ORIGINAL RESEARCH
Key Words: quality of care, bipolar disorder, bipolar depression

Bipolar-I Depression Outpatient Treatment Quality and Costs in Usual Care Practice

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ABSTRACT *~* ***Objective:*** *To examine the longitudinal usual care quality and costs of bipolar-I depression treatment in adults.* ***Experimental Design:*** *Observational study of claims data from a privately insured population, ages 18–64, diagnosed with bipolar-I depression (N = 925), treated in 1999 and 2000, examining depressed phase specific and annualized treatment quality (receipt of antimanic medication and/or psychotherapy). Treatment costs were calculated and stratified by quality.* ***Principal Observations:*** *Little than half (56%) of the patients diagnosed with bipolar-I depression received both an antimanic agent and psychotherapy during their acute phase depression treatment, whereas 15% received an antimanic agent without psychotherapy. Eighteen to 28% of spending was accounted for by treatment that did not meet the standards of practice guidelines—and two-thirds to three-quarters of it was treatment that included an antidepressant without an antimanic agent (care that is advised against by guidelines).* ***Conclusions:*** *Considerable resources were spent in care inconsistent with guidelines—much of that was care that could worsen the course of bipolar illness. This provides an opportunity for policy makers to develop mechanisms of quality improvement that redirect a substantial proportion of resource dollars to care that is more efficacious. Further, when conducting quality assessment and examining outcomes using administrative data, hospital admissions alone are an inadequate measure of bipolar disorder affective instability in claims data.* Psychopharmacology Bulletin. *2008;41(2):24–39.*

INTRODUCTION

Bipolar disorder treatment is complicated and evolving. Maximizing lithium therapy has historically been recommended as the first-line treatment.[1–3] More recently, other agents such as lamotrigine, quetiapine, and a combination of olanzapine and fluoxetine have begun to demonstrate efficacy.[4] However, even after such interventions, many patients continue to have persistent depressive symptoms.[5] The

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role of antidepressants in the treatment of bipolar depression (if, when, which ones, for how long) has been uncertain,[2,5–9] including concerns that they may induce mania or mood cycling, thus worsening the course of illness.[2,3,9–12] And while practice guidelines have long recommended psychotherapy in the treatment of bipolar depression,[3] only recently have specific psychotherapies been shown to demonstrate efficacy in randomized controlled trials.[13–21]

Descriptions of the quality of usual care for bipolar disorder typically have been cross-sectional and indicated that care is often inadequate.[22–27] The Institute of Medicine recommends quality measurement and improvement that utilizes quality measures with a longitudinal scope and includes multiple providers.[28] Still, we are unaware of literature that describes the quality of bipolar care (or bipolar-depression care) over time for multiple providers and levels of care.

In addition to these quality concerns, bipolar disorder is also costly to treat.[26,29–32] Although studies have produced a range of cost estimates (likely due to differing definitions of bipolar disorder and what constitutes appropriate pharmacotherapy), they have found that treating bipolar disorder is costlier than the care of major depression, diabetes, and other general medical, and psychiatric conditions.[26,29,32,33] Also, treating bipolar depression is costlier than other bipolar diagnoses.[30] However, the literature on bipolar disorder treatment costs does not incorporate measures of quality. Given the changes in the organization and financing of mental health care since the 1990s, as well as changes in treatment technology, it is important to understand not only the costs, but also the value associated with those costs of care.

This study aims to extend this literature by describing the usual outpatient care for enrollees treated for bipolar-I depression in a privately insured population in 1999 and 2000, as well as estimating the costs associated with different levels of treatment quality. We focus on bipolar-I depression, rather than bipolar-I disorder in general, because there is less information about treatment quality for bipolar depression specifically, and because of the added complexity of treating bipolar depression. We hypothesize that a significant proportion of patients will not receive guideline concordant care, and that substantial funds are spent on care not recommended by guidelines.

MATERIALS AND METHODS

Determining the Bipolar-I Cohort

We examined administrative medical and pharmacy claims from MarketScan Medstat data for the years 1998 through 2000, representing a national sample of ~3 million enrollees. Nearly all of the insurance

plans represented in the data were managed and ~60% were managed by a behavioral health carve-out specifically. This study was approved by the Harvard Medical School Institutional Review Board.

We limited the cohort to patients diagnosed with bipolar-I for several reasons. First, other bipolar spectrum disorder diagnoses, with their more subtle clinical presentations, may be less accurate in claims data than would bipolar-I diagnoses. Second, treatment guidelines are less clear as to whether all persons with other bipolar spectrum disorders require maintenance antimanic medication treatment. Further, limiting to bipolar-I enabled us to study the treatment quality and associated costs in a population expected to have more homogeneity in illness severity than a broader bipolar spectrum population.

We included adults between ages 18 and 64. Enrollees 65 or older were excluded because they would be eligible for Medicare, and therefore their claims in the private insurance dataset would be an incomplete reflection of their mental health utilization. Additionally, we limited the sample to those who were also enrolled through year 2000 so that we could continue to observe treatment for depressed phases that began in 1999 but did not end by the end of the calendar year 1999. We further limited our sample to those continuously enrolled for at least 10 months in 1999 and in 2000 (over 90% of the bipolar-I depressed population). Our final cohort was 925 patients.

We employed an algorithm to determine the bipolar cohort. First, we excluded enrollees with at least two claims diagnoses of schizophrenia (ICD-9 codes 295.0–295.9) or a hospitalization for schizophrenia. Next, we selected enrollees with at least two claims for bipolar disorder on different service dates (ICD-9 codes: 296.0, 296.1, 296.4–296.8, 301.11, and 301.13). To minimize false positives but also include persons more difficult to engage in treatment, enrollees with only one bipolar claim were included if it represented (1) an inpatient bipolar disorder discharge diagnosis or (2) an outpatient visit diagnosis, but that one visit accounted for at least 50% of the outpatient mental health visits.

Determining the Bipolar-I Depressed Cohort

Persons in the bipolar cohort who received at least one diagnosis of bipolar-I disorder (ICD-9 diagnostic codes: 296.0, 296.1, 296.4–296.7) were selected into our bipolar-I cohort. The bipolar-I depressed population was determined by the presence of at least one diagnosis of either ICD-9 code 296.5 (bipolar depression) or ICD-9 code 296.2/296.3 (major depression) that followed a bipolar-I diagnosis. We used claims from 1998 to ensure that enrollees with in 1999 diagnoses of major depression but 1998 diagnoses of bipolar-I disorder were included in the cohort. To ensure that we could observe at least the first 4 months

of bipolar-I depression treatment in a given depressed phase (i.e., acute phase treatment, a period expected to have the most intensive treatment needs), enrollees were excluded from the analysis if their depression phase in 1999 did not start by September 1st. Since medication prescribing is an important aspect of bipolar-I treatment quality, our final sample included only enrollees diagnosed with bipolar-I depression by psychiatrists (60–70% of the bipolar-I depressed sample).

Depressed Phase Definition

We defined our depressed phases based on "events" that could be observed in the claims: changes in polarity (or remission), inpatient mental health admissions, and restarts (or disruptions) in treatment.

Depressed phase treatment starts were defined by the first observed bipolar-I depression diagnosis in 1999 following either (1) a claim with a manic diagnosis or (2) no mental health visits (based on CPT procedure codes and ICD9 diagnoses), or psychotropic medication prescribed in the prior 60 days. Sixty days was selected to distinguish real interruptions in treatment from missed appointments, or prescription refills while in active treatment.

Depressed phases were considered to have ended at the first observation of claims with the following: (1) fifth-digit diagnosis code indicating remission; (2) psychiatrist diagnosed change in polarity to the manic spectrum (inpatient or outpatient); (3) a mental health (non-manic) hospitalization; (4) disruption of both mental health visits and medications $\geq$60 days; (5) or an "administrative end" (i.e., December 31, 2000 occurring before the ending of a depressed phase). Subsequent new outpatient-depressed phases were considered to start after the first outpatient claim for depression treatment following an inpatient mental health hospitalization. The final sample of 925 enrollees diagnosed with bipolar-I depression included 1,059 depressed phases.

Co-Occurring Conditions

Co-occurring conditions were determined based on a confirmatory ICD-9 diagnosis in the claims. To conservatively estimate psychiatric co-occurring conditions that may be mistakenly diagnosed instead of bipolar disorder, we limited the definition to include those only diagnosed after the first bipolar-I (manic or depressed) diagnosis. We did not apply this temporal constraint to substance-use disorder diagnoses, because the veracity of a substance-use disorder diagnosis would not be affected by the timing of the bipolar diagnosis. General medical co-occurring conditions included those that may affect bipolar disorder course of illness, treatment choices, or adherence [e.g., cardiac, hypertension, hepatic, renal, thyroid, obesity, diabetes, inflammatory, seizure,

cognitive (i.e., HIV, anoxia, Parkinson's Disease, multiple sclerosis, brain tumors, cerebrovascular accidents, dementias), and pregnancy].

Quality Measures

Since we were examining treatments for new episodes of depression in bipolar disorder, these patients should have been receiving maintenance-phase antimanic agents. Expert recommendations and FDA indications for bipolar disorder treatment have evolved since the care was delivered to this cohort of patients from January 1999 through December 2000. The first antipsychotic to receive an FDA indication for treating mania was olanzapine in November 2000—for acute phase treatment. Further, published expert guidelines did not recommend antipsychotic medications for maintenance-phase antimanic treatment until 2004.[34] Therefore, we developed two sets of quality measures that reflected expert consensus during and after the study years.[2,3,8,34,35] One included only non-dopamine blocking antimanic medications (lithium, valproic acid, or carbamazepine—the standard of care at the time our cohort received treatment) and the other a more inclusive definition of maintenance-phase antimanic medications that included antipsychotics. We also considered whether patients received antidepressants (with and without an antimanic medication) and/or any psychotherapy (family, individual or group) during the depressed phases of treatment.

Treatment Quality Hierarchy

Patients were categorized according to the "best" treatment they received during depressed phases that began in 1999. The treatment categories were sorted into four mutually exclusive hierarchical categories of receiving (1) both guideline-recommended treatment modalities (i.e., antimanic agents and psychotherapy), (2) an antimanic medication but no psychotherapy, (3) no antimanic agent and no antidepressant, or (4) an antidepressant without an antimanic agent. Other medications may have been included in these treatment combinations, but were not considered in the classification scheme since one cannot make a quality statement about their presence or absence. Approximately 10% of the patients had more than one depressed phase in 1999. These patients were categorized according to the phase most consistent with guideline recommendations.

Statistical Analysis

We calculated descriptive statistics of the patient and treatment characteristics (Table 1). Also, we calculated the annualized spending on individual patients for mental health treatment. Total spending included the dollars paid by insurers and cost sharing paid by patients for all mental health treatment services—pharmacy, inpatient and outpatient visits.

TABLE 1

PERSON-LEVEL POPULATION DESCRIPTION (N = 925)

CHARACTERISTICS		
Mean age (SD)	44.4 (11.3)	
	N	%
Female	609	66
Comorbid medical disorder present	600	65
Only 1 comorbid medical disorder	268	29
Any anxiety disorder (post bipolar diagnosis)	94	10
ADHD (post bipolar diagnosis)	20	2
SUD (pre or post bipolar diagnosis)	73	8
Any inpatient mental health	95	10
Inpatient manic	22	2
Inpatient depressed	80	8
Number of depressed phases in 1999		
1	831	90
2	69	7
≥3	25	3
Treatment duration for 1999 in days	Mean	SD
Cumulative bipolar treatment (any phase)	289.2	91.7
Cumulative depressed phase treatment	241.6	99.8

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One patient, despite having several visits coded as CPT procedure 90862, had no spending associated with his/her treatment. Therefore, we imputed for that patient's visits the average cost for code 90862 in our data. Since, patients varied in their duration of follow-up, we standardized spending per patient by calculating annualized spending on mental health treatment. Patients and their associated annualized costs were then sorted according to the treatment quality in their "best" treatment phase.

RESULTS

In this cohort, most of the calendar year was spent in the treatment for bipolar disorder in general (289.2 days, SD 91.7), and ~241.6 days (SD 99.8) were spent on depressed phase treatment specifically (Table 1).

Nearly 90% of the outpatient's depressed phases lasted longer than 30 days (Table 2). When considering the "event" leading to depressed phases ending, the largest proportion (42%) was due to an "administrative end." In other words, there was no "event" observed in the claims to signal its termination through the end of the data in December 31, 2000. The next largest proportion of depressed phases ended due to treatment discontinuity (25%). One-fifth of the depressed phases ended due to a change in polarity to mania during outpatient treatment and

TABLE 2

PHASE-LEVEL DESCRIPTIONS (*N* = 1,059 DEPRESSED PHASES)

	N	%
Outpatient depressed phases with duration >30 days	938	88.6
Why Depressed Phases End?		
Remission	22	2
Inpatient manic	24	2
Inpatient depressed	98	9
Outpatient manic	209	20
Treatment break (medications and visits) >60 days	262	25
Treatments Received During Depressed Phases		
Any antimanic medication	739	70
Non-dopamine blocking (lithium, valproic acid, carbamazepine)	655	62
Antipsychotic as sole antimanic medication	84	8
D2 antagonists	22	2
Second generation	69	6
Any antipsychotic	350	33
D2 antagonists	98	9
Second generation	298	28
Any antidepressant	784	74
Medication combinations		
Any antimanic medication + antidepressant	597	56
Non-dopamine blocking antimanic	529	50
Antipsychotic	68	6
Psychotherapy		
Any	802	76
Individual	787	74
Group	55	5
Family	71	7

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2% ended due to a manic hospitalization. An additional 9% ended in a hospitalization due to depression. Few (2%) were coded as remitted.

Seventy percent of the depressed phases included treatment with any antimanic medication; largely non-dopamine blocking antimanic medications (62%) (Table 2). Nearly three-quarters of the depressed phases included antidepressant treatment, but 24% of those phases with antidepressants did not include prescriptions for an antimanic medication. Although antipsychotics were used in one-third of the depressed phases, they were not commonly the sole antimanic agent (8%). Most antipsychotic use, whether as sole antimanic agent or not, was second generation. Over three-quarters of the depressed phases included some form of psychotherapy, largely individual.

Tables 3 and 4 describe how the cohort sorted in terms of the "best" treatment received during a depressed phase beginning in 1999. Table 3

TABLE 3

COSTS FOR ANNUALIZED TREATMENT (ANTIPSYCHOTICS NOT INCLUDED AS ANTIMANIC AGENT)

TREATMENT COMBINATION											
ANTIMANIC AGENT[a]	PSYCHOTHERAPY	ANTIDEPRESSANT	*N*	PERCENTAGE OF *N*	$	PERCENTAGE OF TOTAL COST	MEAN	SD	MEDIAN	2.5%	97.5%
+	+	+/−	467	50	2,270,621	62	4,862	5,906	3,085	434	18,396
+	−	+/−	137	15	369,655	10	2,698	3,795	1,537	163	17,948
−	+/−	−	100	11	257,941	7	2,579	5,784	804	91	15,158
−	+/−	+	221	24	755,678	21	3,419	4,282	2,251	308	15,232
Total			925		3,653,895		3,950	5,346	2,354	182	16,762

[a]Non-dopamine blocking.

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TABLE 4

COSTS FOR ANNUALIZED TREATMENT (ANTIPSYCHOTICS INCLUDED AS ANTIMANIC AGENT)

TREATMENT COMBINATION											
ANTIMANIC AGENT[a]	PSYCHOTHERAPY	ANTIDEPRESSANT	*N*	PERCENTAGE OF *N*	$	PERCENTAGE OF TOTAL COST	MEAN	SD	MEDIAN	2.5%	97.5%
+	+	+/−	521	56	2,617,740	72	5,024	5,907	3,227	452	18,396
+	−	+/−	140	15	372,589	10	2,661	3,763	1,508	163	17,948
−	+/−	−	89	10	212,277	6	2,389	5,924	685	91	15,158
−	+/−	+	175	19	450,864	12	2,576	3,245	1,752	289	13,931
Total			925		3,653,895		3,950	5,347	2,354	182	16,762

[a]Any antimanic agent (dopamine blocking or not).

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describes categories based on pharmacotherapy guideline recommendations during 1999 and 2000 (i.e., receiving a non-dopamine blocking antimanic medication); Table 4 describes the more liberal definition of antimanic medications (i.e., including antipsychotics), consistent with more contemporary guidelines. Nearly 72% received any antimanic medication, whereas 65% received a non-dopamine blocking antimanic medication specifically. Among those who received a non-dopamine blocking antimanic medication, the duration of prescribing was 239 days in 1999 (SD 117) (data not shown), which amounts to over 80% of the time spent in bipolar-I treatment. Only 50% of the cohort received the most guideline-concordant treatment combination (i.e., both a non-dopamine blocking antimanic medication and psychotherapy). Including the people who received an antipsychotic added an additional 6%.

The median annualized treatment cost per person was $2,354 (mean $3,950, SD $5,346). Including antipsychotic medications as antimanic agents in the treatment categories increased the mean and median costs of antimanic treatment (not surprising, given that most of the antipsychotics used were second generation). Considerable resources were spent on care not recommended by expert guidelines. Depending upon whether one considers antipsychotic medications as acceptable maintenance-phase antimanic treatment in the depressed phase, between 18 and 28% of the mental health costs went toward treatment that did not include any antimanic medication: two-thirds to three-quarters of which was spent on care that included an antidepressant in the absence of an antimanic agent.

DISCUSSION

The analysis describes a mixed picture regarding the quality of care received by persons with bipolar-I depression. It is important to consider these results in the context that we used a liberal interpretation of the guidelines when constructing these measures of "best treatment" (i.e., receiving at least one psychotherapy session or at least one non-dopamine blocking antimanic medication prescription).

Throughout the year, only approximately half of the patients received treatment most compatible with the guideline recommendations (i.e., both antimanic medications and psychotherapy). A quarter of the outpatient's depressed phases ended due to a break in treatment for at least 2 months. Only approximately two-thirds received pharmacotherapy consistent with contemporary guideline recommendations; liberalizing the definition of acceptable antimanic medications to include all antipsychotics increased this number to nearly three-quarters.

Nearly three-quarters of the depressed phases included some psychotherapy [but few received family psychotherapy (<7%)]. We cannot

determine from the claims data if the psychotherapy received was consistent with the psychotherapies that have demonstrated efficacy in clinical trials. However, receiving at least some psychotherapy allows the possibility that these patients who have a chronic and disabling illness received needed educational and psychotherapeutic treatment. Prior research by this investigator group using similar Medstat data found that the proportion of persons with bipolar-I disorder receiving any psychotherapy has declined since 1991.[36] Thus, while it appears to be a more positive finding that many of these depressed phases included at least some psychotherapy, further research is needed to determine if rates for bipolar-I depression psychotherapy are declining as well.

Approximately half of the depressed phases were treated with both an antidepressant and a non-dopamine blocking antimanic medication, whereas only 12% with only a non-dopamine blocking antimanic medication (i.e., no antidepressant). Given the often persistence of depressive symptoms, more limited treatment options for persons with bipolar-I depression in 1999 and 2000, and uncertainty in the literature about prescribing antidepressants for patients with bipolar disorder, it is not surprising that a high proportion of those who are on antimanic medications also received an antidepressant. Possibly, with the availability of newer medication and psychotherapy options, and even newer evidence that antidepressants may not be efficacious in treating bipolar depression,[9] this practice pattern is changing.

Twenty percent of these depressed phases ended due to a change in polarity that occurred in the outpatient setting. This is particularly important when one considers that often in mental health quality of care studies using claims data, illness instability is measured by looking at the hospitalization rates. In this cohort, if hospitalization was the only marker of instability examined, then a considerable amount of symptom instability would go unnoticed. Thus, this observation has important implications for bipolar disorder quality assessment using claims data analyses.

As much as 28% of the mental health costs for this population went toward care that did not meet professional guideline standards—and 12–21% were costs for care that experts have deemed to be potentially harmful. We considered the possibility that these patients were possibly more likely to have entered our depressed cohort by inpatient claims and did not transition to outpatient care (thus their costs would be high but we would not observe outpatient treatments that met our quality standards). However, post hoc analyses indicated that patients whose treatment was most concordant with guidelines were more—not less—likely to have been hospitalized (non-dopamine blocking antimanic medication $\chi^2 = 6.6$, d.f. $= 2$, $P = .04$; any antimanic medication: $\chi^2 = 12.4$, d.f. $= 2$, $P = .002$).

A limitation of claims data is that we cannot observe all elements of the clinical history that could dictate treatment and clarify the extent that patients received appropriate care. For example, some patients in our sample who did not receive an antimanic agent may have been stable from a mania perspective (i.e., no manic episode over the past 20 years) and remained free of mania while receiving medications not considered traditional mood stabilizers such as clonazepam or clonidine. Similarly, patients who did not receive psychotherapy during an episode of bipolar depression may have been those who were quickly responsive to medication changes to treat the depressive symptoms. Our observation that patients who received both psychotherapy and antimanic agents were more frequently hospitalized than patients who did not receive both is consistent with this hypothesis that deviations from guideline recommendations may be related, in part at least, to patients' stability. However, it is also important to consider that bipolar depression is often treatment resistant[37–40] and that we would expect poor outcomes in many bipolar-I patients who do not receive a mood stabilizer.[41–44] Therefore, while some of these results may be consistent with tailoring treatment to patients needs, it is more likely that for an overwhelming proportion they represent poor care.

Our data reflect similar spending on mental health treatment when compared with several published studies of bipolar disorder, including a study using data from care delivered in 2004[26,32,33]—a time in which more second-generation antipsychotic medications were receiving FDA approval for acute and maintenance-phase bipolar disorder treatment. These studies were similar to ours in that they used administrative data from multiple health plans, employers, and regions of the United States, as well as similar case finding and treatment definitions. However, two prior studies found considerably lower costs but are not directly comparable with ours due to differing methodology, such as a more limited geographical distribution of enrollees or not including all mental health treatment costs.[29,30]

One potential limitation of this study is our use of administrative data to determine the cohort, which raises the concern of diagnostic accuracy in claims data. However, previous comparisons in a privately insured population found substantial agreement (94%) between claims diagnoses of bipolar disorder and chart review, and that claims data have demonstrated validity in analyses utilizing a bipolar diagnosis to establish the cohort and assess population-based quality of care.[45,46] Additionally, our analysis utilized a more stringent algorithm of the claims data than these studies to determine our bipolar cohort. Even though we did not determine the accuracy bipolar depression diagnoses specifically in the claims data (and to our knowledge there are no published reports on this either), studies examining the agreement between administrative

data and either structured clinical interview or chart review have found fair agreement for depressive disorders.[47,48]

Additionally, we cannot directly observe symptoms in administrative data. Although typically our definition of depressed outpatient treatment phase ends were based on events such as hospitalization, changes in polarity, a gap in treatment, or ICD-9 coding indicating remission, our estimated duration of bipolar-I depression-specific treatment would be inflated if depressive symptoms had resolved but the diagnosis was not coded to a fifth-digit indicating remission. Thus, our estimates of depressed phase duration should be considered as an "upper bound".

Our analysis took into consideration that since 1999 and 2000 (when this cohort received treatment), FDA indications and clinical guidelines have evolved such that antipsychotic medications (particularly second generation) are increasingly acceptable as maintenance monotherapy antimanic medications. In our cohort, most antipsychotic prescribing was in conjunction with a traditional mood stabilizer, not as stand-alone maintenance antimanic treatment. However, analyses conducted by members of this investigator group using data from the Systematic Treatment Enhancing Program for Bipolar Disorder (STEP-BD) study during years 2001 through 2004 indicate that for patients with bipolar-I disorder, there was neither increased likelihood of receiving any antimanic agent over time nor an increased likelihood of receiving an antipsychotic as antimanic monotherapy.[49] Additionally, our antimanic medication rates, hospital rates, and mean mental health costs were similar to a bipolar disorder usual care study examining care as recent as 2004.[50] Thus, we have reason to believe that the practice patterns and costs we observed in this study have persisted at least through 2004. Still, an important area of future research would be to examine current treatment patterns relative to second generation antipsychotic use and maintenance antimanic monotherapy for bipolar-I disorder.

CONCLUSION

This study provides new information regarding the longitudinal quality and costs of care for bipolar depression. A sizable proportion of the treatment dollars spent on persons with new episodes of bipolar-I depression went toward care that did not meet the standards of practice guidelines—and much of that represented treatment advised against by guidelines because it could worsen the course of the illness. This observation provides an important clinical and policy opportunity to redirect resources to be consistent with practice guideline standards. This study also provides evidence that when conducting studies using administrative data, hospital admissions alone do not adequately describe affective instability for patients with bipolar disorder, since much switch in

polarity occurred in the outpatient setting. This knowledge is useful to researchers and policy makers when using administrative data in conducting quality assessment for systems of care. ✤

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