The Diagnosis of Major Depression in Patients With Cancer: A Comparative Approach

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Depressive symptoms not only impair quality of life in cancer patients but constitute an independent risk factor for increased mortality. In order to accurately and efficiently identify depression in cancer patients, the authors developed a biostatistical strategy to identify items of the 21-item, observer-rated Hamilton Rating Scale for Depression (Ham-D) that would optimize the diagnosis of depression among cancer patients. Exhibiting a relatively high sensitivity and specificity, our most optimal diagnostic tool contained six Ham-D items (late insomnia, agitation, psychic anxiety, diurnal mood variation, depressed mood, and genital symptoms). This study may serve as a prototype to generate valid instruments accurate for the diagnosis of major depression in other populations of cancer patients. (Psychosomatics 2006; 47:376–384)

The diagnostic process of an ill patient with comorbid major depression and a medical illness, especially cancer, has historically been an area fraught with controversy.[1] Various diagnostic schema have been proposed in an effort to accurately diagnose major depression in the medically ill patient. In brief, researchers have advocated either the "inclusive approach," that is, counting every depressive symptom,[2] the "exclusive approach," that is, disallowing depressive symptoms common to medical disorders,[3] or the "substitutive approach," in which depressive symptoms such as social avoidance are substituted for neurovegetative symptoms of depression.[4] Moreover, recent reports have advocated the use of abbreviated, structured interviews,[5] or patient self-report scales for the screening[6] or diagnosis of mood disorders.[7] Calculation of the positive predictive value (PPV) of a depression rating scale has provided a measurement of the accuracy of the scale as a diagnostic tool in patients with cancer.[8–11] Receiver operating characteristic (ROC) analyses may assist in setting a "cutoff" score of an observer- or self-rating instrument, above which optimal sensitivity, specificity, and PPV are obtained.[12,13] Last, factor-analytic techniques may help to identify the symptom clustering of mood, cognitive, or somatic symptoms suffered by cancer patients.[14] Indeed, although numerous other studies have utilized short screening tests in medically ill patients, nearly all of these studies have utilized heterogeneous populations of medically ill persons, without specifically focusing upon the depressive symptom psychopathology of patients with cancer.[13,15–17] The challenges of the diagnosis of major depression in the cancer patient are heightened by the depressive symptoms that may be induced by neoplastic progression and/or its treatment, for example, anorexia, fatigue, diminished concentration, sleep disturbance secondary to pain, and so

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forth, whereas other depressive symptoms may be more specific to major depression per se.[1,18,19] However, the critical importance of the diagnosis of major depression has been recently underscored by increasing evidence that depressive symptoms not only impair quality of life in cancer patients but are an independent predictor of mortality,[20–24] although discordant reports exist.[25–29]

We sought to develop a diagnostic tool with high sensitivity and good specificity in order to diagnose major depression in patients with cancer. We hypothesized that use of four groups of individuals, that is, patients with major depression without cancer, normal-comparison individuals, cancer patients with major depression, and cancer patients without major depression, would allow discrimination of which items of the Hamilton Rating Scale for Depression (Ham-D)[30] might be predictive of the presence of major depression in patients with cancer. For the sake of sensitivity, we would want to choose Ham-D items that are endorsed by patients with cancer and major depression. To improve specificity, we would exclude Ham-D items that are unduly endorsed by the nondepressed group of cancer patients. In Figure 1, Ham-D items are accordingly categorized into four types. The "Positive" items are most desirable in terms of both sensitivity and specificity and will be included in the diagnostic tool. On the other hand, the "Negative" items perform poorly in either respect and need not be considered. Whether the "Common" or "Neutral" items should be included in the tool are investigated using logistic-regression models.

METHOD

Subjects

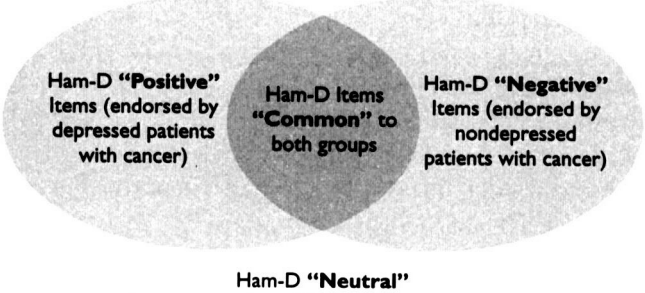
Study subjects with cancer were recruited from outpatients and inpatients at Emory University-affiliated hospitals via referral from medical providers and/or advertisements for "cancer patients with and without depression." Outpatients with major depression and normal-comparison subjects were recruited from Emory and the surrounding community by advertisements or word-of-mouth. After a complete description of the study had been given, 111 potential subjects provided written, informed consent and were then screened in person for the presence of psychiatric disorders, substance abuse, medical illness, and medication intake. Subjects were excluded if they had evidence of bipolar disorder (mania, hypomania, or cyclothymia), schizoaffective disorder, schizophrenia, delirium, or dementia, current alcohol/substance abuse or dependence, or pregnancy. Subjects were between the ages of 18 and 80, had a Mini-Mental State Exam score of at least 24,[31] spoke and read English well enough to complete study questionnaires, and had no untreated endocrine, cardiovascular, hematologic, hepatic, renal, or neurological disease. Subjects were not currently ingesting any medications implicated in causing depression and were not receiving any psychotropic medications for the treatment of symptoms of depression or anxiety. The normal-comparison subjects were without any current or past personal history of a psychiatric disorder except for past alcohol/substance abuse or dependence. The groups of depressed subjects without cancer and the normal-comparison subjects were without significant medical illness on the basis of physical exam, blood and urine analyses, ECG, and chest X-ray.

Sixty-two cancer patients were screened, of which 29 subjects were excluded because of withdrawal from the study (N = 16), current alcohol dependence (N = 4), inability to complete the Ham-D items (N = 3), possible brain metastasis (N = 1), or being without neoplasm discovered after oncologic evaluation (N = 5).

Of 24 subjects screened for the depressed-comparison group, 11 were excluded because of psychiatric disorders (bipolar disorder [N = 2], current alcohol abuse or dependence [N = 2], or numerous Axis I diagnoses [N = 1]); others were excluded because of undiagnosed medical disorders (N = 3), ingestion of a medication that could cause depression (N = 1), marked cognitive dysfunction (N = 1), and lack of depression (N = 1).

Twenty-five potential participants were screened for the normal-comparison group, of which 13 were excluded for the following reasons: a history of depression (N = 3), withdrawal from the study (N = 2), current alcohol abuse (N = 2), pregnancy (N = 1), failure to complete all questionnaires (N = 3), ongoing treatment with an antidepres-

FIGURE 1. Relationship of Ham-D Items Endorsed by Cancer Patients With and Without Major Depression



sant (N = 1), and insufficient language skills to complete the study (N = 1).

Of those screened, 33 cancer patients, 13 patients with major depression without cancer, and 12 normal-comparison subjects completed the study (Table 1). Thirteen (81%) of the 16 depressed cancer patients in the final study sample were recruited from Emory-affiliated hospitals; two (13%) were recruited through advertisement or word-of-mouth, and one (6%) was missing data on site of recruitment. Similarly, of the nondepressed cancer patients who completed the study (N = 17), 16 (94%) were recruited from the hospital, and one (6%) was recruited from advertisement/word-of-mouth. In the depressed comparison group (N = 13), seven (54%) were recruited through word-of-mouth; five (38%) were recruited from Emory University Hospital; and one (8%) was missing data on recruitment. Most of the normal-comparison subjects (N = 7; 58%) were recruited via word-of-mouth; three (25%) were recruited from the Emory-affiliated hospitals where they worked; and two (17%) were missing data on their recruitment site.

Procedures and Methods

The Structured Clinical Interview for DSM-III-R (SCID)[32] and the dimensional 21-item Ham-D[30] were administered to all study participants by a single rater who was either a master's-level nurse or a fourth-year psychiatry resident. Final psychiatric diagnoses were provided by consensus of the research team, comprising the aforementioned individuals and two board-certified psychiatrists.

Of the 16 subjects in the depressed cancer group, the majority (N = 12; 75%) fulfilled diagnostic criteria for major depressive disorder-only; 2 subjects (13%) had both major depressive disorder and dysthymia ("double depression"); 1 subject (6%) fulfilled diagnostic criteria for adjustment disorder with depressed mood; and another (6%) had adjustment disorder with mixed anxiety and depression. The depressed control group comprised 13 subjects, of whom 11 (85%) exhibited an ongoing episode of major depressive disorder-alone; and 2 subjects (15%) fulfilled diagnostic criteria for both major depressive disorder and dysthymia.

Statistical Analyses

We compared demographic and clinical characteristics of the four study groups. One-way analysis of variance (ANOVA) was used to compare the continuous variables. For categorical variables, we used Pearson's chi-square test; Fisher's exact test was used when the cell frequencies were small. Comparison of the 21-item Ham-D scores of the four study groups was performed with one-way ANOVA.

TABLE 1. Demographic and Clinical Characteristics of Normal-Comparison Subjects, Comparison Subjects With Major Depression, and Cancer Patients With and Without Major Depression, N (%)

Characteristics	Normal-Comparison Subjects (N = 12)	Depressed Comparison Subjects (N = 13)	Cancer Patients Without Major Depression (N = 17)	Cancer Patients With Major Depression (N = 16)	p
Gender					0.07
Male	8 (67%)	6 (46%)	9 (53%)	3 (19%)	
Female	4 (33%)	7 (54%)	8 (47%)	13 (81%)	
Ethnicity					0.10
Caucasian	10 (84%)	13 (100%)	12 (71%)	11 (69%)	
Hispanic	0 (0%)	0 (0%)	0 (0%)	1 (6%)	
African American	1 (8%)	0 (0%)	5 (29%)	4 (25%)	
Other	1 (8%)	0 (0%)	0 (0%)	0 (0%)	
Stage of cancer					0.89
I			2 (12%)	3 (19%)	
II			4 (24%)	4 (25%)	
III			4 (24%)	2 (12%)	
IV			7 (42%)	7 (44%)	
Type of Cancer					0.07
Breast			6 (35%)	9 (56%)	
Pancreatic			7 (41%)	5 (31%)	
Esophageal			4 (24%)	0 (0%)	
Gastrointestinal			0 (0%)	2 (13%)	
	Mean (SD)	**Mean (SD)**	**Mean (SD)**	**Mean (SD)**	
Age, years	44.2 (12.4)	51.3 (14.0)	52.4 (13.0)	51.4 (11.5)	0.34
Ham-D score	1.3 (1.6)	24.8 (8.1)	10.3 (6.1)	21.1 (9.1)	**<0.0001**

The Cochran-Armitage trend test was used to determine whether an increased score of each Ham-D item was associated with an increased probability of depression of individuals without, and with, cancer (Table 2). Compared with the commonly-adopted Person chi-square test, the Cochran-Armitage trend test is more powerful in detecting the trend of probability of depression with the increase in Ham-D item score. The sign and value of the Z statistic of the test reflects the direction and magnitude of the trend.

To further determine those Ham-D items that might be "falsely" elevated because of the cancer, we compared Ham-D items between cancer patients without major depression against normal-control subjects by use of the Mantel-Haenszel chi-square test (Table 3).

The Ham-D items of Table 2 and Table 3 were then classified as "Positive," "Common," "Negative," or "Neutral" Ham-D items, as depicted in Figure 1. Utilizing logistic regression, five candidate models indicating the probability of depression of patients with cancer were then constructed using the total scores of the Ham-D items of the aforementioned categories. That is, the predictor in Model I consisted of the total score of "Positive" Ham-D items. The predictor in Model II was the total score of the "Positive" and "Common" Ham-D items. Model III used the total score of the "Positive" and "Neutral" Ham-D items. Model IV used the total score of the "Positive," "Common," and "Neutral' items. Finally, Model V utilized the total score of all 21 items of the Ham-D. The four candidate models (Models I–IV) and Model V were then compared by three criteria: -2 log-likelihood, rescaled generalized coefficient of determination, or what is commonly known as the rescaled R^2, and the area under the receiver operating characteristics (ROC) curve. We used the -2 log-likelihood instead of Akaike Information Criterion (AIC) or Schwarz Criterion (SC) for model comparisons because all five models have one predictor, which is the total score of the corresponding Ham-D items. The -2 log-likelihood and rescaled R^2 are both based on the likelihood of the fitted logistic-regression model and measure the goodness of fit of the model. A more desirable model is indicated by lower -2 log-likelihood and larger rescaled R^2 values. The ROC curve is a plot of the sensitivity of a diagnostic test versus its false-positive rate for all possible "cut-off" scores of the diagnostic test considered by the model. As illustrated by Figure 3, the closer the ROC curve is to the upper left corner, the higher the accuracy of the diagnostic test. The area under the ROC curve is the most popular measure of the accuracy of a

TABLE 2. Increases in Ham-D Items and the Probability of Depression in Patients With and Without Cancer

Ham-D Question (range of score for item)		Depressed Comparison Subjects (N = 13) Versus Normal-Comparison Subjects (N = 12)		Cancer Patients With (N = 16) Versus Without Major Depression (N = 17)	
		Z	p	Z	p
Ham-D #1 (0–4)	Depressed mood	3.79	0.0002	2.89	**0.004**
Ham-D #2 (0–4)	Feelings of guilt	2.86	0.004	1.12	0.264
Ham-D #3 (0–4)	Suicide	2.52	0.012	1.02	0.307
Ham-D #4 (0–2)	Insomnia (early)	2.94	0.003	1.59	0.112
Ham-D #5 (0–2)	Insomnia (middle)	3.15	0.002	1.53	0.127
Ham-D #6 (0–2)	Insomnia (late)	3.19	0.001	2.30	**0.022**
Ham-D #7 (0–4)	Work and activities	4.08	<0.0001	1.80	0.072
Ham-D #8 (0–4)	Retardation	3.74	0.0002	1.29	0.199
Ham-D #9 (0–4)	Agitation	3.23	0.001	2.64	**0.008**
Ham-D #10 (0–4)	Anxiety, psychic	3.34	0.001	3.36	**0.001**
Ham-D #11 (0–4)	Anxiety somatic	3.05	0.002	1.50	0.133
Ham-D #12 (0–2)	Somatic symptoms, gastrointestinal	2.52	0.012	0.59	0.557
Ham-D #13 (0–2)	Somatic symptoms, general	3.74	0.0002	0.471	0.637
Ham-D #14 (0–2)	Genital symptoms	3.48	0.001	2.40	**0.017**
Ham-D #15 (0–4)	Hypochondriasis	2.22	0.027	1.13	0.257
Ham-D #16 (0–2)	Loss of weight	0.85	0.393	0.96	0.338
Ham-D #17 (0–2)	Insight	0.25	0.804	0.48	0.633
Ham-D #18 (0–2)	Diurnal variation	2.88	0.004	2.00	**0.046**
Ham-D #19 (0–4)	Depersonalization and derealization	2.52	0.012	0.71	0.476
Ham-D #20 (0–3)	Paranoid symptoms	2.44	0.015	0.00	1.00
Ham-D #21 (0–2)	Obsessive and compulsive symptoms	1.89	0.059	−0.12	0.907

Ham-D: Hamilton Rating Scale for Depression.

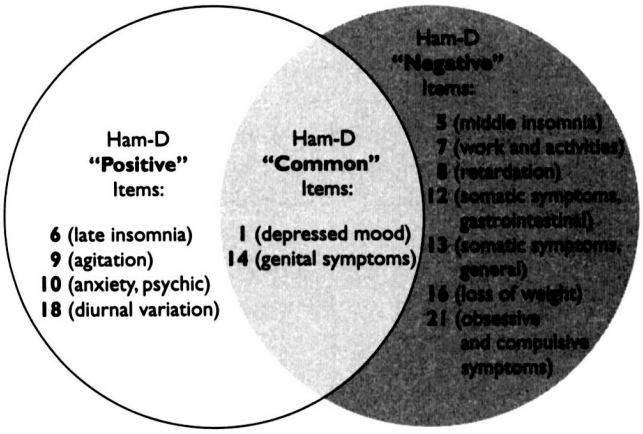
diagnostic test and ranges between 0 and 1, with 0 indicating total inaccuracy and 1 representing perfect accuracy.

RESULTS

The demographic and clinical characteristics of the study participants are presented in Table 1. The study groups did not differ significantly in age ($p = 0.34$), race ($p = 0.10$), or gender, although there was a trend for a higher proportion of women among the depressed cancer patients than in the other three study groups ($p = 0.07$). The stage of cancer was similar between the cancer patients with, and without, major depression ($p = 0.89$), as was the type of cancer ($p = 0.07$). However, the mean 21-item Ham-D scores of the four study groups were significantly different ($p < 0.0001$).

As detailed in Table 2, the probability of depression in the subjects without cancer increased significantly with greater scores in nearly all (18 out of the 21) Ham-D items. The Ham-D items on weight loss, insight, and obsessive and compulsive symptoms were not different in the patients with major depression without cancer than in the normal-control subjects. In the cancer patients, 6 of the 21 Ham-D items were significantly associated with an increased probability of major depression: depressed mood (Z-score = 2.89; $p = 0.004$), late insomnia (Z-score = 2.30; $p = 0.022$), agitation (Z-score = 2.64; $p = 0.008$), psychic anxiety (Z-score = 3.36; $p = 0.001$), genital symptoms (Z-score = 2.40; $p = 0.017$), and diurnal variation (Z-score = 2.00; $p = 0.046$).

FIGURE 2. Ham-D Items Significantly Endorsed by Cancer Patients With and Without Major Depression



Ham-D **"Neutral"** Items: **2** (feelings of guilt), **3** (suicide), **4** (insomnia early), **11** (anxiety, somatic), **15** (hypochondriasis), **17** (insight), **19** (depersonalization and derealization), **20** (paranoid symptoms)

TABLE 3. Increases in Ham-D Items in Cancer Patients Without Major Depression Versus Normal-Comparison Subjects

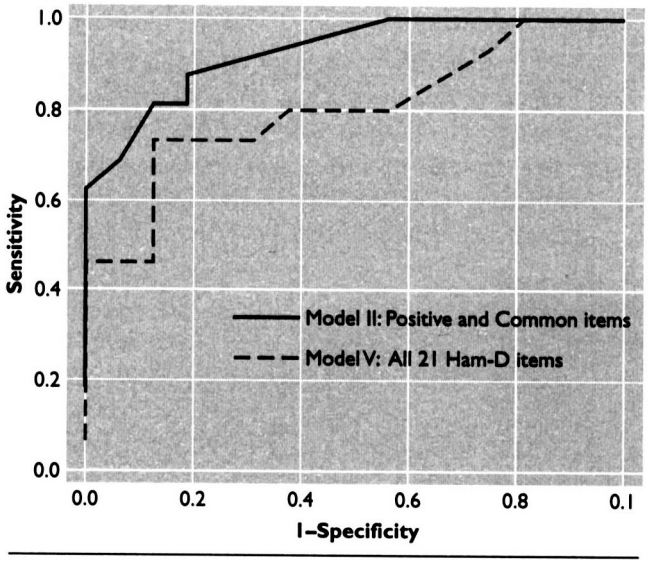
Ham-D Item (range of score for item)		Item Score Mean (SD): Cancer Patients Without Major Depression (N = 17)	Item Score Mean (SD): Normal-Control Subjects (N = 12)	p
Ham-D #1 (0–4)	Depressed mood	0.44 (0.51)	0 (0)	**0.018**
Ham-D #2 (0–4)	Feelings of guilt	0.19 (0.40)	0 (0)	0.159
Ham-D #3 (0–4)	Suicide	0 (0)	0 (0)	0.914
Ham-D #4 (0–2)	Insomnia (early)	0.56 (0.81)	0.17 (0.39)	0.195
Ham-D #5 (0–2)	Insomnia (middle)	0.31 (0.48)	0 (0)	**0.048**
Ham-D #6 (0–2)	Insomnia (late)	0.38 (0.62)	0.08 (0.29)	0.162
Ham-D #7 (0–4)	Work and activities	1.50 (1.15)	0.08 (0.29)	**0.0002**
Ham-D #8 (0–4)	Retardation	0.69 (0.79)	0 (0)	**0.007**
Ham-D #9 (0–4)	Agitation	0.13 (0.50)	0 (0)	0.604
Ham-D #10 (0–4)	Anxiety, psychic	0.38 (0.50)	0.17 (0.39)	0.274
Ham-D #11 (0–4)	Anxiety, somatic	0.44 (0.73)	0.17 (0.39)	0.368
Ham-D #12 (0–2)	Somatic symptoms, gastrointestinal	0.63 (0.72)	0 (0)	**0.007**
Ham-D #13 (0–2)	Somatic symptoms, general	0.94 (0.77)	0.25 (0.62)	**0.013**
Ham-D #14 (0–2)	Genital symptoms	0.69 (0.79)	0 (0)	**0.007**
Ham-D #15 (0–4)	Hypochondriasis	0.63 (0.72)	0.17 (0.39)	0.075
Ham-D #16 (0–2)	Loss of weight	0.81 (0.91)	0 (0)	**0.007**
Ham-D #17 (0–2)	Insight	0.25 (0.58)	0 (0)	0.187
Ham-D #18 (0–2)	Diurnal variation	0.25 (0.45)	0.17 (0.39)	0.618
Ham-D #19 (0–4)	Depersonalization and derealization	0.31 (0.60)	0 (0)	0.104
Ham-D #20 (0–3)	Paranoid symptoms	0.19 (0.40)	0 (0)	0.140
Ham-D #21 (0–2)	Obsessive and compulsive symptoms	0.44 (0.73)	0 (0)	**0.050**

Ham-D: Hamilton Rating Scale for Depression.

As shown in Table 3, there were nine Ham-D items significantly endorsed more often by nondepressed cancer patients than normal-comparison subjects: depressed mood ($p = 0.018$), middle insomnia ($p = 0.048$), diminished work and activities ($p = 0.0002$), retardation ($p = 0.007$), gastrointestinal symptoms ($p = 0.007$), general somatic symptoms ($p = 0.013$), genital symptoms ($p = 0.007$), weight loss ($p = 0.007$), and obsessive and compulsive symptoms ($p = 0.050$).

Utilizing the results of Table 2 and Table 3, the Ham-D items were then inserted into Figure 2. The white circle contains the Ham-D items endorsed by depressed cancer patients from Table 2; the darkest circle contains the Ham-D items endorsed by nondepressed cancer patients from Table 3. Ham-D items significantly endorsed by cancer patients with major depression, and not by the nondepressed cancer patients, that is, the "Positive" Ham-D items, were late insomnia (Item 6), agitation (Item 9), psychic anxiety (Item 10), and diurnal variation in mood (Item 18). Ham-D items significantly endorsed by both cancer patients with and without major depression, that is, the "Common" Ham-D items, were depressed mood (Item 1) and genital symptoms (Item 14). Ham-D items significantly endorsed by nondepressed cancer patients, and not by the depressed cancer patients, that is, the "Negative" Ham-D items, were middle insomnia (Item 5), work and activities (Item 7), retardation (Item 8), gastrointestinal symptoms (Item 12), general somatic symptoms (Item 13), weight loss (Item 16), and obsessive and compulsive symptoms (Item 21). The Ham-D items not endorsed by either the depressed or nondepressed cancer patients, that is, the "Neutral' items, were feelings of guilt (Item 2), suicide (Item 3), early insomnia (Item 4), somatic anxiety (Item 11), hypochondriasis (Item 15), insight (Item 17), depersonalization and derealization (Item 19), and paranoid symptoms (Item 20).

FIGURE 3. ROC Curves for Model II and Model V



In Table 4, we compared the five models by use of the -2 log-likelihood, rescaled R^2, and area under the ROC curve. Models I through IV were all superior to Model V (comprising all 21 items of the Ham-D). Among the four candidate models (Models I–IV), Model II was optimal, according to -2 log-likelihood, rescaled generalized coefficient of determination (or the rescaled R^2), and the area under ROC curve. Figure 3 shows the ROC curves of Model II compared with Model V.

On the basis of observations from Table 4 and Figure 3, the four "Positive" items and two "Common" items of the Ham-D would comprise the diagnostic tool for identifying the presence of depression among cancer patients. Our next step for the diagnostic tool was to choose an optimal cut-off score, which would provide at least 80% sensitivity as well as specificity. As shown in Table 5, the most optimal cut-off score was 6, with a sensitivity of 81.3% and a specificity of 87.5%.

DISCUSSION

Our objective was to develop a diagnostic tool with both high sensitivity and specificity for the optimal diagnosis of depression among cancer patients. Although not originally constructed for use in medically ill patients, the Ham-D continues to have broad use in clinical trials for the treatment of depression, most recently in persons with heart disease.[33,34] Other depression rating scales, for example, the Beck Depression Inventory, have also been successfully utilized in the diagnosis of major depression in patients with diabetes[35] and recent myocardial infarction.[34]

Our final model, Model II, contained "Positive" and "Common" Ham-D items endorsed by cancer patients with major depression. Inclusion of the "Neutral'" Ham-D items (as in Models III and IV) diminished the instrument's accuracy in predicting the presence of major depression in patients with cancer. Of note is the finding that the symptom of anhedonia (included within Ham-D Item 7 "work and activities"), historically cited as a predictor of depression in the heterogeneous populations of medically ill persons,[36,37] is not included within our proposed instrument. Other research groups have also reported that this item is endorsed both by depressed and nondepressed patients with serious medical disorders,[17,36] including cancer pa-

TABLE 4. Comparison of the Five Logistic-Regression Models

Model	Ham-D Items Comprising Logistic-Regression Model	−2Log-Likelihood	R^2	Area Under ROC Curve
I	"Positive"	25.00	0.61	0.912
II	"Positive" + "Common"	22.21	0.67	0.928
III	"Positive" + "Neutral"	29.76	0.49	0.863
IV	"Positive" + "Common" + "Neutral"	27.30	0.55	0.883
V	All 21 Ham-D items	30.55	0.44	0.804

Comparison of the five logistic-regression models shows that Model II is the optimal tool for diagnosis of depression in cancer patients.
Ham-D: Hamilton Rating Scale for Depression; ROC: receiver operating characteristic.

tients receiving chemotherapy[15] and palliative treatment.[37] Although other investigators have utilized psychiatric inpatients with depression[36] to help distinguish depressive symptom patterns between medically ill patients (without and with depression), neither anhedonia, nor "low positive affect," distinguished the depressed medically ill persons from their nondepressed medically ill counterparts. In our study, however, depressed mood remained a useful item in our final model.

Our study's major limitations include a small sample size of cancer patients, with a heterogeneity of cancer diagnoses. Indeed, a more sensitive, and specific, diagnostic tool would likely have arisen from a larger, more homogeneous study population recruiting normal-comparison subjects and patients with major depression similar in age and gender to cancer patients diagnosed with a single type of neoplasm, receiving a uniform anti-cancer regimen. However, given the lack of a "gold standard" for the presence of major depression, even in depressed patients without cancer,[38] this study may serve as a prototype in which similar biostatistical strategies may generate diagnostic instruments accurate in the diagnosis of major depression in cancer as well as other major medical disorders. Although our analyses were performed on a relatively small sample of patients with cancer, our research design included individuals without cancer, that is, patients with major depression and normal-comparison individuals, to identify which Ham-D items would be useful for the detection of major depression in cancer patients. Our final model exhibited greater sensitivity and specificity than the 75% sensitivity and 75% specificity of the 14-item, self-rated Hospital Anxiety and Depression Scale,[12] a scale specifically designed for medically ill patients. Of note is that our most optimal model contained only six Ham-D items, with a relatively low cut-off score of 6, congruent with other reports that accurate identification of major depression in medically ill patients can be achieved with relatively few questions.[13,16,17,39–41] This observer-administered, six-item instrument may support patient "paper-and-pencil" self-report questionnaires, especially if used as a confirmatory follow-up screening instrument to identify those patients who might benefit from antidepressant treatment alone, or in combination with other types of psychosocial interventions. Another potential use of the instrument would be to identify subjects for research protocols where brief tools are used initially.[15,42] Validation of this study's modified Ham-D questionnaire will certainly require additional study of other groups of patients with cancer, especially those patients who may be currently treated with psychotropic medications. Finally, whether cancer patients identified by this (or other) modified dimensional instruments consistently exhibit neurobiologic alterations observed in previous studies of cancer patients with comorbid depression is unknown and is worthy of further investigation.[43,44]

TABLE 5. Sensitivity and Specificity of Cut-Off Scores, From "Positive" and "Common" Ham-D Items

"+Cut-Off" Ham-D Total Score	Sensitivity	Specificity
13	18.8%	100.0%
11	31.3%	100.0%
10	37.5%	100.0%
9	43.8%	100.0%
8	62.5%	100.0%
7	68.8%	93.8%
6	**81.3%**	**87.5%**
5	81.3%	81.3%
4	87.5%	81.3%
3	93.8%	62.5%
2	100.0%	43.8%
1	100.0%	25.0%
0	100.0%	0.0%

Ham-D: Hamilton Rating Scale for Depression.

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