Primary Care Screen for Early Dementia

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OBJECTIVES: To determine whether the Alzheimer's Disease Screen for Primary Care (ADS-PC) is more sensitive to early dementia than the Mini-Mental State Examination (MMSE) and whether it has as high a misclassification rate in minority patients and patients with limited education.

DESIGN: Cross-sectional validation study.

SETTING: Urban geriatric primary care practice.

PARTICIPANTS: Three hundred sixteen African-American and Caucasian patients, including 55 patients with early dementia (Clinical Demential Rating of 0.5).

MEASUREMENTS: The ADS-PC is a two-stage strategy for identifying early dementia that consists of a brief high-sensitivity dementia screen, applied to all patients aged 65 and older, and a second stage to identify memory impairment, applied to patients who fail the first stage. Differences in the sensitivities or specificities of the ADS-PC and the MMSE were evaluated using the McNemar test.

RESULTS: Receiver operating characteristic curves were used to examine differences in the operating characteristics of the ADS-PC across a range of cutscores. When the specificities of both tests were equated (0.90), the sensitivities were significantly different (ADS-PC, 0.75; MMSE, 0.56). The MMSE failed to identify five times as many cases of dementia as the ADS-PC. When the sensitivities were equated, the specificities differed significantly (ADS-PC, 0.95; MMSE, 0.73). The MMSE misclassified five times as many noncases as the ADS-PC. This pattern of significantly higher sensitivity and specificity for the ADS-PC than for the MMSE was repeated in the results according to race and for individuals with high school or more education but not in individuals with less education.

CONCLUSION: The ADS-PC outperformed the MMSE in identifying early dementia in a racially and educationally diverse primary care cohort. **J Am Geriatr Soc 56:206–213, 2008.**

Key words: Alzheimer's disease; primary health care; mass screening; neuropsychological tests; African Americans

Identifying primary care patients with early dementia is critical to delivering the current generation of treatments and the disease-modifying treatments of the future to the seniors who need them. The ethnic and racial composition of primary care cohorts requires strategies that work equally well in different populations so that all patients can benefit from these treatments. Efficient and cost-effective screening for early dementia in primary care could have a major public health effect once progression to clinical dementia can be delayed.[1] Unfortunately, the recognition of dementia by primary care physicians (PCPs) is poor.[2–4] One barrier to early detection is the PCP's uncertainty in diagnosing dementia in its early stage.[3,5] The most widely used approach to dementia screening in primary care relies on mental status testing, particularly the Mini-Mental State Examination (MMSE), to provide a summary of global cognitive function.[6] Misclassification rates for the MMSE are high for minority patients and for individuals with low education.[9] These effects can be diminished through the use of adjusted cutoff scores, although such scores can actually perform worse than unadjusted scores.[8,9]

Alternatives to mental status testing have been developed. A second strategy is to quickly assess several cognitive domains known to be impaired in early dementia, specifically, memory, attention-executive function, and visuospatial ability.[10–12] A third strategy is to assess memory under conditions that control attention and cognitive processing to identify memory impairment that is not secondary to other neuropsychological deficits.[13–16] A fourth strategy is to interview a reliable informant about the patient's cognition and daily activities.[17] Informant interviews have the advantage of being race and education neutral, unlike most performance-based screening tests. Dementia screening instruments have been reviewed with recommendations for general practice.[18,19]

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Effective screening strategies should be accurate (sensitive and specific) and efficient. To optimize accuracy and efficiency, two-stage screening is widely used.[20] Using this approach, sensitive, specific, and time-efficient case-finding strategies that include two stages have been developed.[21] A brief high-sensitivity dementia screen is applied to all patients aged 65 and older in the first stage, and only the patients who fail undergo the more-time-consuming second stage to diagnose memory impairment. The central role of memory in these strategies emerges from the requirement for memory impairment in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IIV) criteria.[22] These strategies have the potential for efficiency, because only individuals likely to have dementia receive the second stage. In developing these strategies, sensitivity was maximized while maintaining the high specificity needed for efficient primary care screening.

The Alzheimer's Disease Screen for Primary Care (ADS-PC) was the most efficient of the strategies developed; only 30% required second-stage testing.[21] It demonstrated good concurrent criterion validity in 262 elderly Caucasian and African-American primary care patients without dementia and 55 cases, most with very mild dementia (Clinical Dementia Rating (CDR) = 0.5). Using a clinical diagnosis as the criterion standard, the ADS-PC had high sensitivity (0.75) and specificity (0.90) for identifying early dementia and higher sensitivity in identifying Alzheimer's disease (AD) (0.85). The ADS-PC worked equally well in African-American and Caucasian patients and in patients with differing educational levels.[21]

This study sought to determine whether the ADS-PC was more sensitive to early dementia than the MMSE and whether it had as high a misclassification rate as the MMSE in African-American patients and in patients with limited education. To answer these questions, the concurrent criterion validity of the two tests was compared in a cohort of primary care patients. Sensitivity and specificity were examined separately using the McNemar Test.

METHODS

Subjects

The study took place in the Geriatric Ambulatory Practice (GAP), an urban academic primary care practice staffed by geriatricians at Montefiore Medical Center in the Bronx, New York following procedures approved by the local institutional review board. Of the 1,041 potential participants from the GAP that were contacted by telephone between January 2003 and December 2005, 35% were ineligible because of ethnicity or language and 9% because of advanced dementia, 18% were not interested, and 7% never completed the baseline assessment. Participants met the following inclusion criteria: aged 65 and older; self-described as white or black, not of Hispanic origin; provided the name of a family member or friend who had known them for at least 5 years; spoke English since age 30; and had adequate vision and hearing to complete the neuropsychological tests. To exclude patients with moderate to severe dementia, patients had to score 18 or higher on the MMSE; two illiterate patients with scores of 13 were included. Each study participant underwent a neuropsychological evaluation (described in detail elsewhere) consisting of a screening battery and an independent diagnostic battery used to determine dementia status.[21]

The data for these analyses were from 316 African-American and Caucasian patients who completed the baseline evaluation. The cognitive status of each participant was established by consensus of a neuropsychologist, a geriatrician, and a geriatric psychiatrist using DSM-IV criteria for dementia[22] and scores from the diagnostic test battery and the informant interview (Table 1). A report was generated for each patient containing the test scores and percentiles for each test in the diagnostic battery based on the performance of GAP patients without dementia at baseline. The presence of functional impairment was determined by informant responses to a structured clinical interview covering six domains of cognitive and daily functioning that were also included in the report.[23]

Raters reviewed the report, made an independent determination of the patient's diagnosis, and then rated the patient's cognitive performance and activities of daily living using the CDR scale.[23] At consensus conferences, patients were discussed when there was any disagreement on diagnostic criteria or CDR box scores. Diagnoses were made without input from the patient's PCP or knowledge of MMSE score or ADS-PC scores to avoid circularity, although two MMSE item scores were known (world backwards and serial subtractions). The consensus CDR score was based on the pattern of box scores.[23] Afterwards, the study neurologist accomplished dementia subtyping

Table 1. Diagnostic Battery

Domain	Instrument
Patient evaluation	
Memory	CERAD verbal recall[24]
	CERAD figure recall[24]
	Name and address recall[25]
	Event recall[26]
Executive functions	"WORLD" backwards[6]
	CERAD problem solving[23]
	Intrusions in CERAD recall[24]
	Serial 7's[6]
	Months backwards[25]
Other cognitive functions	Orientation[23]
	CERAD Figure Copy[24]
	Free and Cued Selective Reminding naming[16]
	Counting up, counting down[25]
	Self-reported ADLs[27]
Mood	Geriatric Depression Scale[28]
Informant interview	
Semistructured Clinical Dementia Interview[25]	Memory
	Orientation
	Problem solving
	Language
	Personality and behavior
	ADLs

CERAD = Consortium to establish a registry for Alzheimer's disease; ADLs = Activities of daily living.

through chart review using established criteria for probable or possible AD,[29] probable or possible vascular dementia (VaD),[30] probable or possible Lewy Body dementia,[31] and frontotemporal dementia.[32] Subtyping decisions were based on detailed review of the patients' paper and computerized medical records, including social and family history, vascular and other risk factors, medications, and laboratory results. Particular attention was paid to the onset, nature, and development of neurological (including cognitive) complaints as noted in the chart and to the reports of neuroimaging when available.

All participants completed both stages of the ADS-PC, whereas in clinical practice, only patients who fail the first stage undergo second-stage testing. Two brief tests constitute the first-stage Rapid Screen: the Memory Impairment Screen (MIS) and Animal Fluency. The MIS, one of the tests recommended by the American Academy of Neurology for dementia screening, is a four-item controlled learning test in which patients identify words (e.g., tango) in response to category cues (dance) that are used later to prompt recall of words not retrieved by free recall.[33] In Animal Fluency, patients have 60 seconds to generate animal names.[34] Scores of 4 or less out of 8 on the MIS or less than 10 animal names trigger the second-stage testing, which is accomplished with Free and Cued Selective Reminding (FCSR), a 16-item controlled learning test to diagnose memory impairment.[13] The 16 pictures are presented four at a time, and participants identify and name each item (e.g., grapes) after its category cue is presented (fruit). Immediate cued recall of the four items is tested before the next set is studied. After all 16 pictures have been studied and retrieved in immediate cued recall, there are three test trials, consisting of free recall, followed by cued recall of items not retrieved in free recall. Impairment is defined as a score of 25 or less in three trials of free recall. FCSR has been used in several aging studies,[15,16,35–38] is well tolerated by patients, and provides clinicians with useful diagnostic information.[38] Race and education do not affect performance.[39,40]

The MMSE was introduced more than 30 years ago to identify cognitive impairment by assessing mental status and includes questions on memory, orientation, language, and attention, for a total of 30 points.[6] The MMSE score used here included performance on the world backwards item instead of serial subtractions because of the lower refusal rate in this cohort.

Statistical Methods

Receiver operating characteristic (ROC) curves were generated for the MMSE and the ADS-PC to visualize differences in their sensitivity and specificity across the full range of cutscores. The misclassification rates of cases and noncases were then compared in a clinically meaningful range of cutscores. The cutscore on the MMSE was manipulated to achieve the same level of sensitivity or the same level of specificity as the ADS-PC, depending upon whether classification accuracy for cases (sensitivity) or noncases (specificity) was being compared. In the comparison of sensitivities, the result was the conditional odds ratio of cases correctly classified by the ADS-PC but misclassified by the MMSE to cases correctly classified by the MMSE but misclassified by the ADS-PC. For specificity comparisons, the result was the conditional odds ratio of the noncases correctly classified by the ADS-PC but misclassified by the MMSE to the noncases correctly classified by MMSE but misclassified by the ADS-PC. The odds ratios were evaluated using the McNemar test for the whole cohort and then separately according to race and education.

RESULTS

Fifty-five participants (17%) met DSM-IV criteria for dementia; 34 (62%) of these had very mild dementia (CDR 0.5), 15 (27%) had mild dementia (CDR 1.0), and six (11%) had moderately severe dementia (CDR 2.0). Subtypes included 25 (47%) with possible or probable AD, eight (15%) with mixed dementia (AD+VaD), 13 (24%) with possible or probable VaD, and eight (15%) with other subtypes. Of the 262 patients who did not meet criteria for dementia, 128 were assigned a CDR rating of 0.0 and 134 a CDR rating of 0.5. The prevalence of amnestic mild cognitive impairment was 9% in the group with a CDR of 0.0 and 37% in the group with a CDR of 0.5 defined using a previously established cutscore on the Free and Cued Selective Reminding Test (FCSRT).[16] Table 2 shows the demographic characteristics and screening test scores and box scores according to dementia status and CDR rating separately for Caucasians and African Americans.

ROC Curves

Figure 1 displays the ROC curves for the MMSE for the whole cohort and FCSR scores for the 93 patients who failed the first stage of the ADS-PC. Because of the multistage, multitest nature of the ADS-PC, the cutscores for the Rapid Screen were fixed at those determined to maximize sensitivity while maintaining the high level of specificity needed for efficient primary care screening (MIS $\leq$4 or Animal Naming $<$10).[21] Ninety-three patients screened positive using these cutscores. Thus, the ROC curve for the ADS-PC shows the sensitivity and specificity of FCSR in these patients at the full range of cutscores for FCSR. The ROC curve for the ADS-PC never reaches perfect sensitivity, because 11 of the 55 patients with the criterion-based diagnosis of dementia were missed in the first stage.

Inspection of Figure 1 indicates that the sensitivity and specificity of the two methods overlap at extreme cutscores but diverge in the clinically relevant range where sensitivity and specificity are acceptable. Using cutscores that yield specificities of at least 0.75 or higher, the ADS-PC appears to have higher sensitivity than the MMSE.

Overall Analysis

To test for differences in sensitivity, the specificity of the MMSE was set equal to the specificity of the ADS-PC (0.90) using a MMSE cutscore of 23 (Table 3). With specificities equated, sensitivity was 0.75 for the ADS-PC and 0.53 for the MMSE. Of the 55 cases of dementia, both tests correctly identified 26 cases and missed 11. Of the remaining cases, the ADS-PC identified 15 that the MMSE missed, and the MMSE identified three that the ADS-PC missed. The conditional odds ratio (15/3) indicates that the MMSE misclassified five times as many dementia cases as the ADS-PC ($P<.01$). Said differently, when the outcome of the two

Table 2. Demographic Information and Screening Test Scores According to Race, Dementia Status, and Clinical Dementia Rating (CDR)

Race	Dementia Status	CDR Scale	N	Age, Mean ± SD	Female, %	Years of Education, Mean ± SD	Median of Sum of Boxes from the CDR	Mini-Mental State Examination Score, Mean ± SD	Memory Impairment Screen Score, Mean ± SD	Animal Fluency Score, Mean ± SD	Free and Cued Selective Reminding Score, Mean ± SD
African American	No dementia	0	70	74.2 ± 6.1	82	12.8 ± 3.0	0.14	27.5 ± 2.4	7.5 ± 0.8	14.7 ± 4.6	32.8 ± 5.8
		0.5	57	77.0 ± 6.1	84	11.3 ± 3.1	1.50	26.1 ± 3.4	6.5 ± 1.5	12.4 ± 4.1	28.4 ± 6.2
	Dementia	0.5	21	80.7 ± 8.0	86	8.9 ± 4.4	3.00	23.1 ± 3.4	5.1 ± 2.4	8.6 ± 3.5	18.9 ± 6.6
		1	7	80.6 ± 8.2	100	11.4 ± 5.2	4.50	20.5 ± 3.5	3.5 ± 3.5	7.0 ± 3.3	18.4 ± 12.0
		2	3	77.0 ± 7.0	100	12.0 ± 0.0	10.0	20.3 ± 2.5	0.3 ± 0.6	9.7 ± 2.9	2.3 ± 3.2
Caucasian	No dementia	0	58	79.1 ± 6.0	90	14.3 ± 3.5	0.04	28.8 ± 1.8	7.4 ± 0.8	16.2 ± 4.4	31.2 ± 5.8
		0.5	77	81.9 ± 6.7	74	13.0 ± 2.8	1.00	27.1 ± 2.4	6.4 ± 1.6	13.7 ± 5.0	25.0 ± 6.8
	Dementia	0.5	13	83.1 ± 6.0	93	12.9 ± 4.0	3.00	27.0 ± 2.4	5.0 ± 2.3	12.9 ± 4.9	21.1 ± 6.2
		1	8	83.7 ± 4.2	67	12.9 ± 4.3	4.50	23.1 ± 3.5	2.0 ± 2.8	8.2 ± 3.5	9.2 ± 6.9
		2	3	77.3 ± 13.9	100	12.3 ± 0.6	9.50	21.0 ± 3.0	1.7 ± 0.6	9.0 ± 5.6	6.7 ± 5.9

SD = standard deviation.

methods diverge, the ADS-PC identified five times as many cases as the MMSE.

To test for differences in specificity, the sensitivity of the MMSE (0.73) was equated to the sensitivity of the ADS-PC (0.75) by using an MMSE cutscore of 26. With sensitivities equated, specificity was 0.90 for the ADS-PC and 0.73 for the MMSE. Of the 262 noncases, both tests correctly identified 183 noncases and misclassified 17 noncases (Table 3). Of the remaining noncases, the ADS-PC correctly classified 52 that the MMSE misclassified, compared with nine noncases that the MMSE classified correctly but that the ADS-PC misclassified. The conditional odds ratio (52/9) indicates that the MMSE misclassified more than five times as many noncases as the ADS-PC ($P<.001$). When the outcomes diverged, the ADS-PC correctly classified more then five times as many noncases as the MMSE.

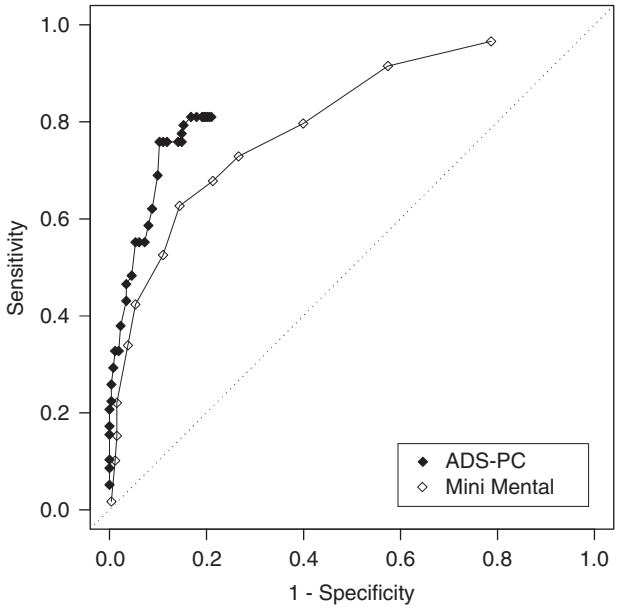

Figure 1. Receiver Operating Characteristic curves for the Alzheimer's Disease Screen for Primary Care (ADS-PC) and the Mini-Mental State Examination. Sensitivity of the ADS-PC does not exceed 80% because 11 of the 55 dementia cases were missed in the first stage and therefore not included in the ROC curve. Two tests, the Free and Cued Selective Reminding Test-Immediate Recall (FCSRT-IR) and the Memory Impairment Screen (MIS), described in the paper are copyrighted by the Albert Einstein College of Medicine (AECOM). Both tests are made freely available from AECOM for teaching and academic research purposes.

Analyses According to Race

There were 158 African-American patients, including 31 with dementia. Using an MMSE cutscore of 21, which equated the specificity of both tests (0.93), sensitivity was 0.81 for the ADS-PC and 0.39 for the MMSE (Table 3). Of the 31 dementia cases, both strategies identified nine and missed three. The ADS-PC identified another 16 cases that the MMSE missed, whereas the MMSE identified three cases that the ADS-PC missed. The MMSE failed to identify more than five times as many cases of dementia as the ADS-PC in African Americans ($P<.006$), the same pattern observed in the overall cohort. Specificities were compared by equating their sensitivities to 0.79, requiring an MMSE cutscore of 24. Under this condition, specificity was 0.94 for the ADS-PC and 0.82 for the MMSE. Of the 127 noncases, both strategies correctly classified 99 noncases and misclassified three cases as having dementia. The ADS-PC correctly classified another 20 noncases that the MMSE misclassified, compared with five noncases that the MMSE correctly classified that the ADS-PC misclassified ($P<.001$).

There were 158 Caucasian patients, including 24 dementia cases. Using an MMSE cutscore of 25, which equated the specificity of both tests (0.89), sensitivity was 0.67 for the ADS-PC and 0.42 for the MMSE (Table 3). Of the 24 dementia cases, both strategies identified 10 and missed eight cases. The ADS-PC identified another six cases that the MMSE missed. The MMSE did not correctly identify any cases that the ADS-PC missed ($P=.04$). Specificities

Table 3. Overall Classification Accuracy and Classification Accuracy According to Race

Comparison	ADS-PC/MMSE COR/COR	ADS-PC/MMSE INC/INC	ADS-PC/MMSE COR/INC	ADS-PC/MMSE INC/COR	Conditional Odds Ratio	McNemar Chi-Square	*P*-Value
Overall cases specificity = 0.90 MMSE ≤ 23	26	11	15	3	5.0	6.72	.01
Overall noncases sensitivity = 0.73 MMSE ≤ 26	183	17	52	9	5.78	28.92	<.001
AA cases specificity = 0.93 MMSE ≤ 21	9	3	16	3	5.33	7.58	.006
AA noncases sensitivity = 0.79 MMSE ≤ 24	99	3	20	5	4.0	13.14	<.001
CA cases specificity = 0.89 MMSE ≤ 24	10	8	6	0	—*	4.17	.04
CA noncases sensitivity = 0.67 MMSE ≤ 27	91	12	25	6	4.17	10.45	.001

* Conditional odds ratio could not be computed.

AA = African American; CA = Caucasian; ADS-PC = Alzheimer's Disease Screener for Primary Care; MMSE = Mini-Mental State Examination; COR/COR = patients correctly classified by both tests; INC/INC = patients incorrectly classified by both tests; COR/INC = patients correctly classified by ADS-PC and misclassified by MMSE; INC/COR = patients incorrectly classified by ADS-PC and correctly classified by MMSE.

were compared by equating their sensitivities as closely as possible (0.67 for the ADS-PC, 0.65 for the MMSE) requiring an MMSE cutscore of 27. Under this condition, specificity was 0.87 for the ADS-PC and 0.72 for the MMSE. Of the 133 noncases, both strategies correctly classified 91 and misclassified 12 noncases. The ADS-PC correctly classified another 25 noncases that the MMSE misclassified, compared with six noncases that the MMSE correctly classified but the ADS-PC misclassified ($P<.001$).

Analysis Stratified According to Educational Level

Eighty-nine participants had less than 12 years of education, including 24 cases (Table 4). With specificities equated (0.85), the sensitivity for the ADS-PC was not significantly higher than the sensitivity of the MMSE (0.75 vs 0.58, $P=.34$). With sensitivities matched (0.75 for the ADS-PC and 0.69 for the MMSE), specificity was 0.85 for the ADS-PC, which was not significantly higher than the specificity of 0.74 for the MMSE ($P=.15$).

Ninety-nine participants had at 12 years of education, including 15 cases (Table 4). Sensitivity was 0.80 for the ADS-PC and 0.47 for the MMSE when the specificities were equated (0.89 for the ADS-PC and 0.91 on the MMSE, $P=.07$). When the sensitivities were equated (0.80), specificity was significantly higher for the ADS-PC than the MMSE (0.89 vs 0.42, $P<.001$).

One hundred twenty-eight participants had more than 12 years of education, including 16 cases (Table 4). Sensitivity was 0.69 for the ADS-PC and 0.38 ($P=.07$) when the specificities were equated (0.94). When the sensitivities were equated (0.69 for the ADS-PC and 0.72 for the MMSE), specificity was significantly higher for the ADS-PC than the MMSE (0.94 vs 0.85, $P=.02$).

Table 4. Classification Accuracy Stratified According to Education

Comparison	ADS-PC/MMSE COR/COR	ADS-PC/MMSE INC/INC	ADS-PC/MMSE COR/INC	ADS-PC/MMSE INC/COR	Conditional Odds Ratio	McNemar Chi-Square	*P*-Value
<12 years specificity = 0.85 MMSE ≤ 22	11	3	7	3	2.33	0.9	.34
<12 years sensitivity = 0.69 MMSE ≤ 23	43	5	12	5	2.40	2.12	.15
12 years specificity = 0.91 MMSE ≤ 24	7	3	5	0	—*	3.2	.07
12 years sensitivity = 0.80 MMSE ≤ 28	34	8	41	1	41.0	36.2	0
>12 years specificity = 0.94 MMSE ≤ 23	6	5	5	0	—*	3.2	.07
>12 years sensitivity = 0.72 MMSE ≤ 26	92	4	13	3	4.33	5.06	.02

* Conditional odds ratio could not be computed.

ADS-PC = Alzheimer's Disease Screen for Primary Care; MMSE = Mini-Mental State Examination; COR/COR = patients correctly classified by both tests; INC/INC = patients incorrectly classified by both tests; COR/INC = patients correctly classified by ADS-PC and misclassified by MMSE; INC/COR = patients incorrectly classified by ADS-PC and correctly classified by MMSE.

DISCUSSION

The purpose of this study was to validate a new two-stage approach to early dementia screening, the ADS-PC, by comparing its accuracy and efficiency with the MMSE in a clinic-based sample. A brief high-sensitivity dementia screen composed of the MIS and Animal Fluency was applied to all patients aged 65 and older in an urban cohort of African-American and Caucasian primary care patients. Patients who failed the first stage underwent the second stage, which was accomplished with FCSR to diagnose memory impairment.

After equating, the ADS-PC outperformed the MMSE in sensitivity (0.75 vs 0.53, respectively) and specificity (0.90 vs 0.73, respectively) in the overall cohort. The MMSE failed to identify five times as many cases as the ADS-PC and misclassified five times as many noncases as the ADS-PC. Significantly higher sensitivity and specificity for the ADS-PC than for the MMSE was found in the results according race. In African Americans, sensitivity was 0.81 for the ADS-PC and 0.39 for the MMSE, indicating that the MMSE failed to identify more than half of the cases with dementia. The MMSE also misclassified more than four times as many African-American noncases as having dementia as the ADS-PC. In Caucasians, the MMSE did not correctly identify a single case of dementia that the ADS-PC missed and misclassified four times as many noncases as the ADS-PC. Stratifying according to educational level resulted in significantly higher specificity and a tendency for higher sensitivity for participants with 12 or more years of education for the ADS-PC than for the MMSE. Although sensitivity and specificity were higher for the ADS-PC than the MMSE for participants with less than 12 years of education, these differences were not significant.

The higher concurrent criterion validity of the ADS-PC can be attributed to the focus on memory in both stages. The MIS in the first stage and the FCSR in the second use controlled learning, procedures that use category cues in the encoding and retrieval phases of the test; in previous studies, these procedures have been shown to discriminate powerfully between normal aging and dementia.[14–16,21,33,35–38,41,42] Controlled learning induces specific semantic processing to minimize inattention and inefficient information processing and provides for maximum cued recall. Controlled learning procedures remediate retrieval deficits that occur in many healthy elderly individuals.[43] In patients with dementia, these procedures have modest benefits.[41] As a consequence, controlled learning procedures increase differences between normal older individuals and those with dementia, thereby improving discriminative validity.

Memory testing is critical to dementia screening, because memory is the one cognitive domain that must be impaired to diagnose dementia,[22] and impaired memory is one of the earliest manifestations of dementia.[44,45] Postmortem series have demonstrated that memory decline precedes decline in mental status in early pathologically defined AD.[46] Other causes of acquired memory impairment in elderly people that are not the result of clinical dementia are rare.[47] Therefore, in the absence of other identifiable etiologies, the identification of impaired memory is highly predictive of a diagnosis of dementia.[13,14,16,21]

Experience with efforts to improve the detection of traditionally underdetected conditions in primary care such as depression indicates that screening or case-finding tools administered by clinic staff generate better results than physician-initiated screening.[48,49] These studies demonstrate that, by itself, the availability of a screening or case-finding tool is not sufficient to change outcomes; diagnosis and treatment improves when responsibility for screening is built into the delivery system independent of physician initiation. When clinic staff in a primary care network performed routine cognitive screening, small but significant increases in new dementia diagnoses, referrals, and medication prescriptions were observed, particularly for patients with more-advanced dementia.[50] Rates of new physician actions may have been higher had the screening test results been clipped to the front of the patient's chart rather than only entered in the electronic medical record.[49] In future studies, neuropsychologists, neurologists, and geropsychiatrists should work with primary care staff to implement and assess the efficiency and cost effectiveness of different case-finding strategies.

Although the results are encouraging, caution is recommended because of the study's limitations. The results are sample-dependent because the measurement properties of the ADS-PC and the MMSE vary according to patient population. Results may differ for samples from different populations, and the optimal cutscores for the ADS-PC could change. Therefore, it is important to replicate the findings in other primary care settings. An apparent limitation is that the analytical methods involved manipulating MMSE cutscores but not ADS-PC cutscores, which were set to maximize sensitivity and specificity. Although this may have conferred an advantage to the ADS-PC, a comparison of the ROC curves for the two methods revealed better operating characteristics for the ADS-PC than the MMSE at cutscores in the clinically relevant range. Two items from the MMSE were used diagnostically, perhaps improving MMSE performance. Although the ADS-PC was superior to the MMSE in African Americans and Caucasians, it did not have an advantage in those with less than a 10th-grade education. In the best-educated group, the sensitivity of the ADS-PC fell slightly. Adjustments for literacy and acculturation may improve the performance of the ADS-PC in these education strata.[51] These approaches are currently being assessed in Latino and Hispanic patients in the hope that the findings can be extended to individuals who do not speak English as their first language. Finally, although the sample was large according to many standards, when the 55 cases of dementia were stratified according to race and education, confidence intervals became broad. Future studies with greater numbers of patients are needed to optimize these procedures.

As new treatments and preventive approaches for AD emerge, they will be implemented in primary care settings, where the majority of the elderly receive their care. The procedures developed in Alzheimer's centers and population studies to identify early dementia may not be practical or appropriate for use in these primary care settings, where base rates of dementia are low and ethno-racial and educational diversity is the rule. As new treatment strategies emerge, they should be tested in the primary care settings in which they will be implemented. These treatments cannot

be implemented in primary care unless efficient procedures are available for identifying eligible patients. The ADS-PC is intended to fill the gap between subspecialty center and population-based research. Once efficient and cost-effective strategies to identify early dementia are developed and implemented, the policy recommendation for early dementia screening can be reconsidered, because dementia would meet criteria of the U.S. Preventive Service Task Force for screening.[52] A policy recommendation for early dementia screening would be warranted if the aggregate benefits of screening and intervention outweighed the aggregate costs. Such a demonstration can occur only after screening tools and treatment programs are fully developed.

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