Depression Predicts Cognitive Disorders in Older Primary Care Patients

Lisa L. Boyle, MD; Anton P. Porsteinsson, MD; Xingjia Cui, MD, MPH, MS; Deborah A. King, PhD; and Jeffrey M. Lyness, MD

Objective: To investigate whether depression is independently associated with increased risk of incident dementia or cognitive disorder not otherwise specified (NOS) in an older primary care population.

Method: This was a prospective 3-year cohort study of 470 patients aged ≥ 65 years without baseline cognitive disorders who were recruited from primary care offices. Annual assessments completed from March 2003 through December 2005 included the use of the Structured Clinical Interview for *DSM-IV* to diagnose major depressive disorder (MDD) and minor depression (MinD) and the Hamilton Depression Rating Scale (HDRS) for depressive symptom severity. The Mini-Mental State Exam, Mattis Dementia Rating Scale-initiation/perseveration subscale, and the Trail Making Tests A and B informed diagnoses of dementia and cognitive disorder NOS.

Results: 36 subjects, representing a cumulative incidence of 13%, developed dementia or cognitive disorder NOS over 3 years. Using Cox proportional hazard survival models to calculate the risk ratio of depression for development of cognitive disorders, MDD and MinD (HR = 3.68; 95% CI, 2.1–6.42 and HR = 1.84; 95% CI, 1.05–3.21, respectively) and HDRS scores (HR = 1.07; 95% CI, 1.02–1.12) predicted new onset dementia or cognitive disorder NOS, when covarying age, gender, and education.

Conclusions: Depressive disorders pose increased risk of incident dementia or cognitive disorder NOS in older primary care patients. Clinicians treating depressed older adults should monitor for development of cognitive disorders.

J Clin Psychiatry 2010;71(1):74–79

Submitted: *September 19, 2008; accepted April 10, 2009 (doi:10.4088/JCP.08m04724gry).*

Corresponding author: *Lisa L. Boyle, MD, Department of Psychiatry, Box Psych, University of Rochester Medical Center, 300 Crittenden Blvd, Rochester, NY 14642 (Lisa_Boyle@urmc.rochester.edu).*

As the population of older adults grows, increasing attention must be placed on age-related illnesses such as cognitive disorders and dementia. Approximately 4.5 million US individuals have Alzheimer's disease (AD), the most common type of dementia, and the population of AD patients is projected to increase at least 3-fold by the year 2050.[1] Moreover, as the number of older adults increases, a larger portion of the population will be at risk for cognitive impairment, including mild cognitive impairment (MCI) and cognitive impairment–no dementia, conditions thought to be on a continuum between normal age-related cognitive decline and dementia. Therefore, the identification of potentially modifiable risk factors for cognitive disorders and dementia is of significant public health interest.

Depression in late life has been associated with cognitive impairment and cognitive decline[2–8] and has been identified as a potential risk factor for subsequent dementia. Some studies have found retrospectively that a past history of depression was associated with increased risk for dementia.[9,10] Other prospective and meta-analytic data have supported depressive symptoms' association with increased risk for subsequent dementia.[11–13] Others have refuted the role of depression as an independent risk factor[14–16] but acknowledge that depression likely represents symptoms of the underlying dementia. Depressive symptoms have also been associated with elevated risk for development of MCI.[17,18] There have been mixed findings whether depression elevates risk for conversion of MCI to AD.[19,20]

Frequently, depressive symptoms are used as a surrogate for depressive disorders in studies examining the association between depression and cognitive disorders. To our knowledge, only one prospective study[19] used formal diagnostic criteria to determine whether major depressive disorder (MDD) is a risk factor for dementia. Additional studies are needed to confirm these findings, increase awareness of the potential risks associated with a clinical diagnosis of depression, and inform future interventions.

Although the vast majority of older adults seek treatment from their primary care physicians as opposed to mental health specialty clinics,[21] few studies have examined the relationship between depression and cognitive disorders in the primary care setting.[18] From earlier work, an estimated 5.1% of older primary care patients have MDD, while 6.6% meet criteria for minor depression (MinD).[22] To our knowledge,

no previous study has examined the role of MinD and subsequent risk for cognitive disorder or dementia.

Similarly, few studies have measured the prevalence of cognitive disorders or dementia in the primary care setting. An estimated 6% of seniors in primary care have dementia, although <20% of those were identified and diagnosed.[23] Certainly, improved identification of those at risk would allow for more efficient and effective strategies to screen, diagnose, and manage those with cognitive disorders and dementia.

This study tested the hypothesis that depression is independently associated with increased risk of subsequent dementia or cognitive disorders in older primary care patients. A rigorously studied cohort of seniors in primary care settings were followed naturalistically as part of a larger study.[22] To our knowledge, this is the first study using systematic diagnoses for both major and minor depression to examine the risk of dementia or cognitive disorders within a cohort of older primary care patients.

METHOD

Participants and Consent

Study procedures have been reported elsewhere.[22] Briefly, from March 2003 through December 2005, all patients aged 65 years and older who presented for care on selected days to private and hospital-affiliated internal medicine, geriatric, and family medicine practices in greater Rochester, New York, and who could provide written informed consent using procedures approved by the University of Rochester Research Subjects Review Board were eligible to participate. Enrolled subjects then underwent semistructured interviews, administered by trained raters who also reviewed each subject's primary care chart. Semistructured interviews and chart reviews were repeated annually for 3 years.

Depression Diagnoses and Measures

The Structured Clinical Interview for *DSM-IV* (SCID)[24] was used to assign subjects to diagnostic groups, defined as follows: (1) current MDD; (2) current MinD (based on *DSM-IV* appendix B criteria); or (3) nondepressed (all others). This trichotomous variable served as an independent predictor in the analyses. The SCID has been validated for use in older patients[25] and has been used as a gold standard for determining depression diagnoses in prior studies.[22,26,27] The other independent variable was the 24-item Hamilton Depression Rating Scale (HDRS).[28] In our research group, interrater reliability has been high, eg, an intraclass correlation coefficient of 0.93 for the HDRS (based on 6 raters and 5 subjects), and κ coefficients for the diagnoses of mood disorders ranging from 0.66 to 0.86 ($P < .001$, based on 6 raters and 3 subjects). To limit any potential confounding effect from shared somatic symptoms common to both depressive and cognitive disorders, we repeated analyses using scoring of only the 12 psychological/affective items from the HDRS (HDRS-P), a modification of the HDRS that we have used in other analyses[29] and adapted from others' prior work.[30] The items included in the HDRS-P were depressed mood, feelings of guilt, suicide, psychic anxiety, hypochondriasis, insight, depersonalization and derealization, paranoid symptoms, obsessive and compulsive symptoms, helplessness, hopelessness, and worthlessness.

Dementia/Cognitive Disorders Diagnoses and Cognitive Measures

Four cognitive measures were used in this study to inform dementia and cognitive disorder not otherwise specified (NOS) diagnoses. The Mini-Mental State Examination (MMSE)[31] was used as a global cognitive measure. Executive function measures included the Mattis Dementia Rating Scale-initiation/perseveration subscale (Mattis-IP),[32] which evaluates category fluency and alternating verbal and psychomotor tasks, and the Trail Making Test B (Trails B).[33] Trails B assesses mental set shifting and response inhibition and was administered along with the Trail Making Test A (Trails A), which measures sustained attention, sequencing, and information processing/motor speed.[33] Trails A and B were analyzed based on completion time in seconds. Analyses included participants who attempted but failed to complete either of these tasks within 300 seconds. This extended time limit was allowed for both Trails A and B in order to test the limits of a subject's abilities.[34] Scores were coded at 300 seconds when participants were unable to complete the task. Study raters administered the cognitive measures according to procedures developed under the supervision of a neuropsychologist.

Clinical application of *DSM-IV* criteria by an experienced geriatric psychiatrist (J.M.L.) was used to inform the diagnosis of dementia using all available information, including participants' overall performance on the cognitive measures, qualitative observations provided by the research raters, and history and examinations recorded in patients' medical records. Cognitive disorder NOS was diagnosed by an experienced geriatric psychiatrist (J.M.L.) using available data from the 4 cognitive measures, based on the following criteria: cognitive impairment ≥1 cognitive domain; evident decline from baseline cognitive function; no significant impairment in overall functional status due to cognition; and not meeting *DSM-IV* criteria for dementia. This approach is similar to MCI criteria adopted in another study.[17] We used a broad definition for cognitive disorder due to the lack of consensus regarding a definition of cognitive impairment that does not meet criteria for dementia. As well, this broader definition is more reflective of usual practice in primary care than diagnoses informed by formal neuropsychometric evaluations.

Data Analyses

Analyses were conducted using SAS, version 9.1 (SAS Institute, Inc, Cary, North Carolina). A time-dependent

Table 1. Demographic and Clinical Characteristics of Older Primary Care Patients

Baseline Characteristic	MDD (n = 20)	MinD (n = 33)	NonD (n = 417)
Age, mean ± SD, y	74.2 ± 5.9	74.6 ± 5.3	74.5 ± 6.5
Education, mean ± SD, y	13.8 ± 2.7	13.7 ± 2.2	14.4 ± 2.5
Female, n (%)	14 (70.0)	24 (72.7)	259 (62.1)
Race, n (%)			
White	20 (100.0)	32 (97.0)	399 (95.7)
Black	0	1 (3.0)	14 (3.4)
Other	0	0	4 (1.0)

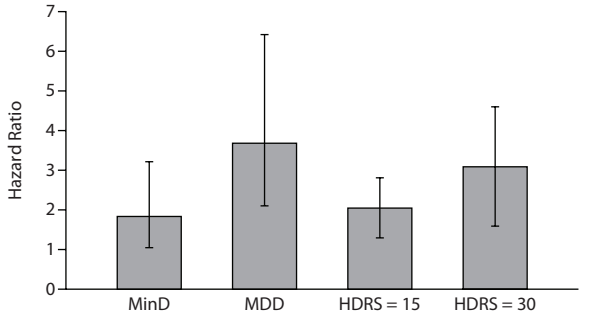
Abbreviations: MDD = major depressive disorder, MinD = minor depression, NonD = nondepressed.

Table 2. HDRS and MMSE Scores by Depression Diagnoses

	MDD		MinD		NonD	
Baseline Characteristics	Mean ± SD	Range	Mean ± SD	Range	Mean ± SD	Range
HDRS score	23.7 ± 5.6	10–34	15.2 ± 5.2	6–26	7.3 ± 4.8	0–26
HDRS-P score	12.6 ± 4.0	4–20	7.4 ± 3.0	1–15	3.2 ± 2.6	0–15
MMSE score	28.1 ± 1.5	24–30	28.0 ± 1.7	23–30	28.8 ± 7.2	17–30

Abbreviations: HDRS = Hamilton Depression Rating Scale, HDRS-P = Hamilton Depression Rating Scale-psychological/affective items, MDD = major depressive disorder, MinD = minor depression, MMSE = Mini-Mental State Examination, NonD = nondepressed.

Figure 1. Hazard Ratios With 95% Confidence Intervals of Depression and Incident Dementia or Cognitive Disorder NOS



Abbreviations: HDRS = Hamilton Depression Rating Scale, MDD = major depressive disorder, MinD = minor depression, NOS = not otherwise specified.

Cox proportional hazards model was used to identify the contribution of depression to the occurrence of dementia or cognitive disorder while simultaneously controlling for other possible predictors such as age, gender, and years of education. Additional sensitivity analyses were conducted by repeating the analyses (1) while also controlling for the Composite Antidepressant Score (CAS)[35] at baseline in order to determine whether antidepressant treatment affected the risk for dementia or cognitive disorders; and (2) while using subsequent MMSE scores as outcome to identify the contribution of depression to the resulting MMSE scores over the 3-year period while simultaneously controlling for age, gender, and years of education. In all analyses, depression diagnosis was entered into the Cox model as a time-dependent covariate, so that only the depression that occurred before the first episode of dementia or cognitive disorder (not after) would be used in the assessment of their contribution. Patients with dementia or cognitive disorder at baseline assessment were excluded from the analyses. The χ^2 test for categorical variables and the nonparametric Wilcoxon test for continuous variables were used for the analyses of attrition based on baseline variables. Two-tailed hypothesis tests were implemented with $\alpha = .05$.

RESULTS

Of 1415 subjects approached for study enrollment, 709 (50.l%) completed intake assessments. As reported elsewhere,[36] while complete information on nonenrolled subjects was not available due to Health Insurance Portability and Accountability Act considerations, enrolled subjects did not differ from nonenrolled patients on age, gender, or 15-item Geriatric Depression Scale[37] score based on available data obtained from routine clinical practice. After excluding subjects who did not participate in any follow-up (n = 222) or who met criteria for cognitive disorder NOS or dementia at baseline (n = 17), 470 of the 709 who enrolled were included in the analyses. There was attrition over the course of 3 years due to death, drop-out, withdrawal, or inability of study personnel to locate subjects. As a result, 426, 324, and 204 subjects participated in years 1, 2, and 3, respectively. Those who did not complete any follow-up assessment did not differ from those who did based on initial age, gender, education, race, cerebrovascular risk factor score, Trails A time, Trails B time, Mattis-IP score, and MMSE score, but they did have higher initial HDRS scores (mean = 10.6 [SD = 6.09] versus mean = 8.5 [SD = 6.4]; Wilcoxon $z = 3.16$, $P = .002$) and a greater overall medical burden according to the Cumulative Illness Rating Scale[38] (mean = 7.93 [SD = 5.79] versus mean = 7.33 [SD = 5.74]; Wilcoxon $z = 1.72$, $P = .04$). The study population's demographic characteristics at baseline are reported in Table 1. These characteristics are categorized by depression diagnoses. The results of HDRS, HDRS-P, and MMSE scores by depression diagnoses are reported in Table 2.

Over the course of 3 years, 12 participants met criteria for dementia and 24 met criteria for cognitive disorder NOS, representing a cumulative incidence of dementia or cognitive disorder of 13%. One subject with incident cognitive disorder NOS subsequently converted to dementia. The hazard ratios (HRs) with 95% confidence intervals (95% CI) for subjects with MDD and MinD and for HDRS scores of 15 and 30 are shown in Figure 1. The HR per unit increase in HDRS-P scores was 1.11 (95% CI, 1.02–1.21), similar to the findings for HDRS scores (HR = 1.07; 95% CI, 1.02–1.12). In the sensitivity analyses that controlled for CAS, there were no significant changes to the study's findings. In the

sensitivity analyses that looked at the relationship between depression and subsequent MMSE scores, depression was not predictive of subsequent MMSE scores over the 3-year follow-up period.

DISCUSSION

Depression was predictive of subsequent onset of dementia or cognitive disorder NOS in older primary care patients independent of age, gender, and years of education. To our knowledge, this is the first study to examine the association of operationally defined major and minor depression with incident cognitive disorders in a primary care older adult population. Both major and minor depression were predictive of subsequent development of dementia or cognitive disorder during the 3 year course of follow-up. Both depressive (HDRS) and isolated psychological/affective (HDRS-P) symptoms predicted subsequent diagnoses of dementia or cognitive disorder NOS. Each 1-point increase in the HDRS and HDRS-P scores raised the risk of subsequent cognitive disorder NOS or dementia by 7% and 11%, respectively. These findings lend additional support to the role of depression as a strong risk marker, as noted in prior studies using depressive symptoms scales and large community samples.[4,12,17] This study extends previous findings[18] by using well-operationalized measures to describe individuals who met criteria for major and minor depression. This has clinical relevance, as it provides a measure of the relationship between depressive symptoms and functioning that depressive symptom scales alone cannot. Another strength of this study was the use of a primary care cohort, as this is the setting in which older depressed individuals are most likely to present. As well, previous findings from community samples may not generalize to primary care populations.

Turning to the results of our sensitivity analyses, antidepressant treatment did not alter our findings, suggesting that there was no association between antidepressant use and subsequent onset of dementia or cognitive disorders following depression. Antidepressant use has not been associated independently with depression outcome in naturalistically followed primary care cohorts, probably because of confounding by indication.[26] Interestingly, previous work[22] in this older adult primary care sample has demonstrated that depression diagnosis and HDRS scores both were independent predictors of decline in some of the executive function tests, ie, scores in Trails B (set-shifting) but not in Trails A (processing speed) or Mattis-IP (category fluency/perseveration) scores. These findings held true when the neurovegetative symptoms of the HDRS were excluded from the analyses. When we examined the relationship between depression (using both diagnosis by SCID and symptom severity by HDRS) and subsequent MMSE scores over the follow-up period, depression was not predictive of subsequent MMSE scores. This may be reflective of the limitations of the MMSE as a measure for detecting mild cognitive impairment or mild dementia,[39] especially in our relatively well-educated sample with higher MMSE scores.

Limitations of the current study include the relatively small number of incident cases of dementia and cognitive disorder NOS, a factor that precluded independent analyses of time to dementia and cognitive disorder NOS as competing outcomes. Additionally, application of the study's criteria to determine dementia or cognitive disorder NOS may have led to an overestimate of the number of incident cases. The *DSM-IV* criteria for dementia capture more broadly those with dementia compared with other diagnostic criteria that are restricted to specific types of dementia (eg, National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association [NINCDS-ADRDA] criteria for Alzheimer's disease[40] or National Institute of Neurological Disorders and Stroke and Association Internationale pour la Recherche et l'Enseignement en Neurosciences [NINDS-AIREN] criteria for vascular dementia[41]). Neither the specific type of dementia (eg, Alzheimer's type or vascular dementia) nor cognitive disorder NOS (eg, MCI) could be determined due to limitations of available neuropsychometrics and other clinical data. Characteristics of this study population may not generalize to other populations given that this was a mostly white and well-educated study cohort. Moreover, there was possible bias of results from participants with incomplete data over the 3 years. The participants who dropped out, died, were lost to follow-up, or did not complete follow-up due to staggered enrollment were more likely to have higher levels of depressive symptoms and medical illness burden. There is the possibility that the group without follow-up assessments may have been more likely to develop incident cognitive impairment or dementia resulting in an underestimate of the number of incident cases in our sample.

This study's data cannot distinguish whether depression represents an independent risk factor or a prodromal feature of dementia or cognitive disorders. To shed light on this question, one would need to examine whether the age at onset and duration of illness of depression moderates the association with incident cognitive disorder, analyses precluded in the present study due to the small number of incident cases. Future prospective studies are needed to examine risk for cognitive disorders in older adults with a remote history of depression in order to help distinguish whether depression confers independent risk. Other investigations into the role of recurrent depression, compared with late onset depression, and subsequent risk for cognitive disorders may also provide increased insight into the relationship between depression and cognitive disorders.

Still, these results highlight the need for better understanding of the role of depression in the pathogenesis of cognitive disorders in older primary care adults in order to

© Copyright 2010 Physicians Postgraduate Press, Inc.

inform improved screening, evaluation, and treatment of those with early signs of cognitive impairment. Clinicians caring for older depressed patients should recognize the importance of monitoring these patients closely for subsequent development of dementia or cognitive disorders. Future well-controlled studies are needed to address our study's limitations and assist practitioners in their efforts to better identify and treat patients at increased risk for developing cognitive disorders.

Author affiliations: Geriatric Psychiatry Program (Drs Boyle, Porsteinsson, King, and Lyness), Alzheimer's Disease Research Program and the Memory Disorders Clinic (Dr Porsteinsson), Department of Psychiatry, University of Rochester Medical Center, Rochester, New York; and Canandaigua VA Medical Center, Canandaigua, New York (Dr Cui).
Potential conflicts of interest: None reported.
Funding/support: This work was supported by grants from the National Institute of Mental Health (R01 MH61429, K24 MH71509, and T32 MH073452). ***Previous presentation***: Presented in part at the American Association for Geriatric Psychiatry Annual Meeting, New Orleans, Louisiana, March 3, 2007 and at the Gerontological Society of America Annual Meeting, San Francisco, California, November 17, 2008.
Acknowledgments: We thank the patients, staff, and providers of the following primary care practices: University of Rochester Medical Center Department of Medicine, Pulsifer Medical, East Ridge Family Medicine, Highland Family Medicine, Olsan Medical, Clinton Crossings Medical, Panorama Internal Medicine, Highland Geriatric Medicine, and Culver Medical. We thank the following for technical assistance: Karen Gibson, MSEd; Constance Bowen, MA; James Evinger, MDiv; Cameron Gardner, MD; Michael New; Andra Niculescu, MD; Jean Sauvain, BS; Jill Scheltz, BA, LMT; and Judy Woodhams, MFA. None reported conflict of interest.

REFERENCES

1. Brookmeyer R, Gray S, Kawas C. Projections of Alzheimer's disease in the United States and the public health impact of delaying disease onset. *Am J Public Health*. 1998;88(9):1337–1342.
2. King DA, Cox C, Lyness JM, et al. Neuropsychological effects of depression and age in an elderly sample: a confirmatory study. *Neuropsychology*. 1995;9(3):399–408.
3. Lichtenberg PA, Ross T, Millis SR, et al. The relationship between depression and cognition in older adults: a cross-validation study. *J Gerontol B Psychol Sci Soc Sci*. 1995;50(1):P25–P32.
4. Yaffe K, Blackwell T, Gore R, et al. Depressive symptoms and cognitive decline in nondemented elderly women: a prospective study. *Arch Gen Psychiatry*. 1999;56(5):425–430.
5. Alexopoulos GS, Kiosses DN, Klimstra S, et al. Clinical presentation of the "depression-executive dysfunction syndrome" of late life. *Am J Geriatr Psychiatry*. 2002;10(1):98–106.
6. Olin JT, Schneider LS, Katz IR, et al. Provisional diagnostic criteria for depression of Alzheimer disease. *Am J Geriatr Psychiatry*. 2002;10(2):125–128.
7. Wilson RS, Mendes De Leon CF, Bennett DA, et al. Depressive symptoms and cognitive decline in a community population of older persons. *J Neurol Neurosurg Psychiatry*. 2004;75(1):126–129.
8. Steffens DC, Otey E, Alexopoulos GS, et al. Perspectives on depression, mild cognitive impairment, and cognitive decline. *Arch Gen Psychiatry*. 2006;63(2):130–138.
9. Speck CE, Kukull WA, Brenner DE, et al. History of depression as a risk factor for Alzheimer's disease. *Epidemiology*. 1995;6(4):366–369.
10. Green RC, Cupples LA, Kurz A, et al. Depression as a risk factor for Alzheimer disease: the MIRAGE Study. *Arch Neurol*. 2003;60(5):753–759.
11. Devanand DP, Sano M, Tang MX, et al. Depressed mood and the incidence of Alzheimer's disease in the elderly living in the community. *Arch Gen Psychiatry*. 1996;53(2):175–182.
12. Wilson RS, Barnes LL, Mendes de Leon CF, et al. Depressive symptoms, cognitive decline, and risk of AD in older persons. *Neurology*. 2002;59(3):364–370.
13. Ownby RL, Crocco E, Acevedo A, et al. Depression and risk for Alzheimer disease: systematic review, meta-analysis, and metaregression analysis. *Arch Gen Psychiatry*. 2006;63(5):530–538.
14. Bassuk SS, Berkman LF, Wypij D. Depressive symptomatology and incident cognitive decline in an elderly community sample. *Arch Gen Psychiatry*. 1998;55(12):1073–1081.
15. Chen P, Ganguli M, Mulsant BH, et al. The temporal relationship between depressive symptoms and dementia: a community-based prospective study. *Arch Gen Psychiatry*. 1999;56(3):261–266.
16. Palmer K, Berger AK, Monastero R, et al. Predictors of progression from mild cognitive impairment to Alzheimer disease. *Neurology*. 2007;68(19):1596–1602.
17. Barnes DE, Alexopoulos GS, Lopez OL, et al. Depressive symptoms, vascular disease, and mild cognitive impairment: findings from the Cardiovascular Health Study. *Arch Gen Psychiatry*. 2006;63(3):273–279.
18. Geda YE, Knopman DS, Mrazek DA, et al. Depression, apolipoprotein E genotype, and the incidence of mild cognitive impairment: a prospective cohort study. *Arch Neurol*. 2006;63(3):435–440.
19. Modrego PJ, Ferrández J. Depression in patients with mild cognitive impairment increases the risk of developing dementia of Alzheimer type: a prospective cohort study. *Arch Neurol*. 2004;61(8):1290–1293.
20. Rozzini L, Chilovi BV, Trabucchi M, et al. Depression is unrelated to conversion to dementia in patients with mild cognitive impairment [letter]. *Arch Neurol*. 2005;62(3):505, author reply 505–506.
21. Olfson M, Pincus HA. Outpatient mental health care in nonhospital settings: distribution of patients across provider groups. *Am J Psychiatry*. 1996;153(10):1353–1356.
22. Cui X, Lyness JM, Tu X, et al. Does depression precede or follow executive dysfunction? outcomes in older primary care patients. *Am J Psychiatry*. 2007;164(8):1221–1228.
23. Boustani M, Callahan CM, Unverzagt FW, et al. Implementing a screening and diagnosis program for dementia in primary care. *J Gen Intern Med*. 2005;20(7):572–577.
24. Spitzer RL, Williams JBW, Gibbon M, et al. *Structured Clinical Interview for DSM-IV, Axis I Disorders (SCID)*. New York, NY: Biometrics Research, New York State Psychiatric Institute; 1995.
25. Segal DL, Hersen M, Van Hasselt VB, et al. Reliability of diagnosis in older psychiatric patients using the Structured Clinical Interview for DSM-III-R. *J Psychopathol Behav Assess*. 1993;15(4):347–356.
26. Lyness JM, Heo M, Datto CJ, et al. Outcomes of minor and subsyndromal depression among elderly patients in primary care settings. *Ann Intern Med*. 2006;144(7):496–504.
27. Unützer J, Katon W, Callahan CM, et al. Collaborative care management of late-life depression in the primary care setting: a randomized controlled trial. *JAMA*. 2002;288(22):2836–2845.
28. Williams JBW. A structured interview guide for the Hamilton Depression Rating Scale. *Arch Gen Psychiatry*. 1988;45(8):742–747.
29. Lyness JM, Cox C, Curry J, et al. Older age and the underreporting of depressive symptoms. *J Am Geriatr Soc*. 1995;43(3):216–221.
30. Zemore R, Eames N. Psychic and somatic symptoms of depression among young adults, institutionalized aged and noninstitutionalized aged. *J Gerontol*. 1979;34(5):716–722.
31. 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(3):189–198.
32. Mattis S. *Dementia Rating Scale (DRS)*. Odessa, FL: Psychological Assessment Resources; 1988.
33. Reitan RM. Validity of the Trail Making Test as an indicator of organic brain damage. *Percept Mot Skills*. 1958;8(7):271–276.
34. Lezak MD. *Neuropsychological Assessment*. 3rd ed. New York, NY: Oxford University Press; 1995.
35. Alexopoulos GS, Meyers BS, Young RC, et al. Recovery in geriatric depression. *Arch Gen Psychiatry*. 1996;53(4):305–312.
36. Sanders ML, Lyness JM, Eberly S, et al. Cerebrovascular risk factors, executive dysfunction, and depression in older primary care patients. *Am J Geriatr Psychiatry*. 2006;14(2):145–152.
37. Sheikh JI, Yesavage JA. Geriatric Depression Scale (GDS): recent evidence and development of a shorter version. In: Brink TL, ed. *Clinical Gerontology: A Guide to Assessment and Intervention*. Binghamton, NY: Haworth Press; 1986:165–173.

38. Linn BS, Linn MW, Gurel L. Cumulative Illness Rating Scale. *J Am Geriatr Soc*. 1968;16:622–626.
39. Petersen RC, Stevens JC, Ganguli M, et al. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter: early detection of dementia: mild cognitive impairment (an evidence-based review). *Neurology*. 2001;56(9): 1133–1142.
40. McKhann G, Drachman D, Folstein M, et al. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology*. 1984;34(7):939–944.
41. Román GC, Tatemichi TK, Erkinjuntti T, et al. Report of the NINDS-AIREN International Workshop. Vascular dementia: diagnostic criteria for research studies. *Neurology*. 1993;43(2):250–260.

Editor's Note: We encourage authors to submit papers for consideration as a part of our Focus on Alzheimer's Disease and Related Disorders section. Please contact Eric M. Reiman, MD, at ereiman@psychiatrist.com.

© Copyright 2010 Physicians Postgraduate Press, Inc.