The Use of the Hamilton Rating Scale for Depression in Elderly Patients With Cognitive Impairment and Physical Illness

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The authors performed a prospective study to assess the impact of cognitive impairment and medical burden on the Hamilton Rating Scale for Depression (Ham-D) scores in older psychiatric inpatients. Over 1 year, all patients admitted to an acute-care geriatric psychiatry unit were assessed with an instrument that includes an anchored version of the 17-item Ham-D. Ham-D scores of 72 patients who met DSM-III-R criteria for a major depressive episode were compared with the scores of 31 patients who did not. The scores of the depressed and nondepressed patients were significantly different on admission but not at discharge. By contrast, the Ham-D scores of 11 depressed patients with a primary dementia did not differ either on admission or at discharge from the scores of 61 depressed patients without dementia. Controlling for psychiatric diagnosis, cognitive impairment had no significant effect on Ham-D scores. Medical burden accounted for less than 6% of the variance in admission Ham-D scores. When properly applied, therefore, the Ham-D yields valid ratings of the severity of depressive symptoms in elderly patients with a broad range of cognitive impairment and physical illness. (American Journal of Geriatric Psychiatry 1994; 2:220–229)

Over the past 30 years, rating scales have been widely used to screen for psychopathology, to obtain a reliable record of psychiatric symptoms, and to derive a quantitative measure of treatment response. Among the many scales available to assess for the presence and severity of depressive symptoms, the Hamilton Rating Scale for

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Depression (Ham-D)[1] has been widely used in many studies of middle-age patients,[2–4] including most studies of newer antidepressant medications.[5] Although the Ham-D has also been used in several studies of late-life depression,[6–12] its validity in older patients, who often present with cognitive impairment and comorbid physical illness, has been questioned. For instance, Sunderland et al.[13] have commented that "several questions on the Ham-D may require cognitive capacities beyond the level of some demented patients (i.e., items concerning feelings of guilt, work and activities, and insight) and thus may not accurately reflect underlying mood" (p. 955).[13] Similarly, Alexopoulos et al.[14] remarked that since the Ham-D uses information from an interview, it requires that the subject have sufficient comprehension and judgment to answer questions related to affect and ideation. In a review on measuring depression in the physically ill, Silverstone[15] stated that among the symptoms rated on the Ham-D "eight might be affected by physical illness ... and thus this rating scale is not suitable for use in the physically ill" (p. 6).[15] Several "geriatric" scales have been developed to address the perceived limitations of the Ham-D in older patients with cognitive impairment and physical illness.[13–17] Nevertheless, a scale validated in both younger and older patients remains useful if one wants to be able to perform comparisons across the life cycle.

Based on pilot results, we hypothesized that the Ham-D could be used with validity in older patients if ratings were based not only on an interview but also on observed behavior reported by reliable informants—as is the case with several "geriatric" scales.[13,14] We performed a prospective study testing the following main hypotheses: 1) on admission to a psychiatric hospital, elderly patients who meet diagnostic criteria for a major depressive episode will have significantly higher scores on the Ham-D than patients who do not, regardless of the presence or absence of dementia; 2) at discharge, patients from various diagnostic groups will not differ in terms of their score on the Ham-D; and 3) differences in Ham-D scores will not be significantly influenced by comorbid medical illness.

METHODS

The Geriatric Clinical Research Unit (GCRU) is a 26-bed acute-care unit at Western Psychiatric Institute and Clinic for the assessment and treatment of late-life mental disorders, a teaching psychiatric hospital that both provides psychiatric care to a large urban catchment area and serves as a referral center for psychiatric patients from suburban and rural southwestern Pennsylvania. During the study period, all patients 50 years old and over admitted to this unit for at least 3 days received a comprehensive evaluation performed by a multidisciplinary team including an attending psychiatrist, a social worker, a physician's assistant (under the supervision of a geriatrician), an occupational therapist, a psychiatric nurse, and a trained research clinician, all with expertise in geriatric psychiatry.[18–23] This comprehensive evaluation included a psychiatric history and mental status examination, a social history, a medical history and physical examination, a battery of blood tests, chest X-ray, electrocardiogram, electroencephalogram, CNS imaging (MRI or CT scan when MRI was contraindicated or when patients were unable to cooperate with the MRI procedures), and other tests, as indicated by the patient's history or examination.

As part of this evaluation, on admission and at discharge, all patients were rated by one of three trained clinicians who was not involved in the patients' clinical care, using a slightly modified standardized version of the Mini-Mental State Exam (MMSE)[24,25] and an instrument yielding ratings on the 17-item Ham-D,[1] the Brief Psychiatric Rating Scale,[26] and Asberg's Side-Effects Scale.[27] The clinician-rated instrument, the Pittsburgh Older Adult Psychopathology Survey

(POAPS, available from the corresponding author) was developed to be used with older, depressed inpatients and outpatients who may present with denial, psychosis, severe psychomotor retardation, or cognitive impairment resulting in a minimization of psychiatric symptoms reported in an interview. In addition to a semi-structured interview, the POAPS includes explicit detailed scoring guidelines allowing scores to be based both on the patient's answers and on his or her observed behavior as documented in the chart or as reported by family and caregiver informants. By use of the "inclusive approach" of studies of depression in the medically ill,[28,29] symptoms were rated without attempting to determine their possible cause. For instance, ratings of weight loss or anergia are based, respectively, on the change in weight observed over the previous 2 weeks and on the characterization of the patient's energy level during the previous 3 days, regardless of the extent to which depression, physical illness, or medication side effects may have contributed to a decrease in weight or energy. Scoring guidelines are consistent with the original psychometric scales and with previously published anchored versions.[1,26,30–33]

The medical burden of each patient was rated using the CIRS-G, a version of the Cumulative Illness Rating Scale,[34–36] operationalized for use in older patients.[37] The CIRS-G yields objectively anchored ratings of disability, morbidity, and threat to life either from physical or mental problems related either to 1 of 13 organ systems or the psychiatric domain. For each system, a score of 0 indicates the absence of any medical problem; 1, a current mild or past significant problem; 2, problems resulting in moderate disability or morbidity or requiring "first line" therapy; 3, problems resulting in severe or constant significant disability or "uncontrollable" chronic problems; 4, end-stage organ failure, problems resulting in severe impairment of function or requiring immediate treatment. For this study, all CIRS-G ratings were completed at discharge by one of three physician assistants working under the supervision of a geriatric physician based on a careful review of all available information, including the results of all laboratory tests and investigations performed during the hospitalization. For each patient, based on the work of Miller et al.,[37] two scores were derived from the CIRS-G: 1) a total score (CIRS-total; range 0–52) was calculated by adding the scores of all 13 organ systems (the CIRS-G rating of psychiatric problems was excluded), thus reflecting the patient's cumulative physical illness burden; and 2) a severity score (CIRS-severity; range: 0–13) was calculated by counting the number of organ systems rated as 3 or 4 on the CIRS-G.

Interrater reliability for the MMSE, Ham-D, and CIRS-total score was assessed near the beginning and the end of the study period with the intraclass correlation procedures described by Fleiss.[38] Each intraclass correlation coefficient (ICC) was based on the concurrent ratings of 10 randomly selected patients by three independent raters. Excellent interrater reliability was established and maintained for the ratings on the MMSE (ICCs: 0.99–1.00), Ham-D (ICCs: 0.81–0.95), and CIRS-total (ICCs: 0.87–0.90).

Shortly after the patient's discharge, consensus research Axis I and Axis II diagnoses were established according to the criteria of the Diagnostic and Statistic Manual, Third Edition, Revised (DSM-III-R).[39] Also, to receive a diagnosis of primary degenerative dementia of the Alzheimer type (PDD) with depression, a patient had to meet DSM-III-R criteria both for PDD and for a major depressive episode. Consensus research diagnoses were made at weekly conferences attended by three to six faculty psychiatrists (including the patient's attending psychiatrist) and the research staff. All available information, including the information obtained from the patient, family, primary care physicians, and old records, was considered. The diagnosis corresponding to the symptoms that precipitated the admission was recorded as the "primary

psychiatric diagnosis." Additional Axis I and Axis II diagnoses were recorded as warranted. During the consensus conference, the patient's list of active physical problems was reviewed, to be subsequently coded on Axis III according to the ICD-9-CM classification system, except that mental disorders and diseases of the brain recorded on Axis I and II were not duplicated. A medical problem was considered active if it was the focus of an investigation or an intervention (e.g., degenerative arthritis with back pain requiring the prescription of a nonsteroidal anti-inflammatory drug would be coded as an active problem, whereas asymptomatic degenerative arthritis of the spine incidentally detected on chest X-ray would not).

Based on consensus research diagnoses, we considered five distinct groups: 1) major depression without psychotic features (single or recurrent), no concurrent Axis I diagnosis of any organic disorder (MD-NP); 2) major depression with psychotic features (single or recurrent), no concurrent Axis I diagnosis of any organic disorder (MD-P); 3) PDD with depression, no concurrent Axis I diagnosis of PDD with delirium, PDD with delusion or organic hallucinosis (PDD-Dep); 4) PDD, uncomplicated, no concurrent Axis I diagnosis of organic hallucinosis (PDD-Unc); and 5) schizophrenia, no concurrent Axis I diagnosis of any organic disorder (Schiz). To test our first and second hypotheses, the first three groups (MD-NP, MD-P, and PDD-Dep) were selected to allow us to evaluate differences and changes in Ham-D scores in patients with and without dementia who meet DSM-III-R criteria for a major depressive episode; the two other groups (PDD-Unc, Schiz) were selected to provide a contrast group of patients with and without dementia who did not meet DSM-III-R criteria for a major depressive episode but who presented with a variety of behavioral symptoms as described previously.[19,22]

We included in the data analysis all patients from these five diagnostic groups who were admitted to the GCRU between September 1, 1991 and August 31, 1992 (for patients who had more than one admission during the study period, only the first admission was considered) and who had completed the MMSE on admission. The 103 patients who met these inclusion criteria had a mean age of 73 ± 9 years (range: 50–91); 69% were female; 87% were white and 13% were black. The mean length of

TABLE 1. Distribution of primary psychiatric diagnoses and characterization of variables in the study sample

	n	Age	MMSE (adm)	Ham-D (adm)	Ham-D (dis)	CIRS-total	CIRS-severity	AXIS III
MD-NP	38	71.5 ± 7.2	26.3 ± 3.3	22.5 ± 3.2	12.5 ± 5.5	12.0 ± 5.3	3.4 ± 3.8	5.5 ± 3.0
MD-P	23	72.6 ± 8.5	25.8 ± 2.8	24.2 ± 4.5	13.1 ± 5.8	10.0 ± 4.8	2.7 ± 3.6	5.5 ± 2.7
PDD-Dep	11	82.5 ± 5.6	15.7 ± 7.4	21.5 ± 6.1	13.1 ± 3.7	13.3 ± 3.9	4.6 ± 3.6	7.1 ± 2.7
PDD-Unc	18	79.3 ± 5.0	7.9 ± 7.2	12.6 ± 3.1	10.5 ± 2.5	9.0 ± 3.2	2.3 ± 3.0	3.9 ± 2.1
Schiz	13	64.4 ± 7.6	24.5 ± 5.0	16.1 ± 4.5	11.4 ± 3.3	9.3 ± 5.7	2.7 ± 4.3	5.2 ± 3.8
All	103	73.4 ± 8.7	21.5 ± 8.6	20.2 ± 5.8	12.2 ± 5.8	10.8 ± 5.0	3.1 ± 3.7	5.3 ± 2.9

Note: Values are means ± SD.

MMSE: Mini-Mental State Exam; Ham-D: Hamilton Rating Scale for Depression; CIRS-total: Cumulative Illness Rating Scale, total score; CIRS-severity: Cumulative Illness Rating Scale, number of organ systems rated 3 or 4; AXIS-III: number of active medical problems coded on Axis III; adm: admission; dis: discharge; MD-NP: major depression, severe, without psychotic features; MD-P: major depression, with psychotic features; PDD-Dep: primary degenerative dementia, with depression; PDD-Unc: primary degenerative dementia, uncomplicated; Schiz: schizophrenia.

hospitalization was 32 ± 17 days (range: 3–82). Table 1 presents, for the entire sample and for each of the five diagnostic groups, the number of patients, mean age, mean MMSE score, mean admission and discharge Ham-D scores, and three measures of medical burden: mean CIRS-total, CIRS-severity, and mean number of active medical problems coded on Axis III (AXIS III).

To test our first and second hypotheses regarding the impact of cognitive impairment on Ham-D scores, analysis of variance (ANOVA, with Tukey's post-hoc comparisons when warranted) were used to compare the mean Ham-D scores of the five diagnostic groups on admission and at discharge. Also, because, by design, our nondepressed subjects (PDD-Unc, Schiz) were expected, on average, to be more cognitively impaired than our depressed subjects (MD-NP, MD-P, and PDD-Dep), an analysis of covariance (ANCOVA) was used to determine the effect of MMSE scores on admission Ham-D scores after controlling for the effect of diagnosis. To test our third hypothesis regarding the impact of medical burden on Ham-D scores, parametric and nonparametric correlations between the three measures of medical burden (CIRS-total, CIRS-severity, AXIS-III) and admission Ham-D scores were calculated in the entire sample. Regression analyses were used to determine whether the association between measures of medical burden and admission Ham-D scores were similar in all diagnostic groups. When significant differences were found, an additional correlation analysis was performed to assess the significance of the impact of medical burden on admission Ham-D scores within each diagnostic group.

RESULTS

We first examined the effect of cognitive impairment on Ham-D scores. On admission, the mean Ham-D score of patients with dementia and depression (PDD-Dep) did not differ significantly from the mean score of depressed patients without dementia (MD-NP, MD-P); by contrast, the mean Ham-D score of each of these three groups of depressed patients (MD-NP, MD-P, and PDD-Dep) differed significantly from the mean score of each of the two groups of nondepressed patients (PDD-Unc, Schiz; F [4,98] = 28.4; $P \leq 0.0001$; Tukey's standardized range significant at the 0.05 level for: MD-NP vs. PDD-Unc, Schiz; MD-P vs. PDD-Unc, Schiz; PDD-Dep vs. PDD-Unc, Schiz). As expected, based on the selection of our depressed groups (MD-NP, MD-P, and PDD-Dep) and nondepressed contrast groups (PDD-Unc, Schiz), a significant association was found between MMSE and admission Ham-D scores (F[1,98] = 44.6; $P \leq$ 0.0001). However, controlling for diagnosis, this association between MMSE and admission Ham-D score was not significant (F [1,93] = 0.89; $P \geq 0.35$). At discharge, after inpatient treatment lasting an average of 1 month, the differences in Ham-D scores between the depressed and nondepressed patients had disappeared and none of the five mean Ham-D scores differed significantly (F[4,95] = 1.0; $P \geq 0.40$).

We next examined the effect of medical burden on Ham-D scores. In the entire sample, although the three measures of medical burden were all highly and significantly correlated with each other (all Ps $\leq$ 0.0001), admission Ham-D scores and measures of medical burden were only marginally associated (Table 2); medical burden, therefore, accounted for, at most, 6% (R^2 = $0.24^2 = 0.058$; $P \leq 0.02$) of the variance in admission Ham-D scores. Assessing for a possible effect of medical burden on Ham-D scores within specific diagnostic groups, we found that the association between CIRS-total and admission Ham-D scores was significantly different in different diagnostic groups (F[4,93] = 2.7; $P \leq 0.04$). A correlation analysis within each diagnostic group showed that Ham-D and CIRS-total scores were significantly correlated only for patients with dementia and without

depression (PDD-Unc), with 23% ($R^2 = 0.48^2 = 0.23$; $P \leq 0.04$) of the variance in admission Ham-D scores explained by the CIRS-total scores for this diagnostic group. When either CIRS-severity or AXIS-III scores were used as a measure of medical burden, there was no significant correlation between either of these two measures of medical burden and admission Ham-D scores within any of the five diagnostic groups (all $Ps \geq 0.10$).

DISCUSSION

To assess the impact of cognitive impairment and medical burden on Ham-D ratings in older psychiatric inpatients, all patients admitted over a period of 1 year to an acute-care geriatric psychiatry unit were systematically assessed with an instrument that includes an anchored version of the 17-item Ham-D. Ham-D ratings were based both on interviews with patients and on observed behavior reported by reliable informants (e.g., family members, ward nurses). As hypothesized, on admission, patients who met diagnostic criteria for a major depressive episode had significantly higher mean scores on the Ham-D than patients who did not, regardless of the presence or absence of dementia. At discharge, depressed and nondepressed patients no longer differed in terms of their score on the Ham-D. Finally, differences in Ham-D scores were not significantly influenced by comorbid medical illness. The implications of these results for the use of the Ham-D in patients with cognitive impairment or physical illness deserves further comment.

Use of the Ham-D in Cognitively Impaired Patients

Gottlieb et al.[40] have previously reported the Ham-D to be a reliable scale for the assessment of depressive features in patients suffering from PDD of mild to high severity. Like ours, their ratings were based both on patients' examination and on observed behavior (as reported by at least one family member). As previously, noted by Alexopoulos et al.[14,17] and Sunderland et al.,[13] the ability to rate not only the patient's subjective symptoms but also his or her objective behavior may be a necessary feature for any scale used to rate depressive symptomatology in cognitively impaired patients. Our results suggest that in elderly patients with cognitive impairment, this method yields not only reliable, but also valid ratings of depression. This conclusion

TABLE 2. Correlations between Hamilton Rating Scale for Depression admission scores and three measures of medical burden

	Ham-D (adm)	CIRS-total	CIRS-severity	AXIS III
Ham-D (adm)	—	0.17 (0.08)	0.15 (0.13)	0.27 (0.005)
CIRS-total	0.18 (0.07)	—	0.75 (0.0001)	0.64 (0.0001)
CIRS-severity	0.17 (0.09)	0.82 (0.0001)	—	0.44 (0.0001)
AXIS-III	0.24 (0.02)	0.62 (0.0001)	0.50 (0.0001)	—

Note: Values above dashes: Spearman correlation coefficients (corresponding *P* values below). Values below dashes: Pearson correlation coefficients (corresponding *P* values below).
Ham-D: Hamilton Rating Scale for Depression; CIRS-total: Cumulative Illness Rating Scale, total score; CIRS-severity: Cumulative Illness Rating Scale, number of organ systems rated 3 or 4; AXIS III: number of active medical problems coded on Axis III; adm: admission.

is supported by the statistically and clinically significant differences between the mean Ham-D admission scores of patients who did and did not meet DSM-III-R criteria for a major depressive episode, regardless of the presence or absence of a clinical dementia. The strength of this evidence is predicated on the correctness of our clinical diagnoses. Though there is not yet a consensus on the best way to diagnose clinically meaningful depression in patients with dementia,[41,42] the use of the criteria for a major depressive episode in the context of a degenerative dementia has been validated both by neuropathological and neurochemical studies of postmortem tissues[43–45] and by clinical studies.[11,19] Furthermore, the apparent sensitivity of the Ham-D to symptomatic change (i.e., treatment response) in older, depressed patients regardless of the presence or absence of dementia provides additional support for its valid use in patients with various degrees of cognitive impairment. Although our depressed patients received fairly standardized antidepressant treatment, as described previously,[12,19,20] the lack of controlled treatments qualifies this finding. Moreover, the duration of our inpatients' hospitalization (1 month on average) was shorter than the duration of antidepressant treatment expected to yield maximal benefits in older, depressed patients.[10,46] Thus, it is possible that significant differences in the symptomatic improvement of our depressed patients with and without dementia would have been detected over a longer interval. However, the absence of a significant association between Ham-D scores and severity of cognitive dysfunction in this and other studies of patients with dementia and without clinical depression[40,47] makes this possibility unlikely.

Use of the Ham-D in Physically Ill Patients

Because of the prominence given by the Ham-D to the physical manifestations of major depression (its so-called neuro-vegetative symptoms), the validity of the Ham-D in elderly patients with physical illness has been questioned.[15,17] However our results strongly support the conclusion that the Ham-D is a valid instrument for quantifying the severity of depression in elderly patients with a broad range of physical illness and medical burden. Though we are not aware of any other published correlation between Ham-D scores and systematic measures of medical burden in a similar sample, our findings are entirely congruent with four recent studies[29,48–50] that, taken together with our results, suggest that endorsement by elderly patients of somatic symptoms on a scale such as the Ham-D is likely to indicate a higher severity of depression, rather than physical illness and medical burden. Lyness et al.[50] have reported that somatic worry in elderly depressed inpatients was associated with a measure of depression severity (Ham-D scores) rather than with a measure of medical burden (CIRS scores). Similarly, Koenig et al.[29] found that both self-rated and observer-rated somatic symptoms were important indicators of depression in older medical inpatients. In a sample of elderly depressed outpatients, Miller et al.[48] found that somatic complaints attributed to antidepressant side effects gradually resolved with successful treatment of depression. In a representative sample of 1,060 community-dwelling elders, Foelker and Shewchuk[49] found no significant correlation between depression severity (as measured by scores on the Center for Epidemiological Studies Depression Scale [CES-D]) and medical burden (as measured by the composite score or the three component scores of the Physical Health Domain Index [PHDI] of the Philadelphia Geriatric Center's Multi-Level Assessment Instrument). Among elders deemed depressed (on the basis of their CES-D score), although the CES-D total score was not associated with the PHDI score or any of its components, there was a significant association between somatization (as measured by the CES-D somatic

subscale) and the PHDI score. Thus clinical depression appears to act as a mediating variable between physical illness and somatic complaints. In other words, major depression may cause an increase in subjective somatic complaints related to underlying physical illness. If this hypothesis is confirmed by other studies, the wisdom of eliminating somatic symptoms from geriatric depression rating scales may be questioned.[16] Similarly, given the considerable overlap between the DSM-III-R criteria for a major depressive episode and the symptoms assessed by the Ham-D, these results suggest that more importance, rather than less, should be given to somatic complaints when diagnosing clinical depression in elderly patients.[51–53] Our data cannot answer this question because this study was designed to test the validity of the Ham-D as an instrument for quantifying and assessing change in the severity of major depression[1] rather than for determining its presence or absence.

CONCLUSION

Limitations to this study involve the retrospective nature of the psychiatric diagnoses (made shortly after discharge), the relatively small number of patients in each diagnostic subgroup, and the inclusion of only older patients admitted to an acute-care psychiatric hospital. Thus our results may not apply to older, depressed patients treated in the community, in medical facilities, or in long-term care facilities over a long period of time. Similarly, this study does not address the usefulness of the Ham-D in quantifying depressive symptoms in elderly patients with subsyndromal ("minor") depression.[17] In light of data suggesting important differences between patient and family assessments of depressive manifestations in Alzheimer's disease,[54] it would have been informative to quantify the relative contribution of the two sources of information on which our ratings were based (i.e., interviews with patients and observed behavior reported by reliable informants). Notwithstanding these limitations, this study supports the hypothesis that, when based both on patient's interview and observed behavior, the Ham-D yields reliable and valid ratings of the severity of depressive symptoms—and of the change in these depressive symptoms in response to treatment—in elderly patients with a broad range of cognitive impairment and physical illness. Thus, given its wide use in younger patients, the Ham-D may provide a suitable instrument for the study of depressive patients throughout the entire adult life span.

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References

1. Hamilton M: Development of a rating scale for primary depressive illness. British Journal of Social and Clinical Psychology 1967; 6:278–296
2. Elkin I, Parloff MB, Hadley SW, et al: NIMH Treatment of Depression Collaborative Research Program. Arch Gen Psychiatry 1985; 42:305–316
3. Spiker DG, Weiss JC, Dealy RS, et al: The pharmacological treatment of delusional depression. Am J Psychiatry 1985; 142:430–436
4. Frank E, Kupfer DJ, Perel JM, et al: Three-year outcomes for maintenance therapies in recurrent depression. Arch Gen Psychiatry 1990; 47:1093–1099
5. Reimherr FW, Chouinard G, Cohn CK, et al: Antidepressant efficacy of sertraline: a double-blind, placebo- and amitriptyline-controlled, multicenter comparison study in outpatients with major depression. J Clin Psychiatry 1990; 51(suppl.):18–27
6. Georgotas A, McCue RE, Hapworth W, et al: Comparative efficacy and safety of MAOIs vs. TCAs in treating depression in the elderly. Biol Psychiatry 1986; 21:1155–1166

7. Cohn CK, Shrivastava R, Mendels J, et al: Double-blind, multicenter comparison of sertraline and amitriptyline in elderly depressed patients. J Clin Psychiatry 1990; 51:28–33
8. Reifler BV, Teri L, Raskind M, et al: Double-blind trial of imipramine in Alzheimer's disease patients with and without depression. Am J Psychiatry 1989; 146:45–49
9. Katz IR, Simpson GM, Curlik SM, et al: Pharmacologic treatment of major depression for elderly patients in residential care settings. J Clin Psychiatry 1990; 51(suppl.):41–47
10. Reynolds CF, Frank E, Perel JM, et al: Combined pharmacotherapy and psychotherapy in the acute and continuation treatment of elderly patients with recurrent major depression: a preliminary report. Am J Psychiatry 1992; 149:1687–1692
11. Alexopoulos GS, Meyers BS, Young RC, et al: The course of geriatric depression with "reversible dementia": a controlled study. Am J Psychiatry 1993; 150:1693–1699
12. Zubenko GS, Mulsant BH, Rifai AH, et al: Impact of acute psychiatric inpatient treatment on major depression in late life and prediction of response. Am J Psychiatry, in press
13. Sunderland T, Alterman IS, Yount D, et al: A new scale for the assessment of depressed mood in demented patients. Am J Psychiatry 1988; 145:955–959
14. Alexopoulos GS, Abrams RC, Young RC, et al: Cornell scale for depression in dementia. Biol Psychiatry 1988; 23:271–284
15. Silverstone PH: Measuring depression in the physically ill. International Journal of Methods in Psychiatric Research 1991; 1:3–12
16. Yesavage JA, Brink TL, Rose TL, et al: Development and validation of a geriatric depression screening scale: a preliminary report. J Psychiatr Res 1983; 17:37–49
17. Alexopoulos GS, Abrams RC, Young RC, et al: Use of the Cornell scale in nondemented patients. J Am Geriatr Soc 1988; 36:230–236
18. Sweet RA, Mulsant BH, Rifai AH, et al: Dyskinesia and neuroleptic exposure in elderly psychiatric inpatients. J Geriatr Psychiatry Neurol 1992; 5:156–161
19. Zubenko GS, Rosen J, Sweet RA, et al: Impact of psychiatric hospitalization on behavioral complications of Alzheimer's disease. Am J Psychiatry 1992; 149:1484–1491
20. Kunik ME, Mulsant BH, Rifai AH, et al: Personality disorders in elderly inpatients with major depression. American Journal of Geriatric Psychiatry 1993; 1:38–45
21. Rifai AH, Mulsant BH, Sweet RA, et al: A study of elderly suicide attempters admitted to an inpatient psychiatric unit. American Journal of Geriatric Psychiatry 1993; 1:126–135
22. Mulsant BH, Stergiou A, Keshavan MS, et al: Schizophrenia in late life: a clinical study of elderly patients admitted to an acute care psychiatric hospital. Schizophr Bull 1993; 19:709–721
23. Sweet RA, Mulsant BH, Kunik ME, et al: Phenomenology and prevalence of neuroleptic-induced akathisia in late life. American Journal of Geriatric Psychiatry 1993; 1:136–142
24. Folstein MF, Folstein SE, McHugh PR: Mini-Mental State: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975; 12:189–198
25. Molloy DW, Alemayehu E, Roberts R: Reliability of a standardized Mini-Mental State Examination compared with the traditional Mini-Mental State Examination. Am J Psychiatry 1991; 148:102–105
26. Overall JE, Gorham DR: The Brief Psychiatric Rating Scale. Psychol Rep 1962; 10:799–812
27. Asberg M, Cronholm B, Sjoqvist F, et al: Correlation of subjective side effects with plasma concentrations of nortriptyline. BMJ 1970; 4:18–21
28. Cohen-Cole SA, Stoudemire A: Major depression and physical illness. Psychiatr Clin North Am 1987; 10:1–17
29. Koenig HG, Cohen HJ, Blazer DG, et al: Profile of depressive symptoms in younger and older medical inpatients with major depression. J Am Geriatr Soc 1993; 41:1169–1176
30. Rhoades HM, Overall JE: The semistructured BPRS interview and rating guide. Psychopharmacol Bull 1988; 24:101–104
31. Tarell JD, Schulz SC: Nursing assessment using the BPRS: a structured interview. Psychopharmacol Bull 1988; 24:105–111
32. Williams JBW: A structured interview guide for the Hamilton Depression Rating Scale. Arch Gen Psychiatry 1988; 45:742–747
33. Woerner MG, Mannuzza S, Kane JM: Anchoring the BPRS: an aid to improved reliability. Psychopharmacol Bull 1988; 24:112–117
34. Linn BS, Linn MW, Gurel L: Cumulative Illness Rating Scale. J Am Geriatr Soc 1968; 16:622–626
35. Waldman E, Potter JF: A prospective evaluation of the Cumulative Illness Rating Scale. Aging 1992; 4:171–178
36. Conwell Y, Forbes NT, Cos C, et al: Validation of a measure of physical illness burden at autopsy: the Cumulative Illness Rating Scale. J Am Geriatr Soc 1993; 41:38–41
37. Miller MD, Paradis CF, Houck PR, et al: Rating chronic medical illness burden in geropsychiatric practice and research: application of the Cumulative Illness Rating Scale (CIRS). Psychiatry Res 1992; 41:237–248
38. Fleiss JL: The Design and Analysis of Clinical Experiments. New York, John Wiley and Sons, 1986
39. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition, Revised. Washington, DC, American Psychiatric Association, 1987
40. Gottlieb GL, Gur RE, Gur RC: Reliability of psychiatric scales in patients with dementia of the Alzheimer type. Am J Psychiatry 1988; 145:857–860

41. Emery VO, Oxman TE: Update on the dementia spectrum of depression. Am J Psychiatry 1992; 149:3:305–317
42. Forsell Y, Jorm AF, Fratiglioni L, et al: Application of DSM-III-R criteria for major depressive episode to elderly subjects with and without dementia. Am J Psychiatry 1993; 150:1199–1202
43. Zubenko GS, Moossy J: Major depression in primary dementia: clinical and neuropathologic correlates. Arch Neurol 1988; 45:1182–1186
44. Zweig RM, Ross CA, Hedreen JC, et al: The neuropathology of aminergic nuclei in Alzheimer's disease. Ann Neurol 1988; 24:233–242
45. Zubenko GS, Moossy J, Kopp U: Neurochemical correlates of major depression in primary dementia. Arch Neurol 1990; 47:209–214
46. Georgotas A, McCue E: The additional benefit of extending an antidepressant trial past 7 weeks in the depressed elderly. International Journal of Geriatric Psychiatry 1989; 4:191–195
47. Miller NE: The measurement of mood in senile brain disease: examiner ratings and self-reports, in Psychopathology in the Aged, edited by Cole JO, Barrett JE. New York, Raven Press, 1980, pp 97–122
48. Miller MD, Pollock BG, Rifai AH, et al: Longitudinal analysis of nortriptyline side effects in elderly depressed patients. J Geriatr Psychiatry Neurol 1991; 4:226–230
49. Foelker GA, Shewchuk RM: Somatic complaints and the CES-D. J Am Geriatr Soc 1992; 40:259–262
50. Lyness JM, Caine ED, Conwell Y, et al: Depressive symptoms, medical illness, and functional status in depressed psychiatric inpatients. Am J Psychiatry 1993; 150:910–915
51. Endicott J: Measurement of depression in patients with cancer. Cancer 1984; 53:2243–2248
52. Rapp SR, Vrana S: Substituting nonsomatic for somatic symptoms in the diagnosis of depression in elderly male medical patients. Am J Psychiatry 1989; 146:1197–1200
53. Kathol RG, Mutgi A, Williams J, et al: Diagnosis of major depression in cancer patients according to four sets of criteria. Am J Psychiatry 1990; 147:1021–1024
54. Mackenzie TB, Robiner WN, Knopman DS: Differences between patient and family assessments of depression in Alzheimer's disease. Am J Psychiatry 1989; 146:1174–1178