Stroke

AHA SCIENTIFIC STATEMENT

Cognitive Impairment After Ischemic and Hemorrhagic Stroke: A Scientific Statement From the American Heart Association/American Stroke Association

Nada El Husseini, MD, MHSc, FAHA, Chair; Irene L. Katzan, MD, MS, FAHA, Vice Chair; Natalia S. Rost, MD, MPH, FAHA; Margaret Lehman Blake, PhD, CCC-SLP; Eeeseung Byun, RN, PhD; Sarah T. Pendlebury, FRCP, DPhil; Hugo J. Aparicio, MD, MPH; María J. Marquine, PhD; Rebecca F. Gottesman, MD, PhD, FAHA; Eric E. Smith, MD, MPH, FAHA; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; Council on Cardiovascular Radiology and Intervention; Council on Hypertension; and Council on Lifestyle and Cardiometabolic Health

PURPOSE: Cognitive impairment is a common consequence of stroke and has direct implications for poststroke functioning and quality of life, including the ability to maintain a job, live independently, sustain interpersonal relationships, and drive a vehicle. In this scientific statement, we critically appraise the literature on the prevalence, diagnosis, and management of poststroke cognitive impairment (PSCI) and provide a framework for clinical care while highlighting gaps that merit further study.

METHODS: We performed a scoping literature review of randomized controlled clinical trials, prospective and retrospective cohort studies, case-control studies, clinical guidelines, review articles, and editorials on the incidence and prevalence, natural history, diagnosis, and management of PSCI. Scoping reviews determine the scope of a body of literature on a given topic to indicate the volume of literature and the studies currently available and provide an overview of its focus.

RESULTS: PSCI is common after stroke, especially in the first year, and ranges from mild to severe. Although cognitive impairment is reversible in some cases early after stroke, up to one-third of individuals with stroke develop dementia within 5 years. The pathophysiology is not yet fully elucidated but is likely attributable to an acute stroke precipitating a series of pathological events, often in the setting of preexisting microvascular and neurodegenerative changes. Screening for associated comorbidities and interdisciplinary management are integral components of the care of individuals with PSCI. There is a need for prospective studies evaluating the individual trajectory of PSCI and the role of the acute vascular event in the predisposition for Alzheimer disease and related dementias, as well as high-quality, randomized clinical trials focused on PSCI management.

Key Words: AHA Scientific Statements ■ cognitive dysfunction ■ depression ■ prevalence ■ prospective studies ■ risk factors ■ stroke

Post-stroke cognitive impairment (PSCI) ranges in severity from mild to severe and occurs in up to 60% of stroke survivors in the first year after stroke, with a higher rate seen shortly after stroke.[1–4] Up to 20% of individuals with mild PSCI recover fully, with the highest rate of recovery seen shortly after stroke.[5] However, improvement in cognitive impairment without return to prestroke levels is more frequent than complete recovery.[6,7] The risk of developing future dementia is increased after stroke even in those with transient cognitive impairment.[8] The American Heart Association/American Stroke Association statement "Vascular Contributions to Cognitive Impairment and Dementia," published in 2011, addressed the construct of vascular cognitive impairment (VCI), which captures the entire spectrum of cognitive disorders associated with all forms of cerebral vascular brain injury, with or without a clinical history of stroke, with a focus on the role of vascular contributions

Stroke is available at www.ahajournals.org/journal/str

 Stroke. 2023;54:e272–e291. DOI: 10.1161/STR.0000000000000430

to dementia.[9] In 2021, the European Stroke Organization and European Academy of Neurology published joint guidelines on PSCI based on evidence from randomized controlled trials, highlighting areas for which robust evidence is lacking and suggesting priority areas for future research.[10] In this scientific statement, we discuss PSCI, defined as cognitive impairment resulting from an overt stroke (ischemic or hemorrhagic) and ranging from mild cognitive impairment to dementia, and provide an actionable summary that delineates a general framework for PSCI screening, diagnosis, and management.

This scientific statement is based on a scoping literature review primarily within the past 10 years of randomized controlled clinical trials, prospective and retrospective cohort studies, case-control studies, clinical guidelines, review articles, and editorials on the incidence and prevalence, natural history, diagnosis, and management of PSCI.

DEFINITIONS

The following are key definitions differentiating VCI and dementia from PSCI and dementia:

VCI refers to cognitive impairment of any severity associated with cerebrovascular disease regardless of the occurrence of stroke symptoms.[11] The types of vascular injuries leading to VCI range from an insidious, progressive accumulation of microvascular pathological changes (eg, diffuse white matter injury detected on magnetic resonance neuroimaging as white matter hyperintensities or leukoaraiosis, cerebral microbleeds, enlarged perivascular spaces, or cortical microinfarcts) to a single or multiple clinical stroke events affecting brain structures critical for cognition.[12]

Vascular dementia is the end of a continuum of severity of clinical manifestations of VCI.[6]

PSCI refers to any severity of cognitive impairment, regardless of cause, noted after an overt stroke.[6,13]

Poststroke dementia (PSD) is the end of a continuum of severity of clinical manifestations of PSCI and refers to all types of dementia after stroke.[6]

PREVALENCE AND INCIDENCE OF PSCI

The prevalence of cognitive impairment after ischemic or hemorrhagic stroke differs by the timing of assessment, diagnostic criteria, demographics (eg, age, race, or ethnicity), era of study publication, and case mix (eg, stroke severity, prior/recurrent stroke, prestroke dementia, population versus hospital based, interval from stroke, inclusion of patients with aphasia), resulting in substantial heterogeneity in reported estimates.[14–16] PSCI is most common in the first year after stroke, occurring in up to 60% (cumulative incidence) of stroke survivors, with the highest rate seen shortly after stroke.[4] About 44% of individuals are impaired in global cognition 2 to 6 months after stroke.[3] However, a large population of stroke survivors have cognitive impairment that is not sufficient to meet diagnostic criteria for dementia but still affects quality of life.[17] A systematic review that included 23 studies published between 1995 and 2017 found a pooled prevalence of PSCI without dementia in the first year after stroke of 38% (95% CI, 32%–43%), thus concluding that 4 in 10 stroke survivors display a level of cognitive impairment that does not meet the criteria for dementia.[18]

In studies in which cognitive performance is assessed after but not before the stroke, the estimates of PSCI may be affected by impairment that may have been present before the stroke onset.[16] For example, in the Nor-COAST multicenter prospective cohort study (Norwegian-Cognitive Impairment After Stroke) of mostly mild stroke (N=617), PSCI (including dementia) was prevalent in 59% of participants at 3 months and 51% at 18 months.[19] In this study, 9% of participants had prestroke mild or major cognitive impairment.[19] In another cohort of individuals with mild stroke (N=220) that excluded prestroke cognitive impairment, the overall frequency of 3-month PSCI was 47.3%.[2]

The prevalence of PSD varies by stroke severity and history of stroke recurrence, and PSD occurs less frequently than milder forms of cognitive impairment.[20,21] PSD rates in the first year after stroke range from 7.4% (95% CI, 4.8%–10.0%) in population-based studies of first-ever stroke in which prestroke dementia was excluded to 41.3% (95% CI, 29.6%–53.1%) in hospital-based studies of recurrent stroke in which prestroke dementia was included. About 10% of patients have dementia before the first stroke; 10% develop new dementia soon after first stroke; and more than one-third have dementia after recurrent stroke.[16]

Racial differences in the frequency and severity of PSCI have been reported.[22] Stroke in Black patients results in a greater cognitive decline and is more frequently associated with dementia within 5 years of ischemic stroke compared with White patients, despite Black patients being younger at the time of the incident stroke.[23]

Prestroke cognitive impairment, PSCI, and dementia are frequent in patients with intracranial hemorrhage (ICH) and higher in those with lobar ICH.[24,25] In a prospective observational cohort study of 218 patients without preexisting dementia, the incidence rate of new-onset dementia at 1 year after ICH was 14.2% (95% CI, 10.0%–19.3%) and at 4 years was 28.3% (95% CI, 22.4%–34.5%).[25] The incidence of new-onset dementia was >2 times higher in patients with lobar ICH (incidence at 1 year, 23.4% [95% CI, 14.6%–33.3%]) than in patients with nonlobar ICH (incidence at 1 year, 9.2% [95% CI, 5.1%–14.7%]).[25]

In subarachnoid hemorrhage (SAH), impairment in at least 1 neuropsychological domain is common. Depending on the assessment tool, the rates of impairment on

global cognitive tests after SAH ranges between 26% to 43% at 3 months and 21% at 12 months.[26,27]

NATURAL HISTORY OF PSCI

The temporal pattern of PSD based on clinical observation is variable. It may (1) start at the onset of stroke and stabilize, (2) start at the onset of stroke and progress, (3) develop after recurrent strokes, (4) develop at the onset of stroke in the presence of preexisting cognitive impairment, or (5) develop >3 to 6 months after stroke.[28]

The majority of studies on cognitive impairment after stroke report a prevalence or cumulative incidence of dementia at specific time points with relatively few data on individual cognitive trajectories that describe the course and cause of cognitive change over time. If cognitive assessment is done in the early poststroke period, estimates of impairment are even more elevated (up to 91.5% at 2 weeks in 1 series).[29] Although early poststroke impairment is common, PSD may be an inappropriate label for these early fluctuations in cognition because improvement may occur, especially within the first 6 months after stroke.[30–33] However, cognitive recovery may be limited in patients with multiple comorbidities, polypharmacy, older age, and previous cognitive decline.[34]

Data on PSCI in the long-term are sparse. In a small study (N=109) of stroke and transient ischemic attack survivors at 7 years after the index event, 37% had mild cognitive impairment and 22% had dementia.[35] Another study reported an overall prevalence of cognitive impairment 3 months after stroke and at annual follow-up up to 14 years after stroke that remained relatively unchanged at 22%.[1] Two large population studies found the longitudinal risk of dementia to vary according to stroke severity.[20,21] In the Atherosclerosis Risk in Communities cohort study (N=15 379 participants free of stroke and dementia at baseline), the risk of dementia compared with no stroke over a median follow-up of 25.5 years by adjusted hazard ratio was 1.76 (95% CI, 1.49–2.00) for 1 minor to mild stroke, 3.47 (95% CI, 2.23–5.40) for 1 moderate to severe stroke, 3.48 (95% CI, 2.54–4.76) for ≥2 minor to mild strokes, and 6.68 (95% CI, 3.77–11.83) for ≥2 moderate to severe strokes.[21] Similarly, in the population-based longitudinal Oxford Vascular Study, compared with population dementia rates for the UK population >65 years of age, postevent dementia incidence in the first year after stroke was higher than expected for all categories of cerebrovascular event, with the age- and sex-adjusted relative incidence ranging from 3.5 (95% CI, 2.5–4.8) after transient ischemic attack and 5.8 (95% CI, 4.4–7.5) after minor stroke to 47.3 (95% CI, 35.9–61.2) after severe stroke, with less marked increased relative incidence thereafter.[20] The 5-year cumulative incidence of new PSD was 33.1% (95% CI, 31.7%–34.5%) after stroke, with 51% of dementia diagnosed within the first year and greater front-loading of risk in those with major than in those with more minor stroke.[20] Because death is a competing risk for dementia (ie, it precludes the occurrence of dementia), exploratory analysis using the cumulative incidence competing-risk methods showed a lower cumulative incidence of dementia associated with severe stroke (National Institutes of Health Stroke Scale score >10) compared with that obtained with Kaplan-Meier methods.[20] Additional studies are needed to better characterize these temporal patterns and possible contributing factors.

DELAYED-ONSET PSCI

Although there is no widely accepted consensus definition, late PSCI is usually defined as new cognitive impairment or dementia with onset >3 to 6 months after the stroke.[36] The risk factors and pathophysiological mechanisms of late poststroke cognitive decline and dementia differ from those of early PSCI. One major risk factor is stroke recurrence, which may be decreased by robust secondary stroke prevention. The incidence of new dementia is much higher after a second stroke.[16,20,21] Among those with late-onset PSCI without recurrent symptomatic stroke, the progression of cerebral small-vessel disease and covert stroke appears to play an important role, although other neurodegenerative diseases such as Alzheimer disease (AD) also need to be considered.[36,37] Other risk factors for late poststroke cognitive decline include older age, baseline cognitive impairment, hypertension, diabetes, and brain atrophy.[36]

In the REGARDS study (Reasons for Geographical and Racial Differences in Stroke), incident first-ever stroke was associated with a stepwise immediate decline in cognitive function, followed by an accelerated risk for future cognitive decline greater than what was expected for age.[22] This acceleration in cognitive decline was greater in older stroke survivors than younger stroke survivors.[22] A systematic review of population-based and hospital-based cohorts found that the overall incidence of new dementia >6 months after stroke was 1.7%/y but varied by stroke severity.[16] In the Framingham study, the 10-year risk of dementia was 19.3% after stroke and 11.0% without stroke. Incident stroke doubled the risk of dementia even after adjustment for age, sex, education, and stroke risk factors.[38]

DIFFERENTIAL DIAGNOSIS

In addition to the direct effects of the stroke, cognitive function after stroke can be affected by other stroke complications (eg, hyponatremia, delirium, depression), as well as by prestroke cognitive decline and coexisting age-related neuropathologies. Delirium is a common complication of stroke, occurring in ≈25% of admitted patients, and should be differentiated from PSCI.[39] The clinical hallmarks of delirium are alterations in arousal

 Stroke. 2023;54:e272–e291. DOI: 10.1161/STR.0000000000000430

and attention, cognition, and behavior that arise over a short period of time, typically in the acute or early subacute phase of stroke, and are not better explained by a neurodegenerative disorder or PSCI.[40] Delirium is more common in patients with stroke who are older and have more severe stroke, poststroke infection, prestroke cognitive decline, and greater brain atrophy.[41] Furthermore, stroke lesion topography has been linked to delirium in patients hospitalized with stroke.[42] Workup for delirium should include assessment of electrolytes; tests of liver and renal function; assessment for infection, constipation, and pain; and a review of medications.

To exclude potentially reversible causes of impairment, the clinician should obtain laboratory testing for thyroid-stimulating hormone and vitamin B_{12}[43] and should consider the potential cognitive effects of mood disorders; sleep disorders, including obstructive sleep apnea and sedating and anticholinergic medications; and hearing and vision impairments. Poststroke depression is common, affecting about one-third of individuals in the first year after stroke.[44] Poststroke depression is often accompanied by cognitive symptoms, which makes differentiating it from primarily PSCI more complex. Because depression-related cognitive symptoms may resolve with the treatment of depression, it is important to screen for poststroke depression, especially when PSCI is suspected.[44] The use of a depression screening tool validated in patients with stroke may aid in recognition of depression.[45] Risk factors for poststroke depression include higher physical disability; prestroke history of depression, anxiety, and cognitive impairment; and lack of social and family support.[44]

Poststroke cognitive decline should be differentiated from prestroke decline. Questioning the patient and an informant about cognitive-related activities of daily living (eg, finances, shopping, and organizing medications) or using a validated questionnaire such as the Informant Questionnaire on Cognitive Decline in the Elderly or the Eight-Item Informant Interview to Differentiate Aging and Dementia may determine whether there was cognitive impairment that predated the stroke.[46–48] Causes of cognitive impairment before stroke can include vascular cognitive disorders such as covert cerebral small-vessel disease related to stroke risk factors and comorbid age-related neurodegenerative diseases such as AD.

In the elderly, it is common for dementia to have multiple causes (also called mixed dementia), most frequently a combination of vascular disease and irreversible neurodegenerative pathologies, particularly AD.[9] More research is needed on how to accurately diagnose AD and other neurodegenerative pathologies in the setting of a recent stroke. Biomarkers of the AD pathophysiological process such as β-amyloid and tau can be measured in cerebrospinal fluid or blood or by positron emission tomography. However, such testing is currently expensive, invasive, or not widely available for routine use.

SYMPTOMS AND COGNITIVE DOMAINS AFFECTED

An individual's cognitive trajectory in the months after stroke might be affected by multiple factors, including the stroke location, preexisting cognitive impairment, small-vessel disease and comorbidities, sociocultural (eg, socioeconomic status) and demographic (eg, age and sex) characteristics of the person experiencing the stroke, and the interventions provided. Stroke location has been linked to the type of cognitive deficits observed but is not perfectly predictive of cognitive impairment. Involvement of strategic locations such as the left frontotemporal region, left thalamus, and right parietal lobe,[49] as well as the left middle cerebral artery territory, has been associated with increased likelihood of PSCI.[50] Support vector regression-based lesion symptom mapping performed 3 to 6 months after an ischemic stroke identified the left angular gyrus, left basal ganglia structures, and white matter around the left basal ganglia as strategic structures for global cognitive impairment after stroke.[51] Larger strokes tend to involve many of these regions, making it hard to differentiate cognitive impairment attributable to regional involvement from that attributable to stroke size and severity. Because aphasia is common after left middle cerebral artery stroke and several commonly used cognitive tests and screening instruments depend on intact language function, the severity of cognitive impairment may be overestimated in individuals with aphasia and with left middle cerebral artery strokes. Furthermore, some studies explicitly exclude individuals with aphasia, leading to difficulties capturing the true rates of cognitive impairment in the broader stroke population.

Global cognitive deficits have been described in the poststroke setting,[52] but this global impairment may reflect the use of global cognitive measures in many studies.[53] Difficulty with executive function and attention (and, in some studies, memory) is common after ischemic stroke[54] but also has been reported to show the most improvement by 3 to 6 months after stroke, whereas impairment in the language domain does not tend to improve.[54,55] Patients with ICH show cognitive deficits similar to those of patients with ischemic stroke,[56] with different domains affected depending on the location (ie, lobar vs nonlobar) of the ICH.[57]

Patients with SAH frequently have less baseline vascular disease or subclinical cerebrovascular disease (both important contributors to PSCI) than other stroke populations. Yet, multiple cognitive domains may be impaired with SAH, with the highest rates of impairment noted in executive function and verbal memory.[58,59]

PATHOPHYSIOLOGY

In the general population, small-vessel disease is the biggest contributor to VCI and dementia, whereas in the poststroke population, there is a relatively greater contribution

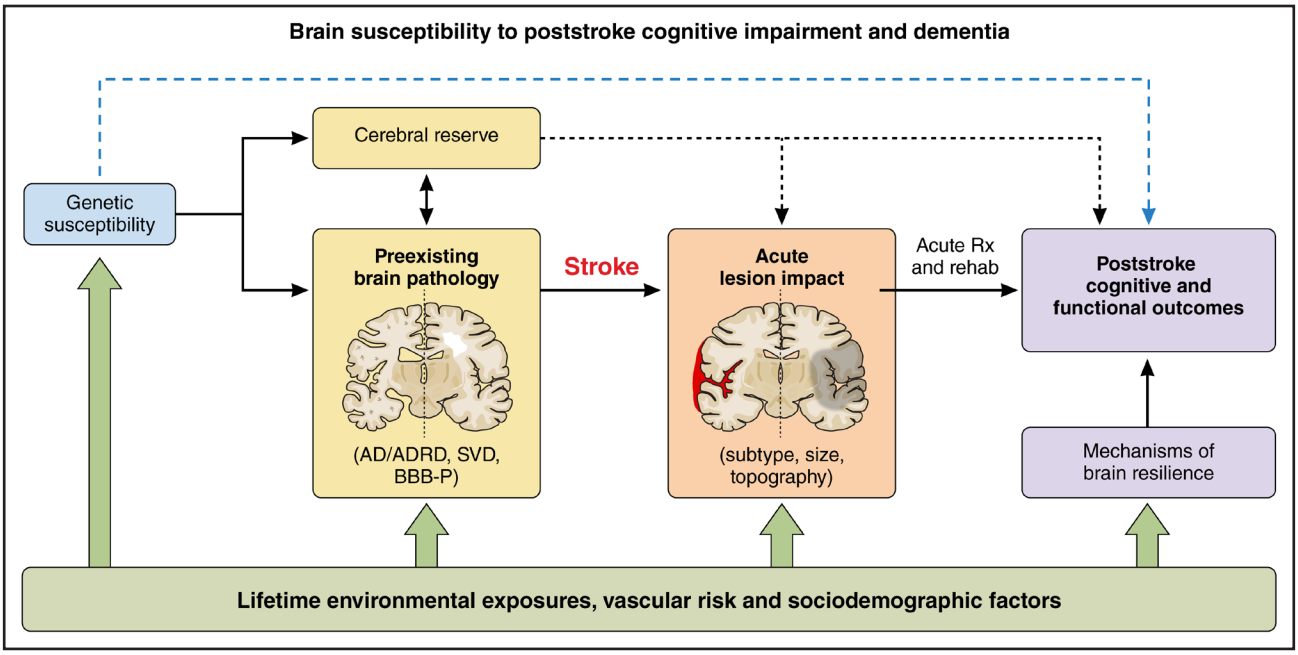

Figure 1. Brain susceptibility to PSCI and dementia.
Conceptual framework for factors contributing to the pathophysiology of poststroke cognitive impairment (PSCI). AD/ADRD indicates Alzheimer disease and related dementias; BBB-P, blood-brain barrier permeability; Rx, treatment; and SVD, small-vessel disease.

from larger, more destructive embolic infarcts. The exact pathophysiology of PSCI is not well understood given the paucity of knowledge about the effects of specific stroke subtypes (ie, acute ischemia, ICH, or aneurysmal SAH), as well as the variable contributions of the severity of the injury, the lesion location, and the interaction between the preexisting brain pathology and an acute stroke event, which may serve as a trigger for or accelerate cognitive decline in a vulnerable brain.[13,60] The constructs of brain reserve and brain resilience as they relate to brain health are evolving.[61,62] Brain reserve is the difference between the degree of brain damage observed in an individual and the clinical manifestation of that damage. Brain resilience is a combination of the capacity of the brain to counteract the lifetime accumulation of damage and the compensatory mechanisms that can be used to mitigate the effects of this damage.[61,62] It is likely that brain reserve and resilience and the factors contributing to them also play a role in the degree of cognitive impairment in the setting of stroke-related brain injury (Figure 1).

In most brains affected by stroke, there are diffuse age-related changes involving the smallest building block of the brain parenchyma, the neurovascular unit, which includes neurons, astrocytes, pericytes, microglia, and blood vessels.[63] The neurovascular unit is the key structural element of what has been called brain health, or the capacity of the brain to operate at its optimal state of structural and functional integrity, in the absence of or despite the impact of insidious or precipitous injuries related to cerebrovascular dysfunction, metabolic disarray, proteinopathies, or inflammatory responses.[64–67] The structural elements of the neurovascular unit are often damaged by stroke-related injury, possibly leading to PSCI (Figure 1).[61,62] However, the same elements can also be considered points of intervention for future treatments, rehabilitation, and prevention strategies involving lifetime environmental exposures, vascular risk factor modification, and even gene therapies.[68]

RISK FACTORS

Risk factors for PSCI reflect prestroke cognitive decline, preexisting cerebral vulnerability/reduced reserve, and the impact of the stroke; a minor stroke may precipitate dementia in an older person with a vulnerable brain.[16,20,36] Key vulnerability factors include age, cerebral small-vessel disease, and neurodegeneration, which may be partially mitigated by higher educational attainment and premorbid intelligence (indicators of cerebral reserve).[16,20,36] Comorbid poststroke depression is also an important factor associated with PSCI, and the 2 disorders frequently coexist, possibly through shared mechanisms. The risk associated with the effects of late-life vascular factors on early poststroke cognitive decline is unclear except for diabetes, which has been associated with an increased risk.[69] Strong social networks may be a protective factor, although evidence specifically in PSCI is sparse.

PSCI is more common with higher stroke lesion load such as in severe or recurrent strokes.[16,20,36] The risk of PSCI varies with stroke subtype (higher in hemorrhagic and cardioembolic stroke compared with lacunar stroke), likely driven partially by the corresponding stroke severity. Lesion location is important because risks are higher

 Stroke. 2023;54:e272–e291. DOI: 10.1161/STR.0000000000000430

in stroke affecting specific brain regions (see the Symptoms and Cognitive Domains Affected section).

In ICH, lobar location carries greater risk than deep location, likely because lobar hemorrhages are associated with underlying cerebral amyloid angiopathy.[25,70,71] In aneurysmal SAH, delayed cerebral ischemia and chronic hydrocephalus predict PSCI, but the underlying biological mechanisms remain poorly understood.[72] Compared with aneurysm coiling, aneurysm clipping in SAH may be associated with a higher rate of executive dysfunction and lower scores on language tests.[58] However, this may be confounded by other underlying patient characteristics.

Brain imaging findings (lesion volume, white matter hyperintensities, atrophy) are proxies for stroke severity and brain vulnerability, with lobar microbleeds and global small-vessel disease burden being important predictors of dementia after hemorrhagic stroke.[25,70,71,73] However, it remains unclear to what extent imaging biomarkers predict PSCI over and above clinical factors, including acute cognitive status (delirium, low cognitive test score), which is a powerful predictor capturing both prestroke decline and lesion impact.[16,36,71] Poststroke delirium is associated with higher risk for PSD and lower survival.[74] *APOE* ε4 homozygous genotype is a possible risk factor for prestroke dementia and PSD, accelerating early decline after major stroke and increasing the probability of later dementia after less severe events.[75]

Knowledge gaps remain, particularly in our understanding of the role of noncerebral factors, including infection, frailty, and social factors. Further studies are needed to understand the independent predictors of poststroke cognitive decline and whether blood and cerebrospinal fluid biomarkers and brain imaging add predictive value over clinical factors.

ASSOCIATION WITH OTHER POSTSTROKE OUTCOMES

PSCI is associated with other adverse outcomes, including physical disability, sleep disorders, depression, personality and behavioral changes, and other neuropsychological changes, all contributing to a lower quality of life.[76] Independently of the occurrence of PSCI, these outcomes are common after stroke (Figure 2).[44,76–82] Risk factors, including older age, stroke severity, history of stroke, multiple comorbidities, lower educational attainment, and social isolation, also overlap.[16,83] Coexisting adverse poststroke outcomes and multimorbidity can complicate timely diagnosis and effective treatment,[84] for example, the exacerbation of cognitive impairment after stroke attributable to undiagnosed depression.[15]

In patients with physical deficits after stroke, functional outcomes, measured with the modified Rankin Scale, Barthel Index, or assessment of activities of daily living, are directly affected by cognitive impairment in that patients with PSCI may have difficulty participating in rehabilitation and experiencing the full benefit of a rehabilitation program. Cognitive dysfunction, however, is not conditional on physical disability; PSCI may occur after mild stroke or transient ischemic attack.[8,16,20]

Along with a cognitive assessment after stroke, patients should be evaluated for problems with physical function, sleep, mood, anxiety, apathy, fatigue, and other personality and behavioral changes both in the acute stage and later during recovery. Although the association between these conditions and PSCI is incompletely understood, they all contribute to reduced quality of life in stroke survivors (Figure 2). Poor access to resources and stigma surrounding diagnoses of dementia, disability, and depression may impede care.[85]

Robust clinical trial data on the impact of neuropsychological treatments or sleep interventions on PSCI are lacking, although improving physical activity[86] and using an antidepressant[87] may provide small or short-term benefits in specific cognitive domains. Further research is needed to understand the effect of sleep interventions such as continuous positive airway pressure for sleep apnea on poststroke cognitive outcomes.[88] Research is also needed to determine the frequency of the co-occurrence of these sleep-related conditions in patients with PSCI.

SCREENING AND DIAGNOSTIC MODALITIES

Cognitive complaints, or subjective reports of cognitive decline, are common in patients after stroke[89,90] and are linked to objective cognitive impairment as determined by performance-based, standardized measures of cognitive function.[90–92] However, several factors affect patients' report of cognitive problems beyond the presence of objective cognitive dysfunction. Higher psychological distress (eg, depression, negative affect) has been linked to increased report of cognitive difficulties after stroke, independently of the severity of objective cognitive impairment.[89,93] Anosognosia, or lack of awareness of the presence or severity of a person's own cognitive deficits, often results in underreporting of cognitive problems.[94] Additional information can be gathered from collateral sources such as family members or caregivers. Informant report is specific but insensitive to PSCI and can be affected by interpersonal and cultural factors.[95] Thus, although the report of cognitive decline by patients and their informants is important, objective cognitive assessment is crucial to accurately identify cognitive dysfunction, particularly when anosognosia is present.

Although there is no gold standard for cognitive screening after stroke, several brief cognitive screening tests (≤30 minutes) have been used to identify PSCI.[96–100]

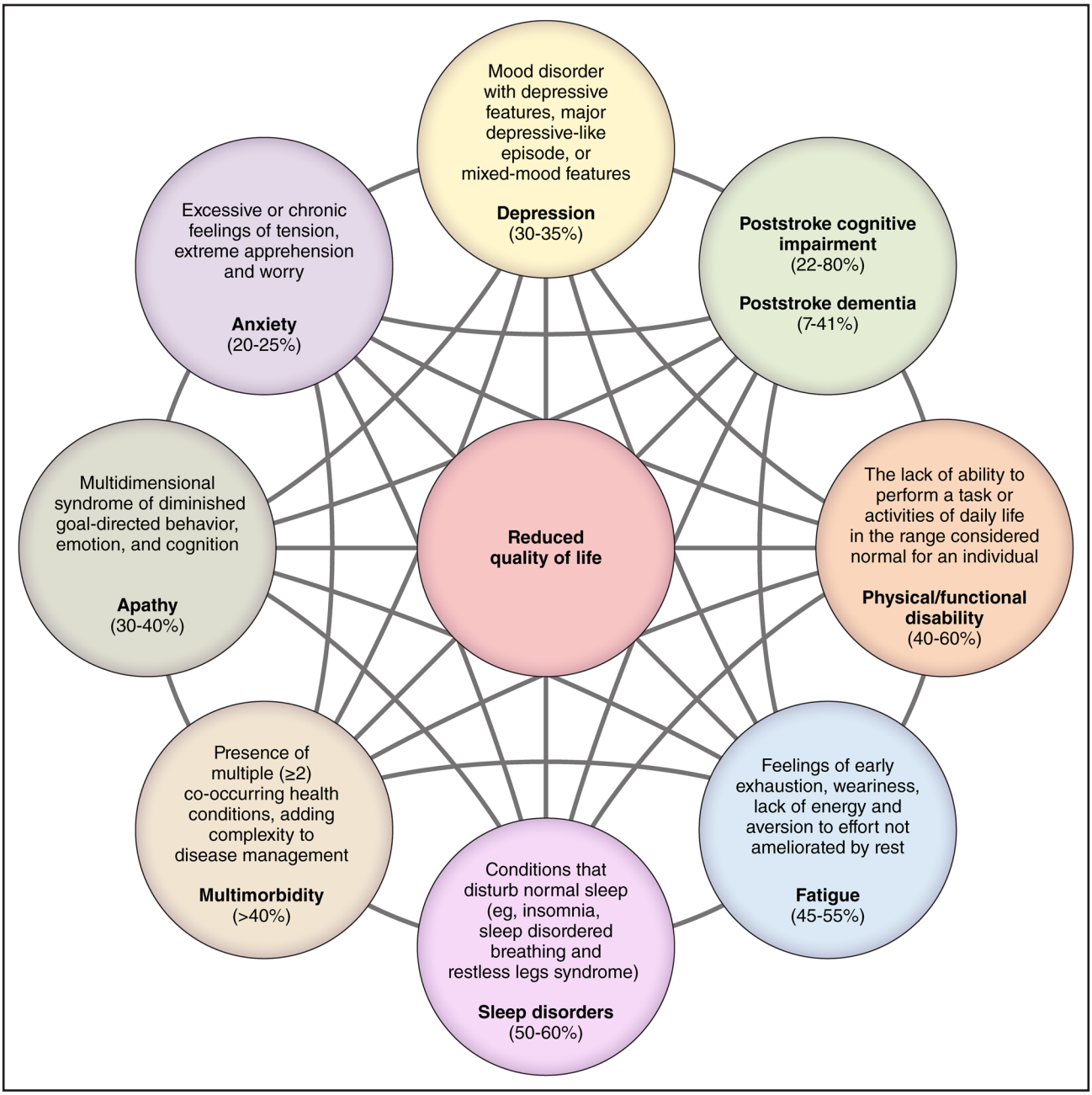

Figure 2. Comorbid conditions occurring in patients with PSCI and dementia contribute to reduced quality of life. Definitions of poststroke outcomes and their approximate incidence or prevalence (percent) within 12 months after stroke.
PSCI indicates poststroke cognitive impairment.

The Mini-Mental State Examination and the Montreal Cognitive Assessment have been the most widely studied cognitive screening instruments,[96,98,99] with the Montreal Cognitive Assessment generally being recommended over the Mini-Mental State Examination,[96,98,101] particularly in subacute phases after stroke,[100] because it has less of a ceiling effect and is more sensitive to mild cognitive impairment. However, several other cognitive screens show initial evidence for their utility in identifying cognitive impairment after stroke.[97–100] The choice of the best screening tool to use for a given patient will vary according to the psychometric properties of the test; demographic (age, sex, educational attainment), cultural, and language characteristics of the patient; circumstances of test administration (eg, time, bedside/clinic/telehealth); and the presence of other stroke-related impairments.[17]

Unfortunately, most screening instruments were not developed to identify the heterogeneous presentation of poststroke cognitive deficit and might miss subtle (yet impactful) poststroke cognitive changes. Furthermore, stroke-related impairments such as motor weakness,

unilateral neglect, and aphasia, as well as demographic factors such as education, language, or culture, may render standard cognitive screening tools inadequate.[104] Tailored comprehensive neuropsychological evaluations that use appropriate normative data; consider demographic (educational attainment, age, and sex), cultural, and linguistic factors; and account for stroke-related deficits may improve diagnostic accuracy, provide a thorough characterization of the patient's cognitive strengths and weaknesses, and identify mild cognitive changes over time.

Early detection of cognitive impairment in the acute stroke unit is essential for informing interventions and for discharge planning; the natural history of PSCI indicates that it is also important to assess for cognitive changes over time. However, the comparative effectiveness of different screening strategies—including whom to screen, when, and how often—has not been evaluated in prospective clinical trials. There are potential downsides to screening, including cost and the potential to falsely label patients as having cognitive impairment on the basis of low test scores from confounding factors such as cultural bias, education bias, test anxiety, or administration in a second language. False-positive diagnoses can cause harm by inducing psychological distress or reducing patient autonomy, for example, by leading to loss of the license to drive or the ability to independently manage financial affairs. These uncertainties notwithstanding, which should be addressed in future research, it is unquestionably necessary to screen whenever there is a cognitive complaint or clinician concern about cognitive ability. Clinician concern should be triggered by unexplained patient difficulties with cognitive-related activities of daily living, following clinician instructions, or providing a reliable history. Stroke systems of care need to be resourced to provide cognitive screening and assessment in patients at risk, including sufficient time for cognitive screens, if indicated, and health care professionals to follow up with detailed assessments and plans for accommodation and rehabilitation.

MANAGEMENT OF PSCI

Interdisciplinary Collaboration

Collaboration among physicians, including neurologists, gerontologists, and primary care physicians, speech language pathologists, occupational therapists, neuropsychologists, nurses, and related health professionals is crucial throughout levels of poststroke care for the optimal identification and management of cognitive problems after stroke. A tailored neuropsychological evaluation is best suited to thoroughly characterize cognitive strengths and weaknesses, which is important for optimal management of PSCI. This also will aid in individualizing care tailored to the patient's needs, such that involvement of all disciplines is not needed for all patients.

For example, speech-language pathologists can identify and treat cognitive and communication deficits after stroke (and dysphagia). Occupational therapists can further evaluate and manage the functional impact of cognitive problems in patients' daily activity contexts. A streamlined, interdisciplinary model of care beyond the acute and subacute phases after stroke is needed for optimal monitoring and management of cognitive deficits. Telehealth services might be a useful tool to implement such a model, provided that barriers to these services are addressed.[105] Although referral patterns differ depending on local resources and expertise, Figure 3 provides a decision tree to help guide collaborations among relevant health care services, particularly in the process of screening and diagnosis of PSCI in postacute care settings, as comprehensive and evidence-based postacute care models are developed. The team composition should be tailored to the symptoms and needs of the individual patient.

Cognitive Rehabilitation

In general, cognitive rehabilitation (including restorative cognitive training and functional cognitive rehabilitation) after stroke results in small improvements in cognitive functioning compared with control conditions (treatment as usual or active sham intervention).[106] Small gains, both immediate and sustained, occur in several cognitive areas (attention, memory, executive function) and visuospatial neglect. Specifically, memory gains occur with strategy training,[107–109] but attention training does not produce consistent benefits.[110,111] Benefits of computerized cognitive training (eg, engaging and gamified cognitive exercises accessed from the patients' own computers or mobile devices) over standard cognitive rehabilitation are inconsistent but tend to be better with clinician-directed programs.[112–115] Emerging evidence, albeit from small or lower-quality studies,[116] suggests potential cognitive benefits of virtual reality tools[117–119] and training and education for family and patients.[120–122]

Physical Activity

Physical activity may have a positive impact on cognitive function after stroke, with a possible advantage for aerobic compared with nonaerobic exercise.[123–125] Small studies suggest cognitive benefits of specific forms of physical activity such as tai chi,[126] boxing,[127] and resistance exercises.[128] Evidence for the added benefit of using virtual reality with physical activity is inconclusive.[129,130]

Medical and Pharmacological Treatments

Because the risk of PSCI increases with stroke recurrence, secondary stroke prevention, including

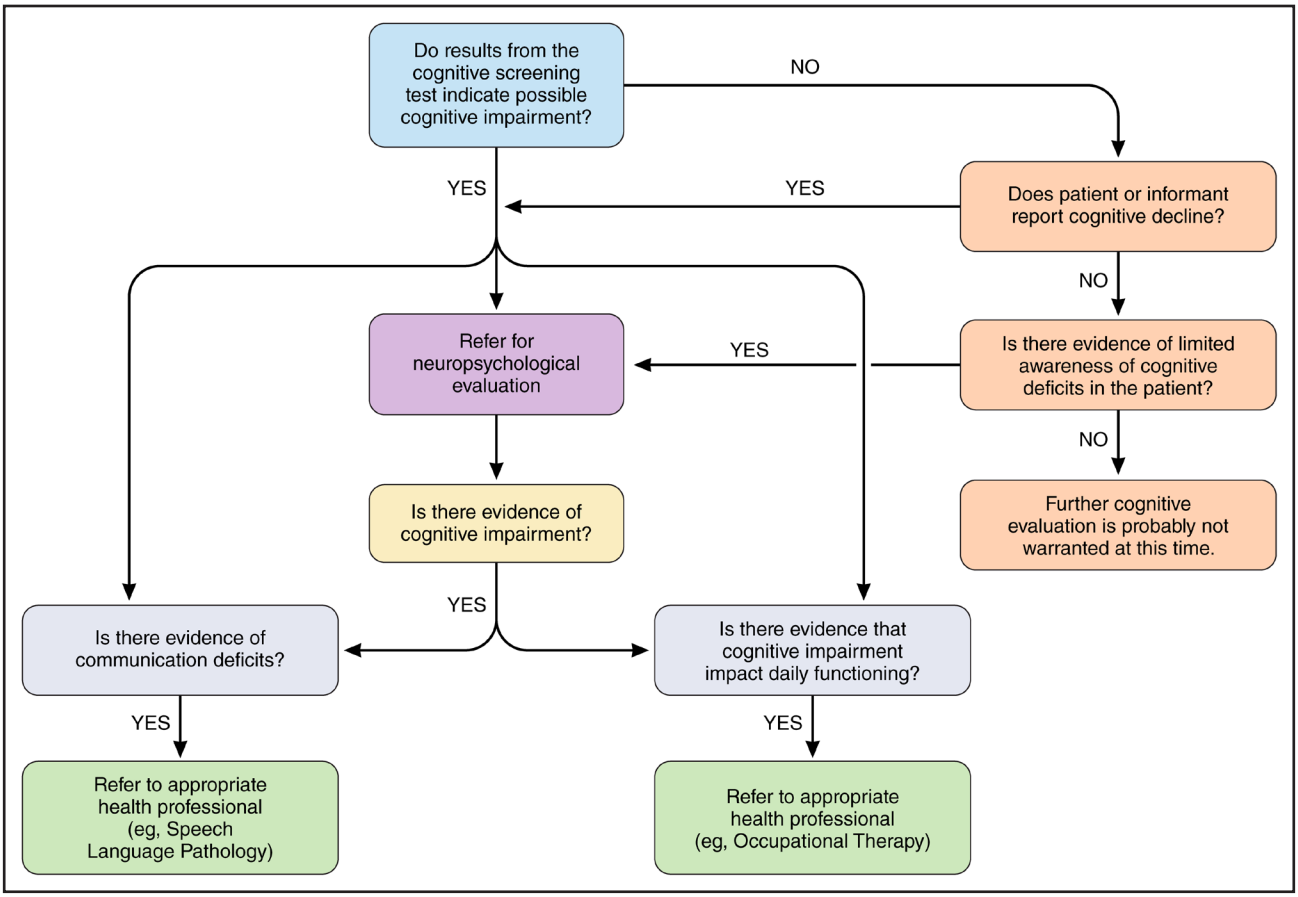

Figure 3. Considerations for assessment and multidisciplinary evaluation of PSCI. PSCI indicates poststroke cognitive impairment.

antihypertensive therapy, statins, diabetes control, and anticoagulation for atrial fibrillation, is an important approach to prevent the risk for or worsening of PSCI.[131] Treatments for hypertension and lifestyle programs to reach target blood pressure after stroke have to date failed to show positive impacts on cognitive function.[132,133] Current evidence is insufficient to prove whether some antihypertensive drug classes are better than others at preserving cognition.[134] Nonetheless, hypertension treatment reduces the risk of incident and recurrent strokes, which are risk factors for PSCI. In the general population, blood pressure lowering with antihypertensive agents compared with control is associated with a reduced risk of cognitive impairment and incident dementia.[135,136] More research is needed to close the gaps in the disparities in hypertension control that extend beyond lifestyle factors and the effect of this on the incidence and progression of PSCI.

There are knowledge gaps in the effect of interventions for smoking, obesity, diabetes, hyperlipidemia, and obstructive sleep apnea for reducing the risk of PSCI, although they are generally considered to be additional important modifiable risk factors for preventing cognitive decline.[137] Simultaneous treatment of multiple vascular risk factors compared with only one or few was associated with a slower cognitive decline in a cohort of patients with AD and could improve or maintain cognitive functioning in at-risk elderly people from the general population.[138,139] Similar studies of multiple simultaneous interventions are needed in patients with PSCI.

Because cognitive outcome has traditionally not been considered an outcome measure in randomized trials investigating the benefit of acute stroke treatments, limited evidence exists with regard to their effect on cognition, although it is postulated that PSCI would be decreased because of a reduction in acute lesion size and improved functional outcome. The few studies that evaluated cognitive outcomes after acute stroke treatments suggest that intravenous thrombolysis and mechanical thrombectomy improve cognitive outcomes (compared with no treatment) but that these benefits are strongly associated with functional outcome.[140–142]

Systematic reviews of dopamine agonists[143] and selective serotonin reuptake inhibitors[144–146] show no consistent beneficial effects on cognition after stroke. Individual small clinical trials have reported various pharmaceutical agents that may have a potential benefit

on global cognition: neurotrophics (Cortexin),[147] peptides such as Cerebrolysin[148] and relaxin,[149] citicoline (cytidine-5′-diphosphocholine),[150] and nitrates (glyceryl trinitrate).[151] Specific pharmaceuticals may affect defined aspects of cognition, including the effects of dopamine agonists on hemi-inattention[152] and selegiline on attention and executive function.[153]

Cholinesterase inhibitors (eg, donepezil, rivastigmine, and galantamine) and memantine, an *N*-methyl D-aspartate receptor antagonist, are sometimes prescribed for patients with dementia after stroke, although more work is needed to define the safety and efficacy of these drugs in this population.[154,155] Randomized trials provide moderate-quality evidence for small improvements in cognition, of uncertain clinical relevance, with donepezil, rivastigmine, galantamine, or memantine; however, they are complicated by adverse events (including dizziness and diarrhea) and patient discontinuation.[156]

Emerging, Complementary, and Integrative Treatments

Small studies have shown the benefits of remote ischemic conditioning for visuospatial, attention, and executive functions[157] and long-term (>6 months) global cognition.[158] Further confirmatory studies with larger samples are warranted.[159] Several studies suggest potential benefit from transcranial magnetic stimulation and transcranial direct current stimulation (tDCS).[160,161] In a meta-analysis of 15 studies (N=820 participants) of tDCS, compared with sham tDCS or control, anodal tDCS was associated with a small improvement in the general cognitive and attention performance but not with memory.[160] Most of these studies, however, were of lower methodological quality and lacked sham tDCS and safety data.[160] Well-designed studies are needed to determine the potential benefits of neuromodulation in the treatment of poststroke cognitive deficits and to establish the optimal treatment protocols.[160] Acupuncture treatments may also have a positive effect on global cognition.[162–164] However, a meta-analysis suggests that the majority of these studies were of low quality.[164] The combination of acupuncture with other therapies (eg, cognitive or physical rehabilitation) may enhance the benefits of either alone.[165,166]

Preliminary and exploratory studies suggest potential cognitive benefits from various herbal treatments and vitamins, including huperzine A,[167] depsides salts from Salvia miltiorrhiza,[168] ginkgo biloba,[169] pomegranate polyphenols,[170] and Cerebralcare Granule,[171] but no benefits from mailuoning,[172] folic acid, and B vitamins.[173] None of these are approved by the US Food and Drug Administration for use in PSCI. Last, there is a paucity of randomized studies on the potential effects of heart-healthy diets (eg, DASH [Dietary Approaches to Stop Hypertension] diet, Mediterranean diet, MIND [Mediterranean-DASH Intervention for Neurodegenerative Delay] diet) on cognition after stroke.

ANTICIPATORY GUIDANCE FOR PATIENTS AND THEIR CAREGIVERS

Actionable Considerations for the Clinician When Cognitive Impairment Is Detected on Screening

Stroke survivors with dementia are at higher risk of death, disability, and institutionalization.[174] When cognitive impairment is detected on screening, comprehensive cognitive evaluation such as a battery of standardized neuropsychological assessments can further help characterize impaired cognitive domains.[175] In addition to the management of poststroke cognitive deficits described previously, other considerations include assessing for safety issues in the home environment, return to work (if applicable), and driving, as well as assessing for caregiver fatigue and connecting patients and caregivers with available community resources when possible. Advance care planning, including personal medical directives and identifying an enduring power of attorney, should also be considered.

Home Safety

Recommendations for home safety after stroke are related predominantly to the ability to perform daily activities of living as a result of limitations in mobility and cognition. The most common issues in the home environment for stroke survivors are using the bathroom and having limited mobility and communication.[176] Examples of recommendations for these issues include providing appropriate equipment for mobility, installing grab bars or raising toilet seats in the bathroom, and establishing a personal emergency system for simplified access to immediate help.[176] Impaired cognition is also associated with falls, and the majority of falls occur at home.[177] To ensure home safety, health care professionals need to assess the home environment, identify home safety issues, and provide appropriate recommendations to stroke survivors and their caregivers. Transitional care processes, especially those that are more intensive, may increase home safety and reduce hospital readmission rates.[178]

Return to Work

Evidence for a relationship between cognitive function and return to work after a stroke comes primarily from

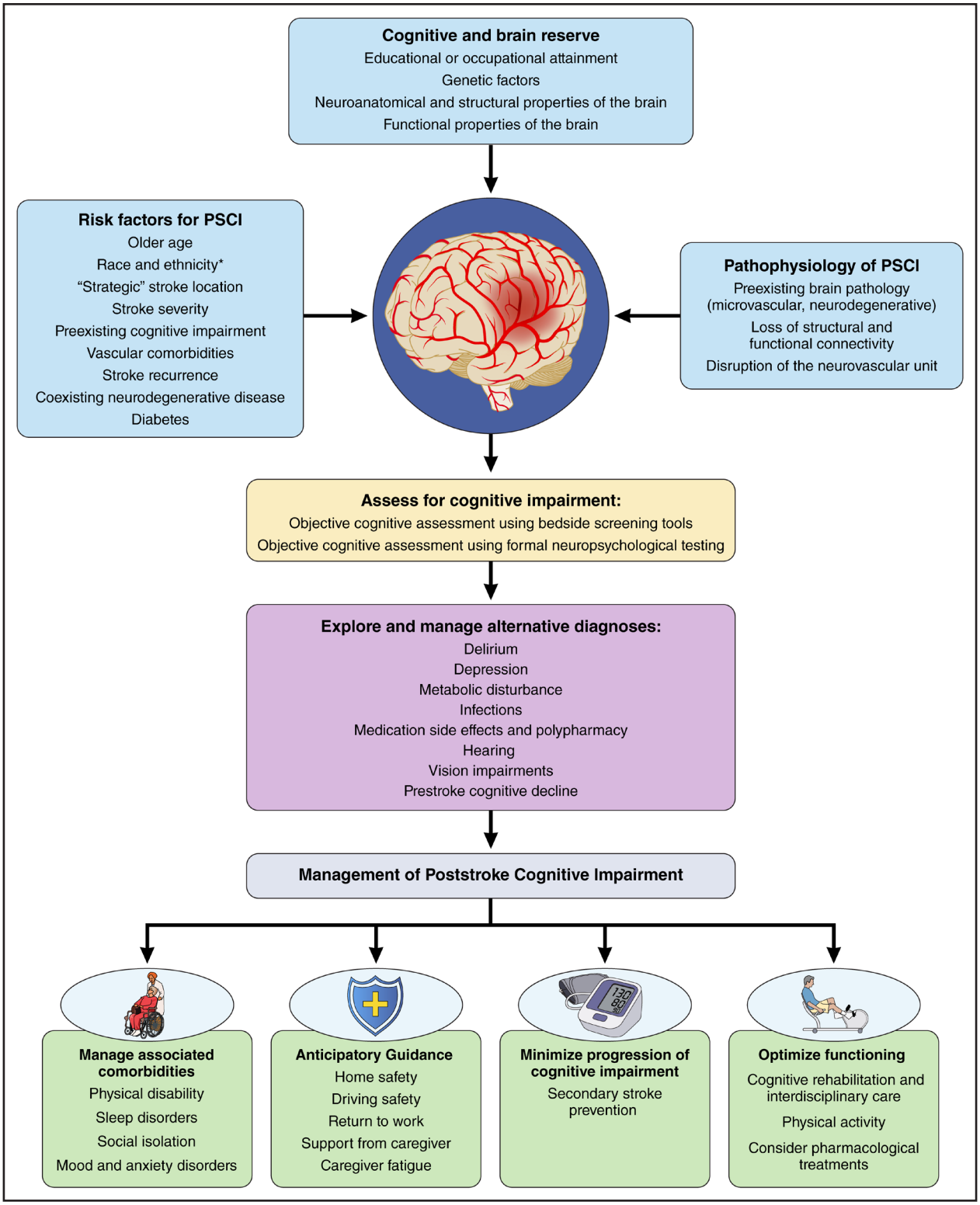

Figure 4. Summary of contributing factors, differential, and considerations for management of PSCI.
PSCI indicates poststroke cognitive impairment.
*For example, in the United States, Black individuals are at higher risk than White individuals.

prospective observational studies. Deficits in global cognitive function[179] and specifically executive function[180] are negatively related to return to work. The risk of cognitive decline at 1 year after stroke is higher for people who were not employed before the stroke and for those who did not return to mentally stimulating jobs after a stroke.[181] Qualitative studies consistently indicate that lack of knowledge of or support for invisible deficits such

Table 1. Considerations for Clinical Practice and Gaps Needing Additional Studies According to Section

Section	Suggestions for clinical practice	Gaps
Prevalence and incidence	There is substantial heterogeneity in the reported prevalence of PSCI explained mostly by the cohort selection criteria. PSCI is most common in the first year after stroke, occurring in up to 60% of stroke survivors: About 38% have mild cognitive impairment, and 7%-41% have dementia.	Estimates of incidence adjusted for competing risk of death, overall and in specific subgroups, including people of underrepresented races and ethnicities and women.
Natural history	PSCI tends to improve over time, with most recovery occurring within the first 3 to 6 mo.	Individual poststroke cognitive trajectories
Delayed-onset cognitive impairment after stroke	Late PSD (onset >3–6 mo after the stroke) occurs in ≈1.7% of stroke survivors per year.	Characterization of the types of late PSD When reporting on delayed-onset cognitive impairment, studies should exclude those with impairment before 3 to 6 mo from the stroke and thus not report the cumulative incidence of cognitive impairment that combines early and delayed onset.
Differential diagnosis	Differential diagnosis: Prestroke cognitive decline Coexisting age-related neuropathologies (example AD) Effects of medical conditions and complications, such as metabolic abnormalities, medication side effects, infections, delirium, sleep disorders, hearing and vision impairments, and depression	Whether fluid (blood/CSF) and imaging biomarkers should be used to assist with the diagnosis of PSCI
Symptoms and cognitive domains affected	Cognitive deficits can be global or limited to specific domains.	Better understanding of how stroke location and size interact with cognitive reserve to cause PSCI with different severities and cognitive profiles.
Pathophysiology	Stroke-related injury to the neurovascular unit, secondary neurodegeneration, and loss of structural and functional connectivity	Better understanding of the mechanisms of PSCI and the effects of specific stroke subtypes (ie, acute ischemia, ICH, or aneurysmal SAH), as well as stroke severity, lesion location, and the complex interaction between the preexisting brain pathology and the acute stroke event.
Risk factors	Risk of cognitive decline is determined by the stroke lesion and cerebral vulnerability/reserve. Key risk factors: older age, prestroke cognitive decline, preexisting white matter disease or neurodegeneration, diabetes, stroke severity, prior/recurrent stroke, stroke location, and acute cognitive status	The role of noncerebral factors, including infection, frailty, and social factors, and the added value of blood, CSF, and brain imaging biomarkers in risk stratification.
Association with other poststroke outcomes	PSCI is associated with other adverse outcomes, including physical disability, sleep disorders, behavioral and personality changes, depression, and other neuropsychological changes, all leading to lower quality of life.	The association and frequency of co-occurrence of PSCI with other poststroke outcomes, including anxiety, apathy, and fatigue. The effect of sleep interventions and treatment of comorbid depression and anxiety on poststroke cognitive outcomes.
Screening and diagnostic modalities in the clinic	Tailored neuropsychological evaluations improve diagnostic accuracy for cognitive impairment after stroke and provide a thorough characterization of the patient's cognitive strengths and weaknesses.	Optimal timing for screening for PSCI, best screening tools, and whether screening affects patient outcomes. Optimal testing to assess the additional impact of stroke on cognitive impairment in individuals who already have a history of dementia. Development of cognitive assessments that can be practically used by busy clinicians and that would capture the heterogeneous nature of PSCI, including in patients with impaired language function.
Management	Interdisciplinary collaboration is essential for the optimal identification and management of PSCI. Clinician-directed behavioral cognitive rehabilitation and physical activity are likely beneficial for poststroke cognition. There are no consistently positive effects of pharmaceutical agents for poststroke cognition, although individual small studies show some benefits.	The impact of heart-healthy diets and of simultaneous treatments of vascular risk factors, as well as management of stroke complications (eg, physical disability, depression, sleep apnea) on poststroke cognitive function. Well-designed studies of pharmacological and nonpharmacological treatments (eg, ischemic conditioning, neuromodulation, and acupuncture) aimed to improve poststroke cognitive function.
Anticipatory guidance	Comprehensive cognitive evaluation with considerations for pharmacological and nonpharmacological treatments, management of stroke risk factors to prevent stroke recurrence, targeting of high-risk populations, evaluation for comorbid complications, and assessment of home safety, driving, and return to work (if applicable) are warranted.	Evaluation of the benefit of multidisciplinary clinics for individuals with stroke and cognitive impairment on quality of life, cognitive function, caregiver burden, and functional outcome.

AD indicates Alzheimer disease; CSF, cerebrospinal fluid; ICH, intracranial hemorrhage; PSCI, poststroke cognitive impairment; PSD, poststroke dementia; and SAH, subarachnoid hemorrhage.

as cognitive impairments is a deterrent to returning to work or maintaining a job after returning to work.[182–184] Return to work may be facilitated by cognitive or vocational rehabilitation.[185]

Driving

In many cultures, driving is a sign of independence, has a strong impact on quality of life, and may be necessary for work or for socializing. After a stroke, approximately one-third of patients require some type of training or rehabilitation to return to driving.[186] Cognitive abilities have been linked to success on driving tests. However, a systematic review of 53 studies did not find strong evidence to recommend any one cognitive assessment tool over another.[187] Although inconsistencies in the methodologies and results of these studies prevent strong conclusions, better attention and executive function are most often related to a return to driving.[188,189] Various training programs exist, although many do not encompass all of the components that affect successful driving (eg, cognitive function, sensory perception, mobility, motivation).[186] A systematic review of 4 randomized controlled trials with 245 participants reported no improvements in on-road performance or any cognitive function after a driving intervention, although driving simulations may be more effective than other training programs.[190]

CONCLUSIONS AND FUTURE DIRECTIONS

PSCI is common and contributes to the poorer health status of stroke survivors. It often occurs in the presence of a variety of stroke-related deficits and other comorbid conditions such as depression, adding complexity to both its diagnosis and its treatment. Management requires a multipronged approach that includes evaluation and management of comorbid conditions, anticipatory guidance for matters such as home safety and driving, implementation of secondary stroke prevention strategies to minimize the progression of cognitive impairment, and administration of treatments to optimize functioning and improve cognition (Figure 4). Thus, the comprehensive management of patients with PSCI should involve an interdisciplinary collaboration of the patient and their caregivers with health professionals, including neurologists, occupational therapists, speech therapists, nurses, neuropsychologists, gerontologists, and primary care physicians. Given the prevalence of PSCI and its association with poor health-related outcomes, the implementation of protocols to systematically evaluate and treat PSCI based on locally available resources is warranted.

As outlined in the Table 1, there are multiple unanswered questions about the pathophysiology, diagnosis, and treatment of PSCI. More studies are needed on the exact mechanisms of PSCI, the effects of specific stroke subtypes, and the interaction among the preexisting brain pathology, sociocultural factors, and the acute stroke event. The DISCOVERY study (Determinants of Incident Stroke Cognitive Outcomes and Vascular Effects on Recovery), is an ongoing prospective, multicenter, observational, nested-cohort study of 8000 patients with ischemic and hemorrhagic stroke without history of dementia enrolled at the time of index stroke from 30 clinical sites across the United States and followed up for a minimum of 2 years with serial cognitive evaluations and assessments of functional outcome. Subsets are undergoing research magnetic resonance imaging, positron emission tomography, and comprehensive genetic/genomic and fluid biomarker testing. The overall scientific objective of this study is to elucidate mechanisms of brain resilience and susceptibility to PSCI in diverse US populations.[13] Future research might inform best practices for cognitive screening after stroke. Perhaps the most pressing need, however, is the development of effective and culturally relevant treatments for PSCI through the conduct of adequately powered clinical trials of cognitive rehabilitative techniques, pharmaceutical agents, and lifestyle modifications in diverse groups of patients. Along with this, studies are required to evaluate whether multidisciplinary clinics or other models of care improve outcomes for patients with PSCI. Given the significant contribution of PSCI to the growing burden of dementia, focusing on these unanswered questions should be considered a priority.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

This statement was approved by the American Heart Association Science Advisory and Coordinating Committee on November 15, 2022, and the American Heart Association Executive Committee on December 13, 2022. A copy of the document is available at https://professional.heart.org/statements by using either "Search for Guidelines & Statements" or the "Browse by Topic" area. To purchase additional reprints, call 215-356-2721 or email Meredith.Edelman@wolterskluwer.com.

The American Heart Association requests that this document be cited as follows: El Husseini N, Katzan IL, Rost NS, Blake ML, Byun E, Pendlebury ST, Aparicio HJ, Marquine MJ, Gottesman RF, Smith EE; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Cardiovascular Radiology and Intervention, Council on Hypertension, and Council on Lifestyle and Cardiometabolic Health. Cognitive impairment after ischemic and hemorrhagic stroke: a scientific statement from the American Heart Association/American Stroke Association. *Stroke.* 2023;54:e272–e291. doi: 10.1161/STR.0000000000000430

The expert peer review of AHA-commissioned documents (eg, scientific statements, clinical practice guidelines, systematic reviews) is conducted by the AHA Office of Science Operations. For more on AHA statements and guidelines development, visit https://professional.heart.org/statements. Select the "Guidelines & Statements" drop-down menu, then click "Publication Development."

Disclosures

Writing Group Disclosures

Writing group member	Employment	Research grant	Other research support	Speakers' bureau/ honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Nada El Husseini	Duke University Medical Center	Site PI, NIA/NINDS U19NS115388*	None	None	None	None	None	None
Irene L. Katzan	Cleveland Clinic	None	None	None	None	None	None	None
Hugo J. Aparicio	Boston University School of Medicine	American Academy of Neurology (AAN Career Development Award, principal investigator)†; NIH (awardee, National Institute of Neurological Disorders and Stroke, NIH Loan Repayment Program L30 NS093634)*; NIH (National Institute on Aging R01AG066524 coinvestigator)*; Alzheimer's Association (Alzheimer's Association Research Grant [AARGD-20-685362], principal investigator)*; Boston University (Boston University's Aram V. Chobanian Assistant Professorship)†	None	None	None	None	None	None
Margaret Lehman Blake	University of Houston	NIH/NIDCD (R01 research grant)*	None	Academy of Neurologic Communication Disorders & Sciences*	None	None	ANCDS (unpaid)*	None
Eeeseung Byun	University of Washington	NIH/NINR (PI for K23NR017404 grant)*; NIH/NIA (pilot project PI for P30AG059304 grant)*; University of Washington Population Health Initiative Tier 1 pilot grant (PI)*	None	None	None	None	None	None
Rebecca F. Gottesman	National Institutes of Health/National Institute of Neurological Disorders and Stroke	None	None	None	None	None	None	None
Maria J. Marquine	University of California, San Diego	NIH (PI of R01MD013502, R01AG070956 and K24AG075240)†	None	None	Federal Defenders Office*	None	None	None
Sarah T. Pendlebury	Wolfson Centre for Prevention of Stroke and Dementia (United Kingdom)	NIHR Oxford Biomedical Research Centre (support for studies on delirium and dementia)†; John Fell Fund (brain imaging algorithm development)†; RCF funding (brain imaging studies)†; RCF funding (decision-making capacity)†	None	None	None	None	Consultancy*	None
Natalia S. Rost	Harvard Medical School	NINDS (U19NS115388, Rost–PI)†	None	None	None	None	None	None
Eric E. Smith	University of Calgary (Canada)	None	None	None	None	None	None	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

*Modest.

†Significant.

Reviewer Disclosures

Reviewer	Employment	Research grant	Other research support	Speakers' bureau/honoraria	Expert witness	Ownership interest	Consultant/ advisory board	Other
Alexa S. Beiser	Boston University School of Public Health	None	None	None	None	None	None	None
Cheryl Bushnell	Wake Forest School of Medicine	None	None	None	None	None	None	None
Saurav Das	University of Kentucky College of Medicine	None	None	None	None	None	None	None
Mary G. George	Eagle Global Scientific LLC	None	None	None	None	None	None	None
Yorito Hattori	National Cerebral and Cardiovascular Center (Japan)	None	None	None	None	None	None	None
Linda S. Williams	Roudebush VA Medical Center	None	None	None	None	None	None	None

This table represents the relationships of reviewers that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all reviewers are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives $5000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns $5000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it is less than "significant" under the preceding definition.

REFERENCES

1. Douiri A, Rudd AG, Wolfe CD. Prevalence of poststroke cognitive impairment: South London Stroke Register 1995-2010. *Stroke*. 2013;44:138–145. doi: 10.1161/STROKEAHA.112.670844
2. Jacquin A, Binquet C, Rouaud O, Graule-Petot A, Daubail B, Osseby GV, Bonithon-Kopp C, Giroud M, Bejot Y. Post-stroke cognitive impairment: high prevalence and determining factors in a cohort of mild stroke. *J Alzheimers Dis*. 2014;40:1029–1038. doi: 10.3233/JAD-131580
3. Lo JW, Crawford JD, Desmond DW, Godefroy O, Jokinen H, Mahinrad S, Bae HJ, Lim JS, Kohler S, Douven E, et al; Stroke and Cognition (STROKOG) Collaboration. Profile of and risk factors for poststroke cognitive impairment in diverse ethnoregional groups. *Neurology*. 2019;93:e2257–e2271. doi: 10.1212/WNL.0000000000008612
4. Ihle-Hansen H, Thommessen B, Wyller TB, Engedal K, Oksengard AR, Stenset V, Loken K, Aaberg M, Fure B. Incidence and subtypes of MCI and dementia 1 year after first-ever stroke in patients without pre-existing cognitive impairment. *Dement Geriatr Cogn Disord*. 2011;32:401–407. doi: 10.1159/000335361
5. Rasquin SM, Lodder J, Verhey FR. Predictors of reversible mild cognitive impairment after stroke: a 2-year follow-up study. *J Neurol Sci*. 2005;229–230:21–25. doi: 10.1016/j.jns.2004.11.015
6. Dichgans M, Leys D. Vascular cognitive impairment. *Circ Res*. 2017;120:573–591. doi: 10.1161/CIRCRESAHA.116.308426
7. Sivakumar L, Kate M, Jeerakathil T, Camicioli R, Buck B, Butcher K. Serial Montreal Cognitive Assessments demonstrate reversible cognitive impairment in patients with acute transient ischemic attack and minor stroke. *Stroke*. 2014;45:1709–1715. doi: 10.1161/STROKEAHA.114.004726
8. Pendlebury ST, Wadling S, Silver LE, Mehta Z, Rothwell PM. Transient cognitive impairment in TIA and minor stroke. *Stroke*. 2011;42:3116–3121. doi: 10.1161/STROKEAHA.111.621490
9. Gorelick PB, Scuteri A, Black SE, Decarli C, Greenberg SM, Iadecola C, Launer LJ, Laurent S, Lopez OL, Nyenhuis D, et al; on behalf of the 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. doi: 10.1161/STR.0b013e3182299496
10. Quinn TJ, Richard E, Teuschl Y, Gattringer T, Hafdi M, O'Brien JT, Merriman N, Gillebert C, Huyglier H, Verdelho A, et al. European Stroke Organisation and European Academy of Neurology joint guidelines on post-stroke cognitive impairment. *Eur Stroke J*. 2021;6:I–XXXVIII. doi: 10.1177/23969873211042192
11. van der Flier WM, Skoog I, Schneider JA, Pantoni L, Mok V, Chen CLH, Scheltens P. Vascular cognitive impairment. *Nat Rev Dis Primers*. 2018;4:18003. doi: 10.1038/nrdp.2018.3
12. Rosenberg GA, Wallin A, Wardlaw JM, Markus HS, Montaner J, Wolfson L, Iadecola C, Zlokovic BV, Joutel A, Dichgans M, et al. Consensus statement for diagnosis of subcortical small vessel disease. *J Cereb Blood Flow Metab*. 2016;36:6–25. doi: 10.1038/jcbfm.2015.172
13. Rost NS, Meschia JF, Gottesman R, Wruck L, Helmer K, Greenberg SM; DISCOVERY Investigators. Cognitive impairment and dementia after stroke: design and rationale for the DISCOVERY study. *Stroke*. 2021;52:e499–e516. doi: 10.1161/STROKEAHA.120.031611
14. Sun JH, Tan L, Yu JT. Post-stroke cognitive impairment: epidemiology, mechanisms and management. *Ann Transl Med*. 2014;2:80. doi: 10.3978/j.issn.2305-5839.2014.08.05
15. Tang EY, Amiesimaka O, Harrison SL, Green E, Price C, Robinson L, Siervo M, Stephan BC. Longitudinal effect of stroke on cognition: a systematic review. *J Am Heart Assoc*. 2018;7:e006443. doi: 10.1161/JAHA.117.006443
16. Pendlebury ST, Rothwell PM. Prevalence, incidence, and factors associated with pre-stroke and post-stroke dementia: a systematic review and meta-analysis. *Lancet Neurol*. 2009;8:1006–1018. doi: 10.1016/S1474-4422(09)70236-4
17. Quinn TJ, Elliott E, Langhorne P. Cognitive and mood assessment tools for use in stroke. *Stroke*. 2018;49:483–490. doi: 10.1161/STROKEAHA.117.016994
18. Sexton E, McLoughlin A, Williams DJ, Merriman NA, Donnelly N, Rohde D, Hickey A, Wren MA, Bennett K. Systematic review and meta-analysis of the prevalence of cognitive impairment no dementia in the first year post-stroke. *Eur Stroke J*. 2019;4:160–171. doi: 10.1177/2396987318825484
19. Aam S, Einstad MS, Munthe-Kaas R, Lydersen S, Ihle-Hansen H, Knapskog AB, Ellekjaer H, Seljeseth Y, Saltvedt I. Post-stroke cognitive impairment: impact of follow-up time and stroke subtype on severity and cognitive profile: the NorCOAST Study. *Front Neurol*. 2020;11:699. doi: 10.3389/fneur.2020.00699
20. Pendlebury ST, Rothwell PM; Oxford Vascular Study. Incidence and prevalence of dementia associated with transient ischaemic attack and stroke: analysis of the population-based Oxford Vascular Study. *Lancet Neurol*. 2019;18:248–258. doi: 10.1016/S1474-4422(18)30442-3
21. Koton S, Pike JR, Johansen M, Knopman DS, Lakshminarayan K, Mosley T, Patole S, Rosamond WD, Schneider ALC, Sharrett AR, et al. Association of ischemic stroke incidence, severity, and recurrence with dementia in the Atherosclerosis Risk in Communities cohort study. *JAMA Neurol*. 2022;79:271–280. doi: 10.1001/jamaneurol.2021.5080
22. Levine DA, Wadley VG, Langa KM, Unverzagt FW, Kabeto MU, Giordani B, Howard G, Howard VJ, Cushman M, Judd SE, et al. Risk factors for poststroke cognitive decline: the REGARDS study (Reasons for Geographic and Racial Differences in Stroke). *Stroke*. 2018;49:987–994. doi: 10.1161/STROKEAHA.117.018529
23. Clark DG, Boan AD, Sims-Robinson C, Adams RJ, Amella EJ, Benitez A, Lackland DT, Ovbiagele B. Differential impact of index stroke on dementia risk in African-Americans compared to Whites. *J Stroke Cerebrovasc Dis*. 2018;27:2725–2730. doi: 10.1016/j.jstrokecerebrovasdis.2018.05.048
24. Banerjee G, Wilson D, Ambler G, Osei-Bonsu Appiah K, Shakeshaft C, Lunawat S, Cohen H, Yousry TD, Lip GYH, Muir KW, et al; CROMIS-2 Collaborators. Cognitive impairment before intracerebral hemorrhage is associated with cerebral amyloid angiopathy. *Stroke*. 2018;49:40–45. doi: 10.1161/STROKEAHA.117.019409
25. Moulin S, Labreuche J, Bombois S, Rossi C, Boulouis G, Henon H, Duhamel A, Leys D, Cordonnier C. Dementia risk after spontaneous intracerebral haemorrhage: a prospective cohort study. *Lancet Neurol*. 2016;15:820–829. doi: 10.1016/S1474-4422(16)00130-7

26. Mayer SA, Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, Claassen J, Du YE, Connolly ES Jr. Global and domain-specific cognitive impairment and outcome after subarachnoid hemorrhage. *Neurology*. 2002;59:1750–1758. doi: 10.1212/01.wnl.0000035748.91128.c2
27. Springer MV, Schmidt JM, Wartenberg KE, Frontera JA, Badjatia N, Mayer SA. Predictors of global cognitive impairment 1 year after subarachnoid hemorrhage. *Neurosurgery*. 2009;65:1043–1050. doi: 10.1227/01.NEU.0000359317.15269.20
28. Rodriguez Garcia PL, Rodriguez Garcia D. Diagnosis of vascular cognitive impairment and its main categories. *Neurologia*. 2015;30:223–239. doi: 10.1016/j.nrl.2011.12.014
29. Jaillard A, Naegele B, Trabucco-Miguel S, LeBas JF, Hommel M. Hidden dysfunctioning in subacute stroke. *Stroke*. 2009;40:2473–2479. doi: 10.1161/STROKEAHA.108.541144
30. Turunen KEA, Laari SPK, Kauranen TV, Uimonen J, Mustanoja S, Tatlisumak T, Poutiainen E. Domain-specific cognitive recovery after first-ever stroke: a 2-year follow-up. *J Int Neuropsychol Soc*. 2018;24:117–127. doi: 10.1017/S1355617717000728
31. Hochstenbach JB, den Otter R, Mulder TW. Cognitive recovery after stroke: a 2-year follow-up. *Arch Phys Med Rehabil*. 2003;84:1499–1504. doi: 10.1016/s0003-9993(03)00370-8
32. Desmond DW, Moroney JT, Sano M, Stern Y. Recovery of cognitive function after stroke. *Stroke*. 1996;27:1798–1803. doi: 10.1161/01.str.27.10.1798
33. Middleton LE, Lam B, Fahmi H, Black SE, McIlroy WE, Stuss DT, Danells C, Ween J, Turner GR. Frequency of domain-specific cognitive impairment in sub-acute and chronic stroke. *NeuroRehabilitation*. 2014;34:305–312. doi: 10.3233/NRE-131030
34. del Ser T, Barba R, Morin MM, Domingo J, Cemillan C, Pondal M, Vivancos J. Evolution of cognitive impairment after stroke and risk factors for delayed progression. *Stroke*. 2005;36:2670–2675. doi: 10.1161/01.STR.0000189626.71033.35
35. Hagberg G, Fure B, Thommessen B, Ihle-Hansen H, Øksengård AR, Nygård S, Pendlebury ST, Beyer MK, Wyller TB, Ihle-Hansen H. Predictors for favorable cognitive outcome post-stroke: a-seven-year follow-up study. *Dement Geriatr Cogn Disord*. 2019;48:45–55. doi: 10.1159/000501850
36. Mok VC, Lam BY, Wong A, Ko H, Markus HS, Wong LK. Early-onset and delayed-onset poststroke dementia: revisiting the mechanisms. *Nat Rev Neurol*. 2017;13:148–159. doi: 10.1038/nrneurol.2017.16
37. Clancy U, Makin SDJ, McHutchison CA, Cvoro V, Chappell FM, Hernandez M, Sakka E, Doubal F, Wardlaw JM. Impact of small vessel disease progression on long-term cognitive and functional changes after stroke. *Neurology*. 2022;98:e1459–e1469. doi: 10.1212/WNL.0000000000200005
38. Ivan CS, Seshadri S, Beiser A, Au R, Kase CS, Kelly-Hayes M, Wolf PA. Dementia after stroke: the Framingham study. *Stroke*. 2004;35:1264–1268. doi: 10.1161/01.STR.0000127810.92616.78
39. Shaw RC, Walker G, Elliott E, Quinn TJ. Occurrence rate of delirium in acute stroke settings: systematic review and meta-analysis. *Stroke*. 2019;50:3028–3036. doi: 10.1161/STROKEAHA.119.025015
40. *Diagnostic and Statistical Manual of Mental Disorders*. American Psychiatric Association; 2013.
41. Oldenbeuving AW, de Kort PL, Jansen BP, Algra A, Kappelle LJ, Roks G. Delirium in the acute phase after stroke: incidence, risk factors, and outcome. *Neurology*. 2011;76:993–999. doi: 10.1212/WNL.0b013e318210411f
42. Rhee JY, Colman MA, Mendu M, Shah SJ, Fox MD, Rost NS, Kimchi EY. Associations between stroke localization and delirium: a systematic review and meta-analysis. *J Stroke Cerebrovasc Dis*. 2022;31:106270. doi: 10.1016/j.jstrokecerebrovasdis.2021.106270
43. Knopman DS, DeKosky ST, Cummings JL, Chui H, Corey-Bloom J, Relkin N, Small GW, Miller B, Stevens JC. Practice parameter: diagnosis of dementia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2001;56:1143–1153. doi: 10.1212/wnl.56.9.1143
44. Towfighi A, Ovbiagele B, El Husseini N, Hackett ML, Jorge RE, Kissela BM, Mitchell PH, Skolarus LE, Whooley MA, Williams LS; on behalf of the American Heart Association Stroke Council; Council on Cardiovascular and Stroke Nursing; and Council on Quality of Care and Outcomes Research. Poststroke depression: a scientific statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2017;48:e30–e43. doi: 10.1161/STR.0000000000000113
45. Prisnie JC, Fiest KM, Coutts SB, Patten SB, Atta CA, Blaikie L, Bulloch AG, Demchuk A, Hill MD, Smith EE, et al. Validating screening tools for depression in stroke and transient ischemic attack patients. *Int J Psychiatry Med*. 2016;51:262–277. doi: 10.1177/0091217416652616
46. Jorm AF. A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): development and cross-validation. *Psychol Med*. 1994;24:145–153. doi: 10.1017/s003329170002691x
47. van Nieuwkerk AC, Pendlebury ST, Rothwell PM; Oxford Vascular Study. Accuracy of the Informant Questionnaire on Cognitive Decline in the Elderly for detecting preexisting dementia in transient ischemic attack and stroke: a population-based study. *Stroke*. 2021;52:1283–1290. doi: 10.1161/STROKEAHA.120.031961
48. Galvin JE, Roe CM, Coats MA, Morris JC. Patient's rating of cognitive ability: using the AD8, a brief informant interview, as a self-rating tool to detect dementia. *Arch Neurol*. 2007;64:725–730. doi: 10.1001/archneur.64.5.725
49. Weaver NA, Kuijf HJ, Aben HP, Abrigo J, Bae H-J, Barbay M, Best JG, Bordet R, Chappell FM, Chen CPLH, et al. Strategic infarct locations for post-stroke cognitive impairment: a pooled analysis of individual patient data from 12 acute ischaemic stroke cohorts. *Lancet Neurol*. 2021;20:448–459. doi: 10.1016/S1474-4422(21)00060-0
50. Weaver NA, Kancheva AK, Lim J-S, Biesbroek JM, McHuenges Wajer I, Kang Y, Kim BJ, Kuijf HJ, Lee B-C, Lee K-J, et al. Post-stroke cognitive impairment on the Mini-Mental State Examination primarily relates to left middle cerebral artery infarcts. *Int J Stroke*. 2021;16:981–989. doi: 10.1177/1747493020984552
51. Zhao L, Biesbroek JM, Shi L, Liu W, Kuijf HJ, Chu WW, Abrigo JM, Lee RK, Leung TW, Lau AY, et al. Strategic infarct location for post-stroke cognitive impairment: a multivariate lesion-symptom mapping study. *J Cereb Blood Flow Metab*. 2018;38:1299–1311. doi: 10.1177/0271678X17728162
52. Dharmasaroja P. Temporal changes in cognitive function in early recovery phase of the stroke. *J Stroke Cerebrovasc Dis*. 2021;30:106027. doi: 10.1016/j.jstrokecerebrovasdis.2021.106027
53. Saa JP, Tse T, Baum C, Cumming T, Josman N, Rose M, Carey L. Longitudinal evaluation of cognition after stroke: a systematic scoping review. *PLoS One*. 2019;14:e0221735. doi: 10.1371/journal.pone.0221735
54. Pinter D, Enzinger C, Gattringer T, Eppinger S, Niederkorn K, Horner S, Fandler S, Kneihsl M, Krenn K, Bachmaier G, et al. Prevalence and short-term changes of cognitive dysfunction in young ischaemic stroke patients. *Eur J Neurol*. 2019;26:727–732. doi: 10.1111/ene.13879
55. Yang Y-M, Zhao Z-M, Wang W, Dong F-M, Wang P-P, Jia Y-J, Han N, Jia Y-L, Wang J-H. Trends in cognitive function assessed by a battery of neuropsychological tests after mild acute ischemic stroke. *J Stroke Cerebrovasc Dis*. 2020;29:104887. doi: 10.1016/j.jstrokecerebrovasdis.2020.104887
56. Donnellan C, Werring D. Cognitive impairment before and after intracerebral haemorrhage: a systematic review. *Neurol Sci*. 2020;41:509–527. doi: 10.1007/s10072-019-04150-5
57. Banerjee G, Summers M, Chan E, Wilson D, Charidimou A, Cipolotti L, Werring DJ. Domain-specific characterisation of early cognitive impairment following spontaneous intracerebral hemorrhage. *J Neurol Sci*. 2018;391:25–30. doi: 10.1016/j.jns.2018.05.015
58. Egeto P, Loch Macdonald R, Ornstein TJ, Schweizer TA. Neuropsychological function after endovascular and neurosurgical treatment of subarachnoid hemorrhage: a systematic review and meta-analysis. *J Neurosurg*. 2018;128:768–776. doi: 10.3171/2016.11.JNS162055
59. Kreiter KT, Copeland D, Bernardini GL, Bates JE, Peery S, Claassen J, Du YE, Stern Y, Connolly ES, Mayer SA. Predictors of cognitive dysfunction after subarachnoid hemorrhage. *Stroke*. 2002;33:200–208. doi: 10.1161/hs0102.101080
60. Wong A, Mok V. Stroke: poststroke cognitive impairment: what are we measuring? *Nat Rev Neurol*. 2015;11:487–488. doi: 10.1038/nrneurol.2015.130
61. Montine TJ, Cholerton BA, Corrada MM, Edland SD, Flanagan ME, Hemmy LS, Kawas CH, White LR. Concepts for brain aging: resistance, resilience, reserve, and compensation. *Alzheimers Res Ther*. 2019;11:22. doi: 10.1186/s13195-019-0479-y
62. Stern Y, Barnes CA, Grady C, Jones RN, Raz N. Brain reserve, cognitive reserve, compensation, and maintenance: operationalization, validity, and mechanisms of cognitive resilience. *Neurobiol Aging*. 2019;83:124–129. doi: 10.1016/j.neurobiolaging.2019.03.022
63. Iadecola C. The neurovascular unit coming of age: a journey through neurovascular coupling in health and disease. *Neuron*. 2017;96:17–42. doi: 10.1016/j.neuron.2017.07.030
64. Gorelick PB, Furie KL, Iadecola C, Smith EE, Waddy SP, Lloyd-Jones DM, Bae HJ, Bauman MA, Dichgans M, Duncan PW, et al; on behalf of the American Heart Association/American Stroke Association. Defining optimal brain health in adults: a presidential advisory from the American Heart Association/American Stroke Association. *Stroke*. 2017;48:e284–e303. doi: 10.1161/STR.0000000000000148

65. Zlokovic BV. Neurovascular pathways to neurodegeneration in Alzheimer's disease and other disorders. *Nat Rev Neurosci*. 2011;12:723–738. doi: 10.1038/nrn3114
66. Iadecola C. The pathobiology of vascular dementia. *Neuron*. 2013;80:844–866. doi: 10.1016/j.neuron.2013.10.008
67. Finger CE, Moreno-Gonzalez I, Gutierrez A, Moruno-Manchon JF, McCullough LD. Age-related immune alterations and cerebrovascular inflammation. *Mol Psychiatry*. 2022;27:803–818. doi: 10.1038/s41380-021-01361-1
68. Hachinski V, Einhaupl K, Ganten D, Alladi S, Brayne C, Stephan BCM, Sweeney MD, Zlokovic B, Iturria-Medina Y, Iadecola C, et al. Preventing dementia by preventing stroke: the Berlin Manifesto. *Alzheimers Dement*. 2019;15:961–984. doi: 10.1016/j.jalz.2019.06.001
69. Lo JW, Crawford JD, Samaras K, Desmond DW, Kohler S, Staals J, Verhey FRJ, Bae HJ, Lee KJ, Kim BJ, et al; STROKOG Collaboration. Association of prediabetes and type 2 diabetes with cognitive function after stroke: a STROKOG collaboration study. *Stroke*. 2020;51:1640–1646. doi: 10.1161/STROKEAHA.119.028428
70. Biffi A, Bailey D, Anderson CD, Ayres AM, Gurol EM, Greenberg SM, Rosand J, Viswanathan A. Risk factors associated with early vs delayed dementia after intracerebral hemorrhage. *JAMA Neurol*. 2016;73:969–976. doi: 10.1001/jamaneurol.2016.0955
71. Smith EE. Cerebral amyloid angiopathy as a cause of neurodegeneration. *J Neurochem*. 2018;144:651–658. doi: 10.1111/jnc.14157
72. Stienen MN, Smoll NR, Weisshaupt R, Fandino J, Hildebrandt G, Studerus-Germann A, Schatlo B. Delayed cerebral ischemia predicts neurocognitive impairment following aneurysmal subarachnoid hemorrhage. *World Neurosurg*. 2014;82:e599–e605. doi: 10.1016/j.wneu.2014.05.011
73. Pasi M, Sugita L, Xiong L, Charidimou A, Boulouis G, Pongpitakmetha T, Singh S, Kourkoulis C, Schwab K, Greenberg SM, et al. Association of cerebral small vessel disease and cognitive decline after intracerebral hemorrhage. *Neurology*. 2021;96:e182–e192. doi: 10.1212/WNL.0000000000011050
74. Melkas S, Laurila JV, Vataja R, Oksala N, Jokinen H, Pohjasvaara T, Leppavuori A, Kaste M, Karhunen PJ, Erkinjuntti T. Post-stroke delirium in relation to dementia and long-term mortality. *Int J Geriatr Psychiatry*. 2012;27:401–408. doi: 10.1002/gps.2733
75. Pendlebury ST, Poole D, Burgess A, Duerden J, Rothwell PM; Oxford Vascular Study. Apoe-ε4 genotype and dementia before and after transient ischemic attack and stroke: population-based cohort study. *Stroke*. 2020;51:751–758. doi: 10.1161/STROKEAHA.119.026927
76. Lanctot KL, Lindsay MP, Smith EE, Sahlas DJ, Foley N, Gubitz G, Austin M, Ball K, Bhogal S, Blake T, et al; Fatigue Following Stroke Best Practice Writing Group, the Heart & Stroke Canadian Stroke Best Practices and Quality Advisory Committee, in collaboration with the Canadian Stroke Consortium. Canadian stroke best practice recommendations: mood, cognition and fatigue following stroke, 6th edition update 2019. *Int J Stroke*. 2020;15:668–688. doi: 10.1177/1747493019847334
77. Remes O, Brayne C, van der Linde R, Lafortune L. A systematic review of reviews on the prevalence of anxiety disorders in adult populations. *Brain Behav*. 2016;6:e00497. doi: 10.1002/brb3.497
78. Cumming TB, Packer M, Kramer SF, English C. The prevalence of fatigue after stroke: a systematic review and meta-analysis. *Int J Stroke*. 2016;11:968–977. doi: 10.1177/1747493016669861
79. van Dalen JW, Moll van Charante EP, Nederkoorn PJ, van Gool WA, Richard E. Poststroke apathy. *Stroke*. 2013;44:851–860. doi: 10.1161/STROKEAHA.112.674614
80. Gallacher KI, Jani BD, Hanlon P, Nicholl BI, Mair FS. Multimorbidity in stroke. *Stroke*. 2019;50:1919–1926. doi: 10.1161/STROKEAHA.118.020376
81. Hasan F, Gordon C, Wu D, Huang HC, Yuliana LT, Susatia B, Marta OFD, Chiu HY. Dynamic prevalence of sleep disorders following stroke or transient ischemic attack: systematic review and meta-analysis. *Stroke*. 2021;52:655–663. doi: 10.1161/STROKEAHA.120.029847
82. Lapchak PA. Neuronal dysregulation in stroke-associated pseudobulbar affect (PBA): diagnostic scales and current treatment options. *J Neurol Neurophysiol*. 2015;6:323. doi: 10.4172/2155-9562.1000323
83. Nijsse B, Visser-Meily JM, van Mierlo ML, Post MW, de Kort PL, van Heugten CM. Temporal evolution of poststroke cognitive impairment using the Montreal Cognitive Assessment. *Stroke*. 2017;48:98–104. doi: 10.1161/STROKEAHA.116.014168
84. MacIntosh BJ, Edwards JD, Kang M, Cogo-Moreira H, Chen JL, Mochizuki G, Herrmann N, Swardfager W. Post-stroke fatigue and depressive symptoms are differentially related to mobility and cognitive performance. *Front Aging Neurosci*. 2017;9:343. doi: 10.3389/fnagi.2017.00343
85. Sarfo FS, Nichols M, Qanungo S, Teklehaimanot A, Singh A, Mensah N, Saulson R, Gebregziabher M, Ezinne U, Owolabi M, et al. Stroke-related stigma among West Africans: patterns and predictors. *J Neurol Sci*. 2017;375:270–274. doi: 10.1016/j.jns.2017.02.018
86. Oberlin LE, Waiwood AM, Cumming TB, Marsland AL, Bernhardt J, Erickson KI. Effects of physical activity on poststroke cognitive function: a meta-analysis of randomized controlled trials. *Stroke*. 2017;48:3093–3100. doi: 10.1161/STROKEAHA.117.017319
87. Jorge RE, Acion L, Moser D, Adams HP Jr, Robinson RG. Escitalopram and enhancement of cognitive recovery following stroke. *Arch Gen Psychiatry*. 2010;67:187–196. doi: 10.1001/archgenpsychiatry.2009.185
88. Aaronson JA, Hofman WF, van Bennekom CA, van Bezeij T, van den Aardweg JG, Groet E, Kylstra WA, Schmand B. Effects of continuous positive airway pressure on cognitive and functional outcome of stroke patients with obstructive sleep apnea: a randomized controlled trial. *J Clin Sleep Med*. 2016;12:533–541. doi: 10.5664/jcsm.5684
89. Lamb F, Anderson J, Saling M, Dewey H. Predictors of subjective cognitive complaint in postacute older adult stroke patients. *Arch Phys Med Rehabil*. 2013;94:1747–1752. doi: 10.1016/j.apmr.2013.02.026
90. Nijsse B, van Heugten CM, van Mierlo ML, Post MWM, de Kort PLM, Visser-Meily JMA. Psychological factors are associated with subjective cognitive complaints 2 months post-stroke. *Neuropsychol Rehabil*. 2017;27:99–115. doi: 10.1080/09602011.2015.1065280
91. Narasimhalu K, Wiryasaputra L, Sitoh YY, Kandiah N. Post-stroke subjective cognitive impairment is associated with acute lacunar infarcts in the basal ganglia. *Eur J Neurol*. 2013;20:547–551. doi: 10.1111/ene.12032
92. van Rijsbergen MW, Mark RE, Kop WJ, de Kort PL, Sitskoorn MM. The role of objective cognitive dysfunction in subjective cognitive complaints after stroke. *Eur J Neurol*. 2017;24:475–482. doi: 10.1111/ene.13227
93. van Rijsbergen MWA, Mark RE, Kop WJ, de Kort PLM, Sitskoorn MM. Psychological factors and subjective cognitive complaints after stroke: beyond depression and anxiety. *Neuropsychol Rehabil*. 2019;29:1671–1684. doi: 10.1080/09602011.2018.1441720
94. Orfei MD, Caltagirone C, Spalletta G. The evaluation of anosognosia in stroke patients. *Cerebrovasc Dis*. 2009;27:280–289. doi: 10.1159/000199466
95. McGovern A, Pendlebury ST, Mishra NK, Fan Y, Quinn TJ. Test accuracy of informant-based cognitive screening tests for diagnosis of dementia and multidomain cognitive impairment in stroke. *Stroke*. 2016;47:329–335. doi: 10.1161/STROKEAHA.115.011218
96. Lees R, Selvarajah J, Fenton C, Pendlebury ST, Langhorne P, Stott DJ, Quinn TJ. Test accuracy of cognitive screening tests for diagnosis of dementia and multidomain cognitive impairment in stroke. *Stroke*. 2014;45:3008–3018. doi: 10.1161/STROKEAHA.114.005842
97. Rodrigues JC, Becker N, Beckenkamp CL, Mina CS, de Salles JF, Bandeira DR. Psychometric properties of cognitive screening for patients with cerebrovascular diseases a systematic review. *Dement Neuropsychol*. 2019;13:31–43. doi: 10.1590/1980-57642018dn13-010004
98. Stolwyk RJ, O'Neill MH, McKay AJ, Wong DK. Are cognitive screening tools sensitive and specific enough for use after stroke? A systematic literature review. *Stroke*. 2014;45:3129–3134. doi: 10.1161/STROKEAHA.114.004232
99. Burton L, Tyson SF. Screening for cognitive impairment after stroke: a systematic review of psychometric properties and clinical utility. *J Rehabil Med*. 2015;47:193–203. doi: 10.2340/16501977-1930
100. Van Heugten CM, Walton L, Hentschel U. Can we forget the Mini-Mental State Examination? A systematic review of the validity of cognitive screening instruments within one month after stroke. *Clin Rehabil*. 2015;29:694–704. doi: 10.1177/0269215514553012
101. Hachinski V, Iadecola C, Petersen RC, Breteler MM, Nyenhuis DL, Black SE, Powers WJ, DeCarli C, Merino JG, Kalaria RN, et al. National Institute of Neurological Disorders and Stroke-Canadian Stroke Network vascular cognitive impairment harmonization standards. *Stroke*. 2006;37:2220–2241. doi: 10.1161/01.STR.0000237236.88823.47
102. Deleted in proof
103. Deleted in proof
104. Lees RA, Hendry Ba K, Broomfield N, Stott D, Larner AJ, Quinn TJ. Cognitive assessment in stroke: feasibility and test properties using differing approaches to scoring of incomplete items. *Int J Geriatr Psychiatry*. 2017;32:1072–1078. doi: 10.1002/gps.4568
105. Chapman JE, Gardner B, Ponsford J, Cadilhac DA, Stolwyk RJ. Comparing performance across in-person and videoconference-based administrations of common neuropsychological measures in community-based survivors of stroke. *J Int Neuropsychol Soc*. 2021;27:697–710. doi: 10.1017/S1355617720001174

106. Rogers JM, Foord R, Stolwyk RJ, Wong D, Wilson PH. General and domain-specific effectiveness of cognitive remediation after stroke: systematic literature review and meta-analysis. *Neuropsychol Rev*. 2018;28:285–309. doi: 10.1007/s11065-018-9378-4
107. Stringer AY, Small SK. Ecologically-oriented neurorehabilitation of memory: robustness of outcome across diagnosis and severity. *Brain Inj*. 2011;25:169–178. doi: 10.3109/02699052.2010.541894
108. Withiel TD, Wong D, Ponsford JL, Cadilhac DA, New P, Mihaljcic T, Stolwyk RJ. Comparing memory group training and computerized cognitive training for improving memory function following stroke: a phase II randomized controlled trial. *J Rehabil Med*. 2019;51:343–351. doi: 10.2340/16501977-2540
109. Chen P, Hartman AJ, Priscilla Galarza C, DeLuca J. Global processing training to improve visuospatial memory deficits after right-brain stroke. *Arch Clin Neuropsychol*. 2012;27:891–905. doi: 10.1093/arclin/acs089
110. Loetscher T, Potter KJ, Wong D, das Nair R. Cognitive rehabilitation for attention deficits following stroke. *Cochrane Database Syst Rev*. 2019;2019:CD002842. doi: 10.1002/14651858.CD002842.pub3
111. van de Ven RM, Murre JM, Veltman DJ, Schmand BA. Computer-based cognitive training for executive functions after stroke: a systematic review. *Front Hum Neurosci*. 2016;10:150. doi: 10.3389/fnhum.2016.00150
112. Wentink MM, Berger MA, de Kloet AJ, Meesters J, Band GP, Wolterbeek R, Goossens PH, Vliet Vlieland TP. The effects of an 8-week computer-based brain training programme on cognitive functioning, QOL and self-efficacy after stroke. *Neuropsychol Rehabil*. 2016;26:847–865. doi: 10.1080/09602011.2016.1162175
113. Zucchella C, Capone A, Codella V, Vecchione C, Buccino G, Sandrini G, Pierelli F, Bartolo M. Assessing and restoring cognitive functions early after stroke. *Funct Neurol*. 2014;29:255–262. doi: 10.4061/2010/652612
114. van de Ven RM, Buitenweg JI, Schmand B, Veltman DJ, Aaronson JA, Nijboer TC, Kruiper-Doesborgh SJ, van Bennekom CA, Rasquin SM, Ridderinkhof KR, et al. Brain training improves recovery after stroke but waiting list improves equally: a multicenter randomized controlled trial of a computer-based cognitive flexibility training. *PLoS One*. 2017;12:e0172993. doi: 10.1371/journal.pone.0172993
115. van de Ven RM, Murre JMJ, Buitenweg JIV, Veltman DJ, Aaronson JA, Nijboer TCW, Kruiper-Doesborgh SJC, van Bennekom CAM, Ridderinkhof KR, Schmand B. The influence of computer-based cognitive flexibility training on subjective cognitive well-being after stroke: a multicenter randomized controlled trial. *PLoS One*. 2017;12:e0187582. doi: 10.1371/journal.pone.0187582
116. Rogers JM, Duckworth J, Middleton S, Steenbergen B, Wilson PH. Elements virtual rehabilitation improves motor, cognitive, and functional outcomes in adult stroke: evidence from a randomized controlled pilot study. *J Neuroeng Rehabil*. 2019;16:56. doi: 10.1186/s12984-019-0531-y
117. Laver KE, Lange B, George S, Deutsch JE, Saposnik G, Crotty M. Virtual reality for stroke rehabilitation. *Cochrane Database Syst Rev*. 2017;11:CD008349. doi: 10.1002/14651858.CD008349.pub4
118. Faria AL, Pinho MS, Bermudez IBS. A comparison of two personalization and adaptive cognitive rehabilitation approaches: a randomized controlled trial with chronic stroke patients. *J Neuroeng Rehabil*. 2020;17:78. doi: 10.1186/s12984-020-00691-5
119. Faria AL, Andrade A, Soares L, Bermúdez i Badia S. Benefits of virtual reality based cognitive rehabilitation through simulated activities of daily living: a randomized controlled trial with stroke patients. *J Neuroeng Rehabil*. 2016;13:96. doi: 10.1186/s12984-016-0204-z
120. Ostwald SK, Godwin KM, Cron SG, Kelley CP, Hersch G, Davis S. Home-based psychoeducational and mailed information programs for stroke-caregiving dyads post-discharge: a randomized trial. *Disabil Rehabil*. 2014;36:55–62. doi: 10.3109/09638288.2013.777806
121. Cheng C, Liu X, Fan W, Bai X, Liu Z. Comprehensive rehabilitation training decreases cognitive impairment, anxiety, and depression in post-stroke patients: a randomized, controlled study. *J Stroke Cerebrovasc Dis*. 2018;27:2613–2622. doi: 10.1016/j.jstrokecerebrovasdis.2018.05.038
122. Zhang L, Zhang T, Sun Y. A newly designed intensive caregiver education program reduces cognitive impairment, anxiety, and depression in patients with acute ischemic stroke. *Braz J Med Biol Res*. 2019;52:e8533. doi: 10.1590/1414-431X20198533
123. Yeh TT, Chang KC, Wu CY. The active ingredient of cognitive restoration: A multicenter randomized controlled trial of sequential combination of aerobic exercise and computer-based cognitive training in stroke survivors with cognitive decline. *Arch Phys Med Rehabil*. 2019;100:821–827. doi: 10.1016/j.apmr.2018.12.020
124. Moore SA, Hallsworth K, Jakovljevic DG, Blamire AM, He J, Ford GA, Rochester L, Trenell MI. Effects of community exercise therapy on metabolic, brain, physical, and cognitive function following stroke: a randomized controlled pilot trial. *Neurorehabil Neural Repair*. 2015;29:623–635. doi: 10.1177/1545968314562116
125. Steen Krawcyk R, Vinther A, Petersen NC, Faber J, Iversen HK, Christensen T, Lambertsen KL, Rehman S, Klausen TW, Rostrup E, et al. Effect of home-based high-intensity interval training in patients with lacunar stroke: Aa randomized controlled trial. *Front Neurol*. 2019;10:664. doi: 10.3389/fneur.2019.00664
126. Song R, Park M, Jang T, Oh J, Sohn MK. Effects of a tai chi-based stroke rehabilitation program on symptom clusters, physical and cognitive functions, and quality of life: a randomized feasibility study. *Int J Environ Res Public Health*. 2021;18:5453. doi: 10.3390/ijerph18105453
127. Ersoy C, Iyigun G. Boxing training in patients with stroke causes improvement of upper extremity, balance, and cognitive functions but should it be applied as virtual or real? *Top Stroke Rehabil*. 2021;28:112–126. doi: 10.1080/10749357.2020.1783918
128. Fernandez-Gonzalo R, Fernandez-Gonzalo S, Turon M, Prieto C, Tesch PA, del Carmen Garcia-Carreira M. Muscle, functional and cognitive adaptations after flywheel resistance training in stroke patients: a pilot randomized controlled trial. *J Neuroeng Rehabil*. 2016;13:37. doi: 10.1186/s12984-016-0144-7
129. Manuli A, Maggio MG, Latella D, Cannavo A, Balletta T, De Luca R, Naro A, Calabro RS. Can robotic gait rehabilitation plus virtual reality affect cognitive and behavioural outcomes in patients with chronic stroke? A randomized controlled trial involving three different protocols. *J Stroke Cerebrovasc Dis*. 2020;29:104994. doi: 10.1016/j.jstrokecerebrovasdis.2020.104994
130. Oh YB, Kim GW, Han KS, Won YH, Park SH, Seo JH, Ko MH. Efficacy of virtual reality combined with real instrument training for patients with stroke: a randomized controlled trial. *Arch Phys Med Rehabil*. 2019;100:1400–1408. doi: 10.1016/j.apmr.2019.03.013
131. Kleindorfer DO, Towfighi A, Chaturvedi S, Cockroft KM, Gutierrez J, Lombardi-Hill D, Kamel H, Kernan WN, Kittner SJ, Leira EC, et al. 2021 Guideline for the prevention of stroke in patients with stroke and transient ischemic attack: a guideline from the American Heart Association/American Stroke Association [published correction appears in *Stroke*. 2021;52:e483–e484]. *Stroke*. 2021;52:e364–e467. doi: 10.1161/STR.0000000000000375
132. Ihle-Hansen H, Thommessen B, Fagerland MW, Oksengard AR, Wyller TB, Engedal K, Fure B. Multifactorial vascular risk factor intervention to prevent cognitive impairment after stroke and TIA: a 12-month randomized controlled trial. *Int J Stroke*. 2014;9:932–938. doi: 10.1111/j.1747-4949.2012.00928.x
133. Bu X, Zhang Y, Bazzano LA, Xu T, Guo L, Wang X, Zhang J, Cui Y, Li D, Zhang F, et al. Effects of early blood pressure reduction on cognitive function in patients with acute ischemic stroke. *Int J Stroke*. 2016;11:1009–1019. doi: 10.1177/1747493016660094
134. Peters R, Yasar S, Anderson CS, Andrews S, Antikainen R, Arima H, Beckett N, Beer JC, Bertens AS, Booth A, et al. Investigation of antihypertensive class, dementia, and cognitive decline: a meta-analysis. *Neurology*. 2020;94:e267–e281. doi: 10.1212/WNL.0000000000008732
135. Hughes D, Judge C, Murphy R, Loughlin E, Costello M, Whiteley W, Bosch J, O'Donnell MJ, Canavan M. Association of blood pressure lowering with incident dementia or cognitive impairment: a systematic review and meta-analysis. *JAMA*. 2020;323:1934–1944. doi: 10.1001/jama.2020.4249
136. Williamson JD, Pajewski NM, Auchus AP, Bryan RN, Chelune G, Cheung AK, Cleveland ML, Coker LH, Crowe MG, Cushman WC, et al; SPRINT MIND Investigators for the SPRINT Research Group. Effect of intensive vs standard blood pressure control on probable dementia: a randomized clinical trial. *JAMA*. 2019;321:553–561. doi: 10.1001/jama.2018.21442
137. Lazar RM, Howard VJ, Kernan WN, Aparicio HJ, Levine DA, Viera AJ, Jordan LC, Nyenhuis DL, Possin KL, Sorond FA, et al; on behalf of the American Heart Association Stroke Council. A primary care agenda for brain health: a scientific statement from the American Heart Association. *Stroke*. 2021;52:e295–e308. doi: 10.1161/STR.0000000000000367
138. Deschaintre Y, Richard F, Leys D, Pasquier F. Treatment of vascular risk factors is associated with slower decline in Alzheimer disease. *Neurology*. 2009;73:674–680. doi: 10.1212/WNL.0b013e3181b59bf3
139. Ngandu T, Lehtisalo J, Solomon A, Levalahti E, Ahtiluoto S, Antikainen R, Backman L, Hanninen T, Jula A, Laatikainen T, et al. A 2 year multidomain intervention of diet, exercise, cognitive training, and vascular risk monitoring versus control to prevent cognitive decline in at-risk elderly people (FINGER): a randomised controlled trial. *Lancet*. 2015;385:2255–2263. doi: 10.1016/S0140-6736(15)60461-5

140. Hajjar K, Fulton RL, Diener HC, Lees KR, Collaborators V, Alexandrov A, Bath PM, Bluhmki E, Claesson L, Curram J, et al. Does the cognitive measure COG-4 show improvement among patients treated with thrombolysis after acute stroke? *Int J Stroke*. 2013;8:652–656. doi: 10.1111/j.1747-4949.2012.00848.x
141. Lopez-Cancio E, Jovin TG, Cobo E, Cerda N, Jimenez M, Gomis M, Hernandez-Perez M, Caceres C, Cardona P, Lara B, et al. Endovascular treatment improves cognition after stroke: a secondary analysis of REVASCAT trial. *Neurology*. 2017;88:245–251. doi: 10.1212/WNL.0000000000003517
142. Lattanzi S, Coccia M, Pulcini A, Cagnetti C, Galli FL, Villani L, Campa S, Dobran M, Polonara G, Ceravolo MG, et al. Endovascular treatment and cognitive outcome after anterior circulation ischemic stroke. *Sci Rep*. 2020;10:18524. doi: 10.1038/s41598-020-75609-1
143. Sami MB, Faruqui R. The effectiveness of dopamine agonists for treatment of neuropsychiatric symptoms post brain injury and stroke. *Acta Neuropsychiatr*. 2015;27:317–326. doi: 10.1017/neu.2015.17
144. Legg LA, Rudberg AS, Hua X, Wu S, Hackett ML, Tilney R, Lindgren L, Kutlubaev MA, Hsieh CF, Barugh AJ, et al. Selective serotonin reuptake inhibitors (SSRIs) for stroke recovery. *Cochrane Database Syst Rev*. 2021;11:CD009286. doi: 10.1002/14651858.CD009286.pub4
145. Damsbo AG, Kraglund KL, Buttenschon HN, Johnsen SP, Andersen G, Mortensen JK. Serotonergic regulation and cognition after stroke: the role of antidepressant treatment and genetic variation. *Cerebrovasc Dis*. 2019;47:72–79. doi: 10.1159/000498911
146. Hankey GJ, Hackett ML, Almeida OP, Flicker L, Mead GE, Dennis MS, Etherton-Beer C, Ford AH, Billot L, Jan S, et al; AFFINITY Trial Collaboration. Twelve-month outcomes of the AFFINITY trial of fluoxetine for functional recovery after acute stroke: AFFINITY Trial Steering Committee on behalf of the AFFINITY Trial Collaboration. *Stroke*. 2021;52:2502–2509. doi: 10.1161/STROKEAHA.120.033070
147. Evzel'man MA, Rova NA. Cognitive impairments in patients with ischemic stroke and their correction. *Neurosci Behav Physiol*. 2015;45:323–326. doi: 10.1007/s11055-015-0074-z
148. Muratova TS, Khramtsov D, Vikarenko M, Galina K, Dobush I, Andryushchenko E. The clinical efficacy of Cerebrolysin in ischemic stroke patients with prestroke mild cognitive impairment: a pilot study. *Eur Stroke J*. 2019;4:790–821. doi: 10.1177/2396987319848124
149. Milia P, Caserio M, Bani D, Rastelli TF, Sonaglia F, Bigazzi B, Bigazzi M. Efficacy of relaxin on functional recovery of post stroke patients. *Ital J Anat Embryol*. 2013;118:92–97.
150. Alvarez-Sabin J, Ortega G, Jacas C, Santamarina E, Maisterra O, Ribo M, Molina C, Quintana M, Roman GC. Long-term treatment with citicoline may improve poststroke vascular cognitive impairment. *Cerebrovasc Dis*. 2013;35:146–154. doi: 10.1159/000346602
151. Woodhouse L, Scutt P, Krishnan K, Berge E, Gommans J, Ntaios G, Wardlaw J, Sprigg N, Bath PM; ENOS Investigators. Effect of hyperacute administration (within 6 hours) of transdermal glyceryl trinitrate, a nitric oxide donor, on outcome after stroke: subgroup analysis of the Efficacy of Nitric Oxide in Stroke (ENOS) trial. *Stroke*. 2015;46:3194–3201. doi: 10.1161/STROKEAHA.115.009647
152. Gorgoraptis N, Mah YH, Machner B, Singh-Curry V, Malhotra P, Hadji-Michael M, Cohen D, Simister R, Nair A, Kulinskaya E, et al. The effects of the dopamine agonist rotigotine on hemispatial neglect following stroke. *Brain*. 2012;135:2478–2491. doi: 10.1093/brain/aws154
153. Bartolo M, Chiara Z, Capone A, Sandrini G, Pierelli F. An explorative study regarding the effect of l-deprenyl on cognitive and functional recovery in patients after stroke. *J Neurol Sci*. 2015;349:117–123. doi: 10.1016/j.jns.2014.12.039
154. Kavirajan H, Schneider LS. Efficacy and adverse effects of cholinesterase inhibitors and memantine in vascular dementia: a meta-analysis of randomised controlled trials. *Lancet Neurol*. 2007;6:782–792. doi: 10.1016/S1474-4422(07)70195-3
155. Battle CE, Abdul-Rahim AH, Shenkin SD, Hewitt J, Quinn TJ. Cholinesterase inhibitors for vascular dementia and other vascular cognitive impairments: a network meta-analysis. *Cochrane Database Syst Rev*. 2021;2:CD013306. doi: 10.1002/14651858.CD013306.pub2
156. McShane R, Westby MJ, Roberts E, Minakaran N, Schneider L, Farrimond LE, Maayan N, Ware J, Debarros J. Memantine for dementia. *Cochrane Database Syst Rev*. 2019;3:CD003154. doi: 10.1002/14651858.CD003154.pub6
157. Feng X, Huang L, Wang Z, Wang L, Du X, Wang Q, Xue S. Efficacy of remote limb ischemic conditioning on poststroke cognitive impairment. *J Integr Neurosci*. 2019;18:377–385. doi: 10.31083/j.jin.2019.04.1192
158. Li YJ, Liang KK, Zhang L, Pan R, Hu YM, Zhao JH. Remote ischemic post-conditioning may improve post-stroke cognitive impairment: a pilot single center randomized controlled trial. *J Stroke Cerebrovasc Dis*. 2020;29:105217. doi: 10.1016/j.jstrokecerebrovasdis.2020.105217
159. Zhao W, Zhang J, Sadowsky MG, Meng R, Ding Y, Ji X. Remote ischaemic conditioning for preventing and treating ischaemic stroke. *Cochrane Database Syst Rev*. 2018;7:CD012503. doi: 10.1002/14651858.CD012503.pub2
160. Yan RB, Zhang XL, Li YH, Hou JM, Chen H, Liu HL. Effect of transcranial direct-current stimulation on cognitive function in stroke patients: a systematic review and meta-analysis. *PLoS One*. 2020;15:e0233903. doi: 10.1371/journal.pone.0233903
161. Tian YK, Wang H, Liu Z. Meta-analysis of transcranial magnetic stimulation to treat post-stroke dysfunction. *Neural Regener Res*. 2011;6:1736–1741.
162. Yang A, Wu HM, Tang JL, Xu L, Yang M, Liu GJ. Acupuncture for stroke rehabilitation. *Cochrane Database Syst Rev*. 2016;2016:CD004131. doi: 10.1002/14651858.CD004131.pub3
163. Liu F, Li ZM, Jiang YJ, Chen LD. A meta-analysis of acupuncture use in the treatment of cognitive impairment after stroke. *J Altern Complement Med*. 2014;20:535–544. doi: 10.1089/acm.2013.0364
164. Su XT, Sun N, Zhang N, Wang LQ, Zou X, Li JL, Yang JW, Shi GX, Liu CZ. Effectiveness and safety of acupuncture for vascular cognitive impairment: a systematic review and meta-analysis. *Front Aging Neurosci*. 2021;13:692508. doi: 10.3389/fnagi.2021.692508
165. Xiong J, Zhang Z, Ma Y, Li Z, Zhou F, Qiao N, Liu Q, Liao W. The effect of combined scalp acupuncture and cognitive training in patients with stroke on cognitive and motor functions. *NeuroRehabilitation*. 2020;46:75–82. doi: 10.3233/NRE-192942
166. Jiang C, Yang S, Tao J, Huang J, Li Y, Ye H, Chen S, Hong W, Chen L. Clinical efficacy of acupuncture treatment in combination with RehaCom cognitive training for improving cognitive function in stroke: a 2 x 2 factorial design randomized controlled trial. *J Am Med Dir Assoc*. 2016;17:1114–1122. doi: 10.1016/j.jamda.2016.07.021
167. Xu ZQ, Liang XM, Juan W, Zhang YF, Zhu CX, Jiang XJ. Treatment with Huperzine A improves cognition in vascular dementia patients. *Cell Biochem Biophys*. 2012;62:55–58. doi: 10.1007/s12013-011-9258-5
168. Zhao JQ, Yan M, Zhao H, Guan T, Chen Y. Effect of depsides salts from *Salvia miltiorrhiza* on cognitive function and serum Hcy, D-dimer and apoA1 in patients with cerebral infarction. *Int J Clin Exp Med*. 2020;13:2589–2596.
169. Li S, Zhang X, Fang Q, Zhou J, Zhang M, Wang H, Chen Y, Xu B, Wu Y, Qian L, et al. Ginkgo biloba extract improved cognitive and neurological functions of acute ischaemic stroke: a randomised controlled trial. *Stroke Vasc Neurol*. 2017;2:189–197. doi: 10.1136/svn-2017-000104
170. Bellone JA, Murray JR, Jorge P, Fogel TG, Kim M, Wallace DR, Hartman RE. Pomegranate supplementation improves cognitive and functional recovery following ischemic stroke: a randomized trial. *Nutr Neurosci*. 2019;22:738–743. doi: 10.1080/1028415X.2018.1436413
171. Zhao L, Liao L, Hu F. Comparing Cerebralcare Granule and aspirin for neurological dysfunction in acute stroke in real-life practice. *Psychogeriatrics*. 2017;17:3–8. doi: 10.1111/psyg.12180
172. Yang W, Shi Z, Yang HQ, Teng J, Zhao J, Xiang G. Mailuoning for acute ischaemic stroke. *Cochrane Database Syst Rev*. 2015;1:CD007028. doi: 10.1002/14651858.CD007028.pub3
173. Hankey GJ, Ford AH, Yi Q, Eikelboom JW, Lees KR, Chen C, Xavier D, Navarro JC, Ranawaka UK, Uddin W, et al; VITATOPS Trial Study Group. Effect of B vitamins and lowering homocysteine on cognitive impairment in patients with previous stroke or transient ischemic attack: a prespecified secondary analysis of a randomized, placebo-controlled trial and meta-analysis. *Stroke*. 2013;44:2232–2239. doi: 10.1161/STROKEAHA.113.001886
174. Mijajlovic MD, Pavlovic A, Brainin M, Heiss WD, Quinn TJ, Ihle-Hansen HB, Hermann DM, Assayag EB, Richard E, Thiel A, et al. Post-stroke dementia: a comprehensive review. *BMC Med*. 2017;15:11. doi: 10.1186/s12916-017-0779-7
175. Brainin M, Tuomilehto J, Heiss WD, Bornstein NM, Bath PM, Teuschl Y, Richard E, Guekht A, Quinn T; Post Stroke Cognition Study Group. Post-stroke cognitive decline: an update and perspectives for clinical research. *Eur J Neurol*. 2015;22:229–238, e13–e16. doi: 10.1111/ene.12626
176. Schulz CH, Hersch GI, Foust JL, Wyatt AL, Godwin KM, Virani S, Ostwald SK. Identifying occupational performance barriers of stroke survivors: Utilization of a home assessment. *Phys Occup Ther Geriatr*. 2012;30:10.3109/02703181.2012.687441. doi: 10.3109/02703181.2012.687441
177. Simpson LA, Miller WC, Eng JJ. Effect of stroke on fall rate, location and predictors: a prospective comparison of older adults with and without stroke. *PLoS One*. 2011;6:e19431. doi: 10.1371/journal.pone.0019431
178. Fonss Rasmussen L, Grode LB, Lange J, Barat I, Gregersen M. Impact of transitional care interventions on hospital readmissions in older medical patients: a systematic review. *BMJ Open*. 2021;11:e040057. doi: 10.1136/bmjopen-2020-040057

179. van der Kemp J, Kruithof WJ, Nijboer TCW, van Bennekom CAM, van Heugten C, Visser-Meily JMA. Return to work after mild-to-moderate stroke: work satisfaction and predictive factors. *Neuropsychol Rehabil*. 2019;29:638–653. doi: 10.1080/09602011.2017.1313746
180. Fride Y, Adamit T, Maeir A, Ben Assayag E, Bornstein NM, Korczyn AD, Katz N. What are the correlates of cognition and participation to return to work after first ever mild stroke? *Top Stroke Rehabil*. 2015;22:317–325. doi: 10.1179/1074935714Z.0000000013
181. Hallevi H, Molad J, Kliper E, Seyman E, Niry D, Bornstein NM, Ben Assayag E. Working status is related to post stroke/TIA cognitive decline: data from the TABASCO study. *J Stroke Cerebrovasc Dis*. 2020;29:105019. doi: 10.1016/j.jstrokecerebrovasdis.2020.105019
182. Balasooriya-Smeekens C, Bateman A, Mant J, De Simoni A. Barriers and facilitators to staying in work after stroke: insight from an online forum. *BMJ Open*. 2016;6:e009974. doi: 10.1136/bmjopen-2015-009974
183. Lindgren I, Brogårdh C, Pessah-Rasmussen H, Jonasson SB, Gard G. Work conditions, support, and changing personal priorities are perceived important for return to work and for stay at work after stroke: a qualitative study. *Disabil Rehabil*. 2022;44:2500–2506. doi: 10.1080/09638288.2020.1836522
184. Palstam A, Tornbom M, Sunnerhagen KS. Experiences of returning to work and maintaining work 7 to 8 years after a stroke: a qualitative interview study in Sweden. *BMJ Open*. 2018;8:e021182. doi: 10.1136/bmjopen-2017-021182
185. Wei X-J, Liu X-F, Fong KN. Outcomes of return-to-work after stroke rehabilitation: a systematic review. *Br J Occup Ther*. 2016;79:299–308. doi: 10.1177/0308022615624710
186. Akinwuntan AE, Wachtel J, Rosen PN. Driving simulation for evaluation and rehabilitation of driving after stroke. *J Stroke Cerebrovasc Dis*. 2012;21:478–486. doi: 10.1016/j.jstrokecerebrovasdis.2010.12.001
187. Smedslund G, Giske L, Fleitscher H, Brurberg KG. *Screening Tools for Cognitive Function and Driving*. Norwegian Knowledge Centre for the Health Services; 2015.
188. Aufman EL, Bland MD, Barco PP, Carr DB, Lang CE. Predictors of return to driving after stroke. *Am J Phys Med Rehabil*. 2013;92:627–634. doi: 10.1097/PHM.0b013e318282bc0d
189. Motta K, Lee H, Falkmer T. Post-stroke driving: examining the effect of executive dysfunction. *J Safety Res*. 2014;49:33–38. doi: 10.1016/j.jsr.2014.02.005
190. George S, Crotty M, Gelinas I, Devos H. Rehabilitation for improving automobile driving after stroke. *Cochrane Database Syst Rev*. 2014;2014:CD008357. doi: 10.1002/14651858.CD008357.pub2