

# Medication Use, Service Utilization, and Medical Costs Associated With New Episodes of Bipolar Disorder: Evidence From a Retrospective Claims Database

Robert L. Ohsfeldt, Ph.D.; Maureen J. Lage, Ph.D.; and Krithika Rajagopalan, Ph.D.

---

**Objective:** To identify resource use patterns and costs incurred during new episodes of bipolar disorder.

**Method:** Researchers examined Medstat MarketScan databases covering the interval of January 1, 1998, to December 31, 2002, to identify 6148 patients with new episodes of bipolar disorder as defined by the *International Classification of Diseases, Ninth Revision*. Resource utilization patterns and costs for the 6 months prior to the index date and for the 30 days and 1 year after the index date were examined. Differences among subcategories of bipolar patients in terms of the resources used before and after the index date were also examined.

**Results:** The majority of the individuals in the study were female (61.3%) and the mean age was 41.9 years. Patients diagnosed as manic had higher bipolar treatment costs ( $p < .01$ ) and were more likely to be hospitalized for mental health diagnoses 30 days ( $p < .01$ ) and 1 year after the index diagnosis ( $p = .02$ ) compared with individuals diagnosed as depressive, mixed, or other/unknown. Median total medical costs in the 1 year after the index date were highest for those diagnosed as depressed ( $p = .02$ ), while patients diagnosed as mixed bipolar had significantly more psychiatrist visits after the index date ( $p < .01$ ). Approximately 15% of patients were not treated with any central nervous system medication, and over 50% of patients were treated with antidepressants.

**Conclusion:** The subcategory of bipolar disorder that an individual is diagnosed as having significantly affects resource use and costs after such diagnosis. Patients diagnosed as manic generally used more resources than other individuals. In addition, results suggest that a large proportion of individuals are not being treated in accordance with recommended treatment guidelines.

(*Prim Care Companion J Clin Psychiatry* 2007;9:280–286)

---

Bipolar disorder is conservatively estimated to affect approximately 2.6% of the population in the United States,<sup>1</sup> and may affect as many as 6.4% if individuals with at least 2 lifetime manic or hypomanic episodes below the threshold for at least 1 week in duration are included.<sup>2</sup> The total annual cost of bipolar disorder in the United States has been estimated to be about \$45.2 million in 1991 dollars, or about \$67.2 million if expressed in 2004 dollars.<sup>3</sup> Worldwide, bipolar disorder is the sixth leading cause of disability.<sup>4</sup>

Patterns of treatment for bipolar disorder are highly complex and varied. Although treatment guidelines have been established,<sup>5,6</sup> divergence from these recommendations in usual clinical practice is widespread.<sup>7</sup> For example, Lim et al.<sup>7</sup> found that only one third of patients who were admitted to psychiatric inpatient units were discharged on medications recommended by expert guidelines as preferred or alternative recommended treatment. Thus, a better understanding of the patterns of treatment received by bipolar patients in usual care is an important initial step in developing interventions to improve the process of care for bipolar disorder.

The objective of this study was to identify patterns of resource use and costs among privately insured patients during new episodes of bipolar disorder. This study used Medstat MarketScan claims data to analyze differences in patterns of resource use and costs across patients grouped by type of index bipolar diagnosis. To the extent possible in claims data, the study team compared the observed patterns of care with treatment guidelines and noted the implications of apparent divergence from treatment guidelines.

## PATIENTS AND METHOD

Medstat's MarketScan Commercial Claims and Encounters (CCE) databases provided the data for these analyses. The CCE database is a Health Insurance Portability and Accountability Act (HIPAA)-compliant, fully de-identified medical claims database that includes private sector health data from approximately 100 payers and contains data on clinical utilization, expenditures, and enrollment across inpatient, outpatient, prescription drug, and carve-out services. The database links paid

---

Received Sept. 19, 2006; accepted Dec. 18, 2006. From Texas A&M Health Science Center, College Station (Dr. Ohsfeldt); HealthMetrics Outcomes Research, LLC, Groton, Conn. (Dr. Lage); and AstraZeneca, Wilmington, Del. (Dr. Rajagopalan). Dr. Rajagopalan is currently employed by Biogenidec, Cambridge, Mass.

This research was supported by AstraZeneca, Wilmington, Del. Dr. Ohsfeldt is a consultant for Auger and Pfizer and has received grant/research support from AstraZeneca. Dr. Lage is a consultant for AstraZeneca, Johnson and Johnson, Amgen, and Eli Lilly. Dr. Rajagopalan has no additional financial or other relationships relevant to the subject of this article.

Corresponding author and reprints: Maureen J. Lage, Ph.D., HealthMetrics Outcomes Research, LLC, 120 Anchorage Circle, Groton, CT 06340 (e-mail: lagemj@hlthmetrics.com).

Table 1. Central Nervous System (CNS) Medications Used by Bipolar Disorder Patients

Category	Medication	
Mood stabilizers/anticonvulsants	Lithium	
	Divalproex	
	Carbamazepine	
	Clonazepam	
	Gabapentin	
	Lamotrigine	
	Levetiracetam	
	Oxcarbazepine	
	Primidone	
	Tiagabine	
	Topiramate	
	Zonisamide	
	Atypical antipsychotics	Olanzapine
		Quetiapine
Risperidone		
Clozapine		
Typical antipsychotics	Ziprasidone	
	Chlorpromazine	
	Haloperidol	
Anxiolytics	Perphenazine	
	Alprazolam	
Antidepressants	Buspirone	
	Chlordiazepoxide	
	Diazepam	
	Hydrazine	
	Lorazepam	
	Oxazepam	
	SSRIs	
	Citalopram	
	Fluoxetine	
	Fluvoxamine maleate	
	Paroxetine hydrochloride	
	Sertraline	
	TCA's	
	Amitriptyline	
Chlordiazepoxide		
Perphenazine		
Amoxapine		
Clomipramine hydrochloride		
Mirtazapine		
Nortriptyline hydrochloride		
Protriptyline hydrochloride		
Trimipramine maleate		
Other antidepressants		
Isocarboxazid		
Phenelzine sulfate		
Tranlycypromine sulfate		
Bupropion hydrochloride		
Nefazodone hydrochloride		
Trazodone hydrochloride		
Venlafaxine hydrochloride		
Other CNS drugs	Any other CNS or psychotropic medication, not elsewhere specified	

Abbreviations: SSRI = selective serotonin reuptake inhibitor, TCA = tricyclic antidepressant.

claims and encounter data to detailed patient information across sites and types of providers over time.

The researchers examined MarketScan data over the interval of January 1, 1998, to December 31, 2002, to identify a population of patients with at least 1 claim for bipolar disorder (as defined by *International Classification of Diseases, Ninth Revision* [ICD-9] codes 296.4x–

Table 2. Demographic Characteristics of Patients With New Episodes of Bipolar Disorder

Variable	Total Sample (N = 6148)
Age, mean (SD)	41.9 (12.6)
Sex, N (%)	
Female	3769 (61.3)
Male	2379 (38.7)
Region, N (%)	
Northeast	1594 (25.9)
North central	1709 (27.8)
West	353 (5.7)
South	2479 (40.3)
Type of bipolar disorder, <sup>a</sup> N (%)	
Depressed	1066 (17.3)
Manic	889 (14.5)
Mixed	1202 (19.6)
Other/unknown	2991 (48.6)

<sup>a</sup>*International Classification of Diseases, Ninth Revision*, codes are as follows: Bipolar-depressed (296.5x), bipolar-manic (296.4x), bipolar-mixed (296.6x), bipolar-other/unknown (296.7x, 296.8x).

296.8x). Note that there were no restrictions placed on where the diagnosis of bipolar disorder occurred, so this analysis considers both inpatient and outpatient diagnoses, as well as diagnoses from general practitioners and specialists. From this initial population, the researchers included in the study only those individuals aged 18 through 64 years who had at least 18 months of continuous eligibility and received at least 2 claims with a bipolar diagnosis code on different dates of service during a 365-day period (with first such date identified as the index date). In addition, to examine “new episodes” of bipolar disorder and to increase the homogeneity of the sample, individuals were required to have no previous diagnosis of bipolar disorder or schizophrenia in the 6 months prior to the index date. There were 6194 patients who fit all the above criteria.

In addition, the researchers screened for extreme outliers. Specifically, patients were excluded from the analysis if (1) total medical care costs during the 6 months prior to the index date were greater than \$1 million; (2) total inpatient days during the 6 months prior to the index date were greater than 90 days; (3) more than 9 hospitalizations occurred during the 6 months prior to the index date; or (4) total medical costs during the initial 6 months of therapy were greater than \$10 million. There were 46 individuals excluded from the analyses using the above criteria, resulting in a final sample of 6148 individuals.

The study team examined medical utilization in the 30 days postdiagnosis, use of inpatient and outpatient services in the 30 days and 1 year postdiagnosis, and medical costs in the 6 months prior to diagnosis and in the 30 days and 1 year postdiagnosis. For medical utilization we examined patient use of mood stabilizers, atypical antipsychotics, typical antipsychotics, anxiolytics, antidepressants, and other central nervous system (CNS) medications. Table 1 provides a complete list of these

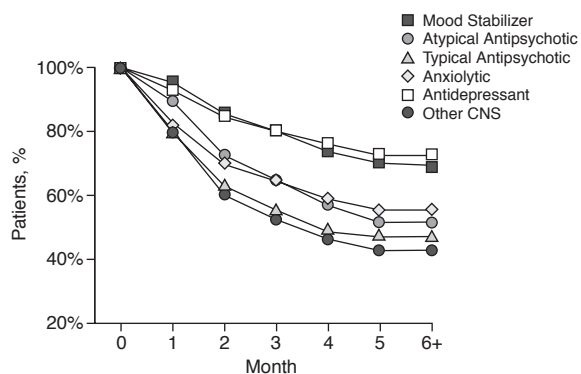
**Table 3. Medication Utilization in the 30 Days Postdiagnosis by Type of Bipolar Disorder**

Variable	Depressive (N = 1066)	Manic (N = 889)	Mixed (N = 1202)	Other/Unknown (N = 2991)	p Value
Initial drug utilization, % <sup>a</sup>					
Mood stabilizer	58.1	64.6	59.7	60.3	.03
New mood stabilizer <sup>b</sup>	13.3	14.8	16.9	18.1	< .01
Atypical antipsychotic	19.7	29.9	20.8	16.6	< .01
New atypical antipsychotic <sup>b</sup>	6.1	11.2	5.7	6.0	< .01
Typical antipsychotic	2.8	5.8	3.3	2.8	< .01
New typical antipsychotic <sup>b</sup>	0.1	1.5	0.7	0.6	< .01
Anxiolytic	32.4	29.6	31.8	26.7	< .01
New anxiolytic <sup>b</sup>	4.2	5.8	3.8	4.0	.09
Antidepressant	62.7	43.6	58.1	58.2	< .01
New antidepressant <sup>b</sup>	7.1	3.0	5.1	6.4	< .01
Other CNS	9.9	9.8	12.0	11.3	.25
New other CNS <sup>b</sup>	2.6	2.8	3.7	2.7	.29
Initial polypharmacy, %					
No CNS categories	14.9	14.6	15.3	15.6	.90
One CNS drug category	24.8	26.4	23.7	25.8	.42
Two CNS drug categories	29.3	29.4	31.2	33.1	.04
Three or more drug categories	31.0	29.6	29.8	25.5	.32

<sup>a</sup>Sum of percentages by subtype may exceed 100% due to initial polypharmacy.

<sup>b</sup>Indicates a new prescription rather than a continuation or reinitiation of a previous therapy.

Abbreviation: CNS = central nervous system.

**Figure 1. Duration of Drug Use by Therapeutic Class**

Abbreviation: CNS = central nervous system.

CNS medications. Inpatient and outpatient services measured in the analysis include physician visits (primary care and psychiatrist), group therapy sessions, outpatient visits (mental health and all diagnoses), and hospitalizations (for bipolar, mental health, and all diagnoses). Medical care costs consisted of all inpatient, outpatient, emergency room, and prescription drug costs.

In the descriptive analyses, the researchers grouped patients by type of bipolar disorder at the index diagnosis. The statistical analyses assess differences in sample proportions across groups using  $\chi^2$  tests, differences in group means for continuous variables using unbalanced analysis of variance, and differences in group medians using the Brown-Mood median test. We considered findings of a p value of  $\leq .05$  to indicate statistically significant

differences between the groups. All analyses were conducted using SAS Version 8.1.<sup>8</sup>

## RESULTS

Table 2 reports descriptive sample statistics. The mean age in the sample is 41.9 years, and 61.3% of the sample is female. In terms of geographic representation, the MarketScan overrepresents the southern region of the United States and underrepresents the western region, and our sample is reflective of this fact. The initial type of bipolar diagnosis is other/unknown (as defined by ICD-9 code 296.7x or 296.8x) for almost half of the sample (48.6%). The least common index diagnosis (14.5%) is the manic subtype (ICD-9 code 296.4x).

Data on prescription drug use within 30 days of the index diagnosis (Table 3) reveal that, overall, about 15% of all patients did not receive any category of CNS drug, whereas about 60% overall received drugs in 2 or more CNS categories. Most patients used a mood stabilizer within 30 days of diagnosis, with use being most common among patients in the manic subtype (64.6%). While antidepressant use also was common overall, a greater percentage of patients in the depressive subtype (62.7%) used antidepressants compared with 43.6% among patients in the manic subtype. The use of antipsychotics (both typical and atypical) was most common among patients in the manic subtype. Anxiolytics were most commonly used by patients in the depressive and mixed subtypes (32.4% and 31.8%, respectively), but were almost as commonly used by those in the manic and other/unknown subtypes (29.6% and 26.7%, respectively). However, in most cases, across all of the CNS drug

Table 4. Inpatient and Outpatient Services by Type of Bipolar Disorder

Variable	Depressive (N = 1066)	Manic (N = 889)	Mixed (N = 1202)	Other/Unknown (N = 2991)	p Value
30 Days postdiagnosis					
Inpatient services					
Hospitalizations—all, mean no.	0.074	0.115	0.076	0.071	< .01
Conditional LOS, <sup>a</sup> mean, d	6.9	9.3	8.4	8.3	< .01
Hospitalizations—mental health, mean no.	0.062	0.098	0.065	0.055	< .01
Hospitalizations—bipolar, mean no.	0.029	0.085	0.052	0.044	< .01
Outpatient services					
Psychiatrist visits, mean no.	1.07	1.03	1.16	0.85	< .01
Primary care physician visits, mean no.	0.89	0.98	0.86	0.96	.20
Group therapy visits, mean no.	0.06	0.06	0.06	0.06	.97
Outpatient visits—all, mean no.	3.99	3.77	3.90	3.78	.15
Outpatient visits—mental health, mean no.	2.99	2.83	2.91	2.79	.23
12 Months postdiagnosis					
Inpatient services					
Hospitalizations—all, mean no.	0.42	0.42	0.39	0.35	.16
Conditional LOS, <sup>a</sup> mean, d	10.7	12.7	12.3	12.6	.39
Hospitalizations—mental health, mean no.	0.25	0.28	0.25	0.20	.02
Hospitalizations—bipolar, mean no.	0.11	0.21	0.17	0.13	< .01
Outpatient services					
Psychiatrist visits, mean no.	4.71	4.66	5.21	4.06	< .01
Primary care physician visits, mean no.	6.47	6.12	5.93	6.37	.41
Group therapy visits, mean no.	0.30	0.51	0.43	0.34	.23
Outpatient visits—all, mean no.	26.9	24.7	26.4	25.6	.05
Outpatient visits—mental health, mean no.	15.0	14.1	14.8	14.1	.17

<sup>a</sup>Conditional LOS: Length of stay for all individuals who were hospitalized.  
Abbreviation: LOS = length of stay.

categories examined, drug use during the first 30 days represented the continuation or reinitiation of drug therapy observed during the 6 month preperiod, rather than the initiation of a new drug therapy.

As shown in Figure 1, many patients discontinued the use of prescription drugs over the first 6 months of therapy. Typical antipsychotic and “other CNS” drugs were most likely to be discontinued, whereas antidepressants and mood stabilizers were least likely to be discontinued over this period. Of patients using typical antipsychotics after the index diagnosis, 62.8% continued therapy for more than 60 days, compared with 85.8% for patients using mood stabilizers and 84.4% of patients using antidepressants. After 6 months, 42.8% of patients using “other CNS” drugs continued to use the drugs, compared with 72.4% of patients using antidepressants and 69.5% of patients using mood stabilizers.

In terms of outpatient and inpatient resource utilization (Table 4), patients with a manic subtype were more likely than patients with other subtypes to be hospitalized for any cause, for any mental health diagnosis, or for bipolar disorder over the first 30 days of therapy. Conditional on having at least 1 hospitalization within the first 30 days, patients with a manic subtype had the longest mean length of stay (9.3 days), and patients with a depressive subtype had the shortest mean length of stay (6.9 days). By contrast, at 1 year following the index diagnosis, the subtypes have the same overall rate of hospitalization and similar rates of hospitalization for general mental health–related conditions (ranging from 0.20 to 0.28); however, at 1 year

following the index diagnosis, patients within the manic subtype have a higher rate of hospitalization specifically related to bipolar disorder. In terms of outpatient care, during the first month of therapy, patients initially diagnosed with a mixed subtype had the most frequent psychiatric office visits (mean = 1.16), and patients with other or unspecified subtypes had the least frequent psychiatric office visits (0.85). There were no statistically significant differences across groups in primary care physician visits, group therapy sessions, or outpatient care visits during the first 30 days of therapy. A similar pattern holds for outpatient care during the first year after the index diagnosis.

Table 5 summarizes the medical care costs for patients grouped by subtype for the index bipolar diagnosis. During the 6-month period prior to the index diagnosis, patients diagnosed with a manic subtype had the highest mean preperiod medical costs, and patients with an other/unknown subtype had the lowest mean preperiod costs. The pattern in median preperiod costs is less apparent, though patients with an other/unknown subtype also had the lowest median preperiod costs. Over a 30-day period following the index diagnosis, there were no statistically significant differences in mean or median total medical costs (all diagnoses) across subtypes. However, if only costs directly related to a bipolar diagnosis are considered, there is a statistically significant difference in median costs, with the highest median bipolar costs among patients with a manic subtype (\$302) and the lowest median bipolar costs among patients with an other/unknown subtype (\$254). There is a trend toward a similar pattern

**Table 5. Medical Costs by Type of Bipolar Disorder**

Variable	Depressive (N = 1066)	Manic (N = 889)	Mixed (N = 1202)	Other/Unknown (N = 2991)	p Value
Prior 6 months total medical costs, \$					
Mean	20,317	22,919	18,118	16,410	.04
Median	3,533	3,490	3,381	3,069	.05
Costs—first 30 days, \$					
Total medical cost—all					
Mean	8,922	8,899	8,458	8,430	.99
Median	818	906	794	780	.09
Total medical cost—bipolar					
Mean	3,028	5,003	4,446	2,841	.09
Median	267	302	265	254	< .01
Drug cost—bipolar					
Mean	186	238	196	175	< .01
Median	54	101	65	52	< .01
Costs—12 months, \$					
Total medical cost—all					
Mean	64,101	52,812	54,498	51,503	.67
Median	10,811	10,372	9,431	10,318	.02
Total medical cost—bipolar					
Mean	11,452	19,317	10,012	15,589	< .01
Median	1,975	2,792	1,651	1,915	< .01
Drug cost—bipolar					
Mean	2,508	3,035	2,333	2,582	< .01
Median	929	1,571	815	981	< .01

in differences in mean bipolar costs, but the differences are not statistically significant at standard levels ( $p = .09$ ). Over the first year following the index diagnosis, there were no statistically significant differences in mean total medical costs (all diagnoses) across subtypes, but median total costs were lowest among patients with a mixed subtype (\$9431). Data on costs directly related to a bipolar diagnosis over the first year reveal that mean and median bipolar costs were highest among patients in the manic subtype (mean = \$19,317; median = \$2792) and lowest among patients in the mixed subtype (mean = \$10,012; median = \$1651).

## DISCUSSION

As might be expected given the complexity of bipolar disorder, the observed patterns of treatment are highly complex and vary considerably across patients. The use of multiple CNS drug agents is common, visits to both primary care physicians and psychiatrists are frequent, and the risk of hospitalization is significant.

Despite the fact that treatment guidelines recommend drug treatment using 1 or more types of CNS drugs for virtually all forms of bipolar disorder,<sup>5</sup> about 15% of the patients in the sample received no CNS drugs within 30 days of the index diagnosis. Given that combination therapy is commonly recommended,<sup>5,9-11</sup> it also is interesting that about one quarter of the sample received only 1 type of CNS drug. Obviously, drug treatment might be contraindicated for some patients, or some patients might have refused to initiate the recommended therapy. Nonetheless, this small but not insignificant percentage of

patients receiving no drug therapy may be a suitable target for quality improvement initiatives. Furthermore, among individuals who used medication, discontinuation rates in the 6 months after the index date ranged from 5% to 57%.

Treatment guidelines also recommend the use of mood stabilizers for most cases of bipolar disorder,<sup>5,9-11</sup> yet only about 65% of patients with a manic subtype received a mood stabilizer, and only about 60% of other patients in the sample received a mood stabilizer.

About 44% of patients with a manic subtype received an antidepressant during the first 30 days following the index diagnosis. About 58% of patients with a mixed subtype received an antidepressant. These high rates of observed antidepressant use predate the publication of the American Psychiatric Association treatment guidelines, which indicate that “antidepressants should be tapered and discontinued if possible.”<sup>5(p4)</sup> This recommendation was based upon evidence that antidepressants have not been shown to be more effective in preventing depressive relapse than mood stabilizers and are associated with an increased risk of antidepressant-induced mood cycling.<sup>12</sup> The high use of antidepressants among these patients prior to the index diagnosis also is likely to reflect the potential for an initial misdiagnosis during an episode of bipolar disorder.

Guidelines also state that psychotherapy may be useful in helping an individual cope with life problems and deal with bipolar disorder.<sup>7</sup> In addition, guidelines suggest that psychotherapy may help prevent future manic and depressive episodes by helping to reduce stress and improve medication compliance. However, in the 1 year after the

index diagnosis, patients have a higher mean number of primary care physician visits than psychiatrist visits and the mean number of psychiatrist visits is approximately 5. These results suggest that many patients may not be regularly meeting with a psychiatrist.

Taken together, the above results suggest that it is not uncommon for individuals diagnosed with bipolar disorder to not be treated in accordance with recommended treatment guidelines. Since medication not only has a significant impact on quality of life, but also significantly enhances the effectiveness of other treatments, inappropriate use of medication can have serious implications for the patient.<sup>13</sup> While treatment guidelines will not fit all individuals, it is important to note that, in general, such guidelines are thought to improve the quality of treatment and increase the accountability of medication treatment.<sup>13</sup> Specifically, it has been argued that the advantages of treatment algorithms for the treatment of mental illness include reducing unnecessary variation in clinical practice patterns, making clinical decision explicit, reducing costs, and improving outcomes.<sup>13</sup>

As to be expected, given the increased resource utilization associated with a diagnosis of bipolar mania or with the use of 2 or more CNS medications before bipolar diagnosis, bipolar manic patients had the highest medical costs. The estimates of bipolar-related medical care costs during 1 year of treatment reported here are substantially greater than the 1-year treatment cost in another recent study using U.S. managed care data.<sup>14</sup> From Table 5, the estimated mean bipolar cost for patients with a depressive subtype is \$11,452, compared with \$5130 in the prior study. Estimates reported in Table 5 for manic and mixed subtypes are \$19,317 and \$10,012, respectively, compared with \$4775 and \$3350 in the prior study. In part, these differences might be attributable to the fact that the costs reported in Table 5 focus on new episodes of bipolar disorder, whereas the prior study calculated costs for a prevalent pool of patients with bipolar disorder. Thus, one might expect higher costs during the initial, more acute phase of treatment than in the maintenance phase of therapy.

It is important to note that this analysis examines new episodes of bipolar disorder and not a new onset of the illness. For example, research has shown that the median age at onset for bipolar disorder is 25 years,<sup>15</sup> while the mean age of individuals in this study is 42. The results presented here may not be typical of individuals with new onset of bipolar disorders.

The findings of this study should be interpreted in the context of the limitations of the study design. For inclusion in this study, individuals had to have been continuously insured for at least 18 months and have no bipolar diagnosis in the 6 months prior to index date. As such, results from this study may not be generalizable to other populations. Second, the use of diagnostic codes to

identify individuals with bipolar disorder is not as rigorous as formal diagnostic assessments. In addition, use of a diagnosis of bipolar disorder with no prior diagnosis in the prior 6 months may not accurately reflect a new episode of bipolar disorder. However, it should be noted that similar types of criteria have been used in other studies that examine mental illness in a retrospective claims database.<sup>16–18</sup> Third, the analysis depends upon prescriptions filled to examine medication use. However, such data may not reflect actual prescriptions issued. Fourth, the use of medical claims data records precludes the inclusion of potentially important factors for consideration, such as the individual's age at onset or substance and/or alcohol abuse. Fifth, the exclusion of very high cost outliers is likely to result in conservative mean costs estimates, but the resulting estimates may be more generalizable. Finally, it is important to note that the analysis focuses on resource utilization and direct medical costs for individuals diagnosed with bipolar disorder, and hence does not include other costs associated with bipolar disorder, such as morbidity, mortality, unemployment, or incarceration.

## CONCLUSION

Although treatment for bipolar disorder is highly complex and varied, some patterns emerge as we examine mental health diagnoses, treatments, hospitalization rates, and costs in the periods immediately preceding and following the bipolar diagnosis. Specifically, a patient's existing mental health diagnosis and his or her use of CNS medications before beginning treatment for bipolar disorder significantly affect resource use and costs after beginning treatment. Patients diagnosed as manic and those who received more than 2 CNS medications prior to their bipolar diagnosis generally used more resources than other individuals. As a result, extra effort in early diagnosis of bipolar disorder and treatment options that improve outcomes for bipolar mania could have large implications for those who bear the burdens—in terms of costs, resources, and quality of life—for bipolar disorder.

*Drug names:* alprazolam (Xanax, Niravam, and others), bupropion (Wellbutrin, Zyban, and others), buspirone (BuSpar and others), carbamazepine (Carbatrol, Equetro, and others), chlordiazepoxide (Librium and others), chlorpromazine (Thorazine, Sonazine, and others), citalopram (Celexa and others), clomipramine (Anafranil and others), clonazepam (Klonopin and others), clozapine (FazaClo, Clozaril, and others), diazepam (Diatat, Valium, and others), divalproex (Depakote), fluoxetine (Prozac, Sarafem, and others), gabapentin (Neurontin and others), haloperidol (Haldol and others), isocarboxazid (Marplan), lamotrigine (Lamictal and others), levetiracetam (Keppra), lithium (Eskalith, Lithobid, and others), lorazepam (Ativan and others), mirtazapine (Remeron and others), nortriptyline (Pamelor and others), olanzapine (Zyprexa), oxcarbazepine (Trileptal), paroxetine (Paxil, Pexeva, and others), phenelzine (Nardil), primidone (Mysoline and others), protriptyline (Vivactil), quetiapine (Seroquel), risperidone (Risperdal), sertraline (Zoloft and others), tiagabine (Gabitril), topiramate (Topamax and others),

tranylcypromine (Parnate and others), trimipramine (Surmontil and others), venlafaxine (Effexor and others), ziprasidone (Geodon), zonisamide (Zonegran and others).

## REFERENCES

1. Kessler RC, Chiu WT, Demier O, et al. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Arch Gen Psychiatry* 2005;62:617–627
2. 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
3. Kleinman L, Lowin A, Flood E, et al. Costs of bipolar disorder. *Pharmacoeconomics* 2003;21:601–622
4. Woods SW. The economic burden of bipolar disease. *J Clin Psychiatry* 2000;61(suppl 13):38–41
5. American Psychiatric Association. Part A: treatment recommendations for patients with bipolar disorder. *Am J Psychiatry* 2002;159(suppl 4): 4–15
6. Keck PE Jr, Perlis RH, Otto MW, et al. The expert consensus guideline series: treatment of bipolar disorder 2004. *Postgrad Med Special Report*. December 2004:1–120
7. Lim PZ, Tunis SL, Edell WS, et al. Medication prescribing patterns for patients with bipolar I disorder in hospital settings: adherence to published practice guidelines. *Bipolar Disord* 2001;3:165–173
8. SAS User's Guide. SAS/STAT User's Guide: Version 8. Cary, NC: SAS Institute; 1999
9. Suppes T, Dennehy EB, Swann AC, et al. Report of the Texas Consensus Conference Panel on Medication Treatment of Bipolar Disorder 2000. *J Clin Psychiatry* 2002;63:288–299
10. The World Federation of Societies of Biological Psychiatry (WFSBP). Guidelines for the biological treatment of bipolar disorders, pt 1: treatment of bipolar depression. *World J Biol Psychiatry* 2002;3:115–124
11. The World Federation of Societies of Biological Psychiatry (WFSBP). Guidelines for the biological treatment of bipolar disorders, pt 2: treatment of mania. *World J Biol Psychiatry* 2003;4:5–13
12. Ghaemi SN, Hsu DJ, Soldani F, et al. Antidepressants in bipolar disorder: the case for caution. *Bipolar Disord* 2003;5:421–433
13. Algorithms and the medication treatment of people with serious mental illnesses [National Association of State Mental Health Program Directors Web site]. Dec 1997. Available at: [http://www.nasmhpd.org/general\\_files/publications/med\\_directors\\_pubs/meddir2.htm](http://www.nasmhpd.org/general_files/publications/med_directors_pubs/meddir2.htm). Accessed Aug 2006
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. Kessler RC, Berglund P, Demler O, et al. Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry* 2005;62:593–602
16. American Psychiatric Association. Practice guidelines for major depressive disorder in adults. *Am J Psychiatry* 1993;150:1–26
17. Birmbaum HG, Cremieux PY, Greenberg PE, et al. Management of major depression in the workplace. *Dis Manage Health Outcomes* 2002;7:163–171
18. Marciniak MD, Lage MJ, Dunayevich E, et al. The cost of treating anxiety: the medical and demographic correlates that impact total medical costs. *Depress Anxiety* 2005;21:178–184