Best Evidence Summaries of Topics in Mental Healthcare

BEST *in* MH *clinical question-answering service*

Question

"How effective, in comparison to other diagnostic tools highlighted by UK clinical guidelines, is the Mini-mental State Examination (MMSE), in the management of cognitive impairments in adults?"

Clarification of question using *PICTRO* structure

Patients:	Adults with cognitive/memory impairment
Index Test:	The Mini-mental State Examination (MMSE)
Comparator Test:	The seven minute screen (7MS), Six-Item Cognitive Impairment Test (6CIT), the General Practitioner Assessment of Cognition (GPCOG), or The Addenbrooke's Cognitive Examination (ACE)
Target Condition:	Adults with cognitive/memory impairment
Reference Standard:	Neuropsychiatric assessment
Outcome:	Sensitivity & specificity

Clinical and research implications

There is some limited evidence, from one diagnostic case control study, that the seven minute screen is a useful screening tool for discriminating patients with dementia from cognitively intact patients and may have higher sensitivity than the Mini-mental State Examination (MMSE) for both Alzheimer's disease and other dementias. A poor quality systematic review suggested that the Six-Item Cognitive Impairment Test (6CIT) should be considered in specialist settings, but no numerical estimates of test performance were presented to support this statement. Evidence from two diagnostic cohort studies suggested that neither MMSE, nor the revised Addenbrooke's Cognitive Examination (ACE-R) had adequate performance to diagnose mild cognitive impairment (MCI) in patients with Parkinson's disease or acute stroke. The results of one further diagnostic cohort study indicated that the ACE-R, but not MMSE, had good sensitivity and specificity for MCI ≥ 1 year after transient ischemic attack (TIA) or stroke.

Further research is needed to provide evidence on the comparative performance of MMSE and the General Practitioner Assessment of Cognition (GPCOG) and the 6CIT, and to provide evidence on the performance of 7MS and ACE-R in a wider range of patient groups and at different degrees of cognitive impairment.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic review, which included five studies relevant to this evidence summary[1], and four primary studies[2-5],which met the inclusion criteria for this evidence summary. One primary study, which was also included in the systematic review, compared the diagnostic performance of 7MS with that of the Mini-Mental State Examination (MMSE),[3] and the remaining primary studies compared the diagnostic performance of the revised Addenbrooke's Cognitive Examination (ACE-R) with that of the MMSE in various patient groups and settings.[2,4,5] No primary studies were identified that compared MMSE with the six-item Cognitive Impairment Test (6CIT), or the General Practitioner Assessment of Cognition (GPCOG).

Main Findings

The systematic review assessed the performance of 29 different multi-domain instruments, which take no longer to administer than the MMSE, for the diagnosis of dementia.[1] It included 44 studies, only 5 of which assessed instruments included in this summary (one study on the seven minute screen (7MS), two studies on 6CIT and two studies on GPCOG.[1] The results of the full Bayesian meta-analysis (including all 29 multi-domain instruments) presented in the review, indicated that 7MS and 6CIT both had satisfactory case finding performance (AUC ≥ 0.80) in specialist settings.[1] There was no evidence that GPCOG had satisfactory performance in any setting or application.[1]

One of the studies included in the systematic review was also identified as a primary study for inclusion in this assessment, because it compared the diagnostic performance of 7MS with that of MMSE.[3] This study was conducted in specialist clinics and reported similar estimates of specificity for any dementia using 7MS at a diagnostic threshold of ≥ 0 (93.5%), or MMSE at a diagnostic threshold of 23 (96.8%).[3] However, the sensitivity of MMSE for Alzheimer's disease (AD) was lower than that of 7MS (71.8% and 92.9%, respectively). Similarly, MMSE also had a lower sensitivity for other dementias than 7MS (59.8% and 89.4%, respectively).[3] This study also reported that both tests were

abnormal in a significant proportion (≈ 30%) of patients who met DSM-IV criteria for depression, but not dementia.[3]

Three primary studies compared MMSE with ACE-R.[2,4,5] All three studies compared the ability of the two instruments to detect mild cognitive impairment (MCI). One study was conducted in non-demented patients with Parkinson's disease.[2] This study found that the overall diagnostic performance, as indicated by the area under the receiver operating characteristic curve (AUC), was higher for ACE-R (0.66) than for MMSE (0.55).[2] However, it should be noted that both of these AUC values are indicative of poor diagnostic performance. The two remaining studies compared MMSE with ACE-R in stroke patients.[4,5] One study was conducted in hospitalised patients immediately after stroke and reported that neither ACE-R or MMSE had an overall performance better than chance; at published diagnostic thresholds, neither test reported both adequate sensitivity (>80%) and adequate specificity (>60%).[4] The final study was conducted in ≥ 1 year after stroke of transient ischemic attack (TIA) and reported that the optimal diagnostic threshold for ACE-R was 92 to 94 (ACE-R < 92 gave a sensitivity of 72% and specificity of 79%; ACE-R < 94 gave a sensitivity 83% and a specificity of 73%).[5] The sensitivity of MMSE for MCI was low, only exceeding 70% at a threshold of < 29.[5]

Authors Conclusions

The systematic review concluded that current evidence suggests that for either the original MMSE or the Abbreviated Mental Test Score (AMTS) should be considered in primary care settings and either 6CIT or the MINI-COG should be considered in specialist settings (MINI-COG is not included in this evidence summary).[1] The primary study of 7MS concluded that it is a useful screening tool for discriminating patients with dementia from cognitively intact patients.[3] Two studies of ACE-R in patients with Parkinson's disease,[2] and in patients with acute stroke,[4] concluded that ACE-R should be used cautiously,[2] or not at all[4] to screen for mild cognitive impairment (MCI). The remaining study, conducted ≥ 1 year after stroke of TIA, concluded that the ACE-R had good sensitivity and specificity for MCI, with optimal thresholds being dependent on application (screening or diagnosis).[5]

Reliability of conclusions/Strength of evidence

The evidence included in this summary was derived from one systematic review and four diagnostic test accuracy studies (three cohort studies and one diagnostic case-control study). The systematic review was of poor quality; reporting of review methods was limited, searches included terms likely limit search sensitivity and pooled estimates of performance were calculated across a wide variety of test using different reference standards. In addition, only 5 of the 44 studies included in the review were relevant to this evidence summary. The case-control design, as used in primary diagnostic accuracy studies is generally associated with a risk of over estimation of index test performance. However, for the study described here, this risk would be likely to apply equally to MMSE and 7MS, thus the reliability of conclusions about the comparative performance of these two tests is unlikely to be affected by the study design. Two of the primary diagnostic accuracy studies included in this summary reported diagnostic thresholds which were derived within the study population.[1,5] This approach is usually considered problematic as it may result in over estimations of test performance. However, as with the case-control design, this risk is likely to apply equally to both index tests being assessed and hence is unlikely to bias conclusions about their relative performance. It should be noted however, that these two studies reported the highest estimates of test performance in this evidence summary. Overall, the available primary studies are of reasonable quality and can be

considered to provide a reasonable estimate of the comparative performance of MMSE and 7MS for the diagnosis of dementia and of MMSE and ACE-R for the diagnosis of MCI.

What do guidelines say?

Nice Guidelines CG42 (2006, updated 2007).

"Clinical cognitive assessment in those with suspected dementia should include examination of attention and concentration, orientation, short and long-term memory, praxis, language and executive function. As part of this assessment, formal cognitive testing should be undertaken using a standardised instrument. The Mini Mental State Examination (MMSE) has been frequently used for this purpose, but a number of alternatives are now available, such as the 6-item Cognitive Impairment Test (6-CIT), the General Practitioner Assessment of Cognition (GPCOG) and the 7-Minute Screen. Those interpreting the scores of such tests should take full account of other factors known to affect performance, including educational level, skills, prior level of functioning and attainment, language, and any sensory impairments, psychiatric illness or physical/neurological problems." (*pg.20*)

SIGN Guidelines CG86 (2006)

“The Addenbrooke’s Cognitive Examination (ACE; *see Annex 7*) is a more comprehensive measure of cognitive function that incorporates the MMSE. It is a 100-point test battery assessing six cognitive domains…Initial cognitive testing can be improved by the use of Addenbrooke’s Cognitive Examination.” (*pg.4*)

The NICE guideline does not include any statement on the comparative performance of MMSE and the other instruments listed, or any recommendation to use a particular instrument; it is, therefore, not contradicted by this evidence summary. By contrast, the SIGN guideline appears to endorse the use of the Addenbrooke’s Cognitive Examination; this evidence summary did not identify sufficient data to support the statement that “initial cognitive testing can be improved by the use of Addenbrooke’s Cognitive Examination.”

Date question received: 26/02/2013
Date searches conducted: 27/02/2013
Date answer completed: 15/03/2013

References

Systematic Review

1. Mitchell, A.J. and Srinivasa, M. (2010) Screening and case finding tools for the detection of dementia. Part 1: Evidence-based meta-analysis of multidomain tests. *The American Journal of Geriatric Psychiaty 18* (**9**) pp. 759-782

Primary Studies

2. Komadina, N.C., Terpening, Z., Huang, Y., Halliday, G.M., Naismith, S.L. and Lewis, S.J.G. (2011) Utility and Limitations of Addenbrooke’s Cognitive Examination-Revised for Detecting Mild Cognitive Impairment in Parkinson’s Disease. *Dementia and Geriatric Disorders* 3*1* pp. 349-357.

3. Meulen, E.F., Schmand, B., van Campen, J.P., de Koning, S.J., Ponds, R.W., Scheltens, P. and Verhev, F.R. (2004) The seven minute screen: a neurocognitive screening test highly sensitive to various types of dementia. *Journal of Neurology, Neurosurgery and Psychiatry* 75 pp. 700-705.
4. Morris, K., Hacker, V. and Berrice Lincoln N. (2012) The validity of the Addenbrooke's Cognitive Examination-Revised (ACE-R) in acute stroke. *Disability and Rehabilitation* 34(3) pp. 189-195.
5. Pendlebury ST, Mariz J, Bull L, Mehta Z, Rothwell PM. (2012) MoCA, ACE-R, and MMSE versus the national institute of neurological disorders and stroke-canadian stroke network vascular cognitive impairment harmonization standards neuropsychological battery after TIA and stroke. *Stroke 43* pp. 464-9.

Guidelines

Scottish Intercollegiate Guideline Network (2006) Management of patients with dementia. A national clinical guideline. CG86. Edinburgh: Scottish Intercollegiate Guideline Network. http://www.sign.ac.uk/pdf/sign86.pdf

National Institute for Health and Clinical Excellence (2006, updated 2007) Dementia. Supporting people with dementia and their carers in health and social care. CG42. London: National Institute for Health and Clinical Excellence. http://www.nice.org.uk/nicemedia/live/10998/30318/30318.pdf

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
Mitchell and Srinivasa (2010)	07/2009	Studies were included if they: assessed the diagnostic performance of brief (taking no longer to complete than MMSE) multi-domain screening method; used a validated reference standard to confirm diagnosis; reported sensitivity and specificity or sufficient data to calculate these measures; included a minimum of 170 participants. Studies were excluded if they: considered only screening for MCI; assessed informant-only interviews.	44 (5 studies assessing tests included in this summary)	This review assessed the performance of multi-domain instruments, which take no longer to administer than the Mini-Mental State Examination (MMSE), for the diagnosis of dementia. The review included 44 studies of brief alternatives to MMSE, with 19 studies reporting direct comparisons with MMSE. Study design was not clearly reported and appeared to include a mixture of diagnostic cohort and diagnostic case-control studies. Criteria for critical appraisal of included studies were described, but the results of this appraisal did not appear to have been used in summarising the results, with the exception that studies where the index test formed part of the diagnostic criteria (reference standard) were excluded. 20 Studies were conducted in memory clinics of secondary care and 24 studies were conducted in primary care, community, or nursing home settings. Studies assessed 29 different instruments, which included 2-29 items and took	The review reported clear and appropriate inclusion criteria. A range of sources were searched a range of sources to identify relevant articles, however, search terms relating to test accuracy study design were used and use of these terms

				between 0.5 and 10 minutes to complete. Studies used a variety of reference standards to confirm diagnosis. Results were summarised, for all instruments, by study setting. The review included only five studies that assessed instruments specified in this evidence summary (Six-item Cognitive Impairment Test (6CIT) 2 studies, General Practitioner Assessment of Cognition (GPCOG) 2 studies and seven minute screen (7MS) 1 study). The results of these studies have bee extracted from the review and are summarised below: 6CIT: Two studies (n=938) assessed 6CIT in secondary care settings. Both studies were single tests assessments with no comparison to MMSE. One study was conducted in patients with mild to severe dementia and one was conducted in patients referred to an Alzheimer's disease centre. One study used DSM-IV and ICD10 diagnostic criteria and the other study relied on diagnosis by a Psychiatrist (method un-specified). Both studies reported a test time of 2 minutes and neither reported any numerical estimate of test performance. One of the studies also reported use of 6CIT in a community setting with participants aged > 65 years (n=344); again the test time was 2 minutes and no numerical	has been shown to reduce search sensitivity (relevant studies may be missed. Details of the review process were not reported, so that it is not clear whether any measures (e.g. checking of data extraction) were taken to reduce error and/or bias. A critical appraisal process was described,

				estimate of test performance was reported. GPCOG: Two studies (n=529) assessed GPCOG in primary care. Both studies were single test assessments, which did not include a comparison with MMSE, and both used DSM-IV as the reference standard. One study was conducted in participants ≥ 50 years old with cognitive problems and the other study did not report details of participants. Both studies reported a test time of 4.5 minutes. One study reported an overall assessment of test performance, area under the receiver operating characteristic curve (AUC), of 0.78 and the other a misclassification rate of 14.2% with no further detail. 7MS: One study (n=424) reported a direct comparison of 7MS with MMSE in a secondary care setting. The study population included participants with AD, vascular dementia, Lewy-body dementia, other dementia, MCI, depression and controls. DSM-IV and the Alzheimer's disease (AD) using National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association (NINCDS-ADRDA) criteria were used to determine diagnosis. The test time for MMSE was 8.5 minutes in non-cognitively impaired participants and 15.6	but the results of this appraisal were not used in summarising the evidence. Broadly appropriate meta-analytic methods were used, though the value of producing summary estimates across a wide range of different instruments and different diagnostic reference standards is questionable.

				minutes in cognitively impaired participants; no test time was reported for MMSE. For AD compared to "intact" participants, the AUC for 7MS was 0.989 and the AUC for MMSE was 0.949. For participants with mild dementia (MMSE >21), the AUC for 7MS was 0.974 and the AUC for MMSE was 0.872. The review reported that 7MS had "better diagnostic accuracy" than MMSE, but no statistical tests were presented to support this statement. Full Bayesian meta-analysis, which included all 29 multi-domain instruments assessed by the review, indicated that 7MS and 6CIT both had satisfactory case finding performance (AUC ≥ 0.80) in specialist settings. There was no evidence that GPCOG had satisfactory performance in any setting or application.	

Primary studies

Author (year)	**Inclusion criteria**	**Number of participants**	**Summary of results**	**Risk of bias**
Komadina et al (2011)	*Participants:* Non-demented patients with PD who satisfied the UKPDS Brain Bank criteria were recruited from the	N = 101	Aim: To assess the performance of ACE-R as a screening tool for mild cognitive impairment in Parkinson's disease (PD-MCI). The mean age of participants with PD-MCI was 65.6 ± 7.3 years and the mean age of participants without MCI was 64.7 ± 9.9	It was not clear whether a consecutive or random sample of participants was recruited, or whether

	Brain and Mind Research Institute's Parkinson's Disease Research Clinic, University of Sydney. All participants had MMSE scores ≥24. *Index test 1:* Addenbrooke's Cognitive Examination-Revised (ACE-R) *Index test 2:* Mini-Mental State Exam (MMSE) *Reference standard:* comprehensive neuropsychological and neurological evaluations: The digit span subtest of the Wechsler Adult Intelligence Scale III; parts A and B of the trail-making test; phonemic fluency (letters F, A, S) and semantic fluency (animal names); Wechsler Memory Scale III logical memory subtest; the National		and 59 participants were male. There were no significant differences in age, gender, years of education, predicted IQ, disease duration, motor UPDRS, Hoehn and Yahr stage, dopamine therapy or depression between participants with and without MCI. The overall accuracy, as indicated by the area under the receiver operating characteristic (ROC) curve, was significantly greater for ACE-R (0.66) than for MMSE (0.55), (p = 0.027). When the fluency sub-domain of ACE-R was used alone the area under the ROC curve was similar to that for the whole tool (0.66). Subgroup analysis indicated that, for individuals with lower levels of education (≤12 years), ACE-R had significantly better diagnostic performance than MMSE (area under the ROC curve 0.76 compared to 0.60, p = 0.018); this difference was not apparent for individuals with higher levels of education (> 12 years). The optimal ACE-R threshold for diagnosing PD-MCI was ≤ 93, which gave sensitivity of 61% and specificity of 64%. Using the fluency sub-domain of ACE-R alone and a threshold of ≤ 10, resulted in increased specificity (92%) and decreased sensitivity (48%). No optimal threshold data were reported for MMSE.	other selection criteria may have been applied. The index tests and reference standard were clearly described, but it was not clear whether the index test was interpreted blind to the reference standard and vice versa. Optimal thresholds for the index test were derived from the study population, which may result in over estimates of test performance. All participants appear to have received both index test and reference standards and tests appear to have been conducted during the same examination.

	Adult Reading Test. Diagnosis of PD-MIC was established using age-adjusted normative data; impairment was defined as ≥ 1.5 SD below predicted IQ. *Outcome:* Sensitivity and specificity for detecting mild cognitive impairment in Parkinson's Disease (PD-MCI).			
Meulen et al. (2004) **Note: this study was included in Mitchell 2010, but more detail is reported in the original study.**	*Participants:* Patients >55 years old, who were referred to geriatric day clinics or memory clinics across the Netherlands for memory complaints. *Index test 1:* The seven minute screen (7MS) *Index test 2:* The Mini-mental State Examination (MMSE) *Reference standard:* Structured interview, neurological	N = 587 (incl. 45 healthy age-matched controls)	Aim: To assess the predictive value of 7MS for various types of dementia, and the influence of depression and other psychiatric conditions on 7MS scores. The study included 542 patients with memory complaints: AD (n=177); vascular dementia (n=62), fronto-temporal dementia (n=43); lewy-body (n=17); other dementia (n=30); MCI (n=87); depression (n=31); other conditions (n=35). 45 Healthy controls were also included. There were no significant differences in age and years of education between controls and patients. The 7MS threshold for dementia was defined as 0 or higher. The sensitivity of 7MS for dementia of any cause versus cognitively intact patients and controls was 91.2% and specificity was 93.5%; sensitivity for AD was 92.9% and sensitivity for other dementias was 89.4%.	The study used a diagnostic case-control type design; i.e. it did not recruit a consecutive sample of symptomatic patients such as might be seen in clinical practice. Diagnostic-case-control type study designs can be associated with over estimations of test performance. The index test and reference standard

	examination, detailed neuropsychological work up, and laboratory investigations (CT or MRI in some patients). Diagnosis was made by a multi-disciplinary team, based on DSM-IV criteria for dementia, vascular dementia, and AD and NINCDS-ADRDA criteria for probable and possible AD, the consensus on frontotemporal lobar degeneration for fronto-temporal dementia, the McKeith citerial for Lewy-body dementia and the Cummings and Benson criteria for subcortical dementia. MCI was defined using the Petersen criteria. *Outcome:* Sensitivity, specificity and positive and negative predictive value.		The diagnostic threshold was defined as 23 for the MMSE score. The specificity of MMSE for dementia of any cause was 96.8%; sensitivity for AD was 71.8% and sensitivity for other dementias was 59.8%. The positive and negative predictive values for 7MS were 98% and 78%. The positive and negative predictive values for MMSE were 99% and 44%. In patients who met DSM-IV criteria for depression, but not dementia, 22 (71%) scored abnormally on 7MS and 18 (58%) scored abnormally on MMSE.	were clearly described and the diagnostic thresholds used did not appear to have been derived from the study population. The reference standard was interpreted blind to index test results in some instances and was otherwise subject to verification. The reference standard appears to have been applied after the index test. All participants appear to have received both index test and reference standards. Time between index test and reference standard was not clear.
Morris, Hacker and Lincoln (2012)	*Participants:* Stroke service patients at Nottingham University Hospitals NHS Trust,	N = 101 61 included in the analysis	Aim: To determine compare the accuracy of ACE-R With that of MMSE for detecting overall cognitive impairment after stroke and to assess the performance of ACE-R subscales.	It was not clear whether a consecutive or random sample of

	which comprises one hyper-acute and three acute stroke wards. Identified by examination of the medical notes. Exclusion criteria were: history of psychiatric problems; blind, deaf, too ill, or too drowsy to be assessed; non-English speaker; moderate or severe aphasia. *Index test 1:* Addenbrooke's Cognitive Examination-Revised (ACE-R) *Index test 2:* Mini-Mental State Exam (MMSE) *Reference standard:* Neuropsychological testing: Logical Memory subtest from the Wechsler Memory Scales III (WMS III); Rey-Osterreith Complex Figure Test recall; Star Cancellation test from the		The median age of participants included in the analysis was 76 years (IQR 67 to 82.5), 31 were male, the median years of education was 9.0 (IQR 9.0 to 11.0). Overall estimates of diagnostic performance, area under the ROC curve (AUC), indicated that neither test performed better than chance; AUC was 0.53 for both MMSE and ACE-R. None of the published diagnostic thresholds, for either test, gave both adequate levels of sensitivity (>80%) and specificity (>60%). For ACE-R, sensitivity estimates ranged from 59% at a threshold of 75 to 90% at a threshold of 88; corresponding specificity values were 40% and 20%. For MMSE, sensitivity estimates were 55% at a threshold of 24 and 80% at a threshold of 27; corresponding specificity estimates were 60% and 20%. No diagnostic threshold for any ACE-R subscale gave both adequate levels of sensitivity and specificity for the detection of impairment in specific areas of cognitive functioning.	participants was recruited, or whether other selection criteria may have been applied. Index tests and reference standard were clearly described, the reference standard was interpreted blind to the index test and the index test was applied before the reference standard. ACE-R and MMSE were applied using published diagnostic thresholds. 40 Patients did not complete neuropsychological testing (discharged from hospital before completion).

	Behavioural Inattention Test; Rey-Osterreith Copy task; Hayling Sentence Completion test; Verbal Fluency test (F,A,S); Letter–Number Sequencing and Digit Span subtests from the WMS-III. *Outcome:* Sensitivity and specificity.			
Pendlebury et al (2012)	*Participants* – Consecutive, non-institutionalised participants, assessed ≥ 1 year after a transient ischaemic attack (TIA) or stroke as part of a larger polupation study (OXVASC 2002). Participants who had problems that interfered with testing (e.g. poor vision, severe hearing impairment, inability to use the right arm, dysphasia, poor English,	N = 91	Aim: To determine the sensitivities and specificities of the MoCA, ACE-R, and MMSE at ≥1 year after transient ischemic attack (TIA) or stroke for detection of MCI. The mean age of study participants was 73.4 ± 11.6 years and 66% were male and 56% were post-stroke. Patients with TIA and stroke were similar in age, education level and gender distribution. Nine participants had incomplete neuropsychology data and three did not have ACE-R. Thirty-nine (42%) participants had MCI (amnestic multiple domain = 10, non-amnestic multiple domain = 9, non-amnestic single domain = 19, amnestic single domain = 1). The overall accuracy for discriminating between MCI and non-cognitively impaired participants, as indicated by the area ROC curve (AUC), was 0.83 (95% CI: 0.75, 0.92) for MMSE and 0.90 (95% CI: 0.83, 0.96) for ACE-R.	Participants were recruited consecutively. Index test and reference standard were appropriate, however, it was not clear whether those undertaking neuropsychological testing were aware of index test results and vice versa. Index test thresholds were derived from the study population.

	or acute illness) were excluded. *Index test 1:* Addenbrooke's Cognitive Examination-Revised (ACE-R) *Index test 2:* Mini-Mental State Exam (MMSE) The study also assessed other tests not included in this summary. *Reference standard* - National Institute of Neurological Disorders and Stroke–Canadian Stroke Network Harmonization Standards Neuropsychological Battery (Trail Test parts A and B, Symbol Digit Modalities Test, Boston Naming Test (30-item version), Rey-Osterrieth complex Figure copy, Hopkins Verbal Learning		The optimal diagnostic threshold for ACE-R was 92 to 94 (ACE < 92, sensitivity 72% and specificity 79%; ACE-R < 94, sensitivity 83% and specificity 73%). The sensitivity of MMSE for MCI was low, only exceeding 70% at a threshold of < 29. Restricting the analysis to multiple-domain MCI gave similar results.	The time between the index tests and reference standard was not explicitly reported, but all appear to have been undertaken at the same assessment. Nine participants (<10%) did not complete neuropsychological assessment.

	Test-Revised and Letter (Controlled Oral Word Association Test) and category (animals) fluency). Impairment was defined as ≥1.5 SD below the age-matched normative mean and MCI was also defined using Petersen criteria. *Target Condition* – Cognitive impairment *Outcome* – Specificity, sensitivity.			

Risk of Bias:

Systematic reviews

Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
Mitchell and Srinivasa (2010)	☺	☹	?	☹	☹

Primary studies

Study	RISK OF BIAS			
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	FLOW AND TIMING
Komadina et al (2011)	?	☹	?	☺
Meulen et al. (2004)	☹	☺	☺	?
Morris, Hacker and Lincoln (2012)	?	☺	☺	☹
Pendlebury et al (2012)	☺	☹	?	☺

☺Low Risk ☹High Risk ? Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
Guidelines			
NICE	Cognitive Impairment MMSE	225	2
SRs and Primary studies			
CENTRAL	1 GPCOG:ti,ab,kw 2GP-COG0 3"General Practitioner Assessment of Cognition"1 4"minute test"34 5"cognitive impairment test"3 6#3 or #4 or #537 7MMSE909 8"mini mental state examination"1100 9#7 or #81396 10#6 and #9 = 1 result	1	
PsycINFO	1. PsycINFO; GPCOG.ti,ab; 10 results. 2. PsycINFO; GP-COG.ti,ab; 1 results. 3. PsycINFO; "General Practitioner Assessment of Cognition".ti,ab; 7 results. 4. PsycINFO; 7MS.ti,ab; 12 results. 5. PsycINFO; 7-MS.ti,ab; 45 results. 6. PsycINFO; "7 minute screen".ti,ab; 16 results. 7. PsycINFO; "seven minute screen".ti,ab; 10 results. 8. PsycINFO; 6-cit.ti,ab; 2 results. 9. PsycINFO; 6CIT.ti,ab; 5 results. 10. PsycINFO; "Six-Item Cognitive Impairment Test".ti,ab; 2 results. 11. PsycINFO; "6 item cognitive impairment test".ti,ab; 4 results. 12. PsycINFO; 1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10 OR 11; 88 results. 13. PsycINFO; MMSE.ti,ab; 3604 results.	25	

	14. PsycINFO; "mini mental state examination".ti,ab; 5065 results. 15. PsycINFO; MINI MENTAL STATE EXAMINATION/; 510 results. 16. PsycINFO; 13 OR 14 OR 15; 6291 results. 17. PsycINFO; 12 AND 16; 25 results.		
EMBASE	18. EMBASE; GPCOG.ti,ab; 12 results. 19. EMBASE; GP-COG.ti,ab; 2 results. 20. EMBASE; "General Practitioner Assessment of Cognition".ti,ab; 9 results. 21. EMBASE; 7MS.ti,ab; 88 results. 22. EMBASE; 7-MS.ti,ab; 872 results. 23. EMBASE; "7 minute screen".ti,ab; 15 results. 24. EMBASE; "seven minute screen".ti,ab; 14 results. 25. EMBASE; 6-cit.ti,ab; 7 results. 26. EMBASE; 6CIT.ti,ab; 6 results. 27. EMBASE; "Six-Item Cognitive Impairment Test".ti,ab; 5 results. 28. EMBASE; "6 item cognitive impairment test".ti,ab; 6 results. 29. EMBASE; 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28; 1000 results. 30. EMBASE; MMSE.ti,ab; 9916 results. 31. EMBASE; "mini mental state examination".ti,ab; 8986 results. 32. EMBASE; MINI MENTAL STATE EXAMINATION/; 13546 results. 33. EMBASE; 30 OR 31 OR 32; 19114 results. 34. EMBASE; 29 AND 33; 35 results.	35	
MEDLINE	35. MEDLINE; GPCOG.ti,ab; 9 results. 36. MEDLINE; GP-COG.ti,ab; 0 results. 37. MEDLINE; "General Practitioner Assessment of Cognition".ti,ab; 5 results. 38. MEDLINE; 7MS.ti,ab; 36 results. 39. MEDLINE; 7-MS.ti,ab; 703 results. 40. MEDLINE; "7 minute screen".ti,ab; 15 results. 41. MEDLINE; "seven minute screen".ti,ab; 12 results. 42. MEDLINE; 6-cit.ti,ab; 3 results. 43. MEDLINE; 6CIT.ti,ab; 5 results. 44. MEDLINE; "Six-Item Cognitive Impairment Test".ti,ab; 5 results.	35	

	45. MEDLINE; "6 item cognitive impairment test".ti,ab; 6 results. 46. MEDLINE; 35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45; 775 results. 47. MEDLINE; MMSE.ti,ab; 5555 results. 48. MEDLINE; "mini mental state examination".ti,ab; 6649 results. 49. MEDLINE; MINI MENTAL STATE EXAMINATION/; 0 results. 50. MEDLINE; 47 OR 48 OR 49; 8728 results. 51. MEDLINE; 46 AND 50; 25 results.		
Summary	**NA**	**NA**	

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