

Prevalence and Effects of Mood Disorders on Work Performance in a Nationally Representative Sample of U.S. Workers

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Objective: Research on the workplace costs of mood disorders has focused largely on major depressive episodes. Bipolar disorder has been overlooked both because of the failure to distinguish between major depressive disorder and bipolar disorder and by the failure to evaluate the workplace costs of mania/hypomania.

Method: The National Comorbidity Survey Replication assessed major depressive disorder and bipolar disorder with the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI) and work impairment with the WHO Health and Work Performance Questionnaire. A regression analysis of major depressive disorder and bipolar disorder predicting Health and Work Performance Questionnaire scores among 3,378 workers was used to estimate the workplace costs of mood disorders.

Results: A total of 1.1% of the workers met CIDI criteria for 12-month bipolar

disorder (I or II), and 6.4% meet criteria for 12-month major depressive disorder. Bipolar disorder was associated with 65.5 and major depressive disorder with 27.2 lost workdays per ill worker per year. Subgroup analysis showed that the higher work loss associated with bipolar disorder than with major depressive disorder was due to more severe and persistent depressive episodes in those with bipolar disorder than in those with major depressive disorder rather than to stronger effects of mania/hypomania than depression.

Conclusions: Employer interest in workplace costs of mood disorders should be broadened beyond major depressive disorder to include bipolar disorder. Effectiveness trials are needed to study the return on employer investment of coordinated programs for workplace screening and treatment of bipolar disorder and major depressive disorder.

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Although bipolar disorder has traditionally been thought to have a lifetime prevalence of about 1% of the population (1, 2), a substantial upward revision of this estimate is occurring based on mounting evidence for a broad bipolar spectrum that includes people with a history of hypomania, subthreshold manic symptoms, and medication-induced manic symptoms (3–5). The bipolar spectrum is now thought to characterize as much as 5% of the general population (6). People with bipolar spectrum disorder spend a considerably higher proportion of time with depressive than manic symptoms (7, 8), resulting in frequent confusion between major depressive episodes due to major depressive disorder or to bipolar disorder (9). Failure to make this distinction can have dire clinical implications.

The same distinction between major depressive disorder and bipolar disorder would be useful to make in depression cost-of-illness studies. However, with rare exceptions, these studies failed to distinguish between major depressive episodes associated with major depressive disorder and those associated with bipolar disorder (10–13).

Furthermore, although several recent cost-of-illness studies (14–16) and reviews (17, 18) have focused on the costs of bipolar disorder, none has presented comparative information on the workplace costs of major depressive disorder and bipolar disorder. The current report does this using data from the recently completed National Comorbidity Survey Replication (NCS-R) (19), a nationally representative survey of the prevalence and costs of mental disorders in the U.S. household population.

Method

Sample

The NCS-R is a nationally representative survey of mental disorders among English-speaking household residents ages 18 and older in the continental United States. Interviews were carried out with 9,282 respondents between February 2001 and April 2003. Verbal informed consent was obtained before data collection. Consent was verbal rather than written to maintain consistency with the baseline NCS. The rate of response was 70.9%. Respondents were given a \$50 incentive for participation. In addition, a probability subsample of hard-to-recruit predesignated respon-

This article is featured in this month's AJP **Audio** and is the subject of an editorial by Dr. Goldman on p. 1490.

TABLE 1. Demographic Distributions and Correlates of 12-Month DSM-IV Bipolar Disorder and Major Depressive Disorder Among 3,378 Employed Respondents to Part 2 of the National Comorbidity Survey Replication

Variable	Demographic Distribution		12-Month Prevalence				Analysis				
			Bipolar Disorder		Major Depressive Disorder		Bipolar Disorder				
	%	SE	%	SE	%	SE	Odds Ratio	95% CI	χ^2	df	p
Sex											
Men	53.4	1.3	0.8	0.2	4.0	0.4	1.0	—			
Women	46.6	1.3	1.5	0.3	9.0	0.9	1.4	0.6–3.2			
χ^2									0.8	1	0.37
Age											
18–29	25.3	1.4	1.6	0.3	7.3	1.0	4.3	0.6–34.1			
30–44	36.6	1.3	1.3	0.3	7.3	0.6	3.8	0.6–22.7			
45–59	32.1	1.2	0.7	0.3	5.3	0.7	2.2	0.2–20.0			
60+	6.0	0.5	0.5	0.5	2.1	0.4	1.0	—			
χ^2									6.3	3	0.10
Race-ethnicity											
Non-Hispanic white	73.5	1.6	1.2	0.2	6.6	0.5	1.0	—			
Non-Hispanic black	11.5	1.0	0.8	0.3	4.8	1.0	0.5	0.2–1.2			
Hispanic	11.3	1.1	1.1	0.5	6.1	1.0	0.6	0.2–1.6			
Other	3.7	0.4	1.5	0.9	7.9	2.6	1.3	0.3–4.9			
χ^2									5.3	3	<0.16
Education											
Less than high school	10.4	0.8	1.6	0.6	6.2	1.4	7.0*	1.8–27.9			
Completed high school	31.0	1.5	1.6	0.4	6.1	0.6	5.6*	2.1–15.1			
Some college	30.4	1.0	1.2	0.3	6.5	0.7	3.8*	1.3–11.2			
Completed college	28.2	1.2	0.4	0.2	6.6	0.9	1.0	—			
χ^2									14.0	3	0.003*
Occupation											
Professional	34.2	0.9	0.9	0.3	7.0	0.8	1.0	—			
Technical	3.0	0.5	0.3	0.4	5.0	2.1	0.2	0.0–2.0			
Service and clerical	21.1	0.8	1.8	0.4	9.3	1.0	0.8	0.3–2.0			
Labor	41.7	1.3	1.0	0.3	4.5	0.5	0.6	0.3–1.3			
χ^2									3.4	3	0.33
Average work hours											
20–34	13.0	0.9	1.8	0.5	7.6	1.2	1.3	0.6–2.7			
35–44	55.5	1.5	1.1	0.2	7.0	0.6	1.0	0.5–2.1			
45+	31.5	1.4	0.9	0.3	4.7	0.7	1.0	—			
χ^2									0.7	2	0.71

*p=0.05, two-tailed.

TABLE 2. Relation of 12-Month DSM-IV Bipolar Disorder and Major Depressive Disorder With Annualized Work Loss Days Due to Absenteeism and Presenteeism Among 3,378 Employed Respondents to Part 2 of the National Comorbidity Survey Replication

Disorder	Individual Level				Aggregate Level (total U.S. labor force) ^a			
	Days per Year		U.S. Dollars per Year		Million Days per Year		Million U.S. Dollars per Year	
	Days	SE	Dollars	SE	Days	SE	Dollars	SE
Bipolar disorder								
Absenteeism	27.7*	7.0	4,067*	1,034	40.7*	10.3	5,973*	1,518
Presenteeism ^b	35.3*	7.7	5,184*	1,137	51.8*	11.4	7,613*	1,670
Total ^c	65.5*	10.4	9,619*	1,527	96.2*	15.3	14,128*	2,242
Major depressive disorder								
Absenteeism	8.7*	2.6	1,420*	418	72.2*	21.2	11,742*	3,456
Presenteeism	18.2*	3.6	2,961*	591	150.5*	30.1	24,482*	4,890
Total ^c	27.2*	4.8	4,426*	784	225.0*	39.9	36,602*	6,485

^a These results are based on a projection to the total civilian U.S. labor force based on data from the 2002 Current Population Survey.^b Presenteeism is defined in lost day equivalents.^c Entries do not sum to the parallel entries for absenteeism and presenteeism because the totals were based on a separate regression equation in which the dependent variable was a measure of total lost days of work rather than the simple summation of the results in the earlier rows.

*p=0.05 level, two-tailed.

dents was selected for a brief telephone nonrespondent survey, the results of which were used to weight the main sample for non-response bias. Nonrespondent survey participants were given a \$100 incentive. The Human Subjects Committees of Harvard Medical School and the University of Michigan both approved these recruitment and consent procedures.

The NCS-R interview was administered in two parts. Part 1 included a core diagnostic assessment of all 9,282 respondents. Part 2 included questions about correlates and additional disorders administered to all part 1 respondents who met lifetime criteria for any core disorder plus a roughly 1-in-3 probability subsample of 5,692 other respondents. The Health and Work Performance

Analysis				
Major Depressive Disorder				
Odds Ratio	95% CI	χ^2	df	p
1.0	—			
2.0	1.4–2.8	18.6	1	<0.001*
4.0*	2.5–6.3			
4.1*	2.6–6.6			
2.9*	1.7–4.8	44.9	3	<0.001*
1.0	—			
1.0	—			
0.6	0.4–1.0			
0.8	0.6–1.2			
0.8	0.6–2.1			
1.1	0.6–2.1	5.3	3	<0.16
1.3	0.6–2.7			
1.1	0.8–1.6			
1.1	0.7–1.8			
1.0	—	0.7	3	0.87
1.0	—			
0.8	0.3–2.1			
1.0	0.7–1.5			
0.7	0.4–1.3	2.8	2	0.43
1.3	0.8–2.1			
1.3	1.0–1.8			
1.0	—	3.3	2	<0.19

Questionnaire assessment of work performance was included in part 2. A subsample of 3,378 part 2 respondents was either employed or self-employed 20 hours or more per week in the month before the interview and had valid data on all measures used in the following analyses. This is the sample used here. The records for these respondents were weighted to adjust for differential probability of selection into part 2 of the interview and for differential nonresponse. A more detailed discussion of NCS-R sampling and weighting is presented elsewhere (20).

Mood Disorders

NCS-R diagnoses were based on version 3.0 of the World Health Organization’s Composite International Diagnostic Interview (CIDI) (21), a fully structured lay-administered measure. DSM-IV criteria were used to define major depressive episodes, dysthymic disorder, bipolar I disorder, and bipolar II disorder. Because of the small sample size, bipolar I disorder and bipolar II disorder were combined into a single category of bipolar disorder for the current analysis. All diagnoses excluded patients with plausible organic causes for their illness. Blind clinical reappraisal interviews with the lifetime nonpatient version of the Structured Clinical Interview for DSM-IV (SCID) (22) were administered to a probability subsample of 325 NCS-R respondents to assess concordance with CIDI hierarchy-free diagnoses. CIDI-SCID concordance was excellent for bipolar disorder, with an area under the receiver-operator-characteristic curve of 0.93, an odds ratio of 582.6, and a nonsignificant McNemar test ($\chi^2=0.6$, $df=1$,

$p=0.45$). The McNemar test evaluated whether the CIDI prevalence estimate differed significantly from the SCID prevalence estimate. Concordance between the CIDI and the SCID was also good for major depression, with an area under the curve of 0.75, an odds ratio of 18.4, and a McNemar test ($\chi^2=7.2$, $df=1$, $p=0.006$). The McNemar test was significant because the CIDI prevalence estimate was conservative relative to the SCID estimate. Concordance between the CIDI and the SCID was not assessed for dysthymia because the number of respondents with dysthymia in the clinical reappraisal sample was too small for reliable analysis.

Once the mood disorders were operationalized, the respondents who were classified as having lifetime bipolar disorder were defined as 12-month patients with 12 months of illness if they experienced a major depressive, a manic, or a hypomanic episode at any time in the 12 months before the interview. The respondents classified as having lifetime major depressive disorder were defined as having 12-month cases if they had experienced a major depressive episode at any time in the 12 months before the interview. The vast majority of respondents with a hierarchy-free diagnosis of 12-month dysthymia also met criteria for 12-month major depressive disorder. These “double depressives” (23) were subsequently compared with other patients with major depressive disorder in the ability to predict their work performance. The handful of respondents with 12-month dysthymia who failed to meet criteria for major depressive disorder was excluded from the analysis because of the group’s low statistical power.

The persistence and severity of 12-month major depressive episodes were compared for respondents with bipolar disorder who had 12-month major depressive episodes and for respondents with 12-month major depressive disorder to determine whether more severe or persistent depression could account for observed differences in work performance between the two subsamples. Persistence was assessed by asking respondents with a 12-month major depressive episode to estimate how many days out of 365 in the past year they had experienced a depressive episode. Severity was assessed with the self-report version of the Quick Inventory of Depressive Symptomatology (24), referring to the 1 month in the past year when the respondents reported their depression as most severe.

Work Performance

Work performance was assessed with the WHO Health and Work Performance Questionnaire (25, 26). This measure uses self-reports about absenteeism (missed days of work) and “presenteeism” (low performance while at work transformed to lost workday equivalents) to generate a summary measure of overall lost workdays in the month before the interview. Absenteeism was defined on a 0–100 scale for the percentage of work days the respondent missed in the past 30 days, while presenteeism was defined on a separate 0–100 scale in which 0 meant doing no work at all on days spent at work and 100 meant performing at the level of a top worker. Absenteeism and presenteeism were combined into a measure of total lost work performance by adding absenteeism to the value $[(100 - \text{absenteeism}) \times (100 - \text{presenteeism})]$. Information about salary was used to transform the measures of lost work performance from a time metric to a salary metric for the purposes of estimating human capital loss associated with mood disorders. Salary was incremented by 25% to estimate fringe benefits.

Control Variables

All analyses included control for sex, age (18–29, 30–44, 45–59, and 60 and over), race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, other), education (less than high school, completed high school, some college, completed college), and occupation (professional, technical, service-clerical, laborer), as well as for average expected hours of work per week (20–34, 35–44, 45 or more).

TABLE 3. Persistence and Severity of 12-Month Major Depressive Episodes With 12-Month DSM-IV Bipolar Disorder or Major Depressive Disorder Among Employed Respondents to Part 2 of the National Comorbidity Survey Replication

Variable	Bipolar Disorder							
	Major Depressive Episode Only (N=7)				Major Depressive Episode and Mania/Hypomania (N=37)			
	Mean	SE	Median	Range	Mean	SE	Median	Range
Persistence (number of days in major depressive episodes in the past 365 days)	134.0	53.5	90.0	30.0–183.0	164.0	19.8	150.0	52.0–250.00
Severity (scores on the Quick Inventory of Depressive Symptomatology Self-Report)	14.1	1.5	15.7	11.5–17.5	17.3	0.8	16.5	15.7–19.6

^a All respondents with a 12-month major depressive episode who had either bipolar disorder or major depressive disorder were compared.

Analysis

Subgroup comparison of prevalence estimates was used to study the sociodemographic correlates of mood disorders, while linear regression analysis was used to estimate associations of mood disorders with work performance. Mood disorders were coded as “yes/no” dummy predictor variables in linear regression equations that included sociodemographic variables (age, sex, race/ethnicity, education, occupation) as controls. The dependent variables in these equations were measures of lost work performance in the metrics of day equivalents and salary equivalents that distinguished absenteeism and presenteeism as well as combined absenteeism and presenteeism into a summary measure of overall lost work performance.

These basic equations were elaborated in three ways. The first distinguished among patients with bipolar disorder who reported 12-month episodes of major depressive episodes only, mania or hypomania only, or both. The second controlled for the severity duration of major depressive episodes. The third evaluated interactions between mood disorders and sociodemographic variables.

The key predictors in the regression equations were measures of the prevalence of 12-month disorders, whereas the outcomes were measures of 1-month (not 12-month) decrements in work performance. The coefficients were multiplied by 12 to estimate decrements in work performance over the past 12 months because of 12-month mood disorders. These individual-level estimates were then projected to the total U.S. civilian labor force by adjusting for 12-month disorder prevalence and for the fact that the seasonally adjusted number of workers in the U.S. civilian labor force ages 18 and over at the time of the NCS-R was 130 million.

A question might be raised as to why the time frame of the measures was not made consistent by using either 12-month decrements in work performance as outcomes or 1-month prevalence of mood disorders as predictors. The former was not possible because methodological research has shown that retrospective self-reports about health-related decrements in work performance are inaccurate beyond a 1-month recall period (27). The latter (i.e., using measures of 1-month mood disorders as predictors) would have been possible but would have left unresolved the possibility that remitted mood disorders continue to have residual adverse effects on work performance after episode resolution. The use of 12-month disorders to predict 1-month work performance resolves this problem by generating an averaged estimate of the effects on 1-month work performance of both active episodes and remitted episodes that were active in the past 12 months. The multiplication of this estimate by 12 then produces an unbiased estimate of the effect of mood disorders active in the past 12 months on decrements in work performance in the same time period.

Because the NCS-R data are weighted and clustered, the Taylor series linearization method (28) implemented in the SUDAAN software system (29) was used to obtain design-based estimates

of statistical significance. Significance tests of sets of coefficients in the logistic regression equations were made using Wald χ^2 tests based on design-corrected coefficient variance-covariance matrices. Statistical significance was consistently evaluated as $p=0.05$, two-tailed.

Results

Prevalence and Sociodemographic Correlates

Twelve-month prevalence estimates of DSM-IV bipolar disorder and major depressive disorder (standard errors in parentheses) among employed NCS-R respondents were 1.1% (SE=0.2) and 6.4% (SE=0.5), respectively. The estimated prevalence of bipolar disorder did not differ significantly by the respondents' sex, age, race/ethnicity, occupation, or expected work hours but was inversely related to education (Table 1). The estimated prevalence of major depressive disorder did not differ significantly by respondent race/ethnicity, education, occupation, or expected work hours but was significantly higher among women than men and inversely related to age. Neither bipolar disorder nor major depressive disorder was related to average hours worked per week.

Associations of Mood Disorders With Work Performance

Bipolar disorder and major depressive disorder both significantly predicted overall lost work performance in the regression analysis, with annualized regression slopes equivalent to 65.5 lost workdays per worker with bipolar disorder and 27.2 lost work days per worker with major depressive disorder (Table 2). Disaggregation showed that absenteeism, while significantly elevated for both people with bipolar disorder (27.7 days) and people with major depressive disorder (8.7 days), was less important than presenteeism (35.3 days for those with bipolar disorder and 18.2 days for those with major depressive disorder). Projections of individual-level associations to the total U.S. civilian labor force yielded estimates of 96.2 million lost workdays and \$14.1 billion salary-equivalent lost productivity per year associated with bipolar disorder and 225.0 million workdays and \$36.6 billion salary-equivalent lost productivity per year associated with major depressive disorder.

		Bipolar Disorder			Analysis	
		Major Depressive Disorder (N=342)				
Mean	SE	Median	Range	z^a	p	
98.1	5.1	60.0	28.0–150.00	2.7	0.01	
14.5	0.3	14.7	11.5–17.5	2.9	0.007	

Variation in Associations Based on the Persistence and Severity of Depressive Episodes

Roughly three-fourths of the respondents with 12-month bipolar disorder had depressive episodes in the 12 months before the interview (63.1% who also had manic/hypomanic episodes and 11.1% who had only depressive episodes). Persistence (days in depressive episodes in the 365 days before the interview) was consistently higher in individuals with bipolar disorder (mean=134.0–164.0, median=90–150) than in those with major depressive disorder (mean=98.1, median=60.0; $z=2.7$, $p=0.01$) (Table 3). Severity (scores on the Quick Inventory of Depressive Symptoms) was also consistently higher in individuals with bipolar disorder (mean=14.1–17.3, median=15.7–16.5) than in those with major depressive disorder (mean=14.5, median=14.7; $z=2.9$, $p=0.007$).

The individual-level elevations of absenteeism, presenteeism, and total lost work performance in individuals with bipolar disorder were consistently higher among respondents with 12-month major depressive episodes than only manic/hypomanic episodes (Table 4). Furthermore, bipolar disorder with major depressive episodes was consistently associated with significantly more lost work performance than major depressive disorder. Statistical control for major depressive episode persistence and severity reduces these discrepancies somewhat but does not make them disappear. Bipolar disorder with only manic/hypomanic episodes, in comparison, is associated with levels of lost work performance roughly equal to those with major depressive disorder.

Variation in Associations Based on Sociodemographic Variables

No significant differences in the associations of bipolar disorder and major depressive disorder with work performance were found by sex ($\chi^2=0.1-1.0$, $df=1$, $p=0.31-0.76$) or, in the case of bipolar disorder, by age ($\chi^2=0.5-0.8$, $df=3$, $p=0.66-0.79$), but the major depressive disorder coefficients varied with age ($\chi^2=8.0-29.0$, $df=3$, $p=0.001-<0.02$) because of larger coefficients among workers in the age range of 30 to 44 years than either younger or older workers. (Detailed results are available upon request from the first author.) We also found variation in associations by oc-

cupation among those with bipolar disorder ($\chi^2=36.8-212.9$, $df=3$, $p<0.0001$) but not major depressive disorder ($\chi^2=1.5-5.9$, $df=3$, $p=0.12-0.67$). The work loss associated with bipolar disorder, although consistently significant in each occupational group, was significantly greater among technical and professional workers in the case of absenteeism and among laborers and professional workers in the case of presenteeism. (Detailed results are available upon request from the first author.)

Discussion

Two potential limitations of this study are the possible existence of inaccuracy in the key measures and the possible existence of unmeasured common causes of the disorders and outcomes. With regard to the first of these two, the accuracy of diagnostic assessment was documented in the SCID reappraisal interviews mentioned in the section on measures. However, fully structured instruments, such as the CIDI, are less able to distinguish mixed episodes than are semistructured clinical interviews, leading to the imposition of a more rigid distinction between major depressive episodes and manic/hypomanic episodes in individuals with major depressive disorder than would have been ideal (30). The accuracy of the Health and Work Performance Questionnaire work performance assessment was evaluated in a series of workplace validity studies (25, 26) that documented strong relationships of questionnaire measures with independent payroll records and supervisor evaluations of job performance.

The possibility of unmeasured common causes is much more difficult to evaluate. To the extent that common causes exist, the estimated effects of bipolar disorder and major depressive disorder on lost work performance will be biased. No definitive way exists to evaluate this possibility other than by experimentally changing the prevalence of these disorders, presumably in a treatment effectiveness trial, and evaluating the effects on work performance. The results of such experiments in representative workplace samples have not been reported either for bipolar disorder or major depressive disorder, although such an experiment is currently underway to evaluate the workplace effects of treating major depressive disorder (31). Despite the absence of experimental evidence, simulations of likely ef-

TABLE 4. Individual-Level Associations of 12-Month DSM-IV Bipolar Disorder Disaggregated by Type of 12-Month Episode and Major Depressive Disorder With Annualized Work Loss Days Due to Absenteeism and Presenteeism With and Without Control for Persistence and Severity of Major Depressive Episodes Among 3,378 Employed Respondents to Part 2 of the National Comorbidity Survey Replication

Variable	Bipolar Disorder							
	Mania/ Hypomania Only		Major Depressive Episodes Only		Both		Major Depressive Disorder	
	Days	SE	Days	SE	Days	SE	Days	SE
Without control for persistence and severity of major depressive episodes								
Absenteeism	12.5	8.6	32.2*	13.9	33.1*	11.9	8.7*	2.6
Presenteeism ^a	27.8*	12.4	62.0*	29.9	33.3*	11.4	18.2*	3.6
Total ^b	39.6*	18.0	105.4*	29.7	69.0*	16.6	27.2*	4.8
With control for persistence and severity of major depressive episodes								
Absenteeism	12.6	8.6	25.6*	13.1	25.4	19.6	2.9	5.5
Presenteeism ^a	28.2*	12.4	42.6	30.2	3.4	15.8	-2.0	9.6
Total ^b	40.1*	17.9	79.4*	24.7	32.5	31.3	3.8	15.3

^a Presenteeism is defined in lost day equivalents.

^b Entries do not sum to the parallel entries for absenteeism and presenteeism because the totals were based on a separate regression equation in which the dependent variable was a measure of total lost days of work rather than the simple summation of the results in the earlier rows. * $p=0.05$, two-tailed.

facts have been carried out using parameter estimates gleaned from clinical trials (32, 33). The estimated decrements in work performance associated with major depressive disorder in these simulations are broadly consistent with the NCS-R estimates. In addition, the results of a recently reported experimental effectiveness trial aimed at increasing work performance by improving the quality of major depressive disorder treatment yielded estimates of effects on work performance broadly consistent with the NCS-R estimates (34).

Within the context of these limitations, the results reported here show that bipolar disorder and major depressive disorder are both common disorders in the U.S. civilian labor force associated with substantial lost work performance. Our prevalence estimates of bipolar disorder and major depressive disorder are consistent with those in other national surveys (35, 36). As noted in the introduction though, bipolar spectrum disorders could be defined more broadly than in the current report (3–5). The same is true for subthreshold depression (37, 38). Future research should investigate the effects of these subthreshold disorders on work performance (5, 39).

Our finding that both bipolar disorder and major depressive disorder are associated with substantial losses in work performance is consistent with other estimates of workplace costs (12, 17, 18, 40, 41). The estimated annual population-level workplace cost of major depressive disorder, \$36.6 billion, is similar in magnitude to the \$31.0 billion estimate reported in another recent study (31). In addition, the workplace cost of major depressive disorder plus bipolar disorder, \$50.7 billion, is very similar to the \$51.5 billion estimate reported elsewhere (12), although the distribution of workplace cost components is quite different across studies. Whereas presenteeism is estimated here to account for about two-thirds of the total workplace costs of illness, the earlier findings were skewed in the opposite direction, with more than two-thirds of

workplace costs estimated to arise from absenteeism (12). The current results are likely to be more accurate than the earlier ones because the Health and Work Performance Questionnaire produces a better measure of the on-the-job component of work performance than the measure used in the previous study. Finally, the only previous estimate of the population-level workplace cost of bipolar disorder, \$2.3 billion in 1990 dollars or in the range of \$3 billion to \$4 billion today (11), is much lower than our \$14.1 billion estimate, presumably reflecting the fact that this earlier report, which was based on synthetic estimation rather than primary data collection, assumed a much lower prevalence than we found to be the case in our nationally representative survey.

By considering bipolar disorder and major depressive disorder simultaneously, we documented that bipolar disorder is associated with substantially more lost work performance than major depressive disorder at the individual level, although aggregate impairment is greater for major depressive disorder than for bipolar disorder because of the higher prevalence of the former than the latter disorder. Decomposition showed that the higher individual-level impairment of bipolar disorder than major depressive disorder was due largely to major depressive episodes being more impairing in the context of bipolar disorder than in major depressive disorder rather than to mania/hypomania being more impairing than major depressive episodes. The finding that mania/hypomania in the absence of major depressive episodes is associated with significantly less work impairment than bipolar disorder with major depressive episodes is consistent with the observation in a prospective patient study that functional impairment was associated with variation in depressive symptoms but not manic symptoms (42). More detailed analysis of the NCS-R data showed that the higher individual-level work impairment of major depressive episodes in bipolar disorder than in major depressive disorder is

due partly to the greater persistence and severity of major depressive episodes in bipolar disorder than in major depressive disorder. However, the persistence/severity of major depressive episodes explained only part of the association between bipolar disorder and work impairment. The remaining part of this association could be due to either imprecision in our measures or the effects of unmeasured correlates of bipolar disorder and work impairment.

An important practical problem related to the finding that most workers with bipolar disorder had major depressive episodes is that major depressive episodes due to bipolar disorder are sometimes incorrectly treated as if they were due to major depressive disorder (43, 44). This problem is exacerbated by people with bipolar disorder reporting more distress because of their depressive than their manic symptoms (40). Because antidepressant medications can trigger the onset of mania, it is important to screen for a history of bipolar disorder at the initiation of depression treatment. A short and valid screen for manic/hypomanic symptoms has recently been developed that could be used for this purpose (45). It is important for the same reason to include a screen for bipolar disorder in workplace depression screening programs. The prevalence and impairments of subthreshold cases should also be examined. Effectiveness trials are needed to calculate the return on investment from the employer's perspective of coordinated workplace bipolar disorder-major depressive disorder screening and treatment (34, 41).

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References

1. Kessler RC, Rubiow DR, Holmes C, Abelson JM, Zhao S: The epidemiology of DSM-III-R bipolar I disorder in a general population survey. *Psychol Med* 1997; 27:1079-1089
2. Robins LN, Helzer JE, Weissman MM, Orvaschel H, Gruenberg E, Burke JD Jr, Regier DA: Lifetime prevalence of specific psychiatric disorders in three sites. *Arch Gen Psychiatry* 1984; 41:949-958
3. Angst J, Gamma A, Benazzi F, Ajdacic V, Eich D, Rössler W: Toward a re-definition of subthreshold bipolarity: epidemiology and proposed criteria for bipolar-II, minor bipolar disorders and hypomania. *J Affect Disord* 2003; 73:133-146
4. Benazzi F, Koukopoulos A, Akiskal HS: Toward a validation of a new definition of agitated depression as a bipolar mixed state (mixed depression). *Eur Psychiatry* 2004; 19:85-90
5. Judd LL, Akiskal HS: The prevalence and disability of bipolar spectrum disorders in the US population: re-analysis of the ECA database taking into account subthreshold cases. *J Affect Disord* 2003; 73:123-131
6. Akiskal HS, Bourgeois ML, Angst J, Post R, Moller H, Hirschfeld R: Re-evaluating the prevalence of and diagnostic composition within the broad clinical spectrum of bipolar disorders. *J Affect Disord* 2000; 59(suppl 1):S5-S30
7. Judd LL, Akiskal HS, Schettler PJ, Endicott J, Maser J, Solomon DA, Leon AC, Rice JA, Keller MB: The long-term natural history of the weekly symptomatic status of bipolar I disorder. *Arch Gen Psychiatry* 2002; 59:530-537
8. Calabrese JR, Hirschfeld RM, Frye MA, Reed ML: Impact of depressive symptoms compared with manic symptoms in bipolar disorder: results of a US community-based sample. *J Clin Psychiatry* 2004; 65:1499-1504
9. Hirschfeld RM, Vornik LA: Recognition and diagnosis of bipolar disorder. *J Clin Psychiatry* 2004; 65(suppl 15):5-9
10. Greenberg PE, Stiglin LE, Finkelstein SN, Berndt ER: The economic burden of depression in 1990. *J Clin Psychiatry* 1993; 54:405-418
11. Greenberg PE, Kessler RC, Nells TL, Finkelstein SN, Berndt ER: Depression in the workplace: an economic perspective, in *Perspectives in Psychiatry: Selective Serotonin Re-uptake Inhibitors*, 2nd ed, vol 5. Edited by Feighner JP, Boyer WF. New York, John Wiley & Sons, 1996, pp 327-363
12. Greenberg PE, Kessler RC, Birnbaum HG, Leong SA, Lowe SW, Berglund PA, Corey-Lisle PK: The economic burden of depression in the United States: how did it change between 1990 and 2000? *J Clin Psychiatry* 2003; 64:1465-1475

13. Rice DP, Miller LS: The economic burden of affective disorders. *Adv Health Econ Health Serv Res* 1993; 14:37–53
14. Wyatt RJ, Henter I: An economic evaluation of manic-depressive illness—1991. *Soc Psychiatry Psychiatr Epidemiol* 1995; 30:213–219
15. Begley CE, Annegers JF, Swann AC, Lewis C, Coan S, Schnapp WB, Bryant-Comstock L: The lifetime cost of bipolar disorder in the US: an estimate for new cases in 1998. *Pharmacoeconomics* 2001; 19:483–495
16. Das Gupta R, Guest JF: Annual cost of bipolar disorder to UK society. *Br J Psychiatry* 2002; 180:227–233
17. Dean BB, Gerner D, Gerner RH: A systematic review evaluating health-related quality of life, work impairment, and healthcare costs and utilization in bipolar disorder. *Curr Med Res Opin* 2004; 20:139–154
18. Kleinman L, Lowin A, Flood E, Gandhi G, Edgell E, Revicki D: Costs of bipolar disorder. *Pharmacoeconomics* 2003; 21:601–622
19. Kessler RC, Merikangas KR: The National Comorbidity Survey Replication (NCS-R): background and aims. *Int J Methods Psychiatr Res* 2004; 13:60–68
20. Kessler RC, Abelson J, Demler O, Escobar JI, Gibbon M, Guyer ME, Howes MJ, Jin R, Vega WA, Walters EE, Wang P, Zaslavsky A, Zheng H: Clinical calibration of DSM-IV diagnoses in the world mental health (WMH) version of the World Health Organization (WHO) Composite International Diagnostic Interview (WMH-CIDI). *Int J Methods Psychiatr Res* 2004; 13:122–139
21. Kessler RC, Ustun TB: The World Mental Health (WMH) Survey Initiative version of the World Health Organization (WHO) Composite International Diagnostic Interview (CIDI). *Int J Methods Psychiatr Res* 2004; 13:93–121
22. First MB, Spitzer RL, Gibbon M, Williams JBW: Structured Clinical Interview for DSM-IV Axis I Disorders, Research Version, Non-Patient Edition (SCID-I/NP). New York, New York State Psychiatric Institute, Biometrics Research, 2002
23. Keller MB, Hirschfeld RM, Hanks D: Double depression: a distinctive subtype of unipolar depression. *J Affect Disord* 1997; 45:65–73
24. Rush AJ, Trivedi MH, Ibrahim HM, Carmody TJ, Arnow B, Klein DN, Markowitz JC, Ninan PT, Kornstein S, Manber R, Thase ME, Kocsis JH, Keller MB: The 16-item Quick Inventory of Depressive Symptomatology (QIDS), Clinician Rating (QIDS-C), and Self-Report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. *Biol Psychiatry* 2003; 54:573–583
25. Kessler RC, Barber C, Beck A, Berglund P, Cleary PD, McKenas D, Pronk N, Simon G, Stang P, Ustun TB, Wang P: The World Health Organization Health and Work Performance Questionnaire (HPQ). *J Occup Environ Med* 2003; 45:156–174
26. Kessler RC, Ames M, Hymel PA, Loeppke R, McKenas DK, Richling DE, Stang PE, Ustun TB: Using the World Health Organization Health and Work Performance Questionnaire (HPQ) to evaluate the indirect workplace costs of illness. *J Occup Environ Med* 2004; 46:S23–S37
27. Laurent A, Cannell CF, Marquis KH: Reporting health events in household interviews: effects of an extensive questionnaire and a diary procedure. *Vital Health Stat* 1972; 2:1–80
28. Wolter KM: Introduction to Variance Estimation. New York, Springer-Verlag, 1985
29. Research Triangle Institute: SUDAAN: Professional Software for Survey Data Analysis. Research Triangle Park, NC, Research Triangle Institute, 2002
30. Bauer MS, Simon GE, Ludman E, Unutzer J: “Bipolarity” in bipolar disorder: distribution of manic and depressive symptoms in a treated population. *Br J Psychiatry* 2005; 187:87–88
31. Stewart WF, Ricci JA, Chee E, Hahn SR, Morganstein D: Cost of lost productive work time among US workers with depression. *JAMA* 2003; 289:3135–3144
32. Kessler RC, Barber CB, Birnbaum HG, Frank RG, Greenberg PE, Rose RM, Simon GE, Wang PS: Depression in the workplace: effects on short-term work disability. *Health Aff (Millwood)* 1999; 18:163–171
33. Simon GE, Barber C, Birnbaum HG, Frank RG, Greenberg PE, Rose RM, Wang P, Kessler RC: Depression and work productivity: the comparative costs of treatment versus nontreatment. *J Occup Environ Med* 2001; 43:2–9
34. Rost K, Smith JL, Dickinson M: The effect of improving primary care depression management on employee absenteeism and productivity: a randomized trial. *Med Care* 2004; 42:1202–1210
35. Grant BF, Stinson FS, Dawson DA, Chou SP, Dufour MC, Compton W, Pickering RP, Kaplan K: Prevalence and co-occurrence of substance use disorders and independent mood and anxiety disorders: results from the National Epidemiologic Survey on Alcohol and Related Conditions. *Arch Gen Psychiatry* 2004; 61:807–816
36. Hirschfeld RM, Calabrese JR, Weissman MM, Reed M, Davies MA, Frye MA, Keck PE Jr, Lewis L, McElroy SL, McNulty JP, Wagner KD: Screening for bipolar disorder in the community. *J Clin Psychiatry* 2003; 64:53–59
37. Judd LL, Akiskal HS, Maser JD, Zeller PJ, Endicott J, Coryell W, Paulus MP, Kunovac JL, Leon AC, Mueller TI, Rice JA, Keller MB: A prospective 12-year study of subsyndromal and syndromal depressive symptomatology in unipolar depressive disorders. *Arch Gen Psychiatry* 1998; 55:694–701
38. Pezawas L, Angst J, Gamma A, Ajdacic V, Eich D, Rossler W: Recurrent brief depression—past and future. *Prog Neuropsychopharmacol Biol Psychiatry* 2003; 27:75–83
39. Rapaport MH, Judd LL: Minor depressive disorder and subsyndromal depressive symptoms: functional impairment and response to treatment. *J Affect Disord* 1998; 48:227–232
40. Calabrese JR, Hirschfeld RM, Reed M, Davies MA, Frye MA, Keck PE, Lewis L, McElroy SL, McNulty JP, Wagner KD: Impact of bipolar disorder on a US community sample. *J Clin Psychiatry* 2003; 64:425–432
41. Wang PS, Simon GE, Kessler RC: The economic burden of depression and the cost-effectiveness of treatment. *Int J Methods Psychiatr Res* 2003; 12:22–33
42. Bauer MS, Kirk GF, Gavin C, Williford WO: Determinants of functional outcome and healthcare costs in bipolar disorder: a high-intensity follow-up study. *J Affect Disord* 2001; 65:231–241
43. Judd LL, Akiskal HS: Depressive episodes and symptoms dominate the longitudinal course of bipolar disorder. *Curr Psychiatry Rep* 2003; 5:417–418
44. Hirschfeld RM: Bipolar depression: the real challenge. *Eur Neuropsychopharmacol* 2004; 14(suppl 2):S83–S88
45. Hirschfeld RM, Holzer C, Calabrese JR, Weissman M, Reed M, Davies M, Frye MA, Keck P, McElroy S, Lewis L, Tierce J, Wagner KD, Hazard E: Validity of the mood disorder questionnaire: a general population study. *Am J Psychiatry* 2003; 160:178–180