# CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

## MOOD, COGNITION AND FATIGUE FOLLOWING STROKE EVIDENCE TABLES

**Vascular Cognitive Impairment: Screening and Assessment**

## Update 2019

*Lanctôt KL, Swartz RH (Writing Group Chairs) on Behalf of the Canadian Stroke Best Practice Recommendations Mood, Cognition and Fatigue following Stroke Writing Group and the Canadian Stroke Best Practice and Quality Advisory Committee, in collaboration with the Canadian Stroke Consortium*

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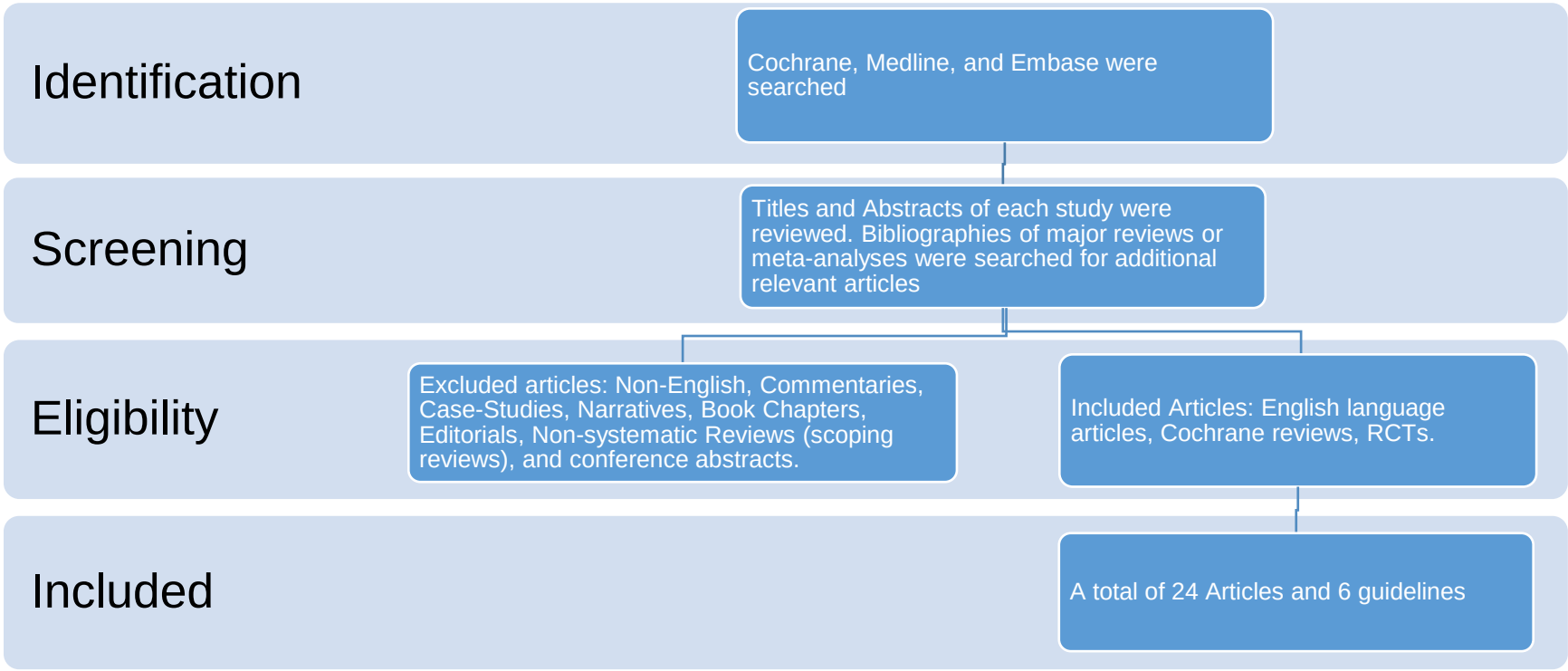
# Search Strategy




The Medline, Embase, PsycInfo, and Cochrane databases were searched using the terms [stroke OR cerebrovascular disorders] and [cognition OR neuropsychology OR mild cognitive impairment OR cognitive training OR cognitive rehabilitation]. The title and abstract of each article was reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 24 articles and 6 guidelines were included and were separated into categories designed to answer specific questions.

# Published Guidelines

| Guideline | Recommendations |
|---|---|
| **Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. (Part 5)** | Practice points<br>All stroke survivors should be screened for cognitive and perceptual deficits by a trained person (e.g. neuropsychologist, occupational therapist or speech pathologist) using validated and reliable screening tools, ideally prior to discharge from hospital.<br><br>Stroke survivors identified during screening as having cognitive deficits should be referred for comprehensive clinical neuropsychological investigations.<br><br>Info Box Practice points<br>Stroke survivors considered to have problems associated with executive functioning deficits should be formally assessed by a suitably qualified and trained person, using reliable and valid tools that include measures of behavioural symptoms. |
| **Smith EE, Saposnik G, Biessels GJ, Doubal FN, Fornage M, Gorelick PB, Greenberg SM, Higashida RT, Kasner SE, Seshadri S; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular Radiology and Intervention; Council on Functional Genomics and Translational Biology; and Council on Hypertension.**<br><br>**Prevention of stroke in patients with silent cerebrovascular disease: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association.**<br><br>***Stroke* 2017;48:e44–e71.**<br>**(selected)** | Summary of Suggestions for Clinical Care of Patients with Silent Cerebrovascular Disease<br><br>*Diagnosis by neuroimaging*<br>MRI has greater sensitivity than CT for diagnosis of silent cerebrovascular disease.<br>Radiology reports should describe silent cerebrovascular disease according to STRIVE.<br>WMHs of presumed vascular origin should be reported with the use of a validated visual rating scale such as the Fazekas scale for MRI.<br><br>*Investigations for patients with silent cerebrovascular disease*<br>Assess common vascular risk factors and assess pulse for atrial fibrillation.<br>Consider carotid imaging when there is silent brain infarction in the carotid territory.<br>Consider echocardiography when there is an embolic-appearing pattern of silent infarction.<br>Consider noninvasive CT or MR angiography when there are large (>1.0 cm) silent hemorrhages. |
| **Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research.**<br><br>**Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.**<br><br>***Stroke* 2016;47:e98–e169.** | Screening for cognitive deficits is recommended for all stroke patients before discharge home. Class 1; LOE B<br><br>When screening reveals cognitive deficits, a more detailed neuropsychological evaluation to identify areas of cognitive strength and weakness may be beneficial. Class IIa; LOE C |
| **Intercollegiate Stroke Working Party. National clinical guideline for stroke,5th Edition. London: Royal College of Physicians, 2016.** | **Cognitive Impairment (general)**<br>People with stroke should be considered to have at least some cognitive impairment in the early phase. Routine screening should be undertaken to identify the person's level of functioning, using standardised measures.<br><br>B Any person with stroke who is not progressing as expected in rehabilitation should receive a detailed assessment to determine whether cognitive impairments are responsible, with the results explained to the person, their family and the multidisciplinary team. |

| Guideline | Recommendations |
|---|---|
| | C People with communication impairment after stroke should receive a cognitive assessment using valid assessments in conjunction with a speech and language therapist. Specialist advice should be sought if there is uncertainty about the interpretation of cognitive test results.<br><br>D People with cognitive problems after stroke should receive appropriate adjustments to their multidisciplinary treatments to enable them to participate, and this should be regularly reviewed.<br><br>E People with acute cognitive problems after stroke whose care is being transferred from hospital should receive an assessment for any safety risks from persisting cognitive impairments. Risks should be communicated to their primary care team together with any mental capacity issues that might affect their decision-making.<br><br>F People with stroke returning to cognitively demanding activities such as driving or work should have their cognition fully assessed.<br>G People with continuing cognitive difficulties after stroke should be considered for comprehensive interventions aimed at developing compensatory behaviours and learning adaptive skills.<br><br>H People with severe or persistent cognitive problems after stroke should receive specialist assessment and treatment from a clinical neuropsychologist/clinical psychologist.<br><br>**Executive Function**<br>A People with stroke who appear to have adequate skills to perform complex activities but fail to initiate, organise or inhibit behaviour should be assessed for the dysexecutive syndrome using standardised measures.<br><br>**Attention and concentration**<br>Any person after stroke who appears easily distracted or unable to concentrate should have their attentional abilities (eg focused, sustained and divided) formally assessed.<br><br>**Memory**<br>A People with stroke who report memory problems and those considered to have problems with learning and remembering should have their memory assessed using standardised measures. |
| **National Stroke Foundation. Clinical Guidelines for Stroke Management 2010 Recommendations. Melbourne Australia.** | **Assessment of Cognition**<br>1. All patients should be screened for cognitive and perceptual deficits using validated and reliable screening tools (GPP).<br>2. Patients identified during screening as having cognitive deficits should be referred for comprehensive clinical neuropsychological investigations (GPP).<br>**Memory**<br>1. Any patient found to have memory impairment causing difficulties in rehabilitation or adaptive functioning should:<br>• Be referred for a more comprehensive assessment of their memory abilities (GPP)<br>• Be assessed to see if compensatory techniques to reduce their disabilities, such as notebooks, diaries, audiotapes, electronic organizers and audio alarms, are useful (D)<br>**Executive functions**<br>1. Patients considered to have problems associated with executive functioning deficits should be formally assessed using reliable and valid tools that include measures of behavioural symptoms (GPP). |
| **Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning: A national clinical guideline, 2010. Edinburgh, Scotland.** | • A full understanding of the patient's cognitive strengths and weaknesses should be an integral part of the rehabilitation plan (GPP).<br>• Stroke patients should have a full assessment of their cognitive strengths and weaknesses when undergoing rehabilitation or when returning to cognitively demanding activities such as driving or work (GPP).<br>• Cognitive assessment may be carried out by occupational therapists with expertise in neurological care, although some patients with more complex needs will require access to specialist neuropsychological expertise (GPP). |
| **VA/DoD clinical practice guideline for the management of stroke rehabilitation 2010.** | **Assessment of cognitive function**<br>1. Assessment of arousal, cognition, and attention should address the following areas:<br>a. Arousal |

| Guideline | Recommendations |
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| | b. Attention deficits<br>c. Visual neglect<br>d. Learning and Memory deficits<br>e. Executive function and problem-solving difficulties<br>2. There is insufficient evidence to recommend for the use of any specific tools to assess cognition. Several screening and assessment tools exist. (See Appendix B for standard screening instruments for cognitive assessment.)<br><br>**Use of standardized assessments**<br>1. Recommend that all patients should be screened for depression and motor, sensory, cognitive, communication, and swallowing deficits by appropriately trained clinicians, using standardized and valid screening tools. [C]<br>2. If depression, or motor, sensory, cognitive, communication, or swallowing deficits are found on initial screening assessment, patients should be formally assessed by the appropriate clinician from the coordinated rehabilitation team. [C] |

# Evidence Tables

## Prevalence and Predictors of Cognitive Impairment after Stroke

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Delavaran et al. 2016**<br><br>**Sweden**<br><br>**Prospective study** | NA | 145 first-ever stroke patients included in the Lund Stroke Register, Sweden, from 2001-2002. Median age was 78 years, 59% male. Median baseline NIHSS score was 3.<br><br>354 age-and sex-matched non-stroke controls were selected from a population - based database. | The development of any post-stroke cognitive impairment (PSCI), defined as Mini-Mental State Examination (MMSE) <27 and/or Montreal Cognitive Assessment (MoCA)<25 and severe cognitive impairment, defined as MMSE<23 and MoCA<20, 10 years following stroke, was established. The prevalences of any and severe cognitive impairment were identified in the controls (using MMSE criteria only). The odds of developing cognitive impairment among stroke survivors was estimated relative to controls. | **Primary outcomes:**<br>Prevalence of long-term PSCI, and to compare scores obtained using MMSE and MoCA<br><br>**Secondary outcomes:**<br>Predictors of severe cognitive impairment | At 10 years, 127 participants with stroke were available for follow-up. Of these, 96 (75.6%) had mRS scores of ≤2; 17 (13.4%) had mRS scores of 3, and 14 (11.0%) had mRS scores of 4or 5.<br><br>Among stroke survivors, the prevalences of any cognitive impairment using MMSE and MoCA criteria were 58 (45.7%) and 75 (61.5%), respectively.<br><br>Among stroke survivors, the prevalences of severe cognitive impairment using MMSE and MoCA criteria were 16 (12.5%) and 35 (28.7%), respectively.<br><br>Among controls, the prevalences of any, and severe cognitive impairment (assessed using only MMSE) were 175 (49.4%) and 43 (12.1%).<br><br>Among the 122 stroke survivors who completed both tests, 49 (40.2%) were classified as cognitively impaired by both tests. Of 75 stroke survivors who were identified as cognitively impaired based on MoCA, 26 had a normal MMSE. 4 stroke survivors with normal MoCA were identified with cognitive impairment based on MMSE.<br><br>The odds of developing severe cognitive impairment were higher among stroke survivors (OR= 2.48, 95% CI 1.34-4.59, p=.004), but not for any cognitive impairment (OR= 1.03, 95% CI 0.66-1.60, p=0.91). |
| **Pendlebury et al. 2015**<br><br>**UK**<br><br>**Prospective study OXVASC** | NA | 1,236 patients recruited from the OXVASC study (n=92,728) who had experienced a stroke or TIA during a defined period (2002-2007) and were included in follow-up to 2014. Mean age was 75 years47% were male, 33% were TIA, 30% major stroke and 5% ICH | Follow-up assessments were conducted at 1 and 6 months and 1 and 5 years by outpatient clinics, home visits or telephone interviews | **Primary outcome:**<br>Post-event dementia, was identified by a post event MMSE score of <24, remaining<24 at all follow-ups, or a MoCA <20 or Telephone Interview for Cognitive Status-modified (TICSm)<22 or Telephone MoCA (T-MoCA<9) | 95 patients had pre-event dementia<br><br>At one-month post stroke, 1,092 patients were alive (947 were assessed). At 6 months, 915 were alive (792 assessed) and at 5 years 673 were alive (567 assessed).<br><br>Incident dementia was identified in 260 patients during 5 years follow-up.<br><br>110 cases of dementia were identified indirectly through medical records, home visits and telephone follow-up, and not through clinic visits.<br><br>The 5-year cumulative incidence of post event |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | | dementia was 29% (26%–32%) overall, but was significantly higher among non-clinic-assessed patients (45% vs. 17%, p< 0.001). |
| **Levine at al. 2015**<br><br>**USA**<br><br>**Prospective study REGARDS** | NA | 23,572 participants ≥ 45 years enrolled in the REGARDS study from 2003-2007, without a history of stroke or cognitive impairment. | Baseline data was collected via telephone interview and home visit. Participants completed follow-up interviews by telephone twice per year, with the cognitive tests administered once per year. The changes in cognitive function following incident stroke were examined, adjusting for baseline cognitive function and other factors. | **Primary Outcome:**<br>Six-Item Screener (SIS)<br><br>**Secondary outcome:**<br>Cognitive impairment as measured by SIS score (<5 impaired vs. ≥5 unimpaired) | Over a median follow-up of 6.1 years, there were 515 strokes. Persons who experienced a stroke were significantly older (68.3 vs. 64.2 years).<br><br>Stroke was associated with acute decline in SIS scores (0.10 points; 95% CI 0.04 to 0.17).<br><br>Among survivors, the difference in the odds of cognitive impairment occurring acutely after stroke vs. immediately before stroke was not statistically significant (OR=1.32, 95% CI, 0.95- 1.83, p= .10); however, there was a significantly faster post-stroke rate of incident cognitive impairment compared with the pre-stroke rate (OR=1.23 per year; 95% CI 1.10-1.38, p < .001). |
| **Qu et al. 2015**<br><br>**China**<br><br>**Cross-sectional study** | NA | 599 stroke survivors (48% of all survivors in the sampled regions) who were residents of 4 communities without a history of dementia or psychiatric disorders | Baseline information was collected by telephone and cognitive assessments (MMSE, MoCA and the Chinese version of the Hachinski Ischemia Scale (HIS), whereby scores of ≤4 indicated Alzheimer's dementia, a score of ≥7 indicated vascular dementia and an intermediate score indicating mixed dementia an average of 4.5 years post stroke. | **Primary outcome:**<br>Post -stroke cognitive impairment (PSCI) based on performance on neuropsychological test | The overall prevalences of PSCI and vascular dementia were 81% and 32%, respectively.<br><br>The risk of PSCI was significantly higher among persons who had experienced a recurrent stroke (OR=2.47, 95% CI 1.47-5.11, p=0.002) and those who suffered medical complications in the acute phase of stroke (OR=3.05, 95% CI 1.84-5.05, p<0.0001). |
| **Sivakumar et al. 2014**<br><br>**Canada**<br><br>**Prospective study** | NA | 100 patients, aged ≥18 years, admitted to hospital within 72 hours of minor ischemic stroke (NIHSS score ≤3) or TIA to a single institution from 2008-2013. Median age was 63 years, 68% were male. 19% of patients had prior history of stroke/TIA. Patients with a history of dementia were excluded | Assessments conducted included MMSE, MoCA, NIHSS, mRS and Geriatric Depression Scale.<br><br>Assessments were conducted at days 7, 30 and 90. | **Primary outcome:**<br>Incidence of cognitive impairment (defined as MMSE≤26 or MoCA<26) and changes in scores over time | Median baseline MoCA and MMSE scores were 26 and 29, respectively (p<0.0001). 54% and 16% of patients were cognitively impaired, using MoCA and MMSE criteria, respectively (p=0.001).<br><br>Over time, there was significant improvement in median MoCA scores (from 27-28-28, p<0.0001), with no change in median MMSE score (remaining unchanged at 29).<br><br>Of the 54 patients with cognitive impairment, as assessed by MoCA, 35 had an increase of ≥2 points by day 30. These patients were younger and 43% had a baseline NIHSS score of 0. These patients demonstrated significant improvement in all 7 MoCA subsets, with the greatest improvement in the recall |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
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| | | | | | domain. |
| **Douiri et al. 2013**<br><br>**UK**<br><br>**Cohort Study** | NA | 4,212 patients with first ever stroke or TIA who were participants of the South London Stroke Register study (1995-2010). | Participants underwent cognitive screening in the acute phase of stroke, 3 months post-stroke onset, and annually thereafter. | **Primary outcome:**<br>Cognitive impairment, defined as MMSE< 24 or Abbreviated Mental Test < 8. (MMSE was used for the 1st five years and the AMT thereafter). | Of the 4,212 participants, 1,618 completed a cognitive assessment and 1,229 completed the 3-month follow-up.<br><br>The prevalence of cognitive impairment was 22% (95% CI 21.2 to 27.8) at 3 months, 22% (95% CI 17.4 to 26.8) and 5 years, and 21% (95% CI 3.6 to 63.6) at 14 years.<br><br>The prevalence of post-stroke cognitive impairment was significantly associated with older age, black ethnicity, and low SES. |
| **Rist et al. 2013**<br><br>**International**<br><br>**Follow-up to RCT** | NA | 6,080 patients with stroke or TIA within 5 years of study enrollment of the PROGRESS trial. Patients with dementia or subarachnoid hemorrhage were excluded as were those with a clear indication or contraindication for treatment with a angiotensin-converting enzyme inhibitor. | As part of the PROGRESS trial, participants were followed for incident dementia and recurrent stroke, which was assessed at baseline, 6 months, 12 months, and annually thereafter. Patients screened positive for dementia if they met one or more criteria: MMSE score ≤25 at any follow-up visit, a decline in the MMSE score of ≥3 points between any 2 follow-up visits, or an MMSE score missing for ≥2 scheduled follow-up visits. Patients with a positive screen were referred to a specialist who used DSM-IV criteria to establish the presence of dementia, which was used to group patients into one of 4 categories (certain dementia, fairly certain (probable) dementia, uncertain (possible) dementia, or no dementia. | **Primary outcome:**<br>The occurrence of dementia, either certain dementia or fairly certain dementia. | At baseline, 41% of participants obtained a score of 30 on the MMSE, 29.1% had a score of 27-29, 22.5% had a score24-26, and 7.4% had a score <24.<br><br>Participants were followed for a mean of 3.8 years, during which time 407 cases of dementia were diagnosed and 709 recurrent strokes occurred.<br><br>Compared with those with a baseline MMSE of 30, those with lower baseline MMSE scores were at significantly greater risk of dementia:<br>MMSE <24: RR 26.8, 95% CI 18.08 to 39.76<br>MMSE 24-27: RR 6.59, 95% CI 4.54 to 9.55<br>MMSE 28-29: RR 2.15, 95% CI 1.43 to 3.24<br><br>The risk of dementia was more strongly associated with baseline MMSE scores in the absence of recurrent stroke. |
| **Bejot et al. 2011**<br><br>**France**<br><br>**Cohort study** | NA | 3,948 patients with first-ever strokes, included in the Dijon Stroke Registry, admitted to hospital between 1985 and 2008. | Cognitive function was evaluated by a neurologist within the first month of stroke. Dementia was diagnosed according to DSM III or IV criteria. | **Primary outcome:**<br>Prevalence of dementia | Of those assessed, 641, (20.4%) were diagnosed with post-stroke dementia.<br><br>The prevalence of dementia varied from 23.7% (95% CI 20 to 27) in 1985-1990 to 19.3% (95% CI 16 to 22) in 1991-1996, 19% (95% CI 16 to 22) in 1997-2002, |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | Prevalence of dementia was assessed over time in 4 increments. | | and 20.2% (95% CI 18 to 23) in 2003-2008.<br><br>Age, vascular risk factors, hemiplegia, and pre-stroke antiplatelet agents were associated with an increased prevalence of post-stroke dementia. |
| **Savva et al. 2010**<br><br>**UK**<br><br>**Systematic review** | NA | 16 articles reporting the incidence of all-cause dementia following symptomatic stroke. | The risk of incident dementia in persons with stroke was compared with persons without stroke. Follow-up periods ranged from 2 to 10 years | **Primary outcome:**<br>Incidence of dementia | The risk of dementia was doubled in persons with stroke aged ≥65 years.<br><br>This increase risk was highest in the period immediately following the index stroke event and decreased over time.<br><br>For individuals >85 years of age, no difference was reported in terms of the incidence of dementia between those with and without a history of stroke. |
| **Pendlebury et al. 2009**<br><br>**UK**<br><br>**Systematic Review & meta-analysis** | NA | 73 articles (n=7511; 22 hospital-based cohorts and 8 population-based cohorts) reporting on consecutive patients with symptomatic stroke followed for at least 3 months. | Studies were included if dementia was assessed using standardized criteria (DSM IV, ICD-10 or MMSE scores<24 and if follow-up was for at least 3 months post stroke | **Primary outcome:**<br>Prevalence and incidence of dementia from 3 months-1-year post stroke, and factors associated with pre-stroke and post-stroke dementia. | The prevalence of pre-stroke dementia at the time of stroke was estimated to be 14.4% (95% CI 12.0 to 16.8) in hospital-based studies and 9.1 (95% CI 6.9 to 11.3) in population-based studies.<br><br>The prevalence of post-stroke dementia was estimated to be 41.3% (95% CI 29.6 to 53.1) for patients with recurrent stroke and 26.5% (95% CI 24.3 to 28.7) for patients with first or recurrent stroke in hospital-based studies (including patients with pre-stroke dementia) and 7.4% (95% CI 4.8 to 10.0) in population-based studies (including patients with first-ever stroke but excluding those with pre-stroke dementia).<br><br>The pooled cumulative incidence of post-stroke dementia was estimated to increase linearly at a rate of 3.0% (95% CI 1.3 to 4.7) per year.<br><br>Some of the factors that were identified as being associated with significantly increased risk of post-stroke dementia include female sex (OR=1.3, 95% CI 1.1-1.6), low education (OR=2.5, 95% CI 1.8 to 3.4), diabetes (OR=1.4, 95% CI 1.2 to 1.7), atrial fibrillation (OR=2.0, 95% CI 1.4 to 2.8), and previous stroke (OR=1.9, 95% CI 1.5 to 2.3), as well as a number of other stroke factors, complications, and brain imaging factors. |

## Test Accuracy of Cognitive Screening Tests for Diagnosis of Dementia or Mild Cognitive Impairment Post Stroke

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Swartz et al. 2017**<br><br>**Canada**<br><br>**Feasibility study** | NA | 1,503 patients attending a stroke prevention clinic between 2012-2014. Diagnoses included persons with stroke (29%) and TIA (34%). Persons were also referred for other non-stroke/TIA events. Mean age was 64 years, 53% were female. | The integrated DOC screening tool includes items to screen for obstructive sleep apnea (DOC-apnea), depression (DOC-mood) and cognitive impairment (DOC-Cog).<br><br>The cognitive impairment (CI) items included the 10-point version of the MoCA (scored 0-10), based on memory, clock drawing and abstraction items.<br><br>The reference standard was a neuropsychological battery (NTP), including Controlled Oral World Association Test of phonemic fluency, Animal Naming task, the California Verbal Learning Test, Digit Symbol Coding and Trails Making A and B.<br><br>Scores were normalized for age, sex. Moderate-severe impairment was defined as ≥2 SDs from the mean score on 2 or more sub-tests of the battery. | **Primary outcome:**<br>Feasibility (defined as 85% of patients completing the entire screen in ≤5 minutes)<br><br>**Secondary outcome:**<br>Validity | Feasibility: all patients completed the DOC screen<br><br>89% of patients completed the screen in less than 5 minutes. Mean time for completion was 4.2 minutes (range 1.6-15.8 minutes)<br><br>Validity: 387 patients completed a NTP.<br>The prevalence of moderate-severe cognitive impairment was 14% (n=53).<br><br>10 patients (27%) scored 0 and were considered to be at low risk of CI; 35 patients (66%) scored 6-9 and were considered to be at intermediate risk of CI and 4 persons (7%) scored ≥5 and were considered to be at high risk of CI.<br><br>Using 2 cut-points, a DOC-Cog score of 0-5 (high-risk) was associated with a specificity of 95% and PPV of 43%; a score of 10 (low-risk) was associated with a sensitivity of 100% and a NPV of 100%. AUC was 0.776, which increased to 0.814 after controlling for age, sex and education. |
| **Zuo et al. 2016**<br><br>**China**<br><br>**Prospective study** | NA | 102 patients aged ≥18 years, recruited from a stroke ward following mild ischemic stroke (n=80) or TIA (n=22) within the previous 7 days. Mean age was 54 years, 67% were male. | The optimal cut-off point for the MoCA-Beijing was evaluated. | **Reference Standard:**<br>Neuropsychological test battery, administered by trained neurologists completed within 14 days after the acute stroke/TIA. Education-adjusted cut-offs of 1.5 SD below the established norms of neuropsychological tests were used to identify cognitive impairment. | 60 patients were identified with cognitive impairment using the reference standard.<br><br>51 persons were identified using the optimal cut-point of ≤22/23 on MMSE. Sensitivity 0.85; specificity 0.88. AUC 0.86 |
| **Lees et al. 2014**<br><br>**UK** | NA | 35 studies that examined the test accuracy of cognitive screening tests compared with | Pooled analyses were conducted, where possible, of cognitive test properties | **Primary outcome:**<br>Sensitivity (SN), specificity (SP) to detect dementia or | 24 different screening tests were used. The most commonly-used tests were MMSE (n=16) and MoCA |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Systematic review** | | a reference standard following stroke. Informant-based tests were excluded. | using different thresholds for cut-off | multidomain cognitive impairment | (n=8). The most commonly used reference standard was a neuropsychological battery (n=21).<br><br>Pooled analyses were reported for 4 screening tests<br><br>MMSE<27/30: SN 0.88, 95% CI 0.82-0.92; SP 0.62, 95% CI 0.50-0.73. Results from 5 studies (n=445) included.<br><br>MoCA<26/30: SN 0.84, 95% CI 0.89-0.98; SP 0.45, 95% CI 0.34-0.57. Results from 4 studies (n=326) included.<br><br>Rotterdam-CAMCOG <33/49: SN 0.81, 95% CI 0.57-0.95, SP 0.92, 95% CI 0.87-0.95. Results from 2 studies (n=421) included<br><br>Addenbrooke's Cognitive Examination-Revised (ACE-R) <88/100: SN 0.96, 95% CI 0.90-1.0; SP 0.70, 95% CI 0.59-0.80 Results from 2 studies (n=192) included.<br><br>Test characteristics performed better when testing was conducted during acute stroke.<br><br>Sensitivities and specificities were similar when the reference standard was a test battery or based on a clinical dementia diagnosis. |
| **Cumming et al. 2013**<br><br>**Australia**<br><br>**Prospective study** | NA | 60 stroke patients ≥18 years, admitted to an acute stroke unit with ischemic or hemorrhagic stroke. Mean age was 72.1 years, 73% male. Patients who were unconscious at admission to hospital and those with major visual, hearing, or language impairments, were excluded. | Trained research assistants administered two screening tools including The Montreal Cognitive Assessment (MoCA), and the Mini Mental State Exam (MMSE), in the participant's place of residence 3 months post-stroke. A second session was completed one week later in which a full neuropsychological testing battery was administered. | **Reference Standard:**<br>A neuropsychological battery, conducted by a physician psychiatrist. The scores across all tests were averaged and a >1 standard deviation in 2 or more domains was the threshold used to identify mild cognitive impairment | Median scores on the MoCA and MMSE were 21 (IQR 17-24) and 26 (IQR 22-27), respectively.<br><br>According to the criterion standard, 39 (65%) patients were cognitively impaired.<br><br>MMSE (at optimal cut-point of 26/27): 37 (62%) patients were identified as cognitively impaired. Sensitivity 0.82; specificity 0.76; AUC 0.84, 95% CI 0.73–0.95<br><br>MoCA (at optimal cut-point of 23/24): 43 (72%) patients were identified as cognitively impaired. sensitivity 0.92; specificity 0.67; AUC 0.87, 95% CI 0.78–0.97<br><br>12 participants were misclassified by the MMSE, 10 were misclassified by the MoCA. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | | As optimized cut points, the positive and negative predictive values were 0.86 and 0.70 for the MMSE and 0.84 and 0.82 for the MoCA, respectively. |
| **Pendlebury et al. 2012**<br><br>**UK**<br><br>**Prospective study** | NA | 100 participants from the OXVASC study were invited at their routine 1- or 5-year follow-up to undergo further cognitive testing. Mean age 73.4 years, 56% were male, 56% stroke, 44% TIA. Individuals residing in a nursing and those with acute illness or deficits that could interfere with testing were excluded. | The Montreal Cognitive Assessment (MoCA), Mini Mental State Exam (MMSE), Addenbrooke's Cognitive Examination-Revised (ACE-R) were administered at follow-up visits. | **Reference standard**: The National Institute of Neurological Disorders and Stroke–Canadian Stroke Network Harmonization Standards Neuropsychological Battery was administered. The identification of mild cognitive impairment (MCI) was based on ≥1.5 standard deviation on at least 1 cognitive domain, compared with age- and education-matched published norms | 91 participants completed all the assessments.<br><br>39 (43%) participants had MCI, using the reference standard.<br><br>MoCA cut-off <25: sensitivity 77%; specificity 83%; cut-off <26, sensitivity 87%, specificity 63%<br><br>ACE-R cut-offs <92: sensitivity 72%, specificity 79%, cut-off <94: sensitivity 83%, specificity 73%.<br><br>MMSE cut-point<29: sensitivity 77%, specificity 81%.<br><br>In ROC analysis, the area under the curve was 0.85 (95% CI 0.78 to 0.93) for the MoCA, 0.83 (95% CI 0.75 to 0.92) for the MMSE, and 0.90 (95% CI 0.83 to 0.96) for the ACE-R. |
| **Dong et al. 2012**<br><br>**China**<br><br>**Prospective Study** | NA | 300 patients, with ischemic stroke or TIA, aged ≥21 years, admitted to a stroke neurology service within 14 days of stroke onset, from 2009-2011. Mean age was 60.21 years. Patients with severe physical disability, severe aphasia or dysarthria, pre-existing dementia, or major psychiatric illness, were excluded. | Cognitive screening measures (MMSE and MoCA) were administered within 14 days of stroke. A formal neuropsychological battery was administered at 3-6-month follow-up, which assessed 7 cognitive domains. Cognitive outcomes were dichotomized as either no to mild (impairment in ≤2 cognitive domains) or moderate to severe (impairment in≥3 cognitive domains) vascular cognitive impairment | **Reference standard:** A neuropsychological test battery. Education-adjusted cutoffs of 1.5 SD below the established norms were used for individual tests. Failure in at least half of the tests in a domain constituted failure in that domain<br><br>Patients with vascular cognitive impairment-no dementia (VCIND) were impaired in at least one domain of the neuropsychological test battery, but did not meet the criteria for dementia. VCIND patients were further classified into VCIND mild (impairment in ≥2 cognitive domains) and VCIND moderate (impairment in ≥3 cognitive domains). Patients with vascular cognitive impairment (VCI) patients were dichotomised into no or mild VCI (NCI and VCIND mild) and moderate to severe VCI | 239 (80%) of participants completed the cognitive assessments. 60 (25%) patients had moderate to severe VCI.<br><br>42.3% of participants demonstrated no or mild cognitive impairment, 32.6% had mild and 22.2% had moderate cognitive impairment without dementia, and 2.9% had dementia.<br><br>Areas under the curve in ROC analysis did not differ significantly between the MoCA (0.85, 95% CI 0.79 to 0.90) and the MMSE (0.83, 95% CI 0.77 to 0.89) in detecting moderate to severe cognitive impairment at 3-6-month follow-up (p>0.05).<br><br>Optimal cut-off points of the standard adjustment method were 21/22 for MoCA (sensitivity 0.88; specificity 0.64) and 25/26 for MMSE (sensitivity 0.88; specificity 0.67).<br><br>No differences were found in between the two tools in terms of their ability to predict domain-specific cognitive impairments 3-6 months post-stroke. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | | | (VCIND moderate and dementia). | |
| **Godefroy et al. 2011**<br><br>**France**<br><br>**Prospective study** | NA | 95 patients admitted to an acute stroke unit within 3 weeks of symptom onset. Patients with severe stroke, were excluded. Mean age was 68.2 years, 63% were male. | Participants completed cognitive assessments, including the Montreal Cognitive Assessment (MoCA), and the Mini Mental State Exam (MMSE), during their inpatient stay. | **Reference standard:** A neuropsychological test battery. A significant deficit was identified by impairment of ≥ 2 cognitive domains. | MoCA and MMSE were performed an average of 6.6 days post stroke.<br><br>64 patients (67%) were cognitively impaired according to reference standard<br><br>Significantly fewer participants were classified as having cognitive impairment according to results using the MMSE than the MoCA (45% vs 82%, p<0.001).<br><br>Sensitively and specificity were 0.70 and 0.97 for the MMSE ≤24 and 0.67 and 0.90 for the MoCA ≤20 respectively.<br><br>The area under the curve in ROC analysis was 0.88 (95% CI 0.82 to 0.95) for the MMSE and 0.89 (95% CI 0.83 to 0.96) for the MoCA. |
| **Bour et al. 2010**<br><br>**Netherlands**<br><br>**Prospective study** | NA | 194 consecutive patients, aged ≥40 years, admitted with supratentorial, first-ever stroke, without pre-stroke cognitive deterioration or MMSE score <15, were excluded. | Participants completed neuropsychological assessments, including the MMSE 1, 6, 12, and 24 months post-stroke onset. | **Reference standard:** A neuropsychological test battery, assessing 10 cognitive domains. | At baseline, 163 patients suffered from at least 1 disturbed cognitive domain, 137 patients from ≥2 and 85 patients suffered from ≥ 4 disturbed cognitive domains. 22 (11%) patients had dementia.<br><br>Using a cut-off of 23/24 on the MMSE to identify dementia, sensitivity was 0.96, specificity was 0.83 and AUC was 0.94<br><br>MMSE score at 1 month was significantly correlated with the number of impaired cognitive domains at 1 (r=-0.68), 6 (r=-0.70), 12 months (r=-0.62), and 24 months (r=-0.69), all at p<0.001.<br><br>Baseline MMSE remained a significant predictor of the number of impaired cognitive domains at each follow-up after controlling for age, sex, and level of education.<br><br>MMSE score at 1-month did not significantly predict cognitive improvement or further deterioration in either univariate or multivariate analyses. |
| **Dong et al. 2010**<br><br>**Singapore**<br><br>**Prospective study** | NA | 100 patients with ischemic stroke or TIA, ≥21 years, admitted to a stroke neurology service within 14 days of stroke onset. Mean age was 62.1 years. Patients with severe physical disability, severe aphasia or dysarthria, pre- | Performance of modified versions of the Montreal Cognitive Assessment (MoCA), and the Mini-Mental State Exam (MMSE), were compared. Patients were also classified into 3 cognitive | **Reference standard:** None | The mean interval between stroke and assessment was 4.2±2.4 days<br><br>Using cut-offs of ≤24 for the MMSE and ≤21 for the MoCA, a total of 43 and 59 participants were classified as being cognitively impaired according to the MMSE and MoCA, respectively. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | existing dementia, or major psychiatric illness, were excluded. | screening test result groups: a) acute vascular cognitive impairment-no dementia (VCIND) moderate (screen positive for both MMSE and MoCA), b) acute VCIND mild (screen positive for either MMSE or MoCA) and c) no cognitive impairment NCI (screen negative for both MMSE and MoCA) | | There were a total of 60 cases of VCIND (41 moderate, 19 severe)<br><br>Using an optimal cut-off, the sensitivity and specificity for MMSE were 85.5% and 82.1%, respectively. Using an optimal cut-off, the sensitivity and specificity for MoCA were 90.3% and 76.8%, respectively.<br><br>18 participants classified as cognitively intact according to the MMSE were identified as being cognitively impaired on the MoCA, whereas only 2 participants were found to be cognitively intact on the MoCA and impaired on the MMSE. |

## Imaging

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Sivakumar et al. 2016**<br><br>**Canada**<br><br>**Prospective study** | NA | 115 patients, aged ≥18 years with acute TIA or minor stroke, recruited within 72 hours of symptom onset, with a NIHSS score ≤3. Patients with aphasia or pre-existing dementia, were excluded. Median age was 66 years, 65% were male. Median baseline MoCA score was 25. 60 patients (52%) were considered cognitively impaired. White matter hyperintensities (WMH) were present in 70 patients (61%). | Patients were assessed using the Montreal Cognitive Assessment (MoCA) MRI – diffusion-weighted imaging and Fluid-Attenuated Inverse Recovery sequences – at baseline, days 7 and 30. Cognitive testing was repeated at day 90. The the relationship between ischemic lesion volumes, WMH volumes, and MoCA scores was examined. | **Primary outcome:**<br>Cognitive impairment, defined as MoCA score <26. | MoCA scores improved significantly over time to 27, 28, and 28 at days 7, 30, and 90, respectively ($p<0.0001$). By day 90, 17% of patients were cognitively impaired.<br><br>The proportion of patients with cognitive impairment was similar in patients with- and without diffusion-weighted imaging lesions:<br>52% vis. 54%, p=0.83<br><br>No relationship was found between diffusion-weighted imaging lesion volume and day 30, but WMH volume at days 30 and 90 predicted MoCA scores.<br><br>WMH at baseline was present in 84% (n=16) of patients with persistent cognitive impairment at day 30, 66% (n=25), of patients with transient deficits and in only 48% (n=23) of patients with no cognitive impairment (p=0.017).<br><br>WMH volumes at baseline were predictive of persistent cognitive deficits after 30 days:<br>β=-0.2.24 (1.956, 45.369), p=0.005, but not after adjustment for age (p=0.093) |
| **Pasi et al. 2015**<br><br>**Italy** | NA | 76 patients with mild cognitive impairment based on Winblad criteria, demonstrating | At baseline, demographic information was collected and both the Montreal | **Primary outcome:**<br>Adjusted partial correlation analysis between MoCA, | Both MoCA and MMSE were significantly associated with age, education, cortical atrophy and medial temporal lobe atrophy. |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| **Prospective study** ***Vascular Mild Cognitive Impairment Tuscany (VMCI-Tuscany) Study*** | | moderate to severe degrees of white matter hyperintensities (WMH) on MRI (modified Fazekas scale). Mean age was 75 years, 55% were male. Mean baseline MoCA and MMSE scores were 18.9 and 26.1, respectively. | Cognitive Assessment (MoCA) and the Mini Mental State Examination (MMSE) were administered. Cut-off values and correction of age and education effects were done using validated norms in the Italian population. Conventional MRI features were collected. Median values of mean diffusivity (MD) and fractional anisotropy of the cerebral white matter were used as DTI derived indices. | MMSE, and DTI-derived indices | MoCA was significantly associated with:<br>Mean diffusivity: r=-0.275, p=0.023<br>Fractional anisotropy: r=0.246, p=0.043<br><br>There were no significant correlations between MMSE- and DTI-derived indices<br><br>Mild cognitive impairment and small vessel disease, diffusion tensor imaging-measured white matter microstructural damage was more related to MoCA than MMSE performance. |
| **Debette et al. 2010**<br><br>**US**<br><br>**Cohort study** | n/a | 2,229 participants from the Framingham Offspring Cohort. | Participants underwent volumetric MRI and neuropsychological assessment. 1,664 participants completed a second neuropsychological assessment approximately 5 years later. Incident stroke, dementia, and mortality were prospectively ascertained. All outcomes were related to white matter hyperintensities volume (WMHV), age-specific extensive WMHV and brain infarcts (BI) adjusting for age and gender. | **Primary outcomes:**<br>Stroke, dementia and death | The mean duration of follow-up was 5.6 years for stroke, 5.9 years for dementia, and 5.2 years for mortality.<br><br>During follow-up, there were 32 strokes (26 ischemic, 5 hemorrhagic, and 1 of unspecified type), 11 cases of dementia (7 AD, 3 vascular dementia, 1 other), and 97 deaths (21 vascular deaths, of which 3 were stroke deaths).<br><br>Extensive WMHV and BI were associated with an increased risk of stroke HR=2.28, 95% CI 1.02-5.13 and HR=0.84, 95% CI 1.32-6.10, respectively).<br><br>WMHV (HR= 2.22, 95% CI 1.3 to 3.7), extensive WMHV (HR= 3.97, 95% CI 1.1 to 14.3), and MRI-detected brain infarcts (HR= 6.12, 95% CI 1.8 to 20.5) were each significantly associated with increased risk of incident dementia, independently of vascular risk factors and interim stroke.<br><br>Both WMHV and EXT-WMHV were associated with a significantly increased risk of death. |
| **Rasquin et al. 2004**<br><br>**Netherlands**<br><br>**Prospective study** ***The Maastricht CODAS (COgnitive Disorders After Stroke) Study*** | NA | 176 consecutively-admitted patients, aged ≥40 years with first-ever ischemic stroke, a Mini Mental State Examination (MMSE) score ≥15, without pre-stroke dementia, other neurological or psychiatric disorders. Mean age was 68 years, 57% were male. Mean | Participants underwent neuropsychological assessment within 1-month of stroke and at 6- and 12-month follow-up. CT scanning was completed at baseline. Cognitive impairment was defined as a score <10th percentile of | **Primary outcomes:**<br>*Dementia*, diagnosed using DSM-IV criteria, *vascular MCI,* diagnosed when patients had at least one cognitive deficit, *vascular cognitive impairment (VCI*), patients with both dementia or vascular MCI. | At 6 months after stroke, 4 patients (2.3%) had died and 13 (7.4%) refused to participate further.<br><br>At 12 months after stroke, a further 5 (3.2%) patients had died and 9 (5.8%) refused to participate.<br><br>At baseline, 17 patients had dementia, 142 had VCI, 125 had vascular MCI and 34 patients had no cognitive disorders |

| Study/Type | Quality Rating | Sample Description | Method | Outcomes | Key Findings and Recommendations |
|---|---|---|---|---|---|
| | | MMSE score was 25.5. | the control group from MAastricht Aging Study (MAAS). Cognitive functioning was assessed using a neuropsychological test battery. | | Significant predictors of dementia (vs. no cognitive impairment)<br>1 month: no significant predictors<br>6 months: Older age (OR= 9.4), low education (OR= 14.7), and territorial infarct (OR=10.6)<br>12 months: Older age (OR 6.2), lower education (OR 4.1), territorial stroke type (OR 4.5), presence of silent infarcts (OR 5.6), and pre-stroke cerebrovascular damage (OR 5.6)<br><br>Significant predictors of VCI (vs. no cognitive impairment<br>1 month: Low education (OR=3.4) and territorial infarct (OR= 2.4)<br>6 months: older age (OR=4.3) and low education (OR=4.1)<br>12 months: Older age (OR= 6.2), lower education (OR= 4.1)<br><br>Significant predictors of vascular MCI (vs. no cognitive impairment<br>1 month: Low education (OR= 4.96) and territorial infarct (OR= 3.58)<br>6 months: Older age (OR=3.4) and lower education (OR=3.7)<br>12 months: Older age (OR=3.5) and lower education (OR=2.28) |
| **Vermeer et al. 2003**<br><br>**Netherlands**<br><br>**Prospective Study** | NA | 1,015 participants included in the prospective, population-based Rotterdam Scan Study, aged 60-90 years, free of dementia and stroke at baseline. Mean age was 72 years, 48% were male. Mean MMSE score was 27.4. | Participants completed a neurological assessment and underwent MRI at baseline and again approximately 4-years later. 739 participants completed the 2nd neuropsychological assessment whereas 629 underwent a 2nd MRI. | **Primary outcome:**<br>Development of dementia | During 3,697 person-years of follow-up (mean per person, 3.6 years), dementia developed in 30 participants (3%), during the study period.<br><br>The risk of developing dementia was significantly higher for participants with silent brain infarcts at baseline (HR= 2.26, 95% CI 1.09 to 4.7), after adjusted for age, sex and level of education. |

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