Distinguishing Bipolar Major Depression From Unipolar Major Depression With the Screening Assessment of Depression-Polarity (SAD-P)

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Background: Patients with bipolar I or II major depression are often misdiagnosed with unipolar major depression. The goal of this study was to develop and validate a brief instrument to screen for bipolar disorder in patients actively ill with major depression.

Method: The sample consisted of subjects who enrolled in the National Institute of Mental Health-Collaborative Program on the Psychobiology of Depression-Clinical Studies from 1978 to 1981 during an episode of major depression and included 91 subjects with bipolar I major depression, 52 with bipolar II major depression, and 338 with unipolar major depression diagnosed according to Research Diagnostic Criteria. Most of the subjects were inpatients at the time of enrollment, and subjects were prospectively followed for up to 20 years. In order to create, test, and cross-validate the screening instrument, a split-sample data analytic procedure was performed. This procedure yielded 3 groups of subjects: the bipolar I index sample, the bipolar I cross-validation sample, and the bipolar II cross-validation sample. Each group included subjects with bipolar major depression and subjects with unipolar major depression. Within the bipolar I index sample, subjects with bipolar I major depression at study intake were compared with subjects with unipolar major depression at study intake on a pool of 59 sociodemographic and clinical candidate variables. The 3 variables showing the greatest disparity between bipolar I subjects and unipolar subjects were selected for the screen, the Screening Assessment of Depression-Polarity (SAD-P). The operating characteristics of the SAD-P were then examined within the bipolar I index sample, bipolar I cross-validation sample, and bipolar II cross-validation sample.

Results: The items selected for the screening instrument were (1) presence of delusions during the current episode of major depression, (2) number of prior episodes of major depression, and (3) family history of major depression or mania. The screen identified bipolar major depression with a sensitivity of 0.82 in the bipolar I index sample, 0.72 in the bipolar I cross-validation sample, and 0.58 in the bipolar II cross-validation sample. With regard to misclassifying subjects with unipolar major depression, the screen provided a positive predictive value of 0.36 in the bipolar I index sample, 0.29 in the bipolar I cross-validation sample, and 0.27 in the bipolar II cross-validation sample.

Conclusion: We suggest using the 3-item SAD-P as a preliminary screen for bipolar disorder in patients who present with an active episode of major depression.

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Patients with bipolar disorder are frequently misdiagnosed with major depressive disorder.[1] One reason is that the mood episode at onset of bipolar disorder is often a depressive episode,[2] and some bipolar patients suffer multiple episodes of major depression prior to their first episode of mania.[3] In addition, observation of patients with bipolar I or II disorder over many years reveals that depressive symptoms occur more frequently than do manic or hypomanic symptoms.[4,5] Finally, patients frequently underreport symptoms of mania.[1] Thus, it is not surprising when patients report that 10 or more years may elapse from the time that they first seek treatment until a clinician finally makes the correct diagnosis of bipolar disorder.[1]

For patients with bipolar depression, an inaccurate diagnosis of unipolar depression will most likely lead to inappropriate treatment with antidepressant monotherapy.

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As a consequence, such patients may suffer poorer outcomes and a course of illness marked by more severe symptoms, chronic mood episodes, increased rates of subsyndromal symptoms and recurrent mood episodes, and more impaired psychosocial functioning. Given the implications for treatment and prognosis, several studies have tried to distinguish bipolar major depression from unipolar major depression by comparing the symptom profile of each syndrome in order to identify consistent differences. Goodwin and Jamison[6] reviewed a number of these studies and found that, compared with unipolar depression, bipolar depression was associated with less physical activity, less weight loss, more time asleep, and more psychomotor retardation. In addition, bipolar depression was associated with less anxiety and anger and fewer somatic complaints.[6] A more recent review found that, compared with unipolar major depression, bipolar depression was more likely to manifest psychosis, psychomotor retardation, persistent and unvarying mood, anhedonia, feelings of worthlessness, hypersomnia, and leaden paralysis.[7]

One methodological limitation noted by Goodwin and Jamison[6] is that, among the studies they reviewed, bipolar patients were often compared to a highly heterogeneous group of depressed nonbipolar patients, rather than a more homogeneous group of unipolar patients with recurrent episodes of endogenous (melancholic) major depression. Another problem is that from one study to the next, the specific symptoms that distinguished bipolar depression from unipolar depression were seldom replicated. This inconsistency has been noted elsewhere.[7]

In addition, results from different studies sometimes contradict each other. For example, Goodwin and Jamison[6] found that bipolar depressed subjects reported more mood lability, whereas a more recent study[8] found bipolar I depressed subjects were significantly more likely to report a persistent and unvarying mood compared with subjects with major depressive disorder. As another example, Goodwin and Jamison[6] found that subjects with bipolar depression reported less anxiety, whereas a recent study[9] found that comorbid panic disorder and generalized anxiety disorder were significantly more common in subjects with bipolar depression compared with those with unipolar major depression.

Taking into account the foregoing issues, the present study reports a means of distinguishing bipolar major depression from unipolar major depression by using a few clinical characteristics that are typically assessed during the initial clinical evaluation of patients with major depression. Specifically, the authors developed and tested a brief screen for bipolar disorder, the Screening Assessment of Depression-Polarity (SAD-P), to be administered by clinicians who are evaluating patients actively ill with major depression. For adults, there is currently 1 self-report screening instrument, the Mood Disorder Questionnaire (MDQ), that has been used to screen for bipolar disorder, both in outpatient psychiatric clinics[10] and in the general community.[11]

The data for the present study come from the National Institute of Mental Health-Collaborative Program on the Psychobiology of Depression-Clinical Studies (Collaborative Depression Study). The Collaborative Depression Study is an ongoing, prospective, observational, longitudinal investigation that has studied the course of illness in mood disorders since 1978.[12] The sample of subjects with bipolar I disorder and the sample with bipolar II disorder are each well characterized by standardized diagnostic criteria and standardized follow-up assessments. The same holds true for the subjects with unipolar major depression. In addition, the subjects with unipolar major depression are largely a homogeneous group of patients with recurrent episodes of endogenous (melancholic) major depression,[13] thus avoiding a limitation of previous studies.[6] Finally, as the Collaborative Depression Study is a longitudinal study, the investigators revise diagnoses of subjects as warranted by their clinical course during prospective follow-up. (For instance, subjects diagnosed with unipolar major depression at study intake may change diagnosis to bipolar II disorder if they suffer an episode of hypomania during prospective follow-up or change diagnosis to bipolar I disorder if they suffer an episode of mania.) Subjects in the Collaborative Depression Study have now been prospectively followed for up to 20 years and assessed frequently throughout the follow-up period.

METHOD

Subjects

From 1978 to 1981, the Collaborative Depression Study investigators recruited inpatients and outpatients receiving treatment for a mood disorder at academic medical centers in Boston, Mass.; Chicago, Ill.; Iowa City, Iowa; New York, N.Y.; and St. Louis, Mo. Inclusion criteria included age of at least 17 years, intelligence quotient greater than 70, the ability to speak English, white race (genetic hypotheses were proposed), no signs of a mood or psychotic disorder secondary to a general medical condition, and written informed consent after the procedures had been fully explained.

Among the patients enrolled into the Collaborative Depression Study, there were 91 subjects with bipolar I major depression at study intake, 52 subjects with bipolar II major depression at study intake, and 338 subjects with unipolar major depression at study intake, whose respective diagnoses of bipolar I disorder, bipolar II disorder, and unipolar major depression remained stable and did not change during the 20-year follow-up period. These 481 subjects constituted the study group examined in the present analyses.

Intake and Follow-Up Assessments

The intake episode of major depression and past psychiatric history were assessed at study intake through an interview with the Schedule for Affective Disorders and Schizophrenia[14] and a review of medical records. Diagnoses were then made according to Research Diagnostic Criteria (RDC).[15] Family psychiatric history was assessed at intake with the Family History-RDC.[16] Follow-up assessments of psychopathology were completed every 6 months for the first 5 years of the study and annually thereafter. Initially, raters used the Longitudinal Interval Follow-up Evaluation[17] during the first 2 years of the study and subsequently used the Longitudinal Interval Follow-up Evaluation II (available upon request) in years 2 through 5 and the Streamlined Longitudinal Interval Continuation Evaluation (available upon request) in the sixth year and beyond.

Data Analytic Procedures: Selection of Screen Items

A split-half data analytic strategy was used to select the 3 items for the SAD-P. Initially, half of the 91 subjects with bipolar I major depression (N = 45) and approximately half of the 338 subjects with unipolar major depression (N = 167) were randomly assigned (using a 1:1 allocation ratio) to a group referred to as the bipolar I index sample. This randomization was done for data analytic purposes only. The remaining subjects with bipolar I major depression (N = 46) and unipolar major depression (N = 171) were assigned to the bipolar I cross-validation sample.

The first analyses involved the bipolar I index sample. Subjects with bipolar I major depression were compared with subjects with unipolar major depression on 59 sociodemographic and clinical candidate variables, mostly related to symptoms of the intake episode of major depression, as ascertained by the Schedule for Affective Disorders and Schizophrenia.[14] These 2 groups of subjects were compared using χ^2 tests for categorical variables, Mann-Whitney U tests for ordinal items, and t tests for continuous variables. No correction for multiple comparisons was used in this exploratory stage of the split-half analyses. The 3 variables showing the greatest disparity between bipolar I subjects and unipolar subjects were selected as items for the screening instrument. Only 3 items were selected, as the objective was to create a brief screen that could easily be incorporated into an initial clinical evaluation. To further facilitate implementation and interpretation of the screen, the 3 items were structured as dichotomous items.

Data Analytic Procedures: Operating Characteristics

The purpose of the SAD-P is to detect bipolar I or II disorder in patients suffering from an episode of major depression. The ability of the SAD-P to achieve this goal was tested by examining the concordance of its results with those of the RDC, the diagnostic "gold standard." Specifically, the following operating characteristics[18] of the screen were examined:

1. Sensitivity: the proportion of subjects with RDC bipolar disorder who screened positive for bipolar disorder on the SAD-P.
2. Specificity: the proportion of subjects with RDC unipolar major depression who screened negative for bipolar disorder with the SAD-P.
3. Positive predictive value: the proportion of subjects who screened positive for bipolar disorder on the SAD-P who had RDC bipolar disorder.
4. Negative predictive value: the proportion of subjects who screened negative for bipolar disorder on the SAD-P who had RDC unipolar major depression.
5. Efficiency: the proportion of subjects for whom the SAD-P and RDC diagnosis agreed.

The operating characteristics of the screening instrument were examined using data from the bipolar I index sample. Next, the operating characteristics of the screen were cross-validated (i.e., replicated) using data from the bipolar I cross-validation sample (hence, the split-half analytic strategy). As a final step, the subjects with bipolar II major depression (N = 52) and the 171 subjects with unipolar major depression, referred to as the bipolar II cross-validation sample, were analyzed to further replicate the results.

The bipolar depressed and unipolar depressed subjects within the bipolar I index sample, the bipolar I cross-validation sample, and the bipolar II cross-validation sample were compared on sociodemographic and clinical variables at study intake. Chi-square tests were used for categorical variables, Mann-Whitney U tests were used for ordinal items, and t tests were used for continuous variables. A 2-tailed alpha level of 0.05 was used for all statistical tests.

RESULTS

The mean (SD) length of follow-up for the entire study sample of 481 subjects was 12.4 (6.7) years. The median length of follow-up was 16 years, and the range was 0.1–20 years.

Sociodemographic and clinical characteristics representative of the bipolar I index sample at study intake are presented in Table 1. The same characteristics of the bipolar I cross-validation sample at study intake are presented in Table 2, and those for the bipolar II cross-validation sample at study intake are presented in Table 3. Across all 3 samples, subjects with bipolar major depression were significantly more likely to enter the study suffering from psychosis, had a significantly greater number of mood epi-

Table 1. Sociodemographic and Clinical Characteristics of the Bipolar I Index Sample at Study Intake

Variable	Bipolar I Major Depression (N = 45)	Unipolar Major Depression (N = 167)	Statistical Test
Age, mean (SD), y	38.2 (13.0)	40.6 (16.1)	t = 1.02 df = 83.99[a] p = .31
Sex, N (%)			χ^2 = 0.02
Male	17 (38)	65 (39)	df = 1
Female	28 (62)	102 (61)	p = .89
Marital status, N (%)[b]			χ^2 = 3.54
Never married	21 (47)	54 (32)	df = 2
Married/live-in	17 (38)	87 (52)	p = .17
Separated, divorced, widowed	7 (16)	26 (16)	
Socioeconomic status, N (%)[b,c]			Mann-Whitney U = 3385
I	1 (2)	11 (7)	p = .29
II	8 (18)	26 (16)	
III	19 (42)	45 (27)	
IV	12 (27)	53 (32)	
V	5 (11)	32 (19)	
Clinical status, N (%)			χ^2 = 1.07
Inpatient	37 (82)	125 (75)	df = 1
Outpatient	8 (18)	42 (25)	p = .30
No. of prior episodes of major depression, N (%)[b]			Mann-Whitney U = 1588 p < .001
0	2 (4)	68 (41)	
1	5 (11)	35 (21)	
2	6 (13)	26 (16)	
3 or more	32 (71)	38 (23)	
Psychosis, N (%)			χ^2 = 6.76
Present	10 (22)	14 (8)	df = 1
Absent	35 (78)	153 (92)	p < .01
Global Assessment Scale score, mean (SD)[d]	36.6 (10.7)	38.3 (10.2)	t = 0.98 df = 210 p = .33
Age at onset of first lifetime mood episode, mean (SD), y	23.0 (10.7)	32.7 (15.3)	t = 4.85 df = 98.00[a] p < .001
Family history of major depression or mania, N (%)[e]			χ^2 = 7.87 df = 1
Positive	37 (82)	97 (58)	p < .01
Negative	8 (18)	70 (42)	
Intake medical center, N (%)[b]			χ2 = 3.93
New York, NY	10 (22)	23 (14)	df = 4
Boston, Mass	7 (16)	28 (17)	p = .42
St. Louis, Mo	8 (18)	45 (27)	
Iowa City, Iowa	12 (27)	51 (31)	
Chicago, Ill	8 (18)	20 (12)	

[a]Satterthwaite's approximation.[19]
[b]Percents do not add to 100 because of rounding.
[c]Hollingshead-Redlich scale: I = highest, V = lowest.[20]
[d]The range for the Global Assessment Scale is 1 to 100, and higher numbers indicate less psychopathology and better functioning.[21]
[e]Parent, sibling, or child.

sodes prior to study intake, and had a significantly younger age at onset compared with subjects with unipolar major depression.

Using data from the bipolar I index sample, subjects with bipolar I major depression and those with unipolar major depression were compared on 59 sociodemographic and clinical variables. On the basis of these comparisons, the following 3 variables were selected for the SAD-P and dichotomized:

1. Number of episodes of major depression prior to the current episode.
   (a) No prior episodes of major depression.
   (b) One or more prior episodes of major depression.
2. Family psychiatric history: first-degree relative (i.e., parent, sibling, or offspring) with a history of either major depression or mania.
   (a) Negative.
   (b) Positive.

Table 2. Sociodemographic and Clinical Characteristics of the Bipolar I Cross-Validation Sample at Study Intake

Variable	Bipolar I Major Depression (N = 46)	Unipolar Major Depression (N = 171)	Statistical Test
Age, mean (SD), y	40.5 (14.1)	40.0 (14.9)	t = 0.21 df = 215 p = .84
Sex, N (%)			χ^2 = 0.05
Male	18 (39)	70 (41)	df = 1
Female	28 (61)	101 (59)	p = .83
Marital status, N (%)[a]			χ^2 = 3.38
Never married	14 (30)	39 (23)	df = 2
Married/live-in	18 (39)	93 (54)	p = .19
Separated, divorced, widowed	14 (30)	39 (23)	
Socioeconomic status, N (%)[a,b]			Mann-Whitney U = 3688
I	0 (0)	7 (4)	p = .50
II	6 (13)	30 (18)	
III	15 (33)	42 (25)	
IV	16 (35)	63 (37)	
V	9 (20)	29 (17)	
Clinical status, N (%)			χ^2 = 8.42
Inpatient	44 (96)	131 (77)	df = 1
Outpatient	2 (4)	40 (23)	p < .005
No. of prior episodes of major depression, N (%)[a]			Mann-Whitney U = 1683 p < .001
0	4 (9)	60 (35)	
1	3 (7)	47 (27)	
2	3 (7)	25 (15)	
3 or more	36 (78)	39 (23)	
Psychosis, N (%)			χ^2 = 23.1
Present	16 (35)	13 (8)	df = 1
Absent	30 (65)	158 (92)	p < .001
Global Assessment Scale score, mean (SD)[c]	31.6 (13.1)	39.1 (10.2)	t = 3.59 df = 60.54[d] p = .001
Age at onset of first lifetime mood episode, mean (SD), y	24.8 (10.2)	31.8 (13.8)	t = 3.82 df = 94.56[d] p < .001
Family history of major depression or mania, N (%)[e]			χ^2 = 0.00 df = 1
Positive	31 (67)	116 (68)	p = 1.00
Negative	15 (33)	55 (32)	
Intake medical center, N (%)			χ^2 = 9.04
New York, NY	9 (20)	11 (6)	df = 4
Boston, Mass	4 (9)	25 (15)	p = .06
St. Louis, Mo	12 (26)	62 (36)	
Iowa City, Iowa	13 (28)	42 (25)	
Chicago, Ill	8 (17)	31 (18)	

[a]Percents do not add to 100 because of rounding.
[b]Hollingshead-Redlich scale: I = highest, V = lowest.[20]
[c]The range for the Global Assessment Scale is 1 to 100, and higher numbers indicate less psychopathology and better functioning.[21]
[d]Satterthwaite's approximation.[19]
[e]Parent, sibling, or child.

3. Presence of delusions of any type during the current episode of major depression (e.g., persecutory, somatic, grandiose, religious, nihilistic, thought insertion or withdrawal).
   (a) No delusions present.
   (b) One or more delusions present.

The SAD-P screen and its scoring are described more fully in Appendix 1.

Operating characteristics of the SAD-P were calculated for the bipolar I index sample, based on a cut score of 2, which achieved a balance between sensitivity and positive predictive value. The results are presented in Table 4. The most clinically relevant results are the sensitivity and positive predictive value. The sensitivity of 0.82 indicates that the SAD-P identified 82% of the subjects with an episode of major depression as having bipolar I disorder. That is, 82% of the subjects with a diag-

Table 3. Sociodemographic and Clinical Characteristics of the Bipolar II Cross-Validation Sample at Study Intake

Variable	Bipolar II Major Depression (N = 52)	Unipolar Major Depression (N = 171)	Statistical Test
Age, mean (SD), y	36.6 (14.7)	40.0 (14.9)	t = 1.58 df = 221 p = .15
Sex, N (%)			χ^2 = 0.82
Male	17 (33)	70 (41)	df = 1
Female	35 (67)	101 (59)	p = .37
Marital status, N (%)			χ^2 = 2.33
Never married	15 (29)	39 (23)	df = 2
Married/live-in	22 (42)	93 (54)	p = .31
Separated, divorced, widowed	15 (29)	39 (23)	
Socioeconomic status, N (%)[a,b]			Mann-Whitney U = 4249
I	1 (2)	7 (4)	p = .62
II	8 (15)	30 (18)	
III	20 (38)	42 (25)	
IV	15 (29)	63 (37)	
V	8 (15)	29 (17)	
Clinical status, N (%)			χ^2 = 0.03
Inpatient	39 (75)	131 (77)	df = 1
Outpatient	13 (25)	40 (23)	p = .96
No. of prior episodes of major depression, N (%)			Mann-Whitney U = 2933 p < .001
0	10 (19)	60 (35)	
1	8 (15)	47 (27)	
2	5 (10)	25 (15)	
3 or more	29 (56)	39 (23)	
Psychosis, N (%)			χ^2 = 5.83
Present	10 (19)	13 (8)	df = 1
Absent	42 (81)	158 (92)	p < .02
Global Assessment Scale score, mean (SD)[c]	36.6 (10.0)	39.1 (10.2)	t = 1.55 df = 221 p = .12
Age at onset of first lifetime mood episode, mean (SD), y	24.6 (10.9)	31.8 (13.8)	t = 3.88 df = 105.92[d] p < .001
Family history of major depression or mania, N (%)[a,e]			χ^2 = 0.45 df = 1
Positive	32 (62)	116 (68)	p = .50
Negative	20 (39)	55 (32)	
Intake medical center, N (%)			χ^2 = 17.34
New York, NY	8 (15)	11 (6)	df = 4
Boston, Mass	11 (21)	25 (15)	p < .01
St. Louis, Mo	4 (8)	62 (36)	
Iowa City, Iowa	16 (31)	42 (25)	
Chicago, Ill	13 (25)	31 (18)	

[a]Percents do not add to 100 because of rounding.
[b]Hollingshead-Redlich scale: I = highest, V = lowest.[20]
[c]The range for the Global Assessment Scale is 1 to 100, and higher numbers indicate less psychopathology and better functioning.[21]
[d]Satterthwaite's approximation.[19]
[e]Parent, sibling, or child.

nosis of bipolar I disorder according to the RDC screened positive for bipolar disorder on the SAD-P. The positive predictive value of 0.36 indicates that 36% of those who screened positive for bipolar I disorder on the SAD-P actually had RDC bipolar I disorder.

The operating characteristics of the SAD-P were calculated for the bipolar I cross-validation sample to provide an independent empirical evaluation of the screen. The operating characteristics of the SAD-P were also calculated for the bipolar II cross-validation sample to provide a second independent empirical evaluation of the screen. The results are presented in Table 4.

DISCUSSION

Bipolar disorder should be part of the differential diagnosis for any patient presenting with depression.[3] The SAD-P, developed in a longitudinal study of subjects with

Table 4. Operating Characteristics of the Screening Assessment of Depression-Polarity

Operating Characteristic	Bipolar I Index Sample (N = 212)	Bipolar I Cross-Validation Sample (N = 217)	Bipolar II Cross-Validation Sample (N = 223)
Sensitivity (95% CI)	0.82 (0.71 to 0.93)	0.72 (0.59 to 0.85)	0.58 (0.45 to 0.71)
Specificity (95% CI)	0.61 (0.54 to 0.68)	0.53 (0.46 to 0.60)	0.53 (0.46 to 0.60)
Positive predictive value (95% CI)	0.36 (0.31 to 0.41)	0.29 (0.25 to 0.33)	0.27 (0.19 to 0.35)
Negative predictive value (95% CI)	0.93 (0.88 to 0.98)	0.87 (0.81 to 0.93)	0.80 (0.73 to 0.87)
Efficiency (95% CI)	0.66 (0.60 to 0.72)	0.57 (0.50 to 0.64)	0.54 (0.47 to 0.61)

Abbreviation: CI = confidence interval.

mood disorders, provides a simple, preliminary assessment that can help clinicians clarify the diagnosis for such patients. It is important to bear in mind that screening instruments in general, and the SAD-P in particular, must not be used to make a definitive diagnosis. Rather, screening instruments are intended to help one decide which patients warrant a more comprehensive assessment. For example, mammograms are used to screen for breast cancer and help clinicians decide which patients warrant a needle biopsy to make the diagnosis. For patients who screen positive on the SAD-P, the diagnosis of bipolar I or II major depression would require, at a minimum, further clinical assessment in the form of an in-depth interview that may need to include family members. Longitudinal follow-up may ultimately be required to definitively establish the diagnosis.

The operating characteristics of the SAD-P are comparable to those of other screening instruments and justify its use for patients who present with an episode of major depression. The instrument consists of only 3 dichotomous questions that are readily administered and commonly included in an initial assessment of major depression. The simplicity of the SAD-P is similar to the 4-item CAGE, which is used to screen for alcohol abuse and dependence in primary care settings, with sensitivity ranging from 43% to 94% and specificity from 70% to 97% (positive predictive values were not reported).[22] The sensitivities and positive predictive values for the SAD-P are consistent with the operating characteristics of screens routinely used in primary care settings for breast cancer,[23] colorectal cancer,[24] cervical cancer,[25] and prostate cancer.[26]

In evaluating the SAD-P, another reference point is the MDQ, a screening assessment for bipolar disorder that was studied in academic psychiatric clinics specializing in the treatment of bipolar and other mood disorders. The MDQ demonstrated a sensitivity of 0.73 and a specificity of 0.90 (positive predictive value was not reported).[10] The MDQ has the advantage of a self-report assessment but comprises 15 items. Recently, the 10-item Conners' Abbreviated Parent Questionnaire was tested as a screen for bipolar disorder in children and adolescents; it yielded a sensitivity of 0.73 and a specificity of 0.86 (positive predictive value was not reported).[27]

The SAD-P might serve a valuable purpose for primary care clinicians, given that they treat many if not the majority of patients with depression.[28] However, the performance characteristics for the SAD-P in primary care settings are unknown.

The data in Tables 1, 2, and 3 show that subjects with bipolar major depression have a significantly younger age at onset compared with subjects with unipolar major depression. This finding is based on comparing age at onset as a continuous variable. The authors attempted to include a dichotomous item for age at onset in the SAD-P; however, these attempts did not improve the operating characteristics of the screen.

As expected, the operating characteristics for each cross-validation sample were smaller than the operating characteristics for the bipolar I index sample. The reason for this is that data from the index sample were used to select the screening items that yielded the best operating characteristics in that sample. The operating characteristics were thus optimized for the bipolar I index sample and, not surprisingly, were reduced in the cross-validation samples. This difference is clearly evident in the item for family history of mania or major depression. The association between family history and diagnosis is larger in the bipolar I index sample (Table 1) than it is in each cross-validation sample (Tables 2 and 3).

The generalizability of the present study is limited in so far as subjects were recruited as they sought treatment at academic medical centers, and more than 75% of the subjects were recruited as inpatients. Thus, the SAD-P may not be relevant for outpatients. It should be noted, however, that the threshold for inpatient hospitalization during the late 1970s and early 1980s, when subjects were recruited, was lower than it is now.

Another limitation is that the items considered for the SAD-P were restricted to a pool of 59 sociodemographic and clinical variables. Biological variables, such as sleep electroencephalographic profiles,[29] may eventually prove to be useful in distinguishing bipolar major depression from unipolar major depression. Furthermore, it is assumed that information ascertained by a clinician is at least as accurate as information obtained by a rater in a research study. Finally, if an item is missing, the screen score cannot be calculated. As with other screens, the SAD-P cannot be used if a patient cannot answer any one of the items.

A previous study from the Collaborative Depression Study compared subjects with bipolar I major depression, bipolar II major depression, or unipolar major depression on a large number of variables at study intake.[30] These analyses found that those with bipolar depression were significantly more likely to manifest psychosis, psychomotor retardation, hypersomnia, and hyperphagia; had a significantly younger age at onset; had a greater number of mood episodes prior to study intake; and had a family history of mania or hypomania.[30]

Some studies have attempted to distinguish bipolar major depression from unipolar major depression by prospectively following patients with an initial diagnosis of unipolar major depression to determine which patients subsequently develop hypomania or mania and to examine whether any clinical characteristics of the intake episode of major depression were significantly associated with a change in diagnosis. Consistent with our findings, such studies have found that psychosis during the intake depressive episode[31–34] and a family history of major affective disorder[35] or mania[31–33] were each significantly associated with subsequent development of mania (numerous other sociodemographic and clinical variables of the intake depressive episode did not predict mania).

In summary, the SAD-P correctly identified a substantial proportion of subjects with bipolar I or II major depression and did not misclassify a disproportionate number of subjects with unipolar major depression. This brief screen is simple and easy to use and does not impose an additional burden upon clinicians; the 3 items are routinely assessed during the initial clinical assessment of patients with major depression. As such, we believe it can help clinicians establish the correct diagnosis in patients who present with major depression.

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Appendix 1. Screening Assessment of Depression-Polarity

The following 3 items comprise the Screening Assessment of Depression-Polarity. Item 3 is derived from item 433 of the Schedule for Affective Disorders and Schizophrenia.[14]

Each item is dichotomous and yields a score of 0 or 1. A total score of 2 or 3 suggests that the patient's episode of major depression may be part of a bipolar disorder and that one should undertake a more in-depth assessment, perhaps including family members. If a patient cannot answer any 1 of the 3 items, the instrument cannot be used.

1. Number of episodes of major depression prior to the current episode
   Score 0: no prior episodes of major depression
   Score 1: 1 or more prior episodes of major depression
2. Family psychiatric history: first-degree relative (i.e., parent, sibling, or offspring) with a history of either major depression or mania
   Score 0: negative family psychiatric history
   Score 1: positive family psychiatric history
3. Presence of delusions of any type during the current episode of major depression (e.g., persecutory, somatic, grandiose, religious, nihilistic, thought insertion or withdrawal)
   Score 0: no delusions present
   Score 1: 1 or more delusions present