Is Bipolar Disorder Overdiagnosed?

Mark Zimmerman, M.D.; Camilo J. Ruggero, Ph.D.;
Iwona Chelminski, Ph.D.; and Diane Young, Ph.D.

Objective: Bipolar disorder, a serious illness resulting in significant psychosocial morbidity and excess mortality, has been reported to be frequently underdiagnosed. However, during the past few years we have observed the emergence of an opposite phenomenon—the overdiagnosis of bipolar disorder. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project, we empirically examined whether bipolar disorder is overdiagnosed.

Method: Seven hundred psychiatric outpatients were interviewed with the Structured Clinical Interview for DSM-IV (SCID) and completed a self-administered questionnaire, which asked the patients whether they had been previously diagnosed with bipolar or manic-depressive disorder by a health care professional. Family history information was obtained from the patient regarding first-degree relatives. Diagnoses were blind to the results of the self-administered scale. The study was conducted from May 2001 to March 2005.

Results: Fewer than half the patients who reported that they had been previously diagnosed with bipolar disorder received a diagnosis of bipolar disorder based on the SCID. Patients with SCID-diagnosed bipolar disorder had a significantly higher morbid risk of bipolar disorder than patients who self-reported a previous diagnosis of bipolar disorder that was not confirmed by the SCID ($p < .02$). Patients who self-reported a previous diagnosis of bipolar disorder that was not confirmed by the SCID did not have a significantly higher morbid risk for bipolar disorder than the patients who were negative for bipolar disorder by self-report and the SCID.

Conclusions: Not only is there a problem with underdiagnosis of bipolar disorder, but also an equal if not greater problem exists with overdiagnosis.

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Received Nov. 1, 2007; accepted Dec. 24, 2007. *From the Department of Psychiatry and Human Behavior, Brown Medical School, and the Department of Psychiatry, Rhode Island Hospital, Providence, R.I.*

The authors report no financial affiliations or other relationships relevant to the subject of this article.

Corresponding author and reprints: Mark Zimmerman, M.D., Bayside Medical Center, 235 Plain St., Providence, RI 02905 (e-mail: mzimmerman@lifespan.org).

Bipolar disorder is a serious illness resulting in significant psychosocial morbidity and excess mortality. During the past few years, a series of research reports, reviews, and commentaries have suggested that bipolar disorder is underrecognized and that many patients, particularly those with major depressive disorder, have, in fact, bipolar disorder.[1–10] Even for those patients diagnosed with bipolar disorder, the lag between initial treatment seeking and the correct diagnosis is often more than 10 years.[11,12] The treatment and clinical implications of the failure to recognize bipolar disorder in depressed patients include the underprescription of mood stabilizing medications, an increased risk of rapid cycling, and increased costs of care.[4,13–15] Recommendations for improving the detection of bipolar disorder include careful clinical evaluations inquiring about a history of mania and hypomania and the use of screening questionnaires.[1,7,8,16]

During the past decade, we have established a clinical research assessment laboratory in which we have incorporated semistructured diagnostic interviews into an outpatient clinical practice. One of the goals of the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project has been to examine diagnostic accuracy and recognition, and several of our initial articles identified problems with the detection of comorbid disorders in clinical practice.[17–20] It became apparent to us soon after initiating the MIDAS project that many more diagnoses were made with a semistructured interview compared to an unstructured clinical evaluation, and a comparison of diagnostic frequencies based on both assessment methods confirmed our clinical impressions.[17–20] Our initial reports documenting the underdetection of diagnostic comorbidity have been subsequently replicated in other settings.[21–23]

With regards to the diagnosis of bipolar disorder, during the past few years we have observed the emergence of an opposite phenomenon—clinician overdiagnosis. A number of patients presenting to our practice have reported that they were previously diagnosed with bipolar disorder, yet a history of a manic or hypomanic episode was not elicited during an evaluation that included both a semistructured interview and a clinical assessment. To be sure, we also have seen patients who presented for the treatment of depression who had not been previously diagnosed with bipolar disorder and in whom we made the diagnosis. However, it seemed to us that more individuals were false positives than false negatives.

In the present report, we sought to empirically examine how often bipolar disorder might be overdiagnosed and underdiagnosed. In fact, it is not straightforward to demonstrate that a psychiatric disorder is being overdiagnosed because of the lack of a valid, gold standard test to prove that a diagnosis is incorrect. By contrast, it is relatively easy to demonstrate that a psychiatric disorder is underdiagnosed. The demonstration of underdetection is a 2-step process. One first needs to reassess a cohort of individuals who initially did not receive the diagnosis of interest to identify a subset who purportedly meet diagnostic criteria after the reassessment. Second, it is necessary to provide evidence of the validity of the newly added diagnoses. Using bipolar disorder as an example, a sample of patients clinically diagnosed with nonbipolar major depressive disorder would be administered a standardized interview such as the Structured Clinical Interview for DSM-IV (SCID).[24] Some of these patients will be diagnosed with bipolar disorder after administration of the semistructured interview. Demonstration of a significantly higher family history loading of bipolar disorder in the patients diagnosed with bipolar disorder according to the SCID would support the validity of the SCID diagnoses and be consistent with the hypothesis that a certain percentage of patients diagnosed with major depressive disorder have undetected bipolar disorder. This approach toward "proving" that a diagnosis is being undetected follows the traditional paradigm of null hypothesis testing. That is, in the aforementioned example, a rejection of the null hypothesis of no difference in rates of familial loading for bipolar disorder in the patients who were and were not diagnosed with bipolar disorder after the SCID supports the conclusion that bipolar disorder was validly diagnosed on the basis of the SCID (i.e., that it had been previously underdiagnosed).

In contrast, proving that a condition is being overdiagnosed is a 3-step process, 1 step of which runs contrary to the tradition of trying to reject the null hypothesis. Again, consider the case of bipolar disorder. First, a cohort of individuals diagnosed with bipolar disorder is reevaluated and a percentage of the patients are rediagnosed with nonbipolar depression. As above, let us assume that familial loading is used as the validator. The second step toward confirming the hypothesis that these patients had been misdiagnosed requires a demonstration of a lower familiar loading of bipolar disorder in the rediagnosed patients compared to patients who retain their bipolar diagnosis. However, this step is not sufficient because, although there may be a difference between these groups, the rediagnosed patients may nevertheless have a higher familial loading of bipolar disorder compared to a cohort that was never diagnosed with bipolar disorder. Thus, a third step is needed to confirm overdiagnosis. That is, one needs to also demonstrate that there is no difference in familial loading between the group rediagnosed as nonbipolar and the group that had always been nonbipolar. Proving nondifference is tantamount to failing to reject the null hypothesis. Because insufficient sample size can result in type II statistical error of incorrectly accepting the null hypothesis, it is important that a study examining overdiagnosis is sufficiently powered.

In the present report from the MIDAS project, we examined whether bipolar disorder is overdiagnosed by using a semistructured interview to diagnose patients who had completed a questionnaire on which they indicated whether they had been previously diagnosed with bipolar disorder. Family history of bipolar disorder was used as an index of diagnostic validity.

METHOD

The MIDAS project represents an integration of research assessment methodology into a community-based outpatient practice affiliated with an academic medical center.[25] A comprehensive diagnostic evaluation is conducted upon presentation for treatment. To date, 2500 patients have been recruited in the MIDAS project from the Rhode Island Hospital Department of Psychiatry outpatient practice. This private practice group predominantly treats individuals with medical insurance (including Medicare but not Medicaid) on a fee-for-service basis, and it is distinct from the hospital's outpatient residency training clinic that predominantly serves lower income, uninsured, and medical assistance patients. Data on referral source were recorded for the last 700 patients enrolled in the study (from May 2001 to March 2005). Patients were most frequently referred from primary care physicians (33.6%), psychotherapists (14.9%), and family members or friends (15.1%).

As part of the initial evaluation, patients were also asked to complete several questionnaires. During the course of the study, we have changed the questionnaires administered. For the last 700 patients, one of the questionnaires asked whether the patient had been diagnosed with bipolar or manic-depressive disorder by a health care professional. These 700 patients are the focus of the present report.

The data in Table 1 show the demographic characteristics of the sample. The majority of the subjects were white, female, married or never married, and high school graduates. The mean age of the sample was 39.9 years (SD = 13.1 years).

Patients were interviewed by a diagnostic rater who administered a modified version of the SCID[24] and the Structured Interview for DSM-IV Personality Disorders (SIDP-IV).[26] The diagnostic raters were highly trained and monitored throughout the project to minimize rater drift. Diagnostic raters were Ph.D.-level psychologists and research assistants with college degrees in the social or biological sciences. Research assistants received 3 to 4 months of training during which they observed at least 20

Table 1. Demographic Characteristics of 700 Psychiatric Outpatients

Characteristic	Value[a]
Gender	
Female	408 (58.3)
Male	292 (41.7)
Education	
Less than high school	50 (7.1)
High school graduate	366 (52.3)
College graduate or greater	284 (40.6)
Marital status	
Married	305 (43.6)
Living with someone	22 (3.1)
Widowed	14 (2.0)
Separated	22 (3.1)
Divorced	121 (17.3)
Never married	216 (30.9)
Race	
White	618 (88.3)
African American	39 (5.6)
Hispanic	17 (2.4)
Asian	5 (0.7)
Portuguese	15 (2.1)
Other	6 (0.9)
Age, mean (SD), y	39.9 (13.1)

[a]Values are expressed as N (%) except where noted.

Table 2. Current DSM-IV Axis I Diagnoses of 700 Psychiatric Outpatients

DSM-IV Diagnosis	N	%
Major depressive disorder	374	53.4
Bipolar disorder	90	12.9
Dysthymic disorder	64	9.1
Generalized anxiety disorder	125	17.9
Panic disorder	149	21.3
Social phobia	179	25.6
Specific phobia	72	10.3
Obsessive-compulsive disorder	45	6.4
Posttraumatic stress disorder	131	18.7
Adjustment disorder	47	6.7
Schizophrenia	3	0.4
Eating disorder	66	9.4
Alcohol abuse/dependence	85	12.1
Drug abuse/dependence	45	6.4
Somatoform disorder	58	8.3
Attention-deficit disorder	43	6.1
Impulse-control disorder	92	13.1

Abbreviation: DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition.

interviews, and they were observed and supervised in their administration of more than 20 evaluations. Psychologists only observed 5 interviews; however, they, too, were observed and supervised in their administration of 15 to 20 evaluations. The majority of the 700 patients in this report were interviewed by psychologists (N = 600, 85.7%). During the course of training, the senior author met with each rater to review the interpretation of every item on the SCID and SIDP-IV. Also during training, every interview was reviewed on an item-by-item basis by the senior rater who observed the evaluation. At the end of the training period, the raters were required to demonstrate exact, or near exact, agreement with a senior diagnostician on 5 consecutive evaluations. Throughout the MIDAS project, ongoing supervision of the raters consisted of weekly diagnostic case conferences involving all members of the team. Written reports of all cases were reviewed by M.Z., who also reviewed the item ratings of every case. Reliability was examined in 48 patients. A joint-interview design was used in which one rater observed another conducting the interview, and both raters independently made their ratings. Of relevance to the present report, the reliability of diagnosing bipolar disorder was $\kappa = 0.85$. The interviewers were blind to the questionnaire data.

Family history diagnoses were based on information provided by the patient. The interview followed the guide provided in the Family History-Research Diagnostic Criteria[27] and assessed the presence or absence of problems with anxiety, mood, substance use, etc., for all first-degree family members. Information about functional impairment, types of treatment, and hospitalizations was also recorded. Morbid risks were calculated using age-corrected denominators or *bezugsiffers* based on Weinberg's shorter method.[28] Thus, relatives over the age of risk for the particular illness were given a value of 1; those within the age for risk were given a value of 0.5, and those below it were given a value of 0. Limits for the ages of risk for bipolar disorder were 15 to 45 years. These ages of risk were based on the distribution of ages at onset in our probands. Morbid risks were compared using the χ^2 statistic.

RESULTS

The data in Table 2 show the current *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition, (DSM-IV) Axis I diagnoses of the 700 patients. The most frequent diagnoses were major depressive disorder (53.4%), social phobia (25.6%), panic disorder (21.3%) and posttraumatic stress disorder (18.7%). Bipolar disorder was diagnosed in 12.9% of the patients. Of the 90 patients diagnosed with bipolar disorder according to the SCID, 26 (28.9%) were diagnosed with bipolar I disorder, 41 (45.6%) with bipolar II disorder, 21 (23.3%) with bipolar disorder not otherwise specified (NOS), and 2 (2.2%) with cyclothymic disorder.

Slightly more than 20% of the sample reported that they had been previously diagnosed as having bipolar disorder (N = 145, 20.7%), significantly higher than the 12.9% rate based on the SCID (McNemar test, $p < .001$). Concordance between the SCID and a self-reported prior diagnosis of bipolar disorder was fair ($\kappa = 0.45$) (Table 3). Fewer than half (43.4%) of 145 patients who reported that they had been previously diagnosed with bipolar disorder were diagnosed with bipolar disorder based on the SCID.

We compared the morbid risk of bipolar disorder in the first-degree relatives of 3 groups: (1) patients diagnosed with bipolar disorder according to the SCID, whether or

Table 3. Association Between the Diagnosis of Bipolar Disorder Based on the Structured Clinical Interview for DSM-IV (SCID) and Patient Report of Previous Diagnosis of Bipolar Disorder

Self-Reported Prior Diagnosis of Bipolar Disorder	SCID Bipolar Disorder Diagnosis		
	Present	Absent	Total
Yes	63	82	145
No	27	528	555
Total	90	610	700

Abbreviation: DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition.

not they self-reported a previous diagnosis of bipolar disorder; (2) patients who self-reported a previous diagnosis of bipolar disorder who were not diagnosed with bipolar disorder according to the SCID interview; and (3) patients without bipolar disorder according to both methods. The data in Table 4 show that patients diagnosed with bipolar disorder according to the SCID had a significantly higher morbid risk of bipolar disorder in first-degree relatives than each of the other 2 groups. Moreover, the patients who self-reported a previous diagnosis of bipolar disorder but who did not receive the diagnosis on the SCID did not have a significantly higher morbid risk for bipolar disorder than the patients who were negative for bipolar disorder by self-report and the SCID.

DISCUSSION

The results of the present study suggest that bipolar disorder is being overdiagnosed. Less than half of the patients who reported that they had been previously diagnosed with bipolar disorder were so diagnosed according to the SCID. Supporting the validity of our diagnoses of bipolar disorder, we found that the patients who we believe were previously overdiagnosed with bipolar disorder had a significantly lower morbid risk of bipolar disorder in their first-degree relatives compared to patients who were diagnosed with bipolar disorder according to the SCID. Moreover, in these presumptively overdiagnosed patients, the morbid risk for bipolar disorder was no different than in patients who were not bipolar according to the SCID.

Our examination of validity was limited to family history analyses. We did not consider other possible validators because these are not specific to bipolar disorder. For example, while bipolar disorder is characterized by a younger age at onset and greater diagnostic comorbidity than nonbipolar depression, the same differences would be predicted to differentiate depressed patients with and without a personality disorder. Because one area of diagnostic confusion is between bipolar disorder and borderline personality disorder, we chose to focus on a validation strategy that was specific to bipolar disorder.

Any study seeking to determine whether a psychiatric disorder is overdiagnosed will find that some patients with the index condition do not have it upon reinterview. Such is the nature of the imperfect reliability of psychiatric diagnosis. The question, then, is not whether some patients previously given a diagnosis do not seem to have it upon reinterview, but rather how many patients do not have it at repeat assessment. It is a value judgment as to how high the percentage should be to call attention to the issue of overdiagnosis. It is our opinion that an overdiagnosis rate of more than 50% represents a problem.

While our findings suggest that bipolar disorder is overdiagnosed, we cannot rule out the possibility that a subset of SCID nonbipolar patients who previously were diagnosed with bipolar disorder did, in fact, have bipolar disorder. During the past few years there has been increasing discussion of the bipolar spectrum and suggestion that DSM-IV criteria for bipolar disorder are overly narrow.[3,5] Thus, some clinicians might have told patients that they have bipolar disorder based on a broader definition of bipolar disorder than that defined in DSM-IV. However, approximately one quarter of the patients diagnosed with bipolar disorder on the SCID were diagnosed with bipolar disorder NOS. Patients who reported a history of multiple hypomanic episodes but in whom we could not establish a 4-day duration for any 1 episode were diagnosed with bipolar disorder NOS.

We agree with other authors who have emphasized the importance of conducting thorough diagnostic evaluations in order to detect bipolar disorder. Consistent with the results of other studies, we found that nearly one third of the 90 patients diagnosed with bipolar disorder on the SCID had not been so diagnosed previously.[3,9] Likewise, in a previous report from the MIDAS project, we found that significantly more patients were diagnosed with bipolar II disorder on the SCID compared to unstructured clinical evaluations.[17–20] However, our results suggest that overdiagnosis of bipolar disorder is as much, if not more, of a problem than underdiagnosis.

Most discussions of the misdiagnosis of bipolar disorder have focused on the personal and societal costs of underdiagnosis. Only occasionally have authors discussed the possible problems associated with overdiagnosis.[2,29] Unnecessary side effects are a significant concern. Mood stabilizers are the treatment of choice for bipolar disorder. Depending on the medication, mood stabilizers have potentially significant health complications affecting renal, endocrine, hepatic, immunologic, or metabolic function. Thus, overdiagnosing bipolar disorder can unnecessarily expose patients to serious medication side effects.

Alternative explanations should be considered to explain the higher rate of prior diagnoses of bipolar disorder. As already noted, we diagnosed bipolar disorder according to the DSM-IV criteria, which have been criticized for being too narrow.[30,31] For example, several studies have challenged the DSM-IV duration criterion and suggested

Table 4. Morbid Risks for Bipolar Disorder in First-Degree Relatives of Psychiatric Outpatients (A) Diagnosed With Bipolar Disorder Based on the Structured Clinical Interview for DSM-IV (SCID), (B) Patients Who Reportedly Were Previously Diagnosed With Bipolar Disorder That Was Not Confirmed by the SCID, and (C) Patients Without Bipolar Disorder

	SCID Bipolar A[a]		Previously Diagnosed Bipolar B[b]		Not Bipolar C[c]		3-Group Test[d]	
Diagnosis	Relatives at Risk, N	Morbid Risk, %	Relatives at Risk, N	Morbid Risk, %	Relatives at Risk, N	Morbid Risk, %	χ^2	p Value
Bipolar disorder	326	7.98	345	3.48	1996	2.45	27.12	< .0001

[a]90 probands.
[b]82 probands.
[c]528 probands.
[d]Group A had higher morbid risk for bipolar disorder than group B ($\chi^2 = 6.35$, $p < .02$) and group C ($\chi^2 = 27.32$, $p < .001$). There was no significant difference between groups B and C ($\chi^2 = 1.21$, $p = .27$).
Abbreviation: DSM-IV = *Diagnostic and Statistical Manual of Mental Disorders,* Fourth Edition.

that individuals with hypomanic episodes of 2 days' duration should be considered to have bipolar disorder.[32] Although we did not adopt a formal rule, we diagnosed bipolar disorder NOS in some patients with repeated hypomanic episodes that barely fell short of the duration requirement. A broader interpretation of bipolar disorder NOS could have resulted in more diagnoses. This could particularly be the case in depressed patients with comorbid borderline personality disorder who frequently experience brief episodes of intense emotions, including euphoria and irritability, that can be interpreted as indicative of bipolar disorder.

Some studies suggest that antidepressant-induced manic and hypomanic symptoms warrant a diagnosis of bipolar disorder.[33–35] It is possible that some of the patients previously diagnosed with bipolar disorder would be considered to have a form of "bipolar spectrum disorder" that does not meet the DSM-IV definition of bipolar disorder. We did not include antidepressant-induced or substance-induced hypomanic episodes as part of the bipolar disorder NOS diagnosis.

Some research suggests that the SCID approach toward assessing bipolar disorder, which uses the mood criterion as a gate question preceding further inquiry, may miss some patients with bipolar disorder.[36,37] Akiskal and Benazzi[37] found that some bipolar patients who initially deny mood disturbance later acknowledge it after hyperactivity is established. They therefore suggested that adequate screening should incorporate an assessment of both hyperactivity and mood disturbance. It is possible that some of the patients previously diagnosed with bipolar disorder whom we did not so diagnose, in fact had bipolar disorder.

Most of the patients who reported a previous diagnosis of bipolar disorder presented for the treatment of depression. Mood-dependent state effects may reduce reporting of prior manic and hypomanic episodes on measures such as the SCID, and this could account for some of the presumptive overdiagnosis.

The impact of marketing efforts and publicity probably also plays a role. Direct-to-consumer advertisements that refer individuals to screening questionnaires can result in patients suggesting to their treaters that they have bipolar disorder. We have seen evidence of this in our practice. This does not necessarily reflect a problem with the performance of a screening questionnaire, but rather how these scales are used. Screening questionnaires maximize sensitivity, at a cost of false positives, because it is presumed that they are followed by expert clinical evaluation. Insufficient diagnostic rigor can result in greater rates of overdiagnosis.

Clinicians are inclined to diagnose disorders that they feel more comfortable treating. We hypothesize that the increased availability of medications that have been approved for the treatment of bipolar disorder might be influencing clinicians who are unsure whether or not a patient has bipolar disorder or borderline personality disorder to err on the side of diagnosing the disorder that is medication responsive. This bias is reinforced by the marketing message of pharmaceutical companies to physicians that has emphasized the literature on the delayed recognition and underrecognition of bipolar disorder, and may be sensitizing clinicians to avoid missing the diagnosis of bipolar disorder. The campaign against underrecognition, which is also illustrated in the titles of published articles in peer-reviewed journals,[1,6] has probably resulted in some anxious, agitated, and/or irritable depressed patients who complain of insomnia and "racing thoughts" being misdiagnosed with bipolar disorder.

Each of these explanations might partially account for a lower prevalence of bipolar disorder according to the SCID than self-reported prior diagnoses of bipolar disorder. However, the family history analyses supported the validity of the SCID assessment. Of course, it is possible that some patients with a prior diagnosis of bipolar disorder had the diagnosis corrected by clinicians who followed them over time. That does not, however, belie the fact that at some point in their history they were incorrectly overdiagnosed with bipolar disorder.

A limitation of the present study is that it was conducted in a single outpatient practice in which the majority of the patients were white, female, and had health

insurance. Replication of the results in other clinical samples with different demographic characteristics is warranted. Another limitation is that prior diagnoses of bipolar disorder were based on patients' reports rather than systematic ascertainment and review of patients' prior records. We did not systematically determine whether psychiatrists, therapists, or primary care providers made prior diagnoses of bipolar disorder, although unsystematic observations indicated that most diagnoses were made by psychiatrists. Strengths of the study are the large sample size and the use of highly trained diagnostic interviewers to reliably administer a semistructured diagnostic interview.

In conclusion, the results of the present study are consistent with prior studies suggesting that there are possible problems with the diagnosis of bipolar disorder. Not only is there a problem with underdiagnosis, but also an equal, if not greater, problem exists with overdiagnosis. With the greater number of medications approved for the treatment of bipolar disorder, along with multiple reports emphasizing the problem with underdiagnosis, it is possible that overdiagnosis has become a greater problem than underdiagnosis. There are potential negative consequences to both underdiagnosis and overdiagnosis. While there is still some uncertainty as to the best assessment approach, we recommend that clinicians use a standardized, validated method in diagnosing bipolar disorder.

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