Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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Current Policy Effective Date: 9/1/24
(See policy history boxes for previous effective dates)

Title: Cognitive Rehabilitation

Description/Background

Cognitive rehabilitation is a therapeutic approach designed to improve cognitive functioning after central nervous system insult. It includes an assembly of therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem solving and executive functions. Cognitive rehabilitation consists of tasks designed to reinforce or re-establish previously learned patterns of behavior or to establish new compensatory mechanisms for impaired neurological systems. Cognitive rehabilitation may be performed by a physician, psychologist, or a physical, occupational, or speech therapist.

Cognitive rehabilitation must be distinguished from occupational therapy (CPT codes 97535–97537); occupational therapy describes rehabilitation that is directed at specific environments (for example, home or work). In contrast, cognitive rehabilitation consists of tasks designed to develop the memory, language, and reasoning skills that can then be applied to specific environments, as described by the occupational therapy codes. Sensory integrative therapy may be considered a component of cognitive rehabilitation. However, sensory integration therapy is considered separately in another policy.

Cognitive rehabilitative services must be provided by a qualified licensed professional and must be prescribed by the attending physician as part of the written care plan. Additionally, there must be a potential for improvement (based on preinjury function), and patients must be able to participate actively in the program. Active participation requires sufficient cognitive function to understand and participate in the program, as well as adequate language expression and comprehension (i.e., participants should not have severe aphasia). Ongoing services are considered necessary only when there is demonstrated continued objective improvement in function.

Medical Policy Statement

The safety and effectiveness of cognitive rehabilitation (as a distinct and definable component of the rehabilitation process) have been established. It may be considered a useful therapeutic option in the rehabilitation of individuals meeting specific selection criteria.

NOTE: Please check individual contract, certificate and rider for specific coverage information.

Inclusionary and Exclusionary Guidelines

Inclusions:
Cognitive rehabilitation is an established procedure when used an as adjunctive treatment of cognitive deficits (e.g., attention, language, memory, reasoning, executive functions, problem solving and visual processing) when all of the following criteria are met:

1. The cognitive deficits have been acquired as a result of neurologic impairment due to traumatic brain injury or stroke, **and**
2. Services must be provided by a qualified licensed professional and must be prescribed by the attending physician as part of the written care plan, and
3. There must be documentation of potential for improvements based on the individual's pre-injury function, **and**
4. Individuals must be able to actively participate in the program. The individual must have sufficient cognitive function to understand and participate in the program as well as adequate language expression and comprehension (i.e., the patient should not have severe aphasia).
5. The individual is expected to make significant cognitive improvement (i.e., individual is not in a vegetative or custodial state).

Excluded diagnoses include, but are not limited to:

- Intellectual disabilities
- Multiple sclerosis
- Cerebral palsy
- Encephalopathy
- S/P brain surgery
- Dementia (e.g., from Alzheimer's disease, HIV-infection or Parkinson's disease)
- Cognitive decline chronic obstructive pulmonary disease
- Behavioral or psychiatric disorders such as attention-deficit/hyperactivity disorder and schizophrenia
- Pervasive developmental disorders
- Post-acute cognitive sequelae of SARS-CoV-2 infection
- Autism spectrum disorders
- Seizure disorders
- Cognitive deficits due to brain tumor or previous treatment for cancer

NOTE:

Suggested therapy guidelines:

a. Duration and intensity of cognitive rehabilitation therapy programs vary. One approach for comprehensive cognitive rehabilitation is a 16-week outpatient program comprising 5 hours of therapy daily for 4 days each week. In another approach, cognitive group treatment occurs for three 2-hour sessions weekly and three 1-hour individual sessions (total, 9 hours weekly). Cognitive rehabilitation programs for specific deficits (for example, memory training) are less intensive and generally have 1 or 2 sessions (30 or 60 minutes) in a week for 4 to 10 weeks.
b. Coverage of outpatient cognitive rehabilitation is subject to applicable benefit plan terms and limitations for physical and occupational therapy. Please check benefit plan descriptions for details.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

97129 97130

Other codes (investigational, not medically necessary, etc.):

N/A

Regulatory Status:

Cognitive rehabilitation is not subject to regulation by the U.S. Food and Drug Administration.

Rationale

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate.

This review evaluates evidence for cognitive rehabilitation delivered by a qualified professional; studies of self-administered computer programs are not considered cognitive rehabilitation for the purposes of this evidence review and are not assessed here.[1-5] Short-term improvements in cognitive test performance measured post-intervention alone will not be considered a health outcome for the purposes of this review. Measurements of daily functioning and quality of life (QOL) are the primary health outcomes of interest. Improvements should be demonstrable after longer term follow-up post-intervention, preferably greater than 6 months.

TRAUMATIC BRAIN INJURY

Clinical Context and Therapy Purpose

The purpose of cognitive rehabilitation delivered by a qualified professional is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation, in patients with cognitive deficits due to traumatic brain injury.

The question addressed in this evidence review is: does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to traumatic brain injury?

The following **PICO** was used to select literature to inform this review.

Populations

The relevant population of interest are individuals with cognitive deficits due to traumatic brain injury. The severity of TBI is commonly objectively assessed using the Glasgow Coma Scale (GCS) based on impairment of conscious level. [8] The GCS measures 3 components - levels of eye, verbal and motor responsiveness. GCS scores can range from 3 (lowest level of responsiveness) to 15 (highest level of responsiveness). Based on associations between GCS score and outcomes, TBI severity has been classified as Mild=GCS of 13 to 15, Moderate=GCS of 9 to 12, and Severe=GCS of 3 to 8.

Interventions

The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators

Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating cognitive rehabilitation delivered by a qualified professional as a treatment for cognitive deficits due to TBI has varying lengths of follow-up. While studies described below all reported at least 1 outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, a minimum of 6 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews
Austin et al (2024) reported results of a systematic review and meta-analysis of cognitive rehabilitation interventions in veterans and service members with traumatic brain injuries.[6] The review included RCTs published by February of 2023 that used adult participants who were US veterans or active duty service members who had a history of mild-to-moderate TBI that tested cognitive rehabilitation treatments designed to improve cognition and/or everyday functioning and reported objective neuropsychological testing as a primary outcome measure. 8 trials (N = 303 in cognitive rehabilitation; N=261 in control; 97% of whom had a history of mild TBI) were included. 7 of the 8 trials were published after 2013. The mean age of participants was 37 years (SD=7) and between 81% and 100% of participants were male. Limited racial and ethnic information was available from the included studies. The mean length of time since TBI was 6 years (SD=52). Cognitive rehabilitation intervention lengths ranged from 4 to 15 weeks (mean=9.5; SD=). Study quality and risk of bias were evaluated using the Cochrane tool. Overall, the studies were rated as having low risk of bias. Given the variation in outcome measures used across studies, effect sizes were transformed into Cohen's d for meta-analysis. Participants in cognitive rehabilitation showed a significant improvement in overall objective neuropsychological functioning compared to controls (d = 0.22; 95% CI, 0.01 to 0.43; p=.04) but not on performance-based measures of functional capacity (d = 0.16; 95% CI, −0.48 to 0.81; p=.62). Participants in cognitive rehabilitation also had comparatively larger improvements in memory (d= 0.42; 95% CI, 0.13 to 0.70; p=.01) and executive functioning (d = 0.26; 95% CI, 0.01 to 0.51; p=.04) but not on attention (d=0.12; 95% CI,−0.12 to 0.35; p=.33). 4 of the RCTs included postintervention follow-up visits to measure durability of treatment effects. In these 4 studies, treatment effects on overall neuropsychological test performance at 10- or 12-week follow-up were also statistically significant favoring cognitive rehabilitation (d = 0.45; 95% CI, 0.01 to 0.90; p=.04).

A 2013 Cochrane review assessed cognitive rehabilitation for executive dysfunction (planning, initiation, organization, inhibition, problem solving, self-monitoring, error correction) in adults with nonprogressive acquired brain damage.[9] Sixteen RCTs (N=660 patients; 395 TBI, 234 stroke, 31 other acquired brain injury) were included in pooled analyses. No statistically significant effects on measures of global executive function or individual component functions were found.

A 2008 TEC Assessment was completed on cognitive rehabilitation in traumatic brain injury.[10] The objective of this Assessment was to determine whether there is adequate evidence to demonstrate that cognitive rehabilitation results in improved health outcomes. Eleven randomized, controlled trials of cognitive rehabilitation for specific cognitive defects showed inconsistent support for cognitive rehabilitation. Out of the 11 studies, 8 reported on health outcomes. Of these 11 studies, 8 reported daily functioning or quality of life (QOL) outcomes. Three studies showed statistically significant differences between intervention groups and control groups on 1 outcome. However, 2 studies were extremely small. Findings were inconsistent across other outcomes measured, and, in 1 study, significant findings after the intervention were

no longer present at 6-month follow-up. All 11 trials also reported outcomes of various cognitive tests. These trials had numerous methodologic limitations, such as small sample sizes, lack of long-term follow-up, minimal interventions, and multiple outcomes. In summary, the RCTs considered in the 2008 TEC Assessment did not show strong evidence for efficacy in the treatment of TBI.

Randomized Controlled Trials

Chiaravalloti et al (2016) conducted an RCT of the Story Memory Technique to improve learning and memory in subjects with TBI.[11] Sixty-nine subjects were randomized to treatment or control. Assessments were performed at the end of treatment (5 weeks) and at 6 months post treatment. Outcomes were statistically significant in favor of the treatment group for several measures assessing memory at 5 weeks. Results at 6 months were less definitive.

das Nair et al (2019) conducted the large (N=328), multicenter, assessor-blinded, A group memory rehabilitation programme for people with traumatic brain injuries (ReMemBrIn) RCT, which involved evaluating a group memory rehabilitation program for people with TBI in 9 sites in England.[12] The group memory rehabilitation intervention involved 10 weekly sessions, each lasting about 1.5 hours, which were delivered by a trained Assistant Psychologist to groups of between 4-6 participants. The intervention focused on retraining memory functions and strategies to improve encoding and retrieval. The control group received usual care, which typically included employment rehabilitation services, self-help groups or receiving specialist charity support. Between 2013 and 2015, 328 individuals were randomized to therapy (N=171) or usual care (N=157). The participants were characterized by a mean age of 45.1 years, a length of initial hospital stay for TBI of 84.2 days, and time since TBI of 100.9 months. On the primary outcome of frequency of memory failures in daily life assessed using the Everyday Memory Questionnaire-patient version (EMQ-p) at 6 months' follow-up, the between-group difference was not clinically important (adjusted difference in mean scores –2.1, 95% confidence interval [CI] –6.7 to 2.5; p = .37). For secondary outcomes, there was a significant improvement in goal attainment both at 6 and 12 months, but no differences on others such as mood or quality of life. Important methodological limitations included lack of an active control arm, incomplete assessment of intervention fidelity, and exclusion of over 20% of the sample from the primary analysis.

Section Summary: Traumatic Brain Injury

Although some randomized control trials (RCTs) have shown improvement in some outcomes with cognitive rehabilitation, systematic reviews have provided mixed findings. In a systematic review of RCTs conducted from 2013 to 2023 including US Veterans with mild to moderate TBI, participants receiving cognitive rehabilitation showed a significant improvement in overall neuropsychological functioning, memory and executive functioning but not in functional capacity or attention compared to controls. The benefits were durable for at least 3 months.

DEMENTIA

Clinical Context and Therapy Purpose

The purpose of cognitive rehabilitation delivered by a qualified professional is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation, in patients with cognitive deficits due to dementia.

The question addressed in this evidence review is: does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to dementia?

The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with cognitive deficits due to dementia.

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators
Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes
The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating cognitive rehabilitation delivered by a qualified professional as a treatment for cognitive deficits due to dementia has varying lengths of follow-up, ranging from 3 months to 2 years. While studies described below all reported at least 1 outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, 2 years of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews
Kudlicka et al (2023) reported results of a Cochrane systematic review of cognitive rehabilitation for people with mild to moderate dementia on outcomes related to everyday functioning.[7] The review included 6 trials (N=1702) published between 2010 and 2022. The mean age of participants in the RCTs ranged from 76 to 80 years and the proportion of male participants ranged from 29% to 79%. Approximately 60% participants had a diagnosis of AD. Risk of bias was rated as relatively low for all domains other than blinding, which is not generally feasible with psychosocial interventions. Extracting data for the outcome of everyday functioning was operationalized by extracting the measure of goal attainment used in the individual studies related to activities targeted in the intervention for that study. Results were provided for outcomes at the end of the cognitive rehabilitation and after 3 to 12 months of follow-up post-rehabilitation.

The authors concluded that there was high-certainty evidence of large positive effects of cognitive rehabilitation relative to control immediately following rehabilitation on participant self-ratings of goal attainment (standardized mean difference (SMD)=1.5; 95% CI, 1.3 to 1.7; 3 RCTs; N=501), informant ratings of goal attainment (SMD=1.6; 95% CI, 1.01 to 2.21; 3 RCTs; N=476), and self-ratings of satisfaction with goal attainment (SMD=1.3; 95% CI, 1.1 to 1.5; 3 RCTs; N=501). The authors also concluded that there was high-certainty evidence showing a large positive effect of cognitive rehabilitation after 3 to 12 months of follow-up post-rehabilitation on participant self-ratings of goal attainment (SMD=1.5; 95% CI, 1.3 to 1.7; 2 RCTs, N=432), informant ratings of goal attainment (SMD=1.3; 95% CI, 0.78 to 1.72; 3 RCTs; N=446), and self-ratings of satisfaction with goal attainment (SMD=1.2; 95% CI, 0.7 to 1.7; 2 RCTs; N=432). There was less certainty regarding whether cognitive rehabilitation had a meaningful effect on other outcomes immediately or after 3 to 12 months such as participant anxiety and quality of life.

In a Cochrane review, Bahar-Fuchs et al (2019) evaluated the use of cognitive training for people with mild to moderate dementia.[13] This review included 33 RCTs published between 1988 and 2018. Most RCTs were small and single-site, with sample sizes of 20 patients or below in each trial arm. Participants in most trials had a mean age between 70 and 80 years and the presumed etiology of the cognitive dysfunction was Alzheimer dementia, and the review authors rated their methodological quality as high or unclear risk of bias due to limitations including lack of allocation concealment and lack of blinding of participants and personnel.

In 2015, Huntley et al performed a meta-analysis of cognitive interventions in dementia.[14] Thirty-three studies were included. Interventions were divided into categories such as cognitive training, cognitive stimulation, and cognitive rehabilitation. Studies classified as cognitive stimulation had a significant effect as measured on the Mini-Mental State Examination (MMSE) and the Alzheimer's Disease Assessment Scale–Cognition (ADAS-Cog). The authors concluded that benefit measured on the ADAS-Cog was generally not clinically significant.

In a 2013 Cochrane review, Bahar-Fuchs evaluated the use of cognitive training (task-focused) or rehabilitation (strategy-focused) in AD and vascular dementia.[15] Evidence from 11 RCTs did not demonstrate improved cognitive function, mood, or activities of daily living in patients with mild to moderate AD or vascular dementia with cognitive *training*. One high-quality RCT [16] of cognitive rehabilitation in 69 patients with early-stage AD (Mini-Mental Status Exam [MMSE] score, ≥18) showed short-term improvements in patient-rated outcomes. A 2011 Cochrane review of interventions for persons with mild cognitive impairment concluded that there was little evidence on the effectiveness and specificity of such interventions because improvements observed were similar to effects seen with active control interventions.[17]

Randomized Controlled Trials

Individual randomized trials not included in the systematic reviews have shown variable outcomes of cognitive rehabilitation; see Tables 1 and 2.

Clare et al (2019) reported on results from the multicenter, assessor-blinded Individual Goal-oriented Cognitive Rehabilitation to Improve Everyday Functioning for People with Early-stage Dementia (GREAT) RCT that compared individual goal-oriented cognitive rehabilitation to treatment as usual in individuals with early-stage dementia.[18] The majority of participants were diagnosed with Alzheimer dementia, their mean age was 78.56 years, and their mean Mini-Mental State Examination (MMSE) score was 23.82 points. The primary outcome was participant-rated 3-month goal attainment. Goals were identified using the semi-structured Bangor Goal-Setting Interview. Attainment was assessed based on a 0-10 scale. Study authors

noted that an improvement of 2 points in the goal attainment rating was considered to be clinically significant. Improvement in goal attainment was significantly greater in the therapy group than in the control group both at 3 months and at 9 months. However, there were no significant between-group differences on any of the secondary outcomes at 3 or 9 months, including self-reported self-efficacy (Generalised Self-Efficacy Scale), mood (Hospital Anxiety and Depression Scale), dementia-specific health-related quality of life. memory, (story recall from the Rivermead Behavioural Memory Test), attention (elevator counting and elevator counting with distraction subtests from the Test of Everyday Attention), or executive function (verbal letter fluency from the Delis-Kaplan Executive Function System). No measure of functional ability was assessed.

Ameiva et al (2016) reported results of the ETNA3 multicenter RCT comparing 4 therapies strategies: standardized programs of cognitive training (group sessions), reminiscence therapy (group sessions), individualized cognitive rehabilitation program (individual sessions), and usual care.[19] Six hundred fifty-three patients with mild-to-moderate AD were randomized in a 1:1:1:1 ratio at 40 French clinical sites. We will focus on the cognitive rehabilitation program and usual care arms. The primary outcome was the rate of survival without moderately severe to severe dementia at 2 years. Secondary outcomes were cognitive impairment, functional disability, behavioral disturbance, apathy, QOL, depression, caregiver burden, and resource utilization. Participants and clinical staff were not blinded to treatment assignment but outcome assessments were done by blinded physicians and psychologists. The cognitive rehabilitation therapy consisted of a “made-to-measure” program and conducted in individual sessions and adapted to patients’ cognitive abilities, with goals selected to be personally relevant to the patient. Intention-to-treat analyses were performed using “missing equal failure” to replace missing values. Approximately 90% of participants had the 3-month follow-up visit and 72% had the 24-month visit. There was no difference between the cognitive rehabilitation group and the usual care group with respect to the primary outcome. However, patients who received cognitive rehabilitation therapy had less functional decline at 24 months compared to the usual care group, as measured by 1 of the 2 scales assessing functional abilities: the Autonomie Gérontologique Groupes Iso-Ressources (AGGIR) scale (p=0.02). The rate of institutionalization was lower in the cognitive rehabilitation therapy group (27%) than in the usual care group (19%). These results are promising but given the lack of consistency in benefits on the 2 functional scales, replication is needed to confirm positive findings.

Regan et al (2017) reported an RCT of a home-based, 4-session, goal-oriented cognitive rehabilitation program versus usual care in 55 patients with mild cognitive impairment (MCI) and early AD.[20] Patients were community-dwelling with a diagnosis of MCI or AD within 6 months of enrollment and a MMSE score greater than 20. The intervention group received 4 weekly 1-hour therapy sessions delivered by experienced therapists with a focus on addressing personally meaningful goals. All participants identified at least 1 goal for improvement. The usual care group had no contact with the research team between their initial and final assessments. The primary outcome measures were goal performance and satisfaction scores on the Canadian Occupational Performance Measure (COPM). Twelve participants in the intervention group and 3 participants in the control group discontinued study participation and were excluded from the final, per-protocol analysis. For the first identified goal, the intervention group had significantly higher improvements in performance and satisfaction on the COPM than the control group. There were no differences in secondary measures of QOL or anxiety and depression. The per-protocol results were biased due to high rate of missing data.

Thivierge et al (2014) in Canada reported a small (N=20), assessor-blinded, block-randomized, crossover trial of an individualized memory rehabilitation program in patients with mild to moderate AD.[21] The Memory Rehabilitation Program comprised 4 weeks of training by a patient's caregiver to improve performance of 1 instrumental activity of daily living (IADL) selected by the patient and caregiver. Errorless learning (assistance provided to minimize errors) and spaced retrieval (expanded delays, from 30 seconds to 8 minutes, between each correct performance of the task) were used to facilitate learning at each patient's own pace. The primary outcome was a measure of assistance required to perform the task correctly at 1, 4, and 8 weeks after training. In comparison with untrained (in period 1) or previously trained (in period 2) controls, statistically significant improvements in performance were observed immediately after training (i.e., at post treatment week 1) in both periods and at post treatment week 4 in period 2. A spontaneous, statistically significant (compared with baseline) improvement in performance occurred in period 1 controls. Performance of the target instrumental activity of daily living (IADL) declined within 2 to 3 months post-training. Improvements in other outcomes (general memory and cognitive ability, overall function, quality of life, and behavioral/psychological symptoms) were not observed.[22]

Kurz et al (2012) conducted an RCT of patients with Alzheimer's disease and early dementia.[23] The population consisted of 201 patients with clinical evidence and dementia and a MMSE score of at least 21/30 points who were randomized to a 12-week cognitive rehabilitation program or standard medical management (site-specific). There were baseline imbalances among the groups, with the intervention group having a lower mean age and higher scores on measures of functional status and quality of life. Outcomes were assessed at 3 months and 9 months following intervention and included a range of measures of functional status, quality of life, cognition, and caregiver burden. There also were no between group differences on any outcome measure. There were also no group differences on subgroup analyses by age, gender, educational level, or baseline cognitive ability, except that depression scores improved significantly for females, but not males, in the intervention group.

Another randomized study of 54 patients by Chapman et al evaluated the combined effect of a cognitive-communication therapy and an acetylcholinesterase inhibitor versus drug treatment alone.[24] A positive effect for the inhibitor cognitive rehabilitation group was found for discourse abilities, functional abilities, emotional symptoms, and overall global performance. Beneficial effects were reported up to 10 months after active intervention.

In 2003, Spector et al published an RCT on 115 patients assigned to a cognitive stimulation program or to a control group.[25] The intervention program ran for 7 weeks, and patients were only evaluated at completion. The treatment group had significantly higher scores on the principal outcome (MMSE), with a group difference of 1.14 points. Differences were also significant for secondary outcomes, a QOL score for AD and an AD assessment scale. The trialists limited assessment of outcomes to the 7-week period of treatment, and concluded that the intervention would need to be continued on a regular basis beyond 7 weeks.

Table 1. Summary of Key RCT Characteristics

Study	Countries	Sites	Dates	Participants	Interventions			
					Therapy 1	*Therapy 2*	*Therapy 3*	*Therapy 4*
Clare et al (2019)[18]	England, Wales	8	2013-2016	Patients with early- stage Alzheimer, vascular or mixed dementia (White, 96.4%; Black, 1.5%; Asian, 1.2%; Mixed, 0.4%; Other, 0.4%)	10 weekly goal-oriented individual cognitive rehabilitation sessions, followed by 4 maintenance sessions over 6 mos (n=281)	Treatment as usual (medication, monitoring, general psychosocial support) (n=208)	NR	NR
Amieva et al (2016)[19]	France	40	2008-2009	Patients diagnosed with Alzheimer disease	CTT (n=170)	RT (n=172)	ICRT (n=157)	Usual medical care (n=154)
Thivierge et al (2014)[21]	Canada	NR	2008-2011	Patients with Alzheimer disease (n=20)	ELL and SR cognitive techniques	Controls	NR	NR
Kurz et al (2012)[23]	Germany	NR	NR	Patients with mild Alzheimer disease (n=201)	12-week cognitive rehabilitation program (n=100)	Standard medical management (site-specific; n=101)	NR	NR
Chapman et al (2004)[24]	U.S.	NR	1999-2001	Patients with mild to moderate Alzheimer disease (n=54)	Combined cognitive-communication therapy plus an acetylcholinesterase inhibitor (n=28)	Drug treatment alone (n=26)	NR	NR
Spector et al (2003)[25]	U.K.	23	NR	Patients with dementia	Cognitive stimulation therapy (n=115)	Control (n=86)	NR	NR

CTT: cognitive training therapy; ELL: errorless learning; ICRT: individualized cognitive rehabilitation therapy; NR: not reported; RT: reminiscence therapy; SR: spaced retrieval.

Table 2. Summary of Key RCT Results

Study	Rate of patients alive and without moderately severe to severe dementia at 24 mos	Survival rate at 24 mos	Direct measure of training	Functional Ability score at 9 mos mean (SD)	Overall cognitive functioning at 1 y	Change in MMSE scores from baseline to 7 wks
Clare et al (2019) [18]	NR	NR	Individual goal attainment at 9 mos	NR	NR	NR
Therapy			N=205, +2.52			
Control			N=211, +0.67			
Mean Difference (95% CI)			1.70 (1.32 to 2.09)			
Amieva et al (2016) [19]			NR	NR	NR	NR
CTT	81 (47.7%)	124 (72.9%)				
RT	78 (45.4%)	118 (68.6%)				
ICRT	85 (54.1%)	121 (77.1%)				
Control	74 (48%)	109 (70.8%)				
Thivierge et al (2014) [21]	NR	NR		NR	NR	NR
Therapy			86.78			
Control			81.12			
Kurz et al (2012) [23]	NR	NR	NR		NR	NR
Therapy				0.729+/-1.82		
Control				0.857+/-1.59		
p-value				.64		
Chapman et al (2004) [24]	NR	NR	NR	NR		NR
Therapy					24.62	
Control					26.96	
Spector et al (2003) [25]	NR	NR	NR	NR	NR	

Therapy						0.9
Control						-0.4
p-value						.044

CI: confidence interval; CTT: cognitive training therapy; ICRT: individualized cognitive rehabilitation therapy; MMSE: Mini-Mental Status Examination; RCT: randomized controlled trial; RT: reminiscence therapy; SD: standard deviation.

Table 3. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Clare et al (2019)[18,]	4. Enrolled populations do not reflect relevant diversity				
Amieva et al (2016)[19,]	4,5. Racial and ethnic demographics for enrolled population are not reported				
Thivierge et al (2014)[21,]			4. Not the intervention of interest		1,2. Follow-up only 24 wks
Kurz et al (2012)[23,]					1,2. Follow-up only 9 mos
Chapman et al (2004)[24,]					
Spector et al (2003)[25,]					

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 4. Study Design and Conduct Gaps

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Follow-Up[d]	Power[e]	Statistical[f]
Clare et al (2019)[18]		1. Participants and clinical staff not blinded				
Amieva et al (2016)[19]		1. Participants and clinical staff not blinded				
Thivierge et al (2014)[21]		1,2. No blinding				
Kurz et al (2012)[23]		1. Not blinded to treatment assignment				
Chapman et al (2004)[24]	1. Randomization process not described					
Spector et al (2003)[25]	3. Allocation concealment unclear	1,2,3. Blinding not clear				

The evidence gaps stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Section Summary: Dementia

A 2023 Cochrane systematic review of cognitive rehabilitation including trials conducted between 2010 and 2022 focusing on outcomes related to everyday function found statistically significantly improved participant self-ratings of goal attainment related to everyday functioning both immediately following rehabilitation and after 3 to 12 months follow-up post-rehabilitation. There was less certainty regarding whether cognitive rehabilitation had a meaningful effect on quality of life. One large RCT with a goal-oriented cognitive rehabilitation program has reported significantly less functional decline on 1 of 2 functional scales and institutionalization in the cognitive rehabilitation group compared to usual care at 24 months. Studies in Alzheimer's disease lack relevant racial and ethnic diversity.

STROKE

Clinical Context and Therapy Purpose
The purpose of cognitive rehabilitation delivered by a qualified professional is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation, in patients with cognitive deficits due to stroke.

The question addressed in this evidence review is: does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to stroke?

The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with cognitive deficits due to stroke.

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators
Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes
The general outcomes of interest are functional outcomes and quality of life.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews
Four Cochrane reviews assessed the effectiveness of cognitive rehabilitation for recovery from stroke.[26-29] The reviews evaluated spatial neglect, attention deficits, and memory deficits. The most recent updates of these reviews for these 3 domains made the following conclusions:

- Spatial neglect: A 2013 update identified 23 RCTs with 628 patients.[26] There was very limited evidence of short-term improvements on tests of neglect with cognitive rehabilitation. However, for reducing disability due to spatial neglect and increasing independence, effectiveness of cognitive rehabilitation remained unproven.

- Attention deficit: A 2013 update identified six RCTs with 223 patients.[27] There was limited evidence of short-term improvement in divided attention (ability to multitask), but no indication of short-term improvements in other aspects of attention. Evidence for persistent effects of cognitive rehabilitation on attention or functional outcomes was lacking. A 2019 update identified no new trials and concluded that the effectiveness of cognitive rehabilitation for attention deficits following stroke remains unconfirmed. [30]
- Memory deficit: A 2016 update identified 13 trials with 514 patients.[29] There were statistically significant benefits in subjective measures of memory in the short term (i.e., the first assessment measurement after the intervention) but not in the longer term (i.e., the second assessment measurement after the intervention). The quality of the evidence ranged from very low to moderate; there was poor quality of reporting in many studies, lack of consistency in the choice of outcome measures, and small sample sizes.

In 2015, Gillespie et al published a review of Cochrane reviews and one subsequently published RCT assessing rehabilitation for post stroke cognitive impairment.[31] Data from 44 trials (N=1,550) were summarized. In addition to post stroke spatial neglect and attention and memory deficits (addressed in the three Cochrane publications previously described), post stroke perceptual disorders, motor apraxia, and executive dysfunction were reviewed. Conclusions were:

- Very little high-quality evidence for the effectiveness of cognitive rehabilitation for post stroke cognitive deficits exists.
- Current evidence indicates that cognitive rehabilitation for spatial neglect, attention deficits, and motor apraxia improve standardized assessments of impairment immediately after treatment. However, durability and clinical significance of these improvements is unclear.
- Evidence for the effectiveness of cognitive rehabilitation for post stroke memory deficits, perceptual disorders, or executive dysfunction was not identified.

A 2001 review of the rehabilitative management of post stroke visuospatial inattention also concluded that long-term impacts of visual scanning and perceptual retraining techniques on overall recovery and functional outcome were unclear.[32]

Randomized Controlled Trials

Zucchella et al (2014) conducted an assessor-blinded RCT of comprehensive cognitive rehabilitation, combining computer training and metacognitive strategies within 4 weeks after stroke.[33] Of 288 consecutive stroke survivors admitted to a neurorehabilitation unit in Italy, 92 (32%) met inclusion criteria and were randomized to cognitive rehabilitation (n=45) or control (n=47). At the end of treatment (i.e., at week 4), no statistically significant differences were found between groups on some measures of memory and visual attention. The clinical significance of these short-term outcomes is unclear.

Section Summary: Stroke

Recent systematic reviews generally report limited effects of cognitive rehabilitation in stroke patients.

MULTIPLE SCLEROSIS

Clinical Context and Therapy Purpose
The purpose of cognitive rehabilitation delivered by a qualified professional in patients with cognitive deficits due to multiple sclerosis (MS) is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition or no rehabilitation.

The question addressed in this evidence review is: does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to MS?

The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with cognitive deficits due to multiple sclerosis.

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators
Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes
The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating cognitive rehabilitation delivered by a qualified professional as a treatment for cognitive deficits due to MS has varying lengths of follow-up, ranging from 6 months to 1 year. While studies described below all reported at least 1 outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Systematic Reviews

Three Cochrane reviews evaluated cognitive rehabilitation in patients with multiple sclerosis (MS) and cognitive impairments.[34-36] In a 2016 update, das Nair et al included 15 studies with 989 patients. There were no differences in subjective reports of memory functioning or mood.[34] There was some evidence of a significant effect of intervention on objective assessments of memory in both the immediate and long-term follow-up and QOL in intermediate follow-up. However, this effect on objective memory outcomes and QOL was no longer statistically significant when studies at high risk of bias were excluded.

Rosti-Otajarvi et al (2014) conducted a subsequent Cochrane review of neuropsychological rehabilitation in MS.[35] Twenty RCTs met inclusion criteria (total N=986), including 7 of the 8 trials in the Cochrane review previously described. Overall quality and comparability of included trials was low due to methodological limitations and variation in interventions and outcome measures across trials, respectively. In meta-analysis, statistically significant improvements in memory span (based on 2 low-quality trials, total N=150; standardized mean difference [SMD], 0.54 [95% CI, 0.20 to 0.88], p=0.002, I^2=0%) and working memory (3 very low-quality trials, total N=288; SMD=0.33 [95% CI, 0.09 to 0.57], p=0.006, I^2=0%) were observed with cognitive training compared with controls. Statistically significant improvements in attention, information processing speed, immediate verbal memory, executive functions, or depression were not observed.

Redero et al (2023) reported results of a systematic review of neuropsychological rehabilitation in patients with relapsing-remitting MS including studies published between 2012 and 2022.[89] 15 studies (N ranging from 9 to 98) were included; 12 were RCTs, 2 were quasi-experimental and 1 had unclear allocation method. The authors found that most of the RCTs published from 2012 to 2022 evaluated rehabilitation interventions delivered through validated computer software. Therefore they are not relevant to this review.

Table 5. Systematic Review & Meta-Analysis Characteristics

Study	Dates	Trials	Participants	Intervention	N. Range	Design	Duration
Rosti-Otajarvi et al (2014)[35]	1993-2013	20	Patients with multiple sclerosis	Neuropsychological rehabilitation	986 (15-240)	RCTs and quasi-randomized trials	Mean 9.5 weeks
Das Nair et al (2016)[36]	1993-2015	15	Patients with multiple sclerosis	Cognitive rehabilitation	989 (19-240)	RCTs and quasi-randomized trials	NR

MS: multiple sclerosis; NR: not reported; RCT: randomized controlled trials.

Table 6. Systematic Review & Meta-Analysis Results

Study	Memory Span Improvement SMD	Working Memory Improvement SMD	Objective Assessment of Memory SMD	Activities of Daily Living SMD
Rosti-Otajarvi et al (2014)[35]	0.54	0.33	NR	NR
95% CI	0.2 to 0.88	0.09 to 0.57	NR	NR
P-value	.002	.006	NR	NR
Das Nair et al (2014)[36]	NR	NR	0.26	-0.03
95% CI	NR	NR	0.03 to 0.49	-0.63 to -0.03
P-value	NR	NR	.03	.03

CI: confidence interval; NR: not reported; SMD: standardized mean difference.

Randomized Controlled Trials

The largest and longest-term RCT conducted in people with MS receiving cognitive rehabilitation was published by Lincoln et al (2020) (Table 7). It is a multicenter, observer-blinded RCT in patients with relapsing-remitting (65%), primary progressive (10%) or secondary progressive MS (25%).[37,38] Participants were recruited between 2015 and 2017 and randomized to 10 weekly sessions of a group cognitive rehabilitation program (N=245) or usual care (N=204). Outcomes were assessed at 6 and 12 months after randomization. Although there were small improvements in mood and everyday memory problems, there were no significant long-term benefits in cognitive abilities, fatigue, employment, or quality of life (Table 8). Its main methodological limitation was that there was no sham cognitive rehabilitation group and participants were not masked to treatment assignment (Tables 9 and 10).

Table 7. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants[2]	Interventions[1]	
					Active	***Comparator***
Lincoln et al (2020)[38]; CRAMMS RCT	England	5	2015-2017	People aged 18 to 69 yrs with MS who reported cognitive problems in daily life	10 weekly sessions of cognitive rehabilitation, delivered by an Assistant Psychologist to groups of 4 to 6 participants; standardized content defined by a treatment manual; n=245	Usual care, n=204

CRAMMS: Cognitive Rehabilitation for Attention and Memory in people with Multiple Sclerosis; MS: multiple sclerosis.

Table 8. Summary of Key RCT Results

Study	Multiple Sclerosis Symptoms Measure	Employment Measures	Quality of Life Measures
Lincoln et al (2020)[38]	387	382	382
	Mean MSIS (SD) Psychological score at 12 mos	Any employment at 12 mos	Mean (SD) EQ-5D visual analog at 12 mos
Cognitive rehabilitation	22.2 (6.1)	60 (29%)	61.6 (19.3)
Usual care	23.4 (6.0)	50 (29%)	59.7 (20.0)
Relative measure	Adjusted mean difference, -0.6; 95% CI, -1.5 to 0.3	Odds ratio, 0.99; 95% CI, 0.60 to 1.63	Adjusted mean difference, 2.6; 95% CI, -0.9 to 6.0

CI: confidence interval; EQ-5D: European Quality-of-Life Five-Level; MSIS: Multiple Sclerosis Impact Scale; SD: standard deviation.

Table 9. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Lincoln et al (2020)[38]			3. Delivery not similar intensity as intervention		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 10. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Lincoln et al (2020)[38]		1. Participants and assistant psychologists aware of allocation				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment
c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
f Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Several additional smaller, single-center and shorter-term RCTs have been conducted (Table 11). These RCTs are heterogeneous in terms of MS type, intervention format, frequency and duration, and outcome assessment methods. Overall, results of the RCTs have been mixed, with the majority of benefits for cognitive rehabilitation only observed in the short-term and either not measured or not sustained in the longer-term.

Table 11. Summary of Small and Shorter-Term Trials in Individuals with MS Undergoing Cognitive Rehabilitation

Author Year	N	MS type	Intervention	Comparator	Summary of Results
Nauta et al (2023)[85]	110	66% relapsing-remitting; 17% secondary progressive; 12% primary progressive	9 weekly group-based sessions of 2.5 hours	Enhanced treatment as usual: 1 individual appointment with MS specialist nurse focused on psycho-education	CRT alleviated cognitive complaints immediately after rehabilitation, but benefits in cognition did not persist to 6 months. At 6-month follow-up, CRT showed benefits on personalized cognitive goals (goals concerning daily life problems identified at baseline for each participant) and processing speed.
Brissart et al (2020)[39,]	110	MS; 22% relapsing-remitting MS	13 2-hour extended cognitive rehabilitation sessions delivered over 6 mos	13 2-hour non-cognitive exercise sessions delivered over 6 mos	Some improvement was observed in the cognitive rehabilitation group in measures of memory function, but there were no differences between groups in executive function or quality of life measures at 6 to 9 mo follow-up.
Chiaravalloti et al (2005)[40,]	117	Primarily relapsing-remitting MS	8 biweekly 45-min cognitive rehabilitation sessions	Control sessions with the same therapist at the same frequency, engaging in nontraining tasks (e.g., reading and recalling a story)	Mixed at 5 and 11 wks. No statistical differences between groups in new learning or emotional functioning. Self-reported improvements in memory were greater in the cognitive rehabilitation group at both time points. Results for other neuropsychological assessments were not reported.
Chiaravalloti et al (2013)[41,]	88	MS	10 biweekly, 45- to 60-min sessions of modified SMT	Control sessions with the same therapist at the same frequency, engaging in nontraining tasks (e.g., reading and recalling a story)	Mixed effects at 5 wks, but majority of benefits were not sustained at 6 months. At 5 wks, there were significant improvements in learning efficiency, objective everyday memory, general contentment (subjective everyday cognition and emotional functioning), apathy, and executive dysfunction, but not awareness level, depression, or anxiety. At 6-mos follow-up, the only persistent between-group difference was general contentment.

Rosti-Otajarvi et al (2013)[42,] Mantynen et al (2014)[43,]	102	Relapsing-remitting MS and attentional deficits	strategy-oriented neuropsychological rehabilitation (13 weekly 60-min sessions)	No intervention	Although no improvement in cognitive performance at wk 13 or at 6 mos, there was improvement in perceived cognitive deficits at both time points and in a subset of patients who completed 1-y follow-up (83% completers in the therapy group vs. 67% in the control group).[a]
Hanssen et al (2016)[44,]	120	MS	4 wks of multidisciplinary cognitive rehabilitation	Standard rehab	Improvement on a health-related quality of life measure relating to psychological health, but no differences in executive function at 4 or 7 mos.
Shahpouri et al (2019)[45,]	56	Primarily relapsing remitting (70%)	10, 2-h individualized sessions held every 7-10 days - approaches developed considering the severity of cognitive impairment and with the aim of optimization of the residual functions	Same number and duration of sessions, but content was not supporting cognitive rehabilitation	Memory, attention, quality of life, and depression were all significantly improved within 3 mos after study initiation.
Chiaravalloti et al (2019)[46,]	20	Learning-impaired participants with primarily relapsing remitting MS (65%)	STEM: 2, 30 to 45 min sessions per wk for 4 wks; guided practice of a set of structured and standardized tasks to train individuals on self-generation, spaced-learning, and retrieval practice.	Participants met individually with the therapist at the same frequency and locations as the treatment group, engaging in non-training oriented tasks.	Although STEM improved measures of subjective cognitive function outcomes immediately following the intervention, it did not lead to improved performance on objective neuropsychological functioning.

MS: multiple sclerosis; SMT: Story Memory Technique; STEM: Strategy-based Training to Enhance Memory.
[a] Due to the possibility that dropout was related to the outcome of interest (e.g., patients with perceived cognitive decline might have been more likely to drop out), findings should be interpreted cautiously.

Section Summary: Multiple Sclerosis

Although numerous RCTs have investigated cognitive rehabilitation in MS, large, high-quality trials are lacking. The ability to make conclusions based on the overall body of evidence is limited by heterogeneity of patient samples, interventions, and outcome measures. Further, results of the available RCTs are mixed, with positive studies mostly reporting short-term benefits. Evidence for clinically significant, durable improvements in cognition is currently lacking.

POST-ACUTE COGNITVE SEQUELAE OF SARS-COV-2 INFECTION

Clinical Context and Therapy Purpose

The purpose of cognitive rehabilitation delivered by a qualified professional is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition or no rehabilitation in patients with cognitive deficits due to post-acute sequelae of SARS-CoV-2 infection (PASC).

The question addressed in this evidence review is: Does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to PASC?

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with cognitive deficits due to PASC infection. The Centers for Disease Control and Prevention define the post-acute period as symptoms persisting at four or more weeks following infection with SARS-CoV-2. [47] The World Health Organization developed the following consensus case definition of 'post COVID-19 condition': individuals with "a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time." [48]

While subjective reports of cognitive impairment (i.e., 'brain fog') have been reported by individuals not requiring hospitalization,[49] current understanding of objective cognitive sequelae of COVID-19 is predominantly limited to individuals who required hospitalization.[50,51], Ceban et al (2022) conducted a meta-analysis of 43 studies with 12 or more weeks follow-up that reported a 22% overall prevalence of cognitive impairment (95% CI, 17% to 28%; I2=98%; N=13232). [52] Subjectively ascertained cognitive impairment (e.g., patient self-report) was reported in 18% of patients (95% CI, 12% to 24%; I2=97.9%; 31 studies), which was significantly lower than in studies with objective ascertainment of cognitive status utilizing validated tools (36%; 95% CI, 27% to 46%; I2=94.9%; 12 studies; p=.002). No significant difference in cognitive symptom prevalence was found in subgroup analyses of hospitalized versus non-hospitalized patients (30% versus 20%; p=.096) or patients with <6 months versus ≥6 months of follow-up (22% versus 21%; p=.794).

Objective cognitive deficits have been reported for verbal fluency, attention, working memory, processing speed, executive functioning, learning, and memory - with no clear pattern of cognitive impairment across studies. While cognitive impairment following intensive treatment of critical illness is not a new phenomenon,[53] the disease course of cognitive impairment experienced by individuals with post-acute sequelae of SARS-CoV-2 infection is an ongoing research priority.[54,55]

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after CNS insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators
Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes
The general outcomes of interest are functional outcomes and quality of life. The natural history of PASC has not been fully categorized, particularly in non-hospitalized individuals. A prospective study measuring cognitive performance among patients who experienced mild disease noted that declines in cognitive scores reported at 6 months spontaneously resolved at 18 month follow-up.[56] Persistent cognitive deficits have been reported in 16% of COVID-19 survivors at 1 year who were treated in the intensive care setting.[57] Therefore, at least 1 to 2 years of follow-up may be considered necessary to demonstrate efficacy and to fully observe outcomes.

The American Academy of Physical Medicine and Rehabilitation Multi-Disciplinary PASC Collaborative issued a consensus guidance statement recommending that patients should be screened for signs of cognitive symptoms using validated tools and instruments, such as the Montreal Cognitive Assessment (MoCA) or MMSE.[50] Additional neuropsychological measures used to assess cognitive and behavioral alterations in PASC are described by De Luca and coworkers [55,] and are listed on the CDC website.[47]

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Review of Evidence
Initial reports of patient rehabilitation after COVID-19 recovery have largely been observational, without clearly identifiable cognitive rehabilitation components within multidisciplinary rehabilitation programs.[58,59] Other reports have primarily focused on respiratory [60,] and physical [61,] rehabilitation.

No studies specifically assessing the efficacy of cognitive rehabilitation programs for PASC were identified.

Section Summary: Post-Acute Cognitive Sequelae of SARS-CoV-2 Infection
No direct evidence on the efficacy of cognitive rehabilitation programs in patients with PASC was identified. Controlled prospective studies in well-defined patient populations with sufficient follow-up duration are necessary to evaluate net health outcomes. Ongoing research continues to elucidate the natural course of cognitive symptoms associated with PASC.

OTHER COGNITIVE DEFICIT CONDITIONS

Clinical Context and Therapy Purpose
The purpose of cognitive rehabilitation delivered by a qualified professional is to provide a treatment option that is an alternative to or an improvement on existing therapies, such as standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation, in patients with cognitive deficits due to epilepsy, autism spectrum disorder, post-encephalopathy, or cancer.

The question addressed in this evidence review is: does cognitive rehabilitation delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits?

The following **PICO** was used to select literature to inform this review.

Populations
The relevant population of interest are individuals with cognitive deficits due to epilepsy, autism spectrum disorder, post-encephalopathy, or cancer.

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system insult. It includes therapy methods that retrain or alleviate problems caused by deficits in attention, visual processing, language, memory, reasoning, problem-solving, and executive functions.

Comparators
Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without specific focus on cognition, or no rehabilitation. Treatment includes counseling, physical and psychological therapy, and dieting and exercise.

Outcomes
The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating cognitive rehabilitation delivered by a qualified professional as a treatment for cognitive deficits due to epilepsy, autism spectrum disorder, post-encephalopathy, or cancer has varying lengths of follow-up, ranging from 2 to 6 months. While studies described below all reported at least 1 outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, 6 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded

Epilepsy/Seizure Disorders
Farina et al (2015) in Italy conducted a systematic review of the literature on cognitive rehabilitation in epilepsy. [62] Literature was searched through December 2013, and 18 articles of different types (reviews, methodological papers, case reports, and experimental studies) were identified. Studies were heterogeneous in-patient characteristics (type of epilepsy, type of previous treatment [surgery, antiepileptic drugs]), intervention modalities (e.g., holistic or focused) and duration, and outcome measures. Reviewers considered the overall quality of the body of evidence to be moderate to low, and results inconsistent (e.g., not all studies showed benefit; some studies showed greater benefit in left-sided seizures and others showed greater benefit in right-sided seizures).

The 2013 updated systematic review by ACRM's Cognitive Rehabilitation Task Force evaluated cognitive rehabilitation in epilepsy.[7] Based on two comparative studies (one randomized; N=156), the Task Force recommended cognitive rehabilitation for attention and memory deficits as a "possibly effective" practice option for seizure-related attention and memory deficits. The randomized trial prospectively enrolled 50 patients with focal seizures who were receiving carbamazepine monotherapy.[63] Patients were randomized to a retraining method, aimed at retraining impaired cognitive functions (n=19); a compensation method, aimed at teaching compensatory strategies (n=17); or a waiting-list control group (n=8). Both interventions focused on divided attention (ability to multi-task). At 6-month follow-up, performance on cognitive tests improved more in both intervention groups compared with control. No difference in inhibitory capacity was observed. Self-reported cognitive complaints, absentmindedness, and quality of life improved more with cognitive rehabilitation. Overall, rehabilitation methods were similarly effective.

Helmstaedter et al (2008), in a nonrandomized study assessed short-term effects of cognitive rehabilitation on memory deficits in two retrospective, matched cohorts of temporal lobe epilepsy surgical patients.[64] Mean age at onset of epilepsy was 4 years, and mean intelligence quotient (IQ) was 105. Patients who received cognitive rehabilitation (n=55) participated in a 1-month program comprising educational sessions about brain function and cognitive exercises. A cohort of 57 patients received no cognitive rehabilitation. Statistically significant improvements in verbal learning and recognition were observed in right-resected patients who received cognitive rehabilitation. Cognitive rehabilitation had non-significant effects in left-resected patients. Limitations of the study include its retrospective design and baseline imbalances in memory and attention deficits (more severe deficits in the control cohort). The limited evidence base precludes conclusions about cognitive rehabilitation for this indication.

Autism Spectrum Disorders

Reichow et al (2013) reported a systematic review of psychosocial interventions administered by nonspecialists for children and adolescents with intellectual disability (IQ<70) or lower-functioning autism-spectrum disorders.[65] Five comparative trials in patients with autism-spectrum disorders (N=255) who received cognitive rehabilitation, training, and support were included. Improvements in school performance and developmental outcomes were inconsistent across trials.

Wang and Reid (2013) conducted a pilot study of a novel virtual reality-cognitive rehabilitation intervention in four children (mean age, 7.4 years) with autism.[66] Children with autism, who are difficult to engage, may respond better to virtual reality approaches than to traditional cognitive rehabilitation. Mean nonverbal IQ ranged from 93 to 139. Each child viewed training programs on laptop computers equipped with tracking webcams; the child's image and movements were projected into virtual environments where he/she was required to manipulate virtual objects. Outcomes were measures of contextual processing, defined as "the ability to determine an object's meaning or relevance in a particular context," and of abstraction and cognitive flexibility, executive functions considered components of contextual processing. After 4 to 6 weeks, all children demonstrated statistically significant improvements in contextual processing and cognitive flexibility. Abstraction scores at baseline were at or close to maximum.

Eack et al (2013) conducted a feasibility study of a comprehensive cognitive rehabilitation intervention, called Cognitive Enhancement Therapy, in 14 "high-functioning" adults (mean age, 25 years) with autism-spectrum disorders.[67] Cognitive Enhancement Therapy, originally developed for schizophrenic patients, provides social interaction and cognitive training focused on attention, memory, and problem solving. Mean full scale IQ of the patient sample was 118 (range, 92 to157). Eleven (79%) of 14 patients completed 18 months of treatment. Statistically significant changes from baseline were observed in mean composite measures of neurocognition, cognitive style, social cognition, and social adjustment. All components of neurocognition (e.g., processing speed, working memory) improved statistically except attention/vigilance.

Postencephalitis

The 2013 systematic review by ACRM's Cognitive Rehabilitation Task Force evaluated cognitive rehabilitation for post-encephalitis cognitive deficits.[7] Eight identified studies were considered poor quality evidence, insufficient for forming conclusions.

Cancer

Cognitive rehabilitation has been investigated in two cancer-related settings: in patients with brain tumors and in cancer survivors whose cognitive deficits are attributed to cancer treatment.

Pediatric Cancer Treatment

For children with cancer receiving cognitive rehabilitation, the evidence includes 1 small (N=46), single-center RCT by Akel et al (2019) (Table 12).[68] The cognitive rehabilitation was delivered in the inpatient treatment clinic of the Department of Pediatric Oncology at University Hospital in Ankara, Turkey. Cognitive skills targeted by the cognitive rehabilitation therapy included place and time orientation, internal and external spatial perception, praxis, attention, visio-motor construction, and thinking operations. Children were characterized by a mean age of 10 years and 55% were male. Cancer diagnoses included non-Hodgkin lymphoma (40%), Hodgkin lymphoma (30%) and bone tumors (30%). Outcomes were evaluated only immediately postintervention. Although compared to the routine therapy groups (Table 13), numerically larger effect sizes for change in fatigue and functional independence were reported for the cognitive

rehabilitation group, it is unknown whether the differences were clinically or statistically significant as the comparative treatment effects were not calculated and clinically significant difference were not prespecified. Significant improvements in cognitive measures were reported pre/post in the intervention group, but no data were reported for the routine therapy group on this outcome. In addition to these inadequate outcome assessment methods, interpretation of these findings are limited by other methodological shortcomings (Tables 14 and 15) including lack of blinding of participants and lack of long-term follow-up. Therefore, this evidence is not sufficient to draw conclusions on effect on health outcomes

Table 12. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants[2]	Interventions[1]	
					Active	***Comparator***
Akel et al (2019)[68.]	Turkey	1	NR	Children aged 6 to 12 yrs receiving oncological treatment with regular inpatient stays for non-brain tumors or brain metastasis and an MMSE for children score >24	15 sessions of structured cognitive rehabilitation that used play to target various cognitive skills; n=25	15 sessions of routine therapy, including relaxation training and task- oriented activity of daily life training; n=21

MMSE: Mini-Mental Status Examination; NR: not reported

Table 13. Summary of Key RCT Results

Study	Cognitive Measures	Fatigue Measures	Functional Independence Measures
Akel et al (2019)[68.]	40	40	40
Measures	Mean total DOTCA-Ch (SD) score pre/post-intervention	Mean (SD) VAS-fatigue pre/post-intervention for post- activity/Effect size/P-value	Mean (SD) WeeFIM total score pre/post-intervention/Effect size/P- value
Cognitive rehabilitation	121.54 ± 13.18/135.36 ± 10.24	5.45 ± 1.01/1.72 ± 0.98/3.69/<.001	52.45 ± 8.90/62.68 ± 9.74/1.15/<.001
Control group	NR	3.16 ± 2.45/2.16 ± 1.79/0.41/.01	52.33 ± 9.29/53.11 ± 8.73/0.08/.068
Relative measure	NA	NR	NR

DOTCA-Ch: Dynamic Occupational Therapy Cognitive Assessment for Children; NA: not applicable; NR: not reported; SD: standard deviation; WeeFIM: Functional Independence Measure for Children; VAS: Visual Analog Scale.

Table 14. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Akel et al (2019)[68]			3. Delivery not similar intensity as intervention	5. Clinical significant difference not prespecified	1. Not sufficient duration for benefit

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 15. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Akel et al (2019)[68]		1. Participants aware of allocation			1. Power calculations not reported	4. Comparative treatment effects not calculated

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Brain Tumors

The 2013 systematic review by ACRM's Cognitive Rehabilitation Task Force evaluated cognitive rehabilitation for adults with brain tumors.[7] In five case reports and case series (total N=36), some patients showed benefit with various cognitive rehabilitation interventions. This evidence was considered insufficient to support any recommendation.

Zucchella et al (2013) conducted an RCT of cognitive rehabilitation in post-neurosurgical adults at a single rehabilitation facility in Italy.[69] Time since craniotomy was not reported. Adjuvant chemotherapy or radiotherapy was not administered until after the study. Of 109 consecutive patients screened for trial participation, 62 (57%) met minimum cognitive deficit and other criteria and were randomized to usual rehabilitative care with (n=30) or without (n=32) cognitive rehabilitation. Treatment sessions were held 4 times weekly for 4 weeks and comprised 45 minutes of therapist-guided computer exercises in 6 cognitive domains (time and spatial orientation, visual attention, logical reasoning, memory, executive function) and15 minutes of cognitive strategizing. At the end of treatment (i.e., at week 4), statistically significant improvements in visual attention and verbal memory were observed in the treatment group compared with controls. Improvements in logical-executive function were not statistically significant. Because of limited follow-up in this study, clinical significance of the findings is unclear.

Cancer Survivors

Systematic Reviews

Fernandes et al (2019) published a systematic review of cognitive rehabilitation programs in adults with non-CNS cancers. It included 1,124 participants (N range, 11 to 242) from 19 studies published between 2007 and 2018 – the majority of which were RCTs (N=12).[70] Waitlist was the most common comparator in the RCTs. As with the previous reviews, most studies in this review assessed the effects of the intervention immediately postintervention or at short-term follow-up (≤6 months) and most trials were conducted in breast cancer survivors. This review did not perform any meta-analyses. Findings across the studies were mixed. Although the review reported that among the RCTs and nonrandomized controlled studies, "87% found short-term improvements on at least one objective cognitive measure," this finding primarily pertained to measurements taken immediately postintervention. In contrast, in the longest-term (26-month follow-up) and largest trials (N=242) included, there were no significant effects on various objective cognitive measures. Only 63% of studies found improvements in short-term quality of life measures and none found any improvements in functional outcomes. An important limitation of all studies is that participants were not blinded to group assignment.

Zeng et al (2016) published a systematic review of a neuropsychologic intervention for cognitive function in cancer survivors.[71] Three case-control studies and 7 RCTs with 433 patients (range, 22-98 patients), published between January 2010 and September 2015, were included. Most trials assessed the effects of the intervention immediately post-intervention or at short-term follow-up (≤6 months). More than half of the trials were conducted in breast cancer survivors. Three trials assessed the effects of cognitive rehabilitation programs and the weighted mean difference for the intervention effect at post-intervention follow-up was -0.19 (95% CI, -2.98 to 2.61).

The 2013 systematic review by ACRM's Cognitive Rehabilitation Task Force evaluated cognitive rehabilitation for cognitive impairments in adult and pediatric cancer survivors.[7] One German RCT showed no benefit with cognitive rehabilitation in 157 adult inpatients that had cognitive impairments after hematopoietic stem cell transplantation.[72] In children and adolescents, two prospective, comparative studies (1 an RCT by Butler et al [2008][73]) evaluated cognitive rehabilitation in survivors of treatment (resection, cranial radiation, and/or chemotherapy) involving the central nervous system (total N=192). Reviewers concluded that process based cognitive rehabilitation techniques (e.g., strategy acquisition and corrective feedback) are "probably effective" in treating attention and memory deficits in these patients. However, the RCT had several methodological limitations.[73] It randomized 161 pediatric survivors of treatment for brain tumors, leukemia, bone marrow transplant involving total body irradiation, and non-Hodgkin lymphoma 2:1 to a cognitive remediation program (n=108) or waiting-list control (n=53). Documented attentional deficit was required for trial eligibility. The cognitive remediation program comprised 2-hour weekly sessions of practice, strategy acquisition, and cognitive-behavioral interventions for up to 20 sessions. Both groups were assumed to receive special education services if needed; this factor was not evaluated in results analysis. The primary outcome was change from baseline in five investigator-developed, multi-test indices (academic achievement, brief focused attention, working memory, memory recall, vigilance) at approximately 6 months after baseline assessments. These indices incorporated results from 11 validated scales completed by blinded study assessors and unblinded parents, teachers, and patients. Mean (SD) patient age was 11 (3) years. Sixty percent of patients in the cognitive remediation group completed the entire program; 80% completed 75% (15 sessions). Six-month follow-up was differential between groups (83% in the cognitive remediation group vs. 98% in the control

group). Analysis was intention to treat. Statistically greater improvement was observed in the cognitive remediation group compared with the control group only in academic achievement, although the treatment effect was small (SMD=0.24), and clinical relevance is uncertain. Given the lack of improvement on neurocognitive scales, it does not appear that improved academic achievement was due to improved neurocognitive function.

Randomized Controlled Trials

For cancer survivors receiving cognitive rehabilitation, the evidence published subsequent to the above-described systematic reviews includes 1 small (N=25), single-center RCT by Richard et al (2019)[74] (Table 16). This RCT randomized 46 participants to Goal Management Training, a Brain Health Program active control that promotes general brain health, and a wait-list control group and reported outcomes immediately following the 8-week treatment period and 4 months following treatment completion. Participants had a mean age of 48 years and 60% were male. Disease characteristics included various tumor types (28% meningioma, 32% low-grade glioma, 24% high-grade glioma) with a mean duration of 23 years since diagnosis. The most common cancer treatment was surgical resection (72%). The most recent type of treatment was whole-brain radiotherapy, which occurred a mean of 3 years prior. The primary outcome measure was change on an investigator-developed executive functioning test composite score. Although compared to the active and wait-list control groups, improvements in executive functioning and real-life functional goal attainment were significantly greater for the Goal Management Training group immediately following treatment, the improvement was only maintained at the 4 month follow-up period for the executive functioning outcome (Table 17). No quality of life measure was reported. Although the improved executive functioning outcome is encouraging, numerous important study and relevance shortcomings seriously limit the interpretation of these findings (Tables 18 and 19). For example, the clinical significance of the executive functioning outcome is unclear as it is not an established measure and its validity is unknown. Additionally, as the executive functioning outcome was not evaluated using an intent-to-treat analysis and excluded a larger proportion of wait-list control group participants than in the Goal Management Training groups (33% vs. 9%), we cannot rule out that the results were biased based on the high and differential exclusions. In addition, interpretation of these findings are limited by other methodological shortcomings including lack of blinding of participants and lack of long-term follow-up. Therefore, this evidence is not sufficient to draw conclusions on effect on health outcomes

Table 16. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants[2]	Interventions[1]	
					Active	***Comparator(s)***
Richard et al (2019)[74]	Canada	1	NR	Adults aged ≥18 yrs with a diagnosis of a primary brain tumor who were ≥3 mos postradiation or surgery with persistent cognitive dysfunction (≤1 SD below executive function testing norms)	8 weekly 2-h individual sessions of a structured and standardized GMT program, a behavioral intervention delivered by a clinical neuropsychologist, with homework between sessions; n=11	8 weekly 2-h individual sessions of a psycho-educational BHP, also with homework of more general "brain challenges"; n=8 Waitlist control; n=6

BHP: brain health program; GMT: goal management training; NR: Not reported; RCT: randomized controlled trial; SD: standard deviation.

Table 17. Summary of Key RCT Results

Study	Cognitive Measures[a]	Functional Outcomes	Quality of Life Outcomes
Richard et al (2019)[74]	19	19	19
Measures	Mean change (SD) in the Executive Functioning Composite at 4 mos follow-up	Functional goal attainment at 4 mos	NR
GMT	+0.69 (0.51)	NR	
BHP	+0.13 (0.50)	NR	NR
WAIT	-0.07 (0.44)	NR	NR
P-value for time-by-group interaction	.046	.064	NR

[a]The Executive Functioning Composite score was calculated by averaging component measure z-scores at each time point across a number of tests including the Trail Making Test B, Test of Everyday Attention (TEA), Sustained Attention to Response Task (SART), Behavioral Assessment of the Dysexecutive Syndrome (BADS), and the Hotel Test.
BHP: Brain Health Program; GMT: Goal Management Training; WAIT: Wait-list control; NR: Not Reported; SD: standard deviation.

Table 18. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Richard et al (2019)[74]				1. Key health outcomes not addressed4. Not establish and validated measurements5. Clinical significant difference not prespecified	1. Not sufficient duration for benefit

The study limitations stated in this table are those notable in the current review; this is not a comprehensive limitations assessment.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4.Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 19. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Richard et al (2019)[74]	3. Allocation concealment unclear	1. Participants aware of allocation		1. High loss to follow-up or missing data (GMT=9%, BHP=25%, WAIT=33%)6. Not intent to treat analysis (per protocol for noninferiority trials).	1. Power calculations not reported	

BHP=Brain Health Program; GMT: Goal Management Training; WAIT: Wait-list control.
The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias. [b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

Section Summary: Other Cognitive Deficit Conditions

Systematic reviews of cognitive rehabilitation for a number of conditions have generally concluded that there is no strong evidence supporting the efficacy of cognitive rehabilitation. Randomized trials of cognitive rehabilitation have numerous methodological flaws that preclude strong conclusions about its efficacy.

SUMMARY OF EVIDENCE

For individuals who have cognitive deficits due to traumatic brain injury who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes randomized controlled trials (RCTs), nonrandomized comparison studies, case series, and systematic reviews. Relevant outcomes are functional outcomes and quality of life. The cognitive rehabilitation trials have some methodologic limitations and have reported some mixed results. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have cognitive deficits due to dementia who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, case series, and systematic reviews. Relevant outcomes are functional outcomes and quality of life. A Cochrane systematic review focusing on outcomes related to everyday function found statistically significantly improved participant self-ratings of goal attainment related to everyday functioning both immediately following rehabilitation and after 3 to 12 months follow-up post-rehabilitation. There was less certainty regarding whether cognitive rehabilitation had a meaningful effect on quality of life. One large RCT with a goal-oriented cognitive rehabilitation program reported significantly less functional decline in 1 of 2 functional scales and lower rates of institutionalization in the cognitive rehabilitation group compared to usual care at 24 months. These results need replication. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to stroke who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs and systematic reviews. Relevant outcomes are functional outcomes and quality of life. Four systematic reviews evaluating 3 separate domains of cognitive function have shown some benefit of cognitive rehabilitation. The evidence is sufficient to determine the effects of the technology on health outcomes.

For individuals who have cognitive deficits due to multiple sclerosis who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs and systematic reviews. Relevant outcomes are functional outcomes and quality of life. Systematic reviews of RCTs have shown no significant effects of cognitive rehabilitation on cognitive outcomes. Although numerous RCTs have investigated cognitive rehabilitation in multiple sclerosis, high-quality trials are lacking. The ability to draw conclusions based on the overall body of evidence is limited by the heterogeneity of patient samples, interventions, and outcome measures. Further,

results of the available RCTs have been mixed, with positive studies mostly reporting short-term benefits. Evidence for clinically significant, durable improvements in cognition is currently lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to post-acute sequelae of SARS-CoV-2 infection who receive cognitive rehabilitation delivered by a qualified professional, no relevant evidence was identified. Relevant outcomes are functional outcomes and quality of life. Systematic reviews have reported on the prevalence and duration of cognitive symptoms among patients with varying acute infection severity and treatment settings. Limited reports examining the outcomes of rehabilitation in patients with post-acute COVID-19 have primarily focused on physical and respiratory rehabilitation. Additionally, the natural history of cognitive deficits experienced by patients who have recovered from acute COVID-19 requires further elucidation. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to epilepsy, autism spectrum disorder, post-encephalopathy, or cancer who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, and case series. Relevant outcomes are functional outcomes and quality of life. The quantity of studies for these conditions is much less than that for the other cognitive rehabilitation indications. Systematic reviews generally have not supported the efficacy of cognitive rehabilitation for these conditions. Relevant RCTs have had methodologic limitations, most often very short lengths of follow-up, that do not permit strong conclusions about efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 20.

Table 20. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01138020	Cognitive Rehabilitation of Blast-induced Traumatic Brain Injury (CRbTBI)	77	Oct 2026
NCT03900806	Internet-based WOrk-related Cognitive Rehabilitation for Cancer Survivors: a Randomized Controlled Trial (i-WORC)	261	Aug 2023
NCT04615390	Recovery Profiles in Patients With COVID-19 Outcomes Undergoing Rehabilitation	200	Nov 2023
NCT03168360	Effect of Intensive Cognitive Rehabilitation in Subacute Stroke Patient	150	Dec 2023
NCT04632719	MentalPlus® for Assessment and Rehabilitation of Cognitive Functions After Remission of Symptoms of COVID-19 (MP-COVID)	200	Dec 2023
NCT05172206	Symptom-based Rehabilitation Compared to Usual Care in Post-COVID - a Randomized Controlled Trial (RELOAD)	132	Dec 2023

NCT05731570	Cognitive Impairment in Long Covid: PhEnotyping and RehabilitatiOn (CICERO)	120	Feb 2024
NCT03225482	Cognitive Rehabilitation for Older Veterans With Mild Cognitive Impairment	216	Mar 2024
NCT04229056	Computer-Assisted Self-Training to Improve Executive Function Versus Unspecific Training in Patients After Stroke, Cardiac Arrest or in Parkinson's Disease: A Randomized Controlled Trial (COMPEX)	700	Dec 2024
NCT05676047	Symptom-Targeted Rehabilitation for Cognitive Complaints in Long COVID (STAR-C3)	100	Dec 2024
NCT03948490	Rehabilitation and Longitudinal Follow-up of Cognition in Adult Lower Grade Gliomas	180	Mar 2025
NCT06021470	The StrokeCog Study: a Randomised Pilot Study of a Novel Cognitive Rehabilitation Intervention in Stroke	64	Oct 2025
NCT05954741	Comparing the Effectiveness of Multidimensional Rehabilitation Programs for Cognitive Impairment in Comorbid Outpatients: a Randomized Controlled Trial	75	Jan 2026
NCT05934786	Rehabilitation of Cognition and Psychosocial Well-being - A Better Life With Epilepsy	70	Dec 2028
NCT05494424	Cognitive Rehabilitation in Post-COVID-19 Condition: A Study Protocol for a Randomized Controlled Trial	240	Jan 2029
Unpublished			
NCT03237676	The Effect of Cognitive Rehabilitation Therapy in Improving Cognitive Function of Attention Following Mild Traumatic Brain Injury	90	Dec 2019
NCT04852718	Evaluate a Rehabilitation Program for the Sequelae of COVID 19 Infection: Description of a Clinical Practice	120	Apr 2021
NCT03679468	Improving Cognition in People With Progressive Multiple Sclerosis: A Multi-Arm, Randomized, Blinded, Sham-Controlled Trial of Cognitive Rehabilitation and Aerobic Exercise.	309	Feb 2023

NCT: national clinical trial.

SUPPLEMENTAL INFORMATION

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2015 Input
In response to requests, input was received from three physician specialty societies and five academic medical centers while this policy was under review in 2015. Input was mixed on cognitive rehabilitation for patients with stroke, MS, brain tumors, or cognitive impairments after previous treatments for cancer. While input was not specifically requested for TBI, the American Association of Physical Medicine & Rehabilitation reasserted its position of support for cognitive rehabilitation after TBI.

2009/2010 Input
In response to requests, input was received from two physician specialty societies and five academic medical centers while this policy was under review in 2009 and 2010. The strongest support was for use of cognitive rehabilitation as part of the treatment of those with TBIs. The level of support varied for other diagnoses such as use in post-stroke patients.

PRACTICE GUIDELINES AND POSITION STATEMENTS
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Physical Medicine and Rehabilitation
The American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Collaborative issued a consensus guidance statement on the assessment and treatment of cognitive symptoms in patients with PASC. [48], PASC cognitive symptom assessment and treatment recommendations are summarized in Table 21.

Table 21. Post-Acute Sequelae of SARS-CoV-2 Infection Cognitive Symptom Assessment and Treatment Recommendations[a]

Assessment Recommendations	
Recommendation #	**Statement**
1	"Patients should be screened for signs of cognitive symptoms using validated tools and instruments."
2	"Patients should be evaluated for conditions that may exacerbate cognitive symptoms and warrant further testing and potential subspecialty referral. [...] Particular areas include: Sleep impairment Mood, including anxiety, depression, and posttraumatic stress disorder Fatigue Endocrine abnormalities Autoimmune disorders Note: Patients often report dissatisfaction with their care because of their persistent symptoms being attributed to psychological factors. It is important to note that mood disorders may be secondary to persistent medical conditions or one of many factors leading to cognitive symptoms."
3	"Patients should have a thorough neurological examination to identify focal neurological deficits."
3a	"For those patients identified with new or worsening focal neurological deficits (including new or worsening cognitive symptoms) an emergent evaluation is warranted; neuroimaging should be considered."

4	"The following basic lab workup should be considered to screen for reversible factors contributing to cognitive symptoms. The initial lab workup in new patients or those without lab workup in the 3 months prior to visit including complete blood count, vitamin B12, thiamine, folate, homocysteine, 1,25-dihydroxy vitamin D, magnesium, liver function tests, comprehensive metabolic panel thyroid function tests (thyroid stimulating hormone, free T3, free T4). In high-risk patients, one may consider syphilis rapid plasma regain and human immunodeficiency virus testing [...]"
5	"Clinicians should conduct a full patient history with review of preexisting conditions and comprehensive medication and supplement review for those that may contribute to cognitive symptoms. Of note, patients with PASC often present on antihistamine, anticholinergic, and antidepressant/anxiolytic medications that can contribute to cognitive symptoms."
5a	"Clinicians should validate patient history through the collection of collateral history, including preexisting function and conditions, from care team/primary care, patient family or care partner, or close contact as available."
6	"Clinicians should assess impact of cognitive symptoms using standardized patient-reported assessments, to include activities of daily living, instrumental activities of daily living, school, work and avocational (ie, hobbies), and quality of life."
Treatment Recommendations	
Recommendation #	**Statement**
1	"For patients who screen positive for cognitive symptoms, refer to a specialist (ie, speech-language pathologist, occupational therapist, neuropsychologist) with expertise in formal cognitive assessment and remediation."
2	"Treat, in collaboration with appropriate specialists, underlying medical conditions, such as pain, insomnia/sleep disorders (including poor sleep hygiene), and mood disorders that may be contributing to cognitive symptoms."
3	"Complete, in collaboration with patient primary care provider, medication polypharmacy reduction, weaning or deprescribing medications if medically feasible with emphasis on medications that may impact cognition."
4	"Reinforce sleep hygiene techniques including nonpharmacologic approaches as first line of sleep remediation."
5	"Similar to patients experiencing “physical” fatigue, patients should be advised to begin an individualized and structured, titrated return to activity program."
5a	"For patients who achieve a return to their normal, daily activities, regular exercise (at least 2–3 times/week of aerobic exercise) may be effective in improving cognition and also contribute to improved sleep patterns."
5b	"Frequent assessment of the impact of return to normal, daily activities (including school, work, driving, operating heavy machinery, etc.) is recommended to ensure that symptoms do not flare and exercise is tolerated."

[a] Adapted from Fine et al (2021).[48,]

In 2023, the American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary Post- Acute Sequelae of SARS-CoV-2 Infection (PASC) Collaborative issued a consensus guidance statement on the assessment and treatment of neurologic symptoms in patients with PASC. PASC neurologic symptom assessment and treatment recommendations are summarized in Table 22.

Table 22. Post-Acute Sequelae of SARS-CoV-2 Infection Neurologic Symptom Assessment and Treatment Recommendations[a]

Assessment Recommendations	
Recommendation #	**Statement**
1	"Clinicians should conduct a full patient history including a review of predisposing comorbidities, prior neurologic symptoms or disorders, relevant hospitalizations, time course and severity of COVID-19 infection(s), COVID-19 treatments, vaccines/boosters, pertinent family history, and social history."
2	"Clinicians should perform a thorough neurological examination to identify focal neurological deficits."
3	"Evaluate for medication and supplement use that may impact signs, symptoms, or assessment parameters"
4	"The following basic lab workup should be considered in new patients or for those without a lab workup in the 3 months prior to the visit: complete blood count with differential; chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein, erythrocyte sedimentation rate, vitamins B1, B6, B12, and D, magnesium, and hemoglobin A1c (HbA1c)."
5	"Assess for history of previous and/or current alcohol and substance use, current diet and exercise habits, physical and cognitive activity levels, and social determinants of health (eg, housing, employment, family, insurance, access to community resources, social stressors, etc.)"
6	"Assess for changes in basic and instrumental activities of daily living, including participation at work, school, community avocational (ie, hobbies) activities."
7	"On initial evaluation, obtain standardized measures of activity performance to compare to normal control values and to guide the initial activity prescription. Repeat the standardized measures of activity performance at follow-up visits to quantify functional changes and guide progression of the activity prescription."
Treatment Recommendations	
Recommendation #	**Statement**
1	"In collaboration with primary care or appropriate specialist treat underlying medical conditions, such as pain, psychiatric, renal/endocrine, cardiovascular, neurological, respiratory, etc., which may be contributing to neurologic symptoms."
2	"In collaboration with primary care or appropriate specialist, consider polypharmacy reduction, weaning or deprescribing medications and supplements where medically feasible."
3	"For patients who achieve a return to their daily activities, consider recommending regular physical activity as tolerated, which may be effective in improving many neurologic symptoms and also contribute to improved sleep patterns."
4	"For patients with neurologic sequelae affecting gait, mobility, cognitive status or activities of daily living, consider referral to physical medicine and rehabilitation physician and/or allied health professionals (eg, physical therapy, occupational therapy, speech language pathology and social work) for patient-specific recommendations to increase function and independence. To optimize functional outcomes, allied health professionals should preferably be familiar with treating sensorimotor deficits, autonomic dysfunction, and post-exertional fatigue."

5	"Provide counseling, referrals to community resources, and education for risk factor modification in the areas of: alcohol and substance use; healthy dietary pattern and hydration; return to activity, as tolerated; medications and supplements; sleep hygiene; social determinants of health."

[a] Adapted from Melamed et al (2023).[86]

American Congress of Rehabilitation Medicine

Based on a 2013 systematic review, the American Congress of Rehabilitation Medicine's Cognitive Rehabilitation Task Force recommended process-based cognitive rehabilitation strategies (e.g., attention process training, strategy acquisition and internalization, self-monitoring, and corrective feedback) to treat attention and memory deficits in children and adolescents with brain cancers who undergo surgical resection and/or radiotherapy.[7]

National Institute for Health and Care Excellence

In 2013 (updated in 2023), NICE guidance on stroke rehabilitation recommends cognitive rehabilitation for visual neglect and memory and attention deficits that impact function.[72] Interventions should focus on relevant functional tasks, e.g., errorless learning and elaborative techniques (mnemonics, encoding strategies) for memory impairments. The guidance states that providers should 'Make special arrangements for people after stroke who have communication or cognitive needs (for example, by holding joint speech and language therapy and physiotherapy sessions for those with communication difficulties).'

In 2018, NICE guidance on dementia management suggested: "Consider cognitive rehabilitation or occupational therapy to support functional ability in people living with mild to moderate dementia." [73]

In 2021 (updated in 2024), NICE issued a rapid guideline on managing the long-term effects of COVID-19. [74] The guideline recommends using a "multidisciplinary approach to guide rehabilitation, including physical, psychological and psychiatric aspects of management." Cognitive rehabilitation was not specifically addressed. Assessing the clinical effectiveness of "different service models of multimodality/multidisciplinary post-COVID-19 syndrome rehabilitation in improving patient-reported outcomes (such as quality of life)" was listed as a key recommendation for research.

The NICE guidance development is a transparent process that provides detailed information on the strength of recommendations and information on potential conflicts of interest for guideline committee members.

Institute of Medicine

The Institute of Medicine published a report in October 2011 titled "Cognitive Rehabilitation Therapy for Traumatic Brain Injury" that included a comprehensive review of the literature and recommendations.[75] The report concluded that "… current evidence provides limited support for the efficacy of CRT interventions. The evidence varies in both the quality and volume of studies and therefore is not yet sufficient to develop definitive guidelines for health professionals on how to apply CRT in practice." The report recommended that standardization of clinical variables, intervention components, and outcome measures was necessary in order to improve the evidence base for this treatment. They also recommended that future studies are needed that have larger sample sizes and include a more comprehensive set of clinical variables and outcome measures.

Veterans Administration
In 2009, the Veterans Administration/Department of Veterans Affairs published guidelines on the treatment of concussion and mild traumatic brain injury,[76] which were updated in 2016 [77] and most recently in 2021.[87,] These guidelines addressed cognitive rehabilitation in the setting of persistent symptoms. The 2021 guidelines stated:

- "We suggest that patients with symptoms attributed to mild traumatic brain injury [mTBI] who present with memory, attention, or executive function problems despite appropriate management of other contributing factors (e.g., sleep, pain, behavioral health, headache, disequilibrium) should be referred for a short trial of clinician-directed cognitive rehabilitation services." [Strength of recommendation: "weak for."]
- "We suggest against the use of self-administered computer training programs for the cognitive rehabilitation of patients with symptoms attributed to mTBI." [Strength of recommendation: "weak against."]

A 2019 Veterans Administration/Department of Defense practice guideline on the management of stroke rehabilitation found "insufficient evidence to recommend for or against the use of any specific cognitive rehabilitation methodology or pharmacotherapy to improve cognitive outcomes" and noted "there has been very little advancement in the evidence regarding the use of specific cognitive rehabilitation strategies or techniques to improve clinical outcomes following stroke."[88,]

Government Regulations

National:
There is no NCD on this topic. In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

Local:
LCD L26884 has been archived and no longer available.

MLN Matters Number: MM11501, effective date 01/01/2020
The CPT Editorial Panel also created, for CY 2020; CPT codes 97129 and 97130 to replace CPT code 97127, which CMS did not recognize. These new codes will effectively replace HCPCS code G0515, which will be deleted, effective January 1, 2020. These codes are designated “sometimes therapy” to permit physicians, NPPs, and psychologists to furnish these services outside a therapy plan of care when appropriate. The CPT long descriptors for the two new “sometimes therapy” codes are:

• CPT code 97129 - Therapeutic interventions that focus on cognitive function (e.g., attention, memory, reasoning, executive function, problem solving, and/or pragmatic functioning) and compensatory strategies to manage the performance of an activity (e.g., managing time or schedules, initiating, organizing and sequencing tasks), direct (one-on-one) patient contact; initial 15 minutes
• CPT code 97130 - Therapeutic interventions that focus on cognitive function (eg, attention, memory, reasoning, executive function, problem solving, and/or pragmatic functioning) and compensatory strategies to manage the performance of an activity (e.g., managing time or schedules, initiating, organizing and sequencing tasks), direct (one-on-one) patient contact; each additional 15 minutes (List separately in addition to code for primary procedure)

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Sensory Integration and Auditory Integration Therapy

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through April 5, 2024, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
4/6/03	4/6/03	4/9/03	Joint policy established; procedure considered experimental and investigational.
08/2005	N/A	N/A	Policy changed to BCN-only policy (see history below)
11/1/12	6/12/12	6/15/12	Policy brought back as a joint policy; policy status changed to established for selected patients with TBI or other neurological injuries including stroke.
4/16/13	4/16/13	4/22/13	Policy references updated; added information to medical policy statement to check individual contract, certificate or rider regarding coverage of cognitive rehab.
1/1/15	10/21/14	11/3/14	Routine maintenance; added additional covered ICD9 diagnosis codes in 432-433 range. Rationale and references updated.
1/1/16	12/10/15	12/10/15	Routine maintenance; added additional references. No change in policy status.
11/1/16	8/16/16	8/16/16	Routine policy maintenance; no change in policy status.
11/1/17	8/15/17	8/15/17	Updated rationale section, added reference # 16, 17, 26, 32, 45 and 53.
5/1/18	2/20/18	2/20/18	Added code 97127. Routine policy maintenance. No change in policy status.
5/1/19	2/19/19		Routine policy maintenance. No change in policy status.
3/1/20	12/17/19		Deleted code 97532 and 97127, added code G0515 for CMS use. Added codes 97129 and 97130. Routine policy maintenance, no change in policy status.

3/1/21	12/15/20		Rationale updated, reference # 12, 17, 35, 36, 50, 52, and 56. Clinical trials section updated. No change in policy status.
3/1/22	12/14/21		Routine maintenance. Minor revision to summary of 2015 Clinical Input from American Association of Physical Medicine & Rehabilitation. Clinical trials section updated. No change in policy status.
3/1/23	12/20/22		•Routine maintenance. •Evidence review and added post-acute cognitive sequelae of SARS-CoV-2 infection was added under Exclusions. •Code G0515 removed from policy as code was deleted eff 1/1/2020. •References updated. (ky)
9/1/23	6/13/23		•Routine maintenance. •References updated. •Vendor: N/A. •Discussion at JUMP – to add autism spectrum disorders, seizure disorders, and cognitive deficits due to brain tumor or previous treatment for cancer under Exclusion section. (ky)
9/1/24	6/14/24		Routine maintenance Added language to Description/Background References updated. Vendor: N/A (ky)

Next Review Date: 2nd Qtr. 2025

BCN Medical Policy History

Policy Date	Comments
10/12/98	BCN policy established
6/14/01	Policy updated
4/6/03 (Joint policy)	Policy converted to a joint policy
11/21/06	Reverted to BCN only policy
6/27/08	Routine maintenance; added BlueCaid coverage information
9/23/09	Policy updated

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: COGNITIVE REHABILITATION

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Coverage for cognitive rehabilitation is available **only** if one of the following conditions are met: 1. The member's certificate does not specifically exclude cognitive rehabilitation (e.g., BCN1, BCN Basic, FEHBP, Non-Group); OR 2. The patient has a specific rider covering cognitive rehabilitation. If eligible for coverage, cognitive rehabilitation is covered only for the diagnosis of either traumatic brain injury or stroke. It is not covered for treatment of patients with chronic progressive brain conditions without reasonable potential for restoration (e.g., Alzheimer's disease, etc.). For BCN certificates that list cognitive rehabilitation as a general benefit exclusion, cognitive rehabilitation is not covered for any condition.
BCNA (Medicare Advantage)	See government section
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- The patient's certificate MUST NOT specifically exclude cognitive rehabilitation services (e.g., BCN1 etc.), OR the patient the patient MUST have a rider explicitly covering cognitive rehabilitation, Check the member's certificate and rider for eligibility for cognitive rehabilitation.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.