

Medical Care Costs and Hospitalization in Patients with Bipolar Disorder Treated with Atypical Antipsychotics

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Background: A large proportion of costs associated with the treatment of bipolar disorder are attributable to patient hospitalization.

Objective: To investigate medical care costs and hospitalization rates among patients with bipolar disorder who were managed with aripiprazole compared with olanzapine, quetiapine, risperidone, or ziprasidone.

Methods: This retrospective cohort study assessed patients who were aged 18 to 64 years, diagnosed with bipolar disorder, and who were receiving therapy with aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone. This study was based on data from the PharMetrics claims database between January 1, 2003, and September 30, 2008. The study used a time-to-event framework. Cox proportional hazards models were used to assess the impact of each atypical antipsychotic on time to hospitalization, including all-cause and mental health-related reasons. Generalized linear models were used to compare costs per treated patient per month between the groups. Aripiprazole therapy was the reference group for all comparisons.

Results: Aripiprazole therapy showed a significantly lower hazard ratio (HR) for all-cause hospitalizations compared with olanzapine (HR, 1.4), quetiapine (HR, 1.4), risperidone (HR, 1.2), and ziprasidone (HR, 1.7); and for mental health-related hospitalizations compared with olanzapine, quetiapine, risperidone (HR, 1.3 each), and ziprasidone (HR, 1.7). Ziprasidone had higher unadjusted all-cause medical costs (US \$1151 ± \$2928) and unadjusted mental health-related costs (US \$711 ± \$2263) than the other antipsychotics that were included in this study, whereas aripiprazole had the lowest all-cause (US \$804 ± \$2523) and mental health-related costs (US \$475 ± \$2145) compared with the other antipsychotics. Quetiapine had the highest all-cause costs (US \$1221; 95% confidence interval [CI], 1180-1263), and ziprasidone had the highest mental health-related costs (US \$823; 95% CI, 754-898). Adjusted inpatient and emergency department all-cause costs were significantly lower for aripiprazole compared with all other atypical antipsychotics ($P < .05$), except olanzapine; however, the adjusted inpatient and emergency department mental health-related costs were significantly lower for aripiprazole only when compared with ziprasidone ($P < .05$).

Conclusions: The costs of medical care for patients with bipolar disorder differ based on the type of medication used, which can affect the rate of hospitalization. Treatment with aripiprazole was associated with fewer hospitalizations, longer time to hospitalization, and therefore the lowest all-cause and mental health-related medical costs compared with olanzapine, quetiapine, risperidone, or ziprasidone. Therefore, aripiprazole may offer an economic advantage over other atypical antipsychotics in patients with bipolar disorder.

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Bipolar disorder is a chronic, recurring disorder associated with frequent episodes of mania and depression. Overall costs for the treatment of bipolar dis-

order are comprised of direct costs of professional services, medication, and hospitalization costs; indirect costs associated with caring for patients; as well as costs asso-

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KEY POINTS

- Patients with bipolar disorder use close to 3- to 4-fold more healthcare resources and incur more than 4-fold greater healthcare costs than patients without the disorder.
- Hospitalization of patients with bipolar disorder is thought to be the single most costly resource, accounting for approximately 33% to 66% of the overall costs of treating patients with this disorder.
- Atypical antipsychotics are increasingly used for patients with bipolar disorder; this study compared the cost of medical care and hospitalization rates for patients who received aripiprazole and those who received olanzapine, quetiapine, risperidone, or ziprasidone.
- The patients using longer-acting antipsychotics had a lower rate of hospital admissions and emergency department visits than those using short half-life antipsychotic agents.
- Ziprasidone had higher unadjusted all-cause medical costs (\$1151) and unadjusted mental health-related costs (\$711) than the other antipsychotics in this study.
- Aripiprazole had the lowest all-cause (\$804) and mental health-related costs (\$475) compared with the other antipsychotics.
- Furthermore, aripiprazole was associated with a significantly lower rate of hospitalizations and a longer time to hospitalization than the other medications in this study.

ciated with the loss of productivity.¹² Notably, 33.5% to 65.2% of the overall cost of treating patients with bipolar disorder is attributable to patient hospitalization,^{3,4} with the majority of patients with bipolar disorder reporting at least 1 psychiatric hospitalization in their lifetime.⁵ Indeed, patient hospitalization is thought to be the single most costly resource in bipolar disorder, accounting for approximately 50% of the cost of medical encounters.⁶

Patients with bipolar disorder have been found to utilize nearly 3 to 4 times more healthcare resources⁶ and to incur more than 4 times greater healthcare costs than patients without bipolar disorder.⁷ An analysis of claims data comparing approximately 28,500 patients with bipolar disorder with approximately 85,500 control patients over a 1-year period established that the annual cost per patient was \$12,764 for a patient with bipolar disorder compared with \$1340 for a control patient, a significant difference ($P < .001$).⁷

Effective pharmacotherapy and psychosocial inter-

ventions are an essential part of the successful treatment of bipolar disorder.⁸ Prescription data indicate that 63.1% to 70.8% of patients with bipolar disorder receive psychotropics (eg, lithium, valproate, carbamazepine), whereas 21.2% to 29.0% of patients receive antipsychotic augmentation therapy.⁹

Atypical antipsychotics, either as monotherapy or as adjunctive treatment to mood stabilizers, are an increasingly common treatment option for patients with bipolar disorder. There may be an association between antipsychotic medication half-life and hospitalization. It has been shown that patients using longer-acting antipsychotics experienced a lower rate of hospital admissions and emergency department visits than patients treated with short half-life antipsychotic agents.¹⁰ Moreover, all atypical antipsychotics have side effects; however, aripiprazole has been shown to have a low metabolic burden among its class.¹¹

Recent claims database analyses have shown that treatment with aripiprazole was associated with a lower risk of and longer time to hospitalization, as well as with lower psychiatric treatment costs and lower total healthcare costs compared with other adjunctive antipsychotic medications.¹²⁻¹⁵ However, these analyses used a limited follow-up time period (ie, 90 days)^{12,13} or focused on long-term (ie, 1-year) cost outcomes using an intent-to-treat (ITT) methodology.^{14,15}

The aim of the current analysis was to evaluate hospitalization and medical care costs for patients during the time they were receiving treatment with aripiprazole compared with patients receiving other atypical antipsychotics (ie, olanzapine, quetiapine, risperidone, or ziprasidone). The analysis presented here is an extension of a previous article covering medical claims from 2003 to 2006,¹⁴ with additional important changes in the methodologic approach.

Methods

Study Design and Data Source

This retrospective cohort analysis was conducted using the PharMetrics Patient-Centric Database, which includes medical and pharmacy claims from January 1, 2003, through September 30, 2008. The PharMetrics database encompasses a composite of 85 health plans across the United States, and it includes information on approximately 47 million patients. The database includes inpatient and outpatient medical claims, diagnosis and procedure codes, as well as pharmacy claims. The PharMetrics database is geographically representative of the US population, and includes a variety of demographic measures.

The sample for this study was restricted to health plans providing comprehensive healthcare data, includ-

ing mental health–related services. The general approach of the analysis was to use baseline measures of health and disease severity, such as baseline comorbidity indices, demographics, drug utilization patterns, and hospitalization rates. Lagged costs as predictors in cost models were not used because of issues with serial correlation. In particular, because healthcare data are extremely skewed, the use of a highly variable predictor may lead to an unstable model.

Selection Criteria

The study included patients aged 18 to 64 years who had 1 or more outpatient or inpatient claims with an *International Classification of Diseases, Ninth Revision* code for bipolar disorder (ie, manic, mixed, or hypomanic [296.0X, 296.1, 296.4X, 6X, 7X, 8X]). A patient’s new start index date was defined as the date of the first prescription claim for an atypical antipsychotic medication in the claims database between January 1, 2003, and September 30, 2008.

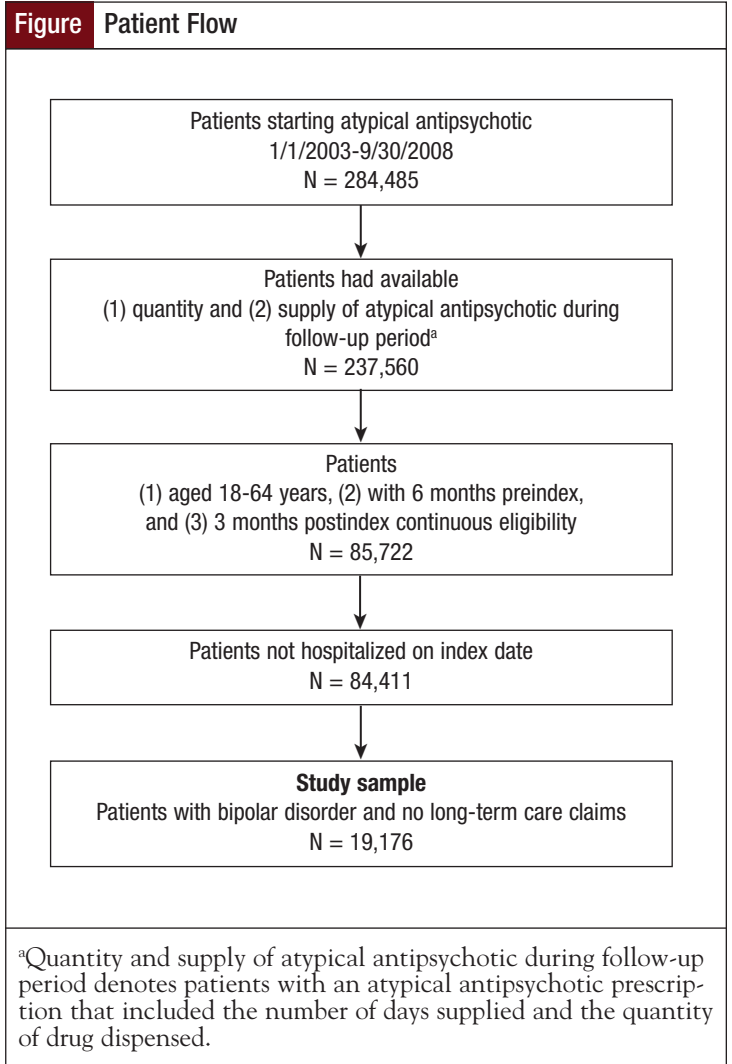
Patients were excluded from the study if they were prescribed an atypical antipsychotic in the 180-day preindex period, or if they had prescriptions for more than 1 atypical antipsychotic agent at the index date. Eligible patients were required to have at least 180 days of continuous enrollment before and after 90 days of continuous enrollment after the index prescription date.

In addition, patients were excluded from the analysis if they resided in a nursing home, hospice facility, or another type of long-term care facility, or if they received prescriptions via mail order. Patients with a diagnosis of schizophrenia spectrum disorder (295.XX), or those who were hospitalized at the time of the index prescription or within 7 days after the index prescription, were excluded from the study.

In the analysis evaluating the impact of atypical antipsychotics on hospitalizations, patients were followed for up to 1 year or until the occurrence of hospitalization, loss of continuous eligibility, or until switching or discontinuation of the index medication occurred (allowing for a gap of 15 days).

In this study, the inpatient and emergency department visit costs and medical costs were also evaluated for patients during their time receiving the index treatment. For this analysis, patients were followed from treatment initiation to the time of switching or discontinuation of the index medication (allowing for a gap of 15 days), loss of continuous eligibility, or the end of the study period (after 1 year).

Costs were reported as costs per treated patient per month (PPPM). Both all-cause and mental health–related outcomes were evaluated. Mental health–related outcomes were identified based on claims with a primary or



a secondary diagnosis code ranging from 290.XX to 319.XX. Costs were adjusted to 2008 US dollars using the medical care component of the Consumer Price Index.

Assessments and Statistical Analyses

The primary analysis of time to hospitalization was addressed using a Cox proportional hazards model, which controlled for baseline factors, such as age, sex, year of index prescription, Charlson comorbidity index, diabetes, hyperlipidemia, glucose and lipid testing, baseline hospitalization rate, and use of mood stabilizers. These control variables were computed using data from the 6-month period before the index date.

The models for medical costs were implemented using a generalized linear framework with a log link and gamma distribution. For the analysis of costs of hospitalization and emergency department visits, a 2-stage multivariate modeling approach was used combining logistic

Table 1 Patient Demographics and Preindex Healthcare Treatment and Resource Use, by Drug: On-Treatment Sample

| Variable | Aripiprazole (N = 3690) | Olanzapine (N = 3038) | Quetiapine (N = 7936) | Risperidone (N = 2997) | Ziprasidone (N = 1515) |
|--|----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
| Mean age, yrs (SD) | 38.50 (12.7) | 40.16 (12.8) ^a | 39.01 (12.2) ^a | 39.24 (12.9) ^a | 39.90 (12.2) ^a |
| Male, N (%) | 1151 (31.2) | 1423 (46.8) ^a | 2968 (37.4) ^a | 1241 (41.4) ^a | 454 (30.0) |
| Index year, N (%) | | | | | |
| 2003 | 130 (3.5) | 523 (17.2) ^a | 404 (5.1) ^a | 320 (10.7) ^a | 70 (4.6) ^a |
| 2004 | 270 (7.3) | 630 (20.7) ^a | 860 (10.8) ^a | 574 (19.2) ^a | 169 (11.2) ^a |
| 2005 | 512 (13.9) | 545 (17.9) ^a | 1306 (16.5) ^a | 550 (18.4) ^a | 280 (18.5) ^a |
| 2006 | 828 (22.4) | 541 (17.8) ^a | 1777 (22.4) ^a | 658 (22.0) ^a | 352 (23.2) ^a |
| 2007 | 1005 (27.2) | 507 (16.7) ^a | 2299 (29.0) ^a | 595 (19.9) ^a | 397 (26.2) ^a |
| 2008 | 945 (25.6) | 292 (9.6) ^a | 1290 (16.3) ^a | 300 (10.0) ^a | 247 (16.3) ^a |
| Mean Charlson comorbidity index (SD) | 0.32 (0.82) | 0.34 (0.96) | 0.34 (0.88) | 0.34 (0.90) | 0.38 (0.88) ^a |
| All-cause hospitalization, N (%) | 831 (22.5) | 922 (30.3) ^a | 2412 (30.4) ^a | 981 (32.7) ^a | 489 (32.3) ^a |
| Mental health–related hospitalization, N (%) | 757 (20.5) | 873 (28.7) ^a | 2246 (28.3) ^a | 914 (30.5) ^a | 465 (30.7) ^a |
| Diabetes, N (%) | 302 (8.2) | 140 (4.6) ^a | 551 (6.9) ^a | 214 (7.1) | 148 (9.8) |
| Hyperlipidemia, N (%) | 696 (18.9) | 538 (17.7) | 1413 (17.8) | 559 (18.7) | 311 (20.5) |
| Glucose testing conducted, N (%) | 1360 (36.9) | 1108 (36.5) | 2958 (37.3) | 1068 (35.6) | 603 (39.8) ^a |
| Lipid testing conducted, N (%) | 717 (19.4) | 552 (18.2) | 1508 (19.0) | 535 (17.9) | 329 (21.7) |
| Use of mood stabilizer, N (%) | 1721 (46.6) | 1037 (34.1) ^a | 3342 (42.1) ^a | 1187 (39.6) ^a | 698 (46.1) |

^a*P* < .05 versus aripiprazole.
SD indicates standard deviation.

regression, generalized linear models, and bootstrapping with 200 repetitions, to account for the fact that many patients had no hospitalizations and emergency department visits and therefore incurred no inpatient or emergency department costs.

All models controlled for the same set of baseline factors used in the Cox proportional hazards model that was stated above. Aripiprazole therapy was used as the reference group for all of the comparisons, with an a priori level of significance set at 0.05 (2-sided).

Results

Patient Disposition and Characteristics

A total of 284,485 patients were identified with a prescription for an atypical antipsychotic in the study database; 19,176 patients had been diagnosed with bipolar disorder, met the study selection criteria, and were therefore included in this analysis. A schematic diagram of patient disposition is shown in the **Figure** (page 381).

Baseline Differences

Of the total number of patients, 3690 were prescribed aripiprazole; 3038 received olanzapine; 7936 quetiapine; 2997 risperidone; and 1515 received ziprasidone (**Table 1**). Baseline patient characteristics for the 5 atypical antipsychotics are displayed in **Table 1**. Patients who were treated with aripiprazole were statistically younger, more likely to be female, and had lower rates of preindex hospitalization and emergency department rates than the comparator atypical antipsychotics. Mean time on treatment ranged from 67 to 74 days (aripiprazole, 71 ± 76; olanzapine, 67 ± 74; quetiapine, 74 ± 84; risperidone, 71 ± 78; ziprasidone, 69 ± 78).

Time to Hospitalization

Results of the Cox proportional hazards model, controlling for differences in baseline patient characteristics, demonstrated a significantly lower hazard ratio (HR) for all-cause and for mental health–related hospitalization

for patients who received aripiprazole compared with those receiving any of the other atypical antipsychotics (Table 2).

Medical and Inpatient Costs (on Treatment Analysis)

The unadjusted PPPM medical costs (ie, outpatient plus inpatient and emergency department) were significantly lower for aripiprazole compared with all the other atypical antipsychotics for all-cause and for mental health-related costs (Table 3).

The unadjusted all-cause medical costs (US \$1151 ± \$2928) and mental health-related costs (US \$711 ± \$2263) associated with ziprasidone treatment were higher than for the other atypical antipsychotics that were assessed, whereas the lowest all-cause (US \$804 ± \$2523) and mental health-related costs (US \$475 ± \$2145) were associated with aripiprazole treatment compared with the other atypical antipsychotics (Table 3).

Results of the generalized linear models regression demonstrated consistent findings for all-cause and for mental health-related medical (ie, outpatient plus inpatient and emergency department) costs, with costs for patients receiving aripiprazole being significantly lower (US \$911; 95% confidence interval [CI], 866-958 and US \$576; 95% CI, 543-610, respectively) compared with other atypical antipsychotics (*P* < .05; Table 4, page 384).

The highest all-cause costs were seen with quetiapine (US \$1221; 95% CI, 1180-1263), and the highest mental health-related costs were seen with ziprasidone (US \$823; 95% CI, 754-898).

The current analysis also indicates lower all-cause and mental health-related inpatient and emergency department costs for patients receiving aripiprazole compared with those receiving all other atypical antipsychotics (Table 5, page 385). The adjusted inpatient and emergency department all-cause costs were significantly lower for aripiprazole compared with all other atypical antipsychotics (*P* < .05), except olanzapine, whereas the adjusted inpatient and emergency department mental health-related costs were significantly lower for this agent only when compared with ziprasidone (*P* < .05).

Discussion

This analysis of commercially insured patients with a diagnosis of bipolar disorder who were receiving atypical antipsychotic treatment established that the HR of hospitalization for patients receiving aripiprazole treatment was significantly lower than for patients receiving other atypical antipsychotics. This translated into lower medical costs for patients prescribed aripiprazole compared with those receiving any of the other atypical antipsychotics.

Table 2 Results of Cox Proportional Hazards Model for All-Cause and Mental Health-Related Hospitalization

| Medication-based hospitalization | Hazard ratio (95% confidence interval) |
|--|--|
| <i>All-cause hospitalization</i> | |
| Olanzapine | 1.4 (1.1-1.7) |
| Quetiapine | 1.4 (1.2-1.6) |
| Risperidone | 1.2 (1.0-1.5) |
| Ziprasidone | 1.7 (1.4-2.1) |
| <i>Mental health-related hospitalization</i> | |
| Olanzapine | 1.3 (1.1-1.6) |
| Quetiapine | 1.3 (1.1-1.5) |
| Risperidone | 1.3 (1.1-1.6) |
| Ziprasidone | 1.7 (1.4-2.1) |

Note: Aripiprazole therapy was the reference group for all comparisons. Estimates are reported after controlling for age, sex, year of index prescription, Charlson comorbidity index, diabetes, hyperlipidemia, glucose and lipid testing, baseline hospitalization rate, and use of mood stabilizers.

Table 3 Medical and Inpatient/Emergency Department Unadjusted Costs: On-Treatment Analysis

| Medication-specific costs | Inpatient and emergency department costs, mean, \$ (± SD) | Medical costs (outpatient + inpatient), mean, \$ (± SD) |
|------------------------------------|---|---|
| <i>All-cause costs</i> | | |
| Aripiprazole | 299 (± 2087) | 804 (± 2523) |
| Olanzapine | 443 (± 3106) | 1038 (± 3771) |
| Quetiapine | 468 (± 2614) | 1089 (± 3450) |
| Risperidone | 453 (± 2598) | 1032 (± 3103) |
| Ziprasidone | 588 (± 2552) | 1151 (± 2928) |
| <i>Mental health-related costs</i> | | |
| Aripiprazole | 225 (± 1893) | 475 (± 2145) |
| Olanzapine | 301 (± 2024) | 621 (± 2382) |
| Quetiapine | 331 (± 2102) | 655 (± 2479) |
| Risperidone | 318 (± 2062) | 674 (± 2453) |
| Ziprasidone | 415 (± 2015) | 711 (± 2263) |

Costs reported as per treated patient per month in 2008 US dollars. SD indicates standard deviation.

Table 4 Generalized Linear Models Regression Analysis for Adjusted Mean Medical Costs: Outpatient plus Inpatient/Emergency Department

| Medication-specific medical costs | Mean adjusted medical costs, \$ (outpatient + inpatient/emergency department) | 95% Confidence interval | |
|---|---|-------------------------|-----------------|
| | | Lower costs, \$ | Upper costs, \$ |
| <i>All-cause costs</i> | | | |
| Aripiprazole | 911 | 866 | 958 |
| Olanzapine | 1100 ^a | 1039 | 1165 |
| Quetiapine | 1221 ^a | 1180 | 1263 |
| Risperidone | 1040 ^a | 984 | 1099 |
| Ziprasidone | 1216 ^a | 1126 | 1312 |
| <i>Mental health-related costs</i> | | | |
| Aripiprazole | 576 | 543 | 610 |
| Olanzapine | 714 ^a | 668 | 762 |
| Quetiapine | 804 ^a | 773 | 836 |
| Risperidone | 757 ^a | 711 | 807 |
| Ziprasidone | 823 ^a | 754 | 898 |
| ^a P <.05 versus aripiprazole. Costs reported as per treated patient per month in 2008 US dollars. Estimates are reported after controlling for age, sex, year of index prescription, Charlson comorbidity index, diabetes, hyperlipidemia, glucose and lipid testing, baseline hospitalization rate, and use of mood stabilizers. | | | |

Most of the antipsychotics examined in the analysis are currently available as generic medications. Therefore, pharmacy expenditure data based on branded antipsychotics from 2003 through 2008 are not applicable for decision-making in today’s marketplace.

These results are consistent with previously published findings.^{12,14,15} For example, Kim and colleagues evaluated commercially insured patients with bipolar disorder who were treated with a mood stabilizer and adjunctive atypical antipsychotic therapy, and observed that after multivariate adjustment for differences in baseline characteristics, aripiprazole was associated with a significantly longer time to hospitalization compared with any of the other atypical antipsychotics.¹³ A companion analysis of

the study also demonstrated that treatment with adjunctive aripiprazole was associated with significantly lower psychiatric-related costs than other atypical antipsychotic agents ($P < .001$).¹²

In a similar study, Kim and colleagues¹⁴ compared the time to psychiatric hospitalization and healthcare costs in commercially insured patients who had bipolar disorder and were being treated with aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone over a 1-year period after initiation of therapy. The current study is an extension of the study by Kim and colleagues.¹⁴ In the study by Kim and colleagues, after a multivariate adjustment for differences in baseline characteristics, aripiprazole was associated with a significantly lower risk of psychiatric hospitalization than ziprasidone, quetiapine, and olanzapine, and significantly lower healthcare costs than quetiapine, but not other atypical antipsychotics.¹⁴

In a real-world study of Medicaid beneficiaries with bipolar disorder who were newly initiating an atypical antipsychotic, those prescribed aripiprazole had a significantly longer time to psychiatric hospitalization than those who were prescribed olanzapine, quetiapine, ziprasidone, or risperidone; however, this difference did not reach significance in the case of the latter.¹⁵ Although adjusted costs of psychiatric hospitalization in beneficiaries initiating aripiprazole were lower compared with all other beneficiaries receiving atypical antipsychotic therapy, this difference was only significant when compared with those initiating treatment with quetiapine.¹⁵

Furthermore, the current study focused solely on medical (ie, outpatient and inpatient) costs. Pharmacy costs were not examined, because most of the antipsychotics examined in the analysis (ie, olanzapine, quetiapine, risperidone, and ziprasidone) are currently available as generic medications. Therefore, pharmacy expenditure data based on branded antipsychotics from 2003 through 2008 are not applicable for decision-making in today’s marketplace.

The present analysis focused on the relative medical costs of patients using each medication, which will likely remain consistent between the study period and current clinical practice. It is also important to note that the time period of the analysis (2003-2008) may have led to the inclusion of some patients in the sample with potential off-label use of aripiprazole for bipolar disorder, because the US Food and Drug Administration approval for this indication was received in September 2004.

Limitations

There are several limitations associated with this analysis. First, the use of medical and pharmacy claims data did not allow for confirmation of a patient’s diagnosis or whether the medication of interest was prescribed

for a specific condition. However, patients included in this study had a diagnosis of bipolar disorder during the study period and were treated with an atypical antipsychotic for that disorder.

Because this was a retrospective database study, lack of randomization may have led to selection bias. Baseline characteristics varied across the cohorts and might have impacted the results. However, the study did adjust for preperiod psychiatric hospitalizations, mood stabilizer use, Charlson comorbidity index score, and other demographic factors to minimize confounding.

It is important to note that the current analysis had less stringent inclusion criteria compared with previously published analyses, namely, that the use of adjunctive mood stabilizers was not required, the follow-up period was long (ie, 365 days), and, most important, cost outcomes were calculated during the time receiving treatment as opposed to an ITT framework projection.

Because outcomes were assessed during a patient's time receiving treatment with the index atypical antipsychotic, the current data provide important information on the effect of atypical antipsychotics on hospitalizations and related costs during the time patients were receiving treatment as opposed to associating post-treatment events with an index medication that was discontinued months earlier. However, it should be noted that the average length of therapy in the current analysis was short (ie, mean time on treatment was 67-74 days) and may not be generalizable to patients using these drugs for a relatively longer period of time.

Conclusions

In this analysis, patients in a commercial plan who were treated with aripiprazole for bipolar disorder had a longer time to hospitalization and fewer hospitalizations compared with patients who were treated with olanzapine, quetiapine, risperidone, or ziprasidone. In addition, patients treated with aripiprazole had the lowest all-cause and mental health-related medical costs compared with those treated with olanzapine, quetiapine, risperidone, or ziprasidone. These data are consistent with previous published findings for patients with bipolar disorder in real-world settings, and they suggest that aripiprazole may offer an economic advantage versus other atypical antipsychotic medications in this patient population. ■

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Table 5 Two-Part Model for Adjusted Inpatient/Emergency Department Costs

| Medication-specific medical costs | Mean adjusted costs, \$ (inpatient/emergency department) | Difference in costs, \$ | 95% Confidence interval | |
|------------------------------------|--|-------------------------|-------------------------|-----------------|
| | | | Lower costs, \$ | Upper costs, \$ |
| <i>All-cause costs</i> | | | | |
| Aripiprazole | 295 | 0 | 0 | 0 |
| Olanzapine | 377 | 82 | -25 | 189 |
| Quetiapine | 421 ^a | 126 | 37 | 214 |
| Risperidone | 388 ^a | 94 | 1 | 190 |
| Ziprasidone | 538 ^a | 243 | 115 | 376 |
| <i>Mental health-related costs</i> | | | | |
| Aripiprazole | 215 | 0 | 0 | 0 |
| Olanzapine | 247 | 31 | -43 | 107 |
| Quetiapine | 283 | 67 | -3 | 138 |
| Risperidone | 264 | 49 | -26 | 115 |
| Ziprasidone | 368 ^a | 153 | 41 | 259 |

^aP <.05 versus aripiprazole.

Costs are reported per treated patient per month in 2008 US dollars. Estimates are reported after controlling for age, sex, year of index prescription, Charlson comorbidity index, diabetes, hyperlipidemia, glucose and lipid testing, baseline hospitalization rate, and use of mood stabilizers.

Author Disclosure Statement

Dr Bergeson, Dr Jing, and Dr Hebden are employed by and own stock in Bristol-Myers Squibb, and Dr Kalsekar and Ms You are employed by Bristol-Myers Squibb. Dr Forbes is a former employee of Otsuka Pharmaceutical Development & Commercialization, Inc.

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STAKEHOLDER PERSPECTIVE

The Potential Value of Benefit Design and Medication Selection for a Total-Cost-of-Care Strategy in Bipolar Disease

PAYERS: The influences of and direction of funding under the Affordable Care Act are shifting the risk of “episodes-of-care” management onto payers under an accountable care organization model. The management of outpatient care that is associated with Medicare and Medicaid coverage involves a risk that is continuing to grow, whereby potentially preventable hospital admissions that are incurred from the inappropriate or the insufficient management of chronic diseases will not be entitled to be reimbursed under federal- and/or state-sponsored programs.

This trend in risk exposure associated with the episode-of-care management strategy is removing the silo approach to management within health plans and is leading to greater collaboration between a plan’s various departments—including care management, pharmacy, and finance—to critically evaluate and create benefit design strategies that consider the total cost of care and not just a single benefit component, such as the pharmacy or the formulary impact alone.

With this development in pharmacy benefit design, traditional formulary-driving influences, such

as generic opportunity and contracting, may not be the final determinants in formulary placement of a specific therapy, although these strategies are still important. Mental health is an important area where this dynamic plays out, and as Dr Bergeson and colleagues demonstrate in their current study in this issue of *American Health & Drug Benefits*, bipolar disease suggests the potential value of medication and formulary selection from an episode-of-care total-cost viewpoint.

PATIENTS: Although not explicitly discussed within the current article, the obvious result from better control of a chronic disease (such as bipolar disorder), a reduction in hospitalizations, and the mitigation of exposure to nosocomial concerns lead the way to a better patient experience, as well as to improved quality of life and quality of care for patients.

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