



CANADIAN STROKE BEST PRACTICE RECOMMENDATIONS

MOOD, COGNITION AND FATIGUE FOLLOWING STROKE EVIDENCE TABLES

Vascular Cognitive Impairment: Management & Cognitive Rehabilitation

Update 2019

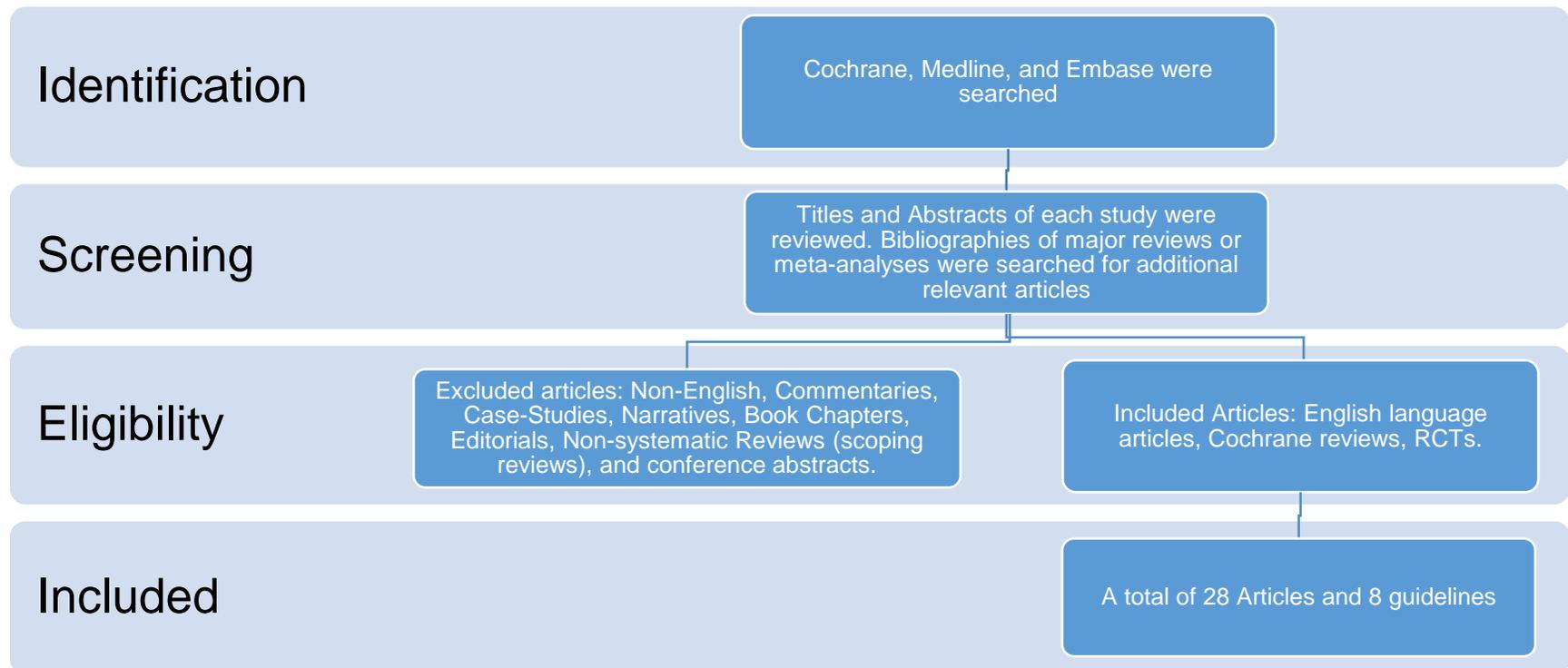
*Lancôt KL, Swartz RH (Writing Group Chairs) on Behalf of the Canadian Stroke Best Practice Recommendations
Mood, Cognition and Fatigue following Stroke Writing Group and the Canadian Stroke Best Practice and Quality Advisory Committee,
in collaboration with the Canadian Stroke Consortium*

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Search Strategy



The Medline, Embase, PsycInfo, and Cochrane databases were searched using the terms [stroke OR cerebrovascular disorders] and [cognition OR neuropsychology OR mild cognitive impairment OR cognitive training OR cognitive rehabilitation]. The title and abstract of each article was reviewed for relevance. Bibliographies were reviewed to find additional relevant articles. Articles were excluded if they were: non-English, commentaries, case-studies, narrative, book chapters, editorials, non-systematic review, or conference abstracts. Additional searches for relevant best practice guidelines were completed and included in a separate section of the review. A total of 28 articles and 8 guidelines were included and were separated into categories designed to answer specific questions.

Published Guidelines

Guideline	Recommendations
<p>Stroke Foundation. Clinical Guidelines for Stroke Management 2017. Melbourne Australia. (Part 6)</p>	<p>Weak Recommendation For stroke survivors with cognitive impairment, meta-cognitive strategy and/or cognitive training may be provided.</p> <p>Consensus-based recommendation For stroke survivors with attentional impairments or those who appear easily distracted or unable to concentrate, a formal neuropsychological or cognitive assessment should be performed.</p> <p>Weak Recommendation For stroke survivors with attention and concentration deficits, cognitive rehabilitation may be used.</p> <p>Weak recommendation New For stroke survivors with attention and concentration deficits, exercise training and leisure activities may be provided.</p> <p>Practice statement Consensus-based recommendations New Stroke survivors with identified perceptual difficulties should have a formal perceptual (i.e. neurological and neuropsychological) assessment. Stroke survivors with an identified perceptual impairment and their carer should receive: • verbal and written information about the impairment; • an assessment and adaptation of their environment to reduce potential risk and promote independence; • practical advice/strategies to reduce risk (e.g. trips, falls, limb injury) and promote independence; • intervention to address the perceptual difficulties, ideally within the context of a clinical trial.</p>
<p>Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD; on behalf of the American Heart Association Stroke Council, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research.</p> <p>Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association.</p> <p><i>Stroke</i> 2016;47:e98–e169.</p>	<p>Enriched environments to increase engagement with cognitive activities are recommended. Class I; LOE A</p> <p>Use of cognitive rehabilitation to improve attention, memory, visual neglect, and executive functioning is reasonable. Class IIa; LOE B</p> <p>Use of cognitive training strategies that consider practice, compensation, and adaptive techniques for increasing independence is reasonable. Class IIa: LOE B</p> <p>Compensatory strategies may be considered to improve memory functions, including the use of internalized strategies (eg, visual imagery, semantic organization, spaced practice) and external memory assistive technology (eg, notebooks, paging systems, computers, other prompting devices). Class IIb; LOE A</p> <p>Some type of specific memory training is reasonable such as promoting global processing in visual-spatial memory and constructing a semantic framework for language-based memory. Class IIb; LOE B</p> <p>Errorless learning techniques may be effective for individuals with severe memory impairments for learning specific skills or knowledge, although there is limited transfer to novel tasks or reduction in overall functional memory problems. Class IIb; LOE B</p> <p>Music therapy may be reasonable for improving verbal memory. Class IIb; LOE B</p> <p>Exercise may be considered as adjunctive therapy to improve cognition and memory after stroke. IIb C</p> <p>Virtual reality training may be considered for verbal, visual, and spatial learning, but its efficacy is not well established. Class IIb; LOE C</p> <p>Anodal tDCS over the left dorsolateral prefrontal cortex to improve language-based complex attention (working memory) remains experimental. Class III; LOE B</p>

Guideline	Recommendations
<p>Intercollegiate Stroke Working Party. National clinical guideline for stroke, 5th Edition. London: Royal College of Physicians, 2016.</p>	<p>Cognitive Impairment (general) People with cognitive problems after stroke should receive appropriate adjustments to their multidisciplinary treatments to enable them to participate, and this should be regularly reviewed.</p> <p>People with continuing cognitive difficulties after stroke should be considered for comprehensive interventions aimed at developing compensatory behaviours and learning adaptive skills.</p> <p>Attention & Concentration People with impaired attention after stroke should have cognitive demands reduced by: – having shorter treatment sessions; – taking planned rests; – reducing background distractions; – avoiding activities when tired. C People with impaired attention after stroke should: – have the impairment explained to them, their family/carers and the multidisciplinary team; – be offered an attentional intervention (e.g. time pressure management, attention process training, environmental manipulation), ideally in the context of a clinical trial; – be given as many opportunities to practise their activities as reasonable under supervision.</p> <p>Executive Functioning People with an impairment of executive function and activity limitation after stroke should be trained in compensatory techniques, including internal strategies (e.g. self-awareness and goal setting), structured feedback on performance of functional tasks and external strategies (e.g. use of electronic reminders or written checklists). People with an executive disorder after stroke should have the impairment and the impact on function explained to them, their family/carers, and the multidisciplinary team.</p> <p>Memory People with memory impairment after stroke causing difficulties with rehabilitation should: – have the impairment explained to them, their family/carers and the multidisciplinary team; – be assessed for treatable or contributing factors (e.g. delirium, hypothyroidism); – have their profile of impaired and preserved memory abilities determined, including the impact of other cognitive deficits e.g. attention; – have nursing and therapy sessions altered to capitalise on preserved abilities; – be trained in approaches that help them to encode, store and retrieve new information e.g. spaced retrieval (increasing time intervals between review of information) or deep encoding of material (emphasising semantic features); – be trained in compensatory techniques to reduce their prospective memory problems (e.g. use of electronic reminders or written checklists); – receive therapy in an environment as similar as possible to their usual environment.</p>
<p>Gorelick PB, Scuteri A, Black SE, et al.</p> <p>Vascular contributions to cognitive impairment and dementia: a statement for healthcare professionals from the American heart association/America stroke association.</p> <p><i>Stroke</i> 2011;42:2672-2713.</p>	<p>Only limited evidence exists to support non-pharmacological modalities for management of VCI.</p> <p>No formal recommendations for therapy are offered. More research with rigorous designs to study the effects of nonpharmacological interventions, including cognitive rehabilitation and acupuncture, is needed.</p>
<p>Cicerone KD, Langenbahn DM, Braden C, Malec JF, Kalmar K, Fraas M, Felicetti T, Laatsch L, Harley JP, Bergquist T, Azulay J.</p>	<p>Remediation of Attention Remediation of attention is recommended during postacute rehabilitation after TBI. Remediation of attention deficits after TBI should include direct attention training and metacognitive training to promote development of compensatory strategies and foster generalization to real world tasks. Insufficient</p>

Guideline	Recommendations
<p>Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008.</p> <p><i>Arch Phys Med Rehabil</i> 2011;92(4):519-30.</p>	<p>evidence exists to distinguish the effects of specific attention training during acute recovery and rehabilitation from spontaneous recovery or from more general cognitive interventions. Level of Recommendation: Practice Standard</p> <p>Computer-based interventions may be considered as an adjunct to clinician-guided treatment for the remediation of attention deficits after TBI or stroke. Sole reliance on repeated exposure and practice on computer-based tasks without some involvement and intervention by a therapist is not recommended. Level of Recommendation (LOR): Practice Option</p> <p>Remediation of Visuospatial and Praxic Deficits Visuospatial rehabilitation that includes visual scanning training is recommended for left visual neglect after right hemisphere stroke. LOR: Practice Standard The use of isolated microcomputer exercises to treat left neglect after stroke does not appear effective and is not recommended. LOR: Practice Guideline Inclusion of limb activation or electronic technologies for visual scanning training may be included in the treatment of neglect after right hemisphere stroke. LOR: Practice Option Systematic training of visuospatial deficits and visual organization skills may be considered for persons with visual perceptual deficits, without visual neglect, after right hemisphere stroke as part of acute rehabilitation. LOR: Practice Option Computer-based interventions intended to produce extension of damaged visual fields may be considered for people with TBI or stroke. LOR: Practice Option Specific gestural or strategy training is recommended for apraxia during acute rehabilitation for left hemisphere stroke. LOR: Practice Standard</p> <p>Remediation of Language and Communication Deficits Cognitive-linguistic therapies are recommended during acute and postacute rehabilitation for language deficits secondary to left hemisphere stroke. LOR: Practice Standard Specific interventions for functional communication deficits, including pragmatic conversational skills, are recommended for social communication skills after TBI. LOR: Practice Standard Cognitive interventions for specific language impairments such as reading comprehension and language formulation are recommended after left hemisphere stroke or TBI. LOR: Practice Guideline Treatment intensity should be considered a key factor in the rehabilitation of language skills after left hemisphere stroke. LOR: Practice Guideline Group based interventions may be considered for remediation of language deficits after left hemisphere stroke and for social-communication deficits after TBI. LOR: Practice Option Computer-based interventions as an adjunct to clinician-guided treatment may be considered in the remediation of cognitive-linguistic deficits after left hemisphere stroke or TBI. Sole reliance on repeated exposure and practice on computer-based tasks without some involvement and intervention by a therapist is not recommended. LOR: Practice Option</p> <p>Remediation of Memory Deficits Memory strategy training is recommended for mild memory impairments from TBI, including the use of internalized strategies (eg, visual imagery) and external memory compensations (eg, notebooks). LOR: Practice Standard Use of external compensations with direct application to functional activities is recommended for people with severe memory deficits after TBI or stroke. LOR: Practice Guideline For people with severe memory impairments after TBI, errorless learning techniques may be effective for learning specific skills or knowledge, with limited transfer to novel tasks or reduction in overall functional memory problems. LOR: Practice Option Group-based interventions may be considered for remediation of memory deficits after TBI. LOR: Practice Option</p>

Guideline	Recommendations
	<p>Remediation of Executive Function Deficits Metacognitive strategy training (self-monitoring and self-regulation) is recommended for deficits in executive functioning after TBI, including impairments of emotional self-regulation, and as a component of interventions for deficits in attention, neglect, and memory. LOR: Practice Standard Training in formal problem-solving strategies and their application to everyday situations and functional activities is recommended during postacute rehabilitation after TBI. LOR:Practice Guideline Group-based interventions may be considered for remediation of executive and problem-solving deficits after TBI. LOR: Practice Option</p> <p>Comprehensive-Holistic Neuropsychologic Rehabilitation Comprehensive-holistic neuropsychologic rehabilitation is recommended during postacute rehabilitation to reduce cognitive and functional disability for persons with moderate or severe TBI. LOR: Practice Standard Integrated treatment of individualized cognitive and interpersonal therapies is recommended to improve functioning within the context of a comprehensive neuropsychologic rehabilitation program, and facilitate the effectiveness of specific interventions. LOR: Practice Option Group-based interventions may be considered as part of comprehensive-holistic neuropsychologic rehabilitation after TBI. LOR: Practice Option</p>
<p>National Stroke Foundation. Clinical Guidelines for Stroke Management 2010 Recommendations. Melbourne Australia.</p>	<p>Attention and Concentration 1. Cognitive rehabilitation can be used in stroke survivors with attention and concentration deficits (C).</p> <p>Memory 1. Any patient found to have memory impairment causing difficulties in rehabilitation or adaptive functioning should: <ul style="list-style-type: none"> • Have their nursing and therapy sessions tailored to use techniques which capitalize on preserved memory abilities (GPP) • Be assessed to see if compensatory techniques to reduce their disabilities, such as notebooks, diaries, audiotapes, electronic organizers and audio alarms, are useful (D) • Be taught approaches aimed at directly improving their memory (GPP) • Have therapy delivered in an environment as like the patient's usual environment as possible to encourage generalization (GPP) </p> <p>Executive functions 1. External cues, such as a pager, can be used to initiate everyday activities in stroke survivors (C). In stroke survivors with impaired executive functioning, the way in which information is provided should be considered (C).</p>
<p>Scottish Intercollegiate Guidelines Network (SIGN). Management of patients with stroke: Rehabilitation, prevention and management of complications, and discharge planning: A national clinical guideline, 2010. Edinburgh, Scotland.</p>	<ul style="list-style-type: none"> • A full understanding of the patient's cognitive strengths and weaknesses should be an integral part of the rehabilitation plan (GPP). • Stroke patients should have a full assessment of their cognitive strengths and weaknesses when undergoing rehabilitation or when returning to cognitively demanding activities such as driving or work (GPP). • Cognitive assessment may be carried out by occupational therapists with expertise in neurological care, although some patients with more complex needs will require access to specialist neuropsychological expertise (GPP). <p>Cognitive rehabilitation: "There is not yet sufficient evidence to support or refute the benefits of cognitive rehabilitation for patients with problems of attention or memory. When cognitive problems are suspected and relatives report personality change, the patient can be referred to a clinical psychologist to provide assessment and where appropriate, psychological intervention which may include carer education and support" (page 22)</p>
<p>VA/DoD clinical practice guideline for the management of stroke rehabilitation 2010.</p>	<p>Non-drug therapies for cognitive impairment a. Recommend that patients be given cognitive re-training, if any of the following conditions are present: a. Attention deficits [A]</p>

Guideline	Recommendations
	<ul style="list-style-type: none"> b. Visual neglect [B] c. Memory deficits [B] d. Executive function and problem-solving difficulties [C] <ol style="list-style-type: none"> 2. Patients with multiple areas of cognitive impairment may benefit from a variety of cognitive re-training approaches that may involve multiple disciplines. [C] 1. Recommend the use of training to develop compensatory strategies for memory deficits in post-stroke patients who have mild short term memory deficits. [B]
<p>Cappa S, Benke T, Clarke S, Rossi B, Stemmer B, van Heugten C; Task Force on Cognitive Rehabilitation; European Federation of Neurological Societies.</p> <p>EFNS guidelines on cognitive rehabilitation: report of an EFNS task force.</p> <p><i>Eur J Neurol</i> 2005;12:665–680.</p>	<p>Memory strategies without electronic aids are possibly effective (Level C recommendation)</p> <p>Specific learning strategies such as errorless learning are probably effective (Level B recommendation)</p> <p>Nonelectronic external memory aids such as diary or notebook keeping are possibly effective (Level C recommendation)</p> <p>Electronic external memory devices such as computers, paging systems, and portable voice organizers are probably effective (Level B recommendation)</p> <p>The use of virtual environments has shown positive effects on verbal, visual, and spatial learning and that memory training in virtual environments is rated as possibly effective (Level C recommendation)</p>

Evidence Tables

Cognitive Rehabilitation

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<i>Attention Deficits</i>					
Wentink et al. 2016 The Netherlands RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	115 patients, aged 45-75 years, with self-perceived cognitive impairments 12–36 months after stroke. Participants were identified from a database of rehabilitation centres. Median age was 59 years, 63% were male. Mean time from stroke onset was 25.5 months.	Participants were randomized to an intervention (n=53) or control group (n=57). The intervention was a computer-based training activity that targeted 5 cognitive domains (attention, speed, memory, flexibility and problem solving), which consisted of gaming at home during for 8 weeks, at least 5 days per week, approximately 15–20 minutes per day (600 minutes in total). Persons in the control group received weekly information about stroke from the study's website.	Primary outcomes: The Cognitive Failures Questionnaire (CFQ), The Trail Making Test (TMT), The Block Span Task, Digit Span Task, Eriksen Flanker Task, The Raven Standard Progressive Matrices, assessed at baseline (T0), weeks 8 (T1) and 16 (T2)	46 persons in the intervention group completed the computer-based intervention (median duration was 528 minutes). CGQ From T0 to T1, and T1 to T2, there were no significant differences between groups in median change in total scores. Attention outcomes: From T0 to T1, there were no significant differences between groups in median change scores for TMT-A or TMT-B (time), or median TMT-A or TMT-B (number of correct items). From T1 to T2, there were no significant differences between groups in median change scores for TMT-A or TMT-B (time), or median TMT-A or TMT-B (number of correct items). There were 3 drop-outs in the intervention group, 0 in control group
Cha & Kim 2013 Korea Systematic review & meta-analysis	NA	12 studies (7 RCTs) including 461 participants who received computer-based cognitive rehabilitation following a stroke, and where a validated tool was used for cognitive assessment. Sample sizes ranged from 1-83. Mean age of participants ranged from 51-73 years. 6 studies included persons with acute stroke, 6 with chronic stroke	Studies used simulator-based training, including Psion organiser, CogRehab, GX-video capture system, 2D Virtual Reality computer program, VTI driving simulator, RehaCom, Wiener Determinationsgerat, UCB s.a. and RoboMemo. Treatment sessions varied from 10-60 minute-sessions and were provided for a duration of 3-6 weeks.	Primary outcome: Treatment effect size (Standardized mean difference) associated with cognitive outcome measures.	SMD=0.54, 95% CI 0.33-0.74, p<0.0001 (medium effect size). Results from 8 studies included. Results were similar for sub groups of acute (n=4 studies) and chronic stroke (n=4 studies) (SMD=0.54 and 0.54, respectively).
Loetscher & Lincoln 2013	NA	6 RCTs (n=223), including patients with attentional deficits following stroke.	Trials compared cognitive rehabilitation to usual care. Interventions aimed to	Primary outcome: Subjective and objective measures of global attention	At the end of the treatment period, cognitive rehabilitation was not associated with significantly greater improvement in measures of subjective reports

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<p>UK</p> <p>Cochrane Review</p>		<p>Trials that included >25% of participants with conditions other than stroke were excluded unless subgroup analyses were reported. The sample sizes ranged from 18-78. Timing of recruitment from stroke onset to study entry varied from within 3-4 months up to 4 years.</p>	<p>either restore attentional functions (n=5), provided compensatory strategies (n=1) or both (n=1) and were provided for 3-11 weeks.</p>	<p>Secondary outcomes: Objective reports of domains of attention</p>	<p>of global attention (SMD=0.53, 95% CI -0.03 to 1.08, p=0.06). Results from 2 trials included.</p> <p>Cognitive rehabilitation was not associated with significant long-term effects (>3 months following the end of treatment) on global attention functions (SMD= 0.16, 95% CI -0.23 to 0.56, p=0.41. Results from 2 trials included.</p> <p>No studies reporting objective measures of global attention, either immediately after treatment, or long-term.</p> <p>Cognitive rehabilitation was associated with significantly greater improvement on divided attention, measured using the Paced Auditory Serial Addition Test (SMD= 0.67, 95% CI 0.35 to 0.98, p<0.001). Results from 4 trials included.</p> <p>There were no significant effects on other domains of attention associated with cognitive rehabilitation.</p>
<p>Barker-Collo et al. 2009</p> <p>New Zealand</p> <p>RCT</p>	<p>CA: <input checked="" type="checkbox"/></p> <p>Blinding: Patient <input checked="" type="checkbox"/></p> <p>Assessor <input checked="" type="checkbox"/></p> <p>ITT: <input checked="" type="checkbox"/></p>	<p>78 patients admitted to hospital within 2 weeks of incident stroke with attention deficits identified through neuropsychological assessment. Patient with severe cognitive impairment (MMSE<20) and medical instability, were excluded. Mean age was 69 years, 60% were male.</p> <p>23.4% of those screened for eligibility were included in the study.</p>	<p>Participants were randomized to receive standard care plus Attention Process Training (APT; n=38) or standard care (n=40). APT is a hierarchical, multilevel intervention that focuses on sustained, selective, alternating, and divided attention. APT was administered by clinical neuropsychologists for a maximum of 30 hours provided in hour sessions over 4 weeks.</p>	<p>Primary outcome: The Integrated Visual Auditory Continuous Performance Test (IVA-CPT) Full-Scale Attention Quotient (FSAQ).</p> <p>Secondary outcomes: IVA-CPT Auditory attention and IVA-CPT visual attention</p>	<p>Participants in the ATP group demonstrated significantly greater improvement on the IVA-CPT FSAQ at both the 5-week (Mean difference in change = 2.76, 95% CI 1.31 to 4.21, p<0.001) and 6-month follow-up (mean difference in change = 2.49, 95% CI 1.24 to 3.74, p<0.001).</p> <p>Participants in the ATP group demonstrated significantly greater improvement on the IVA-CPT (Auditory attention) at 5-weeks (p=0.011), but not 6 months (p=0.208).</p> <p>There were no significant differences in change scores between groups at either 5 weeks or 6 months, for IVA-CPT (Visual attention).</p>
<p>Winkens et al. 2009</p> <p>RCT</p> <p>The Netherlands</p>	<p>CA: <input checked="" type="checkbox"/></p> <p>Blinding: Patient <input checked="" type="checkbox"/></p> <p>Assessor <input checked="" type="checkbox"/></p> <p>ITT: <input checked="" type="checkbox"/></p>	<p>37 patients ≥18 years, referred for cognitive rehabilitation for mental slowness following a stroke, onset of at least 3 months. Patients were recruited as both inpatients and outpatients. Mean age was 52 years, 57% male. Mean time since stroke was 19.3 months (intervention) and 6.9 months (control group).</p>	<p>Patients were randomized to a Time Pressure Management (TPM) group (n=20) or a usual care group (n=17).</p> <p>Persons in the intervention group received 10 hours of treatment teaching patients a strategy to compensate for mental slowness in real-</p>	<p>Primary outcomes: Attention outcomes included Information Intake Task, Mental Slowness Observation Test, Mental Slowness Questionnaire, Paced Auditory Serial Addition Test (PASAT), simple reaction time, Symbol Digit Modalities Test, and Trail Making Test parts A and B. Outcomes were</p>	<p>At the end of treatment, the mean Information intake task (no. of used strategies) was significantly higher from baseline, for the TPM group (0.4 vs. -0.3, p=0.03). There were no other significant differences between groups.</p> <p>At the end of treatment, there was significant improvement in mean Mental Slowness Observation Test (time in seconds) in both groups, but no significant differences between groups (p=0.20).</p>

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			life tasks. Teaching was conducted in three stages and focused on preventative and management strategies	assessed at baseline, at the end of treatment (at 5–10wk), and at 3 months.	At follow-up, the mean Mental Slowness Observation Test (time in seconds) was significantly better from baseline, for the TPM group (p=0.01). There were no other significant differences between groups There were 2 losses to follow-up in TPM group and 1 in the usual care group.
Westerberg et al. 2007 Sweden RCT (pilot)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	21 stroke patients, aged 30-65 years, residing in the community an average of 20 months post stroke, with self-reported attention deficits. Mean age 54 years, 71% were male.	Participants were randomized 12-36 months post-stroke to receive computerized working memory training (n=11) or control (n=10). Participants completed training at home using the RoboMemo® software program in 40-minute sessions, five days per week, for a total of five weeks.	Primary outcome: A neuropsychological test battery (including the Stroop test, Claeson-Dahl, span board, digit span, RUFF 2&7, PASAT, and delayed recall) and the Cognitive Failure Questionnaire (CFQ).	At the end of treatment, participants who received computerized working memory training demonstrated significantly greater improvement in the CFQ scores (Mean 43.0 vs. 29.2, p<0.005), span board (mean 6.2 vs. 5.7, p=0.05), digit span (mean 7.3 vs. 5.7, p=0.005), PASAT (mean 53.6 vs. 47.0, p<0.001) and RUFF 2 & 7 (mean 130.3 sec vs. 112.7 sec, p=0.005). Lost to follow-up: intervention group=18% (n=2), control=10% (n=1).
<i>Memory Deficits</i>					
das Nair & Lincoln 2016 UK Cochrane Review	NA	13 RCTs (n=514) including participants with memory problems following stroke. Trials that included >25% of participants with conditions other than stroke were excluded unless subgroup analyses were reported. Sample sizes ranged from 4-153. Mean age ranged from 31-68 years.	Trials compared various memory rehabilitation strategies, with a control group that received either an alternative form of treatment or no memory intervention. Interventions included computerized memory training (n=5), strategy training (n=2), the use of external memory aides (n=2), imagery mnemonics (n=1). Duration of treatment ranged from 2-10 weeks.	Primary outcome: Subjective memory reports Secondary outcomes: Objective memory reports	Short-term effects (i.e., assessed immediately following the intervention): Memory training was associated with significant improvements in <i>subjective</i> memory measures (SMD= 0.36, 95% CI 0.08-0.64, p=0.01). Results from 7 trials included. Long-Term effects (3-7 months following treatment): Memory training was not associated with significant improvements in <i>subjective</i> memory measures (SMD= 0.31, 95% CI -0.02- 0.64, p=0.063). Results from 3 trials included. Short-term effects (i.e., assessed immediately following the intervention): Memory training was not associated with significant improvements in <i>objective</i> memory measures (SMD= 0.25, 95% CI -0.36 to 0.86, p=0.43). Results from 10 trials included. Long-Term effects (3-7 months following treatment): Memory training was not associated with significant improvements in <i>subjective</i> memory measures (SMD= -0.17, 95% CI -0.74- 0.41, p=0.57). Results from 3 trials included.
Wentink et al. 2016 The Netherlands RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/>	115 patients, aged 45-75 years, with self-perceived cognitive impairments 12–36 months after stroke. Participants were identified from a database of	Participants were randomized to an intervention (n=53) or control group (n=57). The intervention was a	Primary outcomes: The Cognitive Failures Questionnaire (CFQ), The Trail Making Test (TMT), The Block Span Task, Digit Span Task,	46 persons in the intervention group completed the computer-based intervention (median duration was 528 minutes). CGQ

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	rehabilitation centres. Median age was 59 years, 63% were male. Mean time from stroke onset was 25.5 months.	computer-based training activity, that targeted 5 cognitive domains (attention, speed, memory, flexibility and problem solving), which consisted of gaming at home during for 8 weeks, at least 5 days per week, approximately 15–20 minutes per day (600 minutes in total). Persons in the control group received weekly information about stroke from the study's website.	Eriksen Flanker Task, The Raven Standard Progressive Matrices, assessed at baseline (T0), weeks 8 (T1) and 16 (T2)	<p>From T0 to T1, and T1 to T2, there were no significant differences between groups in median change in total scores.</p> <p>Working memory outcomes: From T0 to T1, persons in the intervention group performed significantly better on the (forward) Block Span Test (median change=0.7 vs. -0.1, p=0.02), but not the (backward) Block Span Test (median change=0.3 vs. 0.1, p=0.45). There were no significant differences in median change scores between groups for the Digit Span Test (forward or backwards).</p> <p>From T1 to T2, there were no significant differences between groups in median change scores for The Block Span Test (forwards or backwards) or the Digit Span Test (forward or backwards).</p> <p>There were 3 drop-outs in the intervention group, 0 in control group</p>
Aben et al. 2013, 2014 The Netherlands RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	153 participants, aged 18-80 years, living independently at least 18 months following stroke, with reported subjective memory complaints years. Mean age 58 years, 55% male. Mean time post-stroke was 53.9 months.	<p>Participants were randomly allocated to either Memory Self-Efficacy (MSE) training program (n=77) or active control group (n=76).</p> <p>MSE - 9 twice-weekly group sessions of 1 hour, with ~30 minutes of homework per session. Training consisted of discussions about general information regarding memory and stroke, training in internal and external memory strategies, psycho-education on influence of beliefs and anxiety on memory performance, and realistic goal setting for memory tasks.</p> <p>Control - 9 twice-weekly group sessions of 1 hour, no homework. The control group participated in a peer support group and learned general information about</p>	<p>Primary outcomes: MSE - Metamemory-In-Adulthood questionnaire (MIA) - validated for Dutch. Measures subjective memory experiences in daily living.</p> <p>Memory capacity - Dutch version of Auditory Verbal Learning Test (AVLT) and parallel versions (before/after) of Story Recall from Rivermead Behavioural Memory Test (RBMT). Specifically used delayed recall for both measures as outcomes.</p>	<p>Immediate outcomes (2013) At the end of treatment, improvement of MSE was significantly greater in the MSE training group (p=0.019).</p> <p>There were no significant differences between groups in mean change scores from baseline to end of treatment for AVLT (p=0.802) or RBMT (p=0.378).</p> <p>Long-term outcomes (2014) Improvements in MSE among participants in the training group remained significantly greater compared with control group at both 6 and 12 months after the intervention.</p> <p>15% of the patients in the training group improved by ≥ 1 standard deviation on the MSE scale vs. 4% in the control group.</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			<p>the causes and consequences of stroke.</p> <p>Patients were assessed within 3 weeks prior to intervention, and within 10 days following intervention.</p>		
<p>Zucchella et al. 2014</p> <p>Italy</p> <p>RCT</p>	<p>CA: <input checked="" type="checkbox"/></p> <p>Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/></p> <p>ITT: <input checked="" type="checkbox"/></p>	<p>87 patients, 45-80 years, admitted to a neurorehabilitation unit following first-ever stroke of duration < 4 weeks, with MMSE scores >10 and cognitive deficits, identified in relation to population norms. Mean age was 67 years, 47% were male. Mean MMSE score was 22.</p>	<p>Participants were randomized to a study group and performed cognitive training exercises, including therapist-guided computer exercises (1 hour x 4/week for 4 weeks) or to a control group, which met with a psychologist and discussed general topics, news and their recent activities for a total of 16 hours. Outcomes were assessed before and after the intervention period.</p>	<p>Primary outcomes: Rey Auditory Verbal Learning Test (RAVLT) Delayed and immediate recall, logical memory delayed and immediate recall</p>	<p>At the end of treatment, participants in the study group demonstrated significant improvement in all measures of memory, while those in the control group did not.</p> <p>Mean RALVT scores (immediate recall) were not significantly different between groups at the end of treatment (30 vs. 27.2, p<0.05).</p> <p>Mean RALVT scores (delayed recall) were significantly higher in the study group at the end of treatment (7.2 vs. 3.9, p<0.0001).</p> <p>Mean immediate and delayed logical memory scores were significantly higher in the study group at the end of treatment (4.5 vs. 3.4, p=0.005 and 4.4 vs. 3.2, p=0.009, respectively).</p>
<p>das Nair and Lincoln 2012</p> <p>UK</p> <p>RCT</p> <p>Rehabilitation of Memory in Neurological Disabilities (ReMiND)</p>		<p>72 patients ≥18 years, with reported memory problems due to a traumatic brain injury (n=16), stroke (n=17) or multiple sclerosis (n=39). Mean age was 48 years, 44% male. Mean time since stroke onset was 73 months</p> <p>50.7% of those screened for eligibility were included in the study.</p>	<p>Participants were randomized to one of three study arms: Compensation (n=24), Restitution (n=24), and Self-help (n=24). Each study arm consisted of 10, 1.5-hour sessions administered by research assistants. The use of internal memory aids and errorless learning techniques were taught in both memory programmes. The compensation program additionally taught external memory aids whereas the restitution program additionally included encoding and retrieval exercises. The self-help program consisted of relaxation training with no memory training.</p>	<p>Primary outcome: The Everyday Memory Questionnaire (EMQ).</p> <p>Secondary outcomes: Rivermead Behavioural Memory Test-Extended version (RBMT), General Health Questionnaire-12 (GHQ), and the Nottingham Extended Activities of Daily Living Scale (NEADLS).</p>	<p>No significant between group differences were reported with respect to the primary outcome at either 5 or 7 months.</p> <p>Mean EMQ scores at 5 months were 37.1 (compensation), 42.6 (restitution) and 45.5 (self-help).</p> <p>Mean EMQ scores at 5 months were 36.6 (compensation), 41.0 (restitution) and 44.1 (self-help)</p> <p>Participants in both the compensation and restitution study arms used significantly more internal memory aids than did those in the self-help group (p<0.05).</p> <p>The groups did not differ significantly on measures of mood, adjustment, or activities of daily living.</p> <p>Lost to follow-up: Compensation=16.7%, Restitution=4.2%, Self-help=4.2%.</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Westerberg et al. 2007 Sweden RCT (pilot)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	21 stroke patients, aged 30-65 years, residing in the community an average of 20 months post stroke, with self-reported attention deficits. Mean age 54 years, 71% were male. (Trial was included in Cochrane review of executive function)	Participants were randomized to receive computerized working memory training (n=11) or control (n=10). Participants completed training at home using the RoboMemo® software program in 40 minute sessions, five days per week, for a total of five weeks.	Primary outcome: Subjective memory outcome was the Cognitive Failure Questionnaire (CFQ).	At the end of treatment, participants who received computerized working memory training demonstrated significantly more improvement in the CFQ scores (Mean 43.0 vs. 29.2, p<0.005, effect size 0.80). Lost to follow-up: intervention group=18% (n=2), control=10% (n=1).
<i>Executive Functioning and Problem Solving</i>					
Rozenal-Iluz et al. 2016 Israel RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	39 participants who had a stroke ≥6 six months prior to the study, could walk 10-meters with or without assistance, and with executive dysfunction. Mean age was 60 years, 59% male. Mean time since stroke was 3.5 years.	Secondary analysis from Virtual Reality for Stroke Rehabilitation Trial, in which participants were randomized to an interactive video-game group intervention (n=20) or a traditional group intervention for motor recovery (n=19). The intervention included two, 1-hour group sessions per week for 3 months, either playing video-games or performing traditional exercises/activities.	Primary outcomes: The Executive Function Performance Test (EFPT) (Bill payment sub score), Executive Function Route-finding Task (EFRT), Trail-Making Test Part B (TMT-B). Assessments were completed at baseline, after the intervention and at 3 months.	Mean EFRT scores at baseline, post-intervention and at follow-up were: Intervention group: 3.3, 3.6 and 3.4 Control: group: 3.4, 3.3, and 3.7 There were no significant differences between groups Mean EFPT scores at baseline, post-intervention and at follow-up were: Intervention group: 5.7, 3.9 and 2.8 Control: group: 7.2, 5.0 and 5.0 There were no significant differences between groups Mean TBT-B time (sec) at baseline, post-intervention and at follow-up were: Intervention group: 145.2, 130.8 and 116.9 Control: group: 178.8, 187.5 and 165.7 There were no significant differences between groups There were 3 losses to follow-up in each group
Chung et al. 2013 UK Cochrane Review	NA	19 RCTs (n=907) including participants ≥16 years, with stroke or other non-progressive acquired brain injuries.	Trails examined strategies restoring components of executive function. 13 interventions were described; 7 restorative (self-awareness training, intensive neurorehabilitation, neurorehabilitation including cognitive remediation problem-solving/goal management training, autobiographical memory cueing, working memory training, and verbal feedback), 5 compensative interventions (intensive	Primary outcome: Measures of global executive function, such as the Behavioural Assessment of Dysexecutive Syndrome (BADS) and the Hayling and Brixton Tests. Secondary outcomes: Measures of components of executive function, functional ability in ADLs and extended ADLs, and quality of life.	Cognitive rehabilitation vs. standard care: None of the included trials reported the primary outcome. On the basis of a single RCT (n=86), results significantly favoured cognitive rehabilitation compared to sensorimotor therapy in terms of concept formation (MD= 0.43, 95% CI -0.76 to -0.10) and ADLs (MD=28.3, 95% CI -33.50 to -23.06). Cognitive rehabilitation vs. placebo/no treatment: 4 RCTs (n=184) were included in the meta-analyses. None of the included trials reported the primary outcome. No significant treatment effects were reported with respect to concept formation, planning, flexibility, working memory, or extended ADLs. Comparison of two types of cognitive rehabilitation:

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			neurorehabilitation, standard neurorehabilitation, video-feedback, verbalization, chunking and pacing and directive feedback). There were no trials of adaptive interventions. Control groups included no intervention, standard care and alternative forms of cognitive therapy)		2 RCTs (n=82) reported measures of global executive function: no significant treatment effects were reported (SMD= -0.41, 95% CI -0.85 to 0.03). On the basis of 8 RCTs (n=404), no significant treatment effects were reported for any of the secondary outcomes.
Poulin et al. 2012 Canada Systematic Review	NA	10 studies (n=186), including persons recovering from stroke or mixed etiology (if stroke comprised >50% of sample) experiencing executive function deficits.	Studies examined cognitive rehabilitation strategies to remediate executive function impairments or to improve functional tasks compromised by impairments in executive function, compared to alternative or no treatment. Results were summarized according to stage of recovery and intervention type.	Primary outcome: Measures of some aspect of executive functioning, assessed through neuropsychological or psychological tests or performance of daily activities.	No studies were identified that examined cognitive rehabilitation for executive function during the acute stage of care. In the sub-acute stage of stroke, results from a single pre-post study (n=18) provided limited evidence that computerized dual-task training is associated with significant improvement in executive functioning, compared to no treatment (p<0.05). 9 studies (n=186) examined an intervention during the chronic phase of care. The authors concluded that there is limited evidence to suggest that paging systems are associated with significant improvement in performance on functional tasks that involve executive control, compared to no treatment (p<0.05).
Westerberg et al. 2007 Sweden RCT (pilot)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	21 stroke patients, aged 30-65 years, residing in the community an average of 20 months post stroke, with self-reported attention deficits. Mean age 54 years, 71% were male.	Participants were randomized to receive computerized working memory training (n=11) or control (n=10). Participants completed training at home using the RoboMemo® software program in 40-minute sessions, five days per week, for a total of five weeks.	Primary outcome: A neuropsychological test battery, including the Stroop test, Claeson-Dahl, span board, digit span, RUFF 2&7, PASAT, and delayed recall) and the Cognitive Failure Questionnaire (CFQ).	At the end of treatment, participants who received computerized working memory training demonstrated significantly more improvement in the CFQ scores (Mean 43.0 vs. 29.2, p<0.005), span board (mean 6.2 vs. 5.7, p=0.05), digit span (mean 7.3 vs. 5.7, p=0.005), PASAT (mean 53.6 vs. 47.0, p<0.001) and RUFF 2 & 7 (mean 130.3 sec vs. 112.7 sec, p=0.005). There was no significant difference between groups in mean Stroop raw scores (99.1 vs. 97.8, p<0.05) Lost to follow-up: intervention group=18% (n=2), control=10% (n=1).
Man et al. 2006 Hong Kong Quasi-RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/>	109 patients, aged 18-55 years with acquired brain injury at or within 6 months, (55% stroke) and mild cognitive impairment, assessed through specified cognitive assessments, with an attention span sufficient to	Participants were randomized to one of four study arms: computer-assisted training (CAT, n=30), therapist-administered training (TAT, n=30), online interactive	Primary outcomes: Alternative analogous target insight problems, the Comparing Category Test, Lawton IADL Scale, and Problem Solving Self-Efficacy.	Participants in each of the three intervention groups demonstrated significant improvement from baseline to end of treatment in terms of overall basic and functional problem-solving ability, the Comparing Category Test, and the Lawton IADL Scale (p<0.05), whereas those in the control group did not.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	ITT: ☒	attend the 45-minute training session. Mean age ranged from 43-48 years across treatment groups.	computer-assisted training (ICAT, n=30), and no treatment control (n=20). Participants in each of the active treatment groups completed 20, 45-minute sessions of analogy problem solving skills training.		There were significant improvements of problem solving in the Category test in all intervention groups ($p \leq 0.01$) but not the control group ($p = 0.12$). Lost to follow-up: CAT=6.7% (n=2), TAT=0%, ICAT=16.7% (n=5), Control=0%.

CA: Concealed Allocation; ITT: Intention-to-treat

Cognitive Rehabilitation to Improve Functional Ability

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Hoffmann et al. 2010 Australia Systematic review	NA	4 RCTs including 376 persons ≥ 18 years with cognitive impairment (including attention and concentration, memory, orientation, and/or executive functions) following stroke, in which any non-pharmacological intervention was provided and where either basic or instrumental ADL was assessed.	Interventions included Attention process training (APT), provided for up to 30 hrs; Cognitive skills remediation training administered on an individual basis for 30–40 minutes, 3x per week for an average of 3–4 weeks; feedback of the results from an extensive battery of cognitive assessments to assess specific cognitive functions, including a summarized report with specific recommendations, which was provided to professionals involved in their rehabilitation; and time pressure management (TPM), provided for 10 hours. Control conditions were routine or standard care	Primary outcome: Basic or instrumental ADL	There were no significant differences between groups on any of the ADL measures assessed using the Barthel Index (3 trials) or the modified Rankin Scale (1 trial). There was no significant difference between groups in the single trial that assessed instrumental ADLs using the Extended Activities of Daily Living scale.

Physical Activity

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Oberlin et al. 2017 Australia Systematic review	NA	<p>14 RCTs including 736 persons ≥ 18 years, recovering from ischemic or hemorrhagic stroke. Mean age was 62.5 years, 59% were men. Mean time from stroke onset was 1.9 years. In 7 trials persons with dementia or significant cognitive impairment, were excluded. In 3 trials persons with mild cognitive impairment were included. Baseline cognitive status was not reported in the other 4 trials.</p>	<p>Trials compared a control condition vs. an experimental condition that included a component that aimed to increase physical activity (PA) through aerobic exercise, resistance training, or physiotherapy), and which had a duration of training >4 weeks.</p> <p>The experimental condition in 5 trials involved stretching and toning/physiotherapy, 3 trials consisted only of aerobic exercise training, and 6 trials included a combined PA training program (aerobic exercise + stretching).</p>	<p>Primary outcome: Pooled analyses of validated neuropsychological test of cognition, assessed from pre- to -postintervention</p>	<p>Using the results from all 14 studies, PA was associated with a small to moderate mean effect size (Hedges' $g = 0.304$, 95% CI 0.14–0.47, $p < 0.001$).</p> <p>In sub group analysis, statistically significant effect sizes were observed for chronic stroke (> 3 months), combined PA and stretching/toning programs and for attention/processing speed domains of outcome measures.</p>
Tang et al. 2016 Canada RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	<p>50 persons living in the community, aged 50-80 years, > 1-year post-stroke, able to walk ≥ 5 m with or without assistance and able to participate in an exercise program. Median age was 65 years, 58% were men. Median Montreal Cognitive Assessment was 25.</p>	<p>Participants were randomized 1:1 to a high-intensity Aerobic Exercise (AE) or low-intensity non-aerobic Balance/Flexibility (BF) program for 6 months (3 x 60-min sessions/week)</p>	<p>Secondary outcomes: Verbal Digit Span, Trail Making Part B, and Stroop Tests</p>	<p>There were no significant differences in change scores from baseline to the end of treatment between groups for any outcome.</p> <p>Median scores before and after treatment for the Verbal Digit Span test (forwards) were: AE group 8 and 8; BF group 7 and 7</p> <p>Median scores before and after treatment for the Trail Making Test B (sec) were: AE group 128.9 and 131.6; BF: 161.0 and 163.5</p> <p>Median scores before and after treatment for the Color-Word Stroop Test (sec) were: AE group: 108.5 and 122.0; BF group 131.7 and 141</p> <p>There were no losses to follow-up in the BF group, and 3 in the AE group.</p>
Cumming et al. 2012	NA	<p>12 RCTs and controlled clinical trials ($n=907$) including persons recovering from stroke. Studies</p>	<p>Trials examined the effect of exercise or physical activity on cognition. Trials</p>	<p>Primary outcome: Change in cognitive performance on a range of</p>	<p>9 of the 12 included studies provided sufficient data for pooling.</p>

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Australia Systematic Review		with mixed population were included provided that stroke represented at least one-third of the sample. Cognitive status (impaired vs. intact of participants at admission not reported)	compared different levels and intensities of movement rehabilitation with a standard care or no treatment control group (n=5), 6 vs. 7 days a week of inpatient rehabilitation (n=1), and a specific exercise program with a placebo treatment control group (n=6)	tests, including FIM-Cog, MMSE, Trail making, Symbol Digit, PASAT, WCST, Stroop, SRTT, FIM problem solving, SIS cog domains. In most studies, cognition was not the primary outcome.	Exercise or activity was associated with a significant improvement in cognitive function (SMD=0.2, 95% CI 0.04 to 0.36; p=0.015).
Quaney et al. 2009 USA RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	38 persons recovering from an ischemic stroke with duration of onset ≥6 months, with residual hemiparetic deficits in either the upper or lower extremity, an MMSE score of >23, and adequate cardiac function to adhere to the study protocol. Mean age was 61.5 years, 55% women.	Participants were randomized 1:1 to an aerobic exercise group (AEX group, n = 19), which performed progressive resistive stationary bicycle training at 70% maximal heart rate, or a control group, which performed stretching exercises at home. Each group exercised 3 times a week (45-minute sessions) for 8 weeks.	Primary outcomes: Wisconsin Card Sorting Task (WCST), Stroop task, Trail-Making Task (A, B), Serial Reaction Timed Task (SRTT), Predictive Grip Force Modulation (PGFM)	From baseline to end of treatment, there were no significant differences between groups on any of the cognitive outcomes, with the exceptions of mean SRTT repeated (sec) p=0.024 and mean PGFM color cues (p=0.0380, both favouring the AEX group. From baseline to 8-weeks following treatment, there were no significant differences between groups for any of the cognitive outcomes. There were no losses to follow-up in either group.

CA: Concealed Allocation; ITT: Intention-to-treat

Transcranial Direct Current Stimulation (tDCS)

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Yun et al. 2015 Korea RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	45 patients with cognitive dysfunction following stroke, defined as ≤27 on the Korean version of Mini Mental State Exam (K-MMSE). Mean age was 62.7 years, 44% were male. Mean duration of stroke onset was 39 days.	Patients were randomly assigned to 1 of 3 groups: (1) the left fronto-temporal anode stimulation (left-FTAS) group, (2) the right fronto-temporal anode stimulation (right-FTAS) group, and (3) the sham group. Patients in each group received tDCS treatment for 30 min, five times a week, for 3 weeks.	Primary outcome: K-MMSE, Secondary outcomes: Computerized neurocognitive function tests including forward digit span test (FDST), backward digit span test (BDST), forward visual span test (FVST), backward visual span test (BVST), visual learning test-delayed recall (ViLT-R), verbal learning test-delayed recall (VeLT-R), visual continuous performance test (VCPT), auditory continuous	Within group changes (before vs. after treatment) L-FTAS group: There was significant improvement in mean K-MMSE, BDST, FVST, VeLT-R and K-MBI scores R-FTAS group: There was significant improvement in mean VeLT-R and K-MBI scores Sham group: There was significant improvement in mean K-MMSE, BVST and K-MBI scores. Between group changes Compared with the other 2 groups, patients in the L-FTAS group demonstrated significantly greater improvement in mean changes in VeLT-R scores (10.5 vs. 5.1 and 5.4, p<0.05).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
				performance test (ACPT), and the Korean version of the modified Barthel Index (K-MBI). Assessments were conducted before and after treatment	There were no significant differences in mean change scores between the groups on any of the other outcomes.
Jo et al. 2009 Korea RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	10 patients, < 70 years, with first-ever unilateral right hemisphere stroke, and noticeable cognitive disorder. Mean age was 47.7 years, 70% were male. Mean duration of stroke onset was 2.4 months	Each patient participated in 2 stimulation conditions, anodal dorsolateral prefrontal cortex (2mA) and sham stimulation for duration of 30 minutes within 48 hrs of a washout period. The order of stimulation was randomly assigned.	Primary outcomes: Measures of working memory (accuracy, recognition accuracy and response time)	There were significant improvements in accuracy and recognition accuracy among participants in the active tDCS condition. There were no significant improvements in any outcomes in the sham condition. There were no significant differences between conditions for any of the outcomes.
Kang et al. 2009 Korea RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	10 patients aged 48-84 years with cognitive decline following stroke (MMSE \leq 25). Mean age was 70 years, 60% were male. Mean time since stroke onset was 1.5 years (range 23-3,875 days) 10 aged-match healthy control subjects were also recruited.	Patients received i) 20-minute administration of anodal tDCS (2 mA) to the left dorsolateral prefrontal cortex and ii) sham stimulation in random order. Sessions were at least 2 days apart.	Primary outcome: The “go/no go” test (subjects are presented with 30 figures and must press a button in response to the figure “1”). Number of correct responses and reaction time were evaluated. The go/no go test was administered at baseline, immediately after the intervention, and at 1 and 3 hours post stimulation. In addition, the authors collected subjective descriptions of attention, fatigue, task difficulty and sleep quality (at baseline and 3 hours only).	There were no significant differences between treatment conditions among the control group for either correct responses or reaction time. In the stroke patient portion of the study, active treatment was associated with significant improvement in the number of correct responses (p=0.043). In post-hoc analysis, tDCS stimulation was associated with a significant improvement in correct responses at one hour (p=0.024) which was maintained at 3 hours post treatment (p=0.041). Active stimulation had no significant effect on response time. Assessment of subjective outcomes demonstrated no effect associated with the stimulation intervention.

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Enriched Environments

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Kim et al. 2011 Korea RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/>	28 patients admitted to an inpatient rehabilitation unit following acute stroke with cognitive impairment, identified by a score of 10-24 on the K-	Participants were randomized to receive virtual reality (VR) training (30 minutes, 3x/week for 4 weeks) + computer-assisted	Primary outcomes: Visual & auditory continuous performance tests (CPT), word-color test, forward & backward digit span tests	Within groups, there was significant improvement at the end of treatment from baseline, in the VR group for several outcomes (Visual CPT, Auditory CPT, Forward DSP, and forward and backward VST), but not for persons in the control group.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	MMSE (Korean version of the Mini-Mental Status Examination). Mean age was 64 years, 39% were male. Mean time since stroke onset was 21 days.	cognitive rehabilitation (30 minutes, 2x/weeks, for 4 weeks; n=15) or to a control group (n=13) who underwent computer-assisted cognitive rehabilitation only (same duration as intervention group).	(DST), forward and backward visual span test (VST)	Between groups, there was significantly more improvement among persons in the VR group for the outcomes of visual CPT (mean change from baseline -0.16 vs. -0.03, p<0.01) and the backward VST (mean change 0.9 vs. -0.1, p<0.05).
Sarkamo et al. 2008 Finland RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	60 patients, ≤75 years, who had been discharged from a single institution following middle cerebral artery stroke. Mean ages among the 3 groups were 56, 59 and 61.5 years, 53% were male. Mean time from stroke onset to study entry was 6 days.	Patients were randomly allocated to music listening, language listening or control groups as soon as possible following discharge from acute care. Patients in the music and language listening groups both received portable CD players and CD's of either music or narrated audio books as appropriate & were instructed to listen to the material by themselves for a minimum of 1 hr/day for a period of 2 months. Patients assigned to the control group received no listening material.	Primary outcomes: 10 cognitive domain outcomes including verbal memory (story recall subtest from the Rivermead Behavioural Memory Test), short-term and working memory (digit span subtest from the Wechsler Memory Scale—Revised), focused attention (Stroop subtests). Outcomes were assessed at baseline, 3 and 6 months	The mean changes in verbal memory and focused attention over the study period were significantly more improved among patients in the music listening group (p=0.002 and p=0.012, respectively). There were no other significant changes in mean scores among the groups for any of the other cognitive outcomes. Post hoc analysis of change scores from baseline demonstrated significantly greater improvements in both of these areas associated with music listening at both 3 and 6 months. There were 6 drop-outs.

CA: Concealed Allocation; ITT: Intention-to-treat

Vascular Risk Factor Reduction to Prevent Dementia or Cognitive Decline Following Stroke

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
<i>Blood Pressure</i>					
Williamson et al. 2019 USA Systolic Blood Pressure Intervention Trial-Memory and cognition IN	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	9,250 participants aged ≥ 50 years with SBP ≥130-180 mm Hg and at least one additional CVD risk factor were recruited from 102 clinical sites. Patients with diabetes or previous stroke were excluded. Mean age for patients in both groups was 67.9 years, 36%	Patients were randomized to an intensive BP arm with a goal of SBP <120 mm Hg using 2-drug therapy, if required (n=4,678) vs. a standard arm with a goal of SBP <140 mm Hg (n=4,683) for up to 6 years. Participants were seen	Primary Cognitive outcome: Probable dementia Secondary Cognitive outcomes: Mild cognitive impairment (MCI) and a composite outcome of MCI or probable dementia	Median intervention period was 3.34 years, with a median follow-up of 5.11 years. Over the study period, the mean SBP of patients in the intensive group was lower (121.6 vs. 134.8 mm Hg). There were no cognitive outcomes available for 798 patients (outcomes imputed). Probable dementia occurred in 149 participants in the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
Decreased hypertension (SPRINT-MIND)		were female. Mean Framingham 10 year risk score was 20.1%.<10% of patients in both groups were not taking any antihypertensive agents	monthly for the first 3 months and every 3 months thereafter, with adjustments to medications, as required. Lifestyle modification was encouraged as part of the management strategy		intensive treatment group vs 176 in the standard treatment group (7.2 vs 8.6 cases per 1,000 person-years; HR= 0.83; 95% CI, 0.67-1.04, p=0.10). There were no interactions based on sub group analyses (age, sex, race, history of CVD, kidney disease, SBP at baseline, orthostatic hypotension) The risk of MCI was significantly lower in the intensive group (287 vs. 353 cases per 1,000 persons years; HR=0.81; 95% CI, 0.69-0.95, p=0.007). The risk of the composite outcome was significantly lower in the intensive group (20.2 vs. 24.1 cases per 1,000 person-years; HR=0.85, 95% CI 0.74-0.97, p=0.01)
Bath et al. 2017 UK RCT 'Prevention of Decline in Cognition after Stroke Trial' (PODCAST)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	83 participants recruited from 19 sites (600 planned), functionally independent, who had suffered an ischemic or ICH in the previous 3-7 months, aged ≥70 years with t-MMSE > 16 or age > 60 years and t-MMSE 17 to 20 and SBP 125 to 170 mmHg and total chol of 3 to 8 mmol/l. Mean age was 73 years, 77% were men, median time from stroke onset to randomisation was 4.5 months.	Patients were randomized to an intensive blood pressure lowering program (target SBP< 125 mmHg, n=41) or a moderate blood pressure lowering using guideline standards (target SBP<140 mmHg, n=42), for at least 6 months. In the subset of patients with ischemic stroke, patients were also randomized to receive intensive lipid lowering treatment (target LDL chol <2.0 mmol/L, n=39) or guidelines standard treatment target LDL<3.0 mmol/L, n=38)	Primary outcome: Cognition, assessed annually up to 8 years using Addenbrooke's Cognitive Examination-R (ACE-R) Secondary cognitive outcomes: Stroop test, Trail-Making Tests A and B, category fluency (animal naming); MMSE, Telephone Interview for Cognition Scale-Modified (TICS-M), premorbid cognitive function assessed in an informant interview using the IQCODE and dementia (DSM IV)	Median duration of follow-up was 24 months. Mean baseline SBP and DBP was 147.1 and 82.1 mm Hg. Mean total chol was 4.0 mmol/L. The mean SBP and DBP was reduced significantly more in the intensive BP group (mean difference -10.6 and -5.5 mmHg, p<0.01, respectively). Mean baseline ACE-R scores were 85.7 (intensive BP) and 86.5 (guideline BP). At follow-up, mean ACE-R scores were 80.8 (intensive BP) and 84.4 (guideline BP). The mean difference between groups was not significant (-3.6, 95% CI -9.7, 2.4, p=0.24). There were no significant differences between groups for any of the secondary cognitive outcomes between BP groups Mean total, LDL and non-HDL cholesterol levels were significantly lower in the intensive lipid-lowering group. At follow-up, mean ACE-R scores were 86.5 (intensive lipid reduction + BP lowering) and 78.2 (guideline lipid reduction + BP lowering). The mean difference between groups was not significant (4.4, 95% CI -2.1, 10.9, p=0.18). The intensive lipid group had significantly higher cognition scores, assessed using the Trail Making (time-sec), category fluency (animal naming) the

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
					Stroop (3 accuracy and interference accuracy). Mean mRS was significantly lower, and EQ-VAS was significantly higher in the intensive lipid group. The number of serious adverse events did not differ between groups. The incidence of dementia and death did not differ significantly between groups.
Pearce et al. 2014 USA SPS3 RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	3,020 participants, mean age of 63 years, who were normotensive or hypertensive and had sustained a confirmed lacunar stroke within the previous 180 days. Participants with disabling stroke, or previous ICH or cortical stroke, were excluded.	At least 2 weeks following the event, patients were randomized (1:1) to a SBP target of 130-149 mm Hg or <130 mm Hg (open-label) and 325 mg aspirin+325 mg clopidogrel daily or 32.5 mg aspirin + placebo (double-blind). Patients were followed every 1 or 3 months to ensure that blood pressure remained within target range. Adjustments to medications were made, as appropriate.	Secondary outcome Changes in cognitive function, assessed annually for up to 5 years using the Cognitive Abilities Screening Instrument (CASI)	Median duration of follow-up was 3 years. CASI scores improved slightly in both groups over time, but there were no significant differences between blood pressure groups or antiplatelet groups at 1, 2, 3, 4 or 5 years. Incidence of mild cognitive impairment did not differ among treatment groups (9.7%/year antiplatelet +aspirin, 9.9%/yr aspirin +placebo, 10.0%/yr low BP target and 9.5%/yr higher BP target)
Diener et al. 2008 International PRoFESS RCT (factorial)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	20,332 patients >50 years of age who had suffered an ischemic stroke within 120 days and had two additional risk factors (e.g. diabetes, hypertension, obesity, etc.). Mean age was 66 years, 36% were female	After a median of 15 days following stroke onset, patients were randomly assigned to receive aspirin (25 mg/day) plus extended-release dipyridamole (400 mg/day) or clopidogrel (75 mg/day) and either telmisartan (80 mg/day) or placebo for the study duration (minimum of 18 months).	Secondary outcomes: Mini-Mental State Examination (MMSE) Cognition was assessed at 1 month and 2 years post-stroke and at the end of the study period.	Median duration of follow-up was 2.4 years. At the end of the study period there were no significant differences in the number of patients with MMSE scores ≤24 reported between the two antiplatelet regimens (RR 1.02, 95% CI 0.94 to 1.10) or between the telmisartan and placebo groups (RR 1.01, 95% CI 0.94 to 1.09). There were no significant between group differences in the number of participants who had a decrease of >2 points on the MMSE only the duration of the study (dipyridamole vs. clopidogrel: RR 0.91, 95% CI 0.83 to 1.00; telmisartan vs. placebo: RR 0.95, 95% CI 0.87 to 1.05). A total of 125 patients (0.6%) were lost to follow up.
Peters et al. 2008 UK HYVET-COG RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/> (primary)	3,336 patients >80 years of age with persistent hypertension (160-200 mm Hg sitting systolic pressure). 6% of patients had experienced a previous stroke.	Patients were randomized to receive 1.5 mg of the diuretic indapamide (sustained release) (n=1,933) or placebo (n=1,912). The ACE inhibitor perindopril (2 or 4	Secondary outcomes: Mini-Mental State Examination (MMSE), incident dementia. Cognition was assessed at baseline and annually for the duration of the study.	The median duration of follow-up was 2.2 years. The mean change in MMSE from baseline to the 2-year follow-up was -1.1 (SD 3.9) for participants in the placebo group and 0.7 (SD 4.0) for those in the active treatment group (p<0.05).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
	analysis)		mg), or placebo, was added if necessary to achieve the target blood pressure of 150/80 mm Hg. Target systolic blood pressure was <150 mm Hg and target diastolic blood pressure was < 80 mm Hg. Cognitive decline was defined as a decline of >3 points of a total score of <24 on the MMSE.		Active treatment was not associated with a significant reduction in cognitive decline (HR= 0.93, 95% CI 0.82 to 1.05), incident Alzheimer's disease (HR 0.85, 95% CI 0.63 to 1.15), incident vascular dementia (HR 0.86, 95% CI 0.67 to 1.09), or all incident dementia (HR 0.86, 95% CI 0.67 to 1.09). The number of serious adverse events reported was lower among patients in the active treatment group (358 vs. 448, p = 0.001). Only five of these events (three in the placebo group and two in the active-treatment group) were deemed to be possibly related to the trial medication.
Tzourio et al. 2003 International PROGRESS RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	6,105 patients with a history of stroke (ischemic or hemorrhagic) or TIA within the previous 5 years. No blood pressure criteria was used for study eligibility. 15 patients in each group had MMSE scores of ≤25 at baseline	Patients were randomly assigned to active therapy (n=3,051) or matching placebo (n=3,054). Patients in the active treatment group received a flexible regimen based on perindopril (4 mg daily) with the addition of indapamide (2.5 mg daily) in patients for whom the responsible physician judged there to be no specific indication for or contraindication to treatment with a diuretic.	Secondary outcome: Incident dementia (based on DSM-IV criteria) and cognitive decline, defined as a decline of >2 points from baseline on the MMSE. Timing of assessment: Baseline, 6- and 12-months, and annually for the duration of follow-up.	Mean duration of follow-up was 3.9 years. Cognitive decline was reported in 9.1% of participants in the active treatment group and 11% of participants in the placebo group. Active treatment was associated with a significant reduction in the risk of cognitive decline (risk reduction =19%, 95% CI 4% to 32%) and the composite outcome of cognitive decline and recurrent stroke (risk reduction =45%, 95% CI 21% to 61%). Dementia was diagnosed in 6.4% and 7.1% of participants in the active treatment and placebo groups, respectively. Active treatment was associated with a non-significant reduction in risk of dementia (risk reduction =12%, 95% CI -8% to 28%; p>0.05) and a significant reduction in the composite outcome of dementia and recurrent stroke (risk reduction =34%, 95% CI 3% to 55%).
Forette et al. 2002 European Open-label follow-up of Syst-Eur RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	2,092 patients ≥60 years without dementia with SBP and DBPs of 160-219 and <95 mm Hg. Median age was 68 years	Patients were randomized to receive nitrendipine (10-40 mg/day) with/without enalapril (5-20m g/day) or hydrochlorothiazide (12.5-25 mg/day) or both second line drugs with the aim of lowering SBP to ≤150 mm Hg vs. placebo. At the end of the main phase of the trial, patients in the control group were offered the active treatment. The MMSE was used to	Secondary outcome: Incident dementia	Median duration of follow-up was 3.9 years. Both SBP and DBPs were significantly lower among patients in the active treatment group at all visits. At 8 years, the differences were 4.2 mm Hg systolic and 2.9 mm Hg diastolic (p<0.01). At the end of follow-up there were a total of 64 incident cases of dementia (41 AD, 10 mixed or VaD and 4 of unknown origin). The incidence of dementia was significantly higher among patients in the control group (43 vs. 21; 7.4 cases/1000 vs. 3.3/1000, p<0.0001).

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
			screen patients annually. A score <24 indicated possible dementia, while dementia was confirmed using DSM-III-R criteria + brain imaging.		Nitrendipine was associated with a significantly reduced risk of incidence dementia (HR=0.38, 95% CO 0.23-0.64, p<0.001). An estimated 1000 patients would need to be treated for 5 years to prevent 20 new cases of dementia.
<i>Multicomponent Interventions</i>					
Teuschla et al. 2018 Austria Patient-level meta-analysis	NA	Data from 322 patients included in the ASPIS and Ihle-Hansen et al. 2014 trials, both described below. 157 patients were randomized to the intervention and 165 to the control group	The primary analysis was performed using an intention-to-treat principle where missing data for drop-outs and persons who were not able to perform a cognitive test, were imputed.	Primary outcomes: Trail Making Test (TMT)-A (attention), TMT-B (executive functions) and a 10- word list recall test (verbal memory), assessed at 12 months.	Full cognitive outcomes were available for 259 patients (120 intervention, 139 control). In fully-adjusted models, there were no significant differences for any of the outcomes between groups. In an analysis in which outcomes for drop-outs were imputed but not for patients unable to complete the assessments, there was a significant difference between groups in mean TMT-A scores, favouring the intervention group (p=0.014).
Matz et al. 2015 Austria RCT Austrian Polyintervention Study to Prevent Cognitive Decline After Ischemic Stroke (ASPIS)	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	202 patients, 40-80 years with acute ischemic stroke, with MMSE scores ≥24 with NIHSS scores of 1-14 on admission and mRS of 0-2. Mean age was 62 years, 29% were female. Pre-stroke, 92% of patients were unimpaired.	Within 3 months of stroke, patients were randomized to a 24- month intensive intervention program (n=101), emphasizing blood pressure control (goal of <140/90 mm Hg and <135/85 mm Hg for diabetics), increased physical activity (goal of moderate or vigorous, 3-5x/week), diet (elements of a prudent diet and Mediterranean type diet), while encouraging weight loss in the obese, cognitive training (home-based exercises) and cessation of smoking; or to a control group (n=101), which received care according to standard guidelines.	Primary outcome: Decline in cognitive performance at 24 months, (defined as significant decline in 2/5 of the neuropsychological tests) Secondary outcome: Alzheimer's Disease Assessment Scale cognitive subscore (ADAS-cog) scores at 12 months, QoL (EQ-5D) and depression (CES-D) Assessments were conducted at baseline, 12 and 24 months	166 and 154 patients completed the 12 and 24-month battery of tests. At 24 months, 10.5% of patients in the intervention group and 12.0% in the control group experienced cognitive decline (RR=0.874, 95% CI 0.364-2.098) There were no significant differences between groups in the change in ADAS-cog scores from baseline to 12 or 24 months, between groups (1 vs. 1, p=0.61 and 0 vs. 0, p=0.81, respectively). There were no significant differences between groups in the change in QoL or depression scores from baseline to 12 or 24 months, between groups.
Ihle-Hansen et al. 2014 Norway RCT	CA: <input checked="" type="checkbox"/> Blinding: Patient <input checked="" type="checkbox"/> Assessor <input checked="" type="checkbox"/> ITT: <input checked="" type="checkbox"/>	195 patients who were admitted to the acute stroke unit of a single institution following first-ever stroke or TIA (excluding SAH) who could complete and pass baseline cognitive testing. Mean age was 72 years, 535	Patients were randomized to an intensive program (n=98) including aggressive (i.e. pharmacological, if required) treatment to reach targets (blood pressure ≤140/90, total cholesterol	Primary outcome: Changes in the Trail-Making Test-A (TMT) and the 10-word test from baseline to one-year post stroke. Secondary outcome:	On per-protocol analysis, there were no significant differences in TMT-A change scores from baseline to one-year post stroke between groups (-3.8, 95% CI -11.9 to 4.2, p=0.35) or on the 10-word test (1.1, 95% CI -0.5 to 2.7, 0.17), after adjusting for baseline measurements. The results did not change significantly using ITT analysis.

Study/Type	Quality Rating	Sample Description	Method	Outcomes	Key Findings and Recommendations
		were male	<p>≤5.0 mmol/l, LDL cholesterol ≤3.0 mmol/l, HbA1c ≤7.0%, homocysteine ≤15 mmol/l, and BMI ≤25. Patients were offered smoking cessation courses and encouraged to perform regular moderate physical activity and to adhere to a diet rich in fruit/veg and fish and moderate ETOH, or to a control group, which received treatment as usual by their GPs (n=97).</p>	<p>Incidence of dementia or mild cognitive impairment (MCI) at one year, based on the results of cognitive assessments and additional investigations</p>	<p>The numbers of patients with MCI or dementia did not differ significantly between groups (54% vs. 55%, p=0.91).</p> <p>Significantly more patients in the intervention group achieved targets for blood pressure, LDL chol and homocysteine.</p> <p>85 patients in the intervention group and 93 patients in the control group completed follow-up.</p>

Note: CA: Concealed Allocation; ITT: Intention-to-treat

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