Use of Administrative Data to Identify Health Plan Members With Unrecognized Bipolar Disorder: A Retrospective Cohort Study

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Objective: This retrospective cohort study used an algorithmic case-finding system on claims data from nationwide commercial health plans to validate previously identified predictors of unrecognized bipolar disorder among adults.

Study Design: Retrospective cohort design.

Methods: Using logistic regression, 2 claims data sets were evaluated to explore potential predictors; the first included claims for all healthcare encounters (all-encounters data set); the second excluded mental health provider claims (carve-out data set). A total of 280 244 members aged 18 to 64 years were included from 2 commercial health plans.

Results: Claims related to attention deficit-hyperactivity disorder, depression, depression treated with antipsychotics, use of 3 (of 5) classes of psychotherapeutic drugs, younger age, and sex were all significant predictors of a subsequent diagnosis of bipolar disorder. In the all-encounters data set, a predicted value of 5% or greater yielded a sensitivity of 9.8% and a specificity of 99.9%; a predicted threshold of 3% increased sensitivity to 20.7%; area under the receiver operating characteristic curve (AUC) was 0.82. Performance of the model was acceptable in the carve-out data set, with AUC 0.69.

Conclusions: The case-finding system described here, which compares favorably with other screening tests used in primary care, may have significant value in helping physicians to identify patients with unrecognized bipolar disorder.

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Bipolar disorder is a chronic, disabling mental illness that can have devastating consequences for the patient and poses a substantial burden to the healthcare system. Although bipolar disorder is relatively uncommon, patients with the disorder utilize disproportionate medical and psychiatric healthcare resources.[1,2] Proper treatment of bipolar disorder can prevent psychosocial morbidity and relapses, although patients must be followed closely and treatment regimens may require ongoing adjustment.[3-5]

The prevalence of bipolar disorder is difficult to determine, in large part because of controversy and lack of clarity regarding diagnostic criteria. The diagnosis of bipolar I, characterized by a frank manic episode, is less ambiguous than the diagnosis of bipolar II, which depends on accurate characterization of a hypomanic episode. Whereas estimates of the lifetime prevalence of bipolar disorder range from 1%[6] to 11%[7] across studies, prevalence estimates for clearly defined bipolar disorder I and II generally fall in the range of 1% to 4%, with bipolar I clustering around 1%.

Bipolar illness is frequently misdiagnosed or unrecognized. In 1 survey, 70% of patients with bipolar disorder reported being misdiagnosed at some point,[8] often with major depression. Another study found that on average 8 years elapsed between initial presentation and diagnosis.[9] Such diagnostic and treatment delays can lead to poor outcomes.[10] Inappropriate treatment for (misdiagnosed) unipolar depression may exacerbate symptoms and induce cycling to mania or hypomania.[7,11] Furthermore, retrospective analyses indicate that healthcare costs may be higher for bipolar patients whose diagnosis is delayed.[12,13]

Because earlier identification of bipolar disorder could lead to improved outcomes and lower costs, innovative methods to facilitate its early identification are needed. One recently developed tactic is case-finding systems using standardized claims, prescription fills, and laboratory results data with clinical algorithms to identify patients whose medical care appears to deviate from accepted standards. Such a system can be used to screen large numbers of claims for various treatment patterns that may indicate a missed bipolar disorder diagnosis, prompting contact with the healthcare provider for secondary screening with a brief questionnaire. Several such questionnaires have been validated to screen for bipolar disorder in primary care settings, including the Mood Disorders Questionnaire[14] and the Hypomanic Personality Scale.[15] These instruments have proven useful for identifying patients who may have

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bipolar disorder, but first the physician must consider the diagnosis. A reasonably effective claims-based screening tool could help primary care physicians identify the up to 30% of patients with affective disorders who may have bipolar disorder.[16]

In a previous exploratory case-control study (unpublished), we tested the ability of several claims-codable characteristics (developed by a panel of bipolar disorder experts) to discriminate healthplan members with bipolar disorder from members with unipolar depression or neither diagnosis. We found that diagnoses or medications for unipolar depression, psychotic depression, attention deficit-hyperactivity disorder (ADHD), conduct or impulse control disorders, and prescriptions for multiple classes of psychotropic medications were significant discriminators.

The purpose of this study was to replicate our previous findings using a retrospective cohort design on 2 nationwide commercial health plan claims data sets: 1 including all encounters and 1 with a mental health "carve-out" (missing encounters with the identified mental healthcare system, but not prescriptions). These 2 databases reflected 2 common managed care scenarios and allowed us to replicate the predictive accuracy with mental health services "carved in" and extend the findings to the mental health "carved out" scenario. This study assessed the accuracy of a predictive model of bipolar disorder based on claims clues.

METHODS

To construct and validate the predictive model, we utilized "claims clues" developed by a bipolar disorder expert consensus panel and tested in the previous case-control study. The current study extended the previous findings in additional data sets, using a retrospective cohort design.

Data

The present study utilized the variables from the development study in 2 different data sets representing 2 common mental health payment scenarios: an *all-encounters data set* and a *mental health carve-out data set.* The carve-out data set excluded claims from mental health providers; both included all filled prescriptions. Both data sets contained only members of commercially insured nationwide health maintenance organizations or preferred provider organizations aged 18 to 64 years as of January 1, 2001, who were continuously enrolled from January 1, 2000, through September 30, 2003. The all-encounters set contained all claims for 40 244 members who met the age and enrollment criteria. The carve-out set, representing a different health plan, contained all noncarved-out claims and all prescription fills for 240 000 members who met the age and enrollment criteria.

Procedures

For each data set, we defined an *antecedents period* as containing claims with dates of service in 2000, and a *recognition period* as containing claims with dates of service from January 1, 2001, through September 30, 2003. The algorithmic case-finding system was designed to search for "bipolar clues" in claims from the year 2000, from the standpoint of January 1, 2001.

For the all-encounters set, which included mental health providers' claims, we defined the term "bipolar disorder" based on the presence of at least 2 claims for bipolar disorder (*International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM]* codes 296.1, 296.4-296.8). For the carve-out set, we defined bipolar disorder as the presence of at least 2 claims for bipolar disorder, at least 2 claims for lithium, or at least 2 claims for valproic acid derivatives unless the patient had a claim for any of the following diagnoses: migraine (346.xx); epilepsy (345.xx); convulsions (not otherwise specified) (780.39); undersocialized conduct disorder, aggressive type (312.34); or isolated explosive disorder (312.35). This medication-inclusive definition of bipolar disorder was used to capture individuals with bipolar disorder in the carve-out set who might not have claims with a bipolar disorder diagnosis from providers outside the mental health carve-out.

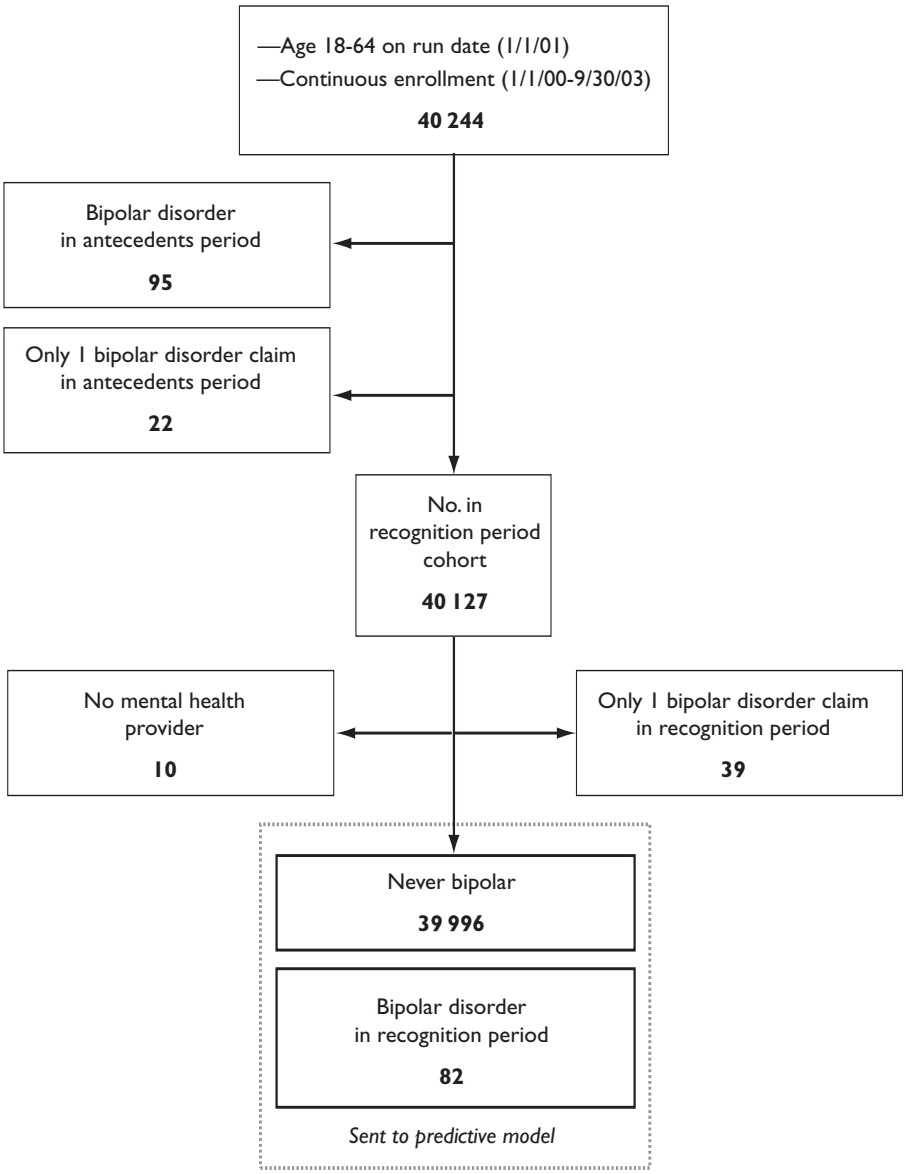
To increase the diagnostic specificity, several types of individuals were excluded from the analysis: individuals with preexisting bipolar disorder, a single bipolar diagnosis during the antecedents period, or only a single bipolar diagnosis during the recognition period. **Figures 1** and **2** describe the categorization based on these restrictions. In the all-encounters data set we considered individuals to have bipolar disorder only when their diagnoses were made by a mental health provider, based on the following criteria: (1) at least 1 hospitalization with a diagnosis in the mental health ICD cluster or (2) at least 2 claims with a CPT code between 90801 and 90899.

In both data sets the base-rates of newly diagnosed bipolar disorder were low. For the all-encounters data set 82 (0.20%) members were identified as having bipolar disorder during the recognition period. For the carve-out set, 1081 (0.45%) members were identified as having bipolar disorder during the recognition period.

Construction of the Predictive Model

A production algorithmic case-finding system (the CareEngine[SM] System, Active Health Management, Inc,

Figure 1. Allocation of Members—All-encounters Data Set



New York) was used to identify possibly unrecognized cases of bipolar disorder. The system applied clinical rules to healthcare encounter claims (*ICD-9-CM* codes), prescription fills (National Drug Codes), age, and sex. All members in each data set who did not have a bipolar disorder diagnosis during the antecedents period were loaded into the case-finding system and evaluated from the standpoint of January 1, 2001. The system evaluated each member using claims with dates of service from January 1, 2000, through December 31, 2000 (the antecedents period), searching for the presence of predictor variables.

For each data set, we also used logistic regression[17] (SPSS V.11, Chicago, Ill) to predict new bipolar diagnosis during the recognition period using all the predictor variables as well as age and sex. For the all-encounters data set 2 variables (impulse control and conduct control disorders) were removed because they were not positive for any of the 82 individuals with a new diagnosis of bipolar disorder; therefore the equation could not be fit with them. Because all of the predictors had been selected based on expert opinion and previously substantiated, we constructed an all-predictors model (regardless of statistical significance). In each data set the model performance was further characterized as area under the curve (AUC) of the receiver operating characteristic (ROC) curve.[18]

RESULTS

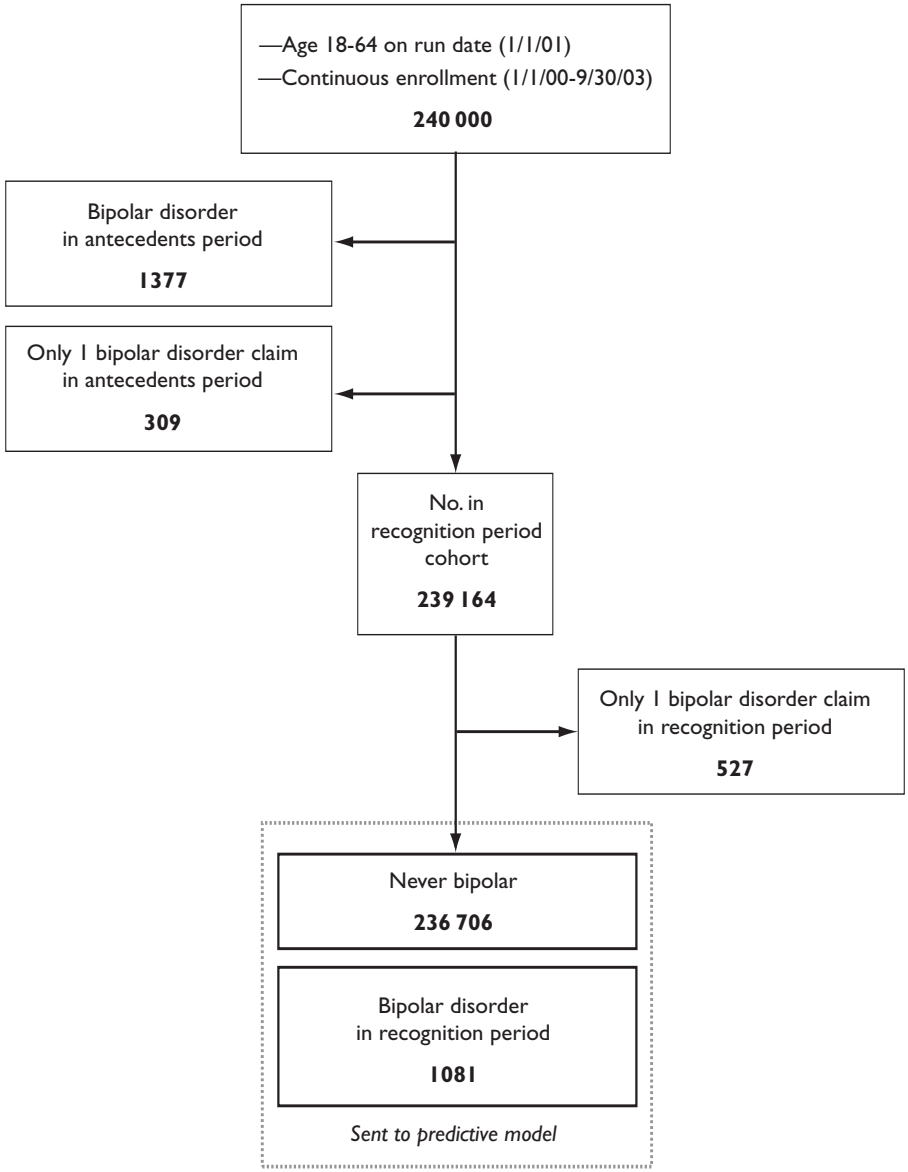
The predictor variables entered into the case-finding system are listed in **Table 1.** In the *all-encounters data set,* no individuals with bipolar disorder diagnosed during the recognition period exhibited the impulse control, conduct disorder, or substance abuse variables. In multivariate logistic regression entering all remaining variables, sex, age, use of 3 (of 5) psychotherapeutic medications, and depression were found to be independently predictive of subsequent recognition of bipolar disorder. Gender was found to have opposite associations in the data sets with subsequent recognition of bipolar disorder, as shown in **Table 2:** negative for the "carve-out" but positive in the "all encounters." The other significant associations appeared in the same direction in both data sets.

Table 2 shows the regression equation fitted from the variables representing those triggered by any patient with bipolar disorder in the all-encounters set, plus sex and age. The overall performance of the model on the all-encounters set can be expressed by the AUC of the

ROC curve. The AUC for the model on the all-encounters set was 0.82 (95% confidence interval [CI], 0.76-0.87). In the larger *carve-out data set,* recognition period patients with bipolar disorder triggered all candidate variables. Although this model did not fit as well to the carve-out set, performance was significantly better than chance, with an AUC of 0.69 (95% CI, 0.67-0.70).

For the all-encounters data set, a threshold of 5% predicted probability of bipolar disorder found 8 of the 82 individuals with bipolar disorder (ie, a sensitivity of 9.8%) and correctly identified 39 940 of the 39 996 individuals without bipolar disorder (for a specificity of 99.9%). Reducing the detection threshold to 3% increased the sensitivity to 20.7%, with 99.4% specificity; however, the number of positive tests needed to identify a case increased from 8 using the 5% threshold to 15.6 with the 3% threshold.

Figure 2. Allocation of Members—Carve-out Data Set



DISCUSSION

The purpose of this study was to create a practical predictive model to support identification of unrecognized bipolar disorder using claims data from commercially insured adults and an algorithmic case-finding system. Using claims for adult members (continuously enrolled for 3.75 years) of 2 commercial health plans, we developed and validated a predictive model based on claims-coded rules for identification of unrecognized bipolar disorder developed by a bipolar expert panel and substantiated in a previous case-control study. The goal of the model was to predict subsequent recognition of bipolar disorder in individuals with no evidence of the disorder during the first year. We validated the model in 2 common scenarios relating to how health plans pay for mental health services. An *all-encounters data set* contained claims for all encounters; a *carve-out data set* excluded claims from mental health providers; both included all prescriptions.

The model demonstrated that in both data sets, sex, age, history of ADHD, psychotic depression, history of use of multiple categories of psychotherapeutic medication, and depression were significantly associated with the subsequent recognition of bipolar disorder. An unexpected finding was that sex was a negative association for "carve-out" but positive for "all-encounters." We postulate that this perplexing finding may relate to the differences in our operational definitions for bipo-

Table 1. Predictor Variables Used by the Case-finding System

Predictor Variable	Operational Definition
ADHD by medications or diagnostic codes	At least 2 claims for ADHD *or* at least 2 claims for an ADHD medication*
Poor response of ADHD to treatment	ADHD (above) and use of 2 or more categories of ADHD medications*
Psychotic depression by medications or diagnostic codes	At least 2 claims for depression or at least 2 claims for medication predominantly used in depression,* plus antipsychotic medication
Prescription of 3 of 5 classes of psychotherapeutic medication	Classes—anticonvulsants, anxiolytics, antidepressants, lithium, antipyschotics (at least 2 claims for each qualifying medication)
Conduct disorder	At least 2 claims (312, 312.0x-312.2x, 312.4x, 312.8x, 312.9x, 313.81)
Impulse control disorder	At least 2 claims (312.3, 312.31, 312,32, 312.34, 312.35)
Significant anxiety disorder	At least 2 claims for excitative-type psychoses (298.1x) or anxiety states (300.0x)
Substance abuse disorder	At least 2 claims (304.xx, 305.xx except 305.1x)
Depression	At least 2 claims for depression (296.2x, 296.3x, 298.0x, 300.4x, 311.xx) or at least 2 claims for medication predominantly used in depression*
Depression and variable: depression and any other single-condition predictor variable	Depression by ICD or meds

Numbers in parentheses indicate *ICD-9-CM* codes. The presence of "x"in an ICD code indicates that any digit, or none, may occupy that place.
*Medication classes used to define "ADHD" included amphetamines, dexmethylphenidate, dextroamphetamine, methylphenidate, and pemoline. Antipsychotic medications included chlorpromazine, clozapine, haloperidol, loxapine, mesoridazine, thioridizine, thiothixene, trifluoperazine molindone, perphenazine, pimozide, olanzapine, quetiapine, risperidone, and ziprasidone. Medications used to define depression included selective serotonin reuptake inhibitors (SSRI); monamine oxidase inhibitors (MAOI), Wellbutrin (only this brand of bupropion), mirtazapine, venlafaxine.
ADHD indicates attention deficit-hyperactivity disorder; *ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification.*

lar disorder, the sequestration of claims in the carved-out mental health networks, or differences in the populations. In the carve-out data set we used a less stringent definition (based on any bipolar diagnoses or specific patterns medication use; see Methods section) that yielded a newly diagnosed bipolar disorder base-rate of 0.45%, whereas in the all-encounters data set we used a more stringent definition of 2 bipolar claims by mental health providers that yielded a base-rate of only 0.20%.

Performance of the algorithmic case-finding system was acceptable for a primary screening tool with low risk of misidentification of false positives, as shown by a sensitivity of 9.8% and a specificity of 99.9% using a predicted diagnosis threshold of 5%, and a sensitivity and specificity of 20.7% and 99.4%, respectively, using a 3% threshold in the carve-out set. Sensitivities in the all-encounters set were slightly higher. A lower sensitivity was expected in the carve-out set, in which some cases of bipolar disorder were identified by relatively (but not completely) specific mood stabilizer therapy. Nevertheless the area under the ROC curve, a test performance measure relating the calculated probability to each individual's actual state, was highly significantly better than chance. The AUC indicated that 82% of the time the model would accurately discriminate a randomly selected individual with bipolar disorder from a randomly selected individual without bipolar disorder. Although individuals in clinical practice who screen positive for bipolar disorder based on this predictive model will in fact have it much less frequently (because of the condition's low prevalence), the positive predictive values at the 5% and 3% prediction thresholds in our study compare favorably with those of many commonly advised primary care screening tests.[19-21] Further improvement of the model's performance with a prospective study could reduce the number needed to secondary screen and capture more individuals with bipolar disorder.

This study looked for subsequent recognition of bipolar disorder during a relatively short prediction interval, 2.75 years. Although this strategy was practical given the turnover commonly observed in health plans, this amount of time may be less than is commonly needed to make an accurate diagnosis,[9] and therefore the possibility exists that more diagnoses of bipolar disorder might have been made with a longer recognition period. Nevertheless, the prevalence of bipolar diagnosis in the mental health carve-out data set was approximately 1%, similar to the preva-

Table 2. Logistic Regression for the 2 Data Sets: All-variables Model

	All-encounters Data Set		Carve-out Data Set	
Indicators	**Coefficient**	**Odds Ratio (95% CI)**	**Coefficient**	**Odds Ratio (95% CI)**
ADHD by *ICD* or medications	0.36	1.43 (0.24, 8.41)	1.198	3.31 (2.30, 4.77)
Poor response of ADHD to treatment	0.50	1.64 (0.10, 27.65)	–0.490	0.61 (0.08, 4.60)
Psychotic depression	0.22	1.247 (0.30, 5.20)	1.630	5.11 (3.52, 7.40)
Use of 3 (of 5) categories of psychotherapeutic medications	2.70	14.90 (3.86, 57.54)	0.31	1.37 (0.59, 3.17)
Conduct disorder	None among patients with BD		–0.41	0.66 (0.09, 4.71)
Impulse control disorder	None among patients with BD		1.58	4.84 (0.56, 41.97)
Anxiety	0.70	2.02 (0.78, 5.20)	0.37	1.45 (1.04, 2.03)
Substance abuse	None among patients with BD		1.25	3.47 (2.26, 5.33)
Depression by *ICD* or medications	2.75	15.58 (9.62, 25.23)	2.04	7.70 (6.72, 8.83)
Age category (Nine 5-year categories: 60-64 years = 0; 18-24 years = 8)	0.22	1.251 (1.13, 1.37)	0.06	1.06 (1.03, 1.09)
Sex (female = 1)	0.68	1.972 (1.19, 3.26)	–0.25	0.78 (0.69, 0.88)
Constant	–8.40		–5.91	

ADHD indicates attention deficit-hyperactivity disorder; BD, bipolar disorder; CI, confidence interval; *ICD, International Classification of Diseases* ; No bipolars, the all-encounters data set contained no bipolar individuals who triggered indicators for conduct disorder, impulse control disorder, or substance abuse). Statistically significant at $P < .05$.

lence cited in epidemiological studies for bipolar I.[6] Furthermore, the time during which claims were examined was sufficient to yield impressive sensitivity and specificity estimates in identifying people who were later recognized as having bipolar disorder.

It may be impractical to execute a claims-based study on a longer-term continuous health plan enrollment data set. A prospective study would address the often-cited diagnostic delay associated with bipolar disorder, as well as the issue of error in ICD coding by physicians.[22-24] Discrepancies across claims-based studies may also be related to differences in criteria for determining who had bipolar disorder. For example, in some claims-based studies, bipolar disorder is defined as a single ICD code and sometimes as a single prescription for a mood stabilizer, without exclusionary diagnoses in the case of valproic acid derivatives. In this study, more rigorous criteria were used to define bipolar disorder, including the absence of exclusionary diagnoses.

Determining a "diagnosis" of ADHD or depression during the antecedents period using medications commonly prescribed for these conditions might yield false-positive ADHD or depression "diagnoses," as these medications may be used to treat other conditions (eg, bupropion for smoking cessation). However, the accuracy of the claims-based ADHD and depression diagnoses is not of primary importance for the predictive model; it is the ability of these claims-based ADHD and depression "diagnoses" to accurately predict missed bipolar disorder that is crucial.

With any screening test, it is important to consider the potential burden of screening results on the physician and the healthcare system. At a predictive threshold of 5% probability (from the regression equation), of 1000 patients identified from the predictive model, 125 would have bipolar disorder; of 1000 patients with bipolar disorder, 98 would be found and 902 missed; the number needed to subject to secondary screening (NNS) to identify 1 case of bipolar disorder would be 8. At the 3% threshold, of 1000 identified from the predictive model, 64 would have bipolar disorder; 207 of 1000 with bipolar disorder would be accurately identified; and NNS would be 15.6. Thus the predictive "score" or threshold could be set to find a reasonable proportion of cases without undue burden, with the knowledge of the likely proportion of missed cases.

METHODS

Early identification and proper treatment of bipolar disorder can reduce healthcare cost and work-loss, and improve psychosocial function. A shorter diagnostic delay means less opportunity for inappropriate treatment (eg, antidepressant monotherapy, which can hasten the switch to mania). Further, delayed treatment is associated with worse outcome.[10] Early identification is also important from the health plan perspective. In the United States alone, the total lifetime cost of care for individuals with bipolar disorder with onset of illness in 1998 was $24 billion.[25] During a 1-year period, patients with bipolar disorder were found to cost nearly 4 times more than age- and sex-matched individuals without the illness ($7663 vs $19 622). The situation is exacerbated for patients with unrecognized bipolar disorder, who have been shown to have higher rates of hospital use and attempted suicide compared with patients with recognized bipolar disorder. Thus, it is reasonable to expect that care providers and health plans could substantially benefit from the use of a predictive model or case-finding algorithm.

Given the routine underrecognition of bipolar disorder, its devastating consequences for patients, and its significant cost to health plans, a case-finding algorithm that could be used to identify patients with risk factors early in the disease course would be expected to contribute substantially to the management of bipolar disorder. Such a system, based on readily available administrative data, has real-world practicality and can be used to screen millions of claims in a day. Indeed, such systems are beginning to see widespread implementation for other conditions.

We propose that such a system could be used to sort individuals identified into 2 levels of intervention based on their predicted likelihood of having bipolar disorder. For example, physicians of patients predicted at greater than 5% risk by regression equation could receive a validated brief screening tool (such as the Mood Disorders Questionnaire); physicians of individuals who triggered a 3% risk by regression equation might receive a recommendation to consider the diagnosis and might be urged to use the screening tool if the physician considers the diagnosis a possibility. We hypothesize that such a system could considerably reduce the biopsychosocial and financial costs of unrecognized bipolar disorder. Prospective studies with a large number of claims and clinical follow-up of identified patients will be needed to determine the actual effect of a case-finding system.

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