 19.8% reported that they had previously received a diagnosis of bipolar disorder from a doctor. A larger percent (31.2%) of those screened positive reported a physician diagnosis of unipolar depression. An additional 49.0% reported no diagnosis of either bipolar disorder or unipolar depression. Of those who screened negative,

Table 1. Demographic Characteristics of Samples (N = 85,358)

Variable	Unweighted %	Weighted % ^a
Sex		
M	35.7	48.0
F	64.3	52.0
Race		
African American	6.3	5.9
White	87.9	87.7
Asian/Pacific Islander	0.8	1.1
Native American	0.6	0.7
Other	1.2	1.4
Unknown	3.3	3.2
Age, y		
18–24	3.2	13.1
25–34	14.0	18.7
35–44	21.2	22.2
45–54	22.3	18.2
55–64	15.8	11.6
≥ 65	23.4	16.2
≥ 65 Region New England Middle Atlantic		
New England	5.2	5.0
Middle Atlantic	14.4	14.4
East N Central	16.9	16.2
West N Central	7.3	6.8
South Atlantic	18.6	18.5
East S Central	6.2	6.2
West S Central	10.8	11.0
Mountain	6.3	6.2
Pacific	14.3	15.6 20,3 14.8 20.6 44.3
Population, urban vs rural		
≤ 100,000 (rural)	21.1	20,3
100,000 to 499,999	15.1	14.8
500,000 to 2,000,000	20.3	20.6
> 2,000,000	43.5	44.3
Household size		70
1	25.4	13.3
2	36.8	13.3 33.4 19.6 18.5
3	15.8	19.6
4	13.3	18.5
5 or more	8.8	15.1
Household income/y		4
< \$20,000	22.2	17.6
\$20,000 to \$34,999	21.0	17.9
\$35,000 to \$54,999	2.2	21.0
\$55,000 to \$84,999	20.0	21.6
≥ \$85,000	14.7	21.9
^a Weighted estimates are deri		Census data

1.4% reported a physician diagnosis of bipolar disorder, and 9.5%, a diagnosis of unipolar depression.

Demographic Predictors of Bipolar Spectrum Disorder

Table 3 presents the results of the logistic regression analyses predicting the positive screens from 6 demographic variables. All variables, with the exception of market size, exhibited significant relationships with the MDQ screen results. The strongest predictor was age, with the highest rates among the 18- through 24-year-olds; the rates progressively decreased with advancing age. Household income was the next strongest predictor, with the highest adjusted lifetime prevalence among those earning less than \$20,000 per year; the prevalence progressively decreased as income increased.

Table 2. Unweighted and Weighted Positive Screen Rates $(N = 85,358)^a$

Variable	Unweighted % (95% CI)	Weighted % (95% CI)	
Total	2.5 (2.4 to 2.6)	3.4 (3.3 to 3.5)	
Sex	,	,	
M	2.7 (2.6 to 2.8)	3.8 (3.7 to 3.9)	
F	2.4 (2.3 to 2.5)	3.0 (2.9 to 3.1)	
Race	,	` ′	
African American	3.3 (3.2 to 3.4)	4.3 (4.2 to 4.4)	
White	2.4 (2.3 to 2.5)	3.1 (3.0 to 3.2)	
Asian/Pacific Islander	2.0 (1.9 to 2.1)	4.1 (4.0 to 4.2)	
Native American	6.2 (6.0 to 6.4)	7.6 (7.4 to 7.8)	
Other	5.1 (5.0 to 5.2)	6.3 (6.1 to 6.5)	
Unknown	3.2 (3.1 to 3.3)	5.2 (5.1 to 5.3)	
Age, y			
18–24	8.9 (8.7 to 9.1)	9.3 (9.1 to 9.5)	
25-34	3.9 (3.8 to 4.0)	3.9 (3.8 to 4.0)	
35-44	3.3 (3.2 to 3.4)	3.2 (3.1 to 3.3)	
45-54	2.7 (2.6 to 2.8)	2.5 (2.4 to 2.6)	
55–64	1.6 (1.5 to 1.7)	1.5 (1.4 to 1.6)	
≥ 65	0.5 (0.5 to 0.5)	0.5 (0.5 to 0.5)	
Region	, ,	` ′	
New England	1.9 (1.8 to 2.0)	2.2 (2.1 to 2.3)	
Middle Atlantic	2.2 (2.1 to 2.3)	2.7 (2.6 to 2.8)	
East N Central	2.4 (2.3 to 2.5)	3.4 (3.3 to 3.5)	
West N Central	2.1 (2.0 to 2.2)	3.1 (3.0 to 3.2)	
South Atlantic	2.5 (2.4 to 2.6)	3.5 (3.4 to 3.6)	
East S Central	3.1 (3.0 to 3.2)	5.2 (5.1 to 5.3)	
West S Central	3.0 (2.9 to 3.1)	3.7 (3.6 to 3.8)	
Mountain	2.9 (2.8 to 3.0)	3.8 (3.7 to 3.9)	
Pacific	2.5 (2.4 to 2.6)	3.2 (3.1 to 3.3)	
Population, urban vs rural	,	` ′	
≤ 100,000 (rural)	3.0 (2.9 to 3.1)	4.1 (4.0 to 4.2)	
100,000 to 499,999	2.9 (2.8 to 3.0)	4.4 (4.3 to 4.5)	
500,000 to 2,000,000	2.5 (2.4 to 2.6)	3.2 (3.1 to 3.3)	
> 2,000,000	2.1 (2.0 to 2.2)	2.7 (2.6 to 2.8)	
Household size	, (,	(,	
1	2.2 (2.1 to 2.3)	2.5 (2.4 to 2.6)	
2	2.0 (1.9 to 2.1)	2.5 (2.4 to 2.6)	
2 3	3.1 (3.0 to 3.2)	3.9 (3.8 to 4.0)	
< 4 ² →	2.9 (2.8 to 3.0)	3.7 (3.6 to 3.8)	
5 or more	3.9 (3.8 to 4.0)	4.8 (4.7 to 4.9)	
Household income/y	(**************************************	, , , , , , , ,	
<\$20,000	3.8 (3.7 to 4.0)	5.7 (5.5 to 5.9)	
\$20,000 to \$34,999	2.9 (2.8 to 3.0)	4.1 (4.0 to 4.2)	
\$35,000 to \$54,999	2.4 (2.3 to 2.5)	3.3 (3.2 to 3.4)	
\$55,000 to \$84,999	1.7 (1.6 to 1.7)	2.4 (2.3 to 2.5)	
≥ \$85,000	1.3 (1.2 to 1.4)	1.9 (1.8 to 2.0)	

^aWeighting accounts for deviations of the responder sample from the demographics of the 2000 U.S. Census.

Comorbidity of Medical Illnesses With Bipolar Spectrum Disorder

Individuals who screened positive were more likely to report a variety of comorbid general medical illnesses. In particular, sizeable (i.e., >10%) adjusted (for demographics) differences between MDQ positive and MDQ negative individuals were found in regard to hypertension, allergies, and alcohol/drug abuse (Table 4). In addition, those with positive screens were likely to report a history of asthma (16.7% vs. 9.7%) and migraine (15.2% vs. 7.0%), over 3 times as likely to report a history of seizure disorder (1.4% vs. 0.4%), and $2^{1/2}$ times as likely to report a history of emphysema/COPD (2.7% vs. 1.1%).

Table 3. Relation of Demographic Variables to Presence or Absence of Bipolar I and II Disorders^a

	Odds			
Variable	Ratio	Wald χ^2	df	p Value
Age	0.96	910.4	1	< .0001
Household income	0.95	391.1	1	< .0001
Gender	1.30	45.5	1	< .0001
Region		50.4	8	< .0001
New England	0.72			
Middle Atlantic	0.82			
East N Central	1.02			
West N Central	0.81			
South Atlantic	1.08			
East S Central	1.30			
West S Central	0.97			
Mountain	1.06			
Race		38.5	5	< .0001
Unknown (C)	1.06			
White	0.69			
African American	0.72			
Asian/Pacific Islande	r 0.86			
Native American	1.15			
Household size	1.07	19.9	1	< .0001
Urban vs rural	1.00	0.1	1	.81

^aResults from logistic regression entering all variables simultaneously. Pacific region was the reference group for odds ratios for region. "Other" was the reference group for odds ratios for race. Gender is coded as 1 = male, 2 = female. Household income coded as 35 separate dollar ranges and entered as a continuation variable. The "urban vs. rural" variable was coded into the 4 categories displayed in Tables 1 and 2.

Family History

In the total sample of 85,358, 36.4% of those who screened positive on the MDQ reported blood relatives with manic-depressive illness or bipolar disorder. In contrast, 10.7% of those who tested negative on the MDQ reported a blood relative with manic-depressive illness or bipolar disorder.

DISCUSSION

The current study is the first large-scale community screen for DSM-IV bipolar I and II disorders. The adjusted and weighted overall positive screen rate for bipolar I and II disorders (3.7%) suggests that the actual prevalence of these disorders may be higher than had previously been thought. The public health significance of bipolar disorder may also be greater than had been estimated from epidemiologic studies that focused on bipolar I disorder.⁷⁻⁹ The broader concept of BSD may more meaningfully capture the diversity of presentation of bipolar symptoms found in clinical settings and their morbidity and mortality.^{2,3,25,26} Thus, the higher positive screen rates reported here have potentially greater relevance to an understanding of the public health significance of bipolar disorder in the United States and are consistent with higher rates for BSD reported in a series of small-scale studies.13

An extremely important finding was that, of those adults identified by the MDQ as screening positive for

bipolar I and II disorders, only 20% had received a diagnosis of bipolar disorder by a physician whereas 31% had received a diagnosis of major depression. Therefore, many patients with bipolar I and II disorders may be misdiagnosed as having unipolar depression. These findings are consistent with 2 surveys of the members of the National Depressive and Manic-Depressive Association (DMDA), conducted nearly a decade apart. Over one third of these patients waited a decade or more to receive a correct diagnosis of bipolar disorder, and 60% received a misdiagnosis of depression.

These current findings have significant clinical implications since the treatment, clinical course, and prognosis for these disorders are different. Of particular concern is that the prescription of antidepressants to a patient with bipolar disorder may worsen the disorder by precipitating mania/hypomania¹⁶ or induce rapid cycling.²⁹ Therefore, whenever clinicians evaluate patients who are depressed, it is critical to assess these patients for a history of any symptoms of mania or hypomania, such as elevated mood, excessive energy, racing thoughts, and reduced need for sleep.

There was significant variation in positive screen rates across a number of other demographic variables. In particular, a higher positive screen rate for bipolar I and II disorders was evident in younger adults, as has been previously reported for bipolar I disorder. Those aged 18 to 24 had an approximately 8-fold greater likelihood of receiving an MDQ score indicative of bipolar disorder relative to those aged 55 or older. The factors responsible for this marked age effect are not clear, but increased mortality associated with bipolar disorder may be a contributing factor.

Household income was also associated with presence/absence of bipolar I and II disorders, with those earning less than \$20,000 per year having approximately 3 times the likelihood of bipolar disorder compared with those earning \$85,000 per year or more. This income effect underscores the persistent impairment in functioning, including school and work functioning, that is associated with BSD.²⁵

Adults with positive screens were more likely to report a number of general medical illnesses compared with those with negative screens. Migraine headaches were reported by more than twice the proportion of those with positive screens compared with those with negative screens. Associations between bipolar disorder and migraine have been described previously. 30,31 Hypertension and asthma were also about twice as common in those with positive screens. Seizure disorders were over 3 times more common in those with positive screens. In understanding these associations between bipolar disorder and general medical illnesses, it is important to take into account that mania can be secondary to neurologic or systemic illnesses. 32,33 These associations, however, suggest

Table 4. Comorbid Medical Illnesses in Individuals That Tested Positive Versus Negative for Bipolar I and II Disorders (N = 85,358)

	Unadjusted Lifetime Prevalence, %		Adjusted Lifetime Prevalence, % (95% CI) ^a		
	Bipolar Disorders	Bipolar Disorders	Bipolar Disorders	Bipolar Disorders	
Illness	Positive	Negative	Positive	Negative	
Alcohol/drug abuse	19.9	2.4	13.3 (11.5 to 15.3)	1.8 (1.5 to 2.0)	
Allergies	40.5	26.6	37.8 (35.7 to 39.9)	25.3 (24.4 to 26.3)	
Hypertension	15.3	12.3	28.7 (26.3 to 31.2)	14.8 (13.9 to 15.7)	
Migraine	23.4	10.1	15.2 (13.7 to 16.8)	7.0 (6.6 to 7.6)	
Asthma	18.3	9.3	16.7 (15.1 to 18.4)	9.7 (9.1 to 10.3)	
Diabetes	7.3	7.0	12.7 (11.0 to 14.6)	9.1 (8.4 to 9.8)	
Emphysema/COPD	2.2	1.5	2.7 (1.9 to 3.7)	1.1 (0.8 to 1.3)	
Seizure disorder	4.9	1.2	1.4 (0.8 to 2.3)	0.4 (0.2 to 0.6)	

^aAdjusted percents are adjusted for age, gender, region of the country, race, household income, and household size

Abbreviation: COPD = chronic obstructive pulmonary disease.

that physicians should consider assessing for these cooccurring general medical conditions in patients with bipolar I and II disorders.

An association between bipolar disorder and alcohol/substance abuse has been previously described,⁷ although the rate found in the current study (adjusted lifetime prevalence of 13.3% for those with bipolar I and II disorders) is lower than reported in these other epidemiologic studies.

A limitation of the current study is that the MDQ is a screening instrument, not a diagnostic instrument. Clinical interview methods are viewed as the gold standard for valid diagnoses within psychiatry. The MDQ, however, has been found to have generally good sensitivity and specificity with regard to research diagnostic interviews obtained from trained interviewers within both clinical²² and, in the current report, nonclinical samples. A McNemar test was nonsignificant; therefore, we would expect that the actual lifetime prevalence of bipolar I and II disorders in the com munity would be near the figure of 3.7%, the positive screen rate. With bipolar disorders, it has been suggested that repeated interviews over time are preferable and that single assessments lead to underdiagnosis due to "statedependent" effects in which individuals currently in a depressed state remember only previous depressions, and those currently in a hypomanic/manic episode remember only previous hypomanic/manic episodes.¹¹ The data reported here may therefore underestimate the true lifetime prevalence of bipolar I and II disorders.

The nonresponse rate of about one third is another limitation of this study. Individuals currently in the midst of a hypomanic/manic or depressive episode are less likely to respond to a survey. To compensate for this limitation, we have presented an adjusted lifetime prevalence rate that, based upon a telephone survey of non-returners, attempts to correct for this bias.

These methodological limitations most likely serve to underestimate the true lifetime prevalence of bipolar I and II disorders. Therefore, the estimate of 3.7% is probably conservative. This estimate also does not take into account many individuals who do not meet fully the criteria for

bipolar I and II disorders, socalled subsyndromal cases, who very likely score just below the threshold for caseness. We know from the unipolar depression literature^{34–36} that the level of suffering and functional impairment in these people is high. These findings and limitations suggest that the clinical and public health significance of bipolar I and II disorders is very high. A separate study will report on

the impact of bipolar I and II disorders on general health, functional impairment, and work productivity.

Financial disclosure: Dr. Hirschfeld has received grant/research support from Abbott, Bristol-Myers, GlaxoSmithKline, Organon, and Wyeth-Ayerst; has served as a consultant or on the advisory board for Abbott, Bristol-Myers, GlaxoSmithKline, Forest, Lilly, Pfizer, Organon, Janssen, Wyeth-Ayerst, Sepracor, and Novartis; and has served on the speaker's bureau for Abbott, Bristol-Myers, Forest, Lilly, Organon, and Pfizer. Dr. Calabrese has received funding from NIMH, Abbott, Ciba-Geigy, Merck, GlaxoSmithKline, Janssen, Lilly, MacArthur Foundation, NARSAD, Parke-Davis, Robert Wood Johnson, Sandoz, SmithKline Beecham, Stanley Foundation, TAP Holdings, UCB Pharma, and Wyeth-Ayerst, and has consulting agreements from or has served on the advisory boards for Abbott, AstraZeneca, Bristol-Myers Squibb/Otsuka, Lilly, GlaxoSmithKline, Janssen-Cilag, Novartis, Parke-Davis/Warner Lambert, Robert Wood Johnson, Shire, SmithKline, TAP Holdings, Teva, and UCB Pharma. Dr. Weissman has served as a consultant for Glaxo and has received grant support from Lilly. Dr. Reed has served as a consultant for and has received grant/ research support from GlaxoSmithKline. Dr. Frye has served as a consultant and on the speakers/advisory board for and has received grant/ research support from GlaxoSmithKline. Dr. Keck is a consultant to, or member of the scientific advisory boards of, Abbott, AstraZeneca, Bristol-Myers, GlaxoSmithKline, Janssen, Lilly, Novartis, Ortho-McNeil, Pharmacia, Pfizer, Shire, and Wyeth-Ayerst and is a principal co-investigator on research studies sponsored by Abbott, AstraZeneca, GlaxoSmithKline, Elan, Lilly, Merck, Organon, Pfizer, and UCB Pharma. Ms. Lewis has received honoraria from GlaxoSmithKline and Abbott and has served on the speakers or advisory boards for GlaxoSmithKline and Lilly. Dr. McElroy has served as a consultant and on the speakers/advisory board for and has received grant/research support and honoraria from GlaxoSmithKline. Dr. McNulty has served as a consultant for and has received honoraria from GlaxoSmithKline. Dr. Wagner has received grant/research support from Abbott, Bristol-Myers, Lilly, Forest, GlaxoSmithKline, Organon, Pfizer, and Wyeth-Ayerst; has served as a consultant for Abbott, Bristol-Myers, Cyberonics, Lilly, Forest, GlaxoSmithKline, Novartis, Janssen, and Pfizer; has served on the speakers bureau for Abbott, Lilly, GlaxoSmithKline, Forest, Janssen, and Pfizer; and has served on the advisory boards for Abbott, Forest, GlaxoSmithKline, Lilly, Novartis, and Pfizer.

REFERENCES

- Keck PE, McElroy SL, Strakowski SM, et al. Twelve-month outcome of bipolar patients following hospitalization for a manic or mixed episode. Am J Psychiatry 1998;155:646–652
- Dilsaver S, Chen Y-H, Swann AC, et al. Suicidality in patients with pure and depressive mania. Am J Psychiatry 1994;151:1312–1315
- 3. Strakowski SM, McElroy SL, Keck PE, et al. Suicidality in mixed and

- manic bipolar disorder. Am J Psychiatry 1996;153:674-676
- Osby U, Brandt L, Correia N, et al. Excess mortality in bipolar and unipolar disorder in Sweden. Arch Gen Psychiatry 2001;58:844

 –850
- Murray CJ, Lopez AD. Global mortality, disability, and the contribution of risk factors: Global Burden of Disease Study. Lancet 1997;349: 1436–1442
- American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Washington, DC: American Psychiatric Press; 1994
- Weissman MM, Bland RC, Canino GJ, et al. Cross-national epidemiology of major depression and bipolar disorder. JAMA 1996;276:293–299
- Weissman MM, Bruce LM, Leaf PJ, et al. Affective disorders. In: Robins LN, Regier DA, eds. Psychiatric Disorders in America: The Epidemiological Catchment Area Study. New York, NY: Free Press; 1991:53–80
- Kessler RC, McGonagle KA, Zhao S, et al. Lifetime and 12-month prevalence of DSM-III-R psychiatric disorder in the United States: results from the National Comorbidity Survey. Arch Gen Psychiatry 1994;51: 8–19
- Akiskal HS, The bipolar spectrum: new concepts in classification and diagnosis. In: Grinspoon L, ed. Psychiatry Update: The American Psychiatric Association Annual Review, vol 2. Washington, DC: American Psychiatric Press; 1983;271–292
- Akiskal HS, Bourgeois ML, Angst J, et al. Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. J Affect Disord 2000;59:S5–S30
- Hirschfeld RMA. Bipolar spectrum disorder: improving its recognition and diagnosis. J Clin Psychiatry 2001;62(suppl 14):5–9
- Angst J. The emerging epidemiology of hypomania and bipolar II disorder. J Affect Disord 1998;50:143–151
- Boerlin HL, Gitlin MJ, Zoellner LA, et al. Bipolar depression and antidepressant-induced mania: a naturalistic study. J Clin Psychiatry 1998; 59:374–379
- Howland RH. Induction of mania with serotonin reuptake inhibitors. J Clin Psychopharmacol 1996;16:425–427
- Calabrese JR, Rapport DK, Kimmel SE, et al. Controlled trials in bipolar I depression: focus on switch rates and efficacy. Eur Neuropsychopharmacol 1999;9(suppl 4):S109–S112
- Stewart WF, Lipton RB, Celentano DD, et al. Prevelance of migraine headache in the United States: relation to age, income, race and other sociodemographic factors. JAMA 1992;267:64–69
- Lipton RB, Stewart WF, Celentano DD, et al. Undiagnosed migraine headache: a comparison of symptom-based and reported physician diagnosis. Arch Intern Med 1992;152:1273–1278
- Lipton RB, Stewart WF, Diamond S, et al. Prevalence and burden of migraine in the United States: data from the American Migraine Study II. Headache 2001;41:646–657
- Lipton RB, Diamond S, Diamond M, et al. Migraine diagnosis and treatment: results from the American Migraine Study II. Headache 2001;41: 638–645

- Population Estimates Program, Population Division, US Bureau of the Census. Monthly Estimates of the United States Population: April 1, 1980 to July 1, 1999, with Short-Term Projections to November 1, 2000. Washington, DC: US Bureau of the Census: Jan 2, 2001
- Hirschfeld RMA, Williams JBW, Spitzer RL, et al. Development and validation of a screening instrument for bipolar spectrum disorder: The Mood Disorder Questionnaire. Am J Psychiatry 2000;157:1873–1875
- First MB, Spitzer RL, Gibbon M, et al. Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P). New York, NY: Biometric Research, New York State Psychiatric Institute; 2001
- Hirschfeld RMA, Holzer C, Calabrese J, et al. Validity of the Mood Disorder Questionnaire: a general population study. Am J Psychiatry. 2003;160: 178–180
- Lewinsohn PM, Klein, DN, Seeley JR. Bipolar disorders in a community sample of older adolescents: prevalence, phenomenology, comorbidity, and course. J Am Acad Child Adolesc Psychiatry 1995;34:454

 –463
- Kessler RC, Rubinow DR, Holmes C, et al. The epidemiology of DSM-III-R bipolar I disorder in a general population survey. Psychol Med 1997:27:1079–1089
- Lish JD, Dime-Meenan S, Whybrow PC, et al. The National Depressive and Manic-Depressive Association (DMDA) survey of bipolar members. J Affect Disord 1994;31:281–294
- 28. Hirschfeld RMA, Lewis L. Perceptions and impact of bipolar disorder: how far have we really come? results of the National Depressive and Manic-Depressive Association 2000 Survey of Individuals With Bipolar Disorder. J Clin Psychiatry. In press
- Wehr TA, Sack DA, Rosenthall NE, et al. Rapid cycling affective disorder: contributing factors and treatment response. Am J Psychiatry 1988;145: 179–184
- Breslau N, Davis GC, Andreski P. Migraine, psychiatric disorders, and suicide attempts: an epidemiological study of young adults. Psychiatry Res 1991;37:11–23
- Merikangas KR, Angst J, Isler H. Migraine and psychopathology. Arch Gen Psychiatry 1990;47:849–853
- Cummings JL. Organic psychoses: delusional disorders and secondary mania. Psychiatr Clin North Am 1986;9:293–311
- Strakowski SM, Keck PE, McElroy SL, et al. The co-occurrence of mania with medical and other psychiatric disorders. Int J Psychiatr Med 1994;24: 305–328
- 34. Judd LL, Paulus MJ, Schettler PJ, et al. Does incomplete recovery from first lifetime major depressive episode herald a chronic course of illness?

 Am J Psychiatry 2000;157:1501–1504
- 35. Judd LL, Akiskal HS. Delineating the longitudinal structure of depressive illness: beyond clinical subtypes and duration thresholds. Pharmacopsychiatry 2000;33:3–7
- 36. Judd LL, Akiskal HS, Zeller PJ, et al. Psychosocial disability during the long-term course of unipolar major depressive disorder. Arch Gen Psychiatry 2000;57:375–380