

Policy Number	THE803.019
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Cognitive Rehabilitation

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
THE803.020 Sensory Integration Therapy and Auditory Integration Therapy

Disclaimer

Carefully check state regulations and/or the member contract.

Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Legislative Mandates

EXCEPTION: For Illinois only: Illinois Public Act 103-0458 [Insurance Code 215 ILCS 5/356z.61] (HB3809 Impaired Children) states all group or individual fully insured PPO, HMO, POS plans amended, delivered, issued, or renewed on or after January 1, 2025 shall provide coverage for therapy, diagnostic testing, and equipment necessary to increase quality of life for children who have been clinically or genetically diagnosed with any disease, syndrome, or disorder that includes low tone neuromuscular impairment, neurological impairment, or cognitive impairment.

EXCEPTION: For members residing in the state of Arkansas: AR 23-79-2902-06 HB 1583 requires, on and after January 1, 2026, coverage for medically necessary treatment related to or because of an acquired brain injury. Required coverage includes: Cognitive rehabilitation therapy; Cognitive communication therapy; Community reintegration services; Functional rehabilitation therapy; Neurocognitive therapy and rehabilitation; Home and community-based treatment; Inpatient services; Neurobehavioral therapy, neurocognitive therapy, and neuropsychological testing; Neurofeedback therapy; Outpatient and day treatment services; and Post-acute care residential treatment services. The coverage must not be subject to a lifetime limitation or an unreasonable annual limitation of the number of days or sessions of medically necessary treatment services. A limitation on rehabilitation services in an inpatient rehabilitation facility shall be separate from and shall not be included in any limitation of post-acute care rehabilitation services; The coverage for an acquired brain injury must not be subject to a greater

deductible, coinsurance, copayment, or out-of-pocket limits than any other benefit provided by a healthcare insurer under a health benefit plan. When a prior auth or preservice review is required, only a clinical peer reviewer may preauthorize coverage or conduct utilization review. A clinical peer reviewer must specialize in and has experiences of the delivery of treatments and services for an individual with acquired brain injuries. This applies to the following: Fully Insured Group, Student, , HMO, EPO, PPO, POS. Unless indicated by the group, this mandate or coverage will not apply to ASO groups.

Coverage

NOTE 1: State Legislation may apply for Cognitive Rehabilitation and Autism Spectrum Disorder (ASD).

Cognitive rehabilitation (CR) (as a distinct and definable component of the rehabilitation process) **may be considered medically necessary** in the rehabilitation of individuals with cognitive impairment and related functional impairment due to moderate to severe traumatic brain injury or stroke when ALL the following criteria are met (see Policy Guidelines):

- CR is provided by a qualified licensed professional within clinician-guided program; AND
- CR is prescribed by the attending physician as part of the written care plan; AND
- The individual is expected to make significant cognitive and functional improvements based on the pre-injury function; AND
- The individual has sufficient cognitive function to understand and willingly participate in the program and has adequate language expression and comprehension (i.e., the individual is not comatose or in a vegetative state and does not have severe aphasia); AND
- Ongoing services are considered necessary only when there is demonstrated continued objective improvement in cognitive functioning toward the quantifiable short- and long-term goals.

Cognitive rehabilitation (as a distinct and definable component of the rehabilitation process) **is considered experimental, investigational and/or unproven** for all other applications, including, but not limited to individuals with:

- Mild traumatic brain injury;
- Mild cognitive impairment;
- Alzheimer's disease;
- Multiple sclerosis;
- Post-acute sequelae of SARS-CoV-2 infection;
- Epilepsy; or
- Cognitive deficits as a result of childhood cancers, adult brain tumors, or non-central nervous system tumors.

Policy Guidelines

For services to be considered medically necessary, they must be provided by a qualified licensed professional and must be prescribed by the attending physician as part of the written

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

Duration and intensity of cognitive rehabilitation (CR) therapy programs vary. One approach for comprehensive cognitive rehabilitation is a 16-week outpatient program comprising 5 hours of therapy daily for 4 days each week. In another approach, cognitive group treatment occurs for three 2-hour sessions weekly and three 1-hour individual sessions (total, 9 hours weekly). CR programs for specific deficits (e.g., memory training) are less intensive and generally have 1 or 2 sessions (30 or 60 minutes) in a week for 4 to 10 weeks (see Background).

Sensory integrative therapy, explicitly identified by CPT code 97533, may be considered a component of cognitive rehabilitation. However, sensory integration therapy is considered separately in Medical Policy THE803.020.

Description

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 comprises tasks to reinforce or reestablish previously learned patterns of behavior or to establish new compensatory mechanisms for impaired neurologic systems. Cognitive rehabilitation may be performed by a physician, psychologist, or a physical, occupational, or speech therapist.

Policy Focus and Scope

Populations

This policy evaluates the efficacy of cognitive rehabilitation (CR) interventions in mitigating cognitive dysfunction among individuals with deficits resulting from traumatic brain injury, stroke, multiple sclerosis, post-acute sequelae of SARS-CoV-2 infection, mild cognitive impairment, or Alzheimer's disease, while specifically excluding other dementia etiologies. The analysis considers the effects of CR on cognitive impairments secondary to epilepsy, without addressing other seizure-related disorders.

The policy also considers the use of CR for cognitive impairments arising from childhood cancers and adult cancers, including brain tumors and non-central nervous system (CNS) tumors. Cancer therapies can induce cognitive changes commonly known as "chemo-brain", manifesting as challenges with memory, focus, and higher-order cognitive skills. These issues may stem from chemotherapy, radiation, or surgical procedures.

The policy does not consider the use of CR for individuals with cognitive deficits due to autism spectrum disorder (ASD) and postencephalopathy:

- Autism Spectrum Disorder encompasses a broad range of conditions affecting social interaction, communication, and behavior. The term "spectrum" highlights the extensive variability of challenges among individuals. ASD includes numerous conditions that impact social interaction, communication, and symptoms, necessitating diverse treatment approaches. These approaches include behavioral and educational interventions, psychopharmacologic interventions, and complementary and alternative therapies.
- Post-encephalitic experiences involve alterations in mental faculties to varying extents, potentially impeding everyday activities. The cognitive impairment patterns following encephalitis vary among individuals, depending on the affected brain systems and the nature of the encephalitis.

Interventions

This policy examines the evidence for CR delivered by qualified professionals within clinician-guided programs. It specifically excludes studies initiated during acute inpatient hospital stays. The review does not evaluate research that is solely based on computerized cognitive training, such as interactive or gamified activities accessed on computers or mobile devices, or the use of virtual reality tools by individuals and their families. Recent research increasingly highlights the effectiveness of computerized cognitive training across diverse populations and cognitive domains.

Outcomes

Short-term improvements in cognitive test performance measured post-intervention alone are insufficient to confirm the utility of CR for this policy. Measurements of daily functioning and quality of life are the primary health outcomes of interest. Improvements should be demonstrable after longer-term follow-up post-intervention, preferably greater than 6 months.

Cognitive Rehabilitation

Cognition-oriented treatments (COTs) is a broad term to describe nonpharmacological interventions designed to engage and enhance cognitive functions. (1) Unlike nonpharmacological interventions, which focus on behavioral, emotional, or physical outcomes, COTs aim to improve cognitive processes and their impact on daily functional abilities. (2) COTs for preventing decline in cognition and functional status in older adults include cognitive training, cognitive behavioral therapy, cognitive stimulation therapy, and CR. Each approach is distinct based on theoretical assumptions, key elements, and target populations, though overlaps exist, making differentiation challenging. Despite available definitions, these terms are often used interchangeably in the literature.

CR is a structured set of therapeutic activities designed to retrain an individual's ability to think, use judgment, and make decisions. The focus is on improving deficits in memory, attention, perception, learning, planning, and judgment. The term CR is applied to various intervention strategies or techniques that attempt to help patients reduce, manage, or cope with cognitive deficits caused by brain injury. The desired outcomes are improved quality of life and function

in home and community life. The term *rehabilitation* broadly encompasses reentry into familial, social, educational, and working environments, the reduction of dependence on assistive devices or services, and general enrichment of quality of life. Patients recuperating from traumatic brain injury have traditionally been treated with some combination of physical therapy, occupational therapy, and psychological services as indicated. CR is considered a separate service from other rehabilitative therapies, with its own specific procedures.

CR focuses on identifying and addressing individual needs and goals, which may require strategies for taking in new information or compensatory methods such as using memory aids. CR is a therapeutic approach that encompasses several key elements: (3)

- It emphasizes functionality in daily activities.
- It focuses on specific activities selected by each participant as important, usually framed as personal goals they aspire to achieve.
- An individualized therapy plan is crafted, aimed at enhancing performance or managing these activities, based on an assessment of the participant's current capabilities and intrinsic capacity, along with an evaluation of the demands of the chosen activities.
- Recognized rehabilitative strategies and methods are employed to help the participant compensate for, manage, or overcome functional limitations concerning the targeted activities.

CR is often categorized into six main domains: complex attention, executive function, learning and memory, language, perceptual-motor control, and social cognition. (97, 98) These areas are commonly evaluated and targeted in rehabilitation programs. The duration and intensity of these programs are customized based on an individual's assessment in these domains. (4, 5) This personalized approach helps create effective treatment plans that address specific cognitive impairments and prioritize functional outcomes.

Regulatory Status

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

Rationale

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

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the

intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Traumatic Brain Injury

Clinical Context and Therapy Purpose

Traumatic brain injury (TBI) is a major cause of death. There were approximately 214,000 TBI-related hospitalizations in 2020 and over 69,000 TBI-related deaths in the United States in 2021. (6) People aged 75 years and older had the highest numbers and rates of TBI-related hospitalizations and deaths. There are three main types of TBI: mild TBI or concussion, moderate TBI, and severe TBI. TBIs can have a significant impact on both individuals and family members/caregivers, resulting in increased impairment in daily activities, depression, anxiety, social isolation, and decreased quality of life. (7) Common symptoms after mild to moderate TBIs include headaches, changes in mood, and cognitive symptoms. Cognitive dysfunction appears to result in higher healthcare utilization, as individuals with cognitive impairment require three times as many hospitalizations as those without cognitive impairment.

The purpose of cognitive rehabilitation (CR) 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 TBI.

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to TBI?

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

Populations

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

Interventions

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

Comparators

Comparators of interest include standard rehabilitation (e.g., physical therapy, occupational therapy) without a 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 one 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.

Methodologically credible studies were selected using the following principles:

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

Systematic Reviews

Chuaykarn et al. (2024) conducted a meta-analysis on the efficacy of nonpharmacological interventions (NPIs) for cognitive function improvement in TBI patients. (4) The review included 21 studies (N=75; age range, 32 to 64 years) published through 2022. Nine studies were from the USA; the remainder were international studies. Twelve were RCTs with TBI severity from mild to severe. Sixteen interventions were categorized into multimodal cognitive training, technology innovation, memory training, executive function training, physical activity, and sensory stimulation. These interventions showed a large effect on memory ($d=0.80$ to $d=2.03$; $p<.000$), processing speed ($d=1.58$; $p<.05$), and cognitive behavior ($d=1.63$ to $d=8.91$; $p=.003$). Executive function ($d=0.5$, $p<.01$ to $d=0.62$; $p<.05$), attention ($d=0.5$; $p<.01$), and intelligence ($d=0.57$ to $d=0.59$; $p=.000$) had medium effects, while visuospatial function and language improved significantly post-intervention.

Austin et al. (2024) reported results of a systematic review and meta-analysis of CR interventions in veterans and service members with TBI. (7) The review included RCTs published by February of 2023 that used adult participants who were U.S. veterans or active-duty service members who had a history of mild-to-moderate TBI that tested cognitive rehabilitation

treatments designed to improve cognition and/or everyday functioning and reported objective neuropsychological testing as a primary outcome measure. Eight trials (N=303 in CR; N=261 in control; 97% of whom had a history of mild TBI) were included. Seven (of 8) trials were published after 2013. The mean age of participants was 37 years (standard deviation, SD=7) and between 81% and 100% of participants were male. Limited racial and ethnic information was available from the included studies. The mean length of time since TBI was 6 years (SD=52). CR intervention lengths ranged from 4 to 15 weeks (mean=9.5; SD=3.7). Study quality and risk of bias were evaluated using the Cochrane tool. Overall, the studies were rated as having low risk of bias. Given the variation in outcome measures used across studies, effect sizes were transformed into Cohen's d for meta-analysis. Participants in CR showed a significant improvement in overall objective neuropsychological functioning compared to controls (d=.22; 95% CI, 0.01 to 0.43; p=.04) but not on performance-based measures of functional capacity (d=.16; 95% CI, -0.48 to 0.81; p=.62). Participants in CR also had comparatively larger improvements in memory (d=.42; 95% CI, 0.13 to 0.70; p=.01) and executive functioning (d=.26; 95% CI, 0.01 to 0.51; p=.04) but not on attention (d=.12; 95% CI, -0.12 to 0.35; p=.33). Four RCTs (50%) included postintervention follow-up visits to measure durability of treatment effects. In these 4 studies, treatment effects on overall neuropsychological test performance at 10- or 12-week follow-up were also statistically significant favoring CR (d=.45; 95% CI, 0.01 to 0.90; p=.04).

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

Randomized Controlled Trials

Numerous RCTs have been conducted and are summarized in the systematic reviews described in the previous section.

Chiaravalloti et al. (2016) conducted an RCT evaluating the Story Memory Technique to improve learning and memory in subjects with moderate-severe TBI. (10) Sixty-nine subjects were randomized to treatment or control. Assessments were performed at the end of treatment (5 weeks) and 6 months posttreatment. Statistically significant outcomes favored the treatment group for several measures assessing memory at 5 weeks, while results at 6 months were less definitive.

das Nair et al. (2019) conducted the large (N=328), multicenter, assessor-blinded RCT, which evaluated a group memory rehabilitation program for people with TBI (ReMemBrIn) in 9 sites in England. (11) 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 to 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 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 years, median GCS closest to admission of 11.5 (25th, 75th percentile=6, 14), a length of initial hospital stay for TBI of 84 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 at 6 months' follow-up, the between-group difference was not clinically important (adjusted difference in mean scores -2.1; 95% CI, -6.7 to 2.5; p=.37). For secondary outcomes, there was a significant improvement in goal attainment both at 6 and 12 months, but no differences on others such as mood or quality of life. Important methodological limitations included lack of an active control arm, incomplete assessment of intervention fidelity, and exclusion of over 20% of the sample from the primary analysis.

Section Summary: Traumatic Brain Injury

While some RCTs have indicated enhancements in certain outcomes with CR for individuals with moderate to severe TBI, systematic reviews have yielded mixed results. One systematic review analyzing 12 RCTs involving individuals with mild to moderate TBI demonstrated notable improvements in memory, processing speed, and cognitive behavior. Executive function, attention, and intelligence showed moderate effects, whereas visuospatial function and language significantly improved following multimodal cognitive training and sensory stimulation. Another systematic review of RCTs focusing on U.S. Veterans with mild to moderate TBI, revealed that participants undergoing CR experienced substantial improvements in overall neuropsychological functioning, memory, and executive function sustained for a minimum of three months. However, these benefits did not extend to functional capacity or attention when compared to control groups.

Mild Cognitive Impairment Or Alzheimer's Disease

Clinical Context and Therapy Purpose

Dementia is an acquired disorder marked by cognitive decline in one or more areas, such as memory, language, executive function, attention, perceptual-motor skills, and social cognition. The Diagnostic and Statistical Manual of Mental Disorders (5th edition, September 2024) defines major neurocognitive disorder as documenting substantial decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing), and steadily progressive, gradual decline in cognition, without extended plateaus. (12) These deficits must be severe enough to impact daily function and independence.

Mild cognitive impairment (MCI) is a state between normal cognition and dementia, with cognitive impairments but no functional decline. MCI can lead to dementia or be reversible. With aging populations, dementia burden increases, requiring clinicians to test for cognitive impairment and manage early signs of Alzheimer's disease and other dementias.

Alzheimer's disease (AD) is the most common dementia in older adults. followed by mixed dementias, and vascular dementia alone. (13, 14) Other forms of dementia include the Parkinsonian dementias, dementia with Lewy bodies, and fronto-temporal dementia. An

estimated 7 million Americans aged 65 years and older are living with AD. That number is expected to double by 2060. AD is increasingly prevalent with advancing age. (15)

CR aims to help patients in the early stages of dementia to maintain memory and higher cognitive function and to devise strategies to compensate for declining function.

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

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

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

Populations

The relevant population of interest is individuals with mild cognitive impairment or Alzheimer's disease.

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating CR 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 one outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, 2 years of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.

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

Systematic Reviews

Hao et al. (2025) conducted a meta-analysis of 32 RCTs, published through July 2024, including 2370 participants, to compare effects of dual-task interventions on cognitive function in individuals aged 60 and older with mild cognitive impairment or dementia. (16) Dual tasking involves the simultaneous or sequential execution of two different tasks, utilizing principles of motor skill acquisition and task relevance to manage multiple tasks efficiently. This review examined three specific dual-task combinations: dual cognitive, motor-cognitive, and dual motor. Dual cognitive task training significantly improved global cognition (SUCRA=79.2%) and motor-cognitive dual task training uniquely enhanced executive function (SMD=1.53). Dual motor task training was most effective for physical function, improving gait (SMD=0.34), muscle strength (SMD=0.28), and balance (SMD=0.90). Motor-cognitive dual task training also resulted in enhancing daily activities (SMD=1.50) and quality of life (SMD=1.20) and reducing depressive symptoms (SMD=-0.96). Overall, dual cognitive task training best enhanced global cognition, while motor-cognitive dual task training significantly improved executive cognition.

Kudlicka et al. (2023) reported results of a Cochrane systematic review of CR for people with mild to moderate dementia on outcomes related to everyday functioning. (3) The review included 6 RCTs (N=1702) published between 2010 and 2022. The mean age of participants in the RCTs ranged from 76 to 80 years and the proportion of male participants ranged from 29% to 79%. Approximately 60% participants had a diagnosis of AD. Risk of bias was rated as relatively low for all domains other than blinding, which is not generally feasible with psychosocial interventions. Extracting data for the outcome of everyday functioning was operationalized by extracting the measure of goal attainment used in the individual studies related to activities targeted in the intervention for that study. Results were provided for outcomes at the end of the CR and after 3 to 12 months of follow-up post-rehabilitation. The authors concluded that there was high-certainty evidence of large positive effects of CR relative to control immediately following rehabilitation on participant self-ratings of goal attainment (standardized mean difference [SMD]=1.5; 95% CI, 1.3 to 1.7; 3 RCTs; N=501), informant ratings of goal attainment (SMD=1.6; 95% CI, 1.01 to 2.21; 3 RCTs; N=476), and self-ratings of satisfaction with goal attainment (SMD=1.3; 95% CI, 1.1 to 1.5; 3 RCTs; N=501). The authors also concluded that there was high-certainty evidence showing a large positive effect of CR after 3 to 12 months of follow-up post-rehabilitation on participant self-ratings of goal attainment (SMD=1.5; 95% CI, 1.3 to 1.7; 2 RCTs, N=432), informant ratings of goal attainment (SMD=1.3; 95% CI, 0.78 to 1.72; 3 RCTs; N=446), and self-ratings of satisfaction with goal attainment (SMD=1.2; 95% CI, 0.7 to 1.7; 2 RCTs; N=432). There was less certainty regarding whether CR had a meaningful effect on other outcomes immediately or after 3 to 12 months such as participant anxiety and quality of life.

Study characteristics of RCTs included in Kudlicka et al. (2023) meta-analysis are summarized in Table 1. The purpose of the limitations tables (Tables 2 and 3) is to display notable limitations identified in each study.

Table 1. Summary of Trial Characteristics of Randomized Trials included in Kudlicka et al. (2023) Meta-Analysis (3)*

Study	Methods	Participants	Interventions	Outcomes
Clarkson et al. (2022); DESCANT (17)	Multicenter, pragmatic, single-blind RCT comparing the effects of introducing memory aids and guidance by dementia support practitioners against treatment as usual (UK)	469 people with mild-to-moderate dementia and their informal carers	A manualized 4-week intervention aiming to improve the abilities, functioning, and independence. A trained dementia support practitioner offered up to 6 hours of guidance and support in using memory aids. Treatment as usual: usual care from memory clinics that involved post-diagnostic counselling and advice from the clinical team, with specialist follow-up if needed	Outcomes were measured at 3 and 6 months. Primary outcome: carer-rated at 6 months. Secondary outcomes for the person with dementia: quality of life, social engagement, activities of daily living, cognition. Outcomes for care partners: mental health status, quality of life, competence in caring.
Clare et al. (2019); GREAT (18)	Parallel-group, multicenter, single-blind RCT comparing CR added to usual care with usual care alone for	475 individuals (248 males) with an ICD-10 diagnosis of AD, vascular or mixed dementia	Participants collaboratively worked on up to 3 CR goals using problem-solving, emotion	Outcomes were measured at 3 and 9 months, focusing on goal attainment, satisfaction, self-efficacy, mood,

	people with dementia, mild-to-moderate. Cognitive impairment, living at home, and with a care partner willing to contribute (UK)		regulation, and behavioral activation strategies. Sessions focused on managing cognitive difficulties, maintaining attention, and supporting care partners (10 weekly sessions over three months plus four maintenance sessions over six months). Treatment as usual: typically consisted of medication, monitoring, and general psychosocial support.	dementia-related quality of life, memory, attention, and executive function. Self-rated goal attainment was the primary outcome at 3 months, while secondary outcomes included various participant and care partner measures evaluated at both time points. Secondary outcomes for carers: self-reported stress, quality of life and health-related quality of life.
Amieve et al. (2016); ETNA3 (19)	Multicenter randomized parallel-group trial, with a two-year follow-up comparing group cognitive training, group reminiscence therapy, individual CR, and usual care (France)	653 people (237 males) with mild-to-moderate AD, ≥50 years old, living at home, and with an identified care partner	Participants underwent CR (individualized) and usual care (control). CR used activities aligning with personal goals and errorless learning. Care included support sessions for partners. Total intervention: 43.5 hours over	Outcomes were collected at multiple intervals, but only data from the 3- and 24-month points were published. The primary outcome was survival rate without severe dementia at 2 years. Secondary outcomes included institutionalization, cognitive ability, behavioral

			24 months, including 30 sessions and telephone support for CR.	symptoms, functional abilities, apathy, depression, quality of life, caregiver burden, and resource utilization.
Thieveryge et al. (2014) (20)	Single-blinded, block-randomized, cross-over, controlled study (Canada)	20 participants with mild-to-moderate AD (3 withdrew and no data available)	Cognitive training: a memory CR program to re-learn instrumental activities of daily living chosen by each participant (twice-weekly sessions over 4 weeks, each lasting 45 to 60 minutes, with evaluation) Controls waiting-list: no intervention	Cross-over. The primary outcome was the performance on the trained IADL as assessed using an observational instrument. Secondary outcomes: global cognition, everyday memory functioning, quality of life. Outcomes completed by care partners were: behavioral, mood, and psychotic symptoms, functional abilities, and carer burden.

* Two RCTs were excluded from this table: Clare et al. 2010 was a pilot study of the GREAT trial (Clare et al. 2019); Hindle et al. 2018 had individuals diagnosed with dementias associated with Parkinson's disease.

Table 2. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Clarkson et al. (2022): DESCANT (17)	5. Enrolled population smaller than target sample				
Clare et al. (2019): GREAT (18)	4. Enrolled populations do not reflect				

	relevant diversity				
Amieva et al. (2016): ETNA3 (19)	4,5. Racial and ethnic demographics for enrolled population are not reported				
Thieverge et al. (2014) (20)			4. Not the intervention of interest		1,2. Follow-up only 24 weeks

The study limitations 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. Study population is unclear; 3. Study population not representative of intended use; 4. Enrolled populations do not reflect relevant diversity; 5. Other.

^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 3. Study Design and Conduct Limitations

Study	Allocation^a	Blinding^b	Selective Reporting^c	Follow-Up^d	Power^e	Statistical^f
Clarkson et al. (2022): DESCANT (17)		1. Participants and clinical staff not blinded	2. Measures listed in the protocol were not reported in primary study			
Clare et al. (2019): GREAT (18)		1. Participants and clinical staff not blinded				
Amieva et al. (2016): ETNA3 (19)		1. Participants and clinical staff not blinded				
Thieverge et al. (2014) (20)		1,2. No blinding				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

^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: Mild Cognitive Impairment Or Alzheimer's Disease

A 2025 meta-analysis reviewed 32 RCTs up to July 2024, including 2370 participants with mild cognitive impairment or dementia. It evaluated three dual-task combinations: dual cognitive, motor-cognitive, and dual motor tasks. Findings indicated dual cognitive task training enhanced global cognition, motor-cognitive dual task training significantly improved executive cognition, and dual motor task training was most effective for physical function. Additionally, a 2023 Cochrane systematic review examined CR trials conducted between 2010 and 2022. Approximately 60% participants had a diagnosis of AD. The review reported statistically significant improvements in participants' self-ratings of goal attainment related to everyday functioning both immediately following rehabilitation and at 3 to 12 months post-rehabilitation. However, there was less certainty regarding the impact of CR on quality of life.

Stroke

Clinical Context and Therapy Purpose

As of 2025, stroke continues to be one of leading causes of significant long-term disability in the United States. (21) An estimated 9.4 million Americans ≥20 years of age self-report having had a stroke. Overall stroke prevalence was an estimated 3.3%. Prevalence of stroke in the United States increases with advancing age in both males and females. Each year, approximately 795,000 people experience a new or recurrent stroke. Approximately 610,000 of these are first clinical episodes and 18,000 are recurrent. Eighty-seven percent (87%) are ischemic, 10% are intracerebral hemorrhages (ICHs), and 3% are subarachnoid hemorrhages (SAHs). Cognitive deficits post-stroke limit participation in daily activities, impacting not just individuals but also their families, caregivers, and society. About 60% of stroke survivors experience cognitive impairments within the first year, (22) with those suffering mild deficits showing the highest recovery rates.

CR targets attention, memory, and executive functioning, focusing on instrumental activities of daily living, such as meal preparation, medication management, housekeeping, financial

responsibilities, time management, and self-care. Rehabilitation can be restorative, aiming to repair impaired functions, or compensatory, providing new strategies and skills when full recovery is not possible. Research to bolster the evidence base for CR continues due to the varied nature of post-stroke cognitive impairments.

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

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to stroke?

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

Populations

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

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating CR delivered by a qualified professional as a treatment for cognitive deficits due to stroke has varying lengths of follow-up. While studies described below all reported at least one outcome of interest, longer follow-up was necessary to fully observe outcomes.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

- Studies with duplicative or overlapping populations were excluded

Systematic Reviews

Four Cochrane reviews have assessed the effectiveness of CR for recovery from stroke. (23-26) The reviews evaluated spatial neglect, attention deficits, and memory deficits. The most recent updates of these reviews for these 3 domains drew the following conclusions:

- Spatial neglect: A 2013 update identified 23 RCTs with 628 patients. (23) There was very limited evidence for short-term improvements on tests of neglect with cognitive rehabilitation. However, for reducing disability due to spatial neglect and increasing independence, the effectiveness of cognitive rehabilitation remained unproven.
- Attention deficit: A 2013 update identified 6 RCTs with 223 patients. (24) There was limited evidence of short-term improvement in divided attention (ability to multitask), but no indication of short-term improvements in other aspects of attention. Evidence for persistent effects of cognitive rehabilitation on attention or functional outcomes was lacking. A 2019 update identified no new trials and concluded that the effectiveness of cognitive rehabilitation for attention deficits following stroke remains unconfirmed. (27)
- Memory deficit: A 2016 update identified 13 trials with 514 patients. (26) 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.

Gillespie et al. (2015) published an overview of Cochrane reviews and a more recent RCT assessing rehabilitation for post-stroke cognitive impairment. (28) Data from 44 trials (N=1,550) were summarized. In addition to post-stroke spatial neglect and attention and memory deficits (addressed in the 4 Cochrane publications previously described), post-stroke perceptual disorders, motor apraxia, and executive dysfunction were reviewed. Conclusions were:

- Very little high-quality evidence exists for the effectiveness of CR for post-stroke cognitive deficits.
- Current evidence has shown that CR for spatial neglect, attention deficits, and motor apraxia improve standardized assessments of impairment immediately after treatment. However, the durability and clinical significance of these improvements are unclear.
- Evidence for the effectiveness of CR 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 the long-term impact of visual scanning and perceptual retraining techniques on overall recovery and functional outcomes were unclear. (29)

Section Summary: Stroke

Recent systematic reviews have generally reported limited effects of CR in stroke patients.

Multiple Sclerosis

Clinical Context and Therapy Purpose

Multiple sclerosis (MS) is the most common progressive neurologic disease of young adults. MS varies per individual, with five clinical presentations: clinically isolated syndrome, relapsing-remitting MS, secondary-progressive MS, primary-progressive MS, and radiologically isolated syndrome. MS symptoms range from single attacks to progressive worsening, with some cases showing MRI abnormalities without symptoms. Treatments can reduce or prevent progression. (30)

Approximately one million Americans are living with MS. (31) The highest prevalence (50%) is observed in the 45-65 age group. (32) Women have a higher prevalence rate (0.55%) compared to men (0.20%), comprising nearly three-quarters of the MS population. Cognitive impairment is a common and debilitating symptom in MS. There is limited evidence that disease-modifying therapies are effective in treating cognitive dysfunction. CR emerges as a promising approach to treat cognitive dysfunction in MS.

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

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to MS?

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

Populations

The relevant population of interest is individuals with cognitive deficits due to MS.

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The 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 one outcome of interest,

longer follow-up was necessary to fully observe outcomes. Therefore, 1 year of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Systematic Reviews

Two Cochrane reviews have evaluated CR for patients with MS and cognitive impairments. das Nair et al. (2016) conducted an updated Cochrane review 'Memory rehabilitation for people with multiple sclerosis' (first published in the Cochrane Library 14 March 2012, Issue 3). (33) This update included 7 studies, bringing the total to 15 studies involving 989 patients. (34) There were no differences in subjective reports of memory functioning or mood. There was some evidence of a significant effect by intervention on objective assessments of memory in both the immediate and long-term follow-up and quality of life in intermediate follow-up. However, this effect on objective memory outcomes and quality of life was no longer statistically significant when studies at high-risk of bias were excluded.

Rosti-Otajarvi and Hamalainen (2014) conducted a Cochrane review of neuropsychological rehabilitation in MS. (35) Twenty RCTs met inclusion criteria (N=986 patients), including 7 (of 8) trials in the das Nair et al. (2016) Cochrane review. Overall quality and comparability of included trials were low due to methodologic limitations and variations in interventions and outcome measures across trials, respectively. In meta-analysis, statistically significant improvements in memory span (based on 2 low-quality trials, n=150 patients; standardized mean difference, 0.54; 95% CI, 0.20 to 0.88; p=.002; $I^2=0\%$) and working memory (3 very low-quality trials, n=288 patients; standardized mean difference, 0.33; 95% CI, 0.09 to 0.57; p=.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, and depression were not observed.

Table 4. Systematic Review & Meta-Analysis Characteristics

Study	Rosti-Otajarvi et al. (2014) (35)	das Nair et al. (2016) 34)
Dates	1993-2013	1993-2015
Trials	20	15
Participants	Patients with MS	Patients with MS
Intervention	Neuropsychological rehabilitation	Cognitive rehabilitation
N (Range)	986 (15-240)	989 (19-240)

Design	RCTs and quasi-randomized trials	RCTs and quasi-randomized trials
Duration	Mean 9.5 weeks	NR

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

Table 5. Systematic Review & Meta-Analysis Results

Study	Memory Span Improvement (SMD)	Working Memory Improvement (SMD)	Objective Assessment of Memory (SMD)	Activities of Daily Living (SMD)
Rosti-Otajarvi et al. (2014) (35)	0.54	0.33	NR	NR
95% CI	0.2 to 0.88	0.09 to 0.57	NR	NR
p-value	.002	.006	NR	NR
das Nair et al. (2014) (34)	NR	NR	0.26	-0.33
95% CI	NR	NR	0.03 to 0.49	-0.63 to -0.03
p-value	NR	NR	.03	.03

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

Randomized Controlled Trials

The largest and longest-term RCT conducted in people with MS receiving CR was published by Lincoln et al. (2020) (Table 7). It was a multicenter, observer-blinded RCT in patients with relapsing-remitting (65%), primary progressive (10%) or secondary progressive MS (25%). (36, 37) Participants were recruited between 2015 and 2017 and randomized to 10 weekly sessions of a group CR 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 7). The main methodological limitation of this trial was that there was no sham CR group, and participants were not masked to treatment assignment (Tables 8 and 9).

Table 6. Summary of Key Randomized Controlled Trial Characteristics

Study; Trial	Lincoln et al. (2020) (37); CRAMMS RCT
Countries	England
Sites	5
Dates	2015-017
Participants	People aged 18 to 69 yrs with MS who reported cognitive problems in daily life
Interventions	
<i>Active</i>	10 weekly sessions of cognitive rehabilitation, delivered by an Assistant Psychologist to groups of 4 to 6 participants; standardized content defined by a treatment manual; n=245
<i>Comparator</i>	Usual care, n=204

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

Table 7. Summary of Key Randomized Controlled Trial Results

Study	Multiple Sclerosis Symptoms Measure	Employment Measures	Quality of Life Measures
Lincoln et al. (2020) (37)	387	382	382
	Mean MSIS (SD) Psychological score at 12 months	Any employment at 12 months	Mean (SD) EQ-5D visual analog at 12 months
Cognitive rehabilitation	22.2 (6.1)	60 (29%)	61.6 (19.3)
Usual care	23.4 (6.0)	50 (29%)	59.7 (20.0)
Relative measure	Adjusted mean difference, -0.6; 95% CI, -1.5 to 0.3	Odds ratio, 0.99; 95% CI, 0.60 to 1.63	Adjusted mean difference, 2.6; 95% CI, -0.9 to 6.0

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

Table 8. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Lincoln et al. (2020) (37)			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 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 9. Study Design and Conduct Limitations

Study	Allocation ^a	Blinding ^b	Selective Reporting ^d	Data Completeness ^d	Power ^e	Statistical ^f
Lincoln et al.		1. Participants and assistant psychologists				

(2020) (37)		aware of allocation				
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The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

^a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment

^c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

^e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

^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 10). 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 CR only observed in the short-term and either not measured or not sustained in the longer-term.

Table 10. Summary of Small and Shorter-Term Trials in Individuals with Multiple Sclerosis Undergoing Cognitive Rehabilitation

Author/Year	N	MS type	Intervention	Comparator	Summary of Results
Nauta et al. (2023) (38)	110	66% relapsing- remitting; 17% secondary progressive; 12% primary progressive	9 weekly group- based sessions of 2.5 hours	Enhanced treatment as usual: 1 individual appointment with MS specialist nurse focused on psycho- education	CRT alleviated cognitive complaints immediately after rehabilitation but benefits in cognition did not persist to 6 months. At 6-month follow-up, CRT showed benefits on personalized cognitive goals (goals concerning daily life problems identified at baseline for each participant) and processing speed.

Brissart et al. (2020) (39)	110	MS; 22% relapsing-remitting MS	13 2-hour extended cognitive rehabilitation sessions delivered over 6 months	13 2-hour non-cognitive exercise sessions delivered over 6 months	Some improvement was observed in the cognitive rehabilitation group in measures of memory function, but there were no differences between groups in executive function or quality of life measures at 6-to-9-month follow-up.
Chiaravalloti et al. (2005) (40)	117	Primarily relapsing-remitting MS	8 biweekly 45-min cognitive rehabilitation sessions	Control sessions with the same therapist at the same frequency, engaging in non-training tasks (e.g., reading and recalling a story)	Mixed at 5 and 11 wks. No statistical differences between groups in new learning or emotional functioning. Self-reported improvements in memory were greater in the cognitive rehabilitation group at both time points. Results for other neuropsychological assessments were not reported.
Chiaravalloti et al. (2013) (41)	88	MS	10 biweekly, 45- to 60-min sessions of modified SMT	Control sessions with the same therapist at the same frequency, engaging in non-training tasks (e.g., reading and recalling a story)	Mixed effects at 5 weeks, but majority of benefits were not sustained at 6 months. At 5 weeks, 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-months follow-up, the only persistent between-group difference was general contentment.
Rosti-Otajarvi et al. (2013) (42) Mantynen et al. (2014) (43)	102	Relapsing-remitting MS and attentional deficits	strategy-oriented neuropsychological rehabilitation (13 weekly 60-min sessions)	No intervention	Although no improvement in cognitive performance at week 13 or at 6 months, there was improvement in perceived cognitive deficits at both time points and in a subset of patients who completed 1-year follow-up (83% completers in the therapy group vs. 67% in the control group). ^a
Hanssen et al. (2016) (44)	120	MS	4 weeks 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 months.
Shahpouri et al. (2019) (45)	56	Primarily relapsing remitting (70%)	10, 2-h individualized sessions held every 7-10 days - approaches developed	Same number and duration of sessions, but content	Memory, attention, quality of life, and depression were all significantly improved within 3 months after study

			considering the severity of cognitive impairment and with the aim of optimization of the residual functions	was not supporting cognitive rehabilitation	initiation.
Chiaravalloti et al. (2019) (46)	20	Learning-impaired participants with primarily relapsing-remitting MS (65%)	STEM: 2, 30-45 min sessions per week for 4 weeks; 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.

CRT: cognitive rehabilitation therapy; h: hour(s); mo: month(s); MS: multiple sclerosis; SMT: Story Memory Technique; STEM: Strategy-based Training to Enhance Memory; wk: week(s).

^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 CR in MS, large, 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 RCTs evaluated are mixed, with positive studies mostly reporting short-term benefits. Evidence for clinically significant, durable improvements in cognition is currently lacking.

Post-Acute Cognitive Sequelae of SARS-CoV-2 Infection

Clinical Context and Therapy Purpose

Although Coronavirus disease 2019 (COVID-19) is primarily a respiratory infectious disease, it has also been associated with a wide range of other clinical manifestations. Post-recovery, many patients report enduring COVID-19-related symptoms, notably affecting cognitive functions such as executive function, memory, attention, and processing speed. These cognitive domains are predominantly linked to SARS-CoV-2 infection (PASC), also known as long-COVID syndrome. (47)

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

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

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

Populations

The relevant population of interest is individuals with cognitive deficits due to PASC infection. The Centers for Disease Control and Prevention define the post-acute period as symptoms persisting at four or more weeks following infection with SARS-CoV-2. (48) The World Health Organization developed the following consensus case definition of 'post COVID-19 condition': individuals with "a history of probable or confirmed SARS CoV-2 infection, usually 3 months from the onset of COVID-19 with symptoms and that last for at least 2 months and cannot be explained by an alternative diagnosis. Common symptoms include fatigue, shortness of breath, cognitive dysfunction but also others and generally have an impact on everyday functioning. Symptoms may be new onset following initial recovery from an acute COVID-19 episode or persist from the initial illness. Symptoms may also fluctuate or relapse over time." (49)

While subjective reports of cognitive impairment (i.e., 'brain fog') have been reported by individuals not requiring hospitalization, (50) current understanding of objective cognitive sequelae of COVID-19 is predominantly limited to individuals who required hospitalization. (51, 52) Ceban et al. (2022) conducted a meta-analysis of 43 studies with 12 or more weeks follow-up that reported a 22% overall prevalence of cognitive impairment (95% CI, 17% to 28%; $I^2=98\%$; $N=13,232$). (53) Subjectively ascertained cognitive impairment (e.g., patient self-report) was reported in 18% of patients (95% CI, 12% to 24%; $I^2=97.9\%$; 31 studies), which was significantly lower than in studies with objective ascertainment of cognitive status utilizing validated tools (36%; 95% CI, 27% to 46%; $I^2=94.9\%$; 12 studies; $p=.002$). No significant difference in cognitive symptom prevalence was found in subgroup analyses of hospitalized versus non-hospitalized patients (30% versus 20%; $p=.096$) or patients with <6 months versus ≥ 6 months of follow-up (22% versus 21%; $p=.794$).

Objective cognitive deficits have been reported for verbal fluency, attention, working memory, processing speed, executive functioning, learning, and memory - with no clear pattern of cognitive impairment across studies. While cognitive impairment following intensive treatment of critical illness is not a new phenomenon, (54) the disease course of cognitive impairment experienced by individuals with post-acute sequelae of SARS-CoV-2 infection is an ongoing research priority. (55, 56)

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The natural history of PASC has not been fully categorized, particularly in non-hospitalized individuals. A prospective study measuring cognitive performance among patients who experienced mild disease noted that declines in cognitive scores reported at 6 months spontaneously resolved at 18-month follow-up. (57) Persistent cognitive deficits have been reported in 16% of COVID-19 survivors at 1 year who were treated in the intensive care setting. (58) Therefore, at least 1 to 2 years of follow-up may be considered necessary to demonstrate efficacy and to fully observe outcomes.

The American Academy of Physical Medicine and Rehabilitation Multi-Disciplinary PASC Collaborative issued a consensus guidance statement recommending that patients should be screened for signs of cognitive symptoms using validated tools and instruments, such as the Montreal Cognitive Assessment (MoCA) or MMSE. (51) Additional neuropsychological measures used to assess cognitive and behavioral alterations in PASC are described by De Luca and coworkers (56) and are listed on the CDC website. (48)

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Initial reports of patient rehabilitation after COVID-19 recovery have largely been observational, without clearly identifiable CR components within multidisciplinary rehabilitation programs. (59, 60) Other reports have primarily focused on respiratory (61) and physical rehabilitation. (62)

Weix et al. (2025) conducted a qualitative systematic review to examine the current evidence surrounding CR interventions and approaches to support persons with PASC. (63) Nineteen

articles published through July 2023 met inclusion criteria and were categorized into five types of intervention: (a) cognitive training, (b) cognitive behavioral therapy, (c) neurostimulation, (d) neurostimulation combined with cognitive training, and (e) multi-component rehabilitation programs. There is evidence that supports cognitive training, moderate supports cognitive behavioral training and low-level evidence supports other interventions provided by occupational therapists to target PASC cognitive symptoms in adults.

Observational studies have assessed the efficacy of CR programs for PASC. Saxon et al. (2025) (n=70 patients, U.S. single-center) found that CR provided by speech-language pathologists led to self-reported improvements in functional cognition and quality of life, especially for those who completed their plan of care, but anxiety before treatment limited these benefits. (64) Braga et al. (2023) (N=208 patients, Brazil single-center) observed discrete improvements in neuropsychological symptoms over 25 months post-infection, though performance often remained below normative standards; better outcomes were noted for individuals who engaged in psychoeducational rehabilitation, had higher education levels, and lower depression scores. (65)

Section Summary: Post-Acute Cognitive Sequelae of SARS-CoV-2 Infection

A systematic review and observational studies indicate that cognitive training may have benefit in adults with PASC. Observational studies highlight persistent cognitive and neuropsychiatric symptoms post-infection, with improvements seen particularly in individuals who complete CR programs, engage in psychoeducation, or have higher education and lower depression scores. Controlled prospective studies in well-defined patient populations with sufficient follow-up duration are necessary to evaluate net health outcomes. Ongoing research continues to elucidate the natural course of cognitive symptoms associated with PASC.

Epilepsy

Clinical Context and Therapy Purpose

Epilepsy is a neurologic condition causing seizures due to improper neuron signals. It is defined by the occurrence of two or more unprovoked seizures separated by more than 24 hours or by the occurrence of a single unprovoked seizure with risk factors indicating an equivalent probability of recurrence. (66) Seizures are either focal, affecting part of one brain hemisphere, or generalized, affecting both hemispheres. Focal seizures can impair awareness and evolve into generalized seizures. (67) Not all seizures are epilepsy related. Conditions like febrile seizures, nonepileptic events, and eclampsia are examples of conditions involving seizures that may not be associated with epilepsy.

Epilepsy affects about 3 million adults in the U.S. and is a chronic, debilitating condition, (68) with the vast majority of these cases originating in the temporal lobe. (69) The management of patients with epilepsy is focused on three main goals: controlling seizures, avoiding treatment adverse effects, and maintaining or restoring quality of life.

The purpose of CR 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.

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to epilepsy?

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

Populations

The relevant population of interest is individuals with cognitive deficits due to epilepsy.

Interventions

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

Comparators

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

Outcomes

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

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

Systematic Reviews

Farina et al. (2015) in Italy conducted a systematic review of the literature on CR for epilepsy. (70) Literature was searched through December 2013, and 18 articles of different types (reviews, methodologic papers, case reports, experimental studies) were identified. Studies

were heterogeneous for patient characteristics (type of epilepsy, type of previous treatment [surgery, antiepileptic drugs]), intervention modalities (e.g., holistic, focused) and duration, and outcome measures. Reviewers considered the overall quality of evidence to be moderate to low, and results inconsistent (e.g., not all studies showed benefit; some showed greater benefit in left-sided seizures, and others showed greater benefit in right-sided seizures).

The 2013 updated systematic review by American Congress of Rehabilitation Medicine (ACRM) evaluated CR in epilepsy. (71) Based on 2 comparative studies (1 randomized; N=156), ACRM recommended CR for attention and memory deficits as a "possibly effective" practice option for seizure-related attention and memory deficits. The RCT by Engelberts et al. (2002) prospectively enrolled 50 patients with focal seizures who were receiving carbamazepine monotherapy. (72) Patients were randomized to a retraining method aimed at retraining impaired cognitive functions (n=19), to a compensation method aimed at teaching compensatory strategies (n=17), or to a wait-list control group (n=8). Both interventions focused on divided attention (ability to multitask). At 6-month follow-up, performance on cognitive tests improved more in both intervention groups than in the control group. No differences in inhibitory capacity were observed. Self-reported cognitive complaints, absentmindedness, and quality of life improved more with CR. Overall, the different rehabilitation methods were similarly effective.

Randomized Controlled Trial

Forthoffer et al. (2025) conducted a prospective, single-blinded multi-center RCT (N=66) to evaluate the efficacy of a CR program called COMETE (COgnitive Rehabilitation of MEmory in Temporal Epilepsy) on episodic memory in patients with temporal lobe epilepsy. (69) Participants were randomly assigned in a 2:4 ratio to either receive the CR intervention or no intervention between neuropsychological assessments. The CR program comprised 12 weekly sessions lasting 45-60 minutes each, held at a hospital. These sessions focused on memory improvement through methods such as facilitation, reorganization, psychoeducation, and exercises, with homework assignments. Patients practiced strategies between sessions using a software program overseen by therapists. Each session included discussion, feedback, exercises, and homework review. Neuropsychologists, who were blinded to the intervention allocation, assessed cognitive performance at baseline, immediate follow-up (3 months post-baseline), and long-term follow-up (10 to 12 months post-baseline). Out of the initial participants, 60 (91%) were randomized. Patients in the CR group significantly improved their performance in the subtests targeted by the program (both verbal and non-verbal memory), with $p < .001$ at both 3 months and at 10-12 months, while patients in the control group did not show such improvement. Specifically, for verbal memory, 56% of the patients in the CR group normalized their performance in verbal memory learning scores, compared to just 7% of the patients in the control group.

Section Summary: Epilepsy

Two systematic reviews, published in the 2000s, have been constrained by the heterogeneity in study design, inconsistency in results, and the low to moderate quality of evidence. A small, single-blinded RCT in France evaluating the effectiveness of the CR program for episodic memory in temporal lobe epilepsy patients demonstrated that the CR group experienced

memory gains up to 12 months post-baseline, with 56% achieving normalized verbal memory scores compared to just 7% in the control group.

Childhood Cancers

Clinical Context and Therapy Purpose

In 2025, approximately 9,550 children in the U.S. will be diagnosed with cancer. (73) Current survival rates show that 85% of these children will survive for five years or more, a significant improvement from the mid-1970s when it was only 58%. Childhood cancers (birth to age 14) and adolescent cancers (ages 15 to 19) differ from adult cancers, with common types including brain and spinal cord tumors, leukemia, lymphoma, neuroblastoma, and osteosarcoma. These require specialized diagnosis, treatment, and care approaches in pediatric oncology. Survivors often experience cognitive dysfunction, especially after treatments for brain tumors or leukemia, with risk factors including young age, cranial irradiation, and chemotherapy.

The purpose of CR 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 cancer.

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to cancer?

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

Populations

The relevant population of interest is individuals with cognitive deficits due to cancer.

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating CR delivered by a qualified professional as a treatment for cognitive deficits due to cancer has varying lengths of follow-up, ranging from 2 to 6 months. While studies described below all reported at least one outcome of interest, longer follow-up was

necessary to fully observe outcomes. Therefore, 6 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

CR has been investigated in 3 cancer-related settings: in children receiving oncological treatment with regular inpatient stays, patients with brain tumors, and cancer survivors whose cognitive deficits are attributed to cancer treatment.

Systematic Reviews

No relevant systematic reviews were identified for this section.

Randomized Controlled Trials

Akel et al. (2019) conducted a single-center RCT (N=40) to investigate the effect of task-oriented inpatient CR on fatigue perception and independence in daily activities. (74) The CR was delivered in the inpatient treatment clinic of the Department of Pediatric Oncology at University Hospital in Ankara, Turkey. Cognitive skills targeted by the CR 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 (Table 11). 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 12), 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 13 and 14) 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 11. Summary of Key Randomized Controlled Trial Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator

Akel et al. (2019) (74)	Turkey	1	NR	Children aged 6-12 years 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
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MMSE: Mini-Mental Status Examination; NR: not reported.

Table 12. Summary of Key Randomized Controlled Trial Results

Study	Cognitive Measures	Fatigue Measures	Functional Independence Measures
Akel et al. (2019) (74)	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 ± 3.18/135.36 ± 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; NA: not applicable; NR: not reported; SD: standard deviation; WeeFIM: Functional Independence Measure for Children; VAS: Visual Analog Scale.

Table 13. Study Relevance Limitations

Study	Population ^a	Intervention ^b	Comparator ^c	Outcomes ^d	Follow-Up ^e
Akel et al. (2019) (74)			3. Delivery not similar intensity as intervention	5. Clinically 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 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. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

^e Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 14. Study Design and Conduct Limitations

Study	Allocation ^a	Blinding ^b	Selective Reporting ^c	Data Completeness ^d	Power ^e	Statistical ^f
Akel et al. (2019) (74)		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 gaps assessment.

^a Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

^b Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician; 4. Unclear blinding of outcome assessment

^c Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

^d Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).

^e Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.

^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: Childhood Cancers

One single-center RCT indicated cognitive benefits, but lacked robust statistical analysis, control data, blinding, and long-term follow-up, limiting conclusions about health outcomes.

Adult Cancers

Clinical Context and Therapy Purpose

In 2025, it is predicated that there will be over 2 million new cancer cases and more than 618,000 cancer-related deaths in the United States. As the population ages, the overall incidence of cancer is expected to rise, with more than 18 million Americans currently living with a history of invasive cancer. (75) Cognitive impairment is a common issue among cancer

patients, including those in remission. Up to 30% of cancer patients show cognitive deficits before treatment begins, 75% may exhibit measurable cognitive impairment during treatment, and 35% of survivors will continue to face cognitive challenges months and years after treatment.

Studies have shown that up to 90% of brain tumor patients encounter difficulties with neurocognitive function during their disease journey. Cognitive changes related to cancer have also been observed in patients with non-central nervous system (non-CNS) cancers prior to initiation of treatment. Cancer therapies such as chemotherapy and radiation can lead to adverse cognitive effects, often referred to as "chemo brain". While some cognitive alterations are mild and transient, others may persist and significantly diminish quality of life. These cognitive deficits include impairments in various cognitive skills such as memory, attention, language, and executive functions.

Patients with brain tumors and those with non-CNS tumors can experience cognitive deficits following treatment.

The purpose of CR 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 cancer.

The question addressed in this medical policy is: Does CR delivered by a qualified professional improve the net health outcome in individuals with cognitive deficits due to cancer?

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

Populations

The relevant population of interest is individuals with cognitive deficits due to cancer.

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating CR delivered by a qualified professional as a treatment for cognitive

deficits due to cancer has varying lengths of follow-up, ranging from 2 to 6 months. While studies described below all reported at least one outcome of interest, longer follow-up was necessary to fully observe outcomes. Therefore, 6 months of follow-up is considered necessary to demonstrate efficacy.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

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

CR has been investigated in 3 cancer-related settings: in children receiving oncological treatment with regular inpatient stays, patients with brain tumors, and cancer survivors whose cognitive deficits are attributed to cancer treatment.

Brain Tumors

Systematic Reviews

Tariq et al. (2025) reviewed CR methods used among brain tumor survivors, analyzing 14 studies, including 8 RCTs. (76) Eight studies focused on adult patients. The review explored various CR interventions, such as neuropsychologist-guided training, holistic mnemonic training, neurofeedback, physical exercises, and computer-based programs - the latter being primary in 4 studies, 3 of which involved pediatric patients. Neuropsychologist-guided training proved effective in enhancing memory, attention, and executive functions, especially in younger and more educated individuals. Holistic mnemonic training and neurofeedback did not affect cognitive functioning. The methodological heterogeneity across studies prevented a meta-analysis, thereby limiting the generalizability of the findings.

Table 15. Studies in Adult Patients included in Tariq et al. (2025) Systematic Review*

Study; Type	Interventions	Participants; Mean Age (years)	Duration	Outcomes
Gehring et al. (2009, 2011) (77, 78); RCT	Neuropsychologic CR program	Intervention: n=70, Control: n=70; Intervention: 42.0; Control: 43.8	6-months	• Significant group differences were found post-treatment in self-reported cognitive functioning (Cohen's d=0.31 to 0.48), which did not persist at the

				6-month follow-up. - At follow-up, there was significant improvement in objective neuropsychologic measures of verbal memory (Cohen's $d=0.48$ and 0.43) and combined attention tests (Cohen's $d=0.23$ to 0.55). - Level of education and age predicted reliable improvement. Odds of improvement increased 0.9 times per year of age and 4.7 times greater for higher education levels vs. low to medium education levels.
Hansen et al. (2020) (79); RCT	Physical and occupational therapy-based interventions individually designed to address participants' deficits or impairments	Intervention, $n=32$, Control, $n=32$; Intervention: 56.1, Control: 52.1	6-weeks	- No significant difference was observed in the overall HRQoL score. - Intervention group had a significantly higher score on HRQoL domain cognitive functioning, fewer symptoms, and greater functional performance outcomes scores.

Locke et al. (2008) (80); Controlled clinical trial	CR and problem solving	Intervention, n=12, Control, n=7; Intervention: 49.8, Control: 56.6	2-weeks, delayed F/U 3-months	Most participants and their caregivers described the intervention as “very helpful” or “somewhat helpful” and would recommend it to another person diagnosed with brain tumor.
Richard et al. (2019) (81); RCT	Goal management training	GMT, n=11, BHP, n=8, WAIT, n=6; 47.7	4-months	- The goal management group reported improvements in executive functions as well as the highest functional goal attainment. - Less cognitive concerns were reported by the intervention groups.
Zucchella et al. (2013) (82); RCT	CR program	Intervention, n=25, Control, n=28; Intervention: 58.7, Control: 52.7	4-weeks	At the end of the treatment period, significant improvement was seen in all the study group’s neuropsychological measures, while the control group trended towards improvement, however, this was not statistically significant.

* Three studies (Dülger et al., 2022; Gehring et al. (2020); van der Linden et al., 2021) were excluded from this table: Dülger et al. (2022) evaluated a combined aerobic-strength training and yoga intervention; Gehring et al. (2020) assessed a home-based remotely coach-exercise intervention; while van der Linden et al. (2021) utilized a computer-based CR program.

CR: cardiac rehabilitation; F/U: follow-up; GMT: goal management training; HRQoL: health-related quality of life; RCT: randomized controlled trial; WAIT: wait-list.

Randomized Controlled Trials

No new RCTs were identified that have been published since the systematic review by Tariq et al. (2025).

Non-Central Nervous System Tumors

Systematic Reviews

Fernandes et al. (2019) published a systematic review of CR 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, of which the majority were RCTs (N=12). (83) 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 meta-analysis of a neuropsychologic intervention for cognitive function in cancer survivors. (84) Three case-control studies and 7 RCTs with 433 patients (range, 22 to 98 patients), published between January 2010 and September 2015, were included. Most trials assessed the effects of the intervention immediately postintervention 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 CR programs and the weighted mean difference for the intervention effect at postintervention follow-up was -0.19 (95% CI, -2.98 to 2.61).

Randomized Controlled Trials

No new RCTs were identified that have been published since the above systematic reviews.

Section Summary: Adult Cancers

A systematic review of 14 studies on CR in brain tumor survivors found that neuropsychologist-guided training improved cognition, while holistic mnemonic training and neurofeedback showed no effect. Aerobic exercises aided executive function. Methodological differences across studies prevented meta-analysis, limiting generalizability, with benefits noted especially for younger, educated individuals. Two systematic reviews examining CR in non-CNS cancers have yielded mixed outcomes. While many studies reported short-term gains in cognition - typically within six months - these improvements were not sustained in larger or longer-term

trials. Neuropsychological interventions, most often studied in breast cancer survivors, demonstrated only minimal benefits.

Summary of Evidence

For individuals who have cognitive deficits due to traumatic brain injury (TBI) who receive cognitive rehabilitation (CR) 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. While some RCTs have indicated enhancements in certain outcomes with CR for individuals with moderate to severe TBI, systematic reviews have yielded mixed results. One systematic review analyzing 12 RCTs involving individuals with mild to moderate TBI demonstrated notable improvements in memory, processing speed, and cognitive behavior. Executive function, attention, and intelligence showed moderate effects, whereas visuospatial function and language significantly improved following multimodal cognitive training and sensory stimulation. Another systematic review of RCTs focusing on US Veterans with mild to moderate TBI, revealed that participants undergoing CR experienced substantial improvements, sustained for a minimum of three months, in overall neuropsychological functioning, memory, and executive function. These benefits did not extend to functional capacity or attention when compared to control groups. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to mild cognitive impairment or Alzheimer's disease (AD) who receive CR delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, case series, and systematic reviews. Relevant outcomes are functional outcomes and quality of life. A 2025 meta-analysis reviewed 32 RCTs up to July 2024, including 2370 participants with mild cognitive impairment or dementia. It evaluated three dual-task combinations: dual cognitive, motor-cognitive, and dual motor tasks. Findings indicated dual cognitive task training enhanced global cognition, motor-cognitive dual task training significantly improved executive cognition, and dual motor task training was most effective for physical function. A 2023 Cochrane systematic review examined CR trials conducted between 2010 and 2022. Approximately 60% of participants had a diagnosis of AD. The review reported statistically significant improvements in participants' self-ratings of goal attainment related to everyday functioning both immediately following rehabilitation and at 3 to 12 months post-rehabilitation. There was less certainty regarding the impact of CR on quality of life. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to stroke who receive CR 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 no benefit of CR or effects of clinical importance. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to multiple sclerosis who receive CR 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 CR on cognitive outcomes. Numerous RCTs have investigated cognitive rehabilitation for multiple sclerosis. The ability to draw conclusions based on the overall body of evidence is limited by the heterogeneity of patient samples, interventions, and outcome measures. Results of the available RCTs have been mixed, with positive studies mostly reporting short-term benefits. Evidence for clinically significant, durable improvements in cognition is currently lacking. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to post-acute sequelae of SARS-CoV-2 (PASC) infection who receive CR delivered by a qualified professional, the evidence includes one systematic review and observational studies. Relevant outcomes are functional outcomes and quality of life. The systematic review and observational studies indicate that cognitive training is the most strongly supported intervention for CR in adults with PASC, while other CR interventions such as neurostimulation and multi-component programs have lower levels of evidence. Small-scale studies highlight persistent cognitive and neuropsychiatric symptoms post-infection, with improvements seen particularly in individuals who complete CR programs, engage in psychoeducation, or have higher education and lower depression scores. Controlled prospective studies in well-defined patient populations with sufficient follow-up duration are necessary to evaluate net health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have cognitive deficits due to epilepsy, who receive CR delivered by a qualified professional, the evidence includes two systematic reviews and one RCT. Relevant outcomes are functional outcomes and quality of life. Both systematic reviews, published in the 2000s, have been constrained by the heterogeneity in study design, inconsistency in results, and the low to moderate quality of evidence. A single-blinded RCT evaluating the effectiveness of the CR program for episodic memory in temporal lobe epilepsy patients demonstrated that the CR group experienced memory gains up to 12 months post-baseline, with 56% achieving normalized verbal memory scores compared to just 7% in the control group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cognitive deficits due to childhood cancers who are treated with CR delivered by a qualified professional, the evidence includes 1 RCT. Relevant outcomes are functional outcomes and quality of life. The single-center RCT indicated cognitive benefits, but lacked robust statistical analysis, control data, blinding, and long-term follow-up, limiting conclusions about health outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cognitive deficits due to adult brain tumors or non-central nervous system (CNS) tumors who are treated with CR delivered by a qualified professional, the evidence

includes systematic reviews and RCTs. A systematic review of 14 studies on CR in brain tumor survivors found that neuropsychologist-guided training improved cognition, while holistic mnemonic training and neurofeedback showed no effect. Methodological differences across studies prevented meta-analysis, limiting generalizability, with benefits noted especially for younger, educated individuals. Two systematic reviews examining CR in non-CNS cancers have yielded mixed outcomes. While many studies reported short-term gains in cognition, typically within six months, these improvements were not sustained in larger or longer-term trials. Neuropsychological interventions, including CR, most often studied in breast cancer survivors, demonstrated only minimal benefits. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Clinical Input

2015

Input was mixed on cognitive rehabilitation for patients with stroke, multiple sclerosis, brain tumors, or cognitive impairments after previous treatments for cancer.

2009/2010

In response to requests, input was received from 2 physician specialty societies and 5 academic medical centers while this policy was under review in 2010. Support was strongest for the use of cognitive rehabilitation as part of the treatment of those with TBI. The level of support varied for other diagnoses (e.g., use in post-stroke patients).

Practice Guidelines and Position Statements

American Academy of Physical Medicine and Rehabilitation

In 2021, the American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Collaborative issued a consensus guidance statement on the assessment and treatment of cognitive symptoms in patients with PASC. (51) PASC cognitive symptom assessment and treatment recommendations are summarized in Table 16.

Table 16. Post-Acute Sequelae of SARS-CoV-2 Infection Cognitive Symptom Assessment and Treatment Recommendations^a

Assessment Recommendations	
Recommendation #	Statement
1	"Patients should be screened for signs of cognitive symptoms using validated tools and instruments."
2	"Patients should be evaluated for conditions that may exacerbate cognitive symptoms and warrant further testing and potential subspecialty referral. [...] Particular areas include: • Sleep impairment

	• Mood, including anxiety, depression, and posttraumatic stress disorder • Fatigue • Endocrine abnormalities • Autoimmune disorders Note: Patients often report dissatisfaction with their care because of their persistent symptoms being attributed to psychological factors. It is important to note that mood disorders may be secondary to persistent medical conditions or one of many factors leading to cognitive symptoms."
3	"Patients should have a thorough neurological examination to identify focal neurological deficits."
3a	"For those patients identified with new or worsening focal neurological deficits (including new or worsening cognitive symptoms) an emergent evaluation is warranted; neuroimaging should be considered."
4	"The following basic lab workup should be considered to screen for reversible factors contributing to cognitive symptoms. The initial lab workup in new patients or those without lab workup in the 3 months prior to visit including complete blood count, vitamin B12, thiamine, folate, homocysteine, 1,25-dihydroxy vitamin D, magnesium, liver function tests, comprehensive metabolic panel thyroid function tests (thyroid stimulating hormone, free T3, free T4). In high-risk patients, one may consider syphilis rapid plasma regain and human immunodeficiency virus testing [...]"
5	"Clinicians should conduct a full patient history with review of preexisting conditions and comprehensive medication and supplement review for those that may contribute to cognitive symptoms. Of note, patients with PASC often present on antihistamine, anticholinergic, and antidepressant/anxiolytic medications that can contribute to cognitive symptoms."
5a	"Clinicians should validate patient history through the collection of collateral history, including preexisting function and conditions, from care team/primary care, patient family or care partner, or close contact as available."
6	"Clinicians should assess impact of cognitive symptoms using standardized patient-reported assessments, to include activities of

	daily living, instrumental activities of daily living, school, work and avocational (i.e., hobbies), and quality of life."
Treatment Recommendations	
Recommendation #	Statement
1	"For patients who screen positive for cognitive symptoms, refer to a specialist (i.e., speech-language pathologist, occupational therapist, neuropsychologist) with expertise in formal cognitive assessment and remediation."
2	"Treat, in collaboration with appropriate specialists, underlying medical conditions, such as pain, insomnia/sleep disorders (including poor sleep hygiene), and mood disorders that may be contributing to cognitive symptoms."
3	"Complete, in collaboration with patient primary care provider, medication polypharmacy reduction, weaning or deprescribing medications if medically feasible with emphasis on medications that may impact cognition."
4	"Reinforce sleep hygiene techniques including nonpharmacologic approaches as first line of sleep remediation."
5	"Similar to patients experiencing "physical" fatigue, patients should be advised to begin an individualized and structured, titrated return to activity program."
5a	"For patients who achieve a return to their normal, daily activities, regular exercise (at least 2–3 times/week of aerobic exercise) may be effective in improving cognition and also contribute to improved sleep patterns."
5b	"Frequent assessment of the impact of return to normal, daily activities (including school, work, driving, operating heavy machinery, etc.) is recommended to ensure that symptoms do not flare and exercise is tolerated."

^a Adapted from Fine et al. (2021). (51)

In 2023, the American Academy of Physical Medicine and Rehabilitation (AAPM&R) Multi-Disciplinary Post-Acute Sequelae of SARS-CoV-2 Infection (PASC) Collaborative issued a consensus guidance statement on the assessment and treatment of neurologic symptoms in patients with PASC. (85) PASC neurologic symptom assessment and treatment recommendations are summarized in Table 17.

Table 17. Post-Acute Sequelae of SARS-CoV-2 Infection Neurologic Symptom Assessment and Treatment Recommendations^a

Assessment Recommendations	
Recommendation #	Statement
1	"Clinicians should conduct a full patient history including a review of predisposing comorbidities, prior neurologic symptoms or disorders, relevant hospitalizations, time course and severity of COVID-19 infection(s), COVID-19 treatments, vaccines/boosters, pertinent family history, and social history."
2	"Clinicians should perform a thorough neurological examination to identify focal neurological deficits."
3	"Evaluate for medication and supplement use that may impact signs, symptoms, or assessment parameters"
4	"The following basic lab workup should be considered in new patients or for those without a lab workup in the 3 months prior to the visit: complete blood count with differential; chemistries including renal and hepatic function tests, thyroid stimulating hormone, c-reactive protein, erythrocyte sedimentation rate, vitamins B1, B6, B12, and D, magnesium, and hemoglobin A1c (HbA1c)."
5	"Assess for history of previous and/or current alcohol and substance use, current diet and exercise habits, physical and cognitive activity levels, and social determinants of health (e.g., housing, employment, family, insurance, access to community resources, social stressors, etc.)"
6	"Assess for changes in basic and instrumental activities of daily living, including participation at work, school, community avocational (i.e., hobbies) activities."
7	"On initial evaluation, obtain standardized measures of activity performance to compare to normal control values and to guide the initial activity prescription. Repeat the standardized measures of activity performance at follow-up visits to quantify functional changes and guide progression of the activity prescription."
Treatment Recommendations	
Recommendation #	Statement
1	"In collaboration with primary care or appropriate specialist treat underlying medical conditions, such as pain, psychiatric, renal/endocrine, cardiovascular, neurological, respiratory, etc., which may be contributing to neurologic symptoms."

2	"In collaboration with primary care or appropriate specialist, consider polypharmacy reduction, weaning or deprescribing medications and supplements where medically feasible."
3	"For patients who achieve a return to their daily activities, consider recommending regular physical activity as tolerated, which may be effective in improving many neurologic symptoms and also contribute to improved sleep patterns."
4	"For patients with neurologic sequelae affecting gait, mobility, cognitive status or activities of daily living, consider referral to physical medicine and rehabilitation physician and/or allied health professionals (e.g., physical therapy, occupational therapy, speech language pathology and social work) for patient-specific recommendations to increase function and independence. To optimize functional outcomes, allied health professionals should preferably be familiar with treating sensorimotor deficits, autonomic dysfunction, and post-exertional fatigue."
5	"Provide counseling, referrals to community resources, and education for risk factor modification in the areas of: alcohol and substance use; healthy dietary pattern and hydration; return to activity, as tolerated; medications and supplements; sleep hygiene; social determinants of health."

^a Adapted from Melamed et al. (2023). (85)

American Congress of Rehabilitation Medicine

In 2013, based on a systematic review, the American Congress of Rehabilitation Medicine recommended process-based cognitive rehabilitation strategies (e.g., attention process training, strategy acquisition and internalization, self-monitoring, corrective feedback) to treat attention and memory deficits in children and adolescents with brain cancers who undergo surgical resection and/or radiotherapy. The strength of evidence for recommendations were determined according to American Academy of Neurology study classification, and no financial conflicts of interest were declared by the authors. (71)

National Institute for Health and Care Excellence (NICE)

In 2013 (updated in 2023), NICE guidance on stroke rehabilitation recommended cognitive rehabilitation for visual neglect and memory and attention deficits that impact function. (86) Interventions should focus on relevant functional tasks (e.g., "errorless learning") and "elaborative techniques" (e.g., "mnemonics," "encoding" strategies) for memory impairments. The guidance states that providers should 'Make special arrangements for people after stroke who have communication or cognitive needs (for example, by holding joint speech and language therapy and physiotherapy sessions for those with communication difficulties).'

In 2018, NICE guidance on dementia management suggested: "Consider cognitive rehabilitation or occupational therapy to support functional ability in people living with mild to moderate dementia." (87)

In 2021 (updated in 2024), NICE issued a rapid guideline on managing the long-term effects of COVID-19. (88) The guideline recommends using a "multidisciplinary approach to guide rehabilitation, including physical, psychological and psychiatric aspects of management." Cognitive rehabilitation was not specifically addressed. Assessing the clinical effectiveness of "different service models of multimodality/multidisciplinary post-COVID-19 syndrome rehabilitation in improving patient-reported outcomes (such as quality of life)" was listed as a key recommendation for research.

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

Institute of Medicine

In 2011, the Institute of Medicine published a report on cognitive rehabilitation for traumatic brain injury that included a comprehensive review of the literature and recommendations. (89) The report concluded that "current evidence provides limited support for the efficacy of CRT [cognitive rehabilitation therapy] 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 to improve the evidence base for this treatment. The Institute of Medicine also recommended future studies with larger sample sizes and more comprehensive sets of clinical variables and outcome measures.

Veterans Administration

In 2009, the Veterans Administration/Department of Veterans Affairs published guidelines on the treatment of concussion and mild traumatic brain injury, (90) which were updated in 2016 (91) and most recently in 2021. (92) These guidelines addressed cognitive rehabilitation in the setting of persistent symptoms. The 2021 guidelines stated:

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

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

use of specific cognitive rehabilitation strategies or techniques to improve clinical outcomes following stroke." (93)

American Heart Association/American Stroke Association

In 2016, the American Heart Association (AHA) and the American Stroke Association published guidelines on adult stroke rehabilitation and recovery. (96) These guidelines provide a synopsis of best clinical practices in the rehabilitative care of adults recovering from stroke, including the following statement on cognitive rehabilitation: "Use of cognitive rehabilitation to improve attention, memory, visual neglect, and executive functioning is reasonable." (Class IIa, Level of Evidence B)

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Below are local coverage determinations (LCDs) pertinent to cognitive rehabilitation:

- L34427 (Outpatient Occupational Therapy; effective date: 04/03/2023): This LCD covers therapeutic procedures aimed at reducing impairments and improving function, including cognitive rehabilitation techniques. (94)
- L33631 (Outpatient Physical and Occupational Therapy Services; effective date: 01/01/2020): This LCD provides guidance on documentation to support the medical necessity of therapy services, including cognitive rehabilitation. (95)

Ongoing and Unpublished Clinical Trials

Some currently ongoing and/or unpublished trials that might influence this policy are listed in Table 18.

Table 18. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
NCT01138020	Cognitive Rehabilitation of Blast-induced Traumatic Brain Injury (CRbTBI)	77	Oct 2027
NCT04615390	Recovery Profiles in Patients With COVID-19 Outcomes Undergoing Rehabilitation	200	Nov 2023 (Last update posted: Jan 2023)
NCT05731570	Cognitive Impairment in Long Covid: PhEnotyping and RehabilitatiOn (CICERO)	78	Sep 2024
NCT03948490	Rehabilitation and Longitudinal Follow-up of Cognition in Adult Lower Grade Gliomas	97	Mar 2026
NCT06021470	The StrokeCog Study: A Randomised Pilot Study of a Novel Cognitive Rehabilitation Intervention in Stroke	64	Oct 2025

NCT05954741	Comparing the Effectiveness of Multidimensional Rehabilitation Programs for Cognitive Impairment in Comorbid Outpatients: A Randomized Controlled Trial	75	Jan 2026
NCT05934786	Rehabilitation of Cognition and Psychosocial Well-being – A better Live with Epilepsy	70	Dec 2028
NCT05494424	Cognitive Rehabilitation in Post-COVID-19 Condition: A Study Protocol for a Randomized Controlled Trial	120	Jan 2029
NCT03168360	Effect of Intensive Cognitive Rehabilitation in Subacute Stroke Patient	150	Dec 2023
NCT04632719	MentalPlus® for Assessment and Rehabilitation of Cognitive Functions After Remission of Symptoms of COVID-19 (MP-COVID)	200	Dec 2023
NCT0517206	Symptom-based Rehabilitation Compared to Usual Care in Post-COVID - a Randomized Controlled Trial (RELOAD)	132	Jan 2024 (published as conference abstract: <i>Am J Respir Crit Care Med</i> 2025; 211:A2426)
NCT03225482	Cognitive Rehabilitation for Older Veterans With Mild Cognitive Impairment	193	Jun 2024
NCT05676047	Symptom – Targeted Rehabilitation for Cognitive Complaints in Long COVID (STAR-C3)	100	Jan 2025

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	97129, 97130
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <<https://www.cms.hhs.gov>>.

Policy History/Revision	
Date	Description of Change
01/01/2026	Document updated. The following changes were made to Coverage: 1) Modified the conditional statement of medical necessity without change to intent; and 2) Added examples to existing list of experimental, investigational and/or unproven indications. Added references 4-6, 12-17, 21, 22, 30-32, 47-69, 73, 75-80, 85, 88, 94, 95, 97, and 98; others removed.
10/15/2024	Document updated with literature review. Coverage unchanged. References 6, 7, 9, 13, 31, 38, 41, and 69 added; others updated.
01/01/2024	Reviewed. No changes.
10/15/2022	Document updated with literature review. Coverage unchanged. Added reference 7 and 63, other references were updated.
01/01/2022	Document updated with literature review. Coverage unchanged. Added references 11, 12, 17, 35-37, 43-44, 51, 53, 57, 59 and 63.
01/01/2021	Reviewed. No changes.
02/15/2019	Document updated with literature review. Coverage unchanged. Added references 16, 17, 26, 32, 45 and 53; several others removed.
07/15/2017	Reviewed. No changes.
02/15/2017	Document updated with literature review. The following change(s) were made to Coverage: 1) "Stroke" moved from experimental/investigational/unproven list to conditionally medically necessary; 2) "Cognitive impairment due to" added to medical necessity

	statement; 3) Cognitive deficits due to brain tumor, prior treatment for cancer, or multiple sclerosis added as experimental/investigational/unproven examples.
01/01/2015	Document updated with literature review. Coverage is unchanged; however, the following additional examples were added to the list of indications that are considered experimental, investigational and/or unproven: 1) Autism spectrum disorders 2) Seizure disorders.
04/15/2012	Document updated with literature review. The following was added: Cognitive rehabilitation (as a distinct and definable component of the rehabilitation process) may be considered medically necessary in the rehabilitation of patients with traumatic brain injury under the following circumstances: 1) Services are prescribed by the attending physician as part of a written care plan; 2) Prescribed services are provided by a qualified licensed professional; 3) There is potential for improvement based on pre-injury function; 4) Patients have sufficient cognitive function to understand and participate in the program, as well as adequate language expression and comprehension, (i.e., participants should not have severe aphasia). NOTE: Ongoing services may be considered necessary only when there is demonstrated continued objective improvement in function. References and rationale updated.
01/01/2010	CPT/HCPCS code(s) updated.
09/15/2009	Revised/updated entire document, no coverage change. Illinois legislation will change on January 1, 2010.
09/01/2007	Revised/updated entire document
09/01/2005	Revised/updated entire document
03/01/2002	Revised/updated entire document
03/01/2000	Revised/updated entire document
09/01/1998	Revised/updated entire document
09/01/1996	New medical document