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Measuring Depression at the End of Life: Is the Hamilton Depression Rating Scale a Valid Instrument?

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Abstract

Depression at the end of life is a common mental health issue with serious implications for quality of life and end of life decision making. This study investigated the reliability and validity of one of the most frequently used measures of depression, the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960, 1967) in 422 patients with terminal cancer admitted to a palliative care hospital. The HAM-D demonstrated high reliability and concurrent validity with a diagnosis of depression, based on Structured Clinical Interview for *DSM-IV* (SCID-I/NP Depression Module). ROC analyses generated an AUC of .91, indicating high sensitivity and specificity. Convergent validity was established through strong correlations with several measures of distress (e.g., hopelessness, desire for hastened death, suicidal ideation). Factor analysis generated four factors (anxiety, depressed mood, insomnia, and somatic symptoms) that accounted for 42% of the variance. Implications for assessing depression in patients with terminal cancer are discussed.

Keywords

Hamilton (HAM-D); Depression; Terminal Illness; Cancer; End of Life

Introduction

The experience of depression among cancer patients has drawn considerable research and clinical attention in the past 25 years. Although widely recognized as one of the most common, and potentially treatable mental health issues facing cancer patients (Wilson, Chochinov, de Faye, & Breitbart, 2000), the nature of depression in patients at the end of life has recently drawn more research attention.

Among the many questions that arise in assessing depression at the end of life is the relationship between physical, cognitive and affective symptoms. Because many physical symptoms occur in terminally ill patients, disentangling the etiology (i.e., depression versus illness) can be complicated. The relationship between anxiety, depression, and “normal adjustment” is also unclear as death approaches. Understanding how depression presents at the end of life may also have important implications for palliative care professionals, by identifying those terminally ill patients who might benefit from psychosocial and pharmacological interventions. This study addresses these questions by examining ratings of depression in a large sample of terminally ill cancer patients using the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960, 1967), one of the most commonly used observer-rated measures of depression.

Since Max Hamilton (1960) first described his depression rating scale, the HAM-D has been frequently used in clinical and research assessments of depression. It should be noted that the HAM-D was designed to measure the *severity* of depression, not to determine the presence or absence of a depressive disorder. The HAM-D has been used extensively to evaluate the efficacy of antidepressant drugs and has been translated (and validated) in several languages (Fava, Kellner, Munari, & Pavan, 1982). In addition, there are at least 20 different versions of the HAM-D (Bagby, Ryder, Schuller, & Marshall, 2004), although the 17- and 21-item scales are the most common.

The validity of the HAM-D has been repeatedly investigated in general clinical populations. A recent review (Bagby et al., 2004) examined the psychometric properties of the HAM-D in 70 published studies, and found adequate internal consistency and discriminant validity. Investigations of the factor structure of the HAM-D across multiple studies, however, have demonstrated inconsistent results. Based on two recent investigations, the most common factors found appear to be those related to general depression, insomnia, and to a lesser degree, anxiety. Bagby et al. (2004) examined the factor stability of the HAM-D, analyzing 15 studies with 17 data sets in which factor analyses had been conducted. The number of factors identified ranged widely, from two to eight. Notably, all but four of the data sets included sleep disruption and general depression factors, and six studies found an anxiety/agitation factor.

Using confirmatory factor analysis, Cole and colleagues (2004) compared factor analyses from six studies that were selected because they had adequate sample sizes, multiple-item factors, and consistent results for subgroups. Of the six latent factor models tested, none had an adequate fit. The best-fitting model, however, was a rationally derived model proposed by the study authors that included four factors: core depression, insomnia, anxiety, and a “visceral” factor comprised of items concerning weight loss, loss of insight, genital symptoms, work and activities, and motor retardation.

Given its ubiquitous use in studies of general psychiatric patients, it is not surprising that the HAM-D has also been frequently used to assess depression co-occurring with a broad range of medical conditions, including Parkinson's disease (Leentjens, Verhey, Lousberg, Spitsbergen, & Wilmsink, 2000), stroke and Alzheimer's disease (Naarding, Leentjens, van Kooten, & Verhey, 2002), chronic obstructive pulmonary disease (Stage, Middleboe, &

Pisinger, 2003), and post-operative effects of mastectomy (Van Heeringen, Van Moffaert, & de Cuypere, 1990). The HAM-D has also been used in research investigations of physically ill elderly patients (Hammond, 1998) and cognitively impaired geriatric patients (Mulsant, Sweet, Rifai, Pasternak, McEachran, & Zubenko, 1994). Unfortunately, many of these studies did not include validity information and those that did reported mixed results. For example, two studies reported high concurrent validity with *DSM-IV* depression diagnosis using Receiver Operator Characteristics Curve (ROC) analysis in patients with Parkinson's disease and Alzheimer's disease (Leentjens et al., 2000; Naarding et al., 2002). Two other studies, however, questioned the use of the HAM-D due to unacceptably low internal consistency in their samples (Stage et al., 2003; Hammond, 1998).

Several factors complicate the diagnosis of depression in the terminally ill cancer patient. First, many of the symptoms used to demonstrate the presence of a major depressive episode present differently in the medically ill patient than they would in a nonmedically ill depressed person. For example, the symptom of anhedonia must be differentiated from the normal response to physical limitations and advancing illness common in the terminally ill. It is not uncommon for patients to become less interested in previously enjoyed activities and refocus their priorities as they become physically weaker and more disabled. Wilson et al. (2000) suggested that researchers and clinicians address this problem by applying the label of anhedonia solely to patients experiencing a *pervasive* loss of interest or pleasure, particularly in regard to the ability to enjoy social interaction with family and friends.

Second, and of greatest importance, is the difficulty in interpreting somatic symptoms in the medically ill patient. Although insomnia, fatigue, psychomotor retardation, loss of appetite, hypochondriasis, and weight loss are all associated with depression in a physically healthy population, they are also symptoms commonly found as a result of severe illness. These symptoms are such frequent sequelae of illnesses, such as cancer, and of many treatments (e.g., chemotherapy) that some researchers have questioned the appropriateness of including somatic symptoms in the diagnosis of depression in this population (Lloyd-Williams, 2003) and others (e.g., Kathol, Mutgi, Williams, Clamon, & Noyes, 1990) have studied various classification systems, including substitutive using criteria developed by Endicott (1984), inclusive, and etiological. In fact, the *DSM-IV* dictates that somatic symptoms be excluded from consideration when they are directly caused by a medical condition. In reality, however, it is often impossible to conclusively determine the etiology of somatic symptoms in a medically ill population. Moreover, as more somatic symptoms of depression are excluded from consideration, it becomes increasingly difficult for patients to meet *DSM-IV* diagnostic criteria for a major depressive episode. The confounding presence of somatic symptoms is particularly problematic when using ratings scales such as the HAM-D. In one investigation of patients with Parkinson's disease, the only somatic item on the HAM-D that was associated with a diagnosis of depression (using the SCID-I) was loss of appetite; other somatic items (e.g., sleep disturbance, fatigue) were uncorrelated with a diagnosis of depression (Leentjens, Marinus, Van Hilten, Lousberg, & Verhey, 2003).

Although the HAM-D is frequently used in psycho-oncology research, very few studies have examined its reliability and validity in patients with cancer. None of the studies examining the HAM-D in patients with cancer have provided data on interrater reliability and only one

study reported internal consistency statistics (Middleboe, Oveson, Mortensen, & Bech, 1994). Only two studies have compared the HAM-D to SCID-I depression diagnoses. One administered the HAM-D as a self-report symptom checklist rather than as clinician-rated instrument and did not compare the two measures regarding the presence or absence of depression (Leentjens et al., 2003). Instead, they used the individual HAM-D items in a discriminant function analysis predicting a diagnosis of depression based on the SCID-I. Another study by Guo et al. (2006) administered the HAM-D and SCID-I (*DSM-III-R*) to four groups: depressed patients with cancer, non-depressed patients with cancer, depressed healthy controls, and a normal comparison group. They did not directly compare the two measures regarding presence or absence of depression, but rather attempted to determine whether an increased score on each Ham-D item was associated with an increased probability of depression in these groups, as indicated by SCID-I depression diagnosis. Using logistic regression and ROC curve analysis, they determined that six HAM-D items were most strongly associated with an increased probability of MDE in the cancer patient sample: depressed mood, late insomnia, agitation, psychic anxiety, genital symptoms, and diurnal variation.

Another study of 36 patients with cancer (Middleboe et al., 1994) analyzed individual HAM-D item-total correlations, finding that depressed mood, middle insomnia, psychic anxiety, and fatigue showed the highest correlations with total HAM-D scores. Items relating to agitation, sexual interest, hypochondriasis, and loss of insight were weakly correlated. The authors note the lack of variance and infrequent endorsement of the latter factors in explaining their poorer psychometric performance.

Unfortunately, given the paucity of research on reliability and validity of the HAM-D in a cancer patient population, few conclusions can be drawn. Furthermore, virtually no research has examined the reliability and validity of the HAM-D in terminally ill patients, which is particularly questionable given the large number of HAM-D items relating to somatic content. This study serves as a first effort to establish the reliability and validity of the HAM-D in patients at the end of life and to empirically evaluate the role of somatic symptoms in depressive disorders in a terminally ill population.

Method

Participants

Terminally ill cancer patients were recruited between December 2000 and August 2004 from a state-of-the-art 200-bed palliative-care facility for people with terminal cancer in New York City. Patients were at least 21 years of age and had a life expectancy of less than six months. All participants were recruited as part of a larger, ongoing study investigating the relationship between depression and the desire for hastened death in the terminally ill (Breitbart, Rosenfeld, & Pessin, 2000). Institutional Review Boards at Calvary Hospital, Memorial Sloan-Kettering Cancer Center, and Fordham University approved the study.

Initially, 439 patients participated in the study. Seventeen patients were omitted from these analyses because of incomplete data on one or both of the depression measures, leaving a total of 422 study participants for inclusion in the present analysis. Of these, 43.4% ($n =$

239) were men and 56.6% ($n = 183$) were women, with an average age of 65.8 years, ($SD = 13.7$, range = 21 to 94) and an average of 13.2 years of education. The majority of participants were Caucasian (68.5%, $n = 289$), with 23.2% African American ($n = 98$) and 6.2% Hispanic ($n = 26$). Half of participants were Catholic (50.5%, $n=213$), with 17.1% Protestant ($n=72$), and 10.4% Jewish ($n=44$). Roughly one-third of the sample (32.2%, $n = 136$) reported having received counseling or treatment for an emotional problem at some point in the past. All participants had cancer; the most common cancer diagnoses included lung/bronchus (17.5%, $n = 74$), colorectal (13.7%, $n = 58$), breast (10.9%, $n = 46$), prostate (7.1%, $n = 30$), pancreatic (6.7%, $n = 28$), and stomach (5%, $n = 21$).

Procedures

Demographic information and psychological variables were collected through review of patient charts and in-person interviews with study participants. All participants were interviewed by trained psychologists or psychology graduate students.

Measures—Depression was assessed using two observer-rated measures of depression, the Structured Clinical Interview for the *DSM-IV* depression module (SCID-I/NP; First, Spitzer, Gibbon, & Williams, 1994) and the Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960), as part of an extensive battery of self-report and clinician-rated instruments assessing potentially relevant constructs such as physical symptoms, psychological well-being, and social support. The depression module of the SCID-I/NP identifies those patients who meet *DSM-IV* diagnostic criteria for a major depressive episode and is considered the “gold standard” in assessing depression in cancer patients (Wilson et al., 2000). The SCID-I has demonstrated superior reliability and validity over standard clinical interviews in several studies (Basco, Bostic, & Davies, 2000; Kranzler, Kannon, & Babor, 1996) and has been used in many studies with cancer patients (e.g., Musselman, Miller, & Porter, 2001; Payne, Hoffman, Theodoulou, Dosik, & Massie, 1999). The SCID-I/NP Depression Module was scored as a dichotomous variable of either “depressed” if patients met *DSM-IV* criteria for a major depressive episode or “not depressed” if patients did not. Reliability for this measure was based on the presence or absence of a diagnosis of depression.

The HAM-D is a 21-item measure of depressive symptoms that yields a severity score from 0 to 63 and has proven to be a reliable and valid measure of depression across many different populations (Mottram, Wilson, & Copeland, 2000; Leentjens, Verhey, & Lousberg, 2000; Bonin-Guillame, Clement, & Leger, 1995; Knesevich et al., 1977). Given the exploratory focus of this study, we include the four “optional” items (e.g., paranoia, diurnal variation) from the HAM-D (Hamilton, 1960) in order to better understand the construct of depression in this population. One HAM-D item assessing “genital symptoms” (i.e., loss of libido) was omitted due to the inappropriate nature of this item given the frail health status of our sample. All analyses in this paper are therefore on the 20-item version of the HAM-D, with a maximum possible total score of 61. A combination of etiological and inclusive approaches was used during the administration of both depression measures. Using these approaches, the investigators attempted to assess the cause of depressive symptoms and then excluded those symptoms most likely resulting from cancer and included those most likely

resulting from depression. When etiology could not be determined, the symptom was considered to be due to depression (the “inclusive” approach).

Several other measures were also included in the study. The Beck Hopelessness Scale (BHS; Beck, Weissman, Lester, & Trexler, 1974) was used to measure patients’ hopelessness and has previously been used in terminally ill populations (e.g., Breitbart et al., 2000; Ganzini, Johnston, McFarland, Tolle, & Lee, 1998; Rabkin, Wagner, & Del Bene, , 2000). A study of terminally ill cancer patients by Abbey, Rosenfeld, Pessin, & Breitbart (2006) demonstrated good internal consistency ($\alpha = .87$), as well as convergent and discriminant validity. Cronbach's coefficient alpha was calculated for the BHS in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .87$) based on an a priori criterion of .70 to reflect adequate reliability (Nunnally & Bernstein, 1994).

The Schedule of Attitudes toward Hastened Death (SAHD; Rosenfeld et al., 1999) measures desire for death and was designed for use with patients with life-threatening illness. It has demonstrated high internal consistency ($\alpha = .89$) in a sample of patients with HIV/AIDS (Rosenfeld et al., 1999) and has demonstrated convergent validity with related measures. Cronbach's coefficient alpha was calculated for the SAHD in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .89$).

The Functional Assessment of Chronic Illness Therapy Spiritual Well-Being Scale (SWB; Brady, Peterman, Fitchett, Mo, & Cella, 1999) was used to assess spirituality. This scale has been used with various medically ill populations and has demonstrated convergent and discriminant validity (e.g., McClain et al., 2003; Peterman, Fitchett, & Brady, 2002; Nelson et al., 2002). Cronbach's coefficient alpha was calculated for the SWB in this analysis ($\alpha = .89$).

The Karnofsky Performance Rating Scale (KPRS; Karnofsky & Burchenal, 1949) is a single-item measure that was used to assess overall functional ability. The KPRS has demonstrated good predictive validity of survival rates of cancer patients (Firat, Bousamra, Gore, & Byardt, 2002; Firat, Byardt, & Gore, 2002).

The Duke-UNC Functional Social Support Questionnaire (FSSQ; Broadhead, Gehlbach, De Gruy, & Kaplan, 1988) was used to assess perceived social support. The FSSQ was initially designed and evaluated among 401 medically ill patients. This measure has demonstrated construct, concurrent, and discriminant validity (Broadhead et al, 1988) and has been used successfully with severely ill cancer patients (Breitbart et al., 2000; McClain et al., 2003). Cronbach's coefficient alpha was calculated for the FSSQ in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .90$).

The Memorial Symptom Assessment Scale Short Form (MSAS; Portenoy et al., 1994) was designed to measure physical and psychological symptoms in cancer patients. It has demonstrated high internal consistency ($\alpha = 0.88$ and 0.83 for physical symptom subscale and psychological symptom subscale, respectively) and high convergent validity with clinical status and quality-of-life measures. Cronbach's coefficient alpha was calculated for the MSAS in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .77$).

The Life Orientation Test-Revised (LOT-R; Scheier, Carver, & Bridges, 1994) has been used in multiple studies involving cancer patients (e.g., Carver, Smith, Antoni, Petronis, Weiss, & Derhagopian, 2005; Carver et al., 1993) and has shown high internal consistency ($\alpha = .71$) in a sample of 312 patients with metastatic cancer (Clarke, Kissane, Trauer, & Smith, 2005). Cronbach's coefficient alpha was calculated for the LOT-R in this analysis ($\alpha = .67$).

The Hospital Anxiety and Depression Scale—Anxiety Subscale (HADS-A; Zigmond & Snaith, 1983) was used to assess patients' anxiety. This measure has been widely used with cancer patients in clinical and research settings and has been demonstrated to have high reliability and validity (e.g., Carroll, Kathol, Noyes, Wald, & Clamon, 1993; Hopwood & Stephens, 2000) in samples of cancer patients. In one study, Rodgers, Martin, Morse, Kendell, and Verrill (2005) found that HADS-A had good internal consistency ($\alpha = 0.79$) in a sample of 110 breast cancer patients. Cronbach's coefficient alpha was calculated for the HADS-A in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .82$).

The Scale for Suicidal Ideation (SSI; Beck, Steer, & Ranieri, 1988) was used to measure suicidality. The SSI has demonstrated high internal consistency and convergent validity in cancer patient samples (e.g., Clarke et al., 2005). Cronbach's coefficient alpha was calculated for the SSI in this analysis and demonstrated adequate internal consistency in our sample ($\alpha = .73$).

Statistical Analyses

The reliability of the HAM-D was evaluated using Cronbach's coefficient alpha, with an a priori criterion of 0.70 to reflect adequate reliability (Nunnally & Bernstein, 1994). Cronbach's alpha was also calculated for other measures given. Measures of interrater reliability (i.e., intraclass correlation coefficient or ICC and Kappa using a random subset of patients who were rated by two independent researchers) were also calculated. Estimates of interrater reliability should be at a minimum of 0.70 (Landis & Koch, 1977). A Mann-Whitney *U*-Test was used to determine the association between individual HAM-D items and a diagnosis of depression based on the SCID-I/NP Depression Module.

A principle components factor analysis (PCA) with Varimax rotation was used to identify the factor structure of the HAM-D in this sample. Optimal number of factors was determined through an inspection of the Scree plot, a review of eigenvalues, and an analysis of the interpretability of various factor solutions (i.e., factor loadings). A conservative a priori criterion of 0.50 was used to identify which items comprise which factors¹. Although a principal axis factor model and/or an oblique rotation were considered, we utilized PCA in order to maximize explained variance in the HAM-D and a Varimax rotation to maximize separation of factors and facilitate interpretation. In fact, a principal axis factor analysis with

¹We additionally conducted a Parallel Analysis using randomly generated data sets to determine the optimal number of factors; however, this analysis resulted in a 2-factor model that explained only 28% of the variance and resulted in only half of the scale items loading on either factor. Given the contradictory findings of these approaches, and the apparent interpretability of the 3rd and 4th factors, we opted to rely on the more “traditional” methods described here.

oblique rotation resulted in a similar overall factor structure, but with uninterpretable third and fourth factors².

Spearman correlation coefficients were calculated between these HAM-D factors and a diagnosis of depression based on the SCID-I/NP Depression Module, as well as with demographic variables and other clinical measures (i.e., the MSAS, LOT-R, KPRS, HADSA, FSSQ, BHS, SWB, and SSI). A Receiver Operating Characteristics (ROC) curve analysis was used to assess the discriminant validity of the HAM-D in distinguishing depressed from nondepressed patients and to determine optimal cutoff scores for maximizing sensitivity and specificity.

Results

Frequency of Depression and HAM-D Item Endorsement

Seventy-two patients (17.1%) met criteria for a current major depressive episode (MDE) according to *DSM-IV* criteria (based on the SCID-I/NP Depression Module). Table 1 lists the frequency of patients' total scores for the HAM-D for the total sample, for patients meeting *DSM-IV* criteria for MDE, and for those patients who did not meet criteria for MDE. Cut-offs listed for mild, moderate, and severe depression are taken from Middleboe et al. (1994).

Table 2 lists the frequency with which individual items on the HAM-D were rated. Seven items (items 1, 5, 7, 10, 12, 13, and 16) were observed (i.e., a score of 1 or greater) in more than 50 percent of the patients. These items were depressed mood, middle insomnia, diminished work and activities, psychic anxiety, gastrointestinal symptoms, general somatic symptoms, and weight loss. At the other extreme, several items were infrequently rated including agitation, loss of insight, paranoia, and obsessive and compulsive symptoms.

Reliability of the HAM-D

In order to test the reliability of the HAM-D, Cronbach's coefficient alpha was calculated for the 20-item version of the HAM-D used in this analysis ($\alpha = .765$). Item-total correlations were also calculated, resulting in a median item-total correlation of .30 and range of -.01 to .59 (see Table 2). Despite the weak item-total correlations for some items (e.g., weight loss and loss of insight), removal of these items increased Cronbach's coefficient alpha only slightly ($\alpha = .774$). Therefore, subsequent analyses utilized the full 20-item scale. Inter-rater reliability was also high, with an ICC of .82 ($n=54$) for the HAM-D and Kappa of .87 ($n=54$) for the diagnosis of MDE based on the SCID-I/NP Depression Module.

A Mann-Whitney *U* test was used to evaluate the hypothesis that patients with MDE would obtain higher HAM-D total scores than those who were not depressed. The results of the test were in the expected direction and significant, $U = 2180, p < .001$.

²Despite the overall similar factor structure, principal axis factor analysis with an oblique rotation resulted in a large number of items that did not load on any factor (8 of 20) and a single item loading on the 3rd factor. Thus, it was determined that PCA analysis with Varimax rotation provided a more coherent factor solution.

A principal components factor analysis with Varimax rotation revealed four factors based on examination of the scree plot (see Figure 1) and eigenvalues above 1.0. This factor solution accounted for 42.0% of the variance in HAM-D scores. Table 3 lists the factor loadings and Table 4 contains a summary of eigenvalues, as well as percent and cumulative explained variance. The first factor, which explained 12.56% of the variance, consisted of four items that related to different aspects of anxiety (psychic anxiety, somatic anxiety, hypochondriasis, and obsessive and compulsive symptoms). The second factor explained 11.4% of the variance and consisted of four items assessing “pure” depressive symptoms: depressed mood, suicidal ideation, diminished interest in work and activities, and motor retardation. The third factor explained 10.4% of the variance and consisted of the three insomnia items, early, middle, and late insomnia. Factor four (7.3% of the variance) consisted of other somatic items including gastrointestinal symptoms, general somatic symptoms, and weight loss. Five items, including agitation, diurnal variation, paranoia, depersonalization, and loss of insight did not load on any of the factors in this solution.

Concurrent Validity of the HAM-D

To assess concurrent validity, bivariate Spearman correlation coefficients were calculated between an MDE diagnosis (SCID-I/NP diagnosis) and individual HAM-D items (see Table 2). Not surprisingly, HAM-D items assessing depressed mood, suicide, and loss of interest in work and activities (i.e., anhedonia) were the most highly correlated with a diagnosis of MDE ($r_s = .55, .46, \text{ and } .41$ respectively). Only two items were not significantly correlated with MDE: loss of insight and diurnal variation, suggesting that these HAM-D items are poor indicators of the presence of a diagnosis of MDE in terminally ill patients.

Table 5 lists the Spearman correlation coefficients between the total HAM-D score and four HAM-D factors with eight measures administered concurrently. The HAM-D total score was significantly correlated with all of these variables ($p < .01$). HAM-D total scores correlated most highly with the HADSA ($r_s = .55$), the MSAS ($r_s = .54$), and SCID-I/NP Depression Module diagnosis ($r_s = .53$).

Validity of the HAM-D Factors

A Mann-Whitney U -test was used to determine the relationship between the four HAM-D factors and MDE diagnoses. Each of the four factors was significantly associated with the presence of an MDE diagnosis: anxiety, $U = 8101.0, p < .001$, depression, $U = 1526.5, p < .001$, insomnia, $U = 7207.5, p < .001$, and somatic, $U = 7225.5, p < .001$.

Examining the correlations between the four HAM-D factors and the other clinical measures revealed that the first factor (Anxiety) was significantly correlated with eight out of nine measures ($p < .01$) (see Table 5). It was most highly correlated with those measures related to anxiety such as the HADSA and MSAS Global Distress Index (which includes several anxiety items). The “pure depression” factor was also significantly correlated with all of the measures ($p < .001$). The strongest correlations were with suicidal ideation (SSI), desire for hastened death (SAHD), optimistic thinking (LOT-R), hopelessness (BHS), and spiritual well-being (SWB). Five of nine variables were significantly correlated with the third, “insomnia” factor ($p < .01$), including the HADSA, MSAS, and SWB. The fourth, “somatic”

factor was also significantly correlated with seven of nine measures, most strongly with the MSAS, a measure of illness-related symptom distress.

Correlations between three demographic variables (gender, age, and years of education) and the HAM-D total and factor scores were also calculated. Age was significantly negatively correlated, albeit weakly, with the anxiety factor ($r_s = -.20$) and with the HAM-D total score ($r_s = -.13$), but not with the other three factors. Gender was significantly associated with the insomnia factor, indicating that women had higher levels of insomnia than men ($r_s = -.16$). Education was not correlated with any of the HAM-D factors or total scores.

Receiver Operating Characteristics Curve Analysis

Receiver Operating Characteristic (ROC) curve analysis indicated a high degree of accuracy using HAM-D scores to predict MDE diagnosis, $AUC = .91$ (95% confidence interval: .88 to .95). The cut-off score for maximum discrimination between depressed and nondepressed patients was determined from the ROC curves as the point at which the highest sensitivity and specificity was reached (see Figure 2). Using a cut-off of 15 or greater for identifying the presence of depression, sensitivity was .79 (57 of 72 patients were correctly classified) and specificity was .87 (311 of 350 patients were correctly identified), resulting in a total “hit rate” of 87%.

Discussion

Clinicians and researchers have identified depression as a common and debilitating disorder in patients with terminal cancer. Depression decreases patients' quality of life, including both physical functioning and overall psychological well-being. Depression can fuel a desire for hastened death and decisions to withdraw or refuse potentially life-extending medical treatments. Despite clinical and research evidence pointing to the importance of identifying and treating depression in the terminally ill, confusion remains about the nature of depression in cancer patients at the end of life. What does it mean to be depressed when one is dying of cancer? Where does “appropriate” sadness at the prospect of impending death end and clinical depression begin? What role do somatic symptoms such as weight loss, insomnia, fatigue, and psychomotor retardation, play in the diagnosis and experience of depression in this population? This study sought to examine these questions through the investigation of one of the most commonly used observer-rated measures of depression, the Hamilton Depression Rating Scale.

Although the HAM-D is often used in studies of cancer patients, there are no published studies specifically evaluating the reliability and validity of the HAM-D in cancer patients at the end of life. The results of this study demonstrate that the HAM-D is a reliable instrument for assessing depression in patients with terminal cancer. The HAM-D demonstrated adequate internal consistency in this sample ($\alpha = .77$) and trained raters were able to achieve a high degree of inter-rater reliability ($ICC = .82$). Although the removal of two items, loss of insight and weight loss, increased Cronbach's coefficient alpha slightly, the increase in internal consistency was minimal ($< .01$).

This study also found the HAM-D to have high degree of concurrent validity in measuring depression in patients with terminal cancer. Although the HAM-D was not intended as a diagnostic instrument, ROC curve analysis indicated that the HAM-D had excellent predictive accuracy ($AUC=.91$) in identifying patients who met *DSM-IV* criteria for a major depressive episode (based on the SCID-I/NP Depression Module). Both Specificity (i.e., correctly identifying non-depressed patients) and Sensitivity (correctly identifying depressed patients) were optimized using a cut-off score of 14/15. This cutoff score is roughly comparable to other studies examining the HAM-D in elderly (Mottram et al., 2000) and medically ill patients (Leentjens et al., 2000; Naarding et al., 2002), that have reported optimal cut-off scores ranging from 13/14 to 15/16. Interestingly, this study found a very similar AUC and sensitivity and specificity to that found by Guo et al. (2006) using a 6-item version of the HAM-D. It is difficult to draw conclusions from their findings, however, given the small sample size ($n = 58$ across 4 groups) and the heterogeneous nature of their sample (both in terms of cancer stage and depression diagnoses).

The results from the factor analysis provide additional support for the validity of the HAM-D, but reveal a number of interesting patterns. We found four stable factors that reflected anxiety, depressed mood, insomnia, and somatic symptoms, and were similar to those found in previous research (Bagby et al., 2004; Cole et al., 2004). Anxiety emerged as the strongest (i.e., first) factor and accounted for the greatest amount of the variance in HAM-D scores. However, this factor had a much weaker correlation with the diagnosis of depression than did the “depressed mood” factor ($r=.23$ versus $.58$). These findings may simply reflect the well-established co-occurrence of anxiety and depression that is typically found among physically healthy patients (e.g., Fava et al., 2000; Fawcett & Kravitz, 1983) but does suggest a prominent role for anxiety at the end-of-life. On the other hand, the depression factor was more highly correlated with many of the “depression” variables (e.g., suicidal ideation, hopelessness, MDE diagnosis), suggesting that the identification of depressed patients may be optimized by using the subset of HAM-D items that most closely tap the construct of depression.

The insomnia and somatic factors observed in this study did not correlate highly with either a diagnosis of MDE or many of the related measures. These findings may reflect the severity of physical illness in this sample, since symptoms such as insomnia, weight loss, and gastrointestinal distress are common consequences of severe illness. Alternatively, these findings may be due to the aggressive palliative care received by patients in the study institution, as physical symptoms were generally well-controlled. In either case, neither insomnia nor other somatic symptoms were highly associated with depression, supporting concerns that these symptoms may not be good indicators of the presence of a depressive disorder in medically ill patients. Likewise, five items (agitation, diurnal variation, depersonalization, paranoia, and loss of insight) failed to load on any of the HAM-D factors, and with the exception of diurnal variation and depersonalization, these items were also infrequently observed in the sample. It is noteworthy that, with the exception of agitation, none of these items are included in the *DSM-IV* criteria for a major depressive episode. Thus, their utility in assessing depression in the terminally ill is questionable.

These findings raise question as to whether the HAM-D would be more useful in research with the terminally ill if some of the items were omitted. Inclusion of items that showed lower correlations with other indices of depression (e.g., the insomnia items) did not detract from either the reliability analyses (coefficient alpha) or the overall scale correlations with concurrently administered measures. Discrepancies between the HAM-D total score and the depression factor in terms of concurrent validity coefficients were quite modest with the exception of suicidal ideation, which was substantially more highly correlated with the depression factor than the total score. This finding is not surprising, given that the HAM-D suicidal ideation item is one of the five items that comprise the depression factor. Thus, the overall pattern of results does not seem to justify modifying the HAM-D, which appears to have robust indicators of reliability and validity in this terminally ill sample despite inclusion of several items of questionable utility. Moreover, given the concerns raised about the HAM-D, in part because of the multiple variations used, different scoring methods for some items, and variable factor structures found (e.g., Bagby et al., 2004), there seems to be little benefit to creating an additional variation for this specific population. That said, the 17-item HAM-D may be more appropriate than the 21-item version for use with cancer patients given that the three of the four items failed to load onto any of the HAM-D factors.

Although the findings from this study provide support for the reliability and validity of the HAM-D for use in patients with terminal cancer, it is important to recognize several limitations. The first potential limitation is the generalizability of the sample. Patients in this study were relatively homogenous in regards to religious affiliation (50.5% were Catholic and another 22.1% were of other Christian faiths). This limitation might have hindered the ability to identify patterns within the HAM-D by restricting the variance on this measure. Another potential limitation to this study is the lack of separate raters for the HAM-D and SCID-I/NP Depression Module. Because one interviewer usually administered both measures to the patient, typically during the same interview, it is possible that some of the concordance found between the HAM-D and SCID-I/NP Depression Module diagnoses was inflated. Future research should use separate raters to address this potential problem.

Despite these limitations, this study provides empirical support for the Hamilton Depression Rating Scale in a large sample of terminally ill cancer patients. Further research is needed to help clarify the relationship between anxiety and depression at the end of life, and assess whether these constructs become more intertwined as death approaches. Likewise, further research might help identify whether abbreviated versions of the HAM-D can be developed that would either facilitate the identification and treatment of depressed cancer patients or help assess depression more accurately. Given the tremendous impact of depression on patient quality of life, the need for accurate assessment techniques that are appropriate for use with terminally ill patients is paramount.

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Figure 1.
Factor Analysis Scree Plot

Figure 2.
ROC Curve Analysis

Table 1

HAM-D Total Scores

HAM-D Score	Total Sample <i>N</i> = 422		SCID-I/NP MDE Diagnosis <i>N</i> = 72		No SCID-I/NP MDE Diagnosis <i>N</i> = 349	
Mild (< 13)	283	67.1%	6	8.3%	277	79.1%
Moderate (13-17)	78	18.5%	27	37.5%	51	14.6%
Severe (> 17)	61	14.5%	39	54.2%	22	6.3%

Chi-square=156.34, df=2, $p < .0001$

Table 2

HAM-D Item Endorsement, Item-Total Correlations, and Correlations with SCID-I

HAM-D Item	Percentage Endorsed or Observed	Item-Total Correlations	SCID-I/NP Total Scores
1. Depressed Mood	68.2%	.59 **	.55 **
2. Guilt	24.9%	.30 **	.25 **
3. Suicide	28.0%	.43 **	.46 **
4. Insomnia-Early	34.6%	.37 **	.26 **
5. Insomnia-Middle	56.2%	.40 **	.23 **
6. Insomnia-Late	43.4%	.36 **	.23 **
7. Work and Activities	77.5%	.39 **	.41 **
8. Retardation	27.0%	.29 **	.29 **
9. Agitation	10.7%	.19 **	.11 *
10. Psychic Anxiety	57.6%	.46 **	.23 **
11. Somatic Anxiety	23.9%	.41 **	.15 **
12. Gastrointestinal Symptoms	57.1%	.31 **	.29 **
13. General Somatic Symptoms	74.9%	.24 **	.15 **
15. Hypochondriasis	29.4%	.42 **	.14 **
16. Weight Loss	52.8%	.18 **	.17 **
17. Loss of Insight	3.6%	-.01	.01
18. Diurnal Variation	30.1%	.29 **	.09
19. Depersonalization	20.9%	.29 **	.21 **
20. Paranoia	6.9%	.23 **	.13 **
21. Obsessions and Compulsions	11.8%	.22 **	.10 *

**
 $p < .01$

*
 $p < .05$

Table 3

HAM-D Factor Loadings

HAM-D Items	Anxiety	Depression	Insomnia	Somatic
1. Depressed Mood	.29	.64	.21	.10
2. Guilt	.30	.29	.14	-.05
3. Suicide	.12	.59	.16	.10
4. Insomnia-Early	.04	.18	.76	-.02
5. Insomnia-Middle	.16	.03	.81	.11
6. Insomnia-Late	.05	.12	.81	.04
7. Work and Activities	.01	.65	.11	.21
8. Retardation	.05	.59	.02	.05
9. Agitation	.46	-.01	.02	-.01
10. Psychic Anxiety	.65	.21	.13	.02
11. Somatic Anxiety	.63	.11	.18	.06
12. Gastrointestinal Symptoms	-.01	.32	.06	.61
13. General Somatic Symptoms	.21	.04	.03	.65
15. Hypochondriasis	.62	.23	.05	.08
16. Weight loss	-.10	.21	.05	.52
17. Loss of Insight	-.01	.19	.01	-.48
18. Diurnal Variation	.49	.08	.08	-.02
19. Depersonalization	.39	.33	-.11	.05
20. Paranoia	.21	.48	-.03	-.27
21. Obsessions and Compulsions	.63	-.03	-.08	-.02

Table 4

Variance Explained by HAM-D Factors

HAM-D	Eigenvalue	Percent Variance	Cumulative Variance
1	2.51	12.56	12.56
2	2.29	11.44	24.00
3	2.08	10.41	34.41
4	1.46	7.31	41.72

Table 5

Correlation of HAM-D Factors and Measures of Physical Symptom, Functioning, Pain, Social Support, and Spiritual Well-Being

HAM-D Factors	Total	Anxiety	Depression	Insomnia	Somatic
<i>Measures</i>					
HADSA	.55 **	.53 **	.39 **	.29 **	.17 *
MSAS	.54 **	.39 **	.34 **	.25 **	.43 **
SCID-I/NP	.53 **	.23 **	.58 **	.28 **	.28 **
SSI	.37 **	.13 *	.50 **	.16 **	.22 **
SAHD	.43 **	.20 **	.48 **	.19 **	.24 **
LOT-R	-.41 **	-.28 *	-.45 **	-.18	-.16
FSSQ	-.16 *	-.18 **	-.18 **	-.07	.01
BHS	.41 **	.27 **	.44 **	.16 *	.20 **
SWB	-.44 **	-.27 **	-.44 **	-.21 **	-.22 **
KPRS	-.16 **	-.08	-.25 **	-.02	-.13 *
<i>Demographics</i>					
Age	-.13 *	-.20 **	-.01	-.09	.06
Gender	-.08	-.07	.00	-.16 **	-.01
Education	.06	.09	.06	-.04	.04

*
 $p < .01$

**
 $p < .001$