Detecting Dementia With the Mini-Mental State Examination in Highly Educated Individuals

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Objective: To evaluate the utility of Mini-Mental State Examination (MMSE) scores in detecting cognitive dysfunction in a sample of highly educated individuals.

Design: Archival data were reviewed on 4248 participants enrolled in the Mayo Clinic Alzheimer Disease Research Center and Alzheimer Disease Patient Registry.

Patients: A total of 1141 primarily white (93%) individuals with 16 or more years of self-reported education were identified. These included 307 (164 men and 143 women) patients with dementia (any type), 176 (106 men and 70 women) patients with mild cognitive impairment, and 658 (242 men and 416 women) control participants without dementia.

Setting: Mayo Clinic Alzheimer Disease Research Center and Alzheimer Disease Patient Registry cohort.

Main Outcome Measures: Diagnostic accuracy estimates (sensitivity, specificity, and positive and negative predictive power) of MMSE cut scores in detecting cognitive dysfunction.

Results: In this sample of highly educated, largely white older adults, the standard MMSE cut score of 24 (23 or below) yielded a sensitivity of 0.66, a specificity of 0.99, and an overall correct classification rate of 89% in detecting dementia. A cut score of up to 27 (26 or below) resulted in an optimal balance of sensitivity and specificity (0.89 and 0.91, respectively) with an overall correct classification rate of 90%. In a cognitively impaired group (dementia and mild cognitive impairment), a cut score of 27 (sensitivity, 0.69; specificity, 0.91) or 28 (sensitivity and specificity, 0.78) might be more appropriate.

Conclusion: Older patients with a college education who present with complaints of cognitive decline (reported by themselves or others) and score less than 27 on the MMSE are at a greater risk of being diagnosed with dementia and should be referred for a comprehensive dementia evaluation, including formal neuropsychological testing.

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Estimates of sensitivity and specificity were calculated for MMSE cut scores from 16 (ie, 15 and below) to 30 (ie, 29 and below). Results comparing control participants without dementia with participants diagnosed with some form of dementia are presented in Table 1 and illustrated with a receiver operating characteristic plot in the Figure. The traditional cut score of 24 (23 or below) yielded a moderate estimate of sensitivity (0.66) with very high specificity (0.99) and an overall correct classification rate of 88.9%. The modest test sensitivity reflects the failure of the traditional cut score to identify a sizeable number of patients with dementia in this highly educated sample. Specifically, 104 patients with dementia (34%) in this sample were misclassified as not having dementia.

An optimal balance between sensitivity (0.89) and specificity (0.91) was obtained with a cut score of 27 (26 or below). This yielded only a slight improvement in the overall correct classification rate (90.1%), but identified 70 of the 104 patients with dementia who were missed using the traditional cutoff. The cut score of 27 yields a likelihood ratio of 9.6, indicating that college graduates...
with an MMSE score of 26 and with complaints of cognitive decline (reported by themselves or others) are nearly 10 times more likely to have dementia than those who obtain a score of 27 or higher.

As expected, the improved sensitivity obtained when the cut score is raised to 27 is achieved by sacrificing specificity. As a result, 61 (9%) participants without dementia fall below the higher cutoff, compared with only 3 (<1%) participants with false-positive identification with the traditional cut score of 24.

Because clinicians regularly evaluate patients with cognitive dysfunction with and without dementia, the above-mentioned analyses were calculated on a cognitively impaired group (mild cognitive impairment and dementia) vs control participants to determine if an appropriate cut score could be obtained. Estimates of sensitivity and specificity are presented in Table 2. The traditional cut score of 24 yields very poor sensitivity (0.45) but perfect specificity (1.0) (Table 2). Raising the cut score to 27 yields an increased sensitivity (0.69) with a concomitantly declined, though still impressive, specificity (0.91).

Although sensitivity and specificity measures are important to establish the diagnostic validity of test measures such as the MMSE, the diagnostic utility of a particular score earned by a particular patient is represented by the test’s predictive values. Positive predictive values (PPV) represent the probability that a patient with a score above cutoff actually has the condition of interest. Conversely, negative predictive values (NPV) represent the probability that a patient with a score above cutoff does not have the condition of interest. Unlike sensitivity and specificity, PPV and NPV are influenced by the base rate of the condition of interest in the target population. In the current study, where the base rate of dementia (dementia-only group) was 32%, the PPV and NPV for the traditional cutoff of 24 were 0.97 and 0.86, respectively. Using a cutoff of 27 yielded a lower PPV (0.82), but a higher NPV (0.94). When looking at the cognitively impaired group (mild cognitive impairment and dementia), the standard cut score of 24 yields very low sensitivity (0.45), but perfect specificity (1.0) (Table 2). Raising the cut score to 27 yields a lower PPV (0.82), but a higher NPV (0.94). The optimal balance of sensitivity and specificity were found at cut scores of 27 (PPV, 0.78; NPV, 0.86) or 28 (PPV, 0.63; NPV, 0.88). Table 3 presents predictive value calculations from the both groups for clinicians who wish to apply these data in settings where base rates of cognitive impairment and/or dementia differ from that of the current study.

The current findings suggest that the traditional MMSE cut score of 24 does not yield optimal classification accuracy in highly educated white patients with dementia. Instead, a more stringent cut score of 27 yields greater clinical utility for identifying dementia in highly educated individu-

### Table 2. Sensitivity and Specificity Estimates for Detecting Cognitive Impairment (Mild Cognitive Impairment and Dementia) Using the MMSE

<table>
<thead>
<tr>
<th>Cut Score</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16</td>
<td>0.14 (0.11-0.18)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;17</td>
<td>0.16 (0.13-0.19)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;18</td>
<td>0.17 (0.14-0.21)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;19</td>
<td>0.20 (0.17-0.24)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>0.22 (0.19-0.26)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;21</td>
<td>0.27 (0.23-0.31)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;22</td>
<td>0.33 (0.29-0.37)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;23</td>
<td>0.38 (0.34-0.43)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;24</td>
<td>0.45 (0.41-0.50)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>&lt;25</td>
<td>0.52 (0.48-0.57)</td>
<td>0.98 (0.97-0.99)</td>
</tr>
<tr>
<td>&lt;26</td>
<td>0.59 (0.54-0.63)</td>
<td>0.96 (0.95-0.98)</td>
</tr>
<tr>
<td>&lt;27</td>
<td>0.69 (0.65-0.73)</td>
<td>0.91 (0.88-0.93)</td>
</tr>
<tr>
<td>&lt;28</td>
<td>0.78 (0.74-0.82)</td>
<td>0.78 (0.74-0.81)</td>
</tr>
<tr>
<td>&lt;29</td>
<td>0.89 (0.86-0.91)</td>
<td>0.57 (0.53-0.61)</td>
</tr>
<tr>
<td>&lt;30</td>
<td>0.96 (0.93-0.97)</td>
<td>0.27 (0.23-0.30)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; MMSE, Mini-Mental State Examination.

### Table 3. The PPV and NPV of Traditional and Optimal MMSE Cut Scores for Highly Educated White Patients Seen in Clinical Settings With Different Base Rates of Dementia or Cognitive Impairment

<table>
<thead>
<tr>
<th>Base Rate</th>
<th>0.01</th>
<th>0.02</th>
<th>0.05</th>
<th>0.10</th>
<th>0.15</th>
<th>0.20</th>
<th>0.25</th>
<th>0.30</th>
<th>0.40</th>
<th>0.50</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cut score of 24 PPV</td>
<td>0.40</td>
<td>0.57</td>
<td>0.78</td>
<td>0.88</td>
<td>0.92</td>
<td>0.94</td>
<td>0.96</td>
<td>0.97</td>
<td>0.98</td>
<td>0.99</td>
</tr>
<tr>
<td>NPV</td>
<td>1.00</td>
<td>0.99</td>
<td>0.98</td>
<td>0.96</td>
<td>0.94</td>
<td>0.92</td>
<td>0.90</td>
<td>0.87</td>
<td>0.81</td>
<td>0.74</td>
</tr>
<tr>
<td>Cut score of 27 PPV</td>
<td>0.09</td>
<td>0.17</td>
<td>0.34</td>
<td>0.52</td>
<td>0.64</td>
<td>0.71</td>
<td>0.77</td>
<td>0.81</td>
<td>0.87</td>
<td>0.91</td>
</tr>
<tr>
<td>NPV</td>
<td>1.00</td>
<td>1.00</td>
<td>0.99</td>
<td>0.99</td>
<td>0.98</td>
<td>0.97</td>
<td>0.96</td>
<td>0.95</td>
<td>0.93</td>
<td>0.89</td>
</tr>
<tr>
<td>Cognitive impairment* Cut score of 24 PPV</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>NPV</td>
<td>0.99</td>
<td>0.99</td>
<td>0.97</td>
<td>0.97</td>
<td>0.94</td>
<td>0.90</td>
<td>0.87</td>
<td>0.83</td>
<td>0.79</td>
<td>0.71</td>
</tr>
<tr>
<td>Cut score of 28 PPV</td>
<td>0.03</td>
<td>0.07</td>
<td>0.16</td>
<td>0.28</td>
<td>0.38</td>
<td>0.47</td>
<td>0.54</td>
<td>0.60</td>
<td>0.70</td>
<td>0.78</td>
</tr>
<tr>
<td>NPV</td>
<td>1.0</td>
<td>0.99</td>
<td>0.99</td>
<td>0.97</td>
<td>0.95</td>
<td>0.93</td>
<td>0.91</td>
<td>0.89</td>
<td>0.84</td>
<td>0.78</td>
</tr>
</tbody>
</table>

Abbreviations: MMSE, Mini-Mental State Examination; NPV, negative predictive values; PPV, positive predictive values.

*Cognitive impairment group includes patients diagnosed with mild cognitive impairment and dementia.

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Educational attainment is often considered a manifestation of cognitive reserve, with higher education levels associated with greater reserve and a greater ability to withstand neuropathological burden before exhibiting detectable signs of disease. Individuals with greater cognitive reserve are believed to maintain higher levels of cognitive functioning in the early stages of degenerative dementia. By the time cognitive symptoms are first obtained, these patients are believed to have significantly greater disease burden and faster subsequent decline. Identifying such individuals at an earlier stage of disease development and progression is desirable for both treatment and research purposes.

There was not enough data in the current sample to test the comparative accuracy of individual cut scores between highly educated individuals across ethnic groups. Therefore, the current findings with white individuals must be tested within ethnic minority populations before generalizations can be made. Additionally, the sample is English-speaking, and caution must be used when attempting to generalize to non-English-speaking individuals or individuals for whom English is a second language. It should also be noted that the MMSE was administered as part of the clinical examination and was not used as part of the inclusion/exclusion criteria for the study database. Therefore, the MMSE was not used as a screening measure of cognitive functioning in this sample and might perform differently when used in this context (eg, epidemiological studies).

The current findings are not intended to encourage the diagnosis of cognitive impairment or dementia based on total MMSE scores alone. Instead these results provide practitioners with revised criteria for appropriate management of highly educated older white patients. Specifically, older patients who present with memory complaints (reported by themselves or others) who have attained a college degree or higher level of education and who score below 27 on the MMSE are at increased risk of cognitive dysfunction and dementia and should be referred for a comprehensive evaluation, including formal neuropsychological studies. When early identification is the primary goal of screening, the cost associated with evaluating individuals further who are subsequently found not to have dementia is outweighed by the benefit of identifying a considerably larger number of individuals who are in the earliest stages of dementia, where early intervention and/or participation in clinical trials may provide maximum benefit.

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Author Contributions: Study concept and design: O’Bryant, Ivnik, Petersen, and Lucas. Acquisition of data: Smith, Ivnik, Graff-Radford, and Lucas. Analysis and interpretation of data: O’Bryant, Humphreys, Smith, and Lucas. Drafting of the manuscript: O’Bryant and Petersen. Critical revision of the manuscript for important intellectual content: O’Bryant, Humphreys, Smith, Ivnik, Graff-Radford, and Lucas. Statistical analysis: O’Bryant and Lucas. Obtained funding: Graff-Radford and Petersen. Administrative, technical, and material support: Humphreys, Smith, Ivnik, and Lucas. Study supervision: Ivnik and Lucas.

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