Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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Current Policy Effective Date: 3/1/21
(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 (i.e., 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.

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 patients meeting specific selection criteria.

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

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

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 patient's pre-injury function, and
4. Patients must be able to actively participate in the program. The patient 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 member is expected to make significant cognitive improvement (e.g., member is not in a vegetative or custodial state).

Excluded diagnoses include, but are not limited to:

- Mental retardation
- 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

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 G0515

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

N/A

Regulatory Status:

N/A

Rationale

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.

This policy was originally based on a 1997 TEC Assessment.[6] The Assessment addressed a broad range of patient indications resulting from neurological insults, including traumatic brain injury, stroke, post-encephalopathy, and aging (including Alzheimer's disease). Eighteen controlled trials were reviewed, primarily focusing on stroke and traumatic brain injury. No controlled trials were available that specifically addressed the remaining patient indications. No clear answer regarding the efficacy of cognitive rehabilitation emerged from the assessment. The evidence was conflicting either because of study design, low power to detect differences, or variation in treatment. The assessment concluded that data were inadequate in the published peer-reviewed literature to validate the effectiveness of cognitive rehabilitation as either an isolated component or one component of a multimodal rehabilitation program.

In 2013, the Cognitive Rehabilitation Task Force of the American Congress of Rehabilitation Medicine (ACRM) published a systematic review of cognitive rehabilitation in medical conditions affecting cognitive function.[7] Literature was searched through the end of 2008. Of 11 clinical conditions reviewed (anoxia/hypoxia, encephalitis, epilepsy, HIV-AIDS encephalopathy, Huntington disease, systemic lupus erythematosus, Lyme disease and other tick-borne encephalopathy, neoplasms, Parkinson disease, and metabolic encephalopathy), there was evidence to support a practice guideline only for children and adolescents with brain tumors who undergo surgical resection and/or radiation therapy. A practice option (based on lower quality evidence) for patients with seizure-related cognitive impairments is discussed next.

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?

The following **PICOs** were used to select literature to inform this review.

Patients

The relevant population of interest are individuals with cognitive deficits due to traumatic brain injury.

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. Patients with cognitive deficits due to TBI are actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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:

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

Systematic Reviews
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.[8] Sixteen RCTs (total 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.[9] 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

RCTs not included in the Cochrane systematic review or TEC Assessment are described next. An RCT comparing a comprehensive neuropsychologic rehabilitation program with standard rehabilitation was published in 2008.[10] Sixty-eight patients were randomized to the 2 intervention groups for 16 weeks of treatment. Principal outcomes were the Community Integration Questionnaire (CIQ) and the Perceived Quality of Life Scale (PQOL). Treatment effectiveness was evaluated by an interaction between intervention pre- and post-treatment. Such an interaction was significant for the CIQ (p=0.042) and the PQOL (p=0.049) but not for any of the secondary neuropsychologic outcomes. The proportion of patients having a clinically significant improvement in CIQ score (4.2 points) was not reported, Follow-up assessments were also done at 6 months post-treatment, but were not subjected to formal statistical analysis. The standard treatment group had further improvements in CIQ scores such that their mean follow-up CIQ score was very similar to that of the intervention group (12.9 vs. 13.2). For PQOL scores, the differences observed at the end of treatment were maintained or had increased by 6 months. This RCT, thus, had mixed findings on the efficacy of comprehensive neuropsychologic rehabilitation for TBI.

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 = 0.37). 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 trials have shown improvement in some outcomes with cognitive rehabilitation, systematic reviews have provided mixed findings, with no consistent evidence of efficacy in patients with TBI.

DEMENTIA, INCLUDING ALZHEIMER'S DISEASE

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?

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

Patients
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. Patients with cognitive deficits due to dementia are actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.

c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. Studies with duplicative or overlapping populations were excluded

Systematic Reviews

In a Cochrane review, Bahar-Fuchs et al (2019) evaluated the use of cognitive training for people with mild to moderate dementia.[14] 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 include 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.[13] 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.[14] 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[15] 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.[16]

Randomized Controlled Trials

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.[17] 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.[18] 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.[19] 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.[20] 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 IADL declined within 2 to 3 months after completion of training. Improvements in other outcomes (general memory and cognitive ability, overall function, quality of life, and behavioral/psychological symptoms[21]) were not observed. Aberrant motor behaviors increased significantly from baseline in treated groups.

Individual randomized trials have shown variable outcomes of cognitive rehabilitation. Kurz et al (2012) conducted an RCT of patients with Alzheimer's disease and early dementia.[22] 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.[23] 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.[24] 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)[17]	England, Wales	8	2013-2016	Patients with Early-Stage Alzheimer, vascular or mixed dementia	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		
Amieva et al (2016)[18]	France	40	2008-2009	Patients diagnosed with Alzheimer disease	CTT (N=170)	RT (n=172)	ICRT (n=157)	Usual medical care (n=154)
Thivierge (2014)[20]	Canada	NR	2008-2011	Patients with Alzheimer disease (n=20)	ELL and SR cognitive techniques	Controls	NR	NR
Kurz et al (2012)[22]	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)[23]	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)[24]	U.K.	23	NR	Patients with dementia	Cognitive stimulation therapy (n=115)	Control (n=86)	NR	NR

RCT: randomized controlled trial; CTT: cognitive training therapy; RT: reminiscence therapy; ICRT: individualized cognitive rehabilitation therapy; ELL: errorless learning; NR: not reported; 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) [17]			Individual goal attainment at 9 mos			
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)[18]						
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 (2014)[20]						
Therapy			86.78			
Control			81.12			
Kurz et al (2012)[22]						
Therapy				0.729+/-1.82		
Control				0.857+/-1.59		
p-value				0.64		
Chapman et al (2004)[23]						
Therapy					24.62	
Control					26.96	
Spector et al (2003)[24]						
Therapy						0.9
Control						-0.4
p-value						0.044

CTT: cognitive training therapy; RT: reminiscence therapy; ICRT: individualized cognitive rehabilitation therapy

Table 3. Relevance Gaps

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Clare et al (2019) [17]					
Amieva et al (2016)[18]					
Thivierge (2014)[20]			4. Not the intervention of interest		1,2. Follow-up only 24 wks
Kurz et al (2012)[22]					1,2. Follow-up only 9 mos
Chapman et al (2004)[23]					
Spector et al (2003)[24]					

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)[17]		1. Participants and clinical staff not blinded				
Amieva et al (2016)[18]	2. Allocation not concealed	1. Participants and clinical staff not blinded				
Thivierge (2014)[20]	2. Allocation not concealed	1,2. No blinding				
Kurz et al (2012)[22]	2. Allocation only concealed from outcome raters	1. Not blinded to treatment assignment				
Chapman et al (2004)[23]	1. Randomization process not described					
Spector et al (2003)[24]	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, Including AD

Systematic reviews of RCTs have generally shown no benefit of cognitive rehabilitation or effects that are clinically important. Most randomized trials either have not showed effects, showed only short-term effects, or did not evaluate long-term outcomes. 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.

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?

The following **PICOs** were used to select literature to inform this review.

Patients

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. Patients with cognitive deficits due to stroke are actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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:

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

Systematic Reviews
Four Cochrane reviews assessed the effectiveness of cognitive rehabilitation for recovery from stroke.[25-28] 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.[25] 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.[26] 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.
- Memory deficit: A 2016 update identified 13 trials with 514 patients.[28] 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.[29] Data from 44 trials involving more than 1500 patients 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.[30]

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.[31] 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 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 multiple sclerosis.

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 **PICOs** were used to select literature to inform this review.

Patients
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. Patients with cognitive deficits due to MS are actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. 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.[32-34] 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.[33] 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.

Table 5. SR & MA Characteristics

Study	Dates	Trials	Participants	Intervention	N. Range	Design	Duration
Rosti-Otajarvi (2014)[33]	1993-2013	20	Patients with multiple sclerosis	Neuropsychological rehabilitation	986 (15-240)	RCTs and quasi-	Mean 9.5 weeks

						randomized trials	
Das Nair (2016)[34]	1993-2015	15	Patients with multiple sclerosis	Cognitive rehabilitation	989 (19-240)	RCTs and quasi-randomized trials	NR

M-A: meta-analysis; MS: multiple sclerosis; NR: not reported; RCT: randomized controlled trials; SR: systematic reviews.

Table 6. SR & MA Results

Study	Memory Span Improvement SMD	Working Memory Improvement SMD	Objective Assessment of Memory SMD	Activities of Daily Living SMD
Rosti-Otajarvi (2014)[33]	0.54	0.33	NR	NR
95% CI	0.2-0.88	0.09-0.57	NR	NR
P-value	0.002	0.006	NR	NR
Das Nair (2014)[34]	NR	NR	0.03-0.49	-0.63 to -0.03
95% CI	NR	NR	0.03-0.49	-0.63 to -0.03
P-value	NR	NR	0.03	0.03

CI: confidence interval; M-A: meta-analysis; P-value NR NR 0.03 0.03
SMD: standardized mean difference; CI: confidence interval.

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%).[35,36] 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 (2019); CRAMMS RCT	England	5	2015-2017	People aged 18-69 yrs with MS who reported cognitive problems in daily life	10 weekly sessions of cognitive rehabilitation, delivered by an Assistant Psychologist to groups of 4-6 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; RCT: randomized controlled trial.

Table 8. Summary of Key RCT Results

Study	Multiple Sclerosis Symptoms Measure	Employment Measures	Quality of Life Measures
Lincoln et al (2020)	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

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

Table 9. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Lincoln et al (2020)			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)		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
Chiaravalloti et al (2005)[37]	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 (eg, 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)[38]	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 (eg, 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)[39] Mantynen et al (2014)[40]	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)[41]	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)[42]	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)[43]	20	Learning-impaired participants with primarily relapsing remitting MS (65%)	STEM: 2, 30-45 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.

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 **PICOs** were used to select literature to inform this review.

Patients
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. Patients with cognitive deficits due to epilepsy, autism spectrum disorder (ASD), post-encephalopathy, or cancer are actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an outpatient clinical setting.

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:

a. To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
b. In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
c. To assess longer term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
d. 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.[44]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 systematic review by ACRM's Cognitive Rehabilitation Task Force evaluated cognitive rehabilitation in epilepsy.[7] Based on two comparative studies (one randomized; total 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.[45] 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.[46] Mean age (SD) was 36 (10) years; mean age (SD) at onset of epilepsy was 4 (1) years; and mean 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

In 2013, Reichow et al 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.[47] Five comparative trials in patients with autism-spectrum disorders (total N=255) who received cognitive rehabilitation, training, and support were included. Improvements in school performance and developmental outcomes were inconsistent across trials.

Wang et al (2013) conducted a pilot study of a novel virtual reality-cognitive rehabilitation intervention in four children (mean age, 7.4 years) with autism.[48] 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.[49] 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, 92-157). 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.

Post-encephalopathy

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).[50] 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)	Turkey	1	NR	Children aged 6-12 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

NR: not reported; MMSE: Mini-Mental Status Examination; RCT: randomized controlled trial.

Table 13. Summary of Key RCT Results

Study	Cognitive Measures	Fatigue Measures	Functional Independence Measures
Akel et al (2019)	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/< 0.001	52.45 ± 8.90/62.68 ± 9.74/1.15/< 0.001
Control group	NR	3.16 ± 2.45/2.16 ± 1.79/0.41/0.01	52.33 ± 9.29/53.11 ± 8.73/0.08/0.068
Relative measure	NA	NR	NR

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

Table 14. Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Akel et al (2019)			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)		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.[51] 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).[52] 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.[53] 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.[54] In children and adolescents, two prospective, comparative studies (1 RCT[55]) 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:[55] Butler et al (2008) 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, multitest 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)[56] (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)	Canada	1	NR	Adults aged ≥ 18 yrs with a diagnosis of a primary brain tumor who were ≥ 3 mos post-radiation or surgery with persistent cognitive dysfunction (≤ 1 SD below executive function testing norms)	8 weekly 2-h individual sessions of a structured and standardizedGMT 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=8Waitlist 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	Functional Outcomes	Quality of Life Outcomes
Richard et al (2019)	19	19	19
Measures	Mean change (SD) in the Executive Functioning Compositea 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	0.046	0.064	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;
GMT: Goal Management Training; BHP: Brain Health Program; WAIT: Wait-list control; NR: Not Reported; RCT: randomized controlled trial; SD: standard deviation.

Table 18. Relevance Limitations

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

The study limitationsstated 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)	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	

GMT: Goal Management Training; BHP=Brain Health Program; WAIT: Wait-list control.
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.

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 sufficient 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. Systematic reviews of RCTs have generally shown no benefit of cognitive rehabilitation or effects that were not clinically important. 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 the effect of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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 the effects of the technology on health outcomes.

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	120	Oct 2021
NCT03237676	The effect of cognitive rehabilitation therapy in improving cognitive function of attention following mild traumatic brain injury	100	Oct 2019
NCT03215342	Cognitive rehabilitation in pediatric acquired brain injury-a randomized controlled trial	80	Jan 2020
NCT03168360	Effect of intensive cognitive rehabilitation in subacute stroke patient	150	Dec 2021
NCT03900806	Internet-based WOrk-related Cognitive Rehabilitation for Cancer Survivors: a Randomized Controlled Trial (i-WORC)	261	May 2021
NCT03948490	Rehabilitation and Longitudinal Follow-up of Cognition in Adult Lower Grade Gliomas	160	Dec 2022
NCT04229056	Computer-Assisted Self-Training to Improve Executive Function Versus Unspecific Training in Patients After Stroke, Cardiac Arrest or in Parkinon's Disease: A Randomized Controlled Trial	300	Dec 2024
Unpublished			
NCT01788618	Cancer and Disorders of Cognitive Functions and Quality of Life: "Cognitive Rehabilitation in Patients Suffering From Cancer and Treated With Chemotherapy"	168	Jul 2017
NCT03306875	Impact of Brain Connectome and Personality on Cognitive Rehabilitation in Multiple Sclerosis	50	Oct 2018

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.

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

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

NICE guidance (2013) on stroke rehabilitation recommends cognitive rehabilitation for visual neglect and memory and attention deficits that impact function.[59] Interventions should focus on relevant functional tasks, e.g., errorless learning and elaborative techniques (mnemonics, encoding strategies) for memory impairments.

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."[60]

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.[61] 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

The VA/Department of Veterans Affairs (DoD) published guidelines on the treatment of concussion/mild traumatic brain injury (TBI) in 2009.[62] These guidelines were updated in 2016 and address cognitive rehabilitation in the setting of persistent symptoms.[63] The guidelines state:

> "Individuals with a history of mTBI who present with symptoms related to memory, attention, and/or executive function problems that do not resolve within 30 to 90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. The Work Group suggests considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). A prolonged course of therapy in the absence of patient improvement is strongly discouraged."

The strength of the recommendation was rated as "weak".

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: MM10303, effective date 01/01/2018
The Centers for Medicare and Medicaid Services (CMS) does not recognize code 97127 for Medicare payment. Instead CMS created code G0515 for this service. G-codes were developed by Medicare for specific programmatic needs that cannot be met using existing codes, such as the G-codes used for functional outcomes reporting. However, G0515 has no connection to the functional outcomes reporting system and should be reported the same was as a CPT code on the claim form.

G0515 contains the same descriptor as former CPT code 97532 and the payment rate is very similar. If speech-language pathologists provide cognitive treatment services to Medicare patients, they should report them with G0515 in the same manner that 97532 was reported.

(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 Therapy
- Coma Stimulation

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through October 2020, 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, added code G0515 for CMS use. 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.

Next Review Date: 4th Qtr. 2021

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.