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## Original Study

## Recall Tests Are Effective to Detect Mild Cognitive Impairment: A Systematic Review and Meta-analysis of 108 Diagnostic Studies

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## A B S T R A C T

**Keywords:**  
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**Background:** Mild cognitive impairment (MCI) is a prevalent symptom associated with the increased risk of dementia. There are many cognitive tests available for detection of MCI, and investigation of the diagnostic performance of the tests is deemed necessary.

**Objective:** This study aims to evaluate the diagnostic performance of different cognitive tests used for MCI detection.

**Data sources:** A list of cognitive tests was identified in previous reviews and from online search engines. Literature searches were performed on each of the cognitive tests in MEDLINE, Embase, and PsycINFO from the earliest available dates of individual databases to December 31, 2016. Google Scholar was used as a supplementary search tool.

**Study selection:** Studies that were used to assess the diagnostic performance of the cognitive tests were extracted with inclusion and exclusion criteria. Each test's performance was compared with the standard diagnostic criteria. Bivariate random effects models were used to summarize the test performance as a point estimate for sensitivity and specificity, and presented in a summary receiver operating characteristic curve. Reporting quality and risk of bias were evaluated.

**Results:** A total of 108 studies with 23,546 participants were selected to evaluate 9 cognitive tests for MCI detection. Most of the studies used the Mini-Mental State Examination (MMSE) ( $n = 58$ ) and the Montreal Cognitive Assessment (MoCA) ( $n = 35$ ). The combined diagnostic performance of the MMSE in MCI detection was 0.71 sensitivity [95% confidence interval (CI): 0.66–0.75] and 0.74 specificity (95% CI: 0.70–0.78), and of the MoCA in MCI detection was 0.83 sensitivity (95% CI: 0.80–0.86) and 0.75 specificity (95% CI: 0.69–0.80). Among the 9 cognitive tests, recall tests showed the best diagnostic performance with 0.89 sensitivity (95% CI: 0.86–0.92) and 0.84 specificity (95% CI: 0.79–0.89). In subgroup analyses, long- or short-delay recall tests have shown better performance than immediate recall tests.

**Conclusions:** Recall tests were shown to be the most effective test in MCI detection, especially for the population with symptoms of memory deterioration. They can be potentially used as the triage screening test for MCI in primary care setting. But when a patient shows cognitive impairments beyond memory deterioration, a more comprehensive test such as the MoCA should be used.

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Mild cognitive impairment (MCI) refers to some measurable cognitive deficits that are associated with normal age-related decline but do not fulfill a diagnosis of dementia.<sup>1,2</sup> The prevalence of MCI is 10% to 20%.<sup>3</sup> The annual progression rate of individuals with MCI to Alzheimer disease (AD) ranges from 10% to 16%.<sup>1,3,4</sup> MCI was classified as a mild neurocognitive disorder in the *Diagnostic and Statistical Manual of Mental Disorder—Fifth Edition*.<sup>5</sup> Some rehabilitation

programs have been shown to be effective in the improvement of cognitive functions for patients with MCI.<sup>3,6</sup> The United States Food and Drug Administration has addressed the importance of treatment investigation for MCI and prodromal AD in 2013.<sup>7</sup> Therefore, screening for MCI can provide a window of opportunity for interventions to improve cognitive function.

However, distinguishing MCI from normal age-related cognitive decline is a challenging task for clinicians.<sup>3</sup> Many neuropsychological tests have been developed, and some of them have been proven to be effective for MCI screening. But the daily administration of the tests is time-consuming in real clinical practice. A systematic review showed that the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) 10-Word List was better than some other cognitive tests with multiple domains.<sup>8</sup> Another systematic review suggested that comprehensive screening tests such as the Montreal Cognitive Assessment (MoCA), Addenbrooke's Cognitive Examination–Revised (ACE-R), and the CERAD had better diagnostic performance than noncomprehensive screening tests such as the Clock Drawing Test (CDT) and the Mini-Cog for MCI detection.<sup>9</sup> Two recent systematic reviews showed that the MoCA had higher sensitivity and specificity than the Mini-Mental State Examination (MMSE) and the Verbal Fluency Test (VFT) for MCI detection.<sup>10,11</sup> However, a comparison across different cognitive tests for the detection of MCI is not readily available. Therefore, the aim of this systematic review is to quantitatively analyze the diagnostic performance of cognitive tests for MCI detection.

## Methods

This study was performed according to the standard guidelines for the systematic review of diagnostic studies, including the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>12</sup> and the guidelines suggested by the Cochrane Diagnostic Test Accuracy Working Group.<sup>13,14</sup>

### Search Strategy

A list of cognitive tests for MCI was identified in previous reviews<sup>8–11</sup> and from web search engines. Literature searches were performed on each of the cognitive tests in MEDLINE, Embase, and PsycINFO with general keywords related to “cognitive impairment,” “MCI,” and “dementia.” The search duration was from the earliest available dates in each database to December 31, 2016. Diagnostic studies comparing the accuracy of the cognitive tests for MCI were identified from the title and abstract preview of all search records. Literature search was also performed in Google Scholar, whose ranking algorithm considers both citation counts and keyword relevance. The first 10 pages of all search results in Google Scholar were scanned. Manual searches were extended to the bibliographies of the review articles and studies that were included in this meta-analysis. The selection was limited to peer-reviewed articles published in the English language.

### Inclusion and Exclusion Criteria

Studies were included if they met at least 1 of the following inclusion criteria:

1. Study participants were screened for MCI in any clinical or community settings.
2. Patients with MCI were confirmed with standard diagnostic criteria, including the Petersen criterion,<sup>1</sup> the report of International Working Group on Mild Cognitive Impairment,<sup>2</sup> the Movement Disorder Society Task Force guidelines for MCI in Parkinson's Disease,<sup>15</sup> or consensus by qualified clinicians using

the Clinical Dementia Rating (CDR)<sup>16</sup> and standardized neuropsychological tests. Studies reporting cases of cognitive impairments with no dementia (CIND), very mild dementia, or questionable dementia were further studied to confirm whether they included subjects with MCI.

3. The total number of participants with normal cognition and MCI was reported.
4. Diagnostic performance of the cognitive tests was summarized in terms of sensitivity and specificity, or data that could be used to derive those values were provided.

Some tests presenting with similar diagnostic methodology were combined in this study. The CDTs in Shulman's<sup>17</sup> and Rouleau's<sup>18</sup> versions are the typical cases in point. We also observed that many studies extracted the part of memory tasks or recall tests from neuropsychological tests, such as the California Verbal Learning Test–Second Edition<sup>19</sup> and the Hopkins Verbal Learning Test–Revised.<sup>20</sup> These recall tests were also included in this study and were further classified into different subgroups—immediate recall, short-delay recall, and long-delay recall for word list or story. Studies were excluded if they were not written in English or the cognitive test was reported in fewer than 4 academic publications.

### Data Extraction

Two investigators (J.Y.C.C. and H.W.H.) independently assessed the relevance of search results and abstracted the data into an Excel spreadsheet. The file was used to record the demographic details of included articles, such as the year of publication, the study location, the number of participants with and without MCI, the mean age of participants, the percentage of male participants, the diagnostic criteria, and the cutoff values used to define patients with MCI. The diagnostic performance of the cognitive tests for MCI was the primary outcome of this study, so we recorded the sensitivity and specificity, or the true-positive, false-positive, true-negative, and false-negative values, of each cognitive test. When a study presented different cutoff values to define a patient with MCI, only the result from a recommended cutoff by the authors of the article was selected. When a study recommended more than 1 cutoff, the cutoff presented in the abstract of the article was chosen. When discrepancies were found regarding study eligibility or data extraction, the third investigator (K.K.F.T.) would make the definitive decision.

### Reporting Quality and Risk of Bias

An 8-point scale was designed to evaluate the study quality, which showed (1) clear definition on study population, (2) details of participant recruitment, (3) sampling of participant selection, (4) data collection plan, (5) reference standard and its rationale, (6) specifications of the cognitive tests, (7) rationales for cutoffs, and (8) methods for calculation of diagnostic accuracy with confidence intervals. Potential risks of bias in each study were evaluated by the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) instrument,<sup>21</sup> which assessed (1) patient selection, (2) execution of the screening instruments, (3) execution of the reference standard, and (4) the patient follow-up and delayed time of receiving reference tests.

### Data Synthesis and Statistical Analysis

The overall sensitivity and specificity of each cognitive test were pooled using a bivariate random effects model.<sup>22</sup> Forest plots were used as the graphical presentation for the combined sensitivity and specificity. A diagnostic odds ratio was used as a single indicator of test performance across a different threshold of cutoff values.<sup>23</sup> Besides, a hierarchical summary receiver operating characteristic (HSROC) curve was generated to present the summary estimates of sensitivity and

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