CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

Vascular Cognitive Impairment Evidence Tables

7th Edition, Update 2024

Screening, Assessment and Diagnosis

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on Behalf of the Canadian Stroke Best Practice Recommendations
Vascular Cognitive Impairment Writing Group and in collaboration with the
Canadian Stroke Consortium CanStroke Recovery Clinical Trials Platform.

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Published Guidelines

Guideline	Recommendations
General Vascular Cognitive Impairment/Dementia Guidelines	
Scottish Intercollegiate Guidelines Network (SIGN). Assessment, diagnosis, care and support for people with dementia and their carers 2023. (SIGN publication no. 168). [November 2023]. **Available from URL: http://www.sign.ac.uk**	Diagnosing suspected vascular dementia NICE guidance indicates that if the dementia subtype is uncertain and vascular dementia is suspected, use MRI. If MRI is unavailable or contraindicated, use CT. Do not diagnose vascular dementia based solely on vascular lesion burden. Be aware that young onset vascular dementia has a genetic cause in some people
Smith EE, Barber P, Field TS, Ganesh A, Hachinski V, Hogan DB, Lanctôt KL, Lindsay MP, Sharma M, Swartz RH, Ismail Z, Gauthier S, Black SE. **Canadian Consensus Conference on Diagnosis and Treatment of Dementia (CCCDTD)5: Guidelines for management of vascular cognitive impairment.** ***Alzheimers Dement (N Y).* 2020 Nov 11;6(1):e12056.**	Magnetic resonance imaging (MRI) is recommended over computed tomography (CT) for investigating vascular cognitive impairment. GRADE 2C Use of standardized criteria (one of: the Vascular Behavioral and Cognitive Disorders [VAS-COG] Society criteria, Diagnostic and Statistical Manual of Mental Disorders [DSM5], Vascular Impairment of Cognition Classification Consensus Study, or the American Heart Association consensus statement) are recommended for the diagnosis of vascular mild cognitive impairment and vascular dementia. GRADE 1C
Ismail Z, Black SE, Camicioli R, Chertkow H, Herrmann N, Laforce R Jr, Montero-Odasso M, Rockwood K, Rosa-Neto P, Seitz D, Sivananthan S, Smith EE, Soucy JP, Vedel I, Gauthier S; CCCDTD5 participants. **Recommendations of the 5th Canadian Consensus Conference on the diagnosis and treatment of dementia.** ***Alzheimer's Dement*. 2020 Aug;16(8):1182-1195.**	*Dementia case finding and detection* Cognitive testing to screen asymptomatic adults for the presence of mild cognitive impairment or dementia, including asymptomatic persons with risk factors such as family history or vascular risk factors, is not recommended. 1C In persons with elevated risk for cognitive disorders or with medical conditions associated with cognitive disorders such as: (a) a history of stroke or transient ischemic attack (TIA); (b) late-onset depressive disorder or a lifetime history of major depressive disorder; (c) untreated sleep apnea; (d) unstable metabolic or cardiovascular morbidity; (e) a recent episode of delirium; (f) first major psychiatric episode at an advanced age (psychosis, anxiety, depression, mania); (g) recent head injury; (h) Parkinson's disease. It is reasonable to ask the patient and an informant about concerns regarding cognition and behavior (2C). If clinically significant cognitive concerns are elicited, then further evaluation using validated assessments of cognition, behavior, and function is appropriate (see subsequent sections for suggestions for valid tools). 1B An objective assessment of the patient's cognitive function could be achieved by using rapid psychometric screening tools such as the Memory Impairment Screen (MIS) + clock drawing test (CDT), the Mini-Cog, the AD8, the four item version of

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(selected)	the MoCA (Clock-drawing, Tap-at-letter-A, Orientation, and Delayed-recall), and the GP Assessment of Cognition (GPCOG). 2B If more time is allowed, preference should be given to using a more comprehensive psychometric screening tool (the Modified Mini-Mental State [3MS] examination, the Mini-Mental State Examination [MMSE], or the Rowland Universal dementia assessment scale [RUDAS]). MMSE remains the most widely used instrument, with high sensitivity and specificity for separating moderate dementia from normal cognition and is recommended in many countries. However, it lacks sensitivity for the diagnosis of mild dementia or MCI. The MoCA is more sensitive to MCI than the MMSE and its use is recommended when mild cognitive impairment is suspected or in cases where there is suspicion of cognitive impairment or concern about the patient's cognitive status, and the MMSE score is in the "normal" range (24+ out of 30). 1B The use of standardized tools to obtain informant report on changes in cognition, function, and behavior increases the diagnostic accuracy when combined with patient-related measures and therefore is recommended. 1C We recommend using one or more informant-based tools that cover cognitive, functional, and behavioral aspects. Specific tools can be selected based on the need for comprehensive assessment versus efficiency depending upon the setting. 1C A number of well-validated instruments exist to help in the process of MCI or dementia diagnosis. However, diagnosis of MCI or dementia should not be solely based on an impaired result on cognitive screening tests. 1B *Use of neuroimaging and fluid biomarkers* Even in older subjects, anatomical neuroimaging is recommended in most situations, using the following list of indications: onset of cognitive signs/symptoms within the past 2 years, regardless of the rate of progression; unexpected and unexplained decline in cognition and/or functional status in a patient already known to have dementia; recent and significant head trauma; unexplained neurological manifestations (new onset severe headache, seizures, Babinski sign, etc.), at onset or during evolution (this also includes gait disturbances); history of cancer, in particular if "at risk" for brain metastases; subject at risk for intracranial bleeding; symptoms compatible with normal pressure hydrocephalus; significant vascular risk factors. 1C Magnetic resonance imaging (MRI) is recommended over computed tomography (CT), especially given its higher sensitivity to vascular lesions as well as for some subtypes of dementia and rarer conditions (2C). If available, and in the absence of contraindications, 3T MRI should be favoured over 1.5 T. (2C) If MRI is performed, we recommend the use of the following sequences: 3D T1 volumetric sequence (including coronal reformations for the purpose of hippocampal volume assessment), fluid-attenuated inversion recovery (FLAIR), T2 (or if available susceptibility-weighted imaging [SWI]) and diffusion-weighted imaging (DWI). 1C We recommend against the routine clinical use of advanced MR sequences such as rs-FMRI, MR spectroscopy, diffusion tensor imaging (DTI), and arterial spin labelling (ASL). However, these sequences are promising research tools that can be incorporated in a research setting or if access to advanced expertise is present. 2C If CT is performed, we recommend a non-contrast CT and coronal reformations are encouraged to better assess hippocampal atrophy. 1C We recommend the use of semi-quantitative scales for routine interpretation of both MRI and CT scans including: the medial

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	temporal lobe atrophy (MTA) scale for medial temporal involvement, Fazekas scale for white matter changes, and global cortical atrophy (GCA) to qualify global atrophy. 1C *Non-cognitive markers of dementia* There is strong evidence that slower gait speed is associated with future dementia, in population studies. When gait speed (cut-off gait speed below 0.8m/s) is coupled with cognitive impairment (subjective or objective) the risk is higher. We recommend testing gait speed in clinics in those patients with cognitive complaints/impairments if time/resources are available. 1B Note: Protocols on how to assess gait speed with stopwatch are available. Testing takes, on average, 3 minutes to perform. Dual-task gait impairment (lower speed or high cost) is associated with future incident dementia. In MCI samples, dual-task gait was shown to predict time to progression to dementia. Variability in the delivery of testing protocols is noted. We recommend that dual-task gait test may be used in specialized clinics (memory clinics) to help identify mild cognitive impairment (MCI) older adults at higher risk of progression to dementia if time/resources are available. 2B Note: Published protocols on how to assess Dual-Task Gait for dementia risk with just a stopwatch are available.
Iadecola C, Duering M, Hachinski V, Joutel A, Pendlebury ST, Schneider JA, Dichgans M. **Vascular Cognitive Impairment and Dementia: JACC Scientific Expert Panel.** ***J Am Coll Cardiol.* 2019 Jul 2;73(25):3326-3344**	*Key Elements* Clinical, neuropsychological, and imaging examination should follow the National Institute of Neurological Disorders–Canadian Stroke Network guidelines. Core domains for cognitive assessment should include executive function, attention, memory, language, and visuospatial function. Definition of major VCI (VaD): clinically significant deficits of sufficient severity in at least 1 cognitive domain (deficits may be present in multiple domains) and severe disruption to IADLs/ ADLs (independent of the motor/sensory sequelae of the vascular event). Patients given a diagnosis of major VCI (VaD) are subcategorized according to the underlying pathology as appropriate. The terms “probable” and “possible” are used to define the available evidence. MRI is a “gold-standard” requirement for a clinical diagnosis of VCI. Probable mild VCI or probable major VCI (VaD) is the appropriate diagnostic category if computed tomography imaging is the only means of imaging available. Post-stroke dementia is defined by an immediate and/or delayed cognitive decline that begins within 6 months after a stroke and that does not reverse. Exclusions from diagnosis: drug/alcohol abuse/dependence within the last 3 months of first recognition of impairment or delirium.
Petersen RC, Lopez O, Armstrong MJ, Getchius TSD, Ganguli M, Gloss D, Gronseth GS, Marson D, Pringsheim T, Day GS, Sager M, Stevens J, Rae-Grant A.	For patients for whom screening or assessing for MCI is appropriate, clinicians should use validated assessment tools to assess for cognitive impairment (Level B). For patients who test positive for MCI, clinicians should perform a more formal clinical assessment for diagnosis of MCI (Level B). For patients with MCI, clinicians should assess for the presence of functional impairment related to cognition before giving a

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Practice guideline update summary: Mild cognitive impairment: Report of the Guideline Development, Dissemination, and Implementation Subcommittee of the American Academy of Neurology. ***Neurol.* 2018 Jan 16;90(3):126-135.** **(selected)**	diagnosis of dementia (Level B). For patients diagnosed with MCI, clinicians should perform a medical evaluation for MCI risk factors that are potentially modifiable (Level B). For patients diagnosed with MCI, clinicians should perform serial assessments over time to monitor for changes in cognitive status (Level B)
Guideline Adaptation Committee. Clinical Practice Guidelines and Principles of Care for People with Dementia. Sydney. Guideline Adaptation Committee; 2016. **A total of 109 Recommendations are included** Dementia-Guideline-Recommendations-WEB-version.pdf (sydney.edu.au)	*Diagnosis of dementia* 28. A diagnosis of dementia should be made only after a comprehensive assessment, which should include: • history taking from the person • history taking from a person who knows the person well, if possible • cognitive and mental state examination with a validated instrument • physical examination • a review of medication in order to identify and minimise use of medications, including over-the-counter products, that may adversely affect cognitive functioning and to simplify medication dosing • consideration of other causes (including delirium or depression). Practice point (PP) 29. At the time of diagnosis of dementia, and at regular intervals subsequently, assessment should be made for medical comorbidities and key psychiatric features associated with dementia, including depression and psychosis, to ensure optimal management of coexisting conditions. PP 30. A basic dementia screen should be performed at the time of presentation, usually within primary care. It should include the following blood tests: • routine haematology • biochemistry tests (including electrolytes, calcium, glucose, and renal and liver function) • thyroid function tests • serum vitamin B12 and folate levels. PP *Cognitive assessment* 38. Clinical cognitive assessment in those with suspected dementia should include examination using an instrument with established reliability and validity. Health and aged care professionals should take full account of other factors known to affect performance, including age, educational level, non-English speaking background, prior level of functioning, aphasia, hearing or visual impairments, psychiatric illness or physical/ neurological problems when interpreting scores. PP *Neuroimaging* 43. Structural imaging (with computed tomography [CT] or magnetic resonance imaging [MRI]) should usually be used in the assessment of people with suspected dementia to exclude other cerebral pathologies and to help establish the subtype diagnosis, unless clinical judgement indicates this inappropriate. Structural imaging may not always be needed in those presenting with moderate-to-severe dementia, if the diagnosis is already clear. 44. Evidence-based Recommendation (EBR) Very low HMPAO SPECT should not be used in people with mild cognitive impairment (MCI) either for the differentiation of dementia from MCI or for the differentiation of progressive from non-progressive MCI.

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Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH. **The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease.** ***Alzheimers Dement*. 2011 May;7(3):270-9.**	Summary of clinical and cognitive evaluation for MCI due to AD *Establish clinical and cognitive criteria* Cognitive concern reflecting a change in cognition reported by patient or informant or clinician (i.e., historical or observed evidence of decline over time) Objective evidence of Impairment in one or more cognitive domains, typically including memory (i.e., formal or bedside testing to establish level of cognitive function in multiple domains) Preservation of independence in functional abilities Not demented *Examine etiology of MCI consistent with AD pathophysiological process* Rule out vascular, traumatic, medical causes of cognitive decline, where possible Provide evidence of longitudinal decline in cognition, when feasible Report history consistent with AD genetic factors, where relevant
Stroke-specific guidelines	
Quinn TJ, Richard E, Teuschl Y et al. **European Stroke Organisation and European Academy Neurology joint guidelines on post-stroke cognitive impairment.** ***Eur J Neurol*. 2021; Vol. 6(3): I–XXXVIII.**	PICO question 6: In patients with stroke does routine use of cognitive screening, compared to no routine screening, improve stroke care? Recommendation Due to a lack of relevant trials in patients with stroke, there is continued uncertainty over the benefits and risks of routine cognitive screening to improve stroke care. Quality of evidence: Very low ⨁ Strength of recommendation: no recommendation (this recommendation applies only to routine screening of all patients presenting with stroke, and does not apply to clinician directed assessment) PICO question 7: In patients with stroke (acute or post-acute), what is the accuracy of Montreal Cognitive Assessment for contemporaneous diagnosis of post-stroke cognitive impairment or dementia? Expert consensus statement Cognitive screening should be considered as part of the comprehensive assessment of stroke survivors. However, there are insufficient data to make recommendations around the timing, the content or the potential benefits of cognitive screening to the patient, their care-givers, and to healthcare systems. Further studies describing the effects of routine cognitive screening following stroke are required. These studies should include acute stroke settings, record feasibility and acceptability, consider effects on care pathways, and describe caregiver outcomes and health economics. Recommendation We suggest that in post-acute stroke settings, screening of cognition using the MoCA is considered.

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	The MoCA should not be used as a substitute for comprehensive clinical assessment. At the conventional threshold for test positivity, MoCA screening will detect most stroke survivors with important cognitive issues but at the cost of substantial false-positives. We suggest that a revised (lower) threshold be considered for stroke populations. Quality of evidence: Low ⨁⨁ Strength of recommendation: Weak for intervention ↑? Expert consensus statement There are inherent limitations to the MoCA, which relies on intact visuospatial and language function for completion. While the MoCA has acceptable test properties for use as an initial screening test in a stroke population, consideration should be given to the development of cognition screening tools that are more acceptable and feasible for those with communication difficulties or spatial neglect. Those utilizing the MoCA cognitive screening test should be fully trained in its administration. Further comprehensive cognitive assessment is recommended in the event of a positive MoCA test result, and findings should be shared with the stroke care team. PICO question 8: In patients with stroke (acute or post-acute), what is the accuracy of Folstein's Mini-Mental State Examination for contemporaneous diagnosis of dementia? Recommendation We suggest that, in acute and post-acute stroke settings, screening of cognition using Folstein's MMSE be considered. The MMSE should not be used as a substitute for comprehensive clinical assessment. At the conventional threshold for test positivity, MMSE screening will exclude most stroke survivors with no important cognitive issues, but at the cost of substantial false-negatives. Quality of evidence: Low ⨁⨁ Strength of recommendation: Weak for intervention ↑? Expert consensus statement There are inherent limitations to the MMSE, which relies on intact visuospatial and language function for completion. While the MMSE has acceptable test properties for use as an initial screening test in a stroke population, consideration should be given to the development of cognition screening tools that are more acceptable and feasible for those with communication difficulties or spatial neglect. Those utilizing the MMSE cognitive screening test should be fully trained in its administration. Further comprehensive cognitive assessment is recommended in the event of a positive MMSE test and findings should be

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	shared with the stroke care team. PICO question 9: In patients with stroke (acute or post-acute), what is the accuracy of Addenbrooke's Cognitive Examination (ACE) for contemporaneous diagnosis of dementia? Recommendation We suggest that in acute and post-acute stroke settings, screening of cognition with one of the versions of ACE can be considered. ACE should not be used as a substitute for comprehensive clinical assessment. Test properties are sensitive to the threshold used to define test positivity, but there were insufficient data to make recommendations around the optimal cut-off for use in stroke. Quality of evidence: Very low ⨁ Strength of recommendation: Weak for intervention ↑? Expert consensus statement There are inherent limitations to the various versions of ACE, which all rely on intact visuospatial and language function for completion. Acceptable test properties for ACE have not been established for use as an initial screening test in a stroke population and consideration should be given to the development of cognition screening tools that are more acceptable and feasible for those with communication difficulties or spatial neglect. Those utilizing the ACE cognitive screening test should be trained in its administration. Further comprehensive cognitive assessment is recommended in the event of a positive ACE test result and findings should be shared with the stroke care team. PICO question 10. In patients with stroke (acute or post-acute), what is the accuracy of the Oxford Cognitive Screen for contemporaneous diagnosis of dementia? Recommendation There is insufficient published evidence to assess the accuracy of the OCS for contemporaneous diagnosis of dementia in the stroke setting. Future research should assess the diagnostic accuracy and utility of the OCS for post-stroke cognitive syndromes. Quality of evidence: Very low ⨁ Strength of recommendation: no recommendation. Expert consensus statement The OCS offers advantages over other screening tools in terms of ease of completion and feasibility for stroke survivors with physical, language or visuospatial impairments.

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	Test accuracy studies of the OCS as a screen for post-stroke dementia are required. Those utilizing the OCS should be trained in its administration. Further comprehensive cognitive assessment is recommended in the event of a positive OCS and findings should be shared with the stroke care team. PICO question 11. In patients with stroke (acute or post-acute), what is the accuracy of remote assessment for contemporaneous diagnosis of dementia? Recommendation We suggest that in post-acute stroke settings, telephone-based screening of cognition can be considered. Telephone-based cognitive screening is not a substitute for comprehensive clinical assessment. At conventional thresholds for test positivity, telephone-based screening will detect most people with important cognitive issues but at the cost of substantial false-positives. Test properties are sensitive to the threshold used to define test positivity, but there were insufficient data to make recommendations around the optimal cut-off for use in stroke. Quality of evidence: Very low ⨁ Strength of recommendation: Weak for intervention ↑? Expert consensus statement There are inherent limitations to telephone-based cognitive screening, but telephone screening can be useful in situations where in-person assessment is not practical. Video call-based cognitive screening shows promise in stroke, but further studies and best practice guidance around application and interpretation of results is needed. Consideration should be given to the development and validation of specific telephone or video call cognitive screening tools or protocols. Those utilizing remote cognitive screening tests should be trained in their administration. Further comprehensive cognitive assessment is recommended in the event of a positive screening test result and findings should be shared with the stroke care team.
Zhang T, Zhao J, Li X, et al. **Chinese Stroke Association guidelines for clinical management of cerebrovascular**	Screening for cognitive impairment is recommended for all patients who had a stroke. When screening suggested cognitive impairment, a more detailed neuropsychological assessment should be used (Class I recommendation, Level B evidence).

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disorders: executive summary and 2019 update of clinical management of stroke rehabilitation. ***Stroke and Vascular Neurology.* 2020 Sep;5(3):260-269.** **(selected)**	
Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. (Part 5)	Practice points 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. Stroke survivors identified during screening as having cognitive deficits should be referred for comprehensive clinical neuropsychological investigations. Info Box Practice points 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. **Prevention of stroke in patients with silent cerebrovascular disease: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2017;48:e44–e71.** **(selected)**	Summary of Suggestions for Clinical Care of Patients with Silent Cerebrovascular Disease *Diagnosis by neuroimaging* MRI has greater sensitivity than CT for diagnosis of silent cerebrovascular disease. Radiology reports should describe silent cerebrovascular disease according to STRIVE. WMHs of presumed vascular origin should be reported with the use of a validated visual rating scale such as the Fazekas scale for MRI. *Investigations for patients with silent cerebrovascular disease* Assess common vascular risk factors and assess pulse for atrial fibrillation. Consider carotid imaging when there is silent brain infarction in the carotid territory. Consider echocardiography when there is an embolic-appearing pattern of silent infarction. Consider noninvasive CT or MR angiography when there are large (>1.0 cm) silent hemorrhages.

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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. **Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.** ***Stroke* 2016;47:e98–e169.**	Screening for cognitive deficits is recommended for all stroke patients before discharge home. Class 1; LOE B 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)** 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. 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. 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. 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. 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. F People with stroke returning to cognitively demanding activities such as driving or work should have their cognition fully assessed. G People with continuing cognitive difficulties after stroke should be considered for comprehensive interventions aimed at

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	developing compensatory behaviours and learning adaptive skills. H People with severe or persistent cognitive problems after stroke should receive specialist assessment and treatment from a clinical neuropsychologist/clinical psychologist. **Executive Function** 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. **Attention and concentration** Any person after stroke who appears easily distracted or unable to concentrate should have their attentional abilities (eg focused, sustained and divided) formally assessed. **Memory** 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.
Hachinski V, Iadecola C, Petersen RC, Breteler MM, Nyenhuis DL, Black SE, Powers WJ, DeCarli C, Merino JG, Kalaria RN, Vinters HV, Holtzman DM, Rosenberg GA, Wallin A, Dichgans M, Marler JR, Leblanc GG. **National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards.** ***Stroke*. 2006 Sep;37(9):2220-41.**	The National Institute for Neurological Disorders and Stroke (NINDS) and the Canadian Stroke Network (CSN) convened researchers in clinical diagnosis, epidemiology, neuropsychology, brain imaging, neuropathology, experimental models, biomarkers, genetics, and clinical trials to recommend minimum, common, clinical and research standards for the description and study of vascular cognitive impairment.
White Paper	
Verdelho A, Wardlaw J, Pavlovic A, Pantoni L, Godefroy O et al. **Cognitive impairment in patients with cerebrovascular disease: A white paper from the links between stroke ESO Dementia Committee.** ***Eur Stroke J*. 2021 Mar;6(1):5-17.**	Summary of investigations to avoid missing modifiable vascular risk factors. • Modifiable vascular risk factors: blood pressure, blood glucose, blood lipids, BMI, lifestyle history, other proxy-risk factors, as obstructive sleep apnea, homocysteine levels. • Sources of emboli and evidence of ischaemic cardiovascular disease: ECG, echocardiogram, doppler ultrasound, CT or MR angiography (intra/extracranial stenosis) • Evidence of cerebrovascular disease: MR or CT brain imaging Summary of suggestions for the management of cerebrovascular disease in patients with Cognitive Impairment (CI). • Clinical appointments due to CI should be considered as an opportunity to check and better control of vascular risk factors.

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	• Brain imaging (made in the context of CI) should be reviewed to verify existence of cerebrovascular disease. • In the case of cerebrovascular component highly suspected/not clear after CT, an MRI should be considered (namely if doubt about hemorrhagic component including microbleeds and cSS, small acute lesions, specific profiles as familiar - e.g.CADASIL, or extension of WMC and SVD) • Specific investigations should be considered in acute lesions, recurrent and multiple strokes (namely neck and intracranial artery imaging and cardiac study) Summary of suggestions concerning treatment of cerebrovascular disease in patients with CI • Implement primary and secondary prevention of stroke; primary prevention applies to all patients. Patients who experienced a stroke should be treated according to secondary prevention guidelines. • No evidence base to support application of secondary stroke prevention treatment strategies for WMH alone. Individualized approach to initiate or modify antithrombotic agents based on weighing the individual patients estimated absolute risk of future ischaemic or haemorrhagic events.

Diagnostic Criteria for Vascular Cognitive Impairment (VCI)

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Skrobot OA, Black SE, Chen C, DeCarli C, Erkinjuntti T, Ford GA, Kalaria RN, O'Brien J, Pantoni L, Pasquier F, Roman GC, Wallin A, Sachdev P, Skoog I; VICCCS group, Ben-Shlomo Y, Passmore AP, Love S, Kehoe PG. **Progress toward standardized diagnosis of vascular cognitive impairment: Guidelines from the Vascular Impairment of Cognition Classification Consensus Study.** ***Alzheimers Dement.* 2018 Mar;14(3):280-292.**	**Summary of the Vascular Impairment of Cognition Classification Consensus Study (VICCCS) diagnosis guidelines** *Definitions and diagnosis of VCI:* Clinical evaluation and neuropsychological protocols as provided in the National Institute of Neurological Disorders–Canadian Stroke Network guidelines are supported. Core domains for assessment should include executive function, attention and memory, as well as language and visuospatial function. Mild VCI: Impairment in at least one cognitive domain and mild to no impairment in instrumental activities of daily living (IADLs)/activities of daily living (ADLs), respectively (independent of the motor/sensory sequelae of the vascular event). Major VCI (VaD): Clinically significant deficits of sufficient severity in at least one cognitive domain (deficits may be present in multiple domains) and severe disruption to IADLs/ADLs (independent of the motor/sensory sequelae of the vascular event). Patients given a diagnosis of major VCI (VaD) are subcategorized according to the underlying pathology as appropriate. A clear temporal relationship (within 6 months) between a vascular event and onset of cognitive deficits is only required for a diagnosis of post-stroke dementia (PSD). *Subtypes of major VCI (VaD)* i) Post-stroke dementia: A patient described as having PSD may or may not have presented evidence of mild cognitive impairment before stroke. The patient will exhibit immediate and/or delayed cognitive decline that begins within 6 months after a stroke and that does not reverse. PSD can result from several different vascular causes and changes in the brain. It encompasses dementia that develops within 6 months of stroke in patients with multiple cortical-subcortical infarcts and strategic infarcts; patients with subcortical ischemic vascular dementia; and those with various forms of neurodegenerative pathology, including Alzheimer's

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	disease (AD). The temporal relationship between the cognitive decline and the stroke differentiates PSD from other forms of major VCI (VaD). ii) Mixed dementias: A standalone umbrella subgroup termed “mixed dementias” includes phenotypes representing each combination between vascular and neurodegenerative disease, that is, VCI-AD, VCI–dementia with Lewy bodies, and so forth. It is recommended that a patient is referred to as having “VCI-AD”, for example, according to the clinically probable phenotypes, rather than the less-specific “mixed dementia”. Where discrimination is possible, the order of terms should reflect the probable relative contribution of the underlying pathology, that is, AD-VCI or VCI-AD. iii) Subcortical ischemic vascular dementia: Small-vessel disease is the main vascular cause of subcortical ischemic vascular dementia. Lacunar infarcts and ischemic white matter lesions are the main type of brain lesions, which are located predominantly subcortically. This diagnosis incorporates the overlapping clinical entities of Binswanger’s disease and the lacunar state. iV) Multi-infarct dementia: Multi-infarct dementia is used to indicate the presence of multiple large cortical infarcts and their likely contribution to the dementia. “Probable” and “possible”—terms for the availability of evidence: Magnetic resonance imaging is a “gold-standard” requirement for a clinical diagnosis of VCI. Probable mild VCI or probable major VCI (VaD) is the appropriate diagnostic category if computed tomography imaging is the only means of imaging available. Recommendations on imaging from the National Institute of Neurological Disorders–Canadian Stroke Network should be followed. Possible mild VCI or possible major VCI (VaD) would be appropriate diagnoses if neither MRI nor computed tomography imaging were available. In diagnosis of VCI when full clinical assessment of the cognitive impairment resulting from the clinical event is impaired by aphasia, patients with documented evidence of normal cognitive function (e.g., annual cognitive evaluations) before the clinical event that caused aphasia could be classified as having probable mild VCI or major VCI (VaD) if imaging is available, and the assessment of ADLs should be made where possible. If imaging is not available, the classification should be possible mild VCI or major VCI (VaD). Those at risk of VCI: It is recommended that greater consideration for diagnosis be given to people who are at risk of VCI if they present with at least 6 months of sustained impairment (even if very mild), rather than transient impairment, as identified through caregiver reporting and clinical observation. All other potential causes of sustained impairment (e.g., depression or vitamin D deficiency, in addition to the already agreed exclusions from diagnosis) should have been excluded. Exclusions from diagnosis: Drug/alcohol abuse/dependence within the last 3 months of first recognition of impairment or delirium. *Clinically significant deficits include moderate severity. Cognitive impairment in mild VCI is differentiated from major (VaD) by not being clinically significant. Definitions were agreed in VICCCS-1 and supported in VICCCS-2.

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Dichgans M & Leys D. **Vascular Cognitive Impairment.** ***Circ Res.* 2017 Feb 3;120(3):573-591.**	Diagnostic Criteria for Vascular Cognitive Impairment (VCI)* VCI refers to all forms of cognitive deficits of vascular origin ranging from MCI to dementia. Diagnosis must be based on cognitive testing involving a minimum of 4 cognitive domains, including executive/attention, memory, language, and visuospatial functions. Vascular dementia (VaD) requires a decline in cognitive function and a deficit in performance in ≥2 cognitive domains that are of sufficient severity to affect activities of daily living. Vascular mild cognitive impairment (VaMCI) includes 4 subtypes: amnestic, amnestic plus other domains, nonamnestic single domain, and nonamnestic multiple domain; VaMCI should be based on the assumption of a decline in cognitive function. Activities of daily living may be normal or mildly impaired. Probable: A diagnosis of probable VaD or VaMCI requires the following: (1) Imaging evidence of cerebrovascular disease and (a) a clear temporal relationship between a vascular event (eg, stroke) and onset of cognitive deficits or (b) a clear relationship between the severity and pattern of cognitive impairment and the presence of diffuse subcortical vascular pathology; (2) Absence of a history of gradually progressive cognitive deficits, suggesting the presence of neurodegenerative disease. Possible: A diagnosis of possible VaD or VaMCI requires imaging evidence of cerebrovascular disease and should be made if there is no clear relationship between vascular disease and cognitive impairment, if the criteria for probable VaD or VaMCI are not fulfilled, if aphasia precludes proper cognitive assessment, or if there is a history of active cancer or psychiatric or metabolic disorders that may affect cognitive function. Unstable VaMCI: subjects with probable of possible VaMCI whose symptoms revert to normal. *The key distinction between VaD and VaMCI is the degree of the functional deficit. The criteria cannot be used in subjects with delirium or an active diagnosis of substance abuse
Sachdev P, Kalaria R, O'Brien J, Skoog I, Alladi S, Black SE, Blacker D, Blazer DG, Chen C, Chui H, Ganguli M, Jellinger K, Jeste DV, Pasquier F, Paulsen J, Prins N, Rockwood K, Roman G, Scheltens P; Internationlal Society for Vascular Behavioral and Cognitive Disorders. **Diagnostic criteria for vascular cognitive disorders: a VASCOG statement.** ***Alzheimer Dis Assoc Disord.* 2014 Jul-Sep;28(3):206-18.**	**Proposed Criteria for Mild Cognitive Disorder and Dementia (or Major Cognitive Disorder)** *Mild cognitive disorder* (A) Acquired decline from a documented or inferred previous level of performance in ≥1 cognitive domains as evidenced by the following (a) Concerns of a patient, knowledgeable informant, or a clinician of mild levels of decline from a previous level of cognitive functioning. Typically, the reports will involve greater difficulty in performing the tasks, or the use of compensatory strategies; and (b) Evidence of modest deficits on objective cognitive assessment based on a validated measure of neurocognitive function (either formal neuropsychological testing or an equivalent clinical evaluation) in ≥1 cognitive domains. The test performance is typically in the range between 1 and 2 SDs below appropriate norms (or between the third and 16th percentiles) when a formal neuropsychological assessment is available, or an equivalent level as judged by the clinician. (B) The cognitive deficits are not sufficient to interfere with independence (ie, instrumental activities of daily living are preserved), but greater effort, compensatory strategies, or accommodation may be required to maintain independence. *Dementia* or major cognitive disorder* (A) Evidence of substantial cognitive decline from a documented or inferred previous level of performance in Z1 of the domains outlined above. Evidence for decline is based on: (a) Concerns of the patient, a knowledgeable informant, or the clinician, of significant decline in specific abilities; and

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	(b) Clear and significant deficits in objective assessment based on a validated objective measure of neurocognitive function (either formal neuropsychological testing or equivalent clinical evaluation) in ≥1 cognitive domains. These typically fall ≥2 SDs below the mean (or below the third percentile) of people of similar age, sex, education, and sociocultural background, when a formal neuropsychological assessment is available, or an equivalent level as judged by the clinician. (B) The cognitive deficits are sufficient to interfere with independence (eg, at a minimum requiring assistance with instrumental activities of daily living, ie, more complex tasks such as managing finances or medications) **DSM-IV and ICD-10 concept of dementia requires deficits in at least 2 domains, 1 of which being memory*
Gorelick PB, Scuteri A, Black SE, et al; American Heart Association Stroke Council, Council on Epidemiology and Prevention, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia. **Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American heart association/ American stroke association.** **Stroke. 2011;42:2672–2713**	*Dementia* 1. The diagnosis of dementia should be based on a decline in cognitive function from a prior baseline and a deficit in performance in 2 cognitive domains that are of sufficient severity to affect the subject's activities of daily living. 2. The diagnosis of dementia must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions. 3. The deficits in activities of daily living are independent of the motor/sensory sequelae of the vascular event. *Probable VaD* 1. There is cognitive impairment and imaging evidence of cerebrovascular disease and a. There is a clear temporal relationship between a vascular event (eg, clinical stroke) and onset of cognitive deficits, or b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (eg, as in CADASIL). 2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder. *Possible VaD* There is cognitive impairment and imaging evidence of cerebrovascular disease but 1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (eg, silent infarcts, subcortical small-vessel disease) and the cognitive impairment. 2. There is insufficient information for the diagnosis of VaD (eg, clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available). 3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (eg, annual cognitive evaluations) before the clinical event that caused aphasia could be classified as having probable VaD. 4. There is evidence of other neurodegenerative diseases or conditions in addition to cerebrovascular disease that may affect cognition, such as a. A history of other neurodegenerative disorders (eg, Parkinson disease, progressive supranuclear palsy, dementia with Lewy bodies); b. The presence of Alzheimer disease biology is confirmed by biomarkers (eg, PET, CSF, amyloid ligands) or genetic studies (eg, PS1 mutation); or c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function. *VaMCI* 1. VaMCI includes the 4 subtypes proposed for the classification of MCI: amnestic, amnestic plus other domains,

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	nonamnestic single domain, and nonamnestic multiple domain. 2. The classification of VaMCI must be based on cognitive testing, and a minimum of 4 cognitive domains should be assessed: executive/attention, memory, language, and visuospatial functions. The classification should be based on an assumption of decline in cognitive function from a prior baseline and impairment in at least 1 cognitive domain. 3. Instrumental activities of daily living could be normal or mildly impaired, independent of the presence of motor/sensory symptoms. *Probable VaMCI* 1. There is cognitive impairment and imaging evidence of cerebrovascular disease and a. There is a clear temporal relationship between a vascular event (eg, clinical stroke) and onset of cognitive deficits, or b. There is a clear relationship in the severity and pattern of cognitive impairment and the presence of diffuse, subcortical cerebrovascular disease pathology (eg, as in CADASIL). 2. There is no history of gradually progressive cognitive deficits before or after the stroke that suggests the presence of a nonvascular neurodegenerative disorder. *Possible VaMCI* There is cognitive impairment and imaging evidence of cerebrovascular disease but 1. There is no clear relationship (temporal, severity, or cognitive pattern) between the vascular disease (eg, silent infarcts, subcortical small-vessel disease) and onset of cognitive deficits. 2. There is insufficient information for the diagnosis of VaMCI (eg, clinical symptoms suggest the presence of vascular disease, but no CT/MRI studies are available). 3. Severity of aphasia precludes proper cognitive assessment. However, patients with documented evidence of normal cognitive function (eg, annual cognitive evaluations) before the clinical event that caused aphasia could be classified as having probable VaMCI. 4. There is evidence of other neurodegenerative diseases or conditions in addition to cerebrovascular disease that may affect cognition, such as a. A history of other neurodegenerative disorders (eg, Parkinson disease, progressive supranuclear palsy, dementia with Lewy bodies); b. The presence of Alzheimer disease biology is confirmed by biomarkers (eg, PET, CSF, amyloid ligands) or genetic studies (eg, PS1 mutation); or c. A history of active cancer or psychiatric or metabolic disorders that may affect cognitive function. *Unstable VaMCI* Subjects with the diagnosis of probable or possible VaMCI whose symptoms revert to normal should be classified as having "unstable VaMCI."
Román GC, Sachdev P, Royall DR, Bullock RA, Orgogozo JM, López-Pousa S, Arizaga R, Wallin A. **Vascular cognitive disorder: a new**	*VCI without dementia (VCI-ND):* (1) The subjects' cognitive impairment did not meet the DSM-III-R criteria for dementia; these criteria require impairment of memory and other cognitive domain causing functional deficits. (2) Cognitive impairment was judged to have a vascular cause as based on presence of signs of ischemia/ infarction; e.g., sudden onset, stepwise progression, patchy cortical deficits on cognitive testing, other evidence of atherosclerosis, and a high Hachinski Ischemic Score (HIS). However, a high HIS score indicating presence of vascular risk factors alone was

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diagnostic category updating vascular cognitive impairment and vascular dementia. ***J Neurol Sci.*** **2004 Nov 15;226(1-2):81-7.**	insufficient for a VCI-ND diagnosis. (3) The requirement for a cognitive deficit to cause functional deficits was defined operationally as follows: Global functional impairment was defined as having difficulty in any two of the following domains: performing household chores, managing money, feeding self, dressing, and incontinence.
Roman GC, Tatemichi TK, Erkinjuntti T, et al. **Vascular dementia: diagnostic criteria for research studies. Report of the NINDS-AIREN International workshop.** ***Neurology*****. 1993;43:250-260**	*Criteria for the diagnosis of vascular dementia.* VaD is a complex disorder characterized by cognitive impairment resulting from ischemic or hemorrhagic stroke or from ischemic-hypoxic brain lesions. The clinical criteria for the diagnosis of probable, possible, and definite vascular dementia are here summarized. I. The criteria for the clinical diagnosis of *probable* vascular dementia include *all* of the following: 1. *Dementia* defined by cognitive decline from a previously higher level of functioning and manifested by impairment of memory and of two or more cognitive domains (orientation, attention, language, visuospatial functions, executive functions, motor control, and praxis), preferably established by clinical examination and documented by neuropsychological testing; deficits should be severe enough to interfere with activities of daily living not due to physical effects of stroke alone. 2. Cerebrovascular disease, defined by the presence of focal signs on neurologic examination, such as hemiparesis, lower facial weakness, Babinski sign, sensory- deficit, hemianopia, and dysarthria' consistent with stroke (with or without history of stroke), and evidence of relevant CVD by brain imaging (CT or MRI) including multiple large-vessel infarcts or a single strategically placed infarct (angular gyrus, thalamus, basal forebrain, or PCA or ACA territories), as well as multiple basal ganglia and white matter lacunes or extensive periventricular white matter lesions, or combinations thereof. 3. A relationship between the above two disorders, manifested or inferred by the presence of one or more of the following: (a) onset of dementia within 3 months following a recognized stroke; (b) abrupt deterioration in cognitive functions; or fluctuating, stepwise progression of cognitive deficits. II. Clinical features consistent with the diagnosis of *probable* vascular dementia include the following: (a) Early presence of a gait disturbance (small-step gait or marche a petits pas, or magnetic, apraxic-ataxic or parkinsonian gait); (b) history of unsteadiness and frequent, unprovoked falls; (c) early urinary frequency, urgency, and other urinary symptoms not explained by urologic disease; (d) pseudobulbar palsy; and (e) personality and mood changes, abulia, depression, emotional incontinence, or other subcortical deficits including psychomotor retardation and abnormal executive function. III. Features that make the diagnosis of vascular dementia uncertain or unlikely include: (a) early onset of memory deficit and progressive worsening of memory and other cognitive functions such as language (transcortical sensory aphasia), motor skills (apraxia), and perception (agnosia), in the absence of corresponding focal lesions on brain imaging; (b) absence of focal neurologic signs, other than cognitive disturbance; and (c) absence of cerebrovascular lesions on brain CT or MRI. IV. Clinical diagnosis of *possible* vascular dementia may be made in the presence of dementia (section 1-1) with focal neurologic signs in patients in whom brain imaging studies to confirm definite CVD are missing; or in the absence of clear temporal relationship between dementia and stroke; or in patients with subtle onset and variable course (plateau or improvement) of cognitive deficits and evidence of relevant CVD. V. Criteria for diagnosis of *definite* vascular dementia are: (a) clinical criteria for *probable* vascular dementia; (b) histopathologic evidence of CVD obtained from biopsy or

Guideline	Recommendations
	autopsy; (c) absence of neurofibrillary tangles and neuritic plaques exceeding those expected for age; and (d) absence of other clinical or pathologic disorder capable of producing dementia. VL Classification of vascular dementia for research purposes may be made on the basis of clinical, radiologic, and neuropathologic features, for subcategories or defined conditions such as cortical vascular dementia, subcortical vascular dementia, ED, and thalamic dementia. The term "AD *with* CVD" should be reserved to classify patients fulfilling the clinical criteria for possible AD and who also present clinical or brain imaging evidence of relevant CVD. Traditionally, these patients have been included with VaD in epidemiologic studies. The term "mixed dementia," used hitherto, should be avoided.

Minimum Imaging Sequences

Guideline	Recommendations
Wardlaw JM, Smith EE, Biessels GJ, et al. **Neuroimaging standards for research into small vessel disease and its contribution to ageing and neurodegeneration.** ***Lancet Neurol*. 2013;12:822-838**	T1-weighted: Important for discriminating lacunes from dilated perivascular spaces; for discriminating grey from white matter, and for studying brain atrophy. Orientation: 2D axial, sagittal, or coronal Target-slice thickness and in-plane resolution: 3–5 mm, and 1 mm × 1 mm Comments: At least one sequence in sagittal or coronal plane is helpful to visualise full extent and orientation of lesions. Diffusion-weighted imaging (DWI): The most sensitive sequences for acute ischaemic lesions; positive for up to several weeks after cerebrovascular event Orientation: 2D axial Target-slice thickness and in-plane resolution:3–5 mm, and 2 mm × 2 mm Comments: Reduced signal on apparent diffusion coefficient map helps to discriminate recent lesions from old lesions T2-weighted: To characterise brain structure; to differentiate lacunes from white matter hyperintensities and perivascular spaces; to identify old infarcts. Orientation: 2D axial Target-slice thickness and in-plane resolution: 3–5 mm, and 1 mm × 1 mm Fluid-attenuated inversion recovery (FLAIR): To identify white matter hyperintensities and established cortical or large subcortical infarcts; to differentiate white matter lesions from perivascular spaces and lacunes. Orientation: 2D axial Target-slice thickness and in-plane resolution: 3–5 mm, and 1 mm × 1 mm T2-weighted gradient-recalled echo (GRE): To detect haemorrhage, cerebral microbleeds, siderosis; for measurement of intracranial volume. Orientation: 2D axial Target-slice thickness and in-plane resolution: 3–5 mm, and 1 mm × 1 mm

Guideline	Recommendations
	Comments: Only reliable routine sequence for detection of hemorrhage

Evidence Tables

Incidence/Prevalence and Predictors of Vascular Cognitive Impairment

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Mild Cognitive Impairment					
Gillis et al. 2019 **USA** **Systematic review & meta-analysis**	NA	7 epidemiological studies that reported the incidence of MCI, amnestic MCI (aMCI) or nonamnestic MCI (naMCI), defined using the revised or original Petersen criteria. Studies that included persons with dementia, were excluded.	The estimates of the age-specific incidence of MCI were calculated, using age categories of 65–69, 70–74, 75–79, 80–84, and ≥85 years.	**Primary outcomes:** Incidence of MCI, amnestic MCI and nonamnestic VCI	Using data from 4 studies, the incidence of MCI per 1,000 person-years by age category was: 75-79 years: 22.5, 95% CI 5.1– 51.4 80-84 years: 40.9, 95% CI 7.7–97.5 ≥85 years: 60.1, 95% CI 6.7–159.0 Using data from 3-5 studies, the incidence of aMCI per 1,000 person-years by age category was: 70-74 years: 22.4, 95% CI 18.2-27.1 75-79 years: 18.7, 95% CI 13.4-24.9 80-84 years: 32.7, 95% CI 16.8-53.7 ≥85 years: 50.5, 95% CI 26.6- 81.3 Using data from 3-4 studies, the incidence of aMCI per 1,000 person-years by age category was: 70-74 years: 23.3, 95% CI 7.9- 46.3 75-79 years: 27.6, 95% CI 15.1-43.6 80-84 years: 31.1, 95% CI 18.1- 47.3 ≥85 years: 54.3, 95% CI 26.9- 90.4 There were no data available to pool for the ages of 65-69 years.
Au et al. 2016 **Canada** **Systematic review & meta-analysis**	30studies were considered to be of higher quality using the Loney tool	56 population or community-based, longitudinal studies in which either the International Working Group or Mayo Clinic criteria were used to detect MCI.	The risks of all MCI, amnestic MCI (aMCI) and nonamnestic VC (naMCI), were calculated for men and women.	**Primary outcomes:** Incidence rate ratio (IRR) and prevalence risk ratios for MCI	The prevalences of all-type MCI and aMCI did not differ between the sexes (RR = 1.02, 95% CI 0.95-1.10, p = 0.61 and RR = 1.09, 95% CI 0.94-1.27, p = 0.24, respectively). The risk of naMCI was significantly lower in men (RR = 0.84, 95% CI = 0.72-0.99, p < 0.05). The risk of all-type MCI did not differ between the sexes (IRR=1.17, 95% CI 0.91-1.52, p =

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					0.23), nor did the risks of aMCI or naMCI (IRR=1.14, 95% CI 0.76-1.71, p = 0.52 and IRR= 1.15, 95% CI 0.91-1.45, p = 0.23, respectively.
Roberts et al. 2012 **USA** **Prospective study**	NA	1,450 adults, ages 70–89 years, recruited from the general population (Olmsted County, MN) who were cognitively intact.	All participants completed a series of neuropsychological tests and underwent follow-up at 15-month intervals. A diagnosis of MCI was determined according to the following criteria: cognitive concern by subject (from interview), informant, nurse, or physician; impairment in ≥1 of the 4 cognitive domains (from cognitive battery); essentially normal functional activities; and absence of dementia.	**Primary outcome:** Age and sex standardized incidence rates of MCI **Secondary outcomes:** Age and sex standardized incidence rates amnestic MCI (aMCI) and nonamnestic VC (naMCI)	During a median follow-up of 3.4 years (4,512.9 person-years), 296 participants developed MCI. 12.2% of participants had 2 assessments, 8.0% had 3, 49.7% had 4, and 10.1% had 5 assessments. The age- and sex-standardized incidence rate of MCI was 63.6 per 1,000 person-years, and was significantly higher in men (72.4 vs. 57.3 per 1,000 person-years; HR=1.40, 95% CI 1.11–1.76). There was an inverse association between the development of MCI and years of education. The risk was significantly higher in persons with <9 years of education (HR=2.07, 95% CI 1.26–3.40). The age- and sex-standardized incidence rate of aMCI was 37.7 per 1,000 person -years and was significantly higher in men (43.9 vs. 33.3 per 1,000 person years; HR=1.40,95% CI 1.05–1.87). The age- and sex-standardized incidence rate of naMCI was 14.7 per 1,000 person -years and was significantly higher in men (20.0 vs.10.9 per 1,000 person years; HR=2.06, 95% CI 1.27–3.34).
VCI/Dementia Following Stroke					
Koton et al. 2022 **USA** **Prospective study**	NA	15,792 participants included in the Atherosclerosis Risk in Communities (ARIC) study with no history of stroke or dementia at baseline (1987 to 1989) who were monitored through 2019. Mean age at baseline was 54.1 years, 55.2% were	Associations between dementia and time-varying ischemic stroke incidence, frequency, and severity were studied across an average of 4.4 visits. Severity was assessed using 4 severity	**Primary outcome:** Dementia risk	Median duration of follow-up was 25.5 years. During follow-up, there were 1,378 ischemic strokes (1,155 incident) and 2,860 cases of dementia diagnosed ≥1 year after incident stroke in participants with stroke. Among persons who did not experience a stroke, 18.2% developed dementia over the study

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		women.	classifications (minor, NIHSS ≤5, 62.8%; mild, NIHSS 6-10, 22.1%; moderate, NIHSS 11-15, 7.9% and severe, NIHSS ≥16, 7.1%).		period compared with 23.3% who had an ischemic stroke (p<0.01). The risk of developing dementia increased with a first and subsequent stroke (any ischemic stroke vs. no stroke: HR=2.02; ≥2 stroke, HR=3.91), by the severity of stroke (≤5, HR=1.79 vs. ≥16, HR=4.70) and with increasing number and severity of stroke (e.g., ≥2 strokes, at least 1 NIHSS ≥11, HR=6.68)
Craig et al. 2022 **UK** **Systematic review**	Using the Newcastle-Ottawa Scale (NOS), 32 studies were categorized as high quality and 10 studies were categorized as moderate quality	44 studies including persons with stroke or TIA. The average age of participants ranged from 56 to 80 years.	The prevalences of dementia at any time post stroke and at one year post stroke, were estimated.	**Primary outcome:** Prevalence of post stroke dementia at any time **Secondary outcome:** Prevalence of post stroke dementia at one year post stroke	Based on the results of 33 studies, the prevalence of dementia at any time following stroke was 16.5% (95% CI 10.4% to 25.1%), excluding prestroke dementia. Including persons with pre-existing dementia, the prevalences of dementia were higher in studies that were hospital based (vs. community), in persons with recurrent stroke, in older studies and in high income countries. Based on the results of 17 studies, the prevalence of dementia at any time following stroke was 22.3% (95% CI 18.8% to 26.2%), including prestroke dementia. Based on the results of 16 studies, the prevalence of dementia at one year following stroke was 18.4% (95% CI 7.4% to 38.7), excluding prestroke dementia. Based on the results of 6 studies, the prevalence of dementia at one year following stroke was 20.4% (95% CI 14.2% to 28.2%), including prestroke dementia. Based on the results from 25 studies, the pooled prevalence for prestroke dementia was 7.6% (95% CI 4.0 to 14.0).
Ismail et al. 2021 **China**	NA	757 patients recruited from a single centre who had sustained a stroke or TIA,	Baseline evaluations including cognitive evaluations (DRS, MoCA	**Primary outcome:** Independent predictors of delayed-onset dementia	Mean and median duration of follow-up was 44.9 and 48 months, respectively.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Prospective study		without a history of dementia. Mean age was 68 years, 45% were women.	and MMSE) were performed 3 to 6 months after stroke/TIA. Patients were then followed up every 12 months. Neuroimaging was performed within one week of event onset.		Median baseline MMSE and MoCA scores were 27 and 21, respectively. 49 patients developed new-onset dementia. The risk of developing delayed-onset dementia was 11.2% by Kaplan–Meier estimate and 10.5% by competing risk analysis. The probability of delayed onset dementia increased throughout the follow-up period. The incidence of delayed-onset dementia was 1.62 per 100 person years. The presence of ≥3 lacunes, a history of IHD, history of ischemic stroke, and a lower baseline MoCA score were significant predictors of dementia.
Pendlebury et al. 2019 **UK** **Prospective study** ***Oxford Vascular Study (OxVASC)***	NA	2,305 patients recruited from the OXVASC study (n=92,728) who had experienced a stroke (70%) or TIA (30%) during a defined period (2002-2012). Mean age was 74.4 years, 49% were men.	The prevalence and incidence of dementia of study participants was compared with published age-matched and sex-matched data for the UK population aged ≥65 years. Dementia was defined as pre-event or post-event according to whether the diagnosis was made before or after the index event. 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	**Primary outcomes:** Standardized prevalence ratio (SPR), Standardized morbidity ratio (SMR).	225 patients had pre-event dementia. The prevalence of pre-event dementia was higher among people with a history of stroke. There was an association between increasing severity of the index stroke and the prevalence of pre-event dementia. Of the 2,080 patients without pre-event dementia, 1982 (95%) were followed up to the end of study or death. Post-event dementia occurred in 432 patients during 5 years of follow-up. The 5-year cumulative incidence of new post-event dementia was 16·2% after TIA and 33·1% after stroke. The incidence of post-event dementia at 1 year was 34·4% in patients with severe stroke (NIHSS score >10), 8·2% in those with minor stroke (NIHSS score <3), and 5·2% in those with TIA. SMR for incident dementia 1 year after index

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			Telephone MoCA (T-MoCA<9) Estimates for the number of years by which dementia was brought forward by cerebrovascular events of differing severity were obtained by visually comparing the plots for age-specific expected prevalence in the UK population with the observed age-specific prevalence in OxVasc survivors at 1 year.		event was significantly higher for both stroke and TIA (3·5, 95% CI 2·5–4·8 and 10·0, 95% CI 8·7–11·5, respectively); and increased with increasing stroke severity (e.g., NIHSS <3; SMR= 5·8, compared with NIHSS >10; SMR=47.3). SMR for incident dementia 1-5 years after index event was significantly higher for both stroke and TIA (1·5, 95% CI 1.1-2·0 and 10·0, 95% CI 8·7–11·5, respectively); and increased with increasing stroke severity (e.g., NIHSS <3; SMR= 2.2, compared with NIHSS >10; SMR=6.5). SMR for any dementia 1 year after index event was not significantly higher for persons with TIA (1·2, 95% CI 0·9–1·6) but was significantly higher for those with stroke (2·7, 95% CI 2·3–3·1) and increased significantly with increasing stroke severity. SPR for any dementia 1-5 years after index event was significantly higher for both stroke and TIA and increased significantly with increasing stroke severity. Significant predictors of post-event dementia included age, event severity, previous stroke, dysphasia, baseline cognition, low education, pre-morbid dependency, leucoaraiosis, and diabetes.
Sexton et al. 2019 **UK** **Systematic review & meta-analysis**	The mean score on the Crowe Critical Appraisal Tool was 30.3/40.	22 hospital-based studies that included consecutively eligible patients and one community-based study that included all eligible persons with strokes (mixed ischaemic and haemorrhagic, or ischaemic stroke) or TIA (if they	The development of cognitive impairment no dementia (CIND) within one-year post-stroke, was estimated.	**Primary outcome:** Pooled prevalence of CIND	Duration of follow-up ranged from one to 12 months. The pooled prevalence of CIND was 38% (95% CI 32– 43%), using data from 21 studies. The criteria used to define CIND varied across studies.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		comprised <25% of the sample), in which cognitive function was assessed using a standardized test, at a defined time post-stroke. Mean age was between 65 and 75.			Range of 1.0 to 2.0 standard deviations below normative population data on 1-3 domains, was used most frequently.
Delavaran et al. 2016 **Sweden** **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. 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:** Prevalence of long-term PSCI, and to compare scores obtained using MMSE and MoCA **Secondary outcomes:** 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. Among stroke survivors, the prevalences of any cognitive impairment using MMSE and MoCA criteria were 58 (45.7%) and 75 (61.5%), respectively. Among stroke survivors, the prevalences of severe cognitive impairment using MMSE and MoCA criteria were 16 (12.5%) and 35 (28.7%), respectively. Among controls, the prevalences of any, and severe cognitive impairment (assessed using only MMSE) were 175 (49.4%) and 43 (12.1%). 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. 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.	NA	1,236 patients recruited	Follow-up assessments	**Primary outcome:**	95 patients had pre-event dementia.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
2015 **UK** **Prospective study** ***Oxford Vascular Study (OxVASC)***		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 years, 47% were male, 33% were TIA, 30% major stroke and 5% ICH.	were conducted at 1 and 6 months and 1 and 5 years by outpatient clinics, home visits or telephone interviews	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)	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). Incident dementia was identified in 260 patients during 5 years follow-up. 110 cases of dementia were identified indirectly through medical records, home visits and telephone follow-up, and not through clinic visits. The 5-year cumulative incidence of post event 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 **USA** **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:** Six-Item Screener (SIS) **Secondary outcome:** 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). Stroke was associated with acute decline in SIS scores (0.10 points; 95% CI 0.04 to 0.17). 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 **China** **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	**Primary outcome:** Post -stroke cognitive impairment (PSCI) based on performance on neuropsychological test	The overall prevalences of PSCI and vascular dementia were 81% and 32%, respectively. 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).

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			dementia, a score of ≥7 indicated vascular dementia and an intermediate score indicating mixed dementia an average of 4.5 years post stroke.		
Sivakumar et al. 2014 **Canada** **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. Assessments were conducted at days 7, 30 and 90.	**Primary outcome:** 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). 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). 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 domain.
Douiri et al. 2013 **UK** **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:** 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. 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. The prevalence of post-stroke cognitive impairment was significantly associated with older age, black ethnicity, and low SES.
Rist et al. 2013 **International**	NA	6,080 patients with stroke or TIA within 5 years of study enrollment of the PROGRESS trial. Patients	As part of the PROGRESS trial, participants were followed for incident	**Primary outcome:** The occurrence of dementia, either certain dementia or fairly certain	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.

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Follow-up to RCT		with dementia or subarachnoid hemorrhage were excluded as were those with a clear indication or contraindication for treatment with a angiotensin-converting enzyme inhibitor.	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.	dementia.	Participants were followed for a mean of 3.8 years, during which time 407 cases of dementia were diagnosed and 709 recurrent strokes occurred. Compared with those with a baseline MMSE of 30, those with lower baseline MMSE scores were at significantly greater risk of dementia: MMSE <24: RR 26.8, 95% CI 18.08 to 39.76 MMSE 24-27: RR 6.59, 95% CI 4.54 to 9.55 MMSE 28-29: RR 2.15, 95% CI 1.43 to 3.24 The risk of dementia was more strongly associated with baseline MMSE scores in the absence of recurrent stroke.
Bejot et al. 2011 **France** **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. Prevalence of dementia was assessed over time in 4 increments.	**Primary outcome:** Prevalence of dementia	Of those assessed, 641, (20.4%) were diagnosed with post-stroke dementia. 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, and 20.2% (95% CI 18 to 23) in 2003-2008. Age, vascular risk factors, hemiplegia, and pre-stroke antiplatelet agents were associated with

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					an increased prevalence of post-stroke dementia.
Savva et al. 2010 **UK** **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:** Incidence of dementia	The risk of dementia was doubled in persons with stroke aged ≥65 years. This increased risk was highest in the period immediately following the index stroke event and decreased over time. 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 **UK** **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:** 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. 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). 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. 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

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					stroke factors, complications, and brain imaging factors.
VCI Following Atrial Fibrillation (AF)					
Liu et al. 2019 **China** **Systematic review & meta-analysis**	NOS scores ranged from 5-8	11 prospective cohort studies including 112,876 persons who were cognitively intact at baseline.	The risk of the development of dementia was compared between persons with and without AF. The most common methods used to identify dementia were DSM-III/IV and MMSE.	**Primary outcome:** Incidence of dementia	Mean duration of follow-up ranged from 1.8 to 26.6 years. AF was independently associated with a significantly increased risk of dementia incidence (HR = 1.34, 95% CI 1.24–1.44).
Chen et al. 2018 **USA** **Prospective study**	NA	12,515 participants from the ARIC Study, recruited from 1990-1992. Mean age was 56.9 years, 56% were women. Persons with AF or dementia were excluded.	The association between incident AF and 20-year change in cognitive performance and incident dementia, was estimated. 3 neuropsychological tests were used to assess cognitive function: the Delayed Word Recall Test (DWRT), the Digit Symbol Substitution Test (DSST) of the Wechsler Adult Intelligence Scale–Revised, and the Word Fluency Test (WFT). The results were also combined to provide a global score. Cognitive function was evaluated at visits 2 (1990–1992), 4 (1996– 1998), and visit (2011–2013). AF diagnoses were obtained from ECGs at study visits and hospital discharge.	**Primary outcome:** Incidence rate and/or risk of cognitive decline and dementia	During 20 years, 2,106 participants developed AF and 1,157 participants developed dementia. After adjusting for age, sex, race, education, occupation, apolipoprotein E, smoking, BMI, systolic blood pressure, diastolic blood pressure, use of hypertensive medication, diabetes mellitus, prevalent coronary heart disease, and prevalent heart failure, the average decline over 20 years in global cognitive Z score was 0.123 (95% CI 0.027–0.230) greater in participants with AF than in those without AF. When further adjusted for incident or prevalent stroke, the difference was slightly attenuated (Z score=0.115, 95% CI 0.215 to 0.014, p=0.03). This translated to a Z score of 0.11 standard deviation lower for persons with AF compared with someone without AF, or 2.75 years difference. AF was also associated with a significantly greater decline in DSST Z scores (0.118, 95% CI 0.194 to 0.041, p= 0.002). When stratified by age (≤57 vs. >57 years), AF was associated with greater decline in global Z, DSST Z, and WFT Z scores in participants aged >57 years but not in those aged ≤57 years.

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					The incidence rate for dementia in persons without AF was 4.48 (95% CI 4.20–4.77) per 1,000 person-years, compared with 21.21 (95% CI 18.28–24.49) in persons with AF. In the fully adjusted model, the risk of dementia was significantly higher in persons with AF (HR=1.23, 95% CI 1.04–1.45). When stratified by age (≤57 vs. >57 years), both the rate and the risk of dementia was higher in persons with AF.
Kalantarian et al. 2013 **USA** **Systematic review & meta-analysis**	7 prospective studies had low risk of bias, 3 cross-sectional studies had a high risk of bias	21 studies including persons with and without AF and with and without a history of stroke	The risks of dementia or cognitive impairment, given AF were estimated. Cognitive impairment was most commonly assessed by using the MMSE, and dementia diagnosis was most commonly confirmed by the DSM criteria.	**Primary outcome:** Cognitive impairment (mild to severe dementia) **Secondary outcomes:** Cognitive impairment and dementia.	*Atrial fibrillation and cognitive impairment in patients with or without history of stroke* Using data from 14 studies, the risk of dementia or cognitive impairment was significantly higher in persons with AF (RR= 1.40, 95% CI 1.19 to 1.64). Using data from 8 studies that assessed dementia, the risk was significantly higher in persons with AF (RR=1.38, 95% CI 1.22 to 1.56). Using data from 8 studies that assessed cognitive impairment or cognitive decline, the risk was significantly higher in persons with AF (RR=1.38, 95% CI 1.11 to 1.71). Using data from 10 studies which included persons without a history of stroke, or those that controlled for stroke history, the risk of dementia or cognitive impairment was significantly higher in persons with AF (RR=1.34, 95% CI 1.13 to 1.58). *Atrial fibrillation and cognitive impairment after stroke* Using data from 7 studies, AF was associated a significantly increased risk of cognitive impairment or dementia after stroke (RR= 2.70, 95% CI 1.82 to 4.00).

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VCI in Persons with Heart Failure					
Li et al. 2020 **China** **Systematic review & meta-analysis**	NA	12 studies. No details or characteristics of the studies provided.	The associations between heart failure and dementia and Alzheimer's disease were examined.	**Primary outcomes:** Dementia, Alzheimer's disease (AD)	The risk of dementia in persons with heart failure was increased significantly, compared with those without heart failure (OR/RR=1.28, 95% CI 1.15-1.43, n=12 studies). The risk of AD was not increased significantly in persons with heart failure (OR/RR= 1.38, 95% CI 0.90 to 2.13, n=4 studies).
Legdeur et al. 2019 **The Netherlands** **Prospective study**	NA	442,428 individuals aged ≥ 65 years included in the Integrated Primary Care Information (IPCI) database, without dementia. Mean age was 72.4 years, 46% were men.	The role of hypertension, diabetes, dyslipidemia, stroke, MI, heart failure, and atrial fibrillation were examined across 6 age categories (increments of 5 years), as potential risk factors for incident dementia, was examined	**Primary outcome:** All-cause dementia (based on the International Classification of Primary Care version 1 (ICPC-1) code P70 determined by the GP or the use of anti-dementia drugs)	Median duration of follow-up was 3.6 years. During 1.4 million person-years (PY) of follow-up, 13,511 people were diagnosed with dementia. Incident dementia increased with age from 1.5/1,000 PY of follow-up at age 65-70 years to 40.0/1,000 PY of follow-up at age ≥90 years. The incidence rate ratio (IRR) was significantly higher in persons with HF compared with no heart failure at ages 65-70 (IRR=2.67, 95% CI 1.76-3.89), 70-75 (IRR=1.38, 95% CI 1.01-1.84), 75-80 (IRR=1.26, 95% CI 1.06-1.49) and 80-85 (IRR=1.15, 95% CI 1.02-1.29), but not in those ≥85 years. The risk of incident dementia was significantly increased in persons with heart failure at ages 65 to 85 years. The HR decreased from 2.62 (95% CI 1.80–3.83) at age 65–70 years to 0.99 (95% CI 0.87–1.11) at age ≥ 90 years (*p* value for trend < 0.001).
Cannon et al. 2017 **UK** **Systematic review & meta-analysis**	Among 21 cross-sectional studies, 13 had a low risk of bias	37 studies (n = 8411 participants), of which 4 were prospective studies, 7 were case control and 26 were cross-sectional.	Depending on the study type, associations between heart failure and cognitive impairment were examined.	**Primary outcome:** Prevalence and risk of cognitive impairment/dementia	Prevalence of cognitive impairment in heart failure cohorts (n = 26 studies, 4,176 participants) was 43% (95% CI 30%–55%). Using data from 5 case control studies (1,414 participants) the odds of cognitive impairment were significantly higher in persons with heart failure (OR=2.64; 95% CI 1.83 to 3.80).

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					4 prospective studies with duration of follow-up of 6 and 24 months and 9 and 10 years including 2,513 participants examined the association between incident cognitive function/ dementia in patients with HF. No results are reported.
VCI Following Valvular Heart Disease					
Rodriguez et al. 2011 **USA** **Prospective study**	NA	2,680 persons ≥65 years included in the Cardiovascular Health Study recruited from 1989-1993 without a clinical history of stroke or TIA. Mean age was 74.5 years, 39.3% were men.	The presence of any annular or valvular calcification (mitral annular calcification [MAC], aortic annular calcification [AAC], or aortic valve sclerosis [AVSc]) was detected by an Echocardiography (ECG) during the 1994-1995 visit. Participants received an MRI during the 1992-93 visit to detect brain infarcts and white matter lesions (WML), graded by a scoring system of 0-9. Covert MRI findings were defined as: 1) high WM grade of >4; 2) the presence of infarcts; or 3) both. The association between valvular calcification and brain infarcts was examined.	**Primary outcomes:** Covert brain infarcts, high white matter lesion grade>4	The prevalence of any annular or valvular calcification was 77.0%. 712 participants (26.6%) had ≥1 covert infarct, and 161 (6.0%) had WM grades 4. Adjusted for age, sex, race, BMI, physical activity, creatinine, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, smoking status (never, former, current), diabetes, and the presence of coronary heart disease or congestive heart failure, the risk of covert brain infarct was increased significantly in persons with any annular or valve calcification (RR=1.24, 95% CI 1.05–1.47). The risk of covert brain infarcts was not increased significantly in persons with MAC, AAC, AVSc or any AV calcification. In adjusted analysis, the risk of high WM grade (>4) was increased significantly in persons with any annular or valve calcification (RR=1.61, 95% CI 1.04–2.49). In adjusted analysis, the risk of covert brain infarcts or high WM grade (>4) was increased significantly in persons with any annular or valve calcification (RR=1.31, 95% CI 1.11–2.54).
VCI Following Congenital Heart Disease (CHD)					
Bagge et al. 2018 **Denmark**	NA	10,632 persons with CHD identified from medical registries and a medical record review covering all	Persons with CHD were followed from January 1, 1981, 30 years of age, or date of first CHD	**Primary outcomes:** All-cause dementia **Secondary outcomes:**	The most common types of CHD diagnoses were atrial (26%) and ventricular (22%) septal defects. 65% of cases were of mild-to-moderate complexity.

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Prospective study		Danish hospitals diagnosed between 1963 and 2012. 62% of participants were born between 1960 and 1982. 46% were men.	registration. Each person with CHD was matched (age and sex) with 10 persons without CHD from the general population. The cumulative incidences and hazard ratios (HRs) of dementia were estimated. Follow-up continued until the date of dementia diagnosis, emigration, death, or end of the study period (December 31, 2012).	Alzheimer disease, vascular dementia, other dementias	The incidence rate of dementia per 1,000 person-years at risk was 0.78 in the CHD cohort and 0.75 in the general population cohort. Compared with the general population, the risks of all-cause dementia and other dementias were significantly higher in persons with CHD (HR=1.61, 95% CI 1.29–2.02 and HR=1.73, 95% CI 1.30–2.30, respectively). The risks of Alzheimer's disease and vascular dementia were not increased significantly in persons with CHD. The risk of early onset dementia (<65 years of age) in the CHD cohort was significantly higher (HR=2.6, 95%CI 1.8−3.8), as was the risk of late-onset dementia (HR=1.3, 95% CI 1.0−1.8).
VCI Following Coronary Artery Disease/Coronary Heart Disease					
Xie et al. 2019 **China** **Prospective study**	NA	7,888 community-dwelling participants aged ≥55 years, recruited from the English Longitudinal Study of Ageing, with no history of stroke or incident stroke during follow-up, MI and/or angina. Mean age was 62.1 years, 58.7% were women.	Participants underwent a cognitive assessment at baseline (wave 1, 2002 to 2003), and at least 1 other time point (from wave 2 [2004 to 2005] to wave 8 [2016 to 2017]). A composite global cognitive Z score was calculated for each participant by averaging the Z scores of cognitive 3 tests. The average annual cognitive decline from baseline of participants who had an incident CHD was compared with those of CHD-free participants.	**Primary outcome:** Change in cognition Models were adjusted for age, sex, BMI, education, marital status, depressive symptoms, current smoking, alcohol consumption, physical activity, hypertension, diabetes, chronic lung disease, asthma, and cancer.	Median duration of follow-up was 12 years. There were 480 (5.6%) incident CHD events (254 MI and 286 angina). The mean difference in change in global cognition Z scores was significantly greater in the incident CHD group (–0.018 SD/year, 95% CI –0.029 to –0.007, p=0.002). The annual rate of cognitive decline before CHD diagnosis in individuals who experienced an incident CHD was similar to those in participants who remained CHD-free throughout follow-up (0.009 SD/year, 95% CI –0.011 to 0.028, p= 0.384). In the years following CHD diagnosis, global cognitive function declined significantly faster than it did before the event (0.039 SD/year; 95% CI: 0.063 to 0.015), after adjustment for calendar time, short-term change in global cognitive

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					function, and baseline covariates, but there was no short-term cognitive decline following CHD diagnosis (0.002 SD/year, 95% CI 0.091 to 0.094).
Deckers et al. 2017 **The Netherlands** **Systematic review & meta-analysis**	Mean NOS score was 6.8, range 3-9.	24 studies (8 cross-sectional, 5 case-control, 10 longitudinal and one nested case-control) including persons with MI, angina pectoris or coronary heart disease (combination of both).	The association between MI, angina and/or coronary heart disease and dementia or cognitive impairment, was examined, using a wide variety of assessment tools/cut-offs	**Primary outcome:** Dementia or cognitive impairment	Coronary heart disease was associated with a significantly increased risk of cognitive impairment or dementia (OR = 1.45, 95%CI = 1.21–1.74, p<0.001, n=10 prospective studies). MI and angina were associated with significantly increased risks of cognitive impairment or dementia (OR = 1.46, 95% CI 1.16–1.84, n=8 prospective studies and OR=1.36, 95% CI 1.12–1.65, n=4 studies, respectively). Using data from case-control (n=4) and cross-sectional studies (n=4), there was so significantly increased risk of dementia or cognitive impairment associated with coronary heart disease.
VCI Following Myocardial Infarction (MI)					
Sundbøll et al. 2018 **Denmark** **Prospective study**	NA	31,4911 patients with first-ever MI identified from the Danish National Patient Registry, included from 1980-2012 and 1,573,193 persons matched for age and sex from the general population. Median age was 70 years, 63% were men.	Dementia diagnosis was obtained through national registries. The risk of dementia in MI and general population cohorts, was estimated. Follow-up continued until the date of dementia diagnosis, emigration, death, or end of the study period (December 31, 2014).	**Primary outcomes:** All-cause dementia **Secondary outcomes:** Alzheimer disease, vascular dementia, other dementias	Median duration of follow-up was 7.7 years for patients with MI and 9.8 years for members of the comparison cohort. During 1 to 35 years of follow-up, 11,334 patients in the MI cohort were diagnosed with dementia of which 32% were Alzheimer disease, 18% were vascular dementia, and 50% comprised other dementias. The cumulative incidence of all-cause dementia in the MI cohort was 8.7% and 13.8% in the comparison cohort. In the fully adjusted model (controlling for heart failure, stable angina pectoris, atrial fibrillation/atrial flutter, valvular heart disease, hypercholesterolemia, myocarditis, cardiomyopathy, hypertension, stroke,

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					intermittent claudication, obesity, diabetes, chronic pulmonary disease, myxedema, alcoholism-related disease, head trauma, osteoarthritis, anemia, chronic kidney disease, depression, a modified Charlson Comorbidity Index score, income, and employment, the risk of dementia), the risks of all-cause dementia, Alzheimer's disease and other dementias were not increased significantly in the MI cohort. The risk of vascular dementia was increased significantly (OR=1.35, 95% CI 1.28–1.43). The risk of dementia was higher in persons who had experienced a stroke within the first year of MI compared with those without stroke within the first year (OR=1.39, 95% CI 1.20–1.62 vs. OR=1.01, 95% CI 0.98-1.03, respectively). The risk of vascular dementia was higher in persons who had experienced a stroke, within the first year of MI, compared with those without stroke within the first year (OR=4.48, 95% CI 3.29–6.12 vs. OR=1.30, 95% CI 1.23–1.37).
VCI Following Cardiac Arrest					
Jaszke-Psonka et al. 2016 **Poland** **Cross-sectional study**	NA	30 cardiac arrest (CA) survivors, whose event occurred between 1-6 months previously (study group). 31 survivors of MI without CA (reference group) and 30 healthy subjects (control group). Mean ages were 52.9, 52.4 and 55.3 years. There were 27 women, in total.	The Digit Span test from the Wechsler Adult Intelligence Scale, Lauretta Bender's Visual-Motor Gestalt Test (BVMT), and the Benton Visual Retention Test (BVRT) were used to assess the presence of cognitive impairment.	**Primary outcome:** Cognitive impairment	53.3% of patients in the study group were cognitively impaired using the BVMT test compared with 32.3% in the reference group and 10% in the control group. Using both versions of the BVRT (version C, method A and version D, method D) a significantly higher percentage of members of the study group were cognitively impaired compared with the reference and control groups. 30% of patients in the study group were cognitively impaired using the Digit Span test compared with 19.4% in the reference group and 13.3% in the control group.
Raina et al. 2015	NA	29 adult patients who had a cardiac arrest (CA) in or out		**Primary outcome:** Change in assessment	There was no significant change in ALFI-MMSE scores at 1, 6 or 12 months. Mean scores (SD)

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USA **Prospective study**		of hospital, survived > 3 days and were admitted to a tertiary care facility. Persons who had sustained a CA due to trauma or following a stroke were excluded. Mean age was 60.8 years, 62% were men.		scores over 12 months.	were 20.75 (2.03), 20.82 (2.51), and 20.96 (2.03). There was no significant change in TICS scores at 1, 6 or 12 months. Mean scores (SD) were 35.43 (5.59) 36.00 (4.46) and 35.57 (5.39).
Risk of Cognitive Decline Following Surgical Repair of Unruptured Intracranial Aneurysm					
Bonares et al. 2016 **Canada** **Systematic review & meta-analysis**	Mean Newcastle-Ottawa score was 4.8.	8 studies including 281 patients, who underwent treatment (either surgical clipping or endovascular coiling) for an unruptured intracranial aneurysm. Mean age was 54.0 years, 75% were women. Patients in 7 studies underwent surgical clipping and either surgical clipping or endovascular coiling in one study.	Cognitive function was assessed before and after treatment. The timing of follow-up testing ranged from one month to one year. Effect sizes were calculated and pooled using the inverse variance method.	**Primary outcomes:** Global cognitive function, executive function, verbal and visual memory, and visuospatial function	At follow-up, there was no significant decline in general cognitive function (ES= -0.22, 95% CI -0.78 to 0.34), executive function (ES= -0.46, 95% CI -0.93 to 0.01), verbal memory (ES=-0.31, 95% CI -1.24 to 0.61), visual memory (ES=1.48, 95% CI -0.36 to 3.31) or visuospatial functions (ES= -0.08, 95% CI -0.30 to 0.45).
Risk of Cognitive Decline Following Elective Non-Cardiac Surgery					
Devereaux et al. 2019 for The NeuroVISION Investigators **Canada** **Prospective study**	NA	1,114 participants aged ≥65 years, recruited from 12 academic centres in 9 countries who underwent elective, non-cardiac surgery and had a brain MRI following surgery and an inpatient stay of ≥2 days. Persons who underwent carotid artery or intracranial surgery were excluded. The mean age was 73 years, 56% were men.	Participants received a standardized cognitive assessment battery before the day of surgery, including the MoCA, the Digit-Symbol Substitution Test (DSST), and the Trail-Making Test Part B (TMT-B). Patients received a brain MRI between 2 and 9 days after surgery, which was reviewed by 2 independent neuroradiologists. The association between	**Primary outcome:** Cognitive decline, defined as a decrease of ≥2 points on the MoCA from preoperative baseline to 1-year follow-up. **Secondary outcomes:** Perioperative covert stroke, cognitive decline at 1-year follow-up based on DSST and TMT-B scores	78 patients had imaging findings consistent with an acute perioperative covert stroke. The primary outcome occurred in significantly more patients who had a perioperative covert stroke compared with those who did not have a perioperative covert stroke (29 [42%] vs. 274 [29%]). Covert stroke was associated with a significantly increased risk of the primary outcome (adjusted OR=1·98, 95% CI 1·22–3·20; p=0·0055). When assessed as a continuous variable, the mean change (decline) in number of correct DSST responses from preoperative to 1-year was significantly greater in the covert stroke group (-2.2 vs. 0.6, adj mean difference= -2.6, 95% CI -5.0 to -0.3, p=0.025).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			perioperative covert stroke and cognitive decline was assessed using regression models.		There was no significant difference in the percentage of persons unable to complete the TMT-B or who took >180 seconds to complete the test (27.3% with convert stroke vs. 26.7% without convert stroke, adj OR=1.10, 95% CI 0.60-2.00). Covert stroke was also associated with a significantly increased risk of overt stroke or TIA at 1-year follow-up (HR= 4·13, 95% CI 1·14-14·99, absolute risk increase 3%; p=0·019).
Risk of Cognitive Decline of Dementia Among Persons with Silent Brain Infarcts					
Sigurdsson et al. 2017 **Iceland** **Prospective study**	NA	2,612 participants from the AGES Reykjavik Study. Mean age was 74 years, 3% of participants had a prevalent stroke at baseline.	All participants underwent brain MRI scans and cognitive testing at baseline and at follow-up. The association between infarct status, divided into 4 groups based on the absence/presence of infarcts: (1) no prevalent and no incident; (2) ≥1 prevalent and no incident; (3) no prevalent and ≥1 incident; and (4) ≥1 prevalent and ≥1 incident and the risk of dementia was examined, using regression models.	**Primary outcome:** Incident dementia	Mean duration of follow-up was 5.2 years. 545 persons had 1,240 new brain infarcts (20.9%) over the study period. The incidences for cortical, cerebellar, and subcortical infarcts detected with MRI were 7.8%, 13.0%, and 4.4%, respectively. The risk of a new infarct was significantly higher in men (RR=1.8; 95% CI 1.5–2.3). Dementia was diagnosed in 358 (13.7%) during the study period. In a model adjusted for age, sex and time from baseline scan, compared with persons with no prevalent or incident infarcts, the risk of dementia was increased significantly in persons with ≥1 incident and no prevalent infarcts (RR=1.5, 95% CI 1.2–2.00) and those with ≥1 prevalent and ≥1 incident infarcts (RR=1.7, 95% CI 1.3–2.2). Compared with persons without infarcts, the risk of dementia was highest in persons with subcortical infarcts (RR=2.6, 95% CI 1.9–3.4).
Vermeer et al. 2003 **The Netherlands**	NA	1,015 participants of the Rotterdam Scan Study, who were aged 60 to 90 years and who were free of dementia and stroke at base	Participants underwent neuropsychological testing and cerebral MRI at baseline (1995 to 1996) and again in 1999	**Primary outcome:** Dementia (defined using standardized criteria) **Secondary outcomes:**	Median per-person duration of follow-up was 3.6 years, during which time 30 persons developed dementia. The risk of developing dementia was significantly

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Prospective study		line. Persons with a history of stroke were excluded. Mean age was 72 years, 52% were women.	to 2000 (n=629) and were monitored for dementia throughout the study period. The association between silent brain infarcts and the risk of dementia and cognitive decline, was examined.	Memory performance, psychomotor speed, global cognitive function	higher in persons with MRI evidence of silent brain infarcts at baseline, adjusting for age, sex and education level (HR=2.26, 95% CI 1.09 to 4.70). 19 persons who developed dementia and 618 without dementia underwent a second cerebral MRI or CT scan. Of these, the percentage of persons with a symptomatic infarct was higher in those who developed dementia (16% vs. 1%), as was the percentage who developed a new silent brain infarct (21% vs. 11%). Global cognitive function was significantly worse in those with silent brain infarcts at baseline (adjusted mean difference in z score=-0.11; 95% CI -0.20 to -0.01) and psychomotor speed (adjusted mean difference in z score=-0.19, 95% CI -0.34 to -0.04). The presence of thalamic silent brain infarcts at baseline was associated with a steeper decline memory performance z score=-0.50, 95% CI -0.87 to -0.13).
Risk of Cognitive Decline in Persons with Diabetes					
Xue et al. 2020 **China** **Systematic review & meta-analysis**	Mean NOS score was 7.75.	144 prospective studies (n=9,359,005) including persons from the general population, who were free from dementia/cognitive impairment, and those who had MCI or dementia. Mean age ranged from 40.4 to 87.8 years, 50% were women.	Among persons with diabetes, and prediabetes, the risk of cognitive impairment including MCI, memory deficits, executive function, processing function, language, attention, visuospatial ability and reasoning was examined, as was the risk of dementia (vascular dementia and AD). The credibility of each	**Primary outcomes:** Cognitive impairment, VCI, and dementia	Mean duration of follow-up ranged from 1.5 to 32 years. Compared to persons without diabetes, the risk of cognitive impairment was significantly increased in persons with diabetes (RR=1.25, 95% CI 1.12-1.39, 20 studies, low-moderate quality of evidence). Compared to persons without diabetes, the risk of MCI was significantly increased in persons with diabetes (RR=1.49, 95% CI 1.26-1.77, 9 studies, moderate quality of evidence, grade A+). Compared to persons without diabetes, the risk

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			meta-analysis result was categorized into four levels: good (G), acceptable (A), suspicious (S) and poor (P) based on three domains: risk of bias, inconsistency, and imprecision		of all-cause dementia was significantly increased in persons with diabetes (RR=1.43, 95% CI 1.33-1.53, 31 studies, grade A+). Compared to persons without diabetes, the risk of vascular dementia was significantly increased in persons with diabetes (RR=1.91, 95% CI 1.61-2.25, 31 studies, grade A+). Compared to persons without prediabetes, the risks of all-cause dementia and vascular dementia were significantly increased in persons with prediabetes (RR=1.18, 95% CI 1.02-1.36, 9 studies, GRADE G and RR=1.47, 95% CI1.01–2.15, grade A+). There was no association between prediabetes and the risk of cognitive impairment, based on the results of 5 studies, grade S-. The risk of dementia was increased with increasing fasting plasma glucose, fasting insulin and HbA1c levels.
Rawlings et al. 2012 **USA** **Prospective study**	NA	13,351 adults aged 48 to 67 years at baseline (1990 to 1992) included in the Atherosclerosis Risk in Communities study. Mean age was 57 years, 56% were women.	The association between cognitive decline over 20 years and diabetes (n=1,779, 13.3%), was examined. Cognitive assessments included the delayed word recall test (DWRT), the digit symbol substitution test (DSST) of the Wechsler Adult Intelligence Scale-Revised, and the word fluency test (WFT). Diabetes was identified by self-reported physician diagnosis or diabetes medication use or HbA1c level of ≥6.5.	**Primary outcome:** Standardized composite global Z scores on cognitive tests, changes in individual cognitive tests Models were adjusted for demographics and vascular risk factors	Results were available for 5,987 persons at the end of follow-up (2001-2013). Diabetes was associated with a significantly greater decline in the scores of all tests except the DWRT. The average decline over 20 years in global cognitive Z score was 0.78 in persons without diabetes and 0.92 in those with diabetes (difference, -0.15 [95% CI, -0.22 to -0.08]), a 19% greater decline among the latter (-0.15 /-0.78). The result remained similar after adjusting for attrition. Increasing duration of diabetes was associated with significantly increased declines in global Z scores, DWRT, DSST and WFT scores, over 14 years.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Persons without diagnosed diabetes but with an HbA1c level of 5.7% to 6.4% at baseline had significantly more cognitive decline over 20 years (adjusted difference in global cognitive Z score, -0.07; p=0.005) than persons without diabetes and with an HbA1c level < 5.7%.
MacKnight et al. 2002 **Canada** **Prospective study**	NA	5,574 persons ≥65 years included in the Canadian Study of Health and Ageing without cognitive impairment at baseline. Mean age was 74 years, 61% were women.	The association between baseline diabetes (identified using self-report, health records, medication list, and/or laboratory testing, n=503) and the risk of incident dementia over a follow-up of 5 years (Alzheimer's Disease [AD] and vascular cognitive impairment) was examined, adjusting for demographics and vascular risk factors	**Primary outcomes:** Dementia, AD and vascular cognitive impairment (VCI) **Secondary outcomes:** Vascular dementia, vascular cognitive impairment no dementia (CIND) and mixed dementia	467 persons were diagnosed with dementia, of whom 267 had Alzheimer's Disease, 89 had vascular dementia and 128 had CIND. The risk of VCI was increased significantly in persons with diabetes, compared with those without (RR=1.62, 95% CI 1.12-2.33). The risks of dementia and AD were not increased significantly in persons with diabetes (RR=1.26, 95% CI 0.90-1.76 and RR=1.30, 95% CI 0.83-2.03, respectively). The risks of vascular dementia and CIND were increased significantly in persons with diabetes (RR=2.03, 95% CI 1.15-3.57 and RR=1.68, 95% CI 1.01-2.78, respectively).
Risk of cognitive decline in persons with renal failure					
Berger et al. 2016 **Australia** **Systematic review & meta-analysis**	Mean NOS score for cohort studies was 5.8/9 and for cross-sectional 5.4/10.	44 studies including 51,575 participants. Mean age was 67.1 years, 52% were women.	The association between cognitive function and kidney function was examined. Kidney disease was satisfied as GFR <60 mL/min/1.73 m^2; GFR<45; <30 and <15.	**Primary outcomes:** Standardized mean differences (SMD) on measures of orientation & attention, perception, memory, language, construction & motor praxis, concept formation & reasoning, executive function and global cognition	Compared with persons with GFR ≥60 mL/min/1.73 m^2, those with GFR <60, had poorer cognitive scores (Orientation & Attention [SMD –0.79, 95% CI, –1.44 to –0.13], Language [SMD –0.63, 95% CI, –0.85 to –0.41], Concept Formation & Reasoning [SMD –0.63, 95% CI, –1.07 to –0.18], Executive Function [SMD –0.53, 95% CI, –0.85 to –0.21], Memory [SMD –0.48, 95% CI, –0.79 to –0.18], and Global Cognition [SMD –0.48, 95% CI, –0.72 to –0.24]). Compared with persons with GFR ≥60 mL/min/1.73 m^2, those with GFR <45, <30 and <15 mL/min/1.73 m^2 had poorer Global Cognition scores (SMD –1.11, 95% CI –2.16 to –0.06, SMD -0.68, 95% CI -0.98 to -0.39 and SMD -0.79, 95% CI -0.86 to -0.72, respectively).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Construction & Motor Praxis and Perception were unaffected by kidney function.
Etgen et al. 2012 **Germany** **Systematic review & meta-analysis**	NA	17 articles including 7 cross-sectional studies and 10 prospective cohort studies, representing 54,779 participants. In the cross-sectional studies, mean age ranged from 36-79 years. One study included only men and one study included only women. In the longitudinal studies, mean age ranged from 64 to 81 years with mean duration of follow-up ranging from 2 to 7 years.	The association between chronic kidney disease (CKD) and cognitive decline/impairment, as defined by the study authors was assessed by pooling of odds ratios. All studies were adjusted for potential confounders.	**Primary outcome:** Cognitive impairment/decline	*Cross sectional studies* The odds of cognitive impairment/decline were significantly higher in persons with CKD compared with those with no CKD, those with GFR >60 vs. GFR 45–60 and in those with GFR >60 vs. GFR <45 (OR=1.65, 95% CI 1.32- 2.05). *Longitudinal studies* The odds of cognitive impairment/decline were significantly higher in persons with CKD compared with those with no CKD, those with GFR >60 vs. GFR 45–60 and in those with GFR >60 vs. GFR <45 (OR=1.39, 95% CI 1.15- 1.68).
Kurella Tamura et al. 2011 **USA** **Cross-sectional study**	NA	3,591 participants included in the Chronic Renal Insufficiency Cohort study. Mean age was 58.2 years, mean eGFR was 43.4 ml/min per 1.73 m^2. Mean MMSE score was 92.	The risk of cognitive impairment (defined as MMSE score >1 standard deviation below the mean score) associated with chronic kidney disease was estimated, using models adjusted for GFR, demographic characteristics (age, sex, race, ethnicity, and traditional vascular risk factors, clinical site and hemoglobin.	**Primary outcome:** Cognitive impairment	The odds of cognitive impairment were lower in those with GFR ≥60 ml/min per 1.73 m^2 compared with those with a GRF of 45-59 ml/min per 1.73 m^2 (unadj OR=0.61, 95% CI 0.39-0.97), but were nonsignificant in the fully adjusted model (OR=0.68, 95% CI 0.38-1.24). The odds of cognitive impairment were significantly higher in those with GFR <30 ml/min per 1.73 m^2 compared with those with a GRF of 45-59 ml/min per 1.73 m^2 (unadj OR=2.29, 95% CI 1.74-3.01), remained significant in a model adjusted for GFR, demographics and stroke (OR=1.41, 95% CI 1.24-1.60), but were nonsignificant in the fully adjusted model (OR=1.28, 95% CI 0.88-1.86).

Sex Differences in Predictors of Cognitive Decline Following Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Gong et al. 2021 **Australia** **Retrospective study**	NA	5,888 participants from the PROGRESS trial. Median age was 64.5 years, 30% were women. Median baseline MMSE score was 29.	Independent predictors of cognitive decline, defined as a ≥3-point decrease in MMSE score from baseline and last recorded score, or dementia, (using DSM-IV criteria + adjudication by 2 neurologists) were identified.	**Primary outcome:** Cognitive decline or dementia	Median duration of follow-up was 4 years. During follow-up, there were 763 cases of cognitive decline (n=610) and dementia (n=394). Active treatment was associated with significantly lower odds of cognitive decline or dementia (OR=0.84, 95% CI 0.72–0.98), with no difference in effect between the sexes. Independent factors that were associated with a decreased risk of the primary outcome were female sex (adj OR=0.78, 95% CI 0.63–0.95), longer years of education (adj OR=0.96, 95% CI 0.94– 0.98 per year) and higher baseline MMSE (adj OR=0.84, 95% CI 0.82–0.86 per point higher). Independent factors that were associated with an increased risk of the primary outcome were higher diastolic blood pressure (adj OR=1.11, 95% CI 1.02–1.20, per 10 mmHg), low estimated glomerular filtration rate (eGFR) <60 ml/min/1.73 m^2 (adj OR=1.27, 95% CI .03–1.58), and peripheral arterial disease (adj OR=1.78,1.26–2.52). Diabetes was more strongly associated with the primary outcome in men compared with women (women-to-men ratio of ORs [ROR]=0.54, 95% CI 0.30–0.98). Low eGFR was more strongly associated with the primary outcome in women (ROR=1.60, 95% CI .03–2.48). Higher Barthel Index scores were less protective for women than men (ROR= 1.07 (1.00–1.14).

Prevalence of Dementia Subtypes

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Goodman et al. 2016 **USA** **Retrospective study**	NA	3,110,654 individuals with a diagnosis of dementia, aged ≥68 years included in the Centers for Medicare & Medicaid (CMS) administrative database from 2011–2013.	The prevalence of dementia subtypes was retrieved.	**Primary outcome:** Dementia subtypes	14.4% of all beneficiaries (21.6 million) had a claim for a service and/or treatment for any dementia subtype. Dementia not otherwise specified was the most common diagnosis (present in 92.9%). The most common subtype was Alzheimer's (43.5%), followed by vascular (14.5%), Lewy body (5.4%), frontotemporal (1.0%), and alcohol induced (0.7%). The prevalence of other types of diagnosed dementia was 0.2%.

Screening vs. Assessment

Study/Type	Key Findings and Recommendations
Roebuck-Spencer et al. 2017 **USA** **Education Paper**	A statement on Screening and Psychological Assessment provided by the Working Group on Screening and Assessment (2014), differentiates between screening tests or measures and psychological assessment. According to the statement, **screening tests**: (a) can be used for the early identification of individuals at potentially high risk for a specific condition or disorder; (b) can indicate a need for further evaluation or preliminary intervention; (c) are generally brief and narrow in scope; (d) may be administered as part of a routine clinical visit; (e) may be used to monitor treatment progress, outcome, or change in symptoms over time; (f) may be administered by clinicians, support staff with appropriate training, an electronic device (such as a computer), or self-administered; (g) can be used by support staff who follow an established protocol for scoring with a preestablished cut-off score and guidelines for individuals with positive scores; and (h) are neither definitively diagnostic nor a conclusive indication of a specific condition or disorder. The limitations of cognitive screening measures are discussed. The 2014 WGSA statement provides direction on neuropsychological assessment. According to the statement, psychological/neuropsychological assessment: (a) provides a more comprehensive clinical picture of an individual; (b) is comprehensive in focusing on the individual's functioning across multiple domains; (c) can aid diagnosis and/or treatment planning in a culturally competent manner; (d) can identify psychological problems and conditions, indicate their severity, and provide treatment recommendations; (e) integrates results from multiple psychological tests, clinical interviews, behavioral observations, clinical record reviews, and collateral information; (f) may include screening measures that are used in conjunction with other information from the assessment, providing a broader context for interpreting the results; (g) may use screening results to determine the choice of instruments for an assessment; and (h) may cover multiple domains of functioning, such as language, memory, visual and verbal problem solving, executive functioning, adaptive functioning, psychological status, capacity for self-care, relevant psychosocial history, and others needed to respond to the referral questions.

Study/Type	Key Findings and Recommendations
Block et al. 2017 **USA** **Clinical review paper**	Two main issues are discussed. 1) clarity around terminology (screening vs. testing vs. assessment) and 2) who should be responsible for the administration and interpretation of cognitive measurement. The authors state that "*the goal of screening is to determine if there is any reason to believe that impairment in a given domain exists, frequently based on a patient's score relative to some pre-specified cut-off."* Further, "*testing refers to the proctoring of one or more individual measures as part of the process of assessment. This assessment process includes not only tests, but also critical components like the clinical interview, consideration of demographic and medical histories, and behavioral observations. As opposed to screening and testing which reflect more narrow processes, assessment is a 'complex process of solving problems in which psychological tests are often used as one* of the many methods of collecting relevant data". While the authors note that clinical neuropsychologists are uniquely prepared to perform neuropsychological assessments, there are certain situations where baseline testing can be conducted by technicians. Cognitive screening and testing may also be performed by individuals with training in basic psychometrics and neuroanatomy/pathology. The distinction between neuropsychological assessment and cognitive evaluations by other specialties is clearly made in the documentation on user qualifications that accompany the majority of neuropsychological tests in use (eg, RBANS). Moreover, many of the user requirements for neuropsychological tests make the distinction between who may be involved in test *administration* versus the user responsible for test *interpretation.*

Test Accuracy of Cognitive Screening Tests for the Diagnosis or Identification of Dementia or Mild Cognitive Impairment

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Post Stroke					
Munthe-Kaas et al. 2021 **Norway** **Prospective study**	NA	521 participants who were able to complete a cognitive assessment 3 months poststroke. Mean age was 71.5 years, 43.6% were women.	Participants underwent a neurological test battery and MoCA to detect the presence of a neurocognitive disorder (NCD) The reference standard was defined as a score of ≥1.5 SD below the normative mean in ≥1 cognitive domain on the cognitive test battery	**Primary outcome:** Sensitivity, specificity, positive predictive value, negative predictive value	280 (53.7%) participants achieved MoCA <26. According to the test battery, 60.5% of patients had an NCD. The AUC of MoCA for NCD was 0.80 (95% CI, 0.76–0.84). At a cut point of <26, sensitivity of MoCA to identify NCD was 0.71 (95% CI 0.66–0.76) with specificity of 0.73 (95% CI 0.67–0.79). The positive predictive value of MoCA was 0.80 (95% CI 0.75–0.85), with negative predictive value of 0.63 (95% CI 0.56–0.69).
Rebchuk et al. 2021 **Canada**	NA	53 persons aged 18-55 years old who had sustained a stroke or TIA within the last 3 years, with an mRS	The performance of the MoCA and the NIH Toolbox Cognition Battery (NIHTB-CB), a	**Primary outcome:** Differences in test scores between stroke and control groups using both	Median MoCA scores were similar between persons with stroke (27.0) and the control group (28.0).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Prospective study		score of 0-1, and at least one subjective cognitive complaint. Median age was 47 years, 36.5% were women. 53 age-matched healthy persons served as a control group. Median age was 44 years, 50.9% were women.	30-minute tablet-based standardized assessment for measuring cognitive impairment across neurological conditions, which is better suited for the evaluation of subtle cognitive deficits, were compared.	assessment tools	63% of persons recovering from stroke and 83% of the control group had a MoCA score ≥26. Mean T-scores for NIHTB-CB Fluid and Crystalized scores were significantly lower in stroke survivors compared with controls (44.9 vs. 54.2 and 53.8 vs. 60.0, respectively) as were total NIHTB-CB scores (49.1 vs. 58.4). In an analysis limited to 77 persons with a MoCA score ≥26, NIHTB-CB Fluid, Crystalized and total scores were significantly lower in the stroke group.
Swartz et al. 2017 **Canada** **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). The cognitive impairment (CI) items included the 10-point version of the MoCA (scored 0-10), based on memory, clock drawing and abstraction items. 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	**Primary outcome:** Feasibility (defined as 85% of patients completing the entire screen in ≤5 minutes) **Secondary outcome:** Validity	Feasibility: all patients completed the DOC screen 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) Validity: 387 patients completed a NTP. The prevalence of moderate-severe cognitive impairment was 14% (n=53). 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. 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.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			Symbol Coding and Trails Making A and B. 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.		
Zuo et al. 2016 **China** **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:** 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. 51 persons were identified using the optimal cut-point of ≤22/23 on MMSE. Sensitivity 0.85; specificity 0.88. AUC 0.86.
Xu et al. 2016 **Singapore** **Prospective study**	NA	405 participants aged ≥50 years with no cognitive impairment (NCI, 23.2%), mild/moderate cognitive impairment- no dementia (CIND, 39.5%) or dementia (37.3%), recruited from 2 hospitals. Mean ages ranged from 67.7 to 76.5 years. 41.2% to 60.3% were women. 21.3% had a previous stroke	All participants completed the NINDS-Canadian Stroke Network (NINDS-CSN) battery including the 60-, 30- and 5-minute versions. Differences in scores between the groups were examined. Receiver operating characteristic (ROC) curves were used to explore the discriminant ability test battery to distinguish between different diagnostic categories.	**Primary outcome:** Ability of testing protocols to distinguish between persons with stroke and controls using area under the curve (AUC) of receiver operator curves	In the whole sample, the AUCs for all combinations of groups (e.g., CIND vs. dementia) ranged from 0.73-0.96 for all 3 test protocols (5, 30- and 60-minute) Among persons with no or primary level of education, the AUCs for all combinations of groups (e.g., CIND vs. dementia) ranged from 0.77-0.93 for the 5-minute protocol, 0.80-0.94 for the 30-minute protocol and 0.81-0.93 for the 60-minute protocol. Among persons with secondary level of education or above, the AUCs for all combinations of groups (e.g., CIND vs. dementia) ranged from 0.68-0.96 for the 5-minute protocol, 0.80-0.97 for the 30-minute protocol and 0.83-0.95 for the 60-minute protocol.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Chen et al. 2015 **China** **Prospective study**	NA	50 Chinese persons aged ≥50 years, who had sustained a mild stroke >3 months previously, recruited from an outpatient clinic. Mean age was 60 years, 48% men. Median NIHSS score was 2. 50 persons recruited from the same outpatient clinic (control group) with an MMSE score >24, with no history of stroke or TIA. Mean age was 63 years, 58% were men.	Three VCI neuropsychological protocols were administered to patients and controls, including 60, 30 and 5-minute versions of Chinese language versions of the NINDS-Canadian Stroke Network (NINDS-CSN). External validity, defined as the ability of the protocol summary scores to differentiate stroke patients from controls, was evaluated. Chinese versions of MMSE and MoCA, Beijing version (MoCA-BJ) were also evaluated	**Primary outcome:** Ability of testing protocols to distinguish between persons with stroke and controls using area under the curve (AUC) of receiver operator curves	Stroke patients had significantly lower summary scores using the 3 testing protocols compared with controls. AUC of 60-minute protocol was 0.88 (95% CI 0.81-0.95), 0.88 (95% CI 0.81-0.94) for 30-minute protocol and 0.86 (95% CI (0.79-0.84) for the 5-minute protocol. AUCs of MoCA-BJ and MMSE were 0.88 (95% CI 0.81-0.95) and 0.75 (95% CI 0.65-0.85), respectively. Based on the MMSE and MoCA cut-off points, 12% of patients were considered to be cognitively impaired on the MMSE, whereas 90% of patients were impaired on the MoCA-BJ. MMSE identified 19.4% of the patients who were cognitively impaired by the 60-min protocol, and MoCA-BJ identified 96.8%. Kappa statistic values were 0.030 between MMSE and MoCA-BJ, 0.154 between the 60-min protocol and MMSE, and 0.208 between the 60-min protocol and MoCA-BJ.
Lees et al. 2014 **UK** **Systematic review**	NA	35 studies that examined the test accuracy of cognitive screening tests compared with a reference standard following stroke. Informant-based tests were excluded.	Pooled analyses were conducted, where possible, of cognitive test properties using different thresholds for cut-off	**Primary outcome:** Sensitivity (SN), specificity (SP) to detect dementia or multidomain cognitive impairment	24 different screening tests were used. The most commonly used tests were MMSE (n=16) and MoCA (n=8). The most commonly used reference standard was a neuropsychological battery (n=21). Pooled analyses were reported for 4 screening tests. 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. 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.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					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 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. Test characteristics performed better when testing was conducted during acute stroke. Sensitivities and specificities were similar when the reference standard was a test battery or based on a clinical dementia diagnosis.
Cumming et al. 2013 **Australia** **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:** 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. According to the criterion standard, 39 (65%) patients were cognitively impaired. 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 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 12 participants were misclassified by the MMSE, 10 were misclassified by the MoCA. 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	NA	100 participants from the OXVASC study were invited	The Montreal Cognitive Assessment (MoCA),	**Reference standard**:	91 participants completed all the assessments.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
UK **Prospective study**		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.	Mini Mental State Exam (MMSE), Addenbrooke's Cognitive Examination-Revised (ACE-R) were administered at follow-up visits.	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	39 (43%) participants had MCI, using the reference standard. MoCA cut-off <25: sensitivity 77%; specificity 83%; cut-off <26, sensitivity 87%, specificity 63% ACE-R cut-offs <92: sensitivity 72%, specificity 79%, cut-off <94: sensitivity 83%, specificity 73%. MMSE cut-point<29: sensitivity 77%, specificity 81%. 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 **China** **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 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	239 (80%) of participants completed the cognitive assessments. 60 (25%) patients had moderate to severe VCI. 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. 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). 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). No differences were found in between the two tools in terms of their ability to predict domain-

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				(impairment in ≥3 cognitive domains). Patients with vascular cognitive impairment (VCI) patients were dichotomized into no or mild VCI (NCI and VCIND mild) and moderate to severe VCI (VCIND moderate and dementia).	specific cognitive impairments 3-6 months post-stroke.
Godefroy et al. 2011 **France** **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. 64 patients (67%) were cognitively impaired according to reference standard. Significantly fewer participants were classified as having cognitive impairment according to results using the MMSE than the MoCA (45% vs 82%, p<0.001). Sensitively and specificity were 0.70 and 0.97 for the MMSE ≤24 and 0.67 and 0.90 for the MoCA ≤20 respectively. 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 **Netherlands** **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. 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. 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

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					(r=-0.62), and 24 months (r=-0.69), all at p<0.001. 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. MMSE score at 1-month did not significantly predict cognitive improvement or further deterioration in either univariate or multivariate analyses.
Dong et al. 2010 **Singapore** **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-existing dementia, or major psychiatric illness, were excluded.	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 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)	**Reference standard:** None	The mean interval between stroke and assessment was 4.2±2.4 days. 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. There was a total of 60 cases of VCIND (41 moderate, 19 severe). 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. 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.
Memory Clinics or Population-based Samples					
Davis et al. 2021 **UK** **Cochrane review**	Using the QUADAS-2 tool, the risk of bias was assessed as	7 cross-sectional studies including 9,422 persons recruited from memory clinics, geriatric hospital clinics or population-derived	The test characteristics of a one-time MoCA test, using the cut-off point selected by the individual authors, to	**Primary outcomes:** Sensitivity (SN), specificity (SP)	*Memory/Geriatric clinic findings (n=5)* The prevalences of dementia were 24%, 48% and 54% for all-cause dementia and 22% and 28% for AD. 3/5 studies used a MoCA cut-point of 25/26. The SNs were 94%, 97% and 100%.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	low or uncertain, while there were few applicability concerns.	samples. Mean/median ages ranged from 61 to ≥75 years.	identify persons with all-cause dementia or Alzheimer's disease (AD) using an accepted reference standard, were examined. The results are presented by care setting.		SPs were 51%, 51% and 60%. In the other two studies, lower thresholds were used. At a cut-point of 24/25, SN/SP was 96% and 88%. In the 5th study, using a cut-18/19, SN/SP was 96% and 88%. *Population-based findings (n=2)* The prevalences of all-cause dementia were 5% and 10%. At a cut-point of 25/26, the SN and SP was 98% and 52% in one study. In the other study, using a cut-point of 20/21, the SN and SP was 77% and 57%.
Ghafar et al. 2019 **Ireland** **Systematic review**	Most studies had low to moderate risk of bias in all domains of the Quality in Prognosis Studies (QUIPS) tool.	15 studies including 4,575 participants, ≥18 years who were interviewed face-to-face and that applied standard diagnostic criteria for detecting VCI, as defined by Gorelick et al. (2011) or Hachinski et al. (1974). Mean age ranged from 51.6 to 75.5 years. The proportion of participants with VCI within each study ranged from 12.8% to 53.4%.	The test properties of various screening methods were examined. Of 27 different methods, the most commonly used tools were the MoCA, MMSE, Clock Drawing Test (CDT), Addenbrooke's cognitive examination–Revised (ACE-R), Combination Clock Drawing Executive Test (CLOX) and trail making test (TMT)	**Primary outcomes:** Sensitivity (SN), specificity (SP), AUC, accuracy, test-retest reliability, inter-rater reliability	Most studies examined ≥1 screening tool. *Differentiating Vascular Dementia from normal cognition* 3 studies used the MoCA with cut-offs of <17 (2 studies) and 21.5. SN ranged from 77% to 92.7%, SP ranged from 92.9% to 97%, AUC ranged from 0.93 to 0.99. Reliabilities were >80%. 3 studies used the MMSE with cut-offs of <26.5 (2 studies) and 26. SN ranged from 62% to 91.8%, SP ranged from 92% to 100%, AUC ranged from 0.86 to 0.99. The CDT and TMT were assessed in 3 studies. SN ranged from 69% to 85.7%, SP ranged from 58% to 83.9%. AUC ranged from 0.73 to 0.88. *Differentiating Vascular Mild Cognitive Impairment from normal cognition* 2 studies used the MoCA with cut-offs of 26 and 26.5. SN were 81% and 96.1%, SP were 75.6% and 79%, AUC were 0.87 to 0.95. Reliabilities were >70%. 2 studies used the Brief Memory and Executive Test with cut-offs of 13. SN were 85% and

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					100%, SP was 84%, AUC was 0.84. 1 study used the MMSE with a cut-off of ≤28. SN was 80%, SP was 70%, AUC was 0.812. Other tests including the TMT and individual components of other tools (e.g, delayed recall), used in 3 studies did not perform as well). *Differentiating between Vascular Dementia and Alzheimer's disease pathology* The most accurate method was the combination of Rey Auditory Verbal Learning Test (RAVLT) recognition and Controlled Word Association (COWAT). SN was 81%, SP was 84% and AUC was 0.89.

Associations between Cognitive Screening and Outcome

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Demeyere et al. 2019 **UK** **RCT** ***(OSC CARE)***	CA: ☑ Blinding: Patient ☒ Assessor ☒ ITT: ☑	821 patients, recruited from 37 different hospital or rehabilitation sites who had sustained a stroke within the previous 10 weeks, were able to concentrate for one hour and had sufficient language comprehension to pass the first orienting tests. Mean age was 69 years, 54% were men. Mean time since stroke was 14 days. Baseline NIHSS score was approximately 4.	Patients were randomized to domain-specific cognitive screening using the Oxford Cognitive Screen (OCS) + tailored management advice (one page domain specific leaflets) or general cognitive screening using the MoCA.	**Primary outcome:** Stroke Impact Scale (SIS), change in stroke severity (NIHSS) at 6 months **Secondary outcome:** Change in cognitive performance from baseline to 6-month follow-up	467 patients (56.9%) completing 6-month follow-up. At baseline, 75% of patients in the OCS group were cognitively impaired in ≥1 cognitive domain vs. 58.37% of patients in the MoCA group, based on a score <26. At 6 months, there were no significant differences between groups in mean SIS scores (41-45 in both groups), NIHSS scores (~2 in both groups) or change in NIHSS scores (~-2 in both groups). At 6 months, there were no significant changes from baseline in cognitive status in either group.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					In the OSC group, 49% of patients improved in cognition, 22% declined and 29% remained stable. In the MoCA group, 40% of patients showed improvement, 22% declined and 38% remained stable.
McKinney et al. 2002 **UK** **RCT**	CA: ☑ Blinding: Patient ☒ Assessor ☑ ITT: ☒	228 patients recruited from 4 hospitals, within 4 weeks of admission for stroke. Mean age was 71 years, 53% were men. 162 caregivers were also included.	Patients were randomized to receive cognitive screening only or to receive a cognitive assessment battery to identify specific cognitive impairments, including general intelligence, memory, perception, language, apraxia, executive function and mood.	**Primary outcome:** Barthel Index (BI) and the Extended Activities of Daily Living Scale (EADL) **Secondary outcomes:** London Handicap Scale, The General Health Questionnaire-28 (GHQ 28), Cognitive Failures Questionnaire (CFQ) **Caregiver outcomes:** Caregiver Strain Index (CSI), GHQ-28 Assessments were conducted at 6 and 12 months	*Patient outcomes* There were no significant differences between groups on measures of functional ability (BI, EADL), perceived disability (LHS) psychological distress (GHQ-28), perceived cognitive ability (CFQ) or satisfaction with care at 6 or 12 months. *Carer outcomes* There were no significant differences between groups on either CSI or CHQ-28 at 6 or 12 months. There were 64 losses in the control group and 57 in the assessment group.

Associations between Diagnostic Imaging and the Development of Post Stroke Dementia

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Ball et al. 2021 **UK** **Systematic review & meta-analysis**	Using the QUPIS tool, the overall risk of bias was determined to be low in 7 studies and moderate in 21 studies.	28 studies including 7,078 persons who had sustained an acute stroke within the previous 30 days and had undergone neuroimaging using CT and cognitive testing ≥3 months later. Mean age ranged from 59.8–78.6 years	The association between brain imaging features using CT, including atrophy, WML, pre-existing stroke lesions (silent brain infarcts, old stroke lesions), pathological stroke type, acute stroke features	**Primary outcomes:** Post-stroke dementia (PSD), post-stroke cognitive impairment (PSCI).	Length of follow-up for PSD and/or PSCI ranged from 3 months to 6 years after stroke. The presence of cerebral atrophy was associated with significantly increased risk of PSD (OR=2.80, 95% CI 1.21–6.51, 4 studies included, n=558), but not PSCI (OR= 2.03, 95% CI 0.74-5.56, 3 studies included, n=501).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			(location, size, number of lesions, swelling), and combinations of neuroimaging features, and cognitive outcomes post stroke was examined.		The presence of WML was associated with an increased risk of PSD (OR=2.46, 95% CI 1.25–4.84, 9 studies included, n=1,054) and PSCI (OR=3.46, 95% CI 2.17-5.52; 4 studies included, n=473). The presence of pre-existing stroke lesions was associated with PSD, OR= 2.38, 95% CI 1.06–5.32; (3 studies included, n=352) but not PSCI. Other CT features were either not associated with cognitive outcome, or there were insufficient data for pooling.
Sivakumar et al. 2016 **Canada** **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:** 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. The proportion of patients with cognitive impairment was similar in patients with- and without diffusion-weighted imaging lesions: 52% vis. 54%, p=0.83 No relationship was found between diffusion-weighted imaging lesion volume and day 30, but WMH volume at days 30 and 90 predicted MoCA scores. 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). WMH volumes at baseline were predictive of persistent cognitive deficits after 30 days: β=-0.2.24 (1.956, 45.369), p=0.005, but not after adjustment for age (p=0.093)
Pasi et al. 2015 **Italy**	NA	76 patients with mild cognitive impairment based on Winblad criteria,	At baseline, demographic information was collected and both	**Primary outcome:** 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***		demonstrating 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.	the Montreal 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: Mean diffusivity: r=-0.275, p=0.023 Fractional anisotropy: r=0.246, p=0.043 There were no significant correlations between MMSE- and DTI-derived indices. Mild cognitive impairment and small vessel disease, diffusion tensor imaging-measured white matter microstructural damage was more related to MoCA than MMSE performance.
Smith et al. 2015 PURE **Prospective study** **Canada**	NA	803 participants aged 35-70 years, with no history of previous stroke, dementia or other neurological conditions, recruited from 4 large Canadian cities from 2010-2012. Mean age was 58 years, 59% were female.	A battery of tests was administered on a one-time basis including Digital Symbol Substitution Test, Montreal Cognitive Assessment tool (MoCA), gait speed (Timed up & Go test), brain MRI.	**Primary outcome:** Associations between cognition, gait tests and MRI findings.	For each 10-year increase in age there was a 0.65-point decrease in MoCA (95% CI 0.45-0.85), a 7.4% decrease in DSST (95% CI 6.1-8.7) and a 0.6 sec increase in TUG (95% CI 0.4-0.8). Each 10-year increase in age was associated with increasing frequency of silent brain infarcts, cerebral microbleeds and white matter hyperintensity (WMH), observed on MRI. There were no significant associations between lower MoCA scores and any MRI findings, adjusting for age, sex and education. Lower DSST scores were associated with higher WMH and lower white matter volume, adjusting for age, sex and education. Slower TUG times were associated with the presence of silent brain infarcts, increased WMH, decreased cortical gray matter and, decreased prefrontal cortex volume, after

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					adjusting for height, age and sex.
Debette et al. 2010 **US** **Cohort study**	NA	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:** 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. 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). 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). 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. Both WMHV and EXT-WMHV were associated with a significantly increased risk of death.
Rasquin et al. 2004 **Netherlands** **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 MMSE score was 25.5.	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 the control group from MAastricht Aging Study (MAAS). Cognitive functioning was assessed using a	**Primary outcomes:** *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. At 12 months after stroke, a further 5 (3.2%) patients had died and 9 (5.8%) refused to participate. At baseline, 17 patients had dementia, 142 had VCI, 125 had vascular MCI and 34 patients had no cognitive disorders. Significant predictors of dementia (vs. no cognitive impairment) 1 month: no significant predictors 6 months: Older age (OR= 9.4), low education

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			neuropsychological test battery.		(OR= 14.7), and territorial infarct (OR=10.6) 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) Significant predictors of VCI (vs. no cognitive impairment 1 month: Low education (OR=3.4) and territorial infarct (OR= 2.4) 6 months: older age (OR=4.3) and low education (OR=4.1) 12 months: Older age (OR= 6.2), lower education (OR= 4.1) Significant predictors of vascular MCI (vs. no cognitive impairment 1 month: Low education (OR= 4.96) and territorial infarct (OR= 3.58) 6 months: Older age (OR=3.4) and lower education (OR=3.7) 12 months: Older age (OR=3.5) and lower education (OR=2.28)

Performance-based Measures of Executive Function

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Poncet et al. 2017 **France** **Scoping review**	NA	21 articles addressing the research question, "*how do assessments measuring an individual's ability to accomplish IADL address EF among persons with ABI?"*	12 tools, developed either to assess executive function (EF) in ADL, independence in ADL considering EF or ADL capacities, were identified. Tools reviewed were Activities of Daily Living Profile (ADL-Profile),	**Primary outcomes:** A general description of the identified tools, their psychometric properties, a comparison of the tools using Lezak's model and how each tool considers the different components of EF, and the tool's applicability	4 tools assessed aspects of executive functioning (CT, MET, MLAT, and NAT), 7 tools assessed the level of independence considering EF (ADL Profile, EFPT, EFRFT, IADL Profile, MPS, RKE-R, R-ADL and one assessed ADL capacity (AMPS). All 12 tools demonstrated adequate reliability and validity.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			Assessment of Motor and Process Skills (AMPS), Cooking Task (CT), Executive Function Performance Test (EFPT), Executive Function Route Finding Task (EFRFT), Instrumental Activities of Daily Living Profile (IADL Profile, Meal Preparation Scale (MPS), Multi-Level Action Test (MLAT), Multiple Errands Test (MET), Naturalistic Action Test (NAT), Rabideau Kitchen Evaluation – Revised (RKE-R), and Rivermead ADL Assessment (R-ADL)		Compliance with Lezak's model (volition, planning and decision making, purposive action; and effective performance) Volition: A single tool fulfilled both criteria for this item (initiate an intension, formulate a goal). ADL-Profile Planning & decision making: 4 tools fulfill all criteria for this item (think of alternatives, weigh and make choices and develop a strategic plan of action). ADL-Profile, CT, IADL-Profile, and MET Purposive action: 5 tools fulfill all criteria for this item (initiate activity, maintain and carry out and stop and / or switch. ADL-Profile, AMPS, CT, IADL-Profile, and MET Effective performance: 8 tools fulfill all criteria for this item (monitor, self-correct and regulate (intensity, tempo, etc.). ADL-Profile, CT, EFPT, EFRFT, IADL-Profile, MLAT, NAT and MET *Applicability* 4 dimensions of applicability (respondent burden examiner burden, distribution of scores and format compatibility) are presented.
Poulin et al. 2013 **Canada** **Review**	NA	41 studies that examined the psychometric properties of assessment tools that evaluated some component of executive function (EF) following stroke or brain injury.	The psychometric properties, of 17 performance-based tools, were reviewed. Tools evaluated were ADL profile, Behavioural assessment of the dysexecutive syndrome (BADS), Complex task performance assessment (CTPA), Execution of a	**Primary outcomes:** Reliability, validity, responsiveness and feasibility	The most common EF components evaluated were planning (n = 13), sequencing (n = 13), problem-solving (n = 11) and monitoring (n = 10), whereas the least frequently assessed components were divided attention (n = 2) and flexibility (n = 3). 14 tools evaluated ≥3 EF components. None evaluated all components. *Reliability* 9 tools have some reliability data available for the population with stroke, with inter-rater reliability (n = 7) and internal consistency (n = 4) being the most commonly reported.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			cooking task, Executive function performance test (FPT), Executive secretarial task (EST), Generation and execution of script: Making a cake, Multiple Errands test (MET), Virtual multiple errands test (VMET), Naturalistic action test, Observed tasks of daily living-revised, Rabideau kitchen evaluation-revised (RKE-R), Virtual action planning supermarket (VAP-S), Assessment of Motor and Process Skills (AMPS), Functional Assessment of Verbal Reasoning and Executive Strategies (FAVRES), Kettle Test (KT), Virtual Environment Technology (VET)-based cognitive assessment program		None of the EF-specific assessments and only 2/4 general assessments with an EF component reported test– retest reliability. AMPS (Excellent: Motor subscore: *r* = 0.88–0.91; and Process subscore: *r* = 0.86–0.90) and Excellent Internal consistency. VET (Test-retest had adequate to excellent *r*=0.528 to 0.926). *Validity* The tools with the strongest evidence of validity were the EFPT and MET. Two EF-specific assessments require further validation in the stroke population are the CTPA and the Rabideau Kitchen Evaluation-Revised. AMPS had the strongest evidence of validity as a general assessment. *Responsiveness* Only AMPS has been formally assessed for responsiveness. *Feasibility* Most of the assessments include daily life tasks that are feasible to accomplish within a clinical setting, and require limited equipment. 12/17 assessments can be completed in <60 minutes. The KT took the shortest time to complete (20 minutes).

Key Findings from Recent White Paper

Study/Type	Key Findings
Verdelho et al. 2021 **UK & EU**	Summary of investigations to avoid missing modifiable vascular risk factors. • Modifiable vascular risk factors: blood pressure, blood glucose, blood lipids, BMI, lifestyle history, other proxy-risk factors, as obstructive sleep apnea, homocysteine levels.

Study/Type	Key Findings
A white paper from the ESO dementia committee	• Sources of emboli and evidence of ischaemic cardiovascular disease: ECG, echocardiogram, doppler ultrasound, CT or MR angiography (intra/extracranial stenosis) • Evidence of cerebrovascular disease: MR or CT brain imaging Summary of suggestions for the management of cerebrovascular disease in patients with Cognitive Impairment (CI). • Clinical appointments due to CI should be considered as an opportunity to check and better control of vascular risk factors. • Brain imaging (made in the context of CI) should be reviewed to verify existence of cerebrovascular disease. • In the case of cerebrovascular component highly suspected/not clear after CT, an MRI should be considered (namely if doubt about hemorrhagic component including microbleeds and cSS, small acute lesions, specific profiles as familiar -e.g.CADASIL, or extension of WMC and SVD) • Specific investigations should be considered in acute lesions, recurrent and multiple strokes (namely neck and intracranial artery imaging and cardiac study) Summary of suggestions concerning treatment of cerebrovascular disease in patients with CI • Implement primary and secondary prevention of stroke; primary prevention applies to all patients. Patients who experienced a stroke should be treated according to secondary prevention guidelines. • No evidence base to support application of secondary stroke prevention treatment strategies for WMH alone. • Individualized approach to initiate or modify antithrombotic agents based on weighing the individual patients estimated absolute risk of future ischaemic or haemorrhagic events.

Abbreviations

AD: Alzheimer's Disease	AUC: area under curve	CA: concealed allocation
CI: confidence interval	DSM: Diagnostic and Statistical Manual of Mental Disorders	DRS: dementia rating scale
GFR: glomerular filtration rate	HR: hazard ratio	ITT: intention-to-treat
MCI: mild cognitive impairment	MMSE: Mini Mental State Examination	MoCA: Montreal Cognitive Assessment
NA: not assessed	NOS: Newcastle-Ottawa Scale	OR: odds ratio
RR: relative risk	VCI: vascular cognitive impairment	

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