Cognitive Rehabilitation for Traumatic Brain Injury in Adults

Assessment
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Executive Summary

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

The term "rehabilitation" broadly encompasses re-entry into familial, social, educational and working environments, the reduction of dependence on assistive devices or services, and the general enrichment of quality of life. The goal of this Assessment is to evaluate the independent effect of a distinct and definable component of the rehabilitation process known as "cognitive rehabilitation."

A 1997 Technology Evaluation Center (TEC) Assessment evaluated the benefits of cognitive rehabilitation in the treatment of cognitive deficit as a consequence of neurological impairment. Available evidence was reviewed to determine whether, when used as an adjunct to conventional rehabilitation or compared with no treatment, cognitive rehabilitation improves the health outcomes of patients with cognitive deficit as a result of neurological impairment. Neurological insults considered in the 1997 Assessment included traumatic brain injury; stroke; post-encephalitic or post-encephalopathy; and aging (including Alzheimer's disease). Cognitive rehabilitation for remediation of cognitive deficit as a result of neurological insult did not meet TEC criteria.

This Assessment is an update to the 1997 TEC Assessment, and focuses on traumatic brain injury in adults. Evidence is reviewed to determine whether, when used as an adjunct to conventional rehabilitation or compared with no treatment, cognitive rehabilitation improves the health outcomes of adult patients with traumatic brain injury (TBI). The health outcomes of interest are improved patient functioning and quality of life.

Based on the available evidence, the Blue Cross and Blue Shield Association Medical Advisory Panel made the following judgments about whether cognitive rehabilitation for traumatic brain injury in adults meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

1. The technology must have final approval from the appropriate governmental regulatory bodies.

Cognitive rehabilitation is a procedure and, therefore, is not subject to U.S. Food and Drug Administration (FDA) regulation.

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2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.

Few controlled studies of cognitive rehabilitation have examined health outcomes. Four comparative trials provided evidence on the effect of cognitive rehabilitation in adults with traumatic brain injury. Three of the 4 studies were randomized, and 1 randomized trial was blinded. Together these studies included 153 treatment patients and 138 controls. Treatment methods varied widely, and included holistic interdisciplinary programs as well as specific cognitive stimulation programs. Control groups were not always specifically defined, but included no treatment, education and phone support, and unstructured attention tasks. Follow-up periods ranged from none to 24 months.

The first study reported that an interdisciplinary community-based outreach program resulted in greater gains in functional skills and independence as compared to a supportive intervention consisting of information. The outreach intervention appeared to be beneficial to those with the most disability. Overall this is a well-designed study that attempted to account for a very heterogeneous study population. The interpretations, however, are complicated by three concerns. The main problem is the appropriateness of the selected outcome measures, in particular, the ceiling effects present in the primary outcome measures. As a result, the study was insensitive to demonstrating change for the majority of patients. The authors attempted to compensate by 1) using a nonparametric test on rank scores of change and 2) creating a Maximal Gain Index (MGI) on the subscale showing the client's greatest improvement from baseline to follow-up. This approach makes it difficult to decipher the true treatment effect. Because change scores and the MGI are influenced by the tails of the intake distributions, and there is some evidence to support the notion that the tail distribution is higher for the outreach patients, then the results are likely artifactual. An analysis of covariance would have controlled for this artifact, and would have diminished the statistical significance.

A second concern involves the assessment and limited treatment and support that took place in the month immediately post-discharge for those patients referred from inpatient rehabilitation. This intervention preceded randomization, and it is unclear what effect it may have had on both the outreach and informational groups. The third problem concerns missing data. As the primary outcome measure was under development during the early stages of the trial, baseline data were not available for all allocated participants. The authors, who describe their study as exploratory, deserve acknowledgement for their attempts to account for the heterogeneity of the population under study. It is a challenge for standardized assessment tools to capture the range of applicable endpoints for such a heterogeneous TBI population, and at the same time capture the extent of change as a result of rehabilitation intervention. The limitations associated with missing data, the outcome measures and the analysis make it difficult to accurately assess the benefits of this program of rehabilitation. It is reasonable to accept the these results as exploratory and encouraging, but given the limitations, it would be premature to accept the results as sufficient support for the benefits of cognitive rehabilitation as delivered in this study's outreach model.

The second reviewed study found that an interdisciplinary inpatient milieu program resulted in no difference in return to work, fitness for military duty or quality of life when compared with a supportive telephone contact intervention. Both groups performed similarly at post-treatment, producing no treatment effect in the statistical analysis. Interpretations on this particular study need to be viewed with caution. First, it is uncertain whether the treatment was initiated too early in the post-acute stage. Patients were on average 38 days out from a severe traumatic brain injury. Typically, treatment programs similar to the one delivered by these investigators are entered into one or more years post-injury. Secondly, the wide disparity in return to work outcomes reported by this study is puzzling in the face of commonly reported figures in the range of 30–40% two or more years post-injury. Plausible explanations include the influence of a military environment or perhaps the patients were less severely impaired than apparent.

These issues bring up important questions about what is operating to cause the reported results, and limit the ability to generalize these results to a broader population. An important observation in this study was the positive trend indicating that more severely impaired patients seemed to benefit from the more intense outreach program. This is a clinically relevant finding. Reasonably,

one can hypothesize that the outreach program may have demonstrated a significant treatment benefit if targeted to severely injured patients able to benefit from the intensity of the effort.

The third study suggested that a residential rehabilitation program resulted in greater improvement in total disability and cognitive and motor function when compared to a variety of alternative treatments, but it is probable that the fundamental weaknesses in design led to bias. These problems include the lack of randomization, the presence of between group differences at baseline, the small sample size, the lack of standardization in the comparison group, and the overall lack of treatment definition.

The fourth study found no difference in functional skills, attention skills or general cognitive abilities when comparing a focused cognitive stimulation strategy to a non-structured strategy in the early post-acute setting. In this study, the treatment intensity may well have been too low. Treatment time was 10 hours total. With the pervasive and life-long cognitive deficits that result from TBI, results from interventions of such limited duration should not be generalized to more sustained interventions. Also, the treatment may have been initiated too early post-injury to be beneficial. The issue of when in the course of the recovery process cognitive rehabilitation is initiated is an important factor for consideration. The timing can determine and influence the nature of the treatment results obtained.

Are there common characteristics among these studies? The first two more rigorous studies share some important commonalities in treatment intervention. Both trials used an interdisciplinary holistic approach that emphasized structured, systematic, and individualized goal setting. The entire study sample of the first study and at least a percentage of the second study sample involved patients with severe TBI. The first study's results, while exploratory, are particularly encouraging when coupled with the positive trend identified by the second study. Is an individually tailored interdisciplinary program of rehabilitation beneficial for patients with more severe TBI injuries, and when in the injury cycle? Future trials are necessary that evaluate a well-defined treatment approach in a carefully selected sample and using carefully selected outcomes to determine treatment effectiveness.

In summarizing the results of these 4 studies, it seems that evidence that is supportive of cognitive rehabilitation as an effective method is mitigated by findings that failed to show beneficial results. These outcome variations may be due in part to key differences in design among the studies including the breadth of treatment focus, intensity of rehabilitation effort, time since onset of injury, heterogeneity among subjects, and outcomes measured. The main deficiencies of the evidence are the inconsistencies in what treatment is under study, in whom, and how effects are being measured. As a result, there is little to no collaborative evidence between studies, and no study is strong enough to stand alone. In the aggregate, these studies do not provide evidence for or against the effect of cognitive rehabilitation. The available data are considered insufficient to make conclusions on whether cognitive rehabilitation results in beneficial health outcomes.

3. The technology must improve the net health outcome; and
4. The technology must be as beneficial as any established alternatives.

The evidence does not permit conclusions on whether cognitive rehabilitation improves health outcomes in adults with traumatic brain injury or is as beneficial as the established alternatives.

5. The improvement must be attainable outside the investigational settings.

Whether cognitive rehabilitation improves health outcomes in adults with traumatic brain injury has not been demonstrated in the investigational setting.

Based on the above, cognitive rehabilitation for traumatic brain injury in adults does not meet the TEC criteria.

Contents

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Assessment Objective

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

The term "rehabilitation" broadly encompasses re-entry into familial, social, educational and working environments, the reduction of dependence on assistive devices or services, and the general enrichment of quality of life. The goal of this Assessment is to evaluate the independent effect of a distinct and definable component of the rehabilitation process known as "cognitive rehabilitation."

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Background

Cognitive Rehabilitation

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

Patient Populations. Cognitive rehabilitation has been used to treat a range of brain insults and neurological impairments. However, the majority of cognitive rehabilitation research and application has focused on two prevalent patient indications, stroke and traumatic brain injury.

Traumatic brain injury (TBI) is broadly defined as brain injury caused by externally inflicted trauma, principally the result of motor vehicle incidents, violence, sports injuries, and falls. Each year, in the U.S., an estimated 70,000–90,000 individuals incur TBI severe enough to cause long-term substantial impairment (National Institutes of Health [NIH] 1999). Advances in emergency care, transport systems and acute medical management have improved survival rates in recent years. The result is a continually increasing number of TBI survivors with long-term disability.

Patients surviving severe TBI often suffer from residual impairments in motor control, communication skills, cognition and social behavior. The cognitive and behavioral deficits are generally among the more problematic impairments, and include a spectrum of changes in memory, language, attention and

* Cognitive rehabilitation is distinct from the group of psychotherapeutic techniques known as "cognitive behavior therapy (CBT)." A treatment for psychological disorder and maladaptive behavior, CBT attempts to change a patient's style of thinking, feeling, and behavior. CBT is used primarily in the treatment of individuals who present with emotional and behavioral difficulties or formal psychiatric disorder. This Assessment does not address the effectiveness of CBT.

concentration, visual processing, reasoning and problem-solving, executive functions, and emotional and behavioral regulation. Resulting psychosocial limitations include high levels of anxiety and depression and pervasive personal loss (e.g., interpersonal relationships, social supports, employment, leisure activity). Consequently, TBI has a profound effect on everyday functioning and independent living.

Models of Brain Injury Rehabilitation. Programs differ in treatment setting, techniques, intensity, duration, and their specific aims. Some programs target an isolated cognitive function while others offer a general mix of rehabilitation therapies. Training may be directed at the improvement of a single task (e.g., a visual reproduction task) or attempt to remediate global impairment, such as memory. Some programs use a single strategy (e.g., computer-assisted training), while others use a range of multidisciplinary approaches.

Cognitive rehabilitation is delivered in a number of different practice settings. The settings overlap to varying degrees and cover the full continuum of care. Cognitive recovery proceeds in overlapping stages, with more marked improvements in some skills occurring at different times. Therefore, the practice setting and the specific interventions used are often linked to the injury stage, with early rehabilitation taking place in more structured settings while later rehabilitation is dispersed to home and community. Table 1 presents a distribution of practice settings adapted from Chestnut et al. (1999).

Therapeutic Strategies. There is significant practice variation in the therapeutic interventions used in brain injury rehabilitation programs. Table 2 lists common cognitive rehabilitation interventions as described by the NIH sponsored Consensus Development Panel on Rehabilitation of Persons with TBI (NIH 1999). In general, therapeutic strategies in cognitive rehabilitation can be divided into approaches that attempt to *recover* cognitive abilities and approaches that attempt to *compensate* for cognitive impairment. The rationale for recovery is that with extensive practice or exercise, it is possible to retrain and improve impaired cognitive function by reestablishing previously learned patterns of behavior. Example techniques include reinforced practice on auditory, visual and verbal tasks, number manipulation, computer-assisted stimulation, and video feedback. In contrast, compensation interventions concede the unrecoverable loss of function and instead focus on adapting to the cognitive deficit. Example compensatory mechanisms include visual cues, memory books, mnemonics, self-monitoring techniques and pagers that trigger behavior. The two approaches are not mutually exclusive, and in practice most cognitive rehabilitation programs combine both restorative and compensatory strategies.

Given the interaction of neurophysical, cognitive and psychologic factors that result from brain injury, individuals are commonly treated by a comprehensive, integrated and holistic program of rehabilitation (Cicerone et al. 2000). Comprehensive rehabilitation is provided by a diverse team of specialists including physicians, physical therapists, occupational therapists, neuropsychologists, clinical psychologists, social workers, speech-language pathologists, rehabilitation nurses, and recreational therapists. In a holistic model, the team of professionals collectively provide an environment for cognitive, behavioral and physical recovery and social reintegration. Specific interventions are individually tailored based on patient attributes and goals to achieve both intermediate goals in cognitive training and more global functional outcomes.

Spontaneous Recovery. Spontaneous recovery refers to the naturally occurring improvements in neuropsychological function following TBI. In the absence of treatment, a variable but expected pattern of improvement occurs, resulting from resolution and absorption of hematomas, decrease in swelling, normalization of blood flow, and return of electrolyte and neurochemical balance (Webster and Scott 1988; Sohlberg and Mateer 1989).

Without further medical complications, patients with TBI typically show progressive gains, with the most pronounced improvement occurring anywhere from the first 3–18 months (Webster and Scott 1988; Rimmele and Hester 1987). However, the time span during which individuals demonstrate the most dramatic recovery rate varies with the severity of injury. The course of recovery for cognitive ability is unpredictable and extremely variable. The window of recovery is generally believed to be approximately 2.5 years, although some recovery is believed to continue at a slowed rate well beyond this point (Donoghue 1995). Functional improvements can continue to improve because of adaptations to the environ-

Table 1. Distribution of Practice Settings for Cognitive Rehabilitation

Setting	General Description
Acute Rehabilitation Programs	– Accepts medically stable patients at the time of discharge from acute hospital – Inpatient rehabilitation hospital environment – Focus on intensive physical and cognitive restorative services in the early months after injury – Multidisciplinary treatment team – Short-term duration
Extended Intensive Rehabilitation Programs	– An extension of the acute rehabilitation program for severely injured patients – Highly structured – Focus on cognitive and memory retraining, speech therapy, ADLs, social behavior and physical therapy – Vocational training and community re-entry typical – Patient remains in program as long as progress is demonstrated – Typical stay 6 to 12 months
Long-term Rehabilitation Programs	– Provides extended rehabilitation and management services in residential setting – Focus on full range of rehabilitation interventions – Treats patients in need of structured environment and making slow improvements – Patient remains in program as long as progress is demonstrated – Generally not for permanent placement
Life-Long Residential Programs	– Accepts patients unable to live independently – For severely injured individuals – Focus on permanent placement – Offers specific activities for cognitive stimulation
Transitional Living Programs	– Prepares patient for maximum independence, teaches community interaction skills – Supervised residential setting – Holistic approach – Specialized programs focus on cognitive, memory, speech and behavioral therapies – Involves education, problem-solving skills, decision-making strategies, planning for life transitions – Offers vocational preparation and training – Individualized to patient needs – Can be offered in variety of facilities such as small group home, community center or special education facility
Day Treatment Programs	– Similar to Transitional Living Program in a non-residential format – Holistic approach – Focus on improving functional skills – Specialized programs focus on cognitive, memory, speech and behavioral therapies – Involves education, problem-solving skills, decision-making strategies, planning for life transitions – Offers vocational preparation and training – Individualized to patient needs
Ambulatory or Home Treatment Programs	– Nursing and rehabilitation interventions delivered in either outpatient setting or in-home – Can be discipline specific or coordinated program of multidisciplinary rehabilitation – Individualized to patient needs – Focus on improving functional skills – Can involve education, problem-solving, coping skills

Table 2. Cognitive Rehabilitation Interventions

Cognitive or academic exercises
Computer-assisted training
Compensatory technique training
External aids
Communication skill training
Psychotherapy
Behavior modification
Comprehensive interdisciplinary (milieu) models
Vocational rehabilitation
Pharmacotherapy
Physical exercise, physical therapy, or aerobic training
Art and music therapy
Nutrition
Spirituality
Alternative or nontraditional therapies

ment, strategic compensation by the individual, use of prosthetic devices or continued neurological development (as in the case of a child). Therefore, the window for cognitive rehabilitation is quite broad and varies from individual to individual (Sohlberg and Mateer 1987).

Health Outcomes. A standard set of outcome measures has not been used in the evaluation of cognitive rehabilitation. The clinical practice of highly individualized treatment in TBI rehabilitation has led to a vast array of outcomes and measures. Practitioners generally agree that the desired outcome of cognitive rehabilitation is improvement in daily function and reduced levels of disability, although historically the more commonly used outcomes have been highly specific intermediate measures (i.e., neuropsychological subtest scores) rather than health outcomes. A progressive change is underway away from the use of intermediate measures and toward quality of life and everyday function. At this time, there are few well-designed controlled studies of cognitive rehabilitation that have investigated health outcomes. In addition to more traditional health outcomes such as quality of life or functional ability, return to work is considered a salient outcome of successful TBI rehabilitation, not only because of the profound effect of brain injury on employability, but also because young adults make up such a significant proportion of the TBI population. Work as a fundamental aspect of lifestyle is crucial to the concept of handicap, and as such is a frequent priority target for rehabilitation.

Systematic Reviews. Systematic reviews of the literature examining the effectiveness of cognitive rehabilitation for TBI have yielded somewhat mixed results.

A review by the former Agency for Health Care Policy and Research (now called the Agency for Healthcare Research and Quality [AHRQ]) evaluated evidence for the effectiveness of cognitive rehabilitation methods to improve outcomes for persons with TBI. Two small randomized controlled trials and one observational study provided evidence that specific forms of cognitive rehabilitation reduce memory failures and anxiety, and improve self-concept and interpersonal relationships for persons with TBI. The durability and clinical relevance of the findings was not established according to the report (Carney et al. 1999). Recommendations suggested the need for future research that makes use of control groups and multivariate methods to address subject variability, and includes standard definitions of the cognitive rehabilitation intervention, and relevant outcome measures that reflect health and function (Carney et al. 1999; Chestnut et al. 1999).

Similar to the AHRQ findings, an NIH sponsored Consensus Development Panel on Rehabilitation of Persons with TBI identified studies that showed improvements in specific cognitive processes (NIH 1999). Demonstrated improvements were found in attention, memory and executive functions, and in some cases involved the use of compensatory aids (such as memory books). Comprehensive, interdisciplinary rehabilitation

programs were the primary intervention in these studies, making it difficult to evaluate program effectiveness due to the heterogeneity of interventions and patients. The panel concluded that evidence does support the use of certain cognitive and behavioral rehabilitation strategies for individuals with TBI, yet the research needs to be replicated in larger, more definitive clinical trials (NIH 1999).

A review by Cicerone et al. (2000) concluded that overall support exists for the effectiveness of several forms of cognitive rehabilitation for individuals with TBI. In particular, evidence was identified to support the effectiveness of treatment for impairments of attention, memory, functional communication and problem-solving after TBI. On the question of comprehensive-holistic cognitive rehabilitation, 15 studies were identified (one Class 1a prospective trial, four Class II non-randomized controlled trials, and 10 Class III studies without controls). The Class 1a trial demonstrated only marginal improvement on neuropsychological measures, and did not report functional outcomes. Three of the class II studies (n=138) compared subjects to non-treated controls and suggested greater reductions in disability with treatment. A fourth Class II study found significant improvements in neuropsychological test scores with cognitive versus interpersonal interventions. Cicerone and colleagues noted evidence to suggest that subject selection factors, particularly the capacity to recognize and adapt to residual cognitive limitations, may be the moderating factor in the effectiveness of holistic rehabilitation programs.

FDA Status. Cognitive rehabilitation is a procedure and, therefore, is not subject to FDA regulation.

Methods

Search Methods

MEDLINE database and PsychINFO database searches of the published literature were performed for the period 1997 through November 2002. Keywords used for the search included: "cognitive rehabilitation," "cognitive retraining," "cognitive training," "neuropsychological rehabilitation," "cognitive remediation," and "cognitive therapy." Additional material was identified through reviews of current relevant journals, reference lists in previously identified articles, meta-analyses, and evidence-based reports.

Study Selection

Studies selected for review met the following criteria:

1. The study sample consisted of 8 or more adults.
2. The study sample consisted exclusively of individuals with TBI, or if a mixed sample was studied, the results were reported by patient indication.
3. Patients underwent a distinct and definable cognitive rehabilitation treatment program.
4. The study was a controlled trial that compared the results of a treatment group to a control group.
5. Health outcomes were reported.
6. Treatment processes, patient selection, and technically adequate measures of health outcome were described in adequate detail.
7. The study was published in a peer-reviewed journal after 1996.

Four studies met these criteria.

Medical Advisory Panel Review

This Assessment was reviewed by the Blue Cross and Blue Shield Association Medical Advisory Panel (MAP) on October 10, 2002. In order to maintain the timeliness of the scientific information in this Assessment, literature searches were performed subsequent to the Panel's review (see "Search Methods," above). If the search updates identified any additional studies that met the criteria for detailed review, the results of these studies were included in the tables and text where appropriate. There were no studies that would change the conclusions of this Assessment.

Formulation of the Assessment

Patient Indications

Adult patients experiencing cognitive deficit as a consequence of traumatic brain injury.

Technologies to be Compared

Cognitive rehabilitation is used as an adjunct to medical management and/or conventional rehabilitation. In the available studies one form of cognitive rehabilitation was: 1) compared with an alternative form of cognitive rehabilitation, or 2) compared with conventional rehabilitation that did not include a distinct cognitive rehabilitation component, or 3) compared with no treatment.

Health Outcomes

It is generally agreed that the desired outcome of cognitive rehabilitation is improvement in daily function or activities of daily living. Functional outcome can be defined in terms of any number of specific, real world outcomes such as independence, social functioning or employment status. In the AHRQ report "Rehabilitation for Traumatic Brain Injury," Chestnut et al. (1999) engaged a panel of technical experts to identify the relevant health outcomes of cognitive rehabilitation for people with TBI. The panel listed the following outcomes:

a. activities of daily living (ADLs);
b. long-term measure of disability (restriction or, as the result of an impairment, inability to perform an activity in the manner or within the range considered normal for a human being);
c. long-term measure of impairment (loss or abnormality of psychological, physiological, or anatomical structure or function);
d. independence, relationships, family life, satisfaction; and
e. long-term financial burden.

In contrast to the health outcomes recommended by Chestnut et al. (1999), intermediate outcomes are generally laboratory-based measures of cognitive function such as neuropsychological test batteries. Neuropsychological tests are measures of highly defined and narrow aspects of human performance, designed to assess brain function rather than to reflect life activities valued by the patient or society. In asking the question of whether intermediate measures of cognitive function associate with health outcomes or employment, Chestnut and colleagues found no association between laboratory-based measures and health outcomes such as functional independence, ADLs or everyday use of memory. In 1996, the American Academy of Neurology (AAN) had also recommended against using neuropsychological test data as a primary indicator for the success of rehabilitation programs (AAN 1996).

This Assessment considers evidence from comparative studies that examine the effects of cognitive rehabilitation on measures of health outcomes as described by Chestnut et al. (1999).

Specific Assessment Question

Does the available evidence demonstrate that cognitive rehabilitation improves the health outcomes of adults with traumatic brain injury?

Review of Evidence

Four controlled trials reported the effects of a cognitive rehabilitation intervention compared to the effects of either an alternative form of rehabilitation or no rehabilitation. Table 3 provides a description of the treatment and alternative interventions used in each of the studies. Table 4 describes the reported outcomes.

All studies reported relevant health outcomes. Three of the 4 studies included randomization and one trial included single-blinding. A total of 291 patients were studied, of which 153 received treatment protocols. Three trials involved severe TBI injuries, while the fourth included a mix of moderate-to-severe injuries. Treatment methods varied, and included comprehensive multidisciplinary programs as well as a specific cognitive stimulation program.

Reported outcomes included a range of measures centered on functional abilities, activities of daily living and return to work: 1) Barthel Index; 2) Brain Injury Community Rehabilitation Outcome-39; 3) Functional Independence Measure; 4) Functional Assessment Measure; 5) various anxiety and depression scales; 6) return to gainful employment; 7) fitness for military duty; 8) modified Health & Activity Limitations Survey; and 9) Community Integration Questionnaire. In addition, various neuropsychologic test batteries and other intermediate measures were reported.

Alternative methods of rehabilitation included 1) information only 2) limited education and weekly phone support 3) undefined rehabilitation in a home, outpatient or long-term care facility or no services and 4) an unstructured program of attention tasks. Treatment settings varied between 1) community outreach 2) post-acute residential and 3) acute inpatient. Treatment intensity ranged from 10 hours total to 8 weeks of inpatient treatment. Mean time since onset of injury ranged from 6 weeks to 3 to 4 years. Follow-up periods ranged from none to 2 years.

Table 3. Rehabilitation Treatment Interventions Used in Studies of Patients with Traumatic Brain Injury

	Treatment Arm		Control Arm	
Study	Setting & Duration	Intervention	Setting & Duration	Intervention
Powell et al. 2002	Home or community setting such as day center 2 visits/week 2-6 hrs/week mean 27.3 weeks (19.1)	Individualized program of multidisciplinary rehabilitation Treatment team led by psychologist and comprised of occupational therapist, physiotherapist, speech and language therapist, clinical psychologist and social worker Treatment components individually tailored based on goals specified in written contracts between patient & therapist Central treatment component: Two weekly outreach visits to the home by relevant therapist/s based on treatment goals Actual interventions provided by therapists not clarified by authors	Home Single visit	Single home visit by one of the team therapists Central treatment component: Provision of a booklet listing range of local and national resources Both treatment and control arms discharged from inpatient rehabilitation received one month of post-discharge community support before being randomized to multidisciplinary outreach group or information-only group

Table 3. Rehabilitation Treatment Interventions Used in Studies of Patients with Traumatic Brain Injury (cont'd)

	Treatment Arm		Control Arm	
Study	Setting & Duration	Intervention	Setting & Duration	Intervention
Salazar et al. 2000	Inpatient minimal nursing unit 8 weeks	High-intensity, protocol-defined structured daily routine, multidisciplinary intervention. Milieu program emphasizing holistic approach. Treatment Team - led by physiatrist with neurologist, rehab nurse, neuropsychologist, OT, speech therapist, and rehab assistants. Consultation by psychiatry and PT. Met weekly to discuss patient goals & facilitate interdisciplinary approach. Goal setting conducted on individual basis. Central treatment components: a. physical fitness training b. group and individual cognitive, speech, occupational and coping skills therapies c. integrated work therapy Specific group therapies: a. planning & organization b. cognitive skills c. pragmatic speech d. milieu e. psychotherapy f. community reentry g. medication Cognitive paradigm followed that emphasized: orientation, attention, memory, visual processing, language, executive functioning and abstract reasoning/problem solving.	Home 8 weeks	Low-intensity, minimal intervention, minimal structure Prior to home discharge a. multidisciplinary evaluation b. one meeting with nurse to plan home stay Instructions to patients upon discharge: a. read at least 30 minutes per day b. play games requiring reasoning skills c. physical exercise at least 30 minutes per day Central treatment component: weekly telephone contact with psychiatric nurse Therapeutic techniques: a. develop therapeutic alliance b. encourage participation in social & community activities c. support coping by providing information d. assist in problem solving by providing names of resources

Table 3. Rehabilitation Treatment Interventions Used in Studies of Patients with Traumatic Brain Injury (cont'd)

	Treatment Arm		Control Arm	
Study	Setting & Duration	Intervention	Setting & Duration	Intervention
Willer et al. 1999	Residential program Mean time between assessments: 8 months ($p<0.05$) Authors did not clarify if treatment was delivered throughout this full period	Broad range of services delivered within a post-acute residential treatment setting. Actual treatment interventions not well-defined by the authors. "All treatment subjects were seen by professionals (e.g., physician, occupational therapist, and physical therapist) on a regular basis. Treatment coordination was provided by a neuropsychologist." Paraprofessionals carry out instructions of the professionals and report progress to treatment team. Paraprofessionals serve as role models in areas of functioning related to community integration.	Variable settings Mean time between assessments: 12.1 months ($p<0.05$) Authors did not clarify if treatment was delivered throughout this full period	Variable range of home-based, outpatient or institutionalized services: 8/23 patients – no services other than family support available through a local support group 15/23 patients – received some combination of component services in either a community home setting or a nursing home setting: occupational therapy (8) physical therapy (10) neuropsychology therapy (12) case management (8) homemaker nurse services (6)
Novack et al. 1996	Post-acute inpatient 30 minutes per day, 5 days per week Mean # of sessions = 20 10 hours total	Focused cognitive stimulation program conducted with a single therapist, one-one format Central treatment component: Hierarchically presented attention tasks progressing from lowest levels (focused and sustained attention) to more challenging tasks requiring selective attention, alternating attention and divided attention Individual goals set and updated weekly Therapeutic techniques: a. increased structure b. removal of physical, auditory and visual cues	Post-acute inpatient 30 minutes per day, 5 days per week Mean # of sessions = 21	Unstructured cognitive stimulation program conducted with a single therapist, 1:1 format Central treatment component: Random tasks focusing on memory or reasoning skills, including orientation questions and games. Emphasis on language-based tasks. Core difference between the two arms: a. Structure versus no structure b. Hierarchical presentation versus no hierarchy

Table 4. Health Outcomes of Cognitive Rehabilitation in Patients with Traumatic Brain Injury

Study	Design	Study Sample	Outcome Measures	Treatment Results	Durability
Powell et al. 2002	Randomized controlled trial Single-blinded Intention to treat analysis	Severe TBI (99%) **Median Time Since Injury** 1.3 years - treatment 1.4 years - control Range 3 months to 20 years 112 randomized **Treatment** n=48 6 lost to follow-up mean age = 34 (11) **Control** n=46 10 lost to follow-up mean age = 35 (10)	Barthel Index (BI) and brain injury community rehab outcome-39 (BICRO-39) focused on levels of activity and participation Functional Independence Measure (FIM) plus Functional Assessment Measure (FAM) focused on functional independence Hospital Anxiety and Depression Scale (HADS)	**BI** Median change = 0; 60% scored ceiling at intake; 35% outreach vs. 20% information improved (p<0.05) **BICRO-39** Mobility, Self-Organization, Psych Well-Being - normal distribution at intake; Personal Care - 70% at floor (total independence); Productive Employment - 75% at ceiling (no activity) Median change score summed across 6 sub-scales greater in outreach (1.58) vs. information (1.04) (p<0.05); Greater gains in self-organization and psych well-being in outreach group (p<0.05) Clinically significant improvement on 6 point scale: 71% outreach vs. 40% information (1.5 point ↑) 40% outreach vs. 20% information (2.0 point ↑) Maximal Gain Index - greater gain in outreach (1.6) vs. information (1.2) (p<0.025) **FIM + FAM** Psych Adjustment & Cognitive Function - normal distrib at intake; Personal Care - 79% at ceiling (total independence); Mobility - 69% at ceiling; Communication - 54% at ceiling No stat sig in between group change scores for either total score (2.8 vs. 2.5) or individual subscales Clinically sig improvement - 40% outreach vs. 20% information (2.0 point ↑); Maximal Gain Index - greater in outreach group (1.6) vs. information (1.2) (p<0.025) **HADS** No difference between groups on anxiety or depression	Mean follow-up 24.8 mos. (18-40 mos.)

Table 4. Health Outcomes of Cognitive Rehabilitation in Patients with Traumatic Brain Injury (cont'd)

Study	Design	Study Sample	Outcome Measures	Treatment Results	Durability
Salazar et al. 2000	Randomized controlled trial Intention to treat analysis	Moderate to severe TBI **Time since injury** 3 months or less mean = 38 days Active duty military personnel 120 randomized **Treatment** n=60 (7 of 67 withdrew) mean age = 25 (6.6) **Controls** n=47 (6 of 53 received additional therapy) mean age = 26 (6.2)	**Primary Measures** Return to gainful employment Fitness for military duty **Secondary Measures** Quality of life as measured by Katz Adjustment Scale Cognitive & behavioral function as measured by neuropsychologic battery	No treatment effect for return to employment Inpatient 90% employed vs. Home 94% (p=.51) Of those working, 91% of inpatient group and 93% of home group working full-time (p=0.99) No treatment effect for fitness for military duty Inpatient 73% vs. Home 66% (p=0.43) Mean time to initiation of medical separation: Inpatient - 6 months from study entry Home - 5 months from study entry (p=0.37) No significant differences found in cognitive and behavioral function scales No significant differences found in quality of life scales Percentage of patients with 1 or more unscheduled outpatient visits in one year post-treatment Inpatient 41% vs. Home 42% (p=0.99)	1 year follow-up

Table 4. Health Outcomes of Cognitive Rehabilitation in Patients with Traumatic Brain Injury (cont'd)

Study	Design	Study Sample	Outcome Measures	Treatment Results	Durability
Willer et al. 1999	Non-randomized, case control study	Severe TBI **Mean Time since injury** 3.0 years (2.9) – treatment 4.6 years (4.6) – controls **Treatment** n= 23 mean age= 33.4 (11.3) **Controls** n=23 mean age = 34.7 (10.7) subjects matched on LOC, age, gender, time since injury & disability	Functional assessment-modified Health & Activity Limitations Survey (HALS) Community Integration Questionnaire (CIQ)	Functional improvements found in both groups, but statistically significant ↑ in total disability score, and cognitive and motor subscales in CR group versus controls Greater improvement in CIQ in CR group, not statistically significant, and limited by initial group differences	No change at 1 year for either group
Novack et al. 1996	Randomized controlled trial Controls matched on age, time since injury, treatment intensity, education	Severe TBI **Mean time since injury** 5.9 weeks (3.3) - treatment 6.4 weeks (4.9) - controls **Treatment** n=22 mean age = 28.7 (13.2) **Controls** n=22 mean age = 26.4 (10.9)	Functional Independence Measure (FIM) Digit Span, Mental Control, Reaction Time Select neuropsych battery	No treatment effect for attention skills, functional skills or general cognitive abilities	No follow-up

LOC loss of consciousness
OT occupational therapy
PT physical therapy

The available studies vary to a substantial extent making reliable comparisons across studies difficult. Treatment methods, alternative methods, therapeutic setting and intensity, time since onset of injury, outcome measures and durability measures are not consistent between studies. These fundamental differences might explain the inconsistencies observed among study results.

1. A community-based program of individualized multidisciplinary rehabilitation resulted in greater gains in functional skills and independence as compared to a community-based intervention consisting of a single therapist visit designed to provide information only (Powell et al. 2002).
2. A high-intensity inpatient program of structured multidisciplinary rehabilitation resulted in no difference in return to work, fitness for military duty or quality of life when compared with a low-intensity home-based intervention consisting of weekly supportive telephone contact (Salazar et al. 2000).
3. A broad-ranging residential rehabilitation program resulted in greater improvement in total disability and cognitive and motor function when compared to a variety of alternative treatments, including no treatment or some form of home, outpatient or nursing home rehabilitation services (Willer et al. 1999).
4. A highly focused inpatient cognitive stimulation program found no difference in functional skills, attention skills or general cognitive abilities when comparing a structured cognitive stimulation strategy to a non-structured strategy (Novack et al. 1996).

Powell et al. (2002). This randomized trial of 96 patients with severe TBI suggests that a community-based multidisciplinary rehabilitation program delivered within an individualized contractual goal setting framework is effective in improving functional ability and independence. Significantly greater improvement was realized by patients receiving the comprehensive multidisciplinary program versus those receiving a single therapist visit consisting of information only. Improvements were seen in practical functioning, independence in a range of activities and psychological well-being. The mean follow-up period was 24.8 months, ranging from a low of 18 months to a high of 40 months.

The Powell study was overall well-designed, and included randomization, concealed allocation to study arm, single-blinding on therapist-assessed outcomes, and intention-to-treat analysis. Of 112 patients randomized to the study, 96 completed both baseline and follow-up assessments. Of the 16 patients lost to follow-up, 3 patients had died, one was in prison, one untraceable, and 11 failed to attend appointments. There was a higher rate of attrition from the control group (18%) versus treatment group (11%).

Once a brain-injured individual has returned to community life, participation in normal life activities can be assessed by any number of relevant outcomes - ability to provide self-care, family relationships, social and recreational pursuits, education, employment, psychological well-being and quality of life. The Powell study used two primary (Barthel Index [BI], Brain Injury Community Rehabilitation Outcome-39 [BICRO-39]), and two secondary measures (Functional Independence Measure plus Functional Assessment Measure [FIM-FAM], Hospital Anxiety and Depression Scale [HADS]) to assess patient outcomes.

The BI, which has been used extensively in inpatient settings, provides a measure of overall disability and is a well-accepted indicator of ability in activities of daily living, such as hygiene, mobilization, and communication. Scores are based on a combination of assessor observation, and client and caregiver interview. The BICRO-39 is a self-report instrument that measures level of activity, participation and psychological aspects of community functioning. Both client and caregiver report are considered. Powell and colleagues prospectively identified 6 of the 8 subscales for measurement—personal care, mobility, self-organization, socializing, productive employment, and psychological well-being. The two family contact/support scales were eliminated because the desired direction of change could vary among subjects.

Baseline and follow-up scores were not uniformly available for all subjects on all measures. The primary outcome measure, BICRO-39 scores, were available for only 35/54 treatment and 40/56 control patients because the instrument was still in development at the early stages of the trial. HADS scores were collected only on patients with the cognitive and linguistic competence to complete the instrument with minimal assistance. Data were available for 20 treatment and 26 control patients. Change scores were available for 48 treatment and 46 control patients on the BI and the FIM+FAM.

The BI median change score was zero for both groups with negative as well as positive changes at follow-up. This result is partially explained by the ceiling effect; 60% of subjects had baseline scores at the ceiling level, and an additional 14% were within 2 points of ceiling (20 maximum). Despite the high baseline scores, 35% of treatment patients and 19.6% of control patients showed improvement at follow-up ($p<0.05$). However, the improvement of one or two points at the upper limit of the index is probably not of clinical significance. It is possible that the BI, which has been validated in inpatient settings, is not a representative measure of disability for a less-disabled community sample.

Total score on the BICRO-39 showed a modest but significantly greater improvement for the treatment group ($p<0.05$). Floor and ceiling effects were apparent at baseline for 2 of 6 subscales. Over 70% of subjects scored within 0.5 points of floor (meaning total independence) on personal care, while 75% scored within 0.5% of ceiling on productive employment (meaning no activity). The remaining 4 scales were normally distributed (mobility, self-organization, psychological well-being and socializing). Two subscales showed significantly greater gains with treatment (self-organization and psychological well-being). Personal care and mobility subscales showed a positive trend ($p=0.08$ and 0.10). When the mobility analysis was limited to the subgroup who demonstrated physical disability at baseline (15 treatment and 14 controls), then a treatment effect was evident ($p<0.05$).

Maximum change on the BICRO-39 is 6 points for a subject who moves from total dependence to maximum independence. Based on this scale, the authors defined clinical significance as a change of at least 1.5 points. According to the authors' definition then, 71% of the treatment group achieved clinically significant change versus 40% of controls. If the criterion is raised to a 2.0-point change, then the difference between groups is 40% versus 20%. In order to look at clinical significance more closely, a "maximal gain index" was computed: a subject-specific change score on the subscale in which the patient showed greatest improvement from baseline to follow-up. A treatment effect was evident for this measure (median scores 1.6 versus 1.0, $p<0.02$).

Total FIM+FAM scores showed similar modest improvements in both groups. No treatment effect was evident in total scores. Ceiling effects were present for 3 of 5 subscales (personal care, mobility and communication), while the remaining 2 subscales were normally distributed (psychological adjustment and cognitive function). Differences between groups on the FIM+FAM subscales did not achieve statistical significance. However, the calculated maximal gain index was significantly greater in the treatment group ($p<0.025$), with most clients demonstrating greatest gain on psychological adjustment. If the clinically significant change criterion is set at 2.0 points (of 6 total points), then clinically significant improvement was demonstrated in 46% of treated patients versus 24% of controls. The groups did not differ in the degree of change on either anxiety or depression on the HADS scale.

There are three main concerns with the interpretation of Powell's results. The main problem is the appropriateness of the selected outcome measures, in particular, the ceiling effects present in the BI, the BICRO-39 and the FIM+FAM. As a result, the study was insensitive to demonstrating change for the majority of patients. The authors attempted to compensate by 1) using a nonparametric test on rank scores of change and 2) creating a Maximal Gain Index (MGI) on the subscale showing the client's greatest improvement from baseline to follow-up. This approach makes it difficult to decipher the true treatment effect.

For example, the median intake score on the BI was 20 for both groups, and the authors state that 60% of participants scored at ceiling (20) at intake. An unanswered question is whether 60% of both groups scored at 20, or if 65% of the informational group and 55% of the outreach group were at ceiling or so on, meaning a greater percentage of outreach patients have a greater potential for change. Both the change scores and the MGI place emphasis on this potential for change. Without knowing true equivalence at baseline, the appropriate statistic would be analysis of covariance, where the baseline measure is the covariate, i.e., adjusting for baseline differences. With the BI, 35% of the outreach group had an improved change score versus 19.6% for the informational group. Although the range of scores at intake was nearly identical, the outreach group may have had a larger proportion in the left tail of the distribution than the informational

group. The change and MGI scores may merely reflect these unknown baseline differences, giving the appearance of real change. Because change scores and the MGI are influenced by the tails of the intake distributions, and there is some evidence to support the notion that the tail distribution is higher for the outreach patients, then the results are likely artifactual. An analysis of covariance would control for this artifact, and would diminish the statistical significance.

A second concern involves the use of post-discharge community support prior to randomization. Patients derived from two sources, those already living in the community and those referred at point of discharge from inpatient rehabilitation. The second group received assessment and limited treatment and support from the outreach team for one month immediately after discharge. The authors considered this step necessary because it was not possible to determine the until the closing days of discharge whether outreach rehabilitation would be appropriate for a given client, leaving insufficient time to make alternative discharge plans. Those for whom treatment goals were definable after about 2 weeks of home assessment were then randomized to either group.

The percentage of subjects receiving the post-discharge service is unclear, as is the exact nature of the treatment and support delivered during this time. Also unclear is the potential confounding effect this intervention may have had on both the outreach and informational groups.

A third problem concerns missing data, particularly with the primary outcome measure. As the BICRO-39 was under development during the early stages of the trial, baseline data were not available for all allocated participants, and analyses were based on 35/54 outreach and 40/56 information subjects who completed both intake and follow-up. The nature of these issues significantly limits the interpretation of Powell's results and precludes meaningful understanding of the treatment effect.

Salazar et al. (2000). A total of 107 active duty military personnel with moderate or severe TBI were randomly allocated to either inpatient or home study arms by concealed methods. An intensive program of multidisciplinary rehabilitation delivered in an inpatient milieu environment was compared with a low-intensity home intervention consisting of weekly telephone support. No differences were observed in return to work or fitness for military duty nor were any significant differences found in cognitive, behavioral and quality of life measures.

Salazar et al. (2000) used a standardized interdisciplinary cognitive rehabilitation program modeled after Prigatano's milieu approach as the treatment intervention (Prigatano et al. 1984; Prigatano et al. 1994). The interdisciplinary program combined group and individual therapies with a milieu-oriented neuropsychological focus. Patients receive individual physical therapy, occupational therapy, speech and language therapy, and cognitive therapies depending on individual need. Several hours of goal-oriented employment work tasks were also included in the daily schedule. The cornerstone of Prigatano's approach is the development of a therapeutic alliance between patient and therapist, and the functioning milieu or environment in which the therapists and patients meet, discuss daily events, provide feedback and confront behaviors that interfere with progress toward independence or ability to work. Because the program was geared toward returning soldiers to duty, most activities, homework and the living environment were modified from Prigatano's work to make them relevant to the military.

Salazar et al. (2000) delivered the milieu model in an inpatient setting; although a previous publication cites the reason for selecting this venue was the lack of military barracks not medical need (Braverman et al. 1999). The interdisciplinary milieu program was compared to a supportive intervention consisting of TBI education and weekly individual phone counseling from a psychiatric nurse.

Return to work and fitness for military duty at 1 year follow-up served as the main outcome measures. Work was defined as either full-time or part-time military or civilian employment. Fitness for duty included those still on active military duty or had received an honorable discharge from the service. Decisions regarding fitness for duty were made independently of the study team. Data were analyzed using intention-to-treat analysis with all randomized subjects.

No between group difference was found in return to work (90% for inpatient treatment versus 94% for home treatment). Among subjects working at 1 year, 91% and 93%

were employed full time. No between group difference was detected in fitness for military duty (73% versus 66%), nor were differences detected in quality of life as measured by the Katz Adjustment Scale or on general measures of cognitive and psychiatric function.

A subgroup analysis suggested a trend toward beneficial effect of the milieu program for patients who were unconscious for more than one hour post injury. Eighty percent of the hospital group (28/35) with period of unconsciousness over one hour versus 58% of the home group (23/40) were evaluated as fit for duty ($p<.05$). Differences in the remaining outcome measures were not reported. The sample size and the fact that the effect was demonstrated in the single outcome "fitness for duty" make it difficult to conclude that the treatment is effective for the general population of patients with loss of consciousness over one hour. This an important finding however, and raises the question of whether the study sample was sufficiently impaired to benefit from the intensive intervention. Patients were included in the trial only if they met a cognitive score of 7 on the Ranchos Los Amigos scale (meaning oriented and appropriate). Thus, subjects had already attained significant cognitive recovery at the time of study inclusion. The authors ability to demonstrate a benefit of cognitive rehabilitation may be limited as a result.

A number of questions are raised by the Salazar report. First, the return to work statistics are uncommonly high (≥90%) in comparison to reported figures which approach roughly 40% after 2-4 years (Prigatano et al. 1994). The mean time since onset of injury was only 38 days, making it difficult to compare these results with the more conventional post-acute programs delivered at roughly 1 to 2 years post severe injury. It is possible, of course, that the unique influences of a military environment had a positive effect on outcomes. Patients in non-military programs may not achieve the same results. Other explanations include the possibility that patients were returned to work inappropriately or that patients were not sufficiently impaired to benefit from the intensive intervention. In fact, the generally high functional level of these subjects seems apparent by their ability to participate in vocational counseling for several hours per day in the early post injury stage. It is reasonable to consider that the treatment intervention as described by Salazar might be effective if targeted to those patients most likely to benefit (i.e., those with greater injury severity). According to the authors, a second, larger multicenter, randomized controlled trial of cognitive rehabilitation for patients with more severe TBI is underway.

Willer et al. 1999. This trial was a case-control study of 46 patients. In total, the Willer findings are not entirely informative due to fundamental weaknesses in the study design. The study lacked randomization and statistical power. Additionally, a highly variable comparison group was used as the alternative form of treatment, the treatment intervention lacked sufficient definition to replicate it, and the results were affected by between group differences present at baseline.

Despite the limitations, Willer et al. suggested a residential program of broad ranging rehabilitation interventions resulted in beneficial treatment effects when compared with variable alternatives. Treatment patients received an 8-month residential post-acute rehabilitation program (described as including a broad range of rehabilitation services although the actual interventions were not well-defined by the authors). Alternative treatment methods were not standardized and included no rehabilitation (8/23) or some combination of rehabilitation services in a home, outpatient or institutionalized setting (15/23).

Positive treatment effects were reported on total disability scores on the Health and Activity Limitations Survey (HALS). The HALS is a global disability index for use across various disease populations. Treatment patients scored at 14.6 (6.6) versus control patients at 18.9 (6.9) ($p<0.001$). Isolated improvements were also observed in motor ($p<0.05$) and cognitive ($p<0.052$) subscales. A brain injury specific scale designed to measure degree of handicap after hospital discharge served as a second outcome measure. Greater improvement was demonstrated by the treatment group on the Community Integration Questionnaire (CIQ) but significant between group differences at baseline confound this finding. The standard method for achieving comparability across comparison groups is randomization, which is absent in this study.

Novack et al. (1996). This report was a randomized controlled trial of 44 patients conducted in the post-acute inpatient setting. No difference in attention skills, functional skills

or general cognitive abilities was found with a structured, therapist-supported cognitive stimulation program when compared to an unstructured cognitive stimulation program. The results are subject to limitations because the treatment intensity was unusually low (10 hours total), and the time since onset of injury was brief (mean 5.9 weeks post injury [3.3] for treatment patients and 6.4 weeks [4.9] for controls). Interpretations should consider whether the treatment intensity was sufficient to cause improvement, and whether the treatment was initiated too acutely for patients to benefit. Given these questions, plus the small sample and lack of follow-up, the Novack results should be viewed with caution.

Summary of Application of the Technology Evaluation Criteria

Based on the available evidence, the Blue Cross and Blue Shield Medical Advisory Panel made the following judgments about whether cognitive rehabilitation for traumatic brain injury in adults meets the Blue Cross and Blue Shield Association Technology Evaluation Center (TEC) criteria.

1. **The technology must have final approval from the appropriate governmental regulatory bodies.**

Cognitive rehabilitation is a procedure and, therefore, is not subject to U.S. Food and Drug Administration (FDA) regulation.

2. **The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes.**

Few controlled studies of cognitive rehabilitation have examined health outcomes. Four comparative trials provided evidence on the effect of cognitive rehabilitation in adults with traumatic brain injury. Three of the 4 studies were randomized, and 1 randomized trial was blinded. Together these studies included 153 treatment patients and 138 controls. Treatment methods varied widely, and included holistic interdisciplinary programs as well as specific cognitive stimulation programs. Control groups were not always specifically defined, but included no treatment, education and phone support, and unstructured attention tasks. Follow-up periods ranged from none to 24 months.

The first study reported that an interdisciplinary community-based outreach program resulted in greater gains in functional skills and independence as compared to a supportive intervention consisting of information. The outreach intervention appeared to be beneficial to those with the most disability. Overall this is a well-designed study that attempted to account for a very heterogeneous study population. The interpretations, however, are complicated by three concerns. The main problem is the appropriateness of the selected outcome measures, in particular, the ceiling effects present in the primary outcome measures. As a result, the study was insensitive to demonstrating change for the majority of patients. The authors attempted to compensate by 1) using a non-parametric test on rank scores of change and 2) creating a Maximal Gain Index (MGI) on the subscale showing the client's greatest improvement from baseline to follow-up. This approach makes it difficult to decipher the true treatment effect. Because change scores and the MGI are influenced by the tails of the intake distributions, and there is some evidence to support the notion that the tail distribution is higher for the outreach patients, then the results are likely artifactual. An analysis of covariance would have controlled for this artifact, and would have diminished the statistical significance.

A second concern involves the assessment and limited treatment and support that took place in the month immediately post-discharge for those patients referred from inpatient rehabilitation. This intervention preceded randomization, and it is unclear what effect it may have had on both the outreach and informational groups. The third problem concerns missing data. As the primary outcome measure was under development during the early stages of the trial, baseline data were not available for all allocated participants. The authors, who describe their study as exploratory, deserve acknowledgement for their attempts to account for the heterogeneity of the population under study. It is a challenge for standardized assessment tools to capture the range of applicable endpoints for such a heterogeneous TBI population, and at the same time capture the extent of change as a result of rehabilitation intervention. The limitations associated with missing data, the outcome measures and the analysis make it difficult to accurately assess the benefits of this program of rehabilitation. It is reasonable to accept the these results as exploratory and encouraging,

but given the limitations, it would be premature to accept the results as sufficient support for the benefits of cognitive rehabilitation as delivered in this study's outreach model.

The second reviewed study found that an interdisciplinary inpatient milieu program resulted in no difference in return to work, fitness for military duty or quality of life when compared with a supportive telephone contact intervention. Both groups performed similarly at post-treatment, producing no treatment effect in the statistical analysis. Interpretations on this particular study need to be viewed with caution. First, it is uncertain whether the treatment was initiated too early in the post-acute stage. Patients were on average 38 days out from a severe traumatic brain injury. Typically, treatment programs similar to the one delivered by these investigators are entered into one or more years post-injury. Secondly, the wide disparity in return to work outcomes reported by this study is puzzling in the face of commonly reported figures in the range of 30-40% two or more years post-injury. Plausible explanations include the influence of a military environment or perhaps the patients were less severely impaired than apparent.

These issues bring up important questions about what is operating to cause the reported results, and limit the ability to generalize these results to a broader population. An important observation in this study was the positive trend indicating that more severely impaired patients seemed to benefit from the more intense outreach program. This is a clinically relevant finding. Reasonably, one can hypothesize that the outreach program may have demonstrated a significant treatment benefit if targeted to severely injured patients able to benefit from the intensity of the effort.

The third study suggested that a residential rehabilitation program resulted in greater improvement in total disability and cognitive and motor function when compared to a variety of alternative treatments, but it is probable that the fundamental weaknesses in design led to bias. These problems include the lack of randomization, the presence of between group differences at baseline, the small sample size, the lack of standardization in the comparison group, and the overall lack of treatment definition.

The fourth study found no difference in functional skills, attention skills or general cognitive abilities when comparing a focused cognitive stimulation strategy to a non-structured strategy in the early post-acute setting. In this study, the treatment intensity may well have been too low. Treatment time was 10 hours total. With the pervasive and life-long cognitive deficits that result from TBI, results from interventions of such limited duration should not be generalized to more sustained interventions. Also, the treatment may have been initiated too early post-injury to be beneficial. The issue of when in the course of the recovery process cognitive rehabilitation is initiated is an important factor for consideration. The timing can determine and influence the nature of the treatment results obtained.

Are there common characteristics among these studies? The first two more rigorous studies share some important commonalities in treatment intervention. Both trials used an interdisciplinary holistic approach that emphasized structured, systematic, and individualized goal setting. The entire study sample of the first study and at least a percentage of the second study sample involved patients with severe TBI. The first study's results, while exploratory, are particularly encouraging when coupled with the positive trend identified by the second study. Is an individually tailored interdisciplinary program of rehabilitation beneficial for patients with more severe TBI injuries, and when in the injury cycle? Future trials are necessary that evaluate a well-defined treatment approach in a carefully selected sample and using carefully selected outcomes to determine treatment effectiveness.

In summarizing the results of these 4 studies, it seems that evidence that is supportive of cognitive rehabilitation as an effective method is mitigated by findings that failed to show beneficial results. These outcome variations may be due in part to key differences in design among the studies including the breadth of treatment focus, intensity of rehabilitation effort, time since onset of injury, heterogeneity among subjects, and outcomes measured. The main deficiencies of the evidence are the inconsistencies in what treatment is under study, in whom, and how effects are being measured. As a result, there is little to no collaborative evidence between studies, and no study is strong enough to stand alone. In the aggregate, these studies do not provide evidence for or against the effect of cognitive rehabilitation. The available data are considered insufficient to

make conclusions on whether cognitive rehabilitation results in beneficial health outcomes.

3. **The technology must improve the net health outcome; and**
4. **The technology must be as beneficial as any established alternatives.**

The evidence does not permit conclusions on whether cognitive rehabilitation improves health outcomes in adults with traumatic brain injury or is as beneficial as the established alternatives.

5. **The improvement must be attainable outside the investigational settings.**

Whether cognitive rehabilitation improves health outcomes in adults with traumatic brain injury has not been demonstrated in the investigational setting.

Based on the above, cognitive rehabilitation for traumatic brain injury in adults does not meet the TEC criteria.

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