# Incurring Greater Health Care Costs: Risk Stratification of Employees With Bipolar Disorder

Richard A. Brook, M.S., M.B.A.; Krithika Rajagopalan, Ph.D.; Nathan L. Kleinman, Ph.D.; James E. Smeeding, R.Ph., M.B.A.; Truman J. Brizee, B.A.; and Harold H. Gardner, M.D.

***Purpose:*** To compare the costs of employees with bipolar disorder with other employee cohorts and to assess cost differences among employees with bipolar disorder of varying severity.

***Methods:*** Retrospective data analysis comparing employees with bipolar disorder (cohort 1) with employees without bipolar disorder (cohort 2), employees with other mental disorders (cohort 3), and employees with no mental disorders (cohort 4). Sick leave, short-term disability, long-term disability, and workers' compensation data were used to compare annual lost time and work-absence costs from January 1, 2001, through December 31, 2002. For bipolar disorder severity and risk stratification, quintiles were identified based on total medical and prescription drug costs and analyzed for many health benefits cost categories.

***Results:*** Cohort 1 was the most costly in nearly every health benefits cost category. All comparisons between cohort 1 and cohorts 2, 3, and 4 yielded significant ($p \leq .05$) differences except for sick leave costs in cohorts 1 and 3. The aggregate health benefits costs for the highest-cost cohort 1 quintile were $70,616, or 21 times greater than the health benefits costs for the lowest-cost quintile ($3385). Medical comorbidity costs accounted for most of this difference ($51,495; $p \leq .05$).

***Conclusion:*** Employees with bipolar disorder are the most costly in nearly every health benefits category, with a small minority (2.4%) accounting for 20% of the costs. Employers need to identify and target high-risk ("high cost") employees with bipolar disorder and coexisting conditions that use resources more frequently for appropriate interventions that may include early screening and diagnosis, appropriate treatment, and/or behavioral strategies for improved adherence. These strategies have the potential to improve quality of patient care and reduce costs.

*(Prim Care Companion J Clin Psychiatry 2006;8:17–24)*

*Received July 1, 2005; accepted Sept. 19, 2005. From the JeSTARx Group, Newfoundland, N.J. (Mr. Brook) and Dallas, Tex. (Mr. Smeeding), Health Economics/Outcomes Research, AstraZeneca Pharmaceuticals, Wilmington, Del. (Dr. Rajagopalan), and Human Capital Management Services, Inc., Cheyenne, Wyo. (Drs. Kleinman and Gardner and Mr. Brizee).*

*Funding, including consultation fees and reimbursement for presenting study findings at meetings, for the research described in this article was provided by AstraZeneca Pharmaceuticals.*

*Mr. Brook is a consultant for, has received grant/research support from, and has received honoraria from AstraZeneca. Dr. Rajagopalan is an employee of AstraZeneca. Drs. Kleinman and Gardner and Messrs. Smeeding and Brizee have received grant/research support from AstraZeneca.*

*Corresponding author and reprints: Richard A. Brook, M.S., M.B.A.,The JeSTARx Group, 18 Hirth Dr., Newfoundland, NJ 07435 (e-mail: rbrook@JeSTARx.com).*

Bipolar disorder is a chronic illness characterized by broad mood swings that include mania, hypomania, depression, and mixed episodes.[1–3] Various subtypes exist, including bipolar I disorder, in which full-fledged manic and major depressive episodes alternate, and bipolar II disorder, which is typified by alternating depression and hypomania. Data from the U.S. National Institute of Mental Health (NIMH) Epidemiologic Catchment Area Program (ECA) and the National Comorbidity Survey (NCS) suggest a 1-year prevalence of clinically significant bipolar disorder of approximately 1%.[4] A more inclusive definition of the illness (taking into account subthreshold cases) supports a lifetime prevalence of up to 6.5%.[5]

There is mounting evidence that bipolar disorder is undertreated. The ECA study reported that only about 60% of people with bipolar disorder actually receive treatment in a given year,[6] while data from the NIMH suggest only one third of such people seek treatment.[7] Moreover, persons with bipolar disorder report problems with employment.[8] They are less likely to be employed over time, and thus some may not be represented in these data.[9]

Nevertheless, the frequent lapses and chronic course of the disease result in significant direct and indirect costs, including increased use of inpatient and outpatient medical services and pharmacotherapy, as well as lost productivity[10] that can be attributed to psychopathology and premature mortality.[11] Thus, bipolar disorder is one of the

most costly diseases, with emerging evidence suggesting that bipolar disorder costs per patient can be greater than they are for other mental illnesses.[11–18]

Unfortunately, patients, caregivers, and primary care clinicians too often fail to correctly recognize, diagnose, and ultimately manage bipolar disorder.[19] Misdiagnosis is especially common if a major depressive episode is the first presentation of the condition.[20] In addition, the frequent presence of comorbid disorders, such as obsessive-compulsive disorder, anxiety disorder, certain personality disorders, and substance abuse, complicates making an accurate diagnosis.[3,20–26]

There is a clear need for early and accurate screening of patients with bipolar disorder in order to make timely and appropriate interventions that can prevent adverse impacts on health and human capital. Moreover, it is possible that patients can present with differing disease and comorbidity characteristics across the spectrum of disease severity. In this context, it is an advantage to both employers and employees to be able to identify high-risk ("high cost") bipolar disorder patients (as defined by coexisting conditions that use resources more frequently compared with low-moderate risk ["low-moderate cost"] patients) and to target these individuals for interventions to ensure appropriate treatment and management of the disease. The current analysis was performed to compare the costs of employees with bipolar disorder with the costs of other employee cohorts and to assess cost differences among employees with bipolar disorder of varying severity over several health benefits cost categories.

## METHOD

### Data Source

This study used data from the Human Capital Management Services (HCMS) Research Reference Database (Human Capital Management Services, Inc., Cheyenne, Wyo.). The HCMS database comprises multiple, geographically diverse, United States–based employers and has a population of more than 230,000 employees with medical and prescription drug coverage. The data cover demographic, payroll, health care, disability, absence, and workers' compensation information from retail, service, manufacturing, and financial industries. This retrospective analysis compared health benefits utilization and costs to employers during a 2-year study period from January 1, 2001, through December 31, 2002. Sources of additional costs were analyzed through cost severity subgrouping. Confidentiality and anonymity of person-level data were maintained in accordance with Health Insurance Portability and Accountability Act (HIPAA)[27] guidelines.

### Sampling and Cohort Selection

Health benefits cost and utilization comparisons were performed among several population cohorts, specifically employees with bipolar disorder (cohort 1) and employees without bipolar disorder (cohort 2). Employees without bipolar disorder were further differentiated into employees with other mental disorders (cohort 3), and employees with no mental disorders (cohort 4). From the full database, cohorts 1–4 were selected based on the presence or absence of International Classification of Diseases, Ninth Revision (ICD-9) criteria[28] for bipolar disorder diagnosis (primary, secondary, or tertiary ICD-9 code of 296.0x, 296.1x, 296.4x, 296.5x, 296.6x, 296.7x, or 296.8x) and other mental disorder diagnosis (primary, secondary, or tertiary ICD-9 code from the Agency for Healthcare Research and Quality "Mental Disorders" category).

For cohort 1, the index date was the date of the first bipolar disorder diagnosis in 2001. For cohort 3, the index date was the date of the first mental disorder diagnosis (non–bipolar disorder) in 2001. For all other cohorts, the index date was calculated as the average index date of subjects in cohort 1. Cohort 1 was mutually exclusive of cohorts 2, 3, and 4. Additionally, cohorts 3 and 4 were mutually exclusive subsets of cohort 2.

A risk-stratification quintile analysis was conducted using costs of health benefits utilization as a severity risk proxy to determine differences within cohort 1, the bipolar disorder cohort. The quintiles were determined by (1) calculating the sum of the medical and prescription drug costs per subject in cohort 1 (N = 761), (2) ranking the subjects in order of cost, and (3) dividing the subjects into groups of 20% increments. The 1st quintile was that with the lowest cost, and the 5th quintile was that with the highest cost. The quintile analysis also provided insight into costs of various comorbid conditions affecting cohort 1 employees.

### Outcome Measures

Measures of outcome among population cohorts included employer costs for medical care, pharmaceuticals, sick leave, short-term disability and long-term disability, workers' compensation, and total costs. Costs were measured during the year following each employee's index date. Using health benefits (medical and pharmaceutical) claims utilization as a marker of bipolar disorder severity, cohort 1 (employees with bipolar disorder) was analyzed by quintiles for the impact of disease severity on various costs, specifically bipolar disorder medical costs, comorbid conditions medical costs, bipolar disorder–related drug costs, other drug costs, sick leave costs, short-term disability and long-term disability costs, and workers' compensation medical and indemnity costs. By the definition of the quintile subgroups, it is expected that medical and drug costs will vary greatly across the different subgroups. However, differences in other cost categories will be of particular interest.

### Statistical Analysis

Regression techniques were used to estimate and compare the differences in costs among the population cohorts. Separate regression models were performed for each of the following dependent variables: medical costs, prescription drug costs, sick leave costs, short-term disability costs, long-term disability costs, workers' compensation costs, and sick leave days. In each case, the regression models controlled for the impact of confounding factors, including age, tenure (the length of time the employee has been with his or her current employer), gender, marital status, race, exempt/nonexempt status, full-time/part-time status, salary, and region as defined by the first digit of the employee's zip code. Exempt employees are generally not paid on an hourly basis and are usually ineligible to receive overtime pay under the Fair Labor Standards Act.[29]

A 2-stage regression model technique was used for all dependent cost variables.[30] For example, when modeling medical costs, logistic regression was used first to predict the likelihood of having any medical costs during the year. Linear regression on the natural log of medical costs was generally used as a second level of analysis rather than generalized linear models to estimate the average annual medical costs for those employees with positive medical costs.[31] These results were then combined to provide estimates of annual medical costs for all employees in the population. The transformation of the multiplicative results from the log-linear models ("patients with bipolar disorder are X times more costly than patients without bipolar disorder") into additive results ("patients with bipolar disorder cost Y dollars more than patients without bipolar disorder") required accommodations for heteroscedasticity (nonconstant variances).[32]

## RESULTS

Table 1 shows descriptive statistics for cohorts 1–4. All variables shown except differences in salary were significantly different (all p values ≤ .05) between cohort 1 (employees with bipolar disorder) and cohort 2 (employees without bipolar disorder). Cohort 1 employees were slightly but significantly older (0.75 years), had longer tenure, were more often female, were less often married, and were more often white than cohort 2 employees. Also, cohort 1 employees had exempt status less often, were more often a full-time employee, and were more concentrated in the Northeast and Mid-Atlantic regions of the United States than cohort 2. There were significant differences between cohort 1 (employees with bipolar disorder) and cohort 3 (employees with other mental disorders) in age, tenure, the percentage of employees who were female, marital status, race, and exempt status.

**Table 1. Descriptive Statistics of Cohorts 1–4**

| Cohort | 1 Bipolar Disorder | 2 Non–Bipolar Disorder | 3 Other Mental Disorders | 4 No Mental Disorders |
|---|---|---|---|---|
| N | 761 | 229,145 | 26,776 | 185,802 |
| Age (at index date), mean, y | 41.16 | 40.41* | 42.07* | 40.11* |
| Tenure (at index date), mean, y | 10.63 | 9.76* | 9.88* | 9.79* |
| Gender, % | | | | |
| Female | 54.40 | 44.48* | 64.05* | 40.14* |
| Married, % | 46.15 | 55.98* | 51.13* | 56.98* |
| Race, % | | | | |
| White | 83.53 | 65.08* | 74.03* | 63.16* |
| Black | 9.12 | 21.26* | 12.24 | 23.20* |
| Hispanic | 4.12 | 7.96* | 7.41 | 7.97* |
| Employment status, % | | | | |
| Exempt | 21.16 | 27.33* | 25.03* | 27.83* |
| Full-time | 89.09 | 85.70* | 91.03 | 84.46* |
| Annual salary | $47,351 | $48,468 | $47,558 | $48,696 |
| Zip code starting with, % | | | | |
| 0 | 18.8 | 12.5* | 10.8* | 12.9* |
| 1 | 22.3 | 15.4* | 12.4* | 16.0* |
| 2 | 18.8 | 14.1* | 15.0* | 13.9* |
| 3 | 14.1 | 22.5* | 26.1* | 22.1* |
| 4 | 3.3 | 5.3* | 3.4 | 5.7* |
| 5 | 0.1 | 0.7 | 0.4 | 0.7 |
| 6 | 2.8 | 3.0 | 2.0 | 3.2 |
| 7 | 5.8 | 9.6* | 14.2* | 8.4* |
| 8 | 4.6 | 4.3 | 5.0 | 4.1 |
| 9 | 9.5 | 12.4* | 10.6 | 12.8* |

*Significant (p ≤ .05) pairwise comparison (versus cohort 1).

### Health Benefits Utilization and Cost

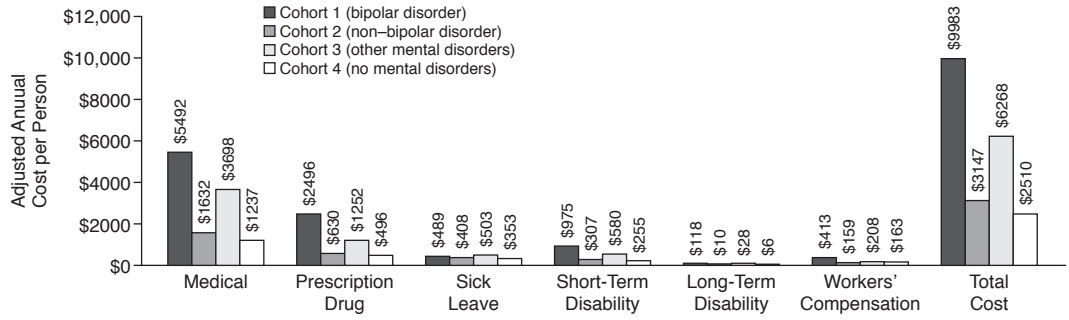
Figure 1, displaying the results of the 2-stage regression models, shows that the employees with bipolar disorder in cohort 1 were the most costly in nearly every health benefits cost category. In total, the mean annual costs of cohort 1 exceeded mean annual costs of cohort 2 by $6836 per person and cohort 3 by $3715 per person. All but one of the comparisons between cohort 1 and cohorts 2, 3, and 4 (cohort 4 consists of employees with no mental disorders) were statistically significant (p ≤ .05). The nonsignificant exception is the comparison between sick leave costs of cohort 1 ($489) and cohort 3 ($503).

### Risk Stratification Quintile Analysis

The analysis indicates that the 5th cost quintile ("highest cost" employees with bipolar disorder), which had 20% of the total medical and prescription drug costs, comprised 2.4% of the bipolar disorder employee population. Conversely, the 1st cost quintile ("lowest cost" employees with bipolar disorder) had the lowest health benefits costs and comprised 61.6% of the population with bipolar disorder.

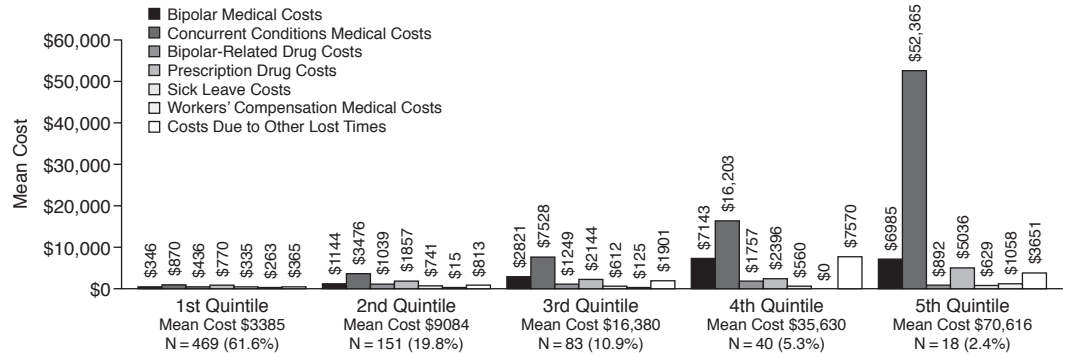
Figure 2 shows that employees in successively higher quintiles had greater aggregate health benefits costs than the preceding quintile, and the difference in aggregate costs was nearly 21 times greater between the 1st quintile

**Figure 1. Comparison of Annual Cost Per Person[a,b]**




[a]Costs were measured during the year following each person's index date. For employees with bipolar disorder, the index date is the date of the first bipolar disorder diagnosis in 2001.
[b]Costs were adjusted using regression modeling and controlling for age, tenure, gender, marital status, race, exempt status, full-time/part-time status, salary, and location.

**Figure 2. Annual Mean Benefit Cost for Employees With Bipolar Disorder by Medical and Drug Cost Quintile[a,b]**




[a]Employees with bipolar disorder were ranked according to their total medical and drug costs during the year following their index date.
[b]Costs were measured during the year following each person's index date. For employees with bipolar disorder, the index date is the date of the first bipolar disorder diagnosis in 2001.

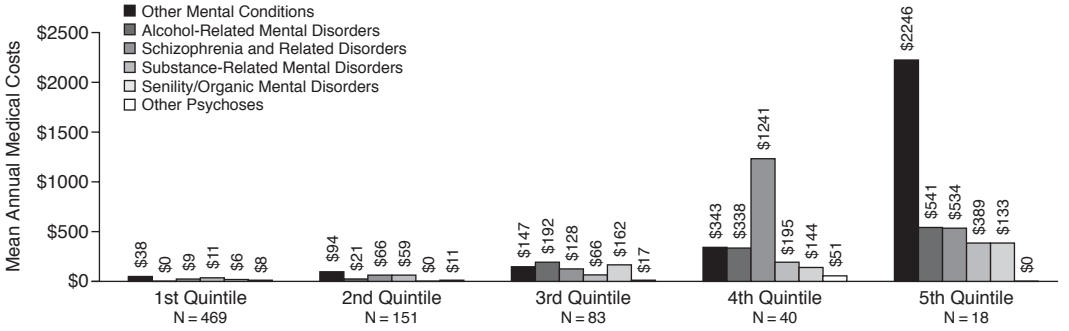
($3385) and the 5th quintile ($70,616). Generally, there was a trend toward greater mean comorbid conditions costs and other drug costs in progressively higher quintiles. The most prominent trend was in mean comorbid conditions medical costs, which were 60 times greater in the 5th quintile ($52,365) than in the 1st quintile ($870). Across quintiles, none of the 95% confidence intervals for comorbid conditions medical costs overlapped, indicating that all differences among the 5 quintiles were significant ($p \leq .05$). The mean cost difference between the highest and lowest quintiles was $51,495 ($p \leq .05$).

There was a consistent increase in the mean other (non–bipolar-specific) drug costs in higher quintiles, and the difference between the 1st and 5th quintiles in other drug costs ($4266) was significant ($p \leq .05$). Mean bipolar disorder–specific medical costs rose steadily and significantly ($p \leq .05$) from the 1st quintile through the 4th quintile but declined in the 5th quintile. Nevertheless, a significant difference in bipolar disorder medical costs ($6639) was observed between the 1st and 5th quintiles ($p \leq .05$).

Nonsignificant cost differences between the highest and lowest quintiles were observed for mean bipolar disorder–related drug costs ($456), sick leave costs ($294), short-term disability and long-term disability costs ($2,877 and –$5, respectively), and workers' compensation medical costs and workers' compensation indemnity costs ($795 and $415, respectively). There was a higher trend in mean bipolar disorder–related drug and short-term disability costs through the 4th quintile, but these costs both declined in the 5th quintile.

Mean sick leave costs showed no consistent trend, and, in fact, sick leave costs were lower in the 5th quintile than the 2nd quintile. Mean workers' compensation medical and workers' compensation indemnity costs also showed no consistent trend up to the 4th quintile but rose significantly ($p \leq .05$) from the 4th quintile to the 5th quintile.

**Figure 3. Annual Mean Comorbid Mental-Health Condition Costs of Employees With Bipolar Disorder by Quintile[a,b]**




[a]Employees with bipolar disorder were ranked according to their total medical and drug costs during the year following their index date.
[b]For employees with bipolar disorder, the index date is the date of the first bipolar disorder diagnosis in 2001.

Employees in the higher quintiles also had much greater mean lost time from work. Employees in the 1st quintile averaged 10.4 health-related lost days from work per year, while employees in the 4th quintiles and 5th quintiles averaged more than 72 health-related lost days per year.

There was a general and consistent trend toward greater mean comorbid conditions costs in higher quintiles, especially mental disorder– and substance abuse–related costs (Figure 3). Compared with the 1st quintile, the mean cost in the 5th quintile was 20 times greater for affective disorders ($427 vs. $8564, respectively), 59 times greater for schizophrenia and related disorders ($9 vs. $534, respectively), and 35 times greater for substance-related mental disorders ($11 vs. $389, respectively). Affective disorders represented the highest health care cost category. Of the remaining categories, mental disorder– and substance abuse–related costs comprised 5 of the top 30 mean costs (ranked by costs in the 5th quintile) for all comorbid conditions, with mean affective disorder costs the most expensive comorbid condition (including physical conditions) in all 5 quintiles.

## DISCUSSION

The study's results demonstrate that health benefits costs for employees with bipolar disorder ($9983) are more than 3 times greater, on average, than for employees without bipolar disorder ($3147) and 59% greater than for employees with other mental disorders ($6268). Similarly, medical and pharmaceutical costs for employees with bipolar disorder are 3 to 4 times greater than those for employees without bipolar disorder.

These results are consistent with other published findings. For example, Bryant-Comstock et al.[14] reported that patients with bipolar I disorder utilize nearly 3 to 4 times the health care resources and incur costs per patient that are more than 4 times greater than age- and sex-matched patients without bipolar disorder during a 1-year period. A separate retrospective study[16] detected a significantly greater ($p < .05$) mean for monthly medical costs ($1179) in patients with unrecognized bipolar disorder in the 12 months following initiation of antidepressant treatment compared with patients with recognized bipolar disorder ($801) and patients without bipolar disorder ($585). On an annual basis, those costs represented $14,148; $9612; and $7020 for the 3 cohorts, respectively.

Thus, there is coherent evidence from the current analysis and published findings that persons with bipolar disorder have significantly greater health benefits costs than those persons without bipolar disorder. Additionally, the approach used in this analysis also examined the source of additional costs through cost severity subgrouping. This cost-risk stratification provided greater insight into the varying levels of cost severity among this population, as evidenced by the employees' health benefits utilization, and also provided insight into the contribution of specific costs.

Using health benefits claims utilization as a proxy for bipolar disorder severity, there was notable severity variation among employees diagnosed with bipolar disorder. The work attendance and health benefits costs of the "highest cost" employees with bipolar disorder (5th quintile) were dramatically different from those of employees in the 1st quintile ("lowest cost"). In fact, the employees with the "highest severity" bipolar disorder, representing 1/40 (2.4%) of the total numbers of employees, incurred 1/5 (20%) of the total health benefits costs. In contrast, almost two thirds of employees with bipolar disorder made up the lowest quintile of health benefits costs (1st quintile). Further analysis of specific cost elements showed that medical costs due to comorbid conditions were the largest expense incurred by the "highest cost" employees with bipolar disorder, and these costs comprised the largest single cost component for all quintiles.

Generally, there was a trend toward significantly greater medical costs due to comorbid conditions in pro-

gressively higher quintiles. These costs were 60 times greater among the "highest cost" employees ($52,365) than among the "lowest cost" employees ($870). Interestingly, the analysis also consistently demonstrated greater (and in some cases significantly greater) bipolar-specific medical costs and bipolar-specific drug costs in progressively higher quintiles, except for the "highest cost" employees quintile, in which these costs actually declined. This intriguing finding may reflect the fact that employees with bipolar disorder in the highest quintile also have a number of expensive comorbid physical conditions that, rather than their mental illness, could be the primary focus of treatment.

Sick leave and workers' compensation costs, on the other hand, showed no consistent trend from the 1st through 4th quintiles. However, workers' compensation costs jumped dramatically in the 5th quintile, while sick leave costs declined. In fact, sick leave costs were less for the "highest cost" employees than those in the 2nd quintile ("low cost" employees). This finding, while superficially counterintuitive, may reflect the fact that sick leave is often capped at a certain number of days allowed per year, depending on the sick leave policy of each employer. Thus, at least some bipolar disorder employees with subsyndromal symptoms or less severe mood episodes (not requiring or qualifying for disability leave) are in the workplace rather than on sick leave. Furthermore, higher quintile employees miss work much more often because of short-term disability leaves than lower quintile employees. For example (from data not shown), 4th quintile employees averaged 57.8 days missed from work annually while on short-term disability, compared with 1st quintile employees, who missed 4.7 days, and 2nd quintile employees, who averaged 9.6 days missed per year ($p < .05$). Overall, employees with bipolar disorder had significantly higher absence costs ($1219), 11.5 additional lost days, and 20% lower adjusted annual productivity output ($p < .05$) per year than those without bipolar disorder.[10]

The principal contribution of comorbid conditions medical costs to the overall health benefits costs of the "highest cost" employees should also be underscored. In this context, results from this analysis indicated that mental disorder– and substance abuse–related costs were major drivers of comorbidity medical costs.

From this analysis, it is clear that not all employees with bipolar disorder have the same cost patterns. A small minority of employees with bipolar disorder (2.4%) has quite severe costs, in contrast to most employees with bipolar disorder who have more modest costs. Employees in the 4th and 5th quintiles also average more than 7 lost weeks per year for health-related reasons, whereas employees in the 1st quintile average about 1½ weeks. Other differences exist as well. For example, "moderate cost" employees with bipolar disorder (3rd quintile) have exempt status at work significantly less often ($p \leq .05$) than employees with bipolar disorder in the 1st quintile (data not shown). This disparity may indicate that employees whose bipolar disorder is more severe (or less well treated) may have more difficulty with white collar jobs than with blue collar jobs, or it may reflect inequities in health care access based on socioeconomic status.

The finding that comorbid condition medical costs are disproportionately greater in employees with more severe disease suggests that mental disorder– and substance abuse–related costs are major contributors to these costs. This situation is not entirely unexpected, given the profile of patients with bipolar disorder. Indeed, high-risk bipolar disorder patients often present with multiple coexisting mental and/or physical conditions, including high rates of comorbid substance abuse and personality disorder.[23–26] The present analysis highlights the differences in profile between the highest and lowest risk bipolar disorder patients and reinforces the need to target high-risk patients with comorbid conditions who disproportionably consume health care resources and require early interventions. At the same time, the findings presented here emphasize the need for employers to identify low- and moderate-risk bipolar disorder employees to ensure appropriate, timely, and differentially targeted types of intervention based on risk levels. This intervention avoids the rapid escalation in cost that accompanies worsening disease.

Unfortunately, the diversity and range of presentation and presence of comorbid personality disorders complicate the diagnosis of bipolar disorder.[21–23] As noted in the introduction, one of the main difficulties is making a correct diagnosis of bipolar disorder in a patient who presents initially with a major depressive episode.[20] This difficulty has been corroborated in studies such as that conducted by the National Depressive and Manic-Depressive Association support group.[33] An analysis of the first 600 completed self-administered surveys sent out by the association to participants diagnosed with bipolar disorder revealed that 69% of those who replied reported that they were initially misdiagnosed, with the most frequent misdiagnosis being unipolar depression. It has been noted by several authors that an accurate diagnosis of bipolar disorder may not be made until several years after the first manifestation, with a common time lag of 10 years until correct diagnosis is made.[20,33,34]

Other common comorbidities include obsessive-compulsive disorder, anxiety disorder, schizophrenia, personality disorder, and substance abuse.[20,34] In a representative sample of bipolar patients (N = 42) treated in community psychiatry programs, 45% had at least 1 comorbid personality disorder, but only 7% had a personality disorder diagnosis recorded in their case notes.[23] The clinical presentation of bipolar disorder can also be deceptive in patients with substance abuse.[26] Although complicating

identification, presentation with multiple comorbid conditions, especially mental and substance abuse–related disorders, should prompt a screen for bipolar disorder by clinicians (including the patient's primary care provider).

Effective screening programs, along with early identification and intervention, are increasingly important in today's economic climate that places enormous emphasis on controlling health care costs and optimizing employee productivity. Accurate and timely recognition of bipolar disorder has the potential to reduce medical costs and indirect costs due to work loss.[16] One such screening instrument is the Mood Disorder Questionnaire (MDQ).[8,34] Thirteen yes/no questions are used to screen for evidence of a lifetime history of mania or hypomania symptoms.[35] The screening instrument takes approximately 5 to 10 minutes to administer and can be self-administered or given by a health care professional.[35] This instrument has good sensitivity (0.73) and specificity (0.90)[35] and allows the primary care physician to identify patients who require further psychiatric evaluation. Successful screening that can be performed by the primary care physician therefore not only improves patient care by enhancing accurate diagnosis of bipolar disorder but improves the chances of successful treatment of depressive episodes and prevents triggering of manic episodes.[35] Not only is patient care improved, but accurate screening allows for more cost-efficient patient management.

Although the current analysis used a unique and rich dataset, retrospective analyses are subject to inherent limitations. Analyses based on insurance claims data are limited by the possibilities of inaccurate diagnoses, coding inaccuracies (which may be relevant in bipolar disorder), missing data, some potential differences among employers' benefit plans for which the study cannot account, and the fact that the study sample is restricted to only those diagnosed with bipolar disorder ICD-9 codes.[4] Potential selection biases also exist, with the possibility that bipolar disorder may be underreported in claims data due to social stigma, practice differences between primary care physicians and specialists, and other factors. It is also likely that patients with the most severe bipolar disorder are not employed and thus are not included in the current analysis.

Traditional management of bipolar disorder has included the use of conventional antipsychotic medications, such as lithium and divalproex for acute mania and lithium and lamotrigine for maintenance therapy. More recently, atypical antipsychotics have been approved for treatment of mania associated with bipolar disorder.[33] One major advantage of the later drugs is that they produce fewer side effects than the typical antipsychotics.[36,37]

While further analysis is needed to determine why some employees with bipolar disorder have high costs and others have more reasonable medical and drug costs, there is increasing evidence for the efficacy of atypical antipsychotic drugs as maintenance and prophylactic therapy.[38] Unfortunately, without continued coverage of maintenance therapies and health insurance, employees with bipolar disorder may experience relapses that complicate care.[3] To better address the needs of such patients, employers and insurers may need to develop programs that identify the disease earlier and identify potential high-cost employees.

Today, employers are increasingly cognizant of the roles of primary care providers in disease management and of employees as effective consumers of health care. Optimizing these roles for both patient and provider could reduce the costs associated with this illness.

In summary, employees with bipolar disorder are the most costly in nearly every health benefits cost category. However, these costs are unevenly distributed. A small minority of employees with bipolar disorder accounts for a disproportionate share of total health benefits costs. Although "highest cost" employees with bipolar disorder make up a small minority of the employed bipolar population, their high attendant comorbidity costs make them prime targets for early diagnosis and intervention. Persons with bipolar disorder, if identified early, can be more effectively managed to prevent adverse impact of the disease on health and human capital and reduce overall costs (not only mental health costs). Additionally, employees with coexisting cardiovascular conditions, cancers, and fractures are likely to need appropriate treatment aimed at improving these conditions. Finally, early bipolar disorder screening of employees (with high costs in areas that are likely to be concurrent conditions of bipolar disorder), appropriate treatment, and aggressive intervention might realize substantial economic savings, especially if targeted at the small minority of "high risk" bipolar patients associated with the highest medical and prescription drug costs.

*Drug names:* divalproex sodium (Depakote), lamotrigine (Lamictal), lithium (Eskalith, Lithobid, and others).

## REFERENCES


1. Goodwin GM. Prophylaxis of bipolar disorder: how and who should we treat in the long term? Eur Neuropsychopharmacol 1999;9:S125–S129
2. Griswold KS, Pessar LF. Management of bipolar disorder. Am Fam Physician 2000;62:1343–1353, 1357–1358
3. Sachs GS. A 25-year-old woman with bipolar disorder. JAMA 2001;285: 454–462
4. Narrow WE, Rae DS, Robins LN, et al. Revised prevalence estimates of mental disorders in the United States: using a clinical significance criterion to reconcile 2 surveys' estimates. Arch Gen Psychiatry 2002;59: 115–123
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. Regier DA, Narrow WE, Rae DS, et al. The de facto US mental and addictive disorders service system: epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. Arch Gen Psychiatry 1993;50:85–94
7. Regier DA, Hirschfeld RM, Goodwin FK, et al. The NIMH Depression

Awareness, Recognition, and Treatment Program: structure, aims, and scientific basis. Am J Psychiatry 1988;145:1351–1357
8. Calabrese JR, Hirschfeld RM, Reed M, et al. Impact of bipolar disorder on a US community sample. J Clin Psychiatry 2003;64:425–432
9. Coryell W, Scheftner W, Keller M, et al. The enduring psychosocial consequences of mania and depression. Am J Psychiatry 1993;150: 720–727
10 Kleinman NL, Brook RA, Rajagopalan K, et al. Lost time, absence costs, and reduced productivity output for employees with bipolar disorder. J Occup Environ Med 2005;47:1117–1124
11. Kleinman L, Lowin A, Flood E, et al. Costs of bipolar disorder. Pharmacoeconomics 2003;21:601–622
12. Begley CE, Annegers JF, Swann AC, et al. The lifetime cost of bipolar disorder in the US: an estimate for new cases in 1998. Pharmacoeconomics 2001;19:483–495
13. Peele PB, Xu Y, Kupfer DJ. Insurance expenditures on bipolar disorder: clinical and parity implications. Am J Psychiatry 2003;160:1286–1290
14. Bryant-Comstock L, Stender M, Devercelli G. Health care utilization and costs among privately insured patients with bipolar I disorder. Bipolar Disord 2002;4:398–405
15. Matza L, de Lissovoy G, Sasane R, et al. The impact of bipolar disorder on work loss. Drug Benefit Trends 2004;16:476–481
16. Birnbaum HG, Shi L, Dial E, et al. Economic consequences of not recognizing bipolar disorder patients: a cross-sectional descriptive analysis. J Clin Psychiatry 2003;64:1201–1209
17. Goetzel RZ, Hawkins K, Ozminkowski RJ, et al. The health and productivity cost burden of the "top 10" physical and mental health conditions affecting six large U.S. employers in 1999. J Occup Environ Med 2003;45:5–14
18. de Zelicourt M, Dardennes R, Verdoux H, et al. Frequency of hospitalisations and inpatient care costs of manic episodes: in patients with bipolar I disorder in France. Pharmacoeconomics 2003;21: 1081–1090
19. Bhugra D, Flick GR. Pathways to care for patients with bipolar disorder. Bipolar Disorders 2005;7:236–245
20. Rush AJ. Toward an understanding of bipolar disorder and its origin. J Clin Psychiatry 2003;64(suppl 6):4–8
21. Zylstra RG, Sanford CE. Bipolar II disorder in a primary care setting: clinical vignette. Prim Care Companion J Clin Psychiatry 1999;1:47–49
22. Brady KT. Difficulties in diagnosis and management of bipolar disorder: three case presentations. J Clin Psychiatry 2000;61(suppl 13):32–37
23. Barbato N, Hafner RJ. Comorbidity of bipolar and personality disorder. Aust N Z J Psychiatry 1998;32:276–280
24. Freeman MP, Freeman SA, McElroy SL. The comorbidity of bipolar and anxiety disorders: prevalence, psychobiology, and treatment issues. J Affect Disord 2002;68:1–23
25. McElroy SL, Altshuler LL, Suppes T, et al. Axis I psychiatric comorbidity and its relationship to historical illness variables in 288 patients with bipolar disorder. Am J Psychiatry 2001;158:420–426
26. Sherwood Brown E, Suppes T, Adinoff B, et al. Drug abuse and bipolar disorder: comorbidity or misdiagnosis? J Affect Disord 2001;65: 105–115
27. Health Insurance Portability and Accountability Act, 42 USC § 1320–d2 (1996)
28. World Health Organization. International Classification of Diseases, Ninth Revision. Geneva, Switzerland: WHO;1997
29. The Fair Labor Standards Act (FLSA). US Department of Labor. Available at http://www.dol.gov/dol/compliance/comp-flsa.htm. Accessed March 14, 2005
30. Blough DK, Madden CW, Hornbrook MC. Modeling risk using generalized linear models. J Health Econ 1999;18:153–171
31. Manning JS, Connor PD, Sahai A. The bipolar spectrum: a review of current concepts and implications for the management of depression in primary care. Arch Fam Med 1998;7:63–71
32. Ai C, Norton E. Standard errors for the retransformation problem with heteroscedasticity. J Health Econ 2000;19:697–718
33. Hirschfeld RM, Lewis L, Vornik LA. 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 2003;64:161–174
34. Hirschfeld RM. The Mood Disorder Questionnaire: A simple, patient-rated screening instrument for bipolar disorder. Prim Care Companion J Clin Psychiatry 2002;4:9–11
35. Hirschfeld RMA. Bipolar depression: the real challenge. Eur Neuropsychopharmacol 2004;14:83S–88S
36. Post RM, Frye MA, Denicoff KD, et al. Beyond lithium in the treatment of bipolar illness. Neuropsychopharmacology 1998;19:206–219
37. Fankhauser MP. Bipolar disorder. In: DiPiro JT, Talbert RL, Yee GC, et al., eds. Pharmacotherapy: A Pathophysiologic Approach, 5th ed. New York, NY: McGraw-Hill; 2002:1273
38. Belmaker RH. Bipolar disorder. N Engl J Med 2004;351:476–486