Cognitive Rehabilitation

Medical Policy #: 08.03.01
Original Effective Date: June 2003
Reviewed: August 2022
Revised: August 2022

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DESCRIPTION

Note: This medical policy is to only address the requests for outpatient cognitive rehabilitation.

According to the American Association of Neurological Surgeons (AANS) in 2020, a traumatic brain injury (TBI) is a disruption in the normal function of the brain that can be caused by a blow, bump or jolt to the head, the head suddenly and violently hitting an object or when an object pierces the skull and enters brain tissue.

Observing one of the following clinical signs constitutes alteration in the normal brain function:

- Loss of or decreased consciousness
- Loss of memory for events before or after the event (amnesia)
- Focal neurological deficits such as muscle weakness, loss of vision, change in speech
- Alteration in mental state such as disorientation, slow thinking or difficulty concentrating

According to D'souza et al., "post-concussion syndrome (PCS), a common sequel of traumatic brain injury (TBI) is a symptom complex comprising of headache, sleep disturbance, neuropsychiatric symptoms, and cognitive impairment. Although it has been described most often in the setting of mild TBI, it occurs after moderate and severe TBI and whiplash injuries as well. Traumatic brain injury has become a global health problem of major concern today, owing to the high incidence of road traffic accidents, sports injuries, terrorist operations, and war-related injuries. Brain trauma leads to diffuse axonal injury (DAI) secondary to abrupt acceleration/deceleration and/or rotational/vibrational forces, which cause axonal shearing. It has been postulated that DAI plays a key role in persistent neurological and cognitive impairments observed after TBI, owing to disruption in connectivity of different regions in the brain."

Cognitive rehabilitation is a therapeutic approach designed to improve cognitive functioning after central nervous system (CNS) 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 designed to reinforce or reestablish previously learned patterns of behavior or to establish new compensatory mechanisms for impaired neurologic systems. The desired outcome of cognitive rehabilitation is an improved quality of life or an improved ability to function in home and community life. Cognitive rehabilitation may be performed by a physician, psychologist, or a physical, occupational or speech therapist.

The two most common approaches to cognitive rehabilitation, usually performed in conjunction with each other are the:

- Remedial, or restorative: Focuses on attempting to restore core areas of cognitive dysfunction by systematic training (e.g., paper and pencil exercises, tabletop tasks, use of computer software) and is based upon the theory that repetitive exercise can restore lost function.
- Compensatory, or adaptive: Geared toward facilitation of activities of everyday living by developing internal substitutes and/or external prosthetic assistance for dysfunctions.

Note: A maintenance program consists of activities that preserve the individual's present level of function and prevents regression of that function. Maintenance begins when the therapeutic goals of a treatment plan have been achieved, or when no additional functional progress is apparent or expected to occur.

Cognitive Rehabilitation Treatment Duration

Based on a review by the Brain Injury Interdisciplinary Special Interest Group, cognitive rehabilitation is effective during the post-acute period - even 1 year or more after injury.

Duration and intensity of cognitive rehabilitation thedrapy programs vary:

- Comprehensive cognitive rehabilitation is a 16-week outpatient program consisting of 5 hours of therapy a day, 4 days per week.
- Cognitive group treatment occurs for three 2-hour sessions each week and three 1-hour session (total of 9 hours per week).
- Cognitive rehabilitation programs for specific deficits, such as memory training or visuo-spatial deficits which may be considered less intensive, generally have 1 or 2 sessions (30 to 60 minutes) per week for 4 to 10 weeks.

Populations
The relevant population of interest is individuals with cognitive deficits due to stroke, traumatic brain injury (TBI), Alzheimer's disease (AD), autism spectrum disorder, coma, COVID-19/post-acute sequelae of SARS-CoV-2, dementia, epilepsy/seizure disorders in adults, Multiple Sclerosis (MS), post-encephalitis, brain tumors, and cancer survivors.

Interventions
The therapy being considered is cognitive rehabilitation delivered by a qualified professional. Cognitive rehabilitation is designed to improve cognitive functioning after central nervous system (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. Individuals with cognitive deficits due to stroke, traumatic brain injury (TBI), Alzheimer's disease (AD), autism spectrum disorder, coma, COVID-19/post-acute sequelae of SARS-CoV-2, dementia, epilepsy/seizure disorders in adults, multiple sclerosis (MS), post-encephalitis, brain tumors, and cancer survivors. actively managed by neurologists, psychologists, psychiatrists, physical therapists, and primary care providers in an *outpatient* clinical setting.

Comparators
Comparators of interest include standard rehabilitation [e.g., physical therapy (PT), occupational therapy (OT)] 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 stroke, traumatic brain injury (TBI), Alzheimer's disease (AD), autism spectrum disorder, coma, COVID-19/post-acute sequelae of SARS-CoV-2, dementia, epilepsy/seizure disorders in adults, multiple sclerosis (MS), post-encephalitis, brain tumors, and cancer survivors 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 six months of follow-up is considered necessary to demonstrate efficacy.

Stroke

Clinical Context and Therapy Purpose

The purpose of cognitive rehabilitation 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 (eg, physical therapy, occupational therapy) without specific focus on cognition or no rehabilitation.

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

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

Populations

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

Interventions

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

Comparators

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

Outcomes

The general outcomes of interest are functional outcomes and quality of life. The existing literature evaluating cognitive rehabilitation 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.

Stroke: Review of Evidence

(2013) The American Congress of Rehabilitation Medicine (ACRM) reports the evidence supports visuospatial rehabilitation after right hemisphere stroke, and interventions for aphasia and apraxia after left hemisphere stroke.

Four Cochrane reviews have assessed the effectiveness of cognitive rehabilitation for recovery from stroke. The reviews evaluated spatial neglect, attention deficits, and memory deficits. The most recent updates of these reviews for these three domains made the following conclusions:

- (2016) das Nair et al. noted for memory deficit: Identified 13 trials with 514 patients. 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.
- (2013) Loetscher et al. noted for attention deficit: Identified 6 RCTs with 223 patients. 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.
- (2013) Bowen et al. noted for spatial neglect: Identified 23 RCTs with 628 patients. 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 unproved.

(2016) das Nair et al. completed a Cochrane database review to determine whether participants who have received cognitive rehabilitation for memory problems following a stroke have better outcomes than those given no treatment or a placebo control. The outcomes of interest were subjective and objective assessments of memory function, functional ability, mood, and quality of life. We considered the immediate and long-term outcomes of memory rehabilitation. They selected randomized controlled trials in which cognitive rehabilitation for memory problems was compared to a control condition. We included studies where more than 75% of the participants had experienced a stroke, or if separate data were available from those with stroke in mixed aetiology studies. Two review authors independently selected trials for inclusion, which was then confirmed through group discussion. They assessed study risk of bias and extracted data. They contacted the investigators of primary studies for further information where required. They conducted data analysis and synthesis in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. We performed a 'best evidence' synthesis based on the risk of bias of the primary studies included. Where there were sufficient numbers of similar outcomes, we calculated and reported standardized mean differences (SMD) using meta-analysis. They included 13 trials involving 514 participants. There was a significant effect of treatment on subjective reports of memory in the short term (standard mean difference (SMD) 0.36, 95% confidence interval (CI) 0.08 to 0.64, P = 0.01, moderate quality of evidence), but not the long term (SMD 0.31, 95% CI -0.02 to 0.64, P = 0.06, low quality of evidence). The SMD for the subjective reports of memory had small to moderate effect sizes. The results do not show any significant effect of memory rehabilitation on performance in objective memory tests, mood, functional abilities, or quality of life. No information was available on adverse events. There are limitations to this review. Many of the studies identified included samples with mixed diagnoses, and although several study authors provided separate data for those with stroke, the sample sizes were small. A sensitivity analysis could have been conducted to compare the stroke-

only studies with those with stroke patients as part of a mixed diagnosis group but given that most trials had small samples further fractionating may have led to further reduction in power, which we felt would lead to inconclusive findings. Mixed diagnoses studies are beneficial in determining the potential for the generalizability of training programs across diagnostic groups and reflect usual clinical practice in many centers, but there are likely to be differential effects of the training based on diagnosis and even severity (Cicerone 2000). This is an area that requires further investigation. The author's concluded participants who received cognitive rehabilitation for memory problems following a stroke reported benefits from the intervention on subjective measures of memory in the short term (i.e., the first assessment point after the intervention, which was a minimum of four weeks). This effect was not, however, observed in the longer term (i.e., the second assessment point after the intervention, which was a minimum of three months). There was, therefore, limited evidence to support or refute the effectiveness of memory rehabilitation. The evidence was limited due to the poor quality of reporting in many studies, lack of consistency in the choice of outcome measures, and small sample sizes. There is a need for more robust, well-designed, adequately powered, and better-reported trials of memory rehabilitation using common standardized outcome measures.

(2015) Gillespie et al. completed a review to provide an overview of the evidence for the effectiveness of cognitive rehabilitation for patients with stroke and to determine the main gaps in the current evidence base. Evidence was synthesized for the six Cochrane reviews relating to rehabilitation for post-stroke cognitive impairment and any subsequently published randomized controlled trials to February 2012. Data arising from 44 trials involving over 1500 patients was identified. Though there was support for the effectiveness of cognitive rehabilitation for some cognitive impairments, significant gaps were found in the current evidence base. All of the Cochrane reviews identified major limitations within the evidence they identified. The authors concluded there is currently insufficient research evidence, or evidence of insufficient quality, to support clear recommendations for clinical practice. Recommendations are made as to the research required to strengthen the evidence base, and so facilitate the delivery of effective interventions to individuals with cognitive impairment after stroke.

(2014) Zucchella et al. conducted an assessor blinded RCT of comprehensive cognitive rehabilitation, combining computer training and metacognitive strategies within 4 weeks after stroke. Of 288 consecutive stroke survivors admitted to a neurorehabilitation unit in Italy, 92 (32%) met inclusion criteria and were randomized to cognitive rehabilitation (n=45) or control (n=47). At the end of treatment (i.e., at week 4), statistically significant differences were found between groups on some measures of memory and visual attention. The clinical significance of these short-term outcomes is unclear.

(2013) Chung et al. completed a Cochrane database review on cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage. They included randomized trials in adults after non-progressive acquired brain injury, where the intervention was specifically targeted at improving cognition including separable executive function data (restorative interventions), where the intervention was

aimed at training participants in methods to compensate for lost executive function (compensative interventions) or where the intervention involved the training in the use of an adaptive technique for improving independence with ADL (adaptive interventions). The primary outcome was global executive function, and the secondary outcomes were specific components of executive function, working memory, ADL, extended ADL, quality of life and participation in vocational activities. We included studies in which the comparison intervention was no treatment, a placebo intervention (i.e., a rehabilitation intervention that should not impact on executive function), standard care or another cognitive rehabilitation intervention. Nineteen studies (907 participants) met the inclusion criteria for this review. We included 13 studies (770 participants) in meta-analyses (417 traumatic brain injury, 304 stroke, 49 other acquired brain injury) reducing to 660 participants once non-included intervention groups were removed from three and four group studies. We were unable to obtain data from the remaining six studies. Three studies (134 participants) compared cognitive rehabilitation with sensorimotor therapy. None reported our primary outcome; data from one study was available relating to secondary outcomes including concept formation and ADL. Six studies (333 participants) compared cognitive rehabilitation with no treatment or placebo. None reported our primary outcome; data from four studies demonstrated no statistically significant effect of cognitive rehabilitation on secondary outcomes. Ten studies (448 participants) compared two different cognitive rehabilitation approaches. Two studies (82 participants) reported the primary outcome; no statistically significant effect was found. Data from eight studies demonstrated no statistically significant effect on the secondary outcomes. We explored the effect of restorative interventions (10 studies, 468 participants) and compensative interventions (four studies, 128 participants) and found no statistically significant effect compared with other interventions. The author's concluded insufficient high-quality evidence to reach any generalized conclusions about the effect of cognitive rehabilitation on executive function, or other secondary outcome measures. Further high-quality research comparing cognitive rehabilitation with no intervention, placebo or sensorimotor interventions is recommended.

Summary of Evidence: Stroke

For individuals who have cognitive deficits due to stroke who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs and systematic reviews. Relevant outcomes are functional outcomes and quality of life. Four systematic reviews evaluating three separate domains of cognitive function have shown limited effects of cognitive rehabilitation or effects of clinical importance. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Traumatic Brain Injury (TBI)

(2019) das Nair et al. completed a health technology assessment to assess the clinical effectiveness and cost-effectiveness of a group memory rehabilitation program for people with TBI. Participants were aged 18-69 years, had undergone a TBI > 3 months prior to recruitment, reported memory problems, were able to travel to a site to attend group sessions, could communicate in English and gave informed consent. Clusters of four to

six participants were randomized to the memory rehabilitation arm or the usual-care arm on a 1:1 ratio. Randomization was based on a computer-generated pseudo-random code using random permuted blocks of randomly varying size, stratified by study site. Participants and therapists were aware of the treatment allocation whereas outcome assessors were blinded. In the memory rehabilitation arm 10 weekly sessions of a manualized memory rehabilitation program were provided in addition to usual care. Participants were taught restitution strategies to retrain impaired memory functions and compensation strategies to enable them to cope with memory problems. The usual-care arm received usual care only. Outcomes were assessed at 6 and 12 months after randomization. Primary outcome: patient-completed Everyday Memory Questionnaire – patient version (EMQ-p) at 6 months' follow-up. Secondary outcomes: Rivermead Behavioural Memory Test – third edition (RBMT-3), General Health Questionnaire 30-item version, European Brain Injury Questionnaire, Everyday Memory Questionnaire – relative version and individual goal attainment. Costs (based on a UK NHS and Personal Social Services perspective) were collected using a service use questionnaire, with the EuroQol-5 Dimensions, five-level version, used to derive quality-adjusted life-years (QALYs). A Markov model was developed to explore cost-effectiveness at 5 and 10 years, with a 3.5% discount applied. The results included randomized 328 participants (memory rehabilitation, n = 171; usual care, n = 157), with 129 in the memory rehabilitation arm and 122 in the usual-care arm included in the primary analysis. We found no clinically important difference on the EMQ-p between the two arms at 6 months' follow-up (adjusted difference in mean scores -2.1, 95% confidence interval -6.7 to 2.5; p = 0.37). For secondary outcomes, differences favoring the memory rehabilitation arm were observed at 6 months' follow-up for the RBMT-3 and goal attainment but remained only for goal attainment at 12 months' follow-up. There were no differences between arms in mood or quality of life. The qualitative results suggested positive experiences of participating in the trial and of attending the groups. Participants reported that memory rehabilitation was not routinely accessible in usual care. The primary health economics outcome at 12 months found memory rehabilitation to be cheaper than usual care but less effective, with an incremental QALY loss of 0.007. Differences in costs and effects were not statistically significant and non-parametric bootstrapping demonstrated considerable uncertainty in these findings. No safety concerns were raised, and no deaths were reported. As a pragmatic trial, we had broad inclusion criteria and, therefore, there was considerable heterogeneity within the sample. The study was not powered to perform further subgroup analyses. Participants and therapists could not be blinded to treatment allocation. The authors concluded the group memory rehabilitation delivered in this trial is very unlikely to lead to clinical benefits or to be a cost-effective treatment for people with TBI in the community. Future studies should examine the selection of participants who may benefit most from memory rehabilitation. (*Trial registration: Current Controlled Trials ISRCTN65792154*)

(2016) Chiaravalloti et al. conducted an RCT evaluating the Story Memory Technique to improve learning and memory in subjects with moderate-severe TBI. 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.

(2013) Chung et al. completed a Cochrane database review on cognitive rehabilitation for executive dysfunction in adults with stroke or other adult non-progressive acquired brain damage. They included randomized trials in adults after non-progressive acquired brain injury, where the intervention was specifically targeted at improving cognition including separable executive function data (restorative interventions), where the intervention was aimed at training participants in methods to compensate for lost executive function (compensative interventions) or where the intervention involved the training in the use of an adaptive technique for improving independence with ADL (adaptive interventions). The primary outcome was global executive function, and the secondary outcomes were specific components of executive function, working memory, ADL, extended ADL, quality of life and participation in vocational activities. We included studies in which the comparison intervention was no treatment, a placebo intervention (i.e., a rehabilitation intervention that should not impact on executive function), standard care or another cognitive rehabilitation intervention. Nineteen studies (907 participants) met the inclusion criteria for this review. We included 13 studies (770 participants) in meta-analyses (417 traumatic brain injury, 304 stroke, 49 other acquired brain injury) reducing to 660 participants once non-included intervention groups were removed from three and four group studies. We were unable to obtain data from the remaining six studies. Three studies (134 participants) compared cognitive rehabilitation with sensorimotor therapy. None reported our primary outcome; data from one study was available relating to secondary outcomes including concept formation and ADL. Six studies (333 participants) compared cognitive rehabilitation with no treatment or placebo. None reported our primary outcome; data from four studies demonstrated no statistically significant effect of cognitive rehabilitation on secondary outcomes. Ten studies (448 participants) compared two different cognitive rehabilitation approaches. Two studies (82 participants) reported the primary outcome; no statistically significant effect was found. Data from eight studies demonstrated no statistically significant effect on the secondary outcomes. We explored the effect of restorative interventions (10 studies, 468 participants) and compensative interventions (four studies, 128 participants) and found no statistically significant effect compared with other interventions. The author's concluded insufficient high-quality evidence to reach any generalized conclusions about the effect of cognitive rehabilitation on executive function, or other secondary outcome measures. Further high-quality research comparing cognitive rehabilitation with no intervention, placebo or sensorimotor interventions is recommended.

Summary of Evidence: Traumatic Brain Injury (TBI)
For individuals who have cognitive deficits due to TBI who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, case series, and systematic reviews. Relevant outcomes are functional outcomes and quality of life. The cognitive rehabilitation trials have methodologic limitations and have reported mixed results, some RCTs have shown improvements in some outcomes with cognitive rehabilitation in individuals with

moderate-severe TBI, systematic reviews have provided mixed findings with no consistent evidence of efficacy in patients with TBI. Systematic reviews have generally concluded that efficacy of cognitive rehabilitation is uncertain. Thus, indicating there is no uniform or consistent evidence base supporting the efficacy of this technique. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes, however, based on Blue Cross Blue Shield Association clinical input obtained in 2015 the following, input was received from three physician specialty societies and five academic medical centers while this policy was under review in 2015. Input was mixed on cognitive rehabilitation for patients with stroke, multiple sclerosis, brain tumors, or cognitive impairments after previous treatments for cancer. While input was not specifically requested for TBI, due to strong support provided in 2009 and no signals of any subsequent evidence or clinical practice changes, the American Association of Physical Medicine & Rehabilitation voluntarily and additionally reasserted its position of support for cognitive rehabilitation after TBI. Therefore cognitive rehabilitation for TBI will be considered medically necessary in certain individuals.

Other Cognitive Deficit Conditions

Alzheimer's Disease (AD)

(2017) Regan et al. reported on a randomized, controlled trial of a home-based, four-session, goal-oriented, cognitive rehabilitation program versus usual care in 55 patients with mild cognitive impairment and early Alzheimer's disease (AD). Patients were community-dwelling, with a diagnosis of mild cognitive impairment or AD within six months of enrollment and an MMSE score greater than 20. The intervention group received four weekly, one-hour therapy sessions, delivered by experienced therapists, with a focus on addressing personally meaningful goals. All participants identified at least one goal for improvement. The usual care group had no contact with the research team between their initial and final assessments. The primary outcome measures were goal performance and satisfaction scores on the Canadian Occupational Performance Measure. A total of 12 participants in the intervention group and three participants in the control group discontinued study participation and were excluded from the final, per-protocol analysis. For the first identified goal, the intervention group had significantly greater improvements in performance and satisfaction on the Canadian Occupational Performance Measure than the control group. There were no differences in secondary measures of QOL or anxiety and depression. The per-protocol results were biased due to the high rate of missing data.

Autism Spectrum Disorder

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

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

(2013) Eack et al. conducted a feasibility study of a comprehensive cognitive rehabilitation intervention, called Cognitive Enhancement Therapy, in 14 "high functioning" adults (mean age, 25 years) with ASD. Cognitive Enhancement Therapy, which was originally developed for patients with schizophrenia, provides social interaction and cognitive training focused on attention, memory, and problem-solving. Mean full scale IQ of the patient sample was 118 (range, 92-157). Eleven (79%) of 14 patients completed 18 months of treatment. Statistically significant changes from baseline were observed in mean composite measures of neurocognition, cognitive style, social cognition, and social adjustment. All components of neurocognition (eg, processing speed, working memory) improved statistically, except attention/vigilance.

Coma

(2020) Li et al. conducted a systematic review of the efficacy of sensory stimulation to improve arousal in comatose individuals after sustaining a traumatic brain injury. A total of 10 eligible studies were included for analysis. The authors noted that there was significant heterogeneity in the studies with respect to duration of observation and the type of sensory stimulation. The studies dated back to 1990 and had sample sizes ranging from 12 to 90 participants distributed amongst 1 to 3 study arms. The review concluded that although there appears to be some evidence that sensory stimulation may increase arousal in comatose individuals, "high-quality clinical trials are needed to establish standard SS [sensory stimulation] protocols."

COVID-19/Post-Acute Sequelae of SARS-CoV-2

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. 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.

While subjective reports of cognitive impairment (i.e., 'brain fog') have been reported by individuals not requiring hospitalization, current understanding of objective cognitive sequelae of COVID-19 is predominantly limited to individuals who required hospitalization.

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, the disease course of cognitive impairment experienced by individuals with post-acute sequelae of SARS-CoV-2 infection is an ongoing research priority.

(2022) Ceban et al. conducted a meta-analysis of 43 studies with 12 or more weeks follow-up that reported a 22% overall prevalence of cognitive impairment (95% CI, 17% to 28%; I2=98%; N=13232). Subjectively ascertained cognitive impairment (eg, patient self-report) was reported in 18% of patients (95% CI, 12% to 24%; I2=97.9%; 31 studies), which was significantly lower than in studies with objective ascertainment of cognitive status utilizing validated tools (36%; 95% CI, 27% to 46%; I2=94.9%; 12 studies; p=.002). No significant difference in cognitive symptom prevalence was found in subgroup analyses of hospitalized versus non-hospitalized patients (30% versus 20%; p=.096) or patients with <6 months versus ≥6 months of follow-up (22% versus 21%; p=.794).

(2021) Albu et al. completed a prospective, observational cohort study investigated the effects of multidisciplinary rehabilitation of post Covid-19 sequelae and persistent symptoms and their impact on patients' functioning and quality of life. From 58 patients referred for neurorehabilitation, 43 were eligible for and participated in the present study. Before and after 8 weeks of rehabilitation, patients underwent physical, neuropsychological and respiratory evaluations and assessment of functional independence, impact of fatigue and quality of life. Forty of 43 individuals (52 ± 11.4 years, 24 male) completed the rehabilitation program. Fatigue (87.5%), dyspnea and/or shortness of breath (62.5%), and cognitive impairment (37.5%) were reported by both previously hospitalized and home-confined patients. Neurological sequelae (35.5%) were present only in hospitalized patients. After 8 weeks of rehabilitation, patients reported significant improvements in motor functional independence, upper and lower limb functionality, impact of fatigue on daily activities, respiratory muscle strength, cognitive performance, and quality of life. The authors concluded post Covid-19 patients present with heterogeneous neurological, physical, and respiratory impairments requiring a multidisciplinary rehabilitation approach to reduce disability and improve functionality and quality of life. A comprehensive assessment of clinical profiles and responses to rehabilitation may facilitate the identification of rehabilitation candidates and help to design effective rehabilitation interventions. Implication for rehabilitation post Covid-19

patients present multiple, heterogeneous neurological, physical and respiratory impairments that are observed in both previously hospitalized and home-confined patients. Eight weeks of multidisciplinary rehabilitation may significantly reduce disability and improve functionality and quality of life. A comprehensive assessment of their clinical profile and response to rehabilitation may facilitate the identification of rehabilitation candidates and help to design more effective rehabilitation interventions.

(2021) Imamura et al. completed a retrospective review noting this study aimed to describe the demographic, clinical, and functional status after the discharge of COVID-19 survivors who underwent intensive multidisciplinary inpatient rehabilitation at the Physical and Rehabilitation Medicine Institute of the University of Sao Paulo Medical School General Hospital and Lucy Montoro Rehabilitation Institute. This was a retrospective study based on electronic medical records. In addition to the severity of COVID-19 and length of hospital stay for the management of COVID-19 and comorbidities, they collected sociodemographic data including age, sex, height, and weight. Functional assessments were performed using the Functional Independence Measure (FIM); Short Physical Performance Battery; Montreal Cognitive Assessment; Depression, Anxiety and Stress Scale; Revised Impact of Events Scale; bioelectrical impedance; Functional Oral Intake Scale; oropharyngeal dysphagia classification; and nutritional assessment. There was a significant improvement in FIM before and after inpatient rehabilitation treatment ($p<0.0001$). Muscle strength and walking capacity were significantly improved ($p<0.01$). The most important factors related to the length of inpatient rehabilitation treatment were improvement in FIM scores (Spearman's $r=0.71$) and gain in lean mass (Spearman's $r=0.79$). The authors concluded rehabilitation of patients after COVID-19 recovery improves their functional status and should be considered in the post-acute phase for selected patients with COVID-19. The main limitations of this retrospective study were missing data on the acute condition and management, pre- and post-respiratory assessments, bioelectrical impedance, and DASS-21; Revised Impact of Events Scale; and the GLIM scores. Another important limitation was the small sample size and the lack of a control group. These should be considered when planning a prospective, observational study with a larger sample size and a control group, whenever feasible.

(2020) Zarrabian et al. reported cognitive rehabilitation therapy (CRT) might be considered as a useful intervention because of the importance of cognitive deficits in cognitive distortions. CRT attempts to enhance functioning and independence. Using different interventions, CRT aims to decline brain functional impairments or to lessen the disabling impact of those impairments. CRT has been proven as an effective way to reduce cognitive biases and increase an individual's capacity for processing and interpretation of information. Among diverse stress management methods, cognitive-behavioral stress management interventions are valuable choices to be considered.

The paper is a commentary letter and did not have any human or animal participants.

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

Dementia
(2019) Bahar-Fuchs et al. completed a Cochrane database review on cognitive training for people with mild to moderate dementia. They searched ALOIS, the Cochrane Dementia and Cognitive Improvement They 33 included trials were published between 1988 and 2018 and were conducted in 12 countries; most were unregistered, parallel-group, single-site RCTs, with samples ranging from 12 to 653 participants. Interventions were between two and 104 weeks long. We classified most experimental interventions as 'straight CT', but we classified some as 'augmented CT', and about two-thirds as multi-domain interventions. Researchers investigated 18 passive and 13 active control conditions, along with 15 alternative treatment conditions, including occupational therapy, mindfulness, reminiscence therapy, and others. The methodological quality of studies varied, but we rated nearly all studies as having high or unclear risk of selection bias due to lack of allocation concealment, and high or unclear risk of performance bias due to lack of blinding of participants and personnel. We used data from 32 studies in the meta-analysis of at least one outcome. Relative to a control condition, we found moderate-quality evidence showing a small to moderate effect of CT on our first primary outcome, composite measure of global cognition at end of treatment (standardized mean difference (SMD) 0.42, 95% confidence interval (CI) 0.23 to 0.62), and high-quality evidence showing a moderate effect on the secondary outcome of verbal semantic fluency (SMD 0.52, 95% CI 0.23 to 0.81) at end of treatment, with these gains retained in the medium term (3 to 12 months post treatment). In relation to many other outcomes, including our second primary outcome of clinical disease severity in the medium term, the quality of evidence was very low, so we were unable to determine whether CT was associated with any meaningful gains. When compared with an alternative treatment, we found that CT may have little to no effect on our first primary outcome of global cognition at end of treatment (SMD 0.21, 95% CI -0.23 to 0.64), but the quality of evidence was low. No evidence was available to assess our second primary outcome of clinical disease severity in the medium term. We found moderate-quality evidence showing that CT was associated with improved mood of the caregiver at end of treatment, but this was based on a single trial. The quality of evidence in relation to many other outcomes at end of treatment and in the medium term was too low for us to

determine whether CT was associated with any gains, but we are moderately confident that CT did not lead to any gains in mood, behavioral and psychological symptoms, or capacity to perform activities of daily living. Limitations were noted as the quality of the studies we reviewed varied but overall was not very high, so the certainty in some of these findings is low. Future studies should continue improving on quality, should continue comparing CT with other treatments, and should follow participants for a longer period to understand whether observed benefits for cognition last beyond the short or medium term. The authors concluded relative to a control intervention, but not to a variety of alternative treatments, CT is probably associated with small to moderate positive effects on global cognition and verbal semantic fluency at end of treatment, and these benefits appear to be maintained in the medium term. Our certainty in relation to many of these findings is low or very low. Future studies should take stronger measures to mitigate well-established risks of bias and should provide long-term follow-up to improve our understanding of the extent to which observed gains are retained. Future trials should also focus on direct comparison of CT versus alternative treatments rather than passive or active control conditions.

(2019) Clare et al. completed a randomized controlled trial to determine whether individual goal-oriented cognitive rehabilitation (CR) improves everyday functioning for people with mild-to-moderate dementia. Parallel group multicenter single-blind randomized controlled trial (RCT) comparing CR added to usual treatment (CR) with usual treatment alone (TAU) for people with an ICD-10 diagnosis of Alzheimer, vascular or mixed dementia, and mild-to-moderate cognitive impairment (Mini-Mental State Examination [MMSE] score ≥ 18), and with a family member willing to contribute. Participants allocated to CR received 10 weekly sessions over 3 months and four maintenance sessions over 6 months. Participants were followed up 3- and 9-months post randomization by blinded researchers. The primary outcome was self-reported goal attainment at 3 months. Secondary outcomes at 3 and 9 months included informant-reported goal attainment, quality of life, mood, self-efficacy, and cognition and study partner stress and quality of life. The results randomized (1:1) 475 people with dementia; 445 (CR = 281) were included in the intention to treat analysis at 3 months and 426 (CR = 208) at 9 months. At 3 months, there were statistically significant large positive effects for participant-rated goal attainment (d = 0.97; 95% CI, 0.75-1.19), corroborated by informant ratings (d = 1.11; 95% CI, 0.89-1.34). These effects were maintained at 9 months for both participant (d = 0.94; 95% CI, 0.71-1.17) and informant (d = 0.96; 95% CI, 0.73-1.2) ratings. The observed gains related to goals directly targeted in the therapy. There were no significant differences in secondary outcomes. The authors concluded CR enables people with early-stage dementia to improve their everyday functioning in relation to individual goals targeted in the therapy. Limitations were noted and should be considered. Due to the constraints of trial design, the goal-setting interview was conducted by researchers not involved in delivering therapy, whereas in clinical practice, the goal-setting process would be undertaken by the therapist and might be more efficient. While participants were invited to select up to three goals, on average, the therapists were able to address two goals per participant. The primary outcome was based on ratings of progress with all goals identified at baseline, rather than just those goals that

were actually addressed; therefore, the overall estimate of improvement in goal attainment is a conservative one. Ratings for the goals that were directly addressed showed a clinically meaningful degree of change. The trial design did not allow us to conclusively demonstrate that benefits were due to the specific effects of CR rather than nonspecific effects of contact with a therapist; however, the observed gains related specifically to improvements in functional ability for goals directly targeted in the therapy, and in the pilot trial, CR demonstrated benefits over an active control condition. In selecting secondary outcome measures, it would have been useful to include a measure of functional ability.

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

(2016) Ameiva et al. reported on results from the group and individual cognitive therapies in Alzheimer's disease (ETNA3) multicenter RCT that compared 4 therapies strategies: standardized programs of cognitive training (group sessions), reminiscence therapy (group sessions), individualized cognitive rehabilitation program (individual sessions), and usual care. Six hundred fifty-three patients with mild-to-moderate AD were randomized in a 1:1:1:1 ratio at 40 French clinical sites. We focus on the cognitive rehabilitation program and usual care arms. The primary outcome was the rate of survival without moderately severe to severe dementia at 2 years. Secondary outcomes were cognitive impairment, functional disability, behavioral disturbance, apathy, quality of life, depression, caregiver burden, and resource utilization. Participants and clinical staff were not blinded to treatment assignment, but outcome assessments were done by blinded physicians and psychologists. The cognitive rehabilitation therapy consisted of a "made-to-measure" program conducted in individual sessions and adapted to patients' cognitive abilities, with goals selected to be personally relevant to the patient. Intention-to-treat analyses were performed using "missing equal failure" to replace missing values. Approximately 90% of participants had a 3-month follow-up visit, and 72% had a 24-month visit. There was no difference between the cognitive rehabilitation group and the usual care group with respect to the primary outcome. However, patients who received

cognitive rehabilitation therapy had a less functional decline at 24 months compared with the usual care group, as measured by 1 of the 2 scales assessing functional abilities: the Autonomie Gérontologique Groupes Iso-Ressources scale (p=.02). The rate of institutionalization was lower in the cognitive rehabilitation therapy group (27%) than in the usual care group (19%). These results are promising but, given the lack of consistency in benefits on the 2 functional scales, replication is needed to confirm these positive findings.

(2015) Huntley et al. performed a meta-analysis of cognitive interventions in dementia. Thirty-three studies were included. Interventions were divided into categories such as cognitive training, cognitive stimulation, and cognitive rehabilitation. Studies classified as cognitive stimulation had a significant effect as measured on the Mini-Mental State Examination (MMSE) and the Alzheimer's Disease Assessment Scale-Cognitive Subscale. Reviewers concluded that benefits measured by the Alzheimer's Disease Assessment Scale-Cognitive Subscale were generally not clinically significant.

Section Summary: Dementia
For individuals who have cognitive deficits due to dementia who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, case series, and systematic reviews. Relevant outcomes are functional outcomes and quality of life. Systematic reviews of RCTs have generally shown no benefit of cognitive rehabilitation or effects of clinical importance. One large RCT evaluating a goal-oriented cognitive rehabilitation program reported a significantly less functional decline in 1 of 2 functional scales and lower rates of institutionalization in the cognitive rehabilitation group compared with usual care at 24 months. These results need replication. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Epilepsy/Seizure Disorders (Adults)
Formal neuropsychologic assessment and cognitive rehabilitation, although understudied, may be helpful for some patients with cognitive complaints. Small studies support the role of cognitive rehabilitation to improve memory after temporal lobe epilepsy surgery. (Last Updated 2021 UptoDate on Epilepsy in Adults)

(2015) Farina et al. in Italy conducted a systematic review of the literature on cognitive rehabilitation for epilepsy. 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).

Multiple Sclerosis (MS)

(2021) Chiaravalloti et al. completed a randomized controlled trial and reported new learning and memory (NLM) impairments are common in multiple sclerosis (MS), negatively impacting daily life. Few studies seek to remediate these deficits to improve everyday functioning. Self-generation, spaced learning and retrieval practice have been shown to improve NLM in healthy persons and have been incorporated into an 8-session treatment protocol, Strategy-based Training to Enhance Memory (STEM). STEM teaches participants about each of the techniques, how to apply them in daily life and provides practice. Participants are taught to restructure a memory-demanding situation to optimize self-generation, spaced learning and retrieval practice. This pilot double-blind, placebo-controlled, randomized clinical trial (RCT) tested the efficacy of STEM in 20 learning-impaired participants with clinically definite MS (9 treatment, 11 control). Significant treatment effects were noted on self-report measures of daily functioning (primary outcome). Objective neuropsychological testing approached significance, showing a medium-large effect on verbal NLM. Results suggest that STEM may improve everyday functioning in individuals with MS. A full-scale RCT is warranted to validate findings in a larger sample so that findings may be generalized to the broader MS community.

(2021) Taylor et al. completed a Cochrane database systematic review to determine whether people with MS who received memory rehabilitation compared to those who received no treatment, or an active control showed better immediate, intermediate, or longer-term outcomes in their: 1. Memory functions, 2. Other cognitive abilities, and 3. Functional abilities, in terms of activities of daily living, mood, and quality of life. They selected RCTs or quasi-RCTs of memory rehabilitation or cognitive rehabilitation for people with MS in which a memory rehabilitation treatment group was compared with a control group. Selection was conducted independently first and then confirmed through group discussion. We excluded studies that included participants whose memory deficits were the result of conditions other than MS, unless we could identify a subgroup of participants with MS with separate results. They added 29 studies during this update, bringing the total to 44 studies, involving 2714 participants. The interventions involved various memory retraining techniques, such as computerized program and training on using internal and external memory aids. Control groups varied in format from assessment-only groups, discussion and games, non-specific cognitive retraining, and attention or visuospatial training. The risk of bias amongst the included studies was generally low, but we found eight studies to have high risk of bias related to certain aspects of their methodology. In this abstract, we are only reporting outcomes at the intermediate timepoint (i.e., between one and six months). We found a slight difference between groups for subjective memory (SMD 0.23, 95% CI 0.11 to 0.35; 11 studies; 1045 participants; high-quality evidence) and quality of life (SMD 0.30, 95% CI 0.02 to 0.58; 6 studies; 683 participants; high-quality evidence) favoring the memory rehabilitation group. There was a small difference between groups for verbal memory (SMD 0.25, 95% CI 0.11 to 0.40; 6 studies; 753 participants; low-quality evidence) and information processing (SMD 0.27, 95% CI 0.00 to 0.54; 8 studies; 933 participants; low-quality evidence), favoring the memory rehabilitation group. We found little to no

difference between groups for visual memory (SMD 0.20, 95% CI -0.11 to 0.50; 6 studies; 751 participants; moderate-quality evidence), working memory (SMD 0.16, 95% CI -0.09 to 0.40; 8 studies; 821 participants; moderate-quality evidence), or activities of daily living (SMD 0.06, 95% CI -0.36 to 0.24; 4 studies; 400 participants; high-quality evidence). The authors concluded there is evidence to support the effectiveness of memory rehabilitation on some outcomes assessed in this review at intermediate follow-up. The evidence suggests that memory rehabilitation results in between-group differences favoring the memory rehabilitation group at the intermediate time point for subjective memory, verbal memory, information processing, and quality of life outcomes, suggesting that memory rehabilitation is beneficial and meaningful to people with MS. There are differential effects of memory rehabilitation based on the quality of the trials, with studies of high risk of bias inflating (positive) outcomes. Further robust, large-scale, multi-center RCTs, with better quality reporting, using ecologically valid outcome assessments (including health economic outcomes) assessed at longer-term are still needed for conclusions to be reported on the effectiveness of memory rehabilitation in people with MS.

(2020) Brissart et al. double-blind multicenter randomized trial. People with multiple sclerosis of 18 to 60 years, Expanded Disability Status Scale ⩽6.0, mild to moderate cognitive impairment. They were randomized into cognitive rehabilitation program (ProCog-SEP) or in a placebo program. ProCog-SEP comprises 13 group's sessions over 6 months and includes psychoeducational advices and cognitive exercises. Placebo program included non-cognitive exercises. No strategy and no cognitive advice were provided. The primary endpoint was the percentage of verbal memory learning measured by the Selective Reminding Test. A comprehensive neuropsychological assessment is carried out before and after interventions by a neuropsychologist blinded to intervention. Effectiveness of the ProCog-SEP versus Placebo has been verified using linear regression models. In total, 128 participants were randomized and 110 were included in the study after planning session in groups; 101 completed this trial (77.2% females); mean age: 46.1 years (±9.6); disease duration: 11.8 years (±7.5). ProCog-SEP was more effective in increasing in learning index (9.21 (95% confidence interval (CI): 1.43, 16.99); p = 0.02) and in working memory on manipulation (0.63 (95% CI: 0.17, 1.09); p = 0.01), and updating capacities (-1.1 (95% CI: -2.13, -0.06); p = 0.04). No difference was observed for other neuropsychological outcomes. Regarding quality-of-life outcomes, no change was observed between the two groups. The authors reported these findings suggest that ProCog-SEP could improve verbal learning abilities and working memory in people with multiple sclerosis. These improvements were observed with 13 group sessions over 6 months. It should be noted a limitation of this study was a small sample size and further robust RCTs are needed.

(2020) de Nair et al. complete a Cochrane database review to determine whether people with MS who received memory rehabilitation showed: 1. Better outcomes in their memory functions compared to those given no treatment or receiving a placebo control; and 2. Better functional abilities, in terms of activities of daily living, mood, and quality of life, than those who received no treatment or a placebo. They selected RCTs or quasi-

randomized trials of memory rehabilitation or cognitive rehabilitation for people with MS in which a memory rehabilitation treatment group was compared to a control group. Selection was conducted independently first and then confirmed through group discussion. They excluded studies that included participants whose memory deficits were the result of conditions other than MS unless we could identify a subgroup of participants with MS with separate results. Three review authors were involved in this update in terms of study selection, quality assessment, and data extraction. We contacted investigators of primary studies for further information where required. We conducted data analysis and synthesis in accordance with the Cochrane Handbook for Systematic Reviews of Interventions (Higgins 2011). We performed a 'best evidence' synthesis based on the methodological quality of the primary studies included.

They added seven studies during this update, bringing the total to 15 studies, involving 989 participants. The interventions involved various memory retraining techniques, such as computerized programs and training on internal and external memory aids. Control groups varied in format from assessment-only groups, discussion and games, non-specific cognitive retraining, and attention or visuospatial training. The risk of bias of the included studies was generally low, but we found eight studies to have high risk of bias related to certain aspects of their methodology. We found significant effect of intervention on objective assessments of memory in both the immediate and long-term follow-ups: standardized mean difference (SMD) 0.23 (95% confidence interval (CI) 0.05 to 0.41) and SMD 0.26 (95% CI 0.03 to 0.49), respectively. We also found significant effect of intervention for quality of life in the immediate follow-up (SMD 0.23 (95% CI 0.05 to 0.41)). These findings showed that the intervention group performed significantly better than the control group. We also found a significant difference for activities of daily living (ADL) in the long-term follow-up (SMD -0.33 (95% CI -0.63 to -0.03)), showing that the control groups had significantly less difficulty completing ADLs than the intervention groups. We found no significant effects, either immediate or long-term, on subjective reports of memory problems (SMD 0.04 (95% CI -0.19 to 0.27) and SMD 0.04 (95% CI -0.19 to 0.27)); on mood (SMD 0.02 (95% CI -0.16 to 0.20) and SMD -0.01 (95% CI -0.21 to 0.20)); and on immediate follow-up for ADL (SMD -0.13 (95% CI -0.60 to 0.33)) and in the long term for quality of life (SMD 0.16 (95% CI -0.03 to 0.36)). We could not complete a sensitivity analysis of intention-to-treat in comparison with per-protocol analysis, due to insufficient information from the included papers. However, a sensitivity analysis of high- versus low-risk studies suggested that while quality of the trials did not affect most outcomes, differences were seen in the objective memory outcomes (both at immediate and long term) and quality of life (immediate) outcome, with studies with higher risk of bias inflating the overall effect size estimates for these outcomes, and the test of overall effect changing from being statistically significant to not significant when studies at high risk of bias were excluded. This suggests that lower-quality studies may have positively influenced the outcomes. The authors concluded there is some evidence to support the effectiveness of memory rehabilitation on memory function, as well as on quality of life. However, the evidence is limited and does not extend to subjective reports of memory functioning or mood. Furthermore, the objective measures used are not ecologically valid measures, and thus potentially limit

generalizability of these findings into daily life. Further robust RCTs of high methodological quality and better quality of reporting, using ecologically valid outcome assessments, are still needed.

(2020) Lincoln et al. completed a Multicenter, pragmatic, randomized controlled trial To assess the clinical and cost-effectiveness of cognitive rehabilitation for attention and memory problems in people with multiple sclerosis. Participants included with multiple sclerosis aged 18–69 years, who reported cognitive problems in daily life and had cognitive problems on standardized assessment with a group cognitive rehabilitation program delivered in 10 weekly sessions in comparison with usual care. The primary outcome was the Multiple Sclerosis Impact Scale Psychological subscale at 12 months after randomization. Secondary outcomes included measures of everyday memory problems, mood, fatigue, cognitive abilities and employment at 6 and 12 months after randomization. In all, 245 participants were allocated to cognitive rehabilitation and 204 to usual care. Mean Multiple Sclerosis Impact Scale Psychological at 12 months was 22.2 (SD = 6.1) for cognitive rehabilitation and 23.4 (SD = 6.0) for usual care group; adjusted difference −0.6, 95% confidence interval (CI) = −1.5 to 0.3, P = 0.20. No differences were observed in cognitive abilities, fatigue, or employment. There were small differences in favour of cognitive rehabilitation for the Multiple Sclerosis Impact Scale Psychological at 6 months and everyday memory and mood at 6 and 12 months. There was no evidence of an effect on costs (−£808; 95% CI = −£2248 to £632) or on quality-adjusted life year gain (0.00; 95% CI = −0.01 to 0.02). The authors concluded this rehabilitation program had no long-term benefits on the impact of multiple sclerosis on quality of life, but there was some evidence of an effect on everyday memory problems and mood. Systematic reviews have generally concluded that efficacy of cognitive rehabilitation is uncertain in the long-term. The evidence is frequently insufficient to determine the effects of the technology on health outcomes.

Section Summary: Multiple Sclerosis (MS)
For individuals who have cognitive deficits due to multiple sclerosis who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs and systematic reviews. Relevant outcomes are functional outcomes and quality of life. Data related to clinical application of these methods are limited and further large, high-quality trials are needed. The ability to draw conclusions based on the overall body of evidence is limited by the heterogeneity of 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. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

Postencephalitis
(2013) The ACRM systematic review also evaluated cognitive rehabilitation for postencephalitis cognitive deficits. Eight identified studies were considered poor quality evidence and insufficient for forming conclusions.

Summary of Evidence: Miscellaneous Indication: Adult Population
For individuals who have cognitive deficits due to aging including individuals with Alzheimer disease (AD), and for individuals with cognitive deficits due to post-encephalopathy, autism spectrum disorder, seizure disorder/epilepsy, multiple sclerosis (MS), coma, brain tumor(s) or previous treatment of cancer, COVID-19, who receive cognitive rehabilitation delivered by a qualified professional, the evidence includes RCTs, nonrandomized comparison studies, and case series. Relevant outcomes are functional outcomes and quality of life. The quantity of studies for these conditions is much less than that for the other cognitive rehabilitation indications. Systematic reviews generally have not supported the efficacy of cognitive rehabilitation for these conditions. Relevant RCTs have had methodologic limitations, most often very short lengths of follow-up, which do not permit strong conclusions about efficacy. Outpatient cognitive rehabilitation is insufficient to permit conclusions. Larger studies with longer follow up are needed to demonstrate durable benefits of cognitive rehabilitation therapy in these individuals. The evidence is not sufficient to draw conclusions on effect on health outcomes.

Cancer
Cognitive rehabilitation has been investigated in three cancer-related settings: in children receiving oncological treatment with regular inpatient stays however the purpose of this medical policy is to review cognitive rehabilitation in the outpatient setting so this is not applicable to the intent of this medical policy and not included individuals with brain tumors, and cancer survivors whose cognitive deficits are attributed to cancer treatment.

Brain Tumors
The 2013 ACRM systematic review evaluated cognitive rehabilitation for adults with brain tumors. In 5 case reports and case series (N=36 patients), some individuals showed benefit with various cognitive rehabilitation interventions. This evidence was considered insufficient to support any recommendations.

(2013) Zucchella et al. conducted an RCT of cognitive rehabilitation in adults after neurosurgery at a single rehabilitation facility in Italy. Time since craniotomy was not reported. Adjuvant chemotherapy or radiotherapy was not administered until after the trial. Of 109 consecutive patients screened for participation, 62 (57%) met minimum cognitive deficit and other criteria and were randomized to usual rehabilitative care with (n=30) or without (n=32) cognitive rehabilitation. Treatment sessions were held 4 times a week for 4 weeks and were comprised of 45 minutes of therapist-guided computer exercises in 6 cognitive domains (time and spatial orientation, visual attention, logical reasoning, memory, executive function) and 15 minutes of cognitive strategizing. At the end of treatment (i.e., at week 4), statistically significant improvements in visual attention and verbal memory were observed in the treatment group compared with controls. Improvements in logical reasoning and executive function were not statistically

significant. Limited study follow-up makes the clinical significance of these findings unclear.

Cancer Survivors

(2019) Fernandes et al. published a systematic review of cognitive rehabilitation programs in adults with non-CNS cancers. It included 1,124 participants (n range, 11 to 242) from 19 studies published between 2007 and 2018, of which the majority were RCTs (N=12). 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. The authors noted they provided specific recommendations to facilitate future research and integration in this field. An important limitation of all studies is that participants were not blinded to group assignment.

(2019) Richard et al. completed a randomized controlled trail in patients with brain tumors face unique quality of life challenges. Executive dysfunction is common and functionally limiting, with no established treatments as standard care. This pilot study evaluated the efficacy of Goal Management Training (GMT), a behavioral intervention combining mindfulness and strategy training, for improving executive and real-life functioning in this population. Twenty-five primary brain tumor survivors were randomized to GMT, an active control (Brain Health Program, BHP), or a wait-list (WAIT) control group. The BHP was a supportive care intervention offering education and activities to promote general brain health, without cognitive strategy training. Participants in GMT and BHP completed eight individual sessions and homework between sessions; those in WAIT received usual care. Assessments at baseline, immediately post-training, and 4-month follow-up used a battery of objective and subjective measures, including functional goal attainment. The results noted an adherence (% sessions completed) was high for both GMT (98.9%) and BHP (84.4%). Executive functions improved with GMT but not BHP or WAIT (repeated measures analysis of variance, time-by-group interaction, post-training $P = 0.077$, follow-up $P = 0.046$). Both intervention groups reported fewer cognitive concerns at post-training ($P = 0.049$) and follow-up ($P < 0.001$). Functional goal attainment was greatest with GMT (post-training $P = 0.027$, follow-up $P = 0.064$). The authors concluded GMT improved executive and real-life functioning in brain tumor survivors, with gains maintained at 4-month follow-up. Clinical implementation of this adaptable program merits consideration for clinically stable patients with cognitive dysfunction. Further development and larger prospective cognitive rehabilitation trials appear warranted.

(Trial registration: ClinicalTrials.gov NCT02489071)

(2016) Zeng et al. published a meta-analysis of a neuropsychologic intervention for cognitive function in cancer survivors. 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 cognitive rehabilitation programs and the weighted mean difference for the intervention effect at postintervention follow-up was -0.19 (95% CI, -2.98 to 2.61). The authors concluded the findings from this meta-analysis indicate that neuropsychological interventions can improve cognitive function in non-CNS cancer survivors and support the need for future research. However, the conclusion from this meta-analysis was based on trials with small sample sizes. Future research should be conducted using a larger sample size. Relevant clinical implications were discussed accordingly.

Cancer Treatment: Pediatric:
(2019) Akel et al. reported for children with cancer receiving cognitive rehabilitation, the evidence includes 1 small (N=46), single-center RCT. The cognitive rehabilitation was delivered in the inpatient treatment clinic of the Department of Pediatric Oncology at University Hospital in Ankara, Turkey. Cognitive skills targeted by the cognitive rehabilitation therapy included place and time orientation, internal and external spatial perception, praxis, attention, visio-motor construction, and thinking operations. Children were characterized by a mean age of 10 years and 55% were male. Cancer diagnoses included non-Hodgkin lymphoma (40%), Hodgkin lymphoma (30%) and bone tumors (30%). Outcomes were evaluated only immediately postintervention. Although compared to the routine therapy groups, 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 is limited by other methodological shortcomings including lack of blinding of participants and lack of long-term follow-up. Therefore, this evidence is not sufficient to draw conclusions on effect on health outcomes.

Practice Guidelines and Position Statements

American Academy of Neurology (AAN)
(2016) The AAN released their "Practice Guideline Update: Disorders of Consciousness" makes no reference to sensory stimulation, cognitive rehabilitation, or coma stimulation as a treatment modality. (*Accessed July 2022*)

American Academy of Physical Medicine and Rehabilitation (AAPM&R)
(2022) 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. PASC cognitive symptom assessment and treatment recommendations are summarized in Table below.

Post-Acute Sequelae of SARS-CoV-2 Infection Cognitive Symptom Assessment and Treatment Recommendations

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."

(*Accessed July 2022*)

American Congress of Rehabilitation Medicine (ACRM)
(2013) The American Congress of Rehabilitation Medicine has developed clinical recommendations for cognitive rehabilitation interventions for individuals with traumatic brain injury (TBI) or stroke.

Summary and Recommendations

- **Brain Neoplasms**
  - Probably effective in treating attention and memory deficits in children and adolescents who undergo resection, radiation, or both after diagnosis of brain neoplasm.
  - Evidence of effectiveness of these approaches in adults with brain neoplasms is equivocal, thus preventing a recommendation to be made for adults in this population.
- **Epilepsy/Seizure Disorders**: practice option that cognitive rehabilitation for attention and memory deficits, with additional techniques for internalization of strategy use, may be effective for individuals with seizure related deficits in attention and memory. It is recommended that further cognitive rehabilitation research involving individuals with seizure disorders consider including strategy use as a specific component of training.
- **Anoxia/Hypoxia**: There is currently insufficient evidence to recommend or contraindicate the use of cognitive rehabilitation in individuals with cognitive impairment from anoxia or hypoxia. It is recommended that foundation cognitive rehabilitation research with this population being with single-subject or small sample studies with careful subject selection (i.e., individuals screened for relatively milder deficits and indications of learning potential), using targeted interventions, and aimed at measurable functional goals.

- **Encephalitis**: There is currently insufficient evidence to make recommendations for the use of cognitive rehabilitation with post-encephalitis cognitive deficits. Eight identified studies were considered poor quality evidence and insufficient for forming conclusions.
- **Toxic Encephalopathy**: There is insufficient evidence to date to support putting forward a treatment recommendation in this area.
- **Parkinson's Disease**: There is insufficient evidence to make recommendations for cognitive rehabilitation for individuals with Parkinson's disease.
- **Huntington Disease**: There is insufficient evidence to date to support putting forward a treatment recommendation in this area.
- **Systemic Lupus Erythematosus**: There is insufficient evidence to date to support a treatment recommendation in this area. It is recommended that researchers of this population focus in areas of cognitive difficulty also common to other diagnostic groups (e.g., attention and/or memory), select individuals with identifiable, yet treatment deficits, and choose intervention methods based in process training and strategy use.

(*Accessed July 2022*)

Institute of Medicine

In 2013, the Institute of Medicine published a report on cognitive rehabilitation for traumatic brain injury that included a comprehensive review of the literature and recommendations.

- The report concluded literature signals evidence of some benefit of certain forms of CRT for TBI, evidence that varies across cognitive domains. The evidence is insufficient overall to provide definitive guidance for translation into clinical practice guidelines, particularly in selecting the most effective treatment(s) for a particular patient. The committee found very little evidence of adverse effects or harm associated with CRT, but it recommended that future studies assess such risks. And, the overall evidence is insufficient to clearly establish whether telehealth technology delivery modes are more or less effective or more or less safe than other means of delivering CRT
- The report also recognized that not all behavioral research follows this methodical sequence. Some treatments are in wide use with little theoretical foundation. Likewise, other treatment packages are in wide use, while little is known about which specific ingredients are most important and for which patients. Some treatments are effective at the group level but differ in their effectiveness for individual people; moderating variables are in play that are poorly understood.
- For CRT to be rigorously shown to be effective, it will require multiple studies, and the goals of those studies will and should differ over time as the research moves through the maturational process. Using treatment theory and enablement theory in combination can guide study designs so researchers do not place unrealistic requirements on treatments while at the same time being most likely to capture the treatment benefits when they exist. He emphasized that, whether or not a research program is moving methodically through the above steps, this outline of the maturational process for CRT is useful as a reference point and for

guiding researchers to regularly ask (1) Where along the path does this treatment dwell right now? and (2) What questions need to be answered in order to move it forward?

(*Accessed July 2022*)

The International Team of Researchers and Clinicians (INCOG) Guidelines for Cognitive Rehabilitation following Traumatic Brain Injury

(2014) The team recommends that individuals have detailed assessments of cognition after resolution of posttraumatic amnesia. Cognitive assessment and rehabilitation should be tailored to the patient's neuropsychological profile, premorbid cognitive characteristics, and goals for life activities and participation. Clinical algorithms and audit tools to evaluate current practice are provided. (*Accessed 2021*)

National Institute of Health and Care Excellence (NICE)

- **COVID-19**
  (2021) NICE issued a rapid guideline on managing the long-term effects of COVID-19. 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. (*Accessed July 2022*)

- **Dementia**
  (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." (*Accessed July 2022*)

- **Stroke**
  (2013) Guidance on stroke rehabilitation recommends cognitive rehabilitation for visual neglect and memory and attention deficits that impact function. Interventions should focus on relevant functional tasks, e.g., errorless learning, and elaborative techniques (mnemonics, encoding strategies) for memory impairments. (*Accessed July 2022*)

Veterans Administration/Department of Veterans Affairs (VA)

- **Guideline on the Management of Stroke Rehabilitation**:
  (2019) 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. (*Accessed July 2022*)

- **Guidelines on the Treatment of Concussion and Mild Traumatic Brain Injury (TBI)**:
  (2016) These guidelines addressed cognitive rehabilitation in the setting of persistent symptoms.
    - "Individuals with a history of mTBI [mild traumatic brain injury] who present with symptoms related to memory, attention, and/or executive function problems that do not resolve within 30 to 90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. The Work Group suggests considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). A prolonged course of therapy in the absence of patient improvement is strongly discouraged." (*Accessed July 2022*)

Regulatory Status
Cognitive rehabilitation is not subject to regulation by the U.S. Food and Drug Administration (FDA).

PRIOR APPROVAL

Not applicable.

POLICY

Note: This medical policy is to only address the requests for outpatient cognitive rehabilitation.

See the Related Medical Policy
- 08.03.04 Sensory Integration Therapy and Auditory Integration Therapy

Medically Necessary
Cognitive rehabilitation may be considered **medically necessary** in the rehabilitation of individuals with a cognitive impairment due to one of following:
- Traumatic Brain Injury (TBI) referring to the disruption of normal brain functioning due to, but not limited to, **one of** the following:
    - Concussion; **and/or**
    - Traumatic cerebral edema; **and/or**
    - Diffuse or focal traumatic brain injury including contusion or traumatic intra-axial hemorrhage of the cerebrum, cerebellum, or brainstem; **and/or**
    - Traumatic extra-axial hemorrhage in the epidural, subdural or subarachnoid spaces

And all of the following criteria must be met:

- Therapy must be prescribed by the attending physician as part of the written care plan; **and**
- The service(s) must be provided by a qualified licensed professional (i.e., physician, a psychologist, physical therapist, occupational therapist and/or speech therapist); **and**
- The individual should have the potential for improvement (based on preinjury function); **and**
- Individuals 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); **and**
- If ongoing services are requested, documentation should demonstrate continued objective improvement in function as identified in short - and long-term goals.

Not Medically Necessary
Cognitive rehabilitation is considered **not medically necessary** when the above criteria is not met.

Cognitive rehabilitation is considered **not medically necessary** for maintenance therapy.

Investigational
Cognitive rehabilitation is considered **investigational** for all other indications including but not limited to the following**:**

- Aging population
- Alzheimer disease
- Autism Spectrum disorder
- Brain Tumors
- Cognitive deficits due to brain tumor or previous treatment for cancer
- Coma Stimulation/Coma Arousal Program/Therapy
- COVID – 19
- Dementia
- Multiple Sclerosis (MS)
- Preventative intervention
- Previous treatment for cancer
- Postencephalitic or Post-encephalopathy individuals
- Seizure disorders
- Stroke

Based on the peer reviewed literature there is insufficient evidence to support the use of cognitive rehabilitation in all other conditions **except for traumatic brain injury** as indicated above, medical literature is limited, and available studies include small study samples and lack of comparison groups and long term follow up.

Policy Guidelines

- Cognitive rehabilitation may be performed by an occupational therapist, physical therapist, speech/language pathologist, neuropsychologist or other psychologist, or a neuropsychiatrist, psychiatrist, or other physician.
- Cognitive rehabilitation must be distinguished from occupational therapy; occupational therapy describes rehabilitation that is directed at specific environments (i.e., home or work). In contrast, cognitive rehabilitation consists of tasks designed to develop the memory, language, and reasoning skills that can then be applied to specific environments.
- Services will be counted toward any applicable therapy visit limits in the individual subscriber contract when cognitive rehabilitation is performed by a physical, occupational and/or speech therapist as part of an outpatient rehabilitation/therapy program for individuals who have suffered a traumatic brain injury.
- Cognitive Rehabilitation Maintenance Therapy - A maintenance therapy program includes activities that maintain the individual's present level of function and prevent regression of that function. Maintenance begins when the therapeutic goals of a treatment plan have been achieved or when no further functional progress is apparent or expected to occur.

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 97129 Therapeutic interventions that focus on cognitive function (eg, attention, memory, reasoning, executive function, problem solving, and/or pragmatic functioning) and compensatory strategies to manage the performance of an activity (eg, managing time or schedules, initiating, organizing, and sequencing tasks), direct (one-on-one) patient contact; initial 15 minutes
- 97130 Therapeutic interventions that focus on cognitive function (eg, attention, memory, reasoning, executive function, problem solving, and/or pragmatic functioning) and compensatory strategies to manage the performance of an activity (eg, managing time or schedules, initiating, organizing, and sequencing tasks), direct (one-on-one) patient contact; each additional 15 minutes (List separately in addition to code for primary procedure)
- S9056 Coma stimulation per diem

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POLICY HISTORY

Date	Reason	Action
August 2022	Annual Review	Policy Revised
August 2021	Annual Review	Policy Revised
August 2020	Annual Review	Policy Revised
August 2019	Annual Review	Policy Revised
August 2018	Annual Review	Policy Revised
August 2017	Annual Review	Policy Revised
August 2016	Annual Review	Policy Revised
September 2015	Annual Review	Policy Revised
October 2014	Annual Review	Policy Revised
October 2013	Annual Review	Policy Renewed
November 2012	Annual Review	Policy Renewed
November 2011	Annual Review	Policy Renewed
October 2010	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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