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Diagnostic Accuracy of the MMSE in Detecting Probable and Possible Alzheimer's Disease in Ethnically Diverse Highly Educated Individuals: An Analysis of the NACC Database

Cynthia C. Spering,[1] Valerie Hobson,[1] John A. Lucas,[2] Chloe V. Menon,[1] James R. Hall,[3,4] and Sid E. O'Bryant[4,5]

[1]Department of Psychology, Texas Tech University, Lubbock.
[2]Mayo Clinic College of Medicine, Jacksonville, Florida.
[3]Department of Psychiatry, University of North Texas Health Science Center, Fort Worth.
[4]Institute for Aging and Alzheimer's Disease Research, University of North Texas Health Science Center, Fort Worth.
[5]Department of Internal Medicine, University of North Texas Health Science Center, Fort Worth.

Address correspondence to Sid E. O'Bryant, PhD, Associate Professor, Department of Internal Medicine; University of North Texas Health Science Center, Fort Worth. Email: Sid.O'Bryant@unthsc.edu.

Background. To validate and extend the findings of a raised cut score of O'Bryant and colleagues (O'Bryant SE, Humphreys JD, Smith GE, et al. Detecting dementia with the mini-mental state examination in highly educated individuals. *Arch Neurol*. 2008;65(7):963–967.) for the Mini-Mental State Examination in detecting cognitive dysfunction in a bilingual sample of highly educated ethnically diverse individuals.

Methods. Archival data were reviewed from participants enrolled in the National Alzheimer's Coordinating Center minimum data set. Data on 7,093 individuals with 16 or more years of education were analyzed, including 2,337 cases with probable and possible Alzheimer's disease, 1,418 mild cognitive impairment patients, and 3,088 nondemented controls. Ethnic composition was characterized as follows: 6,296 Caucasians, 581 African Americans, 4 American Indians or Alaska natives, 2 native Hawaiians or Pacific Islanders, 149 Asians, 43 "Other," and 18 of unknown origin.

Results. Diagnostic accuracy estimates (sensitivity, specificity, and likelihood ratio) of Mini-Mental State Examination cut scores in detecting probable and possible Alzheimer's disease were examined. A standard Mini-Mental State Examination cut score of 24 (≤23) yielded a sensitivity of 0.58 and a specificity of 0.98 in detecting probable and possible Alzheimer's disease across ethnicities. A cut score of 27 (≤26) resulted in an improved balance of sensitivity and specificity (0.79 and 0.90, respectively). In the cognitively impaired group (mild cognitive impairment and probable and possible Alzheimer's disease), the standard cut score yielded a sensitivity of 0.38 and a specificity of 1.00 while raising the cut score to 27 resulted in an improved balance of 0.59 and 0.96 of sensitivity and specificity, respectively.

Conclusions. These findings cross-validate our previous work and extend them to an ethnically diverse cohort. A higher cut score is needed to maximize diagnostic accuracy of the Mini-Mental State Examination in individuals with college degrees.

Key Words: Alzheimer's disease—Dementia diagnosis—Ethnicity—Language—Mini-Mental State Examination.

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THE Mini-Mental State Examination (MMSE) (1) is a commonly administered measure of global cognitive functioning that is used to track change, screen for cognitive impairment, and measure outcome in clinical trials. The MMSE has been shown to be relatively sensitive to overt dementia (2–4), although its utility decreases when assessing patients with psychiatric conditions and mild cognitive decline (5–7).

MMSE performance is moderated by education and age, with less educated and older individuals tending to receive lower scores (5,8). Ethnic minority groups also tend to obtain lower scores than Caucasians; however, ethnicity is often confounded with lower levels of education, particularly in older cohorts who were raised in a segregated educational system (9). Moreover, Ostrosky and colleagues (8) observed a similar confound among Spanish speakers, in that, diagnostic validity (ie, sensitivity and specificity) of the MMSE was found to be better among Spanish speakers with more education compared with those with lower levels of education. Correction formulas have been developed to adjust the negative effects of age and education on MMSE scores (5) but have met with varying levels of success (10).

Table 1. Study Population Characteristics

Characteristics	Total Sample (*n* = 7,093)	Probable and Possible AD (*n* = 2,337)	MCI (*n* = 1,418)	Control (*n* = 3,088)
Sex, *n* (%)				
Male	3622 (51.1)	1,414 (60.5)	778 (55.0)	1,289 (41.7)
Female	3471 (48.9)	923 (39.5)	640 (45.1)	1,799 (58.3)
Age				
Mean (*SD*)	74.0 (10.1)	74.7 (10.1)	75.1 (9.3)	73.2 (10.3)
Range	25–118	26–118	36–107	25–101
Education				
Mean (*SD*)	17.5 (1.6)	17.4 (1.6)	17.5 (1.6)	17.5 (1.5)
Range	16–29	16–27	16–29	16–29
MMSE				
Mean (*SD*)	28.4 (14.4)	23.8 (17.9)	29.0 (10.4)	30 (12.2)
Range	0–30	0–30	0–30	21–30
Race				
Caucasian	6,296 (88.8)	2,111 (90.3)	1,257 (88.6)	2,713 (87.9)
African American	581 (8.2)	149 (6.4)	115 (8.1)	294 (9.5)
AI or AN	4 (0.1)	1 (<0.1)	0	3 (0.1)
NH or PI	2 (<0.1)	1 (<0.1)	0	1 (<0.1)
Asian	149 (2.1)	48 (2.1)	36 (2.5)	59 (1.9)
Other	43 (0.6)	22 (1.0)	7 (0.5)	11 (0.4)
Language				
English	6,764 (95.4)	2,244 (96.0)	1,349 (95.1)	2,940 (95.2)
Spanish	116 (1.6)	42 (2.0)	22 (1.6)	43 (1.4)
Mandarin	25 (0.4)	5 (0.2)	7 (0.5)	10 (0.3)
Cantonese	5 (0.1)	2 (0.1)	2 (0.1)	1 (<0.1)
Russian	10 (0.1)	2 (0.1)	4 (0.3)	3 (0.1)
Japanese	3 (<0.1)	1 (<0.1)	1 (0.1)	1 (<0.1)
Other	104 (1.5)	34 (1.5)	28 (2.0)	37 (1.2)
Unknown	66 (0.9)	7 (0.3)	22 (1.6)	53 (1.7)

Note: AD = Alzheimer's disease; AI = American Indian; AN = Alaska Native; MCI = mild cognitive impairment; MMSE = Mini-Mental State Examination; NH = Native Hawaiian; and PI = Pacific Islander.

The majority of research on the effect of education level on MMSE scores has focused on understanding and adjusting for lower levels of education. However, O'Bryant and colleagues (11) demonstrated that the standard MMSE cut score was not sensitive enough to identify early dementia in highly educated individuals. In that sample of more than 1,000 patients enrolled in the Mayo Clinic Alzheimer's Disease Research Center and Alzheimer's Disease Patient Registry, a cut score of 27 (ie, ≤26) provided the optimal balance between sensitivity (0.89) and specificity (0.91) in detecting cognitive dysfunction associated with dementia in elders with 16 or more years of education. The literature on cognitive reserve suggests that, once diagnosed, patients with probable and possible Alzheimer's disease (AD) who have higher levels of education tend to demonstrate a steeper slope of decline and earlier mortality rates (12,13). As such, the ability to detect disease among such individuals at an earlier stage would allow appropriate intervention strategies to be implemented earlier. Participants in O'Bryant's original sample were primarily Caucasian (93%; 7% identified as African American), and all were tested in English. As such, the generalizability of those findings to ethnically and linguistically diverse populations remains uncertain.

The current study was undertaken to cross-validate and extend the findings of O'Bryant and colleagues (11) through an analysis of a sample of highly educated ethnically diverse individuals drawn from the unified data set (14) of the National Alzheimer's Coordinating Center (NACC). It was hypothesized that a cut score of 27 would yield improved estimates of diagnostic accuracy for highly educated individuals across ethnic and linguistic groups compared with the more commonly utilized cut score of 24 (15).

Methods

Participants

Data were extracted from the July 2008 NACC UDS, which contained data collected from all National Institute on Aging funded Alzheimer's Disease Centers. The inclusion criterion was an educational level of 16 years or more. All participants were evaluated according to standardized protocols that included a trained clinician meeting with the participant and an informant. All participants were assigned a diagnosis by consensus team or single physician according to NACC guidelines. Participants were recruited in numerous ways according to the protocols of the various Alzheimer's Disease Center sites; generally, participants were volunteers or referral cases. See Table 1 for demographic information. The American Indian or Alaskan Native, Native Hawaiian or Pacific Islander, Other, and Unknown groups were not analyzed individually due to low sample size. Of the total sam-

Table 2. MMSE Cutoff Scores for Detection of Probable and Possible AD by Ethnicity

	Cut Score	Sensitivity (95% CI)	Specificity (95% CI	Likelihood Ratio	False-Positive Rate	False-Negative Rate
All ethnicities	24	0.58 (0.56—0.60)	0.98 (0.98- 0.99)	29.00	85	987
	25	0.65 (0.63–0.67)	0.97 (0.96–0.97)	21.70	147	824
	26	0.72 (0.70–0.73)	0.94 (0.93–0.95)	12.00	293	664
	27	0.79 (0.78–0.81)	0.90 (0.89–0.90)	7.90	497	486
	28	0.85 (0.83–0.86)	0.81 (0.80–0.82)	4.50	886	357
African American	24	0.72 (0.64–0.79)	0.98 (0.96–0.99)	36	9	42
	25	0.77 (0.69–0.83)	0.96 (0.93–0.97)	19.25	19	35
	26	0.82 (0.75–0.88)	0.92 (0.89–0.94)	10.25	35	27
	27	0.89 (0.82–0.93)	0.84 (0.80–0.87)	5.56	70	17
	28	0.92 (0.86–0.96)	0.74 (0.69–0.78)	3.54	113	12
Asian	24	0.58 (0.43–0.72)	0.94 (0.88–0.98)	9.71	6	20
	25	0.65 (0.49–0.78)	0.93 (0.86–0.97)	9.32	7	17
	26	0.73 (0.58–0.85)	0.86 (0.78–0.92)	5.21	14	13
	27	0.77 (0.63–0.88)	0.67 (0.50–0.80)	2.33	15	11
	28	0.83 (0.70–0.93)	0.50 (0.34–0.66)	1.70	28	8
Hispanic (all)	24	0.62 (0.48–0.74)	0.93 (0.87–0.97)	8.90	9	23
	25	0.68 (0.55–0.80)	0.91 (0.85–0.95)	7.55	11	19
	26	0.75 (0.62–0.85)	0.88 (0.81–0.93)	6.25	15	15
	27	0.83 (0.71–0.92)	0.79 (0.71–0.86)	3.95	26	10
	28	0.85 (0.73–0.93)	0.69 (0.60–0.77)	2.74	38	9
Mexican American	24	0.56 (0.30–0.80)	1.00	—	0	7
	25	0.63 (0.35–0.85)	1.00	—	0	6
	26	0.69 (0.41–0.89)	0.97 (0.84–1.00)	23	1	5
	27	0.81 (0.54–0.96)	0.88 (0.71–0.96)	6.75	4	3
	28	0.81 (0.54–0.96)	0.78 (0.60–0.91)	3.70	7	3
White	24	0.57 (0.55–0.59)	0.98 (0.98–0.99)	28.5	68	910
	25	0.64 (0.62–0.66)	0.97 (0.97–0.98)	21.33	119	760
	26	0.71(0.69–0.73)	0.94 (0.94–0.95)	11.83	242	614
	27	0.79 (0.77–0.80)	0.90 (0.89–0.91)	7.90	406	449
	28	0.84 (0.83–0.86)	0.82 (0.81–0.84)	4.70	737	330

Note: AD = Alzheimer's disease; CI = confidence interval; and MMSE = Mini-Mental State Examination.

ple, there were 2,337 (1,414 men and 923 women) patients with probable and possible AD, 1,418 patients with mild cognitive impairment (778 men and 640 women), and 3,088 nondemented controls (1,289 men and 1,799 women).

Statistics

Estimates of sensitivity (SN), specificity (SP), and likelihood ratio of a positive result (LR+) were calculated for standard MMSE cut scores ranging from 24 to 28. Sensitivity refers to the proportion of individuals with a given condition that yield a positive test result on a test for that given condition, whereas specificity refers to the proportion of individuals without that condition who receive a negative test finding (16). Sensitivity was established by dividing the number of true positive cases by the sum of true positive cases and false negatives. Specificity was calculated by dividing the number of true negative cases by the sum of true negative cases and false positives (17). LRs represent the relative risk of having a condition given a "positive" test result and is calculated as: LR+ = SN/1 − SP. LRs are more accurate than negative predictive value and positive predictive value because they do not depend on prevalence and can be intuitively interpreted. Diagnostic categorization was dementia and cognitive impairment (ie, mild cognitive impairment and probable and possible AD) versus control. Data were analyzed for all ethnicities together, then separately by ethnicity, primary language, and language of MMSE administration (Tables 2–5). We elected to include all ages in order to maximize external validity.

Results

Probable and Possible AD

For detecting cognitive impairment associated with probable and possible AD (all ethnicities), a traditional cut score of 24 (≤23) resulted in a moderate SN of 0.58 with a very high SP of 0.98 and LR+ of 29 (see Table 2). A cut score of 27 (≤26) yielded a better balance between SN (0.79) and SP (0.90) with a lower, but still good, LR+ of 12.00. The traditional cut score yielded 987 false negatives; that is, the MMSE did not indicate probable and possible AD in 987 individuals who were later diagnosed as demented. This false-negative rate declined significantly to 486 with the new cut score with an increase in false positives from 85 with the traditional cut score to 497 with a cut score of 27.

When viewing the analyses by ethnicity, the revised cut score yielded a better balance between SN and SP across all groups with probable and possible AD than did the traditional cut score of 24. SN and SP estimates for a cut score of 27 were 0.82 and 0.92 for African Americans, 0.73 and 0.86 for Asians, 0.75 and 0.88 for Hispanics, 0.69 and 0.97 for Mexican

Table 3. Cutoff Scores for Detection of Probable and Possible AD by Language of MMSE Administration

	Cut Score	Sensitivity (95% CI)	Specificity (95% CI	Likelihood Ratio	False-Positive Rate	False-Negative Rate
MMSE English	24	0.58 (0.56–0.60)	0.98 (0.98–0.99)	29.00	81	975
	25	0.65 (0.63–0.67)	0.97 (0.97–0.97)	21.70	142	812
	26	0.72 (0.70–0.74)	0.94 (0.93–0.95)	12.00	285	654
	27	0.80 (0.78–0.81)	0.90 (0.89–0.91)	8.00	485	478
	28	0.85 (0.83–0.86)	0.81 (0.80- 0.83)	4.50	871	349
MMSE Spanish	24	0.81 (0.58–0.95)	0.94 (0.84–0.99)	13.50	3	4
	25	0.81 (0.58–0.95)	0.92 (0.81–0.98)	10.12	4	4
	26	0.86 (0.64–0.97)	0.87 (0.74–0.94)	6.61	7	3
	27	0.95 (0.76–1.00)	0.78 (0.65–0.89)	4.32	11	1
	28	0.95 (0.76–1.00)	0.73 (0.58–0.84)	3.52	14	1

Note: AD = Alzheimer's disease; CI = confidence interval; and MMSE = Mini-Mental State Examination.

Americans, and 0.71 and 0.94 for whites. The LR+ 10.25, 5.21, 6.25, 23, and 11.83 in these groups, respectively. The cut score of 27 yielded an SN, SP, and LR+ of 0.72, 0.94, and 12.00 for English speakers and 0.86, 0.87, and 6.61 for Spanish speakers.

Even though the revised cut score of 27 provided a better balance between SN and SP as compared with a traditional cut score of 24 across all groups, as can be seen from Tables 2 and 3, the optimal balance between SN and SP varied by ethnic grouping and by language. In the total sample, which is more ethnically diverse than that from our original analyses, a cut score of both 27 and 28 provided adequate balance in diagnostic accuracy. Among African Americans, cut scores of 27 and 28 each offer a good balance. Among Asians, the optimal balance was found at a cut score of 27. Among all Hispanics, cut scores of 27 and 28 offered adequate balance of SN and SP, whereas the optimal balance for Mexican Americans was a cut score of 28 (SN = 0.81, SP = 0.88, LR+ = 6.75). In this sample, cut scores of 28 (SN = 0.79, SP = 0.90, LR+ = 7.90) and 29 (SN = 0.84, SP = 0.82, LR+ = 4.70) provided optimal balances for white individuals. Optimal balances for English-speaking individuals were found at cut scores of 28 (SN = 0.80, SP = 0.90, LR+ = 8.00) and 29 (SN = 0.85, SP = 0.81, LR+ = 4.50), whereas the optimal balance for Spanish speakers was found at 27.

Table 4. MMSE Cutoff Scores for Detection of MCI/Probable and Possible AD by Ethnicity

	Cut Score	Sensitivity (95% CI)	Specificity (95% CI	Likelihood Ratio	False-Positive Rate	False-Negative Rate
All ethnicities	24	0.38 (0.36–0.39)	1.00 (0.99–1.00)	97.24	13	2333
	25	0.44 (0.42–0.45)	0.99 (0.99–0.99)	55.87	26	2121
	26	0.51 (0.49–0.52)	0.98 (0.98–0.99)	26.42	64	1853
	27	0.59 (0.57–0.60)	0.96 (0.95–0.96)	14.02	140	1547
	28	0.67 (0.66–0.69)	0.90 (0.89–0.91)	6.78	332	1221
African American	24	0.42 (0.36–0.48)	0.98 (0.96–0.99)	26.66	5	153
	25	0.46 (0.40–0.53)	0.97 (0.95–0.99)	16.54	9	140
	26	0.52 (0.46–0.58)	0.94 (0.91–0.96)	8.72	19	126
	27	0.61 (0.55–0.67)	0.87 (0.83–0.91)	4.86	40	102
	28	0.69 (0.64–0.75)	0.79 (0.74–0.83)	3.28	67	81
Asian	24	0.40 (0.30–0.52)	1.00	—	0	50
	25	0.45 (0.34–0.56)	1.00	—	0	46
	26	0.57 (0.46–0.68)	0.98 (0.92–1.00)	37.14	1	36
	27	0.61 (0.49–0.71)	0.98 (0.92–1.00)	39.46	1	33
	28	0.72 (0.62–0.82)	0.89 (0.79–0.96)	6.74	7	23
Hispanic (all)	24	0.44 (0.34–0.54)	0.96 (0.90–0.99)	12.43	3	55
	25	0.48 (0.38–0.58)	0.94 (0.87–0.98)	8.15	5	51
	26	0.56 (0.46–0.66)	0.94 (0.87–0.98)	9.54	5	43
	27	0.70 (0.60–0.79)	0.92 (0.84–0.97)	8.55	7	29
	28	0.79 (0.69–0.86)	0.86 (0.77–0.92)	5.57	12	21
Mexican American	24	0.36 (0.18–0.57)	1.00	—	0	16
	25	0.40 (0.21–0.61)	1.00	—	0	25
	26	0.48 (0.28–0.69)	1.00	—	0	13
	27	0.68 (0.46–0.85)	1.00	—	0	8
	28	0.76 (0.55–0.91)	0.96 (0.78–1.00)	17.48	1	6
White	24	0.37 (0.36–0.39)	1.00	156.73	7	2106
	25	0.43 (0.41–0.45)	0.99 (0.99–1.00)	79.00	16	1914
	26	0.50(0.49–0.52)	0.98 (0.98–0.99)	34.29	43	1672
	27	0.59 (0.57–0.60)	0.97 (0.96–0.97)	18.06	95	1395
	28	0.67 (0.66–0.69)	0.91 (0.90–0.92)	7.78	253	1103

Note: AD = Alzheimer's disease; CI = confidence interval; MCI = mild cognitive impairment; and MMSE = Mini-Mental State Examination.

Table 5. Cutoff Scores for Detection of MCI/Probable and Possible AD by Language of MMSE Administration

	Cut Score	Sensitivity (95% CI)	Specificity (95% CI	Likelihood Ratio	False-Positive Rate	False-Negative Rate
MMSE English	24	0.38 (0.36–0.39)	1.00 (0.99–1.00)	103.98	12	2306
	25	0.44 (0.42–0.45)	0.99 (0.99–1.00)	59.85	24	2094
	26	0.51 (0.49–0.52)	0.98 (0.98–0.99)	26.94	62	1831
	27	0.67 (0.66–0.69)	0.94 (0.93–0.95)	14.15	137	1530
	28	0.68 (0.66–0.69)	0.90 (0.89–0.91)	6.81	327	1205
MMSE Spanish	24	0.53 (0.35–0.70)	0.97 (0.85–1.00)	26.81	1	17
	25	0.53 (0.35–0.70)	0.94 (0.81–0.99)	14.63	2	17
	26	0.64 (0.46–0.79)	0.94 (0.81–0.99)	16.25	2	13
	27	0.78 (0.61–0.90)	0.92 (0.78–0.98)	9.75	3	8
	28	0.80 (0.64–0.92)	0.86 (0.71–0.95)	6.15	5	7

Note: AD = Alzheimer's disease; CI = confidence interval; MCI = mild cognitive impairment; and MMSE = Mini-Mental State Examination.

Cognitively Impaired Group

When considering cognitive impairment in mild cognitive impairment and probable and possible AD across ethnicities, the traditional cut score of 24 resulted in a low SN of 0.38 and very high SP of 1.00 with an LR+ of 97.24 (see Table 4). A better balance was found with a cut score of 27, with SN (0.59) and SP (0.96), with a lower but still good LR+ of 14.02. Lowering the original cut score led to a decrease in false-negative count from 2,333 to 1,547. False positive concurrently increased from 13 to 140.

When these analyses were divided by ethnicity, the new cut score yielded a better balance between SN and SP over the traditional cut score of 24 across all groups with cognitive impairment. Across these groups, the new score yielded the following SN and SP estimates, respectively: for African Americans, 0.61 and 0.87; for Asians, 0.61 and 0.98; for Hispanics, 0.70 and 0.92; for Mexican Americans, 0.68 and 1.00; and for whites, 0.59 and 0.97. For these groups (with the exception of the Mexican American group which was not computed due to having 0 false positives), the LR+ were 4.86, 39.46, 8.55, and 18.06, respectively. For the two language groups, the new cut score of 27 yielded an SN, SP, and LR+ of 0.67, 0.94, and 14.15 for the test administered in English and 0.78, 0.92, and 9.75 for the test administered in Spanish.

As was seen in the probable and possible AD-only group, the new cut score of 27 improved the balance of SN and SP for all groups. However, when considering milder forms of cognitive impairment along with probable and possible AD, a higher cut score of 28 yielded an optimal balance of SN and SP in all ethnic groups and language of MMSE administration.

Discussion

For college-educated individuals, a cut score of 27 generally yields a better balance of estimates of diagnostic accuracy than the traditional cut score of 24 regardless of ethnicity or language of MMSE administration. In a previous study, O'Bryant and colleagues (11) determined that a cut score of 27 (≤26) was most appropriate for detecting possible cognitive impairment associated with dementia in their sample of mostly white individuals. This study also found improved diagnostic accuracy with higher cut scores across ethnically diverse patients with high levels of education. Taken together, it appears that college-educated individuals who present with cognitive complaints and scores lesser than 27 or 28 on the MMSE should be referred for a comprehensive dementia evaluation. However, as is normally the case, a single cut score is typically not applicable across groups. In fact, as can be seen from Table 2, the optimal balance between SN and SP varied between ethnic groups with some cut scores greater than 27 providing the best estimates. As seen in Tables 4 and 5, a cut score of 28 yields an even better balance of SN and SP for many groups. This is the first study to provide a range of cut scores for different ethnic and linguistic groups so that appropriate cut scores can be utilized for the given setting.

It should be noted that, as expected, a higher false-positive rate is associated with the use of higher cut scores. The balance between false-positive and false-negative errors is important for geriatric practitioners to consider when determining the presence of a dementing illness. However, as has been pointed out previously (11), the MMSE should be used in conjunction with a clinical examination, comprehensive assessment including neuropsychological testing, and not as the sole basis for diagnosis. Thus, evidence of probable and possible AD based on screening instruments (including the MMSE) among highly educated elders should be complemented by the conduction of a comprehensive assessment comprising neuropsychological testing. The numerous "costs" associated with dementia evaluations, including financial and emotional strains, are also important to weight out in this process. Nonetheless, the steep decline in cognitive functioning observed in highly educated ethnically diverse populations (16) and commonly thought to reflect possible cognitive reserve, suggests an important need for earlier detection in this particular group. This further speaks to the value of relying on early testing and evaluation in the clinical management of such populations.

Although this study found improved sensitivity, specificity, and rates of false negatives for the new cut score of 27 across ethnicities with high levels of education, it is important to consider other demographic and ability factors in addition to years of education in ethnically diverse groups. For example, Manly and colleagues (18) found that literacy levels are a more important predictor of neuropsychological tests scores than education years alone. Manly and colleagues (18) noted that among minority ethnic groups, education quality is often not accurately reflected in years of education alone, and suggest examining literacy levels over years of education. A possible explanation for the seeming discrepancy between the results of Manly and colleagues and ours could be that all individuals in our study had at least 16 years of education; previous studies, such as Manly and colleagues (18), have examined groups with lower mean years of education. It is possible that individuals attaining 16 or more years of education are exposed to curricula that are more similar than those found in lower levels of education, or perhaps, the individuals attaining those levels of education are more similar themselves (in intellectual ability or socioeconomic status). As our study utilized education levels, further analyses should be conducted to compare our results with those of literacy levels.

An additional consideration for testing ethnically diverse groups lies in the area of test language and administration. For example, clinicians may want to consider that MMSE items function differently among the language of administration (19) and that optimal cut scores may differ among groups. Furthermore, current results indicate that optimal cutoffs differed for Hispanics specified of Mexican origin. Cross-cultural research in neuropsychology should thus also seek to further examine possible discrepancies in the clinical presentation and test performance of populations of different national origins in an attempt to extend the generalizability of available findings.

There are several limitations and clinical issues to consider when interpreting results of this study. For one, the assessment of additional factors that may influence cognitive test performance in patients with probable and possible AD (eg, attentional abilities, anosognosia) was beyond the scope of the current study and should be considered clinically. In addition, it should be noted that there was overlap of some cases between the sample used in O'Bryant and colleagues (11) and the current study, as the sample used in the original study contributes data to the NACC group; however, given the de-identified nature of the data obtained from NACC, it is impossible to know the exact overlap. Last, the MMSE is best suited as a screening instrument for cognitive dysfunction rather than a diagnostic instrument. Therefore, the guidelines resulting from this study can assist clinicians when making referral decisions for highly educated patients of varying ethnic, cultural, and linguistic backgrounds.

Raising the cut score of the MMSE in all highly educated individuals, regardless of ethnicity or language, may lead to early improved detection of cognitive decline. More importantly, this might allow for earlier intervention to attenuate the rapid cognitive decline observed in highly educated people with AD (20) by increasing the amount of time available for treatment of associated symptomatology. In summary, when utilizing the MMSE for screening of cognitive impairment associated with probable and possible AD among ethnically and linguistically diverse elders with high levels of education, a cut score of 27 (or higher) is suggested for determining who should be referred for comprehensive dementia evaluations.

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