Effective Health Care Program

Comparative Effectiveness Review
Number 72

Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults

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Preface

The Agency for Healthcare Research and Quality (AHRQ) conducts the Effective Health Care Program as part of its mission to organize knowledge and make it available to inform decisions about health care. As part of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, Congress directed AHRQ to conduct and support research on the comparative outcomes, clinical effectiveness, and appropriateness of pharmaceuticals, devices, and health care services to meet the needs of Medicare, Medicaid, and the Children's Health Insurance Program (CHIP).

AHRQ has an established network of Evidence-based Practice Centers (EPCs) that produce Evidence Reports/Technology Assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care. The EPCs now lend their expertise to the Effective Health Care Program by conducting comparative effectiveness reviews (CERs) of medications, devices, and other relevant interventions, including strategies for how these items and services can best be organized, managed, and delivered.

Systematic reviews are the building blocks underlying evidence-based practice; they focus attention on the strength and limits of evidence from research studies about the effectiveness and safety of a clinical intervention. In the context of developing recommendations for practice, systematic reviews are useful because they define the strengths and limits of the evidence, clarifying whether assertions about the value of the intervention are based on strong evidence from clinical studies. For more information about systematic reviews, see http://www.effectivehealthcare.ahrq.gov/reference/purpose.cfm.

AHRQ expects that CERs will be helpful to health plans, providers, purchasers, government programs, and the health care system as a whole. In addition, AHRQ is committed to presenting information in different formats so that consumers who make decisions about their own and their family's health can benefit from the evidence.

Transparency and stakeholder input from are essential to the Effective Health Care Program. Please visit the Web site (http://www.effectivehealthcare.ahrq.gov) to see draft research questions and reports or to join an email list to learn about new program products and opportunities for input. Comparative Effectiveness Reviews will be updated regularly.

We welcome comments on this CER. They may be sent by mail to the Task Order Officer named below at: Agency for Healthcare Research and Quality, 540 Gaither Road, Rockville, MD 20850, or by email to epc@ahrq.hhs.gov.

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Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults

Structured Abstract

Objective. To determine the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury (TBI) in adults.

Data Sources: MEDLINE®, Cochrane Database of Systematic Reviews, PsycINFO, and the Physiotherapy Evidence Database (PEDro) bibliographic databases; hand searches of references of relevant systematic reviews.

Review Methods: We screened abstracts and full text articles of identified references for eligibility and reviewed randomized controlled trials (RCTs) and prospective cohort studies to describe intervention characteristics and evaluate evidence on participation outcomes of productivity and community integration and treatment harms. We extracted data, rated quality, and graded strength of evidence. Our primary outcomes included measures of participation in employment, school, or training and select scales measuring community integration (Mayo-Portland Adaptability Inventory [MPAI] and the Craig Handicap Assessment and Reporting Technique [CHART], Craig Handicap Assessment and Reporting Technique Short Form [CHART-SF], and the Community Integration Questionnaire [CIQ]). Data were collected on secondary patient-centered outcomes as well.

Results: We found 16 studies that met our inclusion criteria. Interventions that could be classified as comprehensive holistic day treatment programs were the most often studied model of care. These interventions are characterized as integrated intensive programs delivered to cohorts of patients focusing on cognitive rehabilitation and social functioning. Eight studies that addressed primary outcomes and were assessed to have a low or moderate risk of bias were graded to evaluate effectiveness and comparative effectiveness. We found insufficient evidence on effectiveness. We found a low level of evidence that certain interventions were no different than others in terms of productivity outcomes at 1-year post-treatment. We found a low level of evidence that a comprehensive holistic day treatment program resulted in greater productivity, but not improved community integration, than the standard treatment. However, group differences no longer existed at 6 months post-treatment because the standard rehabilitation group made significant progress during the followup period. Gains made during rehabilitation appear to be sustained at followups 6 months to 1 year post-treatment. Interpretation of community integration from scales is complicated by little attention to minimal clinically important differences. One study addressed harms and found no treatment-related harms.

Conclusions: The body of evidence is not informative regarding effectiveness or comparative effectiveness of multidisciplinary postacute rehabilitation. Further research should address methodological flaws common in these studies and further address effectiveness research questions.

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Executive Summary

Background

Condition and Therapeutic Strategies

Traumatic brain injury (TBI) is an alteration in brain function or other evidence of brain pathology caused by an external force.[1] TBI is a significant public health issue in the United States. Of the approximately 1.7 million TBIs that were recorded annually between 2002 and 2006,[2] 1.37 million patients were treated and released from emergency departments, 275,000 were hospitalized, and 50,000 died.[2] Additional TBIs not reflected in the numbers above are treated in primary care settings and in Federal, military, and Veterans Affairs hospitals. The Department of Defense reported more than 4,500 moderate to severe TBIs among all service members in 2010.[3] Major causes of TBIs include falls (35.2 percent), motor vehicle accidents (17.3 percent), "struck by/against" events (16.5 percent), assaults (10 percent), and other/unknown (21 percent); and, for military personnel, explosions/blasts.[4]

TBIs are categorized as mild, moderate, or severe according to acute injury characteristics that suggest the extent of damage to the brain. Several measures are available to assess severity. Standard criteria include structural imaging findings; duration of loss of consciousness, altered consciousness, and/or post-traumatic amnesia; Glasgow Coma Scale (GCS) scores; and the Abbreviated Injury Severity Scale score (Table A).[5] The GCS is the most widely used scale to determine injury severity. However, the accuracy of this scale can be compromised by certain acute interventions such as intubation and by specific medications; some research suggests that loss of consciousness and post-traumatic amnesia may better predict functional status. Therefore, other measures are also used.[6]

Table A. Criteria used to classify TBI severity[7]

Criteria	Mild	Moderate	Severe
Structural Imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness	< 30 minutes	30 minutes to 24 hours	>24 hours
Alteration of Consciousness/ Mental State	A moment to 24 hours	>24 hours	>24 hours
Post-traumatic Amnesia	0–1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (best available score in 24 hours)	13–15	9–12	3–8
Abbreviated Injury Severity Scale	1–2	3	4–6

Moderate to severe injuries more often require intensive medical care, and 40 percent of those hospitalized with nonfatal TBIs sustain impairments that lead to long-term disability.[5] Different injury types and severity levels are associated with specific impairments. For example, penetrating head injuries can result in cognitive decline related to the location of the injury and the amount of tissue lost.[7] Deficits resulting from penetrating head injuries may be similar to those observed in stroke patients.[8] Closed head injuries are more common and can cause diffuse brain damage that leads to a variety of impairments unique to each individual.[8] Evidence suggests that long-lasting effects of moderate to severe TBI include cognitive deficits, psychiatric morbidities (depressive and

aggressive behaviors, post-traumatic stress disorder, and psychoses), and social functioning deficits.[9] Some long-lasting impairments may not become apparent until well after the injury. By one estimate, two percent of the U.S. population lives with TBI-related disabilities, presumably from moderate to severe TBI.[10]

Patients with moderate to severe TBI are typically treated first in acute medical settings for a duration that varies according to the injury and patient characteristics (e.g., injury severity, impairment level, comorbidities, age) and health care system characteristics. Once the patient is medically stable and deemed ready to engage in intensive rehabilitation, postacute rehabilitation may occur.

Postacute rehabilitation addresses sustained impairments across physical, cognitive, and affective/behavioral domains. Rehabilitation programs strive to maximize functioning and participation according to each individual's capacity. Research during the 1970s and 1980s suggested that domain-specific training may be insufficient to rehabilitate those with frontal lobe damage.[11] Spurred by these findings, clinicians adopted multidimensional approaches to TBI rehabilitation, including vocational and neurobehavioral interventions that incorporated arranged work trials.[11] The current preferred approach is multidisciplinary, with treatments (including treatments for comorbidities) integrated across disciplines or impairment domains.

A recent systematic review of multidisciplinary rehabilitation for brain injury defines "multidisciplinary" as more than one discipline working in coordination;[12] however, the intent of these programs is comprehensive. Multidisciplinary teams often include physiatrists, neurologists, neuropsychologists, clinical psychologists, physical and occupational therapists, speech language pathologists, recreational therapists, social workers, rehabilitation nurses, and technicians. Multidisciplinary programs differ in their settings, components, and emphases. Despite a general understanding that comprehensive multidisciplinary programs comprise many professionals working as a team, program descriptions often do not specify percentages or doses of the various available therapies. This is in part because each individual's sustained impairments are unique and largely determine the composition, intensity, and duration of rehabilitation. Some programs, however, take a more structured approach.

To determine whether rehabilitation programs have met the goal of restoring TBI survivors to previous or newly defined roles requires that we address patient-centered outcomes, which are those valued by patients.[13] To identify these outcomes, we looked to the International Classification of Functioning Disability and Health's (ICF) participation domain.[14] For many brain injury survivors, a final goal of community integration may be to return to work, school, or training, all of which are often classified as "productivity" outcomes. Additionally, researchers and practitioners agree that "community integration" outcomes, related to the resumption of societal roles, are important indicators of effectiveness for TBI rehabilitation.[15]

However, patient-centered outcomes can be subjective and are often measured with scales that do not translate into clinically relevant measures of change. It is difficult to know whether a given change in a certain scale score is clinically meaningful, even when the change may be statistically significant. Efforts to interpret effectiveness depend on identifying the level of change in a particular scale score that equates to meaningful improvement for patients and their families. This is known as the minimal important difference[16] or the minimum clinically important difference (MCID). Yet, the

identification and use of the appropriate MCID raises challenges, including issues related to contextual factors, the population used to determine clinical significance, and the method used to calculate MCID.[17]

Scope and Key Questions

Although experts in the field believe that comprehensive multidisciplinary postacute rehabilitation is the best approach for addressing impairments from moderate to severe TBI, access to these services can be problematic. Health insurance reimbursement policies may limit the degree to which patients can participate in rehabilitation programs.[8, 18] Uncertainty about which patients are likely to benefit from specific rehabilitation programs contributes to lack of full coverage, and impedes advocacy efforts for appropriate care.

This uncertainty does not reflect insufficient efforts to synthesize evidence, but rather unsatisfactory conclusions. Dozens of related systematic reviews have yielded seemingly conflicting results. Differences in conclusions across reviews reflect methodological decisions about populations, outcomes, and included study designs. For instance, reviews by Cicerone et al.[19-22] are widely cited as demonstrating the effectiveness of cognitive rehabilitation. Cicerone's latest review[22] and a recent Cochrane review of multidisciplinary rehabilitation for acquired brain injury in working age adults[12] concluded that these programs improve outcomes.[12] However, a recent Institute of Medicine (IOM) review reported that the evidence on the effectiveness or comparative effectiveness of multimodal cognitive rehabilitation for moderate to severe TBI was not informative.[23] The conclusions of the IOM review drew heavily from randomized controlled trial (RCT) data and relied on a rigorous evidence assessment, while the conclusions from the Cicerone reviews were drawn from a variety of study designs and used a less rigorous evidence assessment. The Cochrane review relied on RCTs, but included studies with populations of any acquired brain injury. Outcomes selected for review can also lead to inconsistent findings across reviews. Many previous reviews appear to have based their determinations of effectiveness on any outcome measures used in the original studies.

Our review differs from prior efforts in several ways. We emphasize selected patient-centered participation outcomes of productivity and community integration, thus offering an important perspective unique from other reviews. In addition, many treatments target specific functional difficulties regardless of etiology. Therefore, rehabilitation programs often enroll both TBI patients and those with non-traumatic brain injuries (primarily stroke patients). However, stroke patients differ distinctly from TBI survivors. Further, evidence suggests that TBI patients achieve greater functional outcomes than stroke patients when matched on age and demographic characteristics.[24] Therefore, we specifically address the moderate- to severe-TBI population.

Finally, our review includes prospective cohort studies in addition to RCTs. We examine evidence of effectiveness and comparative effectiveness of multidisciplinary rehabilitation programs in restoring individuals with moderate to severe TBI to participation in their communities. Our full report provides a detailed description of this systematic review.[25] We address the following Key Questions (KQs):

Key Question 1

How have studies characterized multidisciplinary postacute rehabilitation for TBI in adults?

Key Question 2

What is the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI?

a. Do effectiveness and comparative effectiveness vary by rehabilitation timing, setting, intensity, duration, or composition?
b. Do effectiveness and comparative effectiveness vary by injury characteristics?
c. Do effectiveness and comparative effectiveness vary by patient characteristics, preinjury or postinjury?

Key Question 3

What evidence exists to establish a minimum clinically important difference (MCID) in community reintegration as measured by the Mayo-Portland Adaptability Inventory (MPAI) for postacute rehabilitation for TBI in adults?

Key Question 4

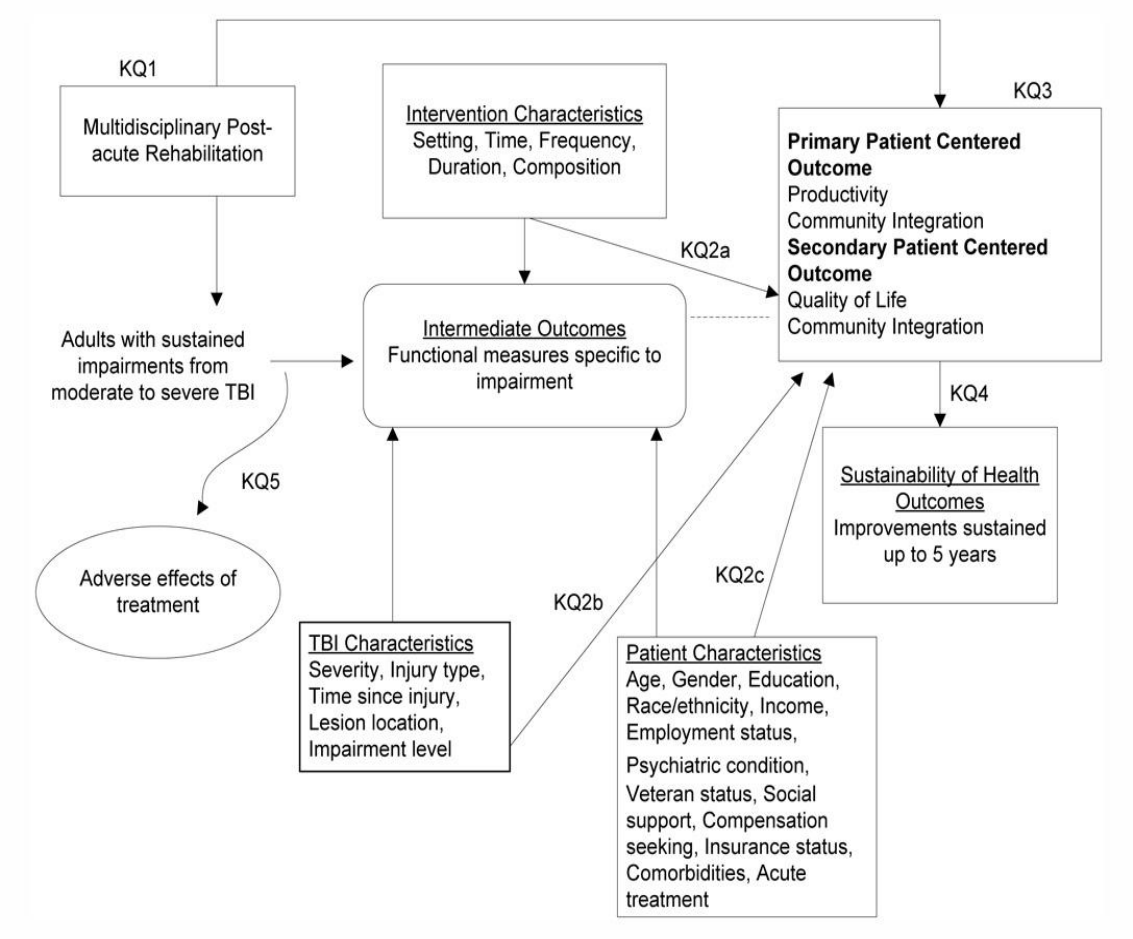
Are improvements in outcomes achieved via multidisciplinary postacute rehabilitation for TBI sustained over time?

Key Question 5

What adverse effects are associated with multidisciplinary postacute rehabilitation for TBI?

We address these KQs in the context of our analytical framework (Figure A). This framework greatly simplifies the complex process navigated by those with sustained impairments from moderate to severe TBI. For instance, spontaneous recovery may occur simultaneously with rehabilitation, which complicates efforts to distinguish natural improvements from those due to treatment.[8] Furthermore, rate of progress and level of effectiveness with rehabilitation can be affected by characteristics of patients and families, injuries and comorbidities, and interventions, and by relationships among these characteristics. Multiplicity of outcomes presents another challenge. Often, progress in response to particular therapies is monitored with measures that evaluate isolated impairments (e.g., memory, attention, or aggressive behavior). Other intermediate measures are used to assess the progress of individuals in rehabilitation settings. Finally, patient-centered outcomes evaluate the success of rehabilitation in returning TBI survivors to roles in the community.

Figure A. Analytic framework for multidisciplinary postacute rehabilitation for TBI in adults



KQ = Key Question; TBI = traumatic brain injury

Methods

Topic Refinement and Review Protocol

Our final KQs were determined after several iterations of the original publically nominated topic of rehabilitation for TBI. We recruited Key Informants representing various roles related to TBI rehabilitation, including researchers, providers in several professions, and one caretaker. Key Informants helped identify salient issues and refine the project's scope. We posted preliminary KQs for public comments, and recruited a panel of technical experts in the field. This panel recommended that we further refine the KQs to focus on comprehensive or multidisciplinary programs, and identified participation outcomes as most relevant to the evaluation of the effectiveness of these programs.

Literature Search Strategy

We developed a comprehensive search strategy consisting of a combination of controlled vocabulary and natural language terms for each bibliographic database (such as MeSH for MEDLINE), for two concepts (rehabilitation and TBI). We used filters for study design when possible. We searched the following bibliographic databases from 1980 to January 2012:

- MEDLINE
- Cochrane Central Register of Controlled Trials (CENTRAL)
- PsycINFO
- Physiotherapy Evidence Database (PEDro)

We searched for RCTs and prospective cohort studies. We supplemented this search with backwards citation searches of relevant systematic reviews. Two investigators independently reviewed each citation, and full text when deemed necessary, to determine its eligibility for inclusion. Disagreements were decided by consultation between investigators or with a third investigator. We also identified relevant systematic reviews. Studies were excluded if they:

- Had insufficient data (i.e. abstract only).
- Had no original data.
- Did not have full text available in English.
- Covered the pediatric population only.
- Reported on fewer than 75 percent patients with moderate to severe TBI.
- Did not study an intervention.
- Were not either an RCT or a prospective cohort study.
- Did not study subjects in the postacute stage.
- Only included impairment-specific interventions.
- Contained no comparison group (i.e., case series).
- Contained no relevant comparison.
- Reported no outcomes of interest for this review.

We determined relevant data fields to extract for each KQ, and data were extracted into evidence and outcomes tables by one investigator. A second investigator confirmed

for accuracy. We did not contact authors to request data not reported in the original studies.

Risk of Bias Assessment of Individual Studies

Risk of bias assessment forms were developed specifically for this project. For RCTs, we modified the Cochrane Risk of Bias Tool[26] by adding items to capture potential risk of bias specific to this topic, such as that associated with intervention definition and implementation, along with the outcomes measures used to assess effectiveness. We obtained these additional items from the RTI Observational Studies Risk of Bias and Precision Item Bank.[27] We also created a risk of bias assessment form for observational studies by selecting items from this item bank that corresponded to those in the modified Cochrane tool; we then added items to assess potential selection bias. Two investigators used the appropriate form to independently assess the risk of bias of eligible studies. Investigators assigned summary scores of low, moderate, or high based on their judgment about the collective risk of bias created by the assessments of the individual items and the magnitude of collective risk of bias created by those items. Investigators consulted to reconcile discrepancies in overall risk of bias assessments. When necessary, a third investigator was consulted.

Data Synthesis

The diversity of study settings, populations, interventions, controls, outcomes, and outcome measures precluded quantitative synthesis of results. Qualitative syntheses grouped studies by population, intervention setting or type, and outcomes in order to identify meaningful patterns. Therefore, all studies meeting inclusion criteria are used to answer KQ1, but only those with a low or moderate risk of bias are used to answer KQ2–5.

Strength of the Body of Evidence

We evaluated the overall strength of evidence (SOE) for eligible studies for each primary outcome or comparison using methods developed by the Agency for Healthcare Research and Quality (AHRQ) and its Effective Health Care Program.[28] We did not include studies with a high risk of bias when determining SOE. We evaluated SOE based on four required domains (risk of bias, consistency, directness, and precision). Two investigators worked independently to qualitatively rate each component and overall SOE. Overall assessments reflected the investigators‘ subjective assessments and relied heavily on their in-depth knowledge of each study, as well as the assessments of each component. Project team members reconciled disagreements through discussion. We rated the overall evidence for each outcome and comparison as high, moderate, low, or insufficient.

Applicability

We determined applicability by reviewing whether included characteristics of population or injury differed from those described by population studies of postacute TBI, and whether included postacute rehabilitation programs or services were those typically used or accessible in current practice.[29]

Results

Results of Literature Searches

We searched four bibliographic databases (Ovid MEDLINE, PschINFO, Cochrane CENTRAL Register of Controlled Trials and PEDro) from 1980 through January of 2012 and identified 1,681 unique references. Review of titles and abstracts identified 170 references meriting full text review. Hand searching identified 12 references meriting full text review, for a total of 182 references. Full text screening identified 16 unique studies meeting inclusion criteria. The most common reason for exclusion was the lack of a comparison group; 59 studies were excluded on this basis. Other common reasons for exclusion included the lack of an intervention, lack of a primary or secondary outcome, ineligible study design, and wrong population—not 75 percent moderate to severe TBI. The full report includes the literature flow diagram, outcomes, evidence, SOE tables, and risk of bias assessment forms and results.[25]

Key Question 1. Characterizing the Interventions

All 16 studies were used to characterize the interventions. Many studies provided limited definitions of the examined interventions. Generally, definitions or details about the content of the interventions appeared to improve over time (i.e., more recent studies provided better definitions). Table B provides a summary of various intervention characteristics. Despite the lack of a consistent taxonomy, interventions could be grouped on several levels. Studies of comprehensive or multidisciplinary approaches to moderate to severe TBI rehabilitation differed by: (1) target populations for which the interventions were designed; (2) settings; (3) methods of intervention delivery; (4) models of care used to develop the intervention; and (5) the intensity and duration of the interventions. Studies focused on evaluating new models of care, comparing different models of care, or assessing particular components added to a standard program. Four studies assessed certain rehabilitation programs and compared results to those not participating in the program.[30-33] Six studies compared new models of care being delivered by their institution or agency with the standard care typically delivered.[34-39] Five studies compared different models of care.[30, 40-43] Two studies compared an additional component added to a standard program with the standard program alone.[44, 45]

Most of the programs addressed TBI survivors whose impairments had persisted more than 6 months postinjury. However, three interventions addressed patients earlier in the postacute period, within 6 months of injury.[38, 42, 43] Two interventions began in the earlier postacute period and continued to the chronic stage.[44, 45] Other programs specifically addressed survivors of severe injuries[38, 39, 45] or military populations.[42, 43]

Programs typically engaged a similar variety of providers from several disciplines, including physiatrists, neurologists, neuropsychologists, clinical psychologists, physical and occupational therapists, speech language pathologists, recreational therapists, social workers, rehabilitation nurses, and technicians. Eight programs used models of care originally described by Ben-Yishay, Prigatano, and others.[30-32, 34, 35, 37, 41, 42] These programs were fairly structured and emphasized cognitive rehabilitation and an integrated approach to treatment. They delivered therapies to small groups of individuals that progressed through rehabilitation together. All interventions in these eight studies were

delivered as intensive daily treatments with a variety of therapy session types, primarily in groups, and with a vocational component. Most were day-treatment programs in outpatient rehabilitation centers and enrolled chronically impaired patients. However, two were residential treatment programs,[37, 42] and a single program addressed TBI survivors earlier in the postacute period.[42] Despite their many similarities, interventions based on this model of care varied in duration from 6 weeks to 6 months.

Other programs described outreach to TBI survivors;[40] community-based care;[36] specific approaches to remediation of skills;[43] multidisciplinary programs without mentioning a specific model;[38] residential communities of TBI survivors;[39] and an outdoor experiential education program.[33] Specific components of multidisciplinary programs that were studied included case management[45] and telephone counseling.[44]

Table B. Summary of postacute rehabilitation programs studied

Program Characteristics	Studies Reporting
Setting	
Inpatient rehabilitation	3[37, 42, 43]
Outpatient rehabilitation center	7[30-32, 34-36, 41]
Combination inpatient/outpatient	2[38, 45]
Home/community-based	3[33, 36, 42, 44]
Residential/transitional living	1[39]
Model of Care	
Holistic day treatment	8[30-32, 34, 35, 37, 41, 42]
Outward Bound	1[33]
Cognitive-didactic	1[43]
Functional treatment concepts	1[43]
Cognitive rehabilitation and community adaptation	1[39]
Delivery	
Small groups	10[30-35, 37, 41-43]
Individuals	9[34-36, 38, 39, 42-45]
Approximate Program Duration	
4 weeks	2[41, 43]
6 weeks	2[37, 42]
8 weeks	1[42]
16 weeks	3[30, 34, 35]
6 months	3[31-33]
9 months	1[44]

Note: This table briefly summarizes characteristics of the studied interventions. More detailed descriptions can be found in the full report.

Key Question 2. Effectiveness and Comparative Effectiveness

Of the 16 eligible studies, 12 assessed a primary outcome and 8 assessed secondary outcomes. Of the 12 studies assessing primary outcomes, 4 were judged to have a high risk of bias, and were thus excluded from analysis,[30, 32, 36, 39] leaving 8 studies (4 RCTs and 4 cohort studies) used to assess SOE. Of these eight studies, one was rated low risk of bias, and seven were rated moderate risk of bias.

Sample sizes for the eight studies ranged from 36 to 366. Six studies were conducted in the United States and two in other countries (United Kingdom and Finland). Subjects were predominantly male (85 percent) and young relative to the adult population of the United States (mean age, 31). Other demographic statistics were less often reported. Studies restricted to TBI populations often included only closed head injuries. Median time since injury varied widely among studies, from 1 to 45 months with a median of 19 months. Two studies specifically restricted enrollees to those within 3[42] or 6[43] months of injury.

Productivity. Heterogeneity in populations and comparisons across studies precluded an overall summary SOE for productivity; instead SOE was calculated for each comparison. Only one of the eligible studies assessing productivity compared the intervention to a no-treatment group.[31] This small cohort study found no significant differences in return to work between groups at a timepoint between 6 and 24 months post-treatment. However, this study was likely underpowered and did not use currently accepted methodology to adequately control for confounding; thus it provided insufficient evidence about effectiveness.

Six studies assessed comparative effectiveness with respect to productivity outcomes.[35, 37, 41-43, 45] Two larger RCTs found no productivity differences soon after injury between groups of patients in different treatment groups.[42, 43] Another single-center RCT found that a 4-month Intensive Cognitive Rehabilitation Program (ICRP) compared to standard treatment at an outpatient rehabilitation center resulted in a moderate effect size increase in productivity for chronically impaired civilian survivors of predominantly moderate to severe TBI; productivity rose among ICRP participants from 9 percent to 47 percent, and among those in standard care from 12 percent to 21 percent.[35] This difference disappeared at the 6-month post-treatment followup, by which time productivity among participants in the standard program had improved to a level (50 percent) no longer significantly different from the ICRP rate (60 percent). This provided a low SOE that the ICRP improved productivity over and above that of standard rehabilitation immediately post-treatment, but that differences were not maintained by 6 months post-treatment. We assessed SOE as low because it was derived from one moderately sized RCT with a moderate risk of bias. The remaining three studies provided insufficient evidence of comparative effectiveness.

Community integration. Neither of the two studies that evaluated community integration with the Community Integration Questionnaire (CIQ) found significant group differences in CIQ scores post-treatment (ICRP = 12.9, standard rehabilitation = 11.7 in an RCT[35]; ICRP = 16.8, standard rehabilitation = 16.1, unadjusted in a cohort study[34]), despite the authors' suggestion of greater improvement for the ICRP group.[34] The RCT detected a statistically significant increase in the CIQ score from pretreatment to post-treatment, without a significant improvement in the standard rehabilitation group. However, group differences were not statistically significant. In addition, the cohort study

detected a greater rate of clinically meaningful change in the ICRP group, with 52 percent showing clinically significant improvement (of 4.2 points) compared to 31 percent in the standard rehabilitation group. The evidence indicated that participation in ICRP versus standard rehabilitation achieved equivalent improvements in CIQ (with low SOE). We assessed SOE as low because the evidence was derived from one moderately sized RCT with a moderate risk of bias. Results from the RCT were primarily used to assess SOE because the cohort study provided unadjusted results for clinically meaningful changes.

Key Question 3. Minimal Clinically Important Differences

Because we found no studies establishing minimum clinically important differences (MCIDs) for the MPAI, we investigated the use of MCIDs with respect to the CIQ. In their pilot study of the ICRP, Cicerone and colleagues derived a "reliable change index" of 4.2 of the total CIQ score to evaluate the incidence of clinically significant changes in community integration. The authors calculated the reliable change index that indicated whether individuals made positive change, no change, or negative change in community integration based on psychometric data from a previous sample of TBI patients. Changes were considered reliable changes if they exceeded the 90 percent confidence interval. However, in a later RCT, the same authors evaluated the ICRP but did not use a reliable change index when evaluating effectiveness.[35]

Key Question 4. Sustainability of Intervention Effectiveness

Two primary outcomes studies incorporated followup outcome measurements.[35, 45] These data provided a low SOE that outcomes achieved during rehabilitation did not deteriorate between the timepoints studied. We assessed SOE as low for these comparisons, because each was derived from one moderately sized RCT with a moderate risk of bias.

Key Question 5. Adverse Events

The single study (low risk of bias) that mentioned adverse events reported that no adverse events were observed.[43]

Discussion

Key Findings and Strength of Evidence

The evidence we reviewed emphasized the complexity of TBIs and of the interventions to rehabilitate individuals suffering from associated sustained impairments. While several studies have addressed this topic, the heterogeneity of the populations studied (in terms of time since injury, injury severity, impairment types and severity, and interventions) precluded combining studies to draw broader conclusions or to strengthen evidence. This is largely a result of the complexity of the condition and of the interventions and not a weakness of the included studies.

We first sought to assess how these multidisciplinary postacute rehabilitation programs were characterized in the eligible studies. Studies of multidisciplinary postacute

rehabilitation often fail to define interventions sufficiently. Newer studies provide more useful definitions than those published prior to 2000. Still, it remains difficult to decipher what the individual components of the program entailed and how, when, and why individuals received specific therapies. We recognize that such detailed definitions are not generally included in journal articles, yet we found few references to manuals containing treatment content or algorithms.

Our review, like others, found the currently available evidence insufficient to draw conclusions about the effectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI. Although we found stronger evidence on the comparative effectiveness of different approaches to multidisciplinary postacute rehabilitation for participation outcomes, we found a limited number of eligible studies and no clear demonstration that one approach was superior to another. Table C summarizes our conclusions regarding comparative effectiveness.

Many of the eligible comparative effectiveness studies demonstrated improvements in patient-centered outcomes in all treated groups. However, the available evidence showed no clear benefit of one approach over another. Two studies demonstrated equivalent participation results in comparison groups with regard to productivity; however, these equivalent results may be an embodiment of the context in which the studies were conducted. For instance, Salazar, et al. enrolled patients whose functional status and social support was sufficient to allow for randomization to home care.[42] Thus, the fact that this group experienced similar improvements to those randomized to inpatient rehabilitation may be specific to their relatively low level of impairment. Validating this possibility, the authors‘ post hoc subgroup analysis of those with more serious injuries found greater improvements from inpatient rehabilitation. A similar situation occurred in the Vanderploeg study, in which certain patient subgroups fared better with one rehabilitation approach versus the other as detected in post hoc analysis.[43] Similar findings relevant to a specific subgroup are evident with regard to the CIQ.[34] The prospective cohort study delivered the ICRP to a more chronically impaired group and achieved a greater rate of clinically significant improvement, suggesting that this approach might be better suited to these individuals. Yet, it could be that this group made more improvements because its members had accumulated more total hours of rehabilitation during this longer timeframe. Although these programs achieved equivalent outcomes, the studies also hinted at possibilities that different patient subgroups responded better to certain types of treatments. While conclusions cannot be drawn from these subgroup analyses, they do emphasize that patients might best be rehabilitated when matched to the program most likely to benefit them. Future research to identify and test hypothesized combinations between patient types and intervention approaches would have important clinical implications.

Evidence suggested that the ICRP may lead to earlier productivity than standard rehabilitation (low SOE). However, evidence also indicated that rates of productivity between groups were not significantly different at 6 months post-treatment (low SOE). Only one eligible study used an MCID to assess effectiveness. This study suggested that a 4.2 change in CIQ score is necessary for meaningful improvement.[34] Improvements in participation measures were sustained 6 months post-treatment for all treatment groups (low SOE), however, no group differences were observed. Few studies addressed harms related to rehabilitation with one study reporting that no harms were observed.

Conducting and synthesizing research on this topic is impeded by the complexity of the condition, the significant number of variables and interactions among variables that affect recovery and rehabilitation outcomes (comorbidities, social support, impairment levels, etc.), and by the complexity of the associated interventions. These factors heighten the challenge faced by primary research in achieving the high SOE required for robust conclusions about effectiveness.

The outcomes selected for this review reflect current views on the importance of social participation as an outcome of rehabilitation. Arguments can be made for the importance of other outcomes. However, the recent IOM review, which considered the outcomes of cognitive functioning, quality of life, and functional status, reached conclusions similar to ours.[23]

Table C. Summary and strength of evidence (SOE) of effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI

Population	Intervention/Comparator	Outcome	Conclusion	SOE
Active-duty military personnel with moderate to severe closed head injury treated within 3 months of injury (Salazar 2000)[42]	Inpatient hospital rehabilitation program (8 weeks) vs. limited home treatment	Return to gainful employment at 1 year post-treatment	No difference between groups	Low (moderate risk of bias, single study)
		Fitness for military duty at 1 year post-treatment	No difference between groups	Low (moderate risk of bias, imprecise, single study)
Veterans or active duty military personnel with moderate to severe closed head injury treated within 6 months of injury (Vanderploeg 2008)[43]	Functional-experiential vs. Cognitive-didactic rehabilitation programs for varying durations	Return to gainful employment at 1-year post-treatment	No difference between groups	Low (low risk of bias, imprecise, single study)
Chronically impaired patients with primarily moderate to severe TBI (Cicerone 2004; Cicerone 2008)[34, 35]	Intensive cognitive rehabilitation (16 weeks) vs. standard rehabilitation (16 weeks)	Community-based employment at end of treatment	Statistically higher proportion Intensive cognitive rehabilitation group employed	Low (moderate risk of bias, single study)
		Community-based employment at 6 months post-treatment	No difference between groups	Low (moderate risk of bias, single study)
		CIQ at end of treatment	No difference between groups	Low (moderate risk of bias, imprecise, consistent)
		CIQ at 6 months post-treatment	No difference between groups	Low (moderate risk of bias, single study)

CIQ = Community Integration Questionnaire; SOE = strength of evidence; TBI = traumatic brain injury.
Note: This table presents a summary of the findings for this systematic review.

Applicability

The studies evaluated for this review may be applicable to the specific populations targeted by the examined interventions (e.g. military populations, those with significant disabilities, those without other psychiatric diagnoses, chronically impaired populations, etc.), and the time periods in which they were studied. Even then, many of the interventions and control conditions seemed to be embodiments of their local rehabilitation systems, making replicability in other contexts challenging. This is especially evident in studies of military and Veterans Affairs health systems, in which rehabilitation services may differ markedly from those available in civilian facilities. Because rehabilitation for TBI is a rapidly evolving field, studies conducted in the 1980s and 1990s may not be applicable to current rehabilitation programs. Additionally, most studies excluded individuals with substance abuse or psychiatric diagnoses, both of which are common in the TBI population.[46] Inconsistent insurance coverage for rehabilitation[8] may limit applicability of these results. TBI disproportionately affects males, those ages 15 to 24, and those of lower socioeconomic status,[9] all groups recognized to have lower rates of health insurance. Knowledge of which treatments are most effective is less likely to benefit those who lack insurance coverage to receive the services.

Research Gaps

Despite many attempts to synthesize evidence relevant to the effectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI in adults, research gaps remain. Additional comparative effectiveness reviews cannot bridge these gaps until additional high quality studies are completed. A followup study and report outlining the future research needs for this topic is forthcoming. Conceptual work to overcome the shortcomings of current research may be the highest priority. Formal research synthesis efforts should aim to identify combinations of patient groups and rehabilitation approaches most likely to achieve success. Effectiveness trials can then be conducted to test hypothesized relationships. Efficacy research requires a no-treatment control and is unlikely to be conducted due to ethical concerns. However, comparative effectiveness studies may be more feasible, and the idea of waitlist controls more amenable, in studies of chronic impairments.

Conceptual work could help advance knowledge in the field. For example, the development and consistent use of taxonomies of TBI impairments and treatments could foster consistent reporting in research. This would enable researchers to better define impairment domains and levels of impairment, which is critical to understanding which interventions work best for which patients. Additionally, as with many postacute rehabilitation topics, the taxonomy of treatment is underdeveloped.[47] Future research should continue to engage relevant disciplines to advance the development and consistent use of a taxonomy for rehabilitation interventions. This taxonomy would enhance patients‘ understanding of rehabilitation programs and enable more informed decisionmaking.

Evidence regarding effectiveness is needed from RCTs and well-designed cohort studies; in particular, regarding which programs work for which impairments and types of patients or injuries. However, additional small-scale RCTs may not move the field forward toward a substantially stronger evidence base. Progress towards a stronger evidence base will require addressing common methodological weaknesses, including (1) specificity of study populations, interventions and comparators, and outcomes used to measure effectiveness, and (2) small sample sizes. Larger studies may be able to address many of the current gaps. For example, the

data collected about patients, injuries, and interventions from larger sample sizes in RCTs could be used to statistically control for the many confounding variables inherent in this complex condition and relevant interventions, when randomization does not achieve balanced groups.

Additionally, alternative approaches proposed as better suited for studying the comparative effectiveness of complex interventions should be further pursued. These studies are likely more feasible and relevant for TBI rehabilitation effectiveness research. The practice-based evidence approach[48] could help overcome certain shortcomings of the available research. This approach incorporates a prospective cohort design and allows for multiple concurrent interventions and inclusion of diverse patient populations and treatment settings. Heterogeneity is controlled for statistically. Studies with much larger sample sizes, enhanced applicability, and rich data to answer the question "What works for whom?" would address many of the knowledge gaps regarding the effectiveness of TBI rehabilitation

Several additional methodological concerns should be addressed in future research on TBI rehabilitation. First, related to larger sample sizes, studies must be appropriately powered to detect differences between treatment groups. Methodological problems in cohort studies often relate to the selection of the comparison group. Planners of cohort studies should carefully select comparison groups as similar as possible to the treatment group. While blinding of participants and providers may not be feasible, outcomes assessors can and should be blinded. Risk of bias could be reduced by adequately defining interventions and ensuring the effective implementation of the interventions and controls. Finally, a lower risk of bias related to outcomes in these intervention studies could be achieved by selecting a priori primary patient-centered outcomes; limiting the number of outcomes scales and comparisons; using consistent and appropriate psychometrically justifiable outcomes scales; establishing MCIDs in these scales; and adjusting for multiple comparisons. All these steps would help create a stronger evidence base.

Aside from questions about enhancing the groundwork and methodology of intervention studies, several additional research questions should be addressed. One question involves timing to treatment effect. Studies we reviewed demonstrated similar outcomes across treatment groups at 1-year followup intervals, but we could not decipher whether treatments yielded similar outcomes throughout the postintervention interval, or whether timing to effect differed between the groups but equalized prior to measurement.

Additionally, we identified few studies that addressed the sustainability of intervention effectiveness. Because impairments sustained from TBI may persist for several years, researchers should collect longer-term followup data on patient-centered outcomes measures. The most frequently studied programs used the comprehensive holistic day-treatment model of care. Given the apparent support for this approach in the TBI community, additional studies should be undertaken to compare this approach with standard rehabilitation programs. Because recent consensus development efforts (e.g., the Common Data Elements TBI Outcomes Workgroup) have recommended certain outcomes for use in research on these topics,[49] future studies should incorporate these measures into their effectiveness research. Further guidance that would match measures most appropriate for specific patients and interventions (e.g., through a complex conceptual model) would enhance the utility of this consensus recommendation.

The TBI Model Systems programs offer settings and populations for conducting patient-centered outcomes research on rehabilitation topics.[50] However, effectiveness research is not the primary mission of the program, and obstacles stand in the way of conducting high quality intervention studies in these settings. Additional incentives and resources could enhance the usefulness of the model systems programs for conducting intervention studies.

Ultimately, the available evidence provides little information about the overall effectiveness or comparative effectiveness of postacute multidisciplinary rehabilitation for adults with for moderate to severe TBI. **However, our failure to draw broad conclusions must not be misunderstood to be evidence of ineffectiveness.** This topic, like many other complex topics, merely lacks high quality conclusive evidence of effectiveness or ineffectiveness from rigorously conducted systematic reviews. This type of evidence is a high bar currently met by only a small portion of medical interventions (and an even smaller portion of rehabilitation interventions). The limited evidence on this topic stems from the fact that the complexity of the condition and treatments results in limited research, and from the limitations within that research of ability to answer salient research questions about what works for which patients. In light of the attention dedicated to this topic, demonstrated by the number of recent reviews and media stories, future research to better establish the evidence base for rehabilitation interventions for the TBI population is of utmost importance.

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Introduction

Background

Definition and Severity of Traumatic Brain Injury

Traumatic brain injury (TBI) is an alteration in brain function or other evidence of brain pathology caused by an external force.[1] TBI is a significant public health issue in the United States, with an estimated 1.7 million TBIs per year from 2002 to 2006.[2] Of those injured each year from 2002 to 2006, 1.37 million were treated and released from emergency departments, 275,000 were hospitalized, and 50,000 died from their injuries.[2] Additional TBIs not reflected in these numbers are treated in primary care settings and in Federal, military, and Veterans Affairs hospitals. The Department of Defense reported over 4,500 moderate to severe TBIs among all service members in 2010.[3] Incidence is highest among children, adolescents, and young adults, but hospitalization and death occur most often among those age 75 and older.[4] Major causes of TBIs include falls (35.2 percent), motor vehicle crashes (17.3 percent), struck by/against events (16.5 percent), assaults (10 percent), and other/unknown (21 percent); and, for military personnel or survivors of terrorist attacks, explosions/blasts. Blast incidents account for the majority of combat injuries, 60 percent of which result in TBI.[4, 5]

TBIs are categorized as mild, moderate, or severe according to acute injury characteristics that suggest the extent of damage to the brain. Multiple measures are used to assess severity, including structural imaging findings; duration of loss of consciousness, altered consciousness and/or post-traumatic amnesia; the Glasgow Coma Scale (GCS) score; and the Abbreviated Injury Severity Scale score.[6] The GCS is the most widely used scale to determine injury severity. However, GCS has significant limitations. For example, it is used at several timepoints, and studies of TBI do not always report which GCS measurement timepoint was used to assess severity. Additionally, GCS may not be the most accurate determinant of severity. Certain acute interventions such as intubation or specific medications can compromise the accuracy of the GCS score.[7] Some experts have begun to support the use of other measures for severity based on research suggesting that loss of consciousness and posttraumatic amnesia may better predict functional status.[7] Table 1 lists the various criteria and commonly used cut points for evaluating TBI severity:

- Structural imaging findings
- Duration of loss of consciousness
- Duration of altered consciousness
- Duration of post-traumatic amnesia
- Glasgow Coma Scale score

Table 1. Criteria used to classify TBI severity[4]

Criteria	Mild	Moderate	Severe
Structural Imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness	< 30 minutes	30 minutes to 24 hours	>24 hours
Alteration of Consciousness/ Mental State	A moment to 24 hours	>24 hours	>24 hours
Post-traumatic Amnesia	0–1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (best available score in 24 hours)	13–15	9–12	3–8

TBI = traumatic brain injury.
Note: This table describes the predominant ways in which TBI severity is assessed.

Sustained Impairments From Moderate to Severe TBI

Moderate to severe TBIs more often require intensive medical care, and 40 percent of those hospitalized with nonfatal moderate to severe TBI sustain impairments that lead to long-term disability.[6] The Institute of Medicine (IOM) recently conducted a systematic review to identify long-term outcomes following TBI, which include seizures, growth hormone insufficiency, Alzheimer's disease, endocrine dysfunction, Parkinsonism, adverse social functioning, neurocognitive deficits, diabetes insipidus, psychosis, and premature death.[4] These outcomes have led some to encourage classifying TBI as the beginning of an ongoing, perhaps lifelong process, that affects multiple organ systems and may cause and accelerate disease.[8] By one estimate, two percent of the U.S. population lives with TBI-related disabilities, presumably from moderate to severe TBI.[9]

Different injury types and severity levels are associated with specific impairments. For example, penetrating head injuries can result in cognitive decline related to injury location and amount of tissue lost;[4] these injuries are associated with long-term unemployment and deficits similar to those observed in stroke patients.[10] Closed head injuries, which are more common, result in diffuse brain damage that leads to impairments unique to the individual.[10] Evidence suggests that long-lasting effects of moderate to severe TBI include cognitive deficits, psychiatric outcomes (depressive and aggressive behaviors, posttraumatic stress disorder in military populations, and psychoses), and social functioning (unemployment and diminished social relationships).[11]

Specifically, sustained *physical* impairments may reduce endurance, cause headaches and seizures, and affect muscle tone, vision, hearing, smell, taste, and speech.[12] Sustained *cognitive* deficits may affect memory, attention, judgment, communication, planning, and spatial orientation.[12] Sustained *affective/behavioral* impairments include changes in mood, behavior, or personality that manifest as impulsiveness, passivity, agitation, loss of empathy, or emotional lability.[10] The constellation of impairments following moderate to severe TBI can impede function and societal participation for months or years after injury.[10]

The degree of heterogeneity in number, types, and severity of impairments from moderate to severe TBI in adults must be noted. Many factors contribute to the wide range of impairments and impairment severity including injury type, extent and location of the brain tissue damaged, and patient factors such as age. Additionally, because TBI results from incidents such as motor vehicle crashes or blasts, TBI patients often have other injuries. Other injuries also occur frequently among certain population groups, such as falls in older individuals more likely to be living with preexisting conditions. Certain injuries occur under circumstances that initiate other disease processes, such as post-traumatic stress disorder. These factors and the interactions among them can affect recovery and response to rehabilitation, which creates challenges for intervention research on this topic.

Spontaneous Recovery

Spontaneous recovery refers to the restoration of function that naturally occurs after a brain injury. Controversy persists around the period and extent of spontaneous recovery after moderate to severe TBI. It is clear that some recovery of function occurs following traumatic brain injury,

even with no rehabilitation.[10] Additionally, certain psychiatric impairments may become more apparent several years postinjury.[11]

Treatment for Moderate to Severe TBI

Patients with moderate to severe TBI are typically treated first in acute medical settings for a duration that depends on injury severity, impairment level, other injuries, patient age, and specific patient and healthcare system characteristics. Once the patient is medically stable, postacute care including rehabilitation may occur. This review includes any rehabilitation that occurs after acute medical treatment is complete; patients are medically stable, and able to participate in intensive rehabilitation programs. Those with multiple long-lasting impairments might participate in impairment-specific therapies, such as memory training. This report does not address such impairment-specific therapies. Those with multiple long-lasting impairments may enter multidisciplinary or comprehensive postacute rehabilitation programs.

Multidisciplinary Postacute Rehabilitation

Postacute rehabilitation programs address sustained impairments across physical, cognitive, and affective/behavioral domains and strive to improve functioning and participation. During the 1970s and ‘80s, research emerged suggesting that domain-specific training may be insufficient to rehabilitate those with damage to the frontal lobe.[13] Spurred by these findings, clinicians began to adopt holistic approaches to TBI rehabilitation, including vocational and neurobehavioral interventions that incorporate arranged work trials.[13] While a standard definition for these comprehensive programs does not exist, the current preferred approach is multidisciplinary, with treatments (including for comorbidities) integrated across disciplines or impairment domains.

A recent systematic review of multidisciplinary rehabilitation post brain injury defines ―multidisciplinary‖ as more than one discipline working in coordination.[14] In the literature, these programs are described by a variety of terms including multidisciplinary, interdisciplinary, comprehensive, holistic, neurobehavioral, neurorehabilitation, and integrated. Multidisciplinary teams often include physiatrists; neurologists; neuropsychologists; clinical psychologists; physical and occupational therapists; speech language pathologists; recreational therapists; social workers; rehabilitation nurses; and technicians. Multidisciplinary programs differ in their settings, components, emphases, and degree of structure. Furthermore, an individual‘s sustained impairments may largely determine the composition, intensity, and duration of rehabilitation. While there appears to be a general understanding that comprehensive programs are comprised of many different professionals working as a team, it is difficult to find program descriptions that specify percentages or doses of the various available therapies. Instead, programs are often variable and seen as a function of specific patients‘ presumed needs.

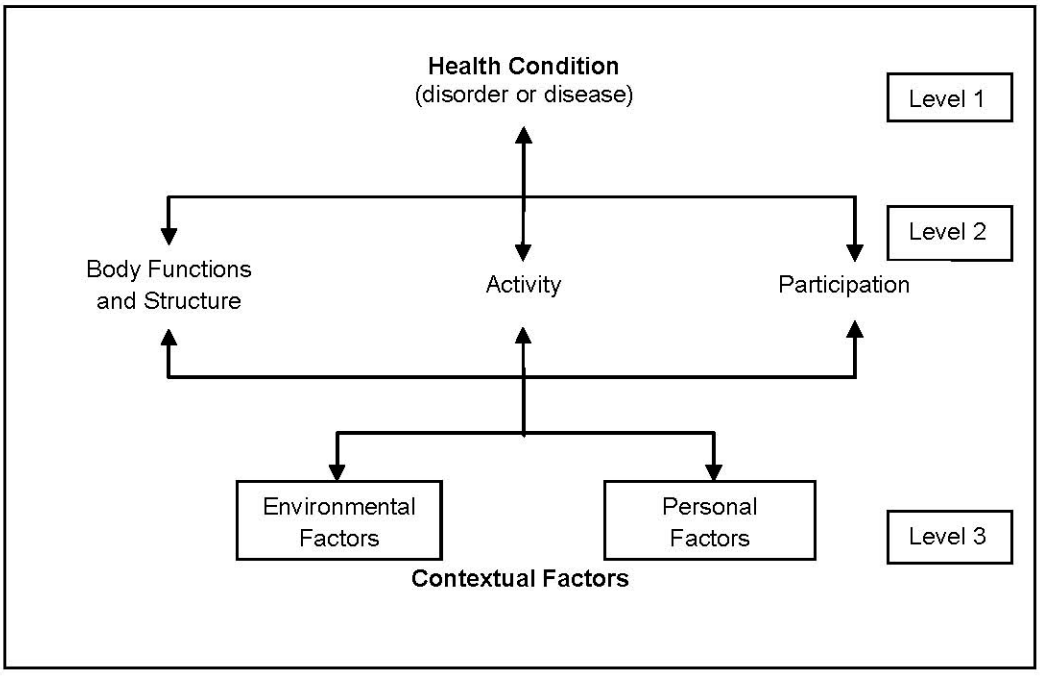
Multidisciplinary rehabilitation programs for brain injury lack a clear and consistent taxonomy.[14] Malec and Basford describe four types of programs: neurobehavioral, residential community reintegration, comprehensive (holistic) day treatment, and outpatient community re-entry. Neurobehavioral programs provide behavioral interventions for patients with significant behavioral disturbances.[15] Residential community reintegration programs treat those who either lack access to outpatient services, or have impairments that preclude it. These programs integrate cognitive, emotional, behavioral, physical, and vocational rehabilitation. Malec defines comprehensive (holistic) day treatment programs as those that offer integrated multimodal rehabilitation emphasizing self-awareness.[15] Outpatient community reintegration programs offer circumscribed rehabilitation treatments and vocational and social reintegration.[15] Depending on

impairment type and access, individuals may or may not participate in postacute rehabilitation, or may cycle through several programs. Adults with TBI who are not enrolled in a specific program may instead participate in community-based rehabilitation services.[15]

Outcomes of Postacute Rehabilitation

Clinicians and researchers have used various outcomes measures to assess the effectiveness of postacute rehabilitation. Patient-centered outcomes are those valued by patients.[16] Patient-centered outcomes for rehabilitation of moderate to severe TBI impairments likely reflect the participation domain of the International Classification of Functioning, Disability, and Health (ICF) framework, created to classify and assess function and disability associated with health conditions.[17] This multidimensional framework (Figure 1): (1) rests on a positive description of human functioning rather than emphasizing the negative consequences of disease; (2) incorporates several levels of influence; and (3) attempts to explicitly acknowledge the dynamic nature of disablement, which fluctuates based on a number of contributing factors across stages of recovery. The ICF emphasizes the complex way in which condition and contextual factors may modify outcomes including participation. One study examined this complexity by conducting pathway analysis of a sample of severe TBI patients to explore the causal, predictive relationships that affect outcomes after TBI.[18] Their modeling suggested that cognitive status and premorbid status were important predictors of outcomes, and that these factors may be more important than injury severity for longer term outcomes such as participation. Nonetheless, participation remains a widely recognized goal of rehabilitation, despite many factors that may influence this outcome.[19-21]

Figure 1. The International Classification of Function, Disability, and Health (ICF)



Ultimately, survivors of TBI and their families hope for reintegration into previous roles and activities. Therefore, the goal of TBI rehabilitation is to help patients resume meaningful participation in their homes and social environments, regardless of whether specific impairments

can be eliminated.[20] For many brain injury survivors, a final goal of community integration may be to return to work, school, or training, all of which are often classified as "productivity" outcomes. Additionally, researchers and practitioners agree that "community integration" outcomes, related to the resumption of societal roles, are important indicators of effectiveness for TBI rehabilitation.[20]

Several scales are available for assessing community reintegration in the brain injury population, such as the Mayo-Portland Adaptability Index (MPAI)[22] and the Community Integration Questionnaire (CIQ)[23]. However, interpreting whether scale score changes are meaningful presents a challenge. Research using scale scores as outcomes is complicated because we don't know exactly what statistically significant changes in scale scores mean clinically to patients. It is imperative to identify the level of change in a particular scale score that equates to a meaningful improvement for patients and their families. Interpreting effectiveness and comparative effectiveness hinges on adequately understanding this meaningful level of change, often called the minimal important difference or the minimum clinically important difference (MCID). MCID has been defined as the smallest difference in an outcome scale that can be perceived by patients as being beneficial.[24] However, the identification and use of MCID raises challenges as well, such as the applicability of the context and methodology in which MCID is established.[25]

Decisional Dilemmas

Treatment decisions for those with impairments from moderate to severe TBI are complex. First, the research on this topic is limited and lacks conclusive findings. This is understandable given the relative newness of the practice of rehabilitation for TBI,[26] and the challenges associated with studying complex conditions and interventions. This complexity makes it difficult for studies to offer clear evidence about which treatments are necessary, when, and for whom. Experts in the field support comprehensive multidisciplinary postacute rehabilitation as the best approach for addressing impairments from moderate to severe TBI. However, access is problematic. Inconsistent health insurance reimbursement policies may limit access to rehabilitation. Lack of coverage may be a problem of particular concern for those who are in the chronic phases of recovery or who need specific types of rehabilitation, such as cognitive rehabilitation.[10, 27] Uncertainty about which patients are likely to benefit from specific rehabilitation programs may contribute to lack of full coverage.

Reimbursement policies for brain injury rehabilitation remain contentious, as demonstrated by the widely publicized 2010 media investigation into Tricare's coverage for cognitive rehabilitation in brain injured soldiers and the related systematic review.[28] Lack of conclusive evidence for effectiveness has also confounded ongoing efforts to advocate for appropriate care coverage. Improved understanding of which patients are likely to benefit from which rehabilitation programs would provide justification for appropriate insurance coverage.

Focus of Review

Persistent decisional dilemmas regarding the effectiveness of rehabilitation for moderate to severe TBI do not reflect a lack of attempts to synthesize evidence. Dozens of systematic reviews have evaluated the effectiveness of rehabilitation for brain injury, with more than 10 completed since 2009. Several are directly relevant to this review:

- The Cochrane Collaborative recently updated their previous review[29] of the effectiveness of multidisciplinary postacute rehabilitation for all severities of acquired brain injury (ABI),

which comprises TBI patients as well as those who have suffered strokes and other brain injuries.[14] The first version of the Cochrane review was supplemented with one comparing study eligibility criteria.[30]

- Several reviews examine various settings for brain-injury rehabilitation. Geurtsen et al. reviewed and compared comprehensive rehabilitation programs in the chronic phase after severe brain injury.[31] Doig et al. compared day hospital versus home-based rehabilitation settings for brain injury.[32] Evans and Brewis evaluated the efficacy of community-based rehabilitation programs.[33]
- The most common sustained impairments from TBI are cognitive and behavioral in nature, thus several recent reviews of related treatments are salient to our report. Cicerone recently updated previous reviews[34-36] of cognitive rehabilitation effectiveness for brain injury.[37] The updated review concluded that comprehensive integrated neuropsychologic rehabilitation can improve community integration, functional independence, and productivity, even for those who are many years postinjury.[37] The Institute of Medicine recently released the prepublication version of their comprehensive evidence review of cognitive rehabilitation for TBI (sponsored by the Department of Defense) in October 2011.[38] This review concluded that the evidence was not informative regarding the efficacy of multimodal programs on cognitive functioning, quality of life, functional status, or sustainability of treatment effects. While not quite as recent, the controversial[28] 2009 Emergency Care Research Institute (ECRI) review[39] on cognitive rehabilitation for TBI (also sponsored by the Department of Defense) provides context for the renewed and lasting interest in determining effectiveness via systematic review. This review concluded that the evidence on cognitive rehabilitation therapy to treat multiple deficits versus alternative treatments was insufficient to draw conclusions. The review also found that comprehensive holistic cognitive rehabilitation versus alternative treatment improved quality of life measures with a small effect size (low SOE), but results for return to work were inconclusive. The ECRI review sparked controversy when it was cited in a media investigation of insurance coverage for cognitive rehabilitation among injured soldiers. TBI experts criticized the limitations on study design (RCTs only) imposed by the review.[28] Finally, Cattelani reviewed treatments for behavioral impairments after ABI and concluded that comprehensive holistic rehabilitation programs are effective in treating people with acquired neurobehavioral impairments and psychosocial problems.[40,41]
- Two recently completed systematic reviews have similarly focused on community integration.[42, 43] One of these is a "module" developed by the Evidence-Based Review of Moderate to Severe Acquired Brain Injury (ABIER) project. ABIER sponsors, conducts, and publishes ongoing modules on various brain injury rehabilitation topics.[44] Their Community Integration module concluded that more intense and structured cognitive rehabilitation in both group and individual settings improve cognitive functioning and satisfaction with community integration compared to standard, less structured multidisciplinary rehabilitation. They further concluded that multidisciplinary rehabilitation program may enhance return to driving postinjury.
- Other highly relevant ABIER reports have evaluated the efficacy of various models of care, one on cognitive interventions, and one on communication interventions. Each made several highly specific conclusions about effectiveness:[44]

- *Inpatient Rehabilitation Conclusions:* Intensive rehabilitation is associated with improved functional outcomes at 2 and 3 months after discharge, but not necessarily at 6 months and beyond.
- Multidisciplinary inpatient rehabilitation may be more effective than a single discipline approach.
- Early rehabilitation is associated with better outcomes (shorter comas and lengths of stay, higher cognitive levels, better Functional Independence Measure (FIM) scores, greater likelihood of discharge to home).
- Inpatient rehabilitation results in a higher rate of change on functional measures in patients aged 18 to 54 than patients aged 55 or older.
- Transitional living settings during the last weeks of inpatient rehabilitation are associated with greater independence than inpatient rehabilitation alone.
- *Outpatient Rehabilitation Conclusions:* Structured multidisciplinary rehabilitation in community settings can improve social functioning.

The complexity of this condition and associated interventions requires more contextualization of the evidence than has been provided by previous reviews. Therefore, in addition to assessing the effectiveness of interventions, we sought to evaluate how and why the data contribute to answering important questions. For example, many treatments target specific functional difficulties, and thus intervention programs often enroll both TBI and non-TBI patients. However, the non-TBI population consists largely of stroke patients, who differ distinctly from TBI survivors. Additionally, evidence suggests that TBI patients achieve greater functional outcomes when matched on age and demographic characteristics.[45] Therefore, we specifically address the TBI population and exclude studies with a significant number of subjects with non-traumatic acquired brain injuries (i.e. stroke or aneurysm patients).

This complexity also affects RCTs, making them more complicated to conduct and possibly restrict enrollment in ways that limit applicability of results. It is therefore important to include well-designed observational studies in this review. Additionally, clearly defined primary outcomes are necessary to ensure quality in a systematic review.[46] Inadequately defined outcomes can result in unreliable conclusions, especially when an abundance of outcome measures are used in individual studies. Previous systematic reviews have not always prespecified primary outcomes, and may suffer from bias created by multiple comparisons.[47] Therefore, we restricted our review to studies evaluating the patient-centered outcomes of productivity and community integration, and identified specific variables and scales a priori. Conclusions based on these outcomes reflect the priorities of patients and their families. Finally, our review includes prospective cohort studies as opposed to restricting eligibility to RCTs. This review examines evidence of effectiveness and comparative effectiveness of multidisciplinary rehabilitation programs in restoring individuals with moderate to severe TBI to active participation in their communities. We address the following Key Questions:

Key Questions

Key Question 1

How have studies characterized multidisciplinary postacute rehabilitation for TBI in adults?

Key Question 2

What is the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI?

a. Do effectiveness and comparative effectiveness vary by rehabilitation timing, setting, intensity, duration, or composition?
b. Do effectiveness and comparative effectiveness vary by injury characteristics?
c. Do effectiveness and comparative effectiveness vary by patient characteristics, preinjury or postinjury?

Key Question 3

What evidence exists to establish a minimum clinically important difference in community reintegration as measured by the Mayo-Portland Adaptability Inventory (MPAI-4) for postacute rehabilitation for TBI in adults?

Key Question 4

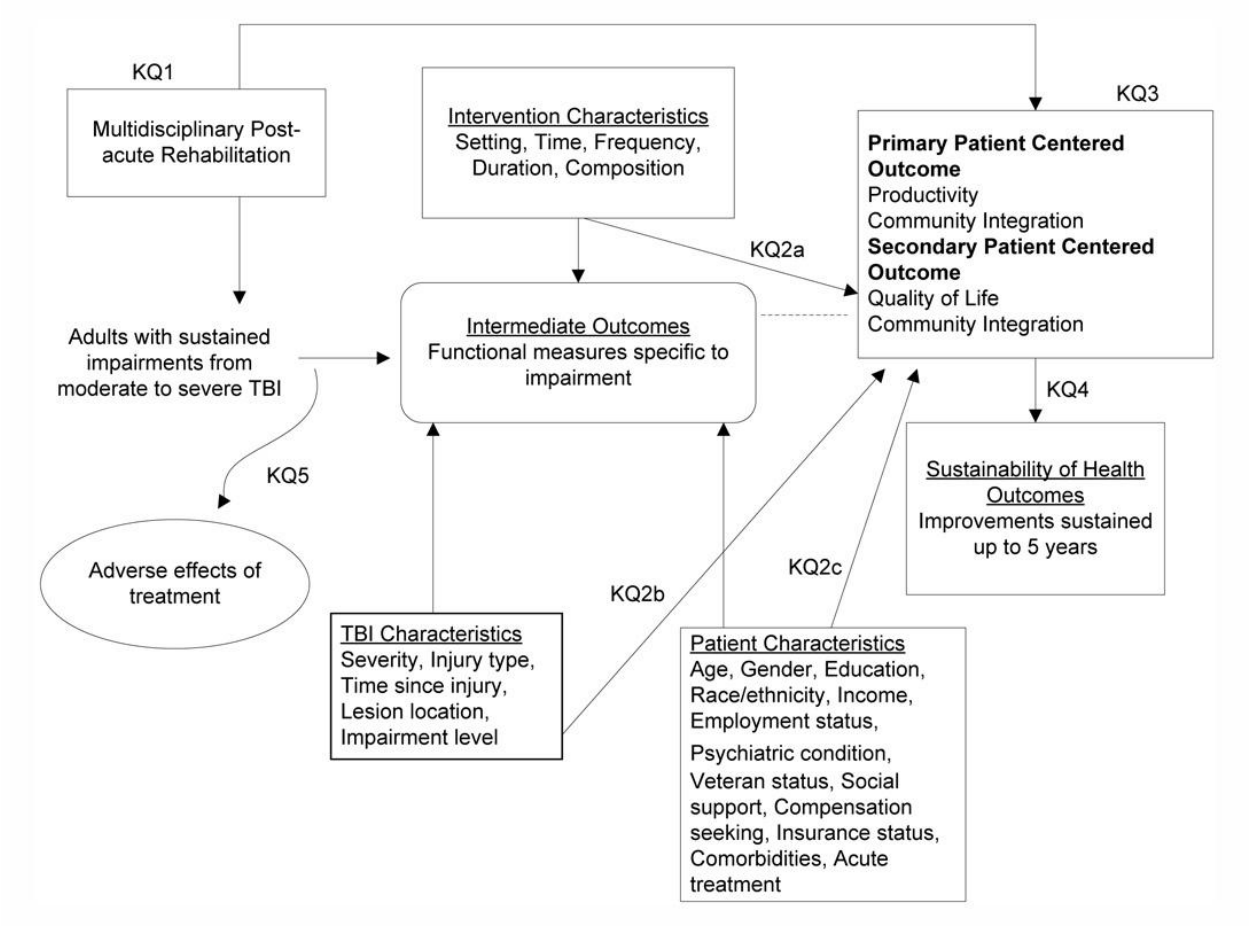
Are improvements in outcomes achieved via multidisciplinary postacute rehabilitation for TBI sustained over time?

Key Question 5

What adverse effects are associated with multidisciplinary postacute rehabilitation for TBI?

We address these Key Questions in the context of our analytical framework (Figure 2). This framework greatly simplifies the complex process navigated by those with sustained impairments from moderate to severe TBI. For instance, spontaneous recovery may occur simultaneously with rehabilitation, which complicates efforts to distinguish natural improvements from those due to treatment.[10] Furthermore, rate of progress and level of effectiveness with rehabilitation can be affected by characteristics of patients and families, injuries and comorbidities, and interventions, and by relationships between these characteristics. Multiplicity of outcomes presents another challenge. Often, progress in response to particular therapies is monitored with measures that evaluate isolated impairments (e.g., memory, attention, or aggressive behavior). Other intermediate measures are used to assess the progress of individuals in rehabilitation settings. Finally, patient-centered outcomes evaluate the success of rehabilitation in returning TBI survivors to roles in the community.

Figure 2. Analytic framework



Methods

Topic Refinement

The initial topic of rehabilitation for TBI for this comparative effectiveness review was nominated to the Effective Healthcare Program through a public process. The topic development materials and our conversations with AHRQ and the nominator clarified the intent of the nomination as follows: to evaluate all forms or types of rehabilitation for all ages and severity levels of TBI, with an emphasis on rehabilitation services provided more than 6 months after the initial injury. Subsequent to the nomination, we recruited Key Informants, including content experts, who cautioned against a review of all ages and severity levels because these are separate bodies of evidence. Specifically, TBI in children and early adolescents is associated with additional complications caused by early stages of brain development.[10] Additionally, any impairments sustained after mild TBI tend to differ from those related to moderate to severe TBI.[4] Key Informants also argued against an arbitrary 6-month cutoff, emphasizing that rehabilitation timing is unique to each injury. They suggested a more meaningful clinical designation, such as postacute reflecting the time in which patients were considered medically stable and ready to participate in rehabilitation. We formulated initial Key Questions with information gleaned from Key Informant discussions and preliminary literature searching, while maintaining the intent of the original nomination. After approval from AHRQ, we posted preliminary Key Questions to the public Effective Healthcare website. These questions proposed evaluating evidence of effectiveness or comparative effectiveness for most types of postacute rehabilitation (any intervention addressing sustained cognitive, physical, or behavioral impairments) at the specific intervention level or overall program level.

The public comment period provided valuable feedback to our Key Questions, especially: (1) that our proposed scope was excessively broad and might result in conclusions with little meaning; and (2) that multidisciplinary rehabilitation is the commonly accepted approach to sustained impairments from moderate to severe TBI. Based on this feedback—with which members of our Technical Expert Panel (TEP) agreed—we significantly revised the Key Questions to avoid an overly broad scope that could add complexity to an already complicated topic. A broader scope would also have overlapped with the IOM systematic review of cognitive rehabilitation that was already underway. The topic nominator emphasized two priority areas: the effectiveness of multidisciplinary rehabilitation and of cognitive rehabilitation. Thus, our review evaluates the evidence of effectiveness for multidisciplinary postacute rehabilitation for moderate to severe TBI in adults as determined by the primary outcomes of productivity and community integration.

Search Strategy

We searched relevant bibliographic databases to identify evidence for this review. These databases included:

- MEDLINE
- Cochrane Central Register of Controlled Trials (CENTRAL)
- PsycINFO
- Physiotherapy Evidence Database (PEDro)

We searched for randomized controlled trials (RCTs) and prospective cohort studies published from 1980 to the January 2012. The nature of postacute rehabilitation has transformed

over the last 30 years, and studies conducted since1980 reflect programs and services most relevant to the topic today.[48]

Our search strategy was based on a concept analysis that identified key concepts and relevant controlled vocabulary and natural language. We combined these bibliographic database searches with backwards citations searches of relevant recent systematic reviews. The concept analysis and search strategy appear in Appendix A. We adapted the strategy to conform to controlled vocabulary and indexing used in the other bibliographic databases.

Triage and Screening

We screened bibliographic database search results to identify eligible studies in two stages: triage and screening. During triage, two independent investigators reviewed titles and abstracts of all references resulting from the bibliographic database searches to exclude ineligible studies. Studies not excluded by both investigators during triage underwent screening. Two independent investigators reviewed full text to determine if studies met inclusion criteria. Differences in screening decisions were resolved by discussion or, if necessary, with the help of a third investigator. Eligibility status and one exclusion reason were documented for all studies evaluated at the screening stage.

Inclusion Criteria

We included controlled trials and prospective cohort studies assessing multidisciplinary postacute rehabilitation for moderate to severe TBI in adults age 16 and over (consistent with the definition of adult used by the TBI Model Systems programs and similar research conducted in other countries).

We aimed to include all studies of multidisciplinary interventions. We chose the term ―multidisciplinary" for this topic because a clear definition of comprehensive programs does not exist. However, screening studies to determine whether interventions were multidisciplinary was challenging and could result in an inappropriate set of included studies. For example, the ―multidisciplinary" screening criterion could lead to inconsistent inclusion of studies of similar interventions simply because some more clearly specified the disciplines involved. Further, clinical practice typically involves many disciplines in delivering these interventions, thus the interventions are to a degree inherently ―multidisciplinary." For these reasons, we chose not to explicitly screen by the term ―multidisciplinary." Finally, our emphasis on community integration outcomes helped assure exclusion of studies examining very specific interventions, such as those aimed at improving memory or gait. We also specifically excluded domain- or impairment-specific interventions such as specific skill building to enhance memory or social skills training even if provided by a multidisciplinary team.

We limited studies to those enrolling at least 75 percent moderate to severe TBI patients. Certain rehabilitation programs are geared to the broader brain injury populations or can include mild TBI patients. However, because our emphasis was on moderate to severe TBI, we felt that including studies addressing the broader brain injury population would not provide the relevant data to draw conclusions specific to this population.

Studies were deemed eligible if they reported one of our preselected primary or secondary outcomes. Primary outcomes included:

- Return to school, work, or training (or other measures of productivity)
- Community Integration as measured with (described in Table 2):

- The Mayo-Portland Adaptability Inventory (MPAI)
- Craig Handicap Assessment and Reporting Technique (CHART)
- Craig Handicap Assessment and Reporting Technique Short Form (CHART-SF)
- Community Integration Questionnaire (CIQ)

As the most relevant outcome, we selected participation demonstrated by productivity or community integration measures. We accepted any definitions of productivity and selected measures deemed most appropriate for measuring community integration. We selected four primary outcome measurement instruments, as follows. First, we selected the MPAI as the most appropriate outcome measurement scale for the population addressed in this review (current version, MPAI-4). The MPAI was specifically developed to evaluate rehabilitation programs in the postacute brain injury population.[22] Additionally, the MPAI was recommended by the TBI Common Data Elements Outcomes Workgroup as a supplemental global outcome measure that summarizes overall impact and incorporates functioning, activities, and participation.[49] This group also cited the utility of this measure in evaluating progress in rehabilitation. The second scale we selected, the Craig Handicap Assessment and Reporting Technique (CHART), is another promising measure that incorporates community integration assessment in the postacute TBI population. The CHART addresses the ICF's participation domain and has been tested in TBI populations.[50] This scale is available both in the full version and a short form (SF) version. The CHART-SF has been suggested as a core measure of social participation by the TBI Common Data Elements Outcomes Workgroup.[49] Finally, we selected the Community Integration Questionnaire (CIQ), which was developed for and has been used extensively in TBI populations and within the TBI model systems programs.[51]

We did not prespecify all secondary outcome measurement instruments. Instead, we chose to include studies with scales that incorporated community integration or quality, satisfaction with life or other measures of global functioning applicable to community settings. Prespecified secondary outcomes scales included the Extended Glasgow Outcome Scale (GOS-E), the Disability Rating Scale (DRS), and the Satisfaction with Life Scale (SWLS). We identified other scales during the screening process. Descriptions of all secondary outcome measures appear in Table 3. Other measures considered secondary outcomes during the screening process (i.e. not selected a priori) included the EuroQOL (EQ 5D); the Perceived Quality of Life Scale (PQOL); the Brain Injury Community Rehabilitation Outcome-39 (BICRO-39); the Quality of Life Inventory (QOLI); Quality of Community Integration Questionnaire (QCIQ); and the Newcastle Independence Assessment Form (NIAF). We deemed outcomes patient-centered if they (1) directly related to life participation; (2) encompassed indicators of resumption to previous roles in the family and community or quality of life; or (3) addressed functioning in as community settings.

We also included prospective cohort studies because of the ethical and operational challenges inherent in conducting rehabilitation RCTs. We considered only studies with comparators of no or alternative interventions, because the extent and timing of spontaneous recovery is not clear (e.g. studies with controls at later stages postinjury were not considered adequate). Additionally, given the number of known and unknown confounding variables affecting rehabilitation outcomes, we paid special consideration to risk of bias in grading of evidence.

Limiting included studies to those published in English is not ideal; however, studies conducted in English are more likely to be applicable to U.S. multidisciplinary postacute rehabilitation programs. We describe specific exclusion criteria used in triage and screening in Table 4. Studies meeting these inclusion criteria were used to address all Key Questions.

Table 2. Primary outcome scales measuring community integration

Primary outcomes	Definition	Scoring
Community Integration Questionnaire (CIQ)[23]	Clinician- or self-reported 15-item scale evaluating home integration, social integration, and productive activities, and focusing on behaviors rather than emotional states.	Scores range from 0-29, with higher scores indicating greater independence and integration.
Craig Handicap Assessment and Reporting Technique Short Form (CHART-SF)[52-54]	A proxy- or self-reported 19-item interview questionnaire that assesses how people with disabilities function as active members of their communities. The CHART-SF assesses physical independence, cognitive independence, mobility, occupation, social integration, and economic self-sufficiency.	Scores range from 0-600, with higher scores indicating less handicap and greater social participation.
Craig Handicap Assessment and Reporting Technique (CHART)[55]	A proxy- or self-reported 32-item interview questionnaire that assesses how people with disabilities function as active members of their communities. The CHART assesses physical independence, mobility, occupation, social integration, and economic self-sufficiency.	Scores range from 0-500, with a higher score indicating less handicap and greater social participation.
Mayo-Portland Adaptability Inventory (MPAI-4)[56]	A proxy or self-reported 29-item questionnaire designed to assist in the clinical evaluation of people during the postacute (posthospital) period following acquired brain injury (ABI) and assist in the evaluation of rehabilitation programs designed to serve these people. Scale measures abilities, adjustment, and participation.	Scores range from 0-4 per item, with higher scores indicating greater disability and problems.

Note: This table describes key elements of scales measuring community integration selected as primary outcomes for the review.

Table 3. Descriptions of secondary outcomes scales

Secondary outcomes	Definition	Scoring
Brain Injury Community Rehabilitation Outcome-39 (BICRO-39)[57]	A proxy or patient-reported 39-item questionnaire assessing problems of brain-injured subjects living in the community. Eight domains are included: personal care, mobility, self-organization, socializing, productive employment, psychological function, and parent/sibling/child/partner contact.	Scores range from 0-5 per question, with higher scores indicating greater dependency.
Disability Rating Scale (DRS)[58]	A clinician-reported, 8-item questionnaire designed to measure general functioning in moderate to severe TBI subjects over the course of recovery. Its components measure cognition, level of functioning, and employability.	Scores range from 0-29 with 0 designated as no disability and 29 as extreme vegetative state
Glasgow Outcome Scale-Extended (GOS-E)[59]	A clinical-reported single item scale of 8 categories: Dead, Vegetative State, Lower Severe Disability, Upper Severe Disability, Lower Moderate Disability, Upper Moderate Disability, Lower Good Recovery, and Upper Good Recovery.	Assessments correspond to one of the eight categories.
EuroQol[49]	Generic self-rating instrument that uses the dimensions of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression to assess health-related quality of life and health status. Combined with clinical data (e.g., survival) it gives quality-adjusted life years. Recommendations for the Use of Common Outcome Measures in Traumatic Brain Injury.	Each dimension has three levels, reflecting "no health problems," "moderate health problems," and "extreme health problems." A dimension for which there are no problems is said to be at level 1, while a dimension for which there are extreme problems is said to be at level 3.
Newcastle Independence Assessment Form - Research (NIAF-R)[60]	A clinician-reported 55-item measure of global functional independence designed to measure recovery from the acute rehabilitation stage to that of independent living in the community.	Scores range from 1-5 (per item), with a 1 as “unable to do task” and a 5 as “needs no help or assistance.”
Perceived Quality of Life Scale (PQOL)	An interviewer- or self-administered 19-item questionnaire that measures patients’ perceptions of their position in life.	Scores range from 0-10 (per item), with 0 designated as extremely dissatisfied/ unhappy and 10 extremely satisfied/ happy.
Quality of Community Integration Questionnaire (QCIQ)[61]	This 15-question tool, designed to evaluate participants’ satisfaction with their functioning after cognitive rehabilitation and complement the Community Integration Questionnaire, queries 2 types of satisfaction: (1) individuals’ subjective satisfaction with their level of community integration (quality of community integration ; 9 questions) and (2) individuals’ satisfaction with their current level of cognitive functioning as it affects their ability to function in specific areas of their lives; 6 questions).	QCI questions each rated on a 4-point scale (range: 1, very dissatisfied to 4, very satisfied). Total possible scores on the QCI scale range from 9 to 36. QCOG questions rated on a 4-point scale (range: 1, very dissatisfied to 4, very satisfied). Total possible scores on the QCOG range from 6 to 24.
Quality of Life Inventory (QOLI)[62]	Clinical validation of the Quality of Life Inventory. A measure of life satisfaction for use in treatment planning and outcome assessment. The QOLI assesses individuals’ quality of life through self-report of the importance they attach to each of 16 life domains (on a 3-point rating scale) as well as their current satisfaction with each domain (on a 6-point rating scale).	Importance scores are multiplied by satisfaction scores for each domain, and then these results are summed to determine an overall current quality of life for each individual. Higher scores indicate a higher overall quality of life.

Note: This table describes key elements of scales selected as secondary outcomes for the review.

Table 4. Exclusion criteria

Study Domain	Exclusion Reason
Publication Type	• Published as abstract only • No original data • Full text not available in English
Population	• Pediatric population • Not 75% moderate to severe TBI
Intervention	• No intervention • Not postacute intervention • Impairment-specific intervention
Comparison	• No comparison group • Not relevant comparison (e.g. comparison group receives same treatment at the same time)
Outcome	• No primary or secondary outcome reported
Study Design	• Case series, retrospective study design

Data Extraction

We determined fields to be extracted for each Key Question and extracted data from eligible studies into tables for evidence and relevant outcomes. We believed that the complexity and heterogeneity of this condition and of multidisciplinary postacute rehabilitation required extensive data extraction. We extracted basic study information such as author; year of publication; subject inclusion and exclusion criteria; intervention and control characteristics (program or service components, timing, frequency, duration); followup duration; participant baseline demographics and other relevant preinjury and postinjury characteristics; comorbidities; injury etiology and severity; and descriptions and results of primary outcomes and adverse effects. One investigator extracted select data elements into evidence and outcomes tables, and a second investigator confirmed data extractions for accuracy.

Risk of Bias

Several tools are available to evaluate risk of bias among primary studies. Recommended practice when selecting instruments to evaluate risk of bias when conducting systematic reviews is to use instruments designed specifically for this purpose and to avoid instruments that calculate composite scores.[63] We developed risk of bias assessment forms specifically for this project. For RCTs, we modified the Cochrane Risk of Bias tool[64] to address specific items that may lead to risk of bias on this topic. Due to the complex nature of the interventions, we incorporated items from the RTI Observational Studies Risk of Bias and Precision Item Bank[65] to evaluate intervention and comparison definitions, implementation, and outcomes issues (consistent measurement, validity and reliability of scales, objective vs. subjective measures, providers versus self-report). Building on the work of other researchers,[66] we assessed whether the intervention definitions provided adequate detail, including identification of the theory or model driving the specific studied intervention, thorough details about intervention components, and documentation of the intervention in manuals or other publications. We also reviewed studies for validation that the interventions were effectively implemented via staff training and/or fidelity checks. Because many of the outcomes were measured using scales, we added an item assessing the quality and validity of the scale to our risk of bias assessment forms. We also modified the Cochrane questions to simplify the evaluation of each component by directly answering questions instead of assessing the degree of risk of bias for individual elements. We

dropped the element related to blinding of participants and personnel because such blinding is unlikely with these interventions. The resulting items on our RCT risk of bias assessment forms included sequence generation; allocation concealment; blinding of outcome assessment; intervention and control description; intervention implementation; outcome measurement; incomplete outcome data; selective outcome reporting; and other issues.

We created a risk of bias assessment form for cohort studies from the RTI Observational Studies Risk of Bias and Precision Item Bank.[65] We selected items for consistency with items on the RCT form, and additional items relevant to selection bias and statistical analysis. Final versions of these forms (Appendix B) contained individual items with guidance and space for responses and comments. The last item on each of the forms assigned an overall risk of bias to the study.

Two investigators independently assessed each item using the appropriate form, and then assigned an overall risk of bias assessment of low, moderate, or high to each study. Risk of bias assessments were performed only for primary outcomes. An ‗uncertain' response was available for particular items on the forms when the determination could not be made based upon what was reported in the study (e.g. no report of blinding of outcomes assessors). We did not contact study authors for additional information. Overall assessments were subjective based upon the assessment of individual items, the magnitude of individual items and the collective risk of bias created by the individual items. Investigators reconciled discrepancies for overall risk of bias by consulting with each other and, when necessary, with a third investigator. RCTs and cohort studies with an overall assessment of high risk of bias were not used to draw conclusions about effectiveness.

Data Synthesis

The diversity of the setting, populations, interventions, controls, outcomes, and outcome measures studied precluded any quantitative synthesis of results. All eligible studies were used to address KQ1. Only studies rated low or moderate risk of bias were used to answer KQ2 – KQ5. Study results are not reported for studies rated high risk of bias. Qualitative syntheses grouped studies by population, intervention setting or type, and outcomes. We evaluated outcomes within groups when more than one study could be appropriately grouped. Results from studies evaluating program effectiveness utilizing measures we selected as secondary outcomes were used to determine consistency of effect with the participation measures selected as primary outcomes.

Grading the Evidence

We evaluated the overall strength of evidence for each primary outcome or comparison using methods developed by the Agency for Healthcare Research and Quality and the Effective Health Care Program.[67] We evaluated strength of the evidence on four required domains:

1. Risk of bias (do the studies for a given outcome or comparison have good internal validity). The risk of bias, based on study design and conduct, is rated low, moderate, or high. Because studies were assessed for risk of bias at the study level and assessments were based on the given study design, evidence level risk of bias assessments are downgraded one level for observational studies.
2. Consistency (the degree of similarity in the effect sizes—i.e., same direction of effect—of the included studies). Consistency is rated consistent or inconsistent if possible. When

evidence on comparisons was based upon a single study, we recorded "single study" for this domain and did not downgrade SOE.

3. Directness (reflecting a single, direct link between the intervention of interest and the outcome). Directness can either be direct or indirect. Because we assessed SOE only for primary outcomes, we considered all evidence to be direct.
4. Precision (degree of certainty surrounding an effect estimate of a given outcome). Precision is either precise or imprecise. A precise estimate is one that would yield a clinically meaningful conclusion. Relative risk estimates for dichotomous outcomes were determined imprecise if relative risk increases or reductions exceeded 25 percent; continuous outcomes were considered imprecise if the upper or lower confidence interval crossed an effect size of 0.5 in either direction.[68]

Two investigators worked independently to qualitatively rate each component and overall strength of evidence. Disagreements were reconciled through discussion among project team members. We rated the overall evidence for each outcome and comparison as:

1. High: High confidence that the evidence reflects the true effect; further research is very unlikely to change the confidence in the estimate of effect.
2. Moderate: Moderate confidence that the evidence reflects the true effect; further research may change our confidence in the estimate of effect and may change the estimate.
3. Low: Low confidence that the evidence reflects the true effect; further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.
4. Insufficient: Evidence either is unavailable or does not permit a conclusion.

Assessing Applicability

We determined applicability of the studies according to the PICOTS format at the evidence level. Study characteristics that affected applicability include (but are not limited to): narrow eligibility criteria; patient or injury characteristics different than that described by population studies of postacute TBI; and postacute rehabilitation programs or services not typically used in current practice.[69]

Results

Our bibliographic database searches, conducted through January of 2012, identified 1,681 unique references.

- Triage of titles and abstracts identified 170 references meriting comprehensive screening. Backward citation searches of relevant systematic reviews identified an additional 12 references, for a total of 182 for screening. Figure 3 describes the literature search and screening process. Full text screening identified 16 unique studies meeting inclusion criteria. The most common reason for exclusion was the lack of a comparison group (59 studies). Other common reasons for exclusion included no intervention, no primary or secondary outcome, ineligible study design, and sample comprised of less than 75 percent moderate to severe TBI survivors. A complete listing of excluded studies appears in Appendix C.

All studies assessed a prespecified primary outcome or a secondary outcome determined a priori or during the screening process as described in this report's Methods section. We identified eight scales that we categorized as patient-centered secondary outcomes because they reflected or incorporated broader outcomes relative to participation, quality of life, or functioning in a community setting.

Table 5 provides an overview of eligible studies listing the primary and secondary outcomes assessed. The overall risk of bias assessments are also documented in Table 5. All studies were used to answer KQ1, but only studies with a low or moderate risk of bias were used to answer KQ2-5. Details describing these assessments are provided in Appendix B, Table 1.

Previous Systematic Reviews

We identified several relevant systematic reviews with Key Questions, included populations or outcomes that differed from ours; thus we considered them partially relevant and used them in a limited fashion. We reviewed their lists of included studies for eligibility in this review. In the Discussion section of this report, we compare our conclusions with those of other reviews.

Description of Eligible Studies

Evidence tables describing the studies appear in Appendix E, Table E-1. Four RCTs and eight cohort studies addressed primary outcomes. Cicerone et al. conducted two studies, a prospective cohort study[61] and an RCT,[70] to assess the effectiveness of an intensive cognitive rehabilitation program (ICRP) as compared to standard treatment in chronically impaired moderate to severe TBI survivors. Vanderploeg et al. conducted an RCT comparing two intensive impatient rehabilitation approaches for veterans or active duty military personnel with moderate to severe TBI.[71] Salazar et al. conducted an RCT to assess the comparative effectiveness of an intensive inpatient cognitive rehabilitation program to a limited home-based rehabilitation program.[72] Greenwood et al. conducted an RCT by randomizing hospitals to complement existing rehabilitation services with case management and compared results to the group of hospitals not adding the service.[73] Ponsford et al. compared a cohort participating in a community-based postacute rehabilitation program to a group of patients participating in the center-based program it replaced.[74] Hashimoto et al. compared patients in a day treatment program to controls not participating in the program.[75] Sarajuuri et al. compared a cohort of moderate to severe TBI survivors enrolled in an intensive inpatient program to those receiving standard care.[76] Prigatano et al. conducted two cohort studies comparing neuropsychological

rehabilitation to nonparticipants.[77, 78] Rattock et al. studied three treatment mixes for comparative effectiveness.[79] Willer et al. evaluated the comparative effectiveness of a residential rehabilitation program to standard care.[80]

Four studies assessed only secondary outcomes, two RCTs and two cohort studies. Bell et al. conducted an RCT to evaluate the comparative effectiveness of a telephone counseling and education program to the standard program without the additional service.[81] Powell conducted an RCT to compare an outreach program to an information-only intervention.[82] Thomas evaluated the effectiveness of an outdoor experiential education program adapted to TBI survivors with chronic impairments as compared to patients that did not enroll in the program.[83] Semlyen et al. compared the effectiveness of a coordinated multidisciplinary program provided at a regional rehabilitation center to care provided by other facilities.[60]

Figure 3. Literature flow diagram

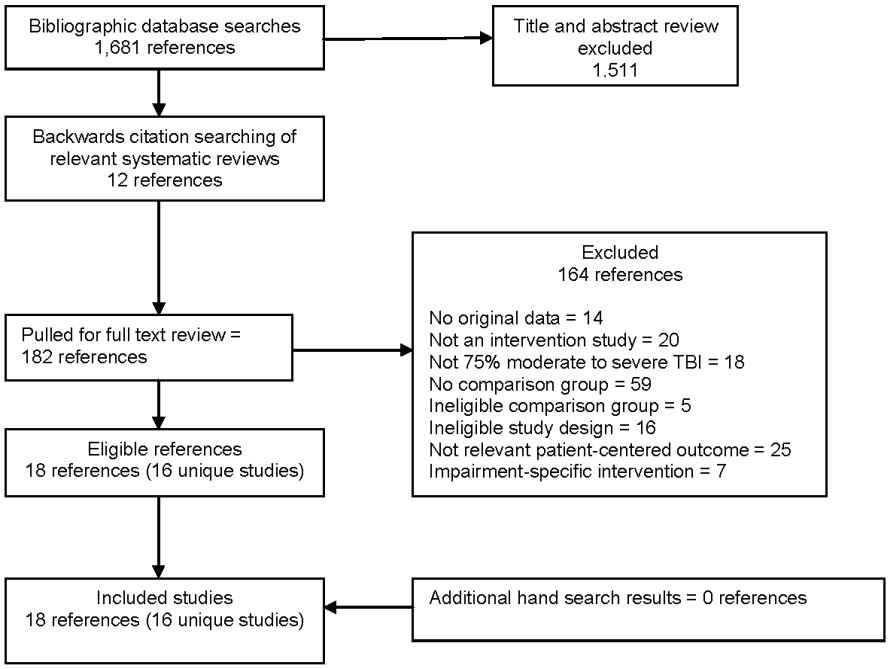


Table 5. Overview of included studies

Study	Study design	Productivity	Community Integration Questionnaire (CIQ)	Mayo-Portland Adaptability Inventory (MPAI-4)	Craig Handicap Assessment and Reporting technique Short form (CHART-SF)	Secondary Patient-Centered Outcome	Overall Risk of Bias Assessment
Cicerone 2008[70]	RCT	✓	✓			PQoL	Moderate
Vanderploeg 2008[71]	RCT	✓				DRS	Low
Salazar 2000[72]	RCT	✓					Moderate
Greenwood 1994[73]	RCT	✓				DRS, GOS-E	Moderate
Ponsford 2006[74]	Cohort	✓		✓	✓		High
Sarajuuri 2005[76]	Cohort	✓					Moderate
Prigatano 1994[78]	Cohort	✓					High
Rattok 1992[79]	Cohort	✓					Moderate
Prigatano 1984[77]	Cohort	✓					Moderate
Hashimoto 2006[75]	Cohort		✓				High
Cicerone 2004[61]	Cohort		✓			QCI	Moderate
Willer 1999[80]	Cohort		✓				High
Bell 2005[81]	RCT					GOS-E, EuroQol, MPQoL	Moderate
Powell 2002[82]	RCT					BICRO-39	Moderate
Thomas 2004[83]	Cohort					QOLI®	High
Semlyen 1998[60]	Cohort					NIAF-R	High
Total number of studies eligible		9	4	1	1	8	
Less High Risk of Bias		2	2	1	1	NA	
Studies used to assess SOE		7	2	0	0	NA	

BICRO-39 = Brain Injury Community Rehabilitation Outcome scale; EuroQol = a quality-of-life instrumented developed by the EuroQol Group; GOS-E =Glasgow Outcome Score-Extended; MPQol =modified Perceived Quality of Life; NA = not applicable; NIAF-R = Newcastle Independence Assessment Form - Research; PQoL = Perceived Quality of Life; QOLI® = Quality of Life Inventory; RCT = randomized controlled trial; SOE = strength of evidence. **Note:** This table lists the 16 studies meeting inclusion criteria. The primary and secondary patient-centered outcomes reported in those studies and the overall risk of bias assessment for studies assessing a primary outcome are also documented. The net number of studies for which SOE was assessed in evaluating effectiveness Key Questions is described.

Key Question 1. How have studies characterized multidisciplinary postacute rehabilitation for TBI in adults?

Key Points

Studies of multidisciplinary postacute rehabilitation for moderate to severe TBI in adults do not always adequately define intervention and control treatments.

Multidisciplinary postacute rehabilitation is delivered in a variety of settings, including inpatient and outpatient rehabilitation centers, community- and home-based settings.

Most interventions do not appear to be theoretically based. However, references to certain models of care are frequently reported. Multidisciplinary rehabilitation programs based on models of care described by Ben-Yishay, Prigatano, and others are the most frequently studied.

Studies rarely report efforts that demonstrate effective implementation of interventions, such as the availability of manuals or other documentation outlining the interventions, staff training, and/or fidelity checks.

Detailed Analysis

All 16 eligible studies were used to characterize interventions. Many studies did not provide detailed definitions of examined interventions. Definitions appeared to improve over time, with more recent studies providing more detailed definitions. Table 6 describes characteristics of studied interventions and Appendix E, Table E-2 provides the intervention definition data extractions. Despite the lack of a consistent taxonomy, interventions could be grouped on several levels. Interventions differed by target populations for which the interventions were designed; setting in which intervention took place; the models of care used to develop the intervention; how the intervention was delivered; and intervention intensity and duration.

Studies focused on evaluating new models of care, comparing different models of care, or assessing particular components added to a standard program. Four studies assessed certain rehabilitation programs and compared results to those not participating in the program.[61, 75, 77, 78, 83] Six studies compared new models of care delivered by their institution or agency to a standard care typically delivered to that community.[60, 61, 70, 74, 76, 80] Five studies compared different models of care where the interventions varied by setting, intensity, or approach.[71, 72, 79, 82] Two studies examined an additional component added to a standard program.[73, 81]

Most of the programs studied were geared towards TBI survivors whose impairments were chronic or had lasted on average more than 6 months postinjury. However, three interventions addressed patients earlier in the postacute period.[60, 71, 72] Two interventions began earlier in the postacute period and continued to the chronic stage.[73, 81] Other programs specifically addressed survivors of severe injuries[60, 73, 80] or military populations.[71, 72]

Programs typically engaged a similar variety of disciplines. Eight programs described programs based upon models of care originally described by Ben-Yishay, Prigatano, and others.[61, 70, 72, 75-79] These programs have been called "comprehensive holistic day treatment," and the interventions emphasized cognitive rehabilitation and an integrated approach. They also included therapies delivered in a similar manner, in which small groups of five to eight participants progressed through rehabilitation together. These programs typically involved substantial group therapy when compared to standard rehabilitation programs. A variety of therapy types were provided, with vocational rehabilitation as a core component. Most were day-treatment programs in outpatient rehabilitation centers, but two were residential treatment programs.[72, 76] A single program citing this model of care addressed TBI survivors in the early

postacute period, within 3 months from injury.[72] Despite their many similarities, interventions based upon this model varied in duration of treatment from 6 weeks to 6 months.

Other programs described outreach to TBI survivors;[82] community-based care;[74] specific approaches to remediation of skills;[71] multidisciplinary programs without mentioning a specific model;[60] residential communities of TBI survivors;[80] and an outdoor experiential education program.[83] Specific components of programs that were studied included case management[73] and telephone counseling.[81]

Program Characteristics

Several postacute multidisciplinary rehabilitation programs were studied.[60, 61, 70-72, 74-80, 82, 83] Three programs compared the effectiveness of programs delivered to TBI survivors earlier in the postacute period.[60, 71, 72]

Vanderploeg et al. compared two inpatient approaches to rehabilitate TBI survivors within 6 months of injury[71]. In addition to daily occupational and physical therapy, study participants received 1.5 to 2.5 hours per day of either cognitive-didactic treatment or functional-experiential therapy. The cognitive-didactic approach targeted four cognitive domains; practiced trial and error in performing exercises; emphasized self-awareness; and aimed to directly rehabilitate the cognitive deficits that underlie functional deficits after TBI, a restorative approach. Cognitive-didactic treatments were delivered to participants on an individual basis. The functional-experiential approach used real-life situations to remediate or compensate for the functional deficits. Treatments were delivered in group settings; with an errorless learning strategy; and with an emphasis on repetition to rebuild functional status.

Salazar et al. compared two rehabilitation programs delivered in different settings targeted to relatively mildly impaired survivors of moderate to severe TBI within 3 months of injury.[72] The 8-week inpatient treatment consisted of interdisciplinary cognitive rehabilitation combining group and individual therapies. This program was based on a model of care previously described by Prigatano and others. The program was structured and involved group and individual cognitive, speech, occupational, and coping skills therapies, and vocational rehabilitation. Participants in the home rehabilitation program received 30 minutes of weekly telephone counseling and education from a psychiatric nurse. They also received educational materials and advice about strategies for enhancing cognitive and organizational skills.

Semlyen et al. described a coordinated, multidisciplinary rehabilitation service provided by the local rehabilitation center.[60] Combined inpatient and outpatient services were delivered on an individual basis as determined by patient needs. Patient goals were established and reviewed weekly in concert with the care team.

Programs based on the comprehensive holistic model (except as studied by Salazar et al.)[72] addressed chronic impairments of moderate to severe TBI.[61, 70, 75-79] Of these, all but one[76] were outpatient day-treatment programs.

Cicerone and colleagues conducted two studies to assess the comparative effectiveness of the ICRP, an alternative model of comprehensive day treatment implemented at a postacute brain injury rehabilitation center.[61, 70] This structured, intensive 16-week group intervention provided 15 hours of combined individual and group therapies, 3 days per week. The program emphasized integration of interventions for impairments across domains, and treatments focused on compensatory approaches to address chronic limitations. Groups of five to eight participants progressed together through the program, which utilized extensive group sessions supplemented with a lesser number of individual sessions.

Prigatano et al. also evaluated this model in two separate studies.[77, 78] Characteristics of their program suggested an intensive and coordinated approach. Groups progressed through the program and participated in four sessions per week, 6 hours per day, for 6 months. Group and individual therapy sessions emphasized self-awareness, acceptance of residual impairments retraining, and compensatory approaches to cognitive deficits.[77] The later study described a similar intervention called a "work re-entry program," composed of interdisciplinary therapies. Small groups participated in therapies 4 to 5 mornings per week for 6 months. Sessions taught patients to participate responsibly as members of small communities, stressing social integration and simulated community situations. After 6 to 8 weeks in the program, participants devoted afternoons to protected work trials of 15 to 20 hours per week.

Hashimoto et al. implemented variations of programs based on the comprehensive holistic model of care.[75] Their program varied in intensity and duration, but maintained the same basic approach. Social skills training based on the positive behaviorist support program was a key component.

Rattock et al. studied three treatment mixes in a program delivered to chronically impaired TBI survivors.[79] All contained training to alleviate attention disorders, therapeutic recreation, and individual counseling. The first treatment mix was a balanced approach that supplemented the above components with cognitive remediation and small group social skills training. The second treatment mix emphasized the social skills training without cognitive remediation. The third treatment mix emphasized individual cognitive skills training without social skills training.

Sarajuuri et al. studied a program based upon the comprehensive holistic day-treatment model of care, targeting chronic impairments from moderate to severe TBI.[76] This 6-week inpatient program (called INSURE) was conducted in Finland for select groups of patients with TBI. Groups of five to eight patients received 7.5 hours daily of neuropsychological rehabilitation core therapies, with individual therapies incorporated as needed. The INSURE program emphasized the therapeutic alliance between the patient and the care team, and consisted of goal setting; group and individual psychotherapy; group cognitive sessions emphasizing compensatory approaches; group speech and language coaching; and, finally, group sessions focused on self-awareness, quality of life, and therapeutic recreation.

Other examined programs reflected additional models or theories. Thomas evaluated an outdoor experiential education program adapted to brain injury survivors with chronic impairments.[83] The author cited a theoretical model describing four tasks of adjustment to brain injury as the underpinning for the intervention. The program was developed through a partnership between a local brain injury service and Outward Bound Australia. The program had three stages; the first focused on raising funds for participation in the program, and clarification of program objectives. The second stage was the 9-day Outward Bound "Discovery" course, adapted for this population from the traditional course, and based on a range of challenging outdoor activities. Participants were encouraged to accept increasing responsibility and attend to activities of daily living in a basic camping environment. The 3- to 4-month followup phase (after returning from the outdoor program) consisted of regular group work. The continued group sessions were intended to help participants use the insights and gains from the outdoor program to achieve personal goals. Key focus areas included social skills, vocational training, and increased independence. Rehabilitation staff members facilitated the groups with the goal of restructuring tasks through activities.

The remaining studies did not report being based on specific models of care or describe the theories on which their programs were based.[74, 80, 82] Ponsford et al. evaluated a program change

from center-based outpatient rehabilitation to community-based services.[74] The community-based program conducted assessments and therapies in the home, workplace, or other relevant community setting. Specific goals and therapeutic interventions were planned based on assessment and discussion with patients and families. Treatment was provided by a variety of professionals, with each specific therapy offered once a week or less. Sessions also involved training for all caretakers involved in the rehabilitation process.

Powell et al. compared two approaches rehabilitation for chronically impaired TBI survivors.[82] The more intensive outreach program offered 2 to 6 weekly hours of individualized treatments in patients' homes or other community settings. Interventions were based on initial assessments and identified treatment goals. The less intensive program involved information only, with one home visit from a team therapist and the provision of an informational booklet highlighting resources in the community of potential benefit to the patient.

Willer et al. studied a residential postacute rehabilitation program providing a broad range of services.[80] Treatments were coordinated by a neuropsychologist, with specific therapies designed to meet each patient's needs. After extensive training, paraprofessionals delivered treatments and served as role models for social skills. All support staff were trained in issues relevant to TBI impairments and rehabilitation.

Two studies evaluated a single component of comprehensive rehabilitation programs.[73, 81] Both of these programs offered services beginning earlier in the postacute period that continued through the chronic period of recovery. Bell et al, studied a telephone intervention.[81] First contact with the TBI survivor or a caregiver occurred within 2 weeks of discharge from inpatient rehabilitation. Subsequent contact occurred at 4 weeks, and at 2, 3, 5, 7, and 9 months. Calls were scheduled to last between 30 and 45 minutes. Each telephone contact contained three basic elements: (1) a followup to concerns raised on the previous call; (2) identification of current concerns; and (3) the recommended intervention in response to current concerns. Calls were supplemented with informational mailings as determined relevant. Staff providing the phone counseling were trained in principles of motivational interviewing. Greenwood et al. studied a case management program added to standard rehabilitation services.[73] The case management intervention involved the formulation of a detailed rehabilitation plan, and the facilitation of cooperation from appropriate professionals to implement the plan. No formal professional services were provided by case managers.

Implementation of Multidisciplinary Rehabilitation Treatments

Adequately implementing the interventions is as important as adequately describing them. Few studies reported implementation efforts such as the availability of manuals defining treatments, staff training, and fidelity or adherence checks. Few studies reported a manual or other detailed documentation with thorough intervention content.[72, 76, 77, 83] Two studies reported staff training prior to beginning of the study.[71, 80] Two studies described efforts to ensure fidelity to treatment protocol.[70, 71]

Table 6. Characteristics of studied interventions

Study location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
Bell 2005[81] United States	Early Postacute through Chronic Moderate to Severe	Telephone counseling		Home (telephone)	Individuals	30-45 min/wk 9 mos	18-27 (incremental)
Cicerone 2004[61], 2008[70] United States	Chronic Moderate to Severe	Intensive Cognitive Rehabilitation Program	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	15 hrs/wk 16 wks	240
Greenwood 1994[73] UK	Early Postacute through Chronic Severe	Case management		Home	Individuals	NR	NR
Hashimoto 2006[75] Japan	Chronic Moderate to Severe	Comprehensive Day Treatment Program	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	8-16 hrs/wk 3-6 mos	96-144
Pondsford 2006[74] Australia	Postacute Moderate to Severe	Community-based therapy program	NR	Community	Individuals	NR	NR
		Hospital-based outpatient treatment	NR	Outpatient rehabilitation center	Individuals	NR	NR
Powell 2002[82] UK	Chronic Severe	Outreach	NR	Home or community	Individuals	2-6 hrs/wk 27 wks (mean)	NR
		Information	NR	Home	Individuals	1 hr 1 session	1
Prigatano 1984[77], 1994[78] United States	Chronic Moderate to Severe	Neuropsychological rehabilitation	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	24 hrs/wk 6 mos	576
Rattok 1992[79] United States	Chronic Moderate to Severe	Treatment Mix 1 (balanced)	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	5 hrs/wk 4 wks	200
		Treatment Mix 2 (interpersonal)	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	5 hrs/wk 4 wks	200
		Treatment Mix 3 (cognitive)	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	5 hrs/wk 4 wks	200

Table 6. Characteristics of studied interventions (continued)

Study location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
Salazar 2000[72] United States	Active duty military Early postacute Moderate to severe Mild impairments	Inpatient Cognitive Rehabilitation	Holistic Day Treatment	Inpatient	Small groups	NR 6 wks	NR
	Active duty military Early postacute Moderate to severe Mild impairments	Home rehabilitation	NR-	Home	Individuals	.5 hr/wk 8 wks;	4
Sarajuuri 2005[76] Finland	Chronic Moderate to Severe	Comprehensive neurorehabilitation	Holistic Day Treatment	Inpatient	Small groups	37.5 hrs/wk 6 wks	225
Semlyen 1998[60] UK	Early postacute Severe	Multidisciplinary rehabilitation	NR	Combination Inpatient/outpatient rehabilitation center	Individuals	NR	NR
Thomas 2004[83] Tasmania	Chronic Moderate to Severe	Outdoor Experiential Education	Outward Bound	Camp-like setting Community	Small groups	OEE – 9 wks Follow-up groups – 3-4 mos.	NR
Vanderploeg 2008[71] United States	Active-duty military, veterans Early postacute Moderate to Severe	Cognitive didactic	Cognitive-didactic	Inpatient	Individuals	7.5-15 hrs/wk 32 days (mean)	NR
		Functional-experiential	Functional treatment concepts	Inpatient	Small groups	21.5-30 hrs/wk 33 days (mean)	NR
Willer 1999[80] United States	Chronic Severe Multiple disabilities	Community-based residential rehabilitation	Cognitive rehabilitation and community adaptation	Residential	Individuals	NR 1-3 yrs	NR

Note: This table briefly describes characteristics of the studied interventions.

Key Question 2. What is the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI?

a. Do effectiveness and comparative effectiveness vary by rehabilitation timing, setting, intensity, duration, or composition?
b. Do effectiveness and comparative effectiveness vary by injury characteristics?
c. Do effectiveness and comparative effectiveness vary by patient characteristics, preinjury or postinjury?

Key Points

Table 7 summarizes the populations, interventions, outcomes, timing of outcome measurement, and direction of effect for all primary outcomes studies.

One small cohort study compared treatment to no treatment, and provided insufficient evidence to determine whether neuropsychological rehabilitation for impairments from moderate to severe TBI was effective at improving return to work at 6 to 24 months post-treatment.

A low strength of evidence demonstrated that the cognitive-didactic approach was no more effective than functional-experiential approach during the early postacute phase in achieving productivity outcomes 1-year post-treatment in a military and veteran population with moderate to severe closed head injuries.

A low strength of evidence demonstrated that a 6-week inpatient postacute rehabilitation program was no more effective than limited home-based rehabilitation during the early postacute period in achieving productivity outcomes 1-year post-treatment in a military population.

A low strength of evidence demonstrated that the ICRP during the chronic phase was more effective than standard rehabilitation at improving productivity outcomes, but not community integration outcomes, immediately post-treatment in a civilian population. However, group differences were no longer significant at 6 months post-treatment.

Table 7. Overview of primary outcomes with strength of evidence

Treatments; Study Design	Study Populations	Outcome Definition	Post-Treatment Assessment	Followup post-Treatment Assessment
Intensive cognitive rehabilitation versus Standard neurorehabilitation Study 1 RCT[70] Study 2 non-RCT[61]	Study 1: 68 American TBI patients (mild 13%), at least 3 months post-injury, in a post-acute brain injury rehabilitation center within a suburban rehabilitation hospital. Mean age 37, Male 68%. Study 2: 57 American TBI patients (mild ~10%) in community-based, post-acute outpatient brain injury rehabilitation program Mean age 37, Male 71%.	Engaged in community-based employment Community Integration Questionnaire	↑↑ 16 weeks (Study 1) Low strength of evidence (SOE) ↔ 16 weeks (Study 1 and Study 2) Low SOE	↔ 6 months (Study 1) Low SOE ↔ 6 months (Study 1) Low SOE
Functional-experiential versus Cognitive-didactic[71] RCT	360 American Veterans Affairs inpatients (active duty or veteran) with non-penetrating TBI within the preceding 6 months. Mean age 32, Male >90%.	Paid employment or school enrollment, either full or part time	not reported	↔ 1 year (n=331)[a] Low SOE
Hospital treatment versus Home treatment[72] RCT	120 American active duty military patients with a closed head injury within 3 months of randomization. All subjects had a Rancho Los Amigos cognitive level of 7 (oriented, appropriate). Mean age 25, Male >90%	Gainful military or civilian employment, either full or part time	not reported	↔ 1 year Low SOE
Case management Versus Conventional rehabilitation [73] RCT (hospitals, not patients)	126 British TBI patients with closed head injury. Case-managed patients were more severely injured at study entry (Glasgow coma score and amnesia P<0.05 between groups). Mean age 31, Male 73%	At competitive work	↔ 6 months (n=95) Insufficient SOE	↔ 1 year (n=77) Insufficient SOE ↔ 2 years (n=46) Insufficient SOE
Comprehensive neurorehabilitation (INSURE) versus Conventional rehabilitation[76] Non-RCT	39 Finnish TBI patients who were independent in daily life and had only slight physical disabilities. Comprehensive neurorehabilitation was in an inpatient setting. Mean age 30, Male 85%	Working, studying, or participating in volunteer activities	not reported	↑ 2 years Insufficient SOE

Table 7. Overview of primary outcomes with strength of evidence (continued)

Treatments; Study Design	Study Populations	Outcome Definition	Post-Treatment Assessment	Followup post-Treatment Assessment
Neuropyschological rehabilitation versus Controls[77] Non-RCT	35 American closed head injury outpatients in a neuropsychological rehabilitation program compared to similar head injury controls. Mean age 25, Male 86%	Gainfully employed or actively engaged in a realistic school program	not reported	↔ Unclear, following 6 months treatment (n=32) Insufficient SOE
Treatment Mix 1 (balanced package, including cognitive remediation and small group interpersonal communication training) versus Treatment Mix 2 (similar to Mix 1 stressing small group inter-personal communication training but without cognitive remediation) versus Treatment Mix 3 (emphasis on individualized cognitive remediation but without small group interpersonal communication training)[79] Non-RCT	59 American TBI (open or closed) patients that had been discharged from inpatient rehabilitation and had been living at home with relatives. In most cases, traditional methods of rehabilitation had failed to stabilize patients in terms of their personal and social adjustments and their return to work. Mean age 27, Male 71%	Productive employment	not reported	↔ 9 months Insufficient SOE

↑↑ Moderate or greater effect (statistically significant) between treatment arms (Relative risk >2.0 or effect size >0.5)
↑ Small effect (statistically significant) between treatment arms (Relative risk <2.0 or effect size <0.5)
↔ No statistically significant differences between treatment arms
[a] Number of patients evaluated reported here if different from baseline
Note: This table describes primary outcomes and strength of evidence with the populations and interventions to which they apply.

Detailed Analysis

Of the 16 studies eligible studies, 13 assessed primary outcomes and eight assessed secondary outcomes. Nine of the primary outcomes studies assessed productivity or employment (four RCTs, five cohort studies). Two of the cohort studies were evaluated to have a high risk of bias and thus excluded from analysis.[74, 78] One cohort study assessed MPAI-3 and the CHART-SF. However, this study was evaluated as having a high risk of bias,[74] leaving no eligible studies using either the MPAI or the CHART-SF. Four studies assessed effectiveness with the CIQ (one RCT and three cohort studies). Two of the cohort studies were evaluated as having a high risk of bias and excluded,[75, 80] leaving two studies for analysis (one RCT and one cohort study).[61, 70] Of the eight studies used to analyze primary outcomes, one was rated low risk of bias,[71] and eight were rated moderate risk of bias[61, 70, 72, 73, 76, 77, 79] for respective outcomes.

The eight studies were heterogeneous in terms of populations, interventions, controls, and outcomes definition and measurement. Study characteristics are summarized in Table 8. Sample sizes ranged from 36 to 366. Six studies were conducted in the United States,[61, 70-72, 77, 79] one in the United Kingdom,[73] and one in Finland.[76] Subjects were predominantly male (85 percent) and young relative to the adult population of the United States (mean age of 31). Studies rarely reported other demographic statistics. Median time since injury varied widely among studies, from 1 to 45 months with a median of 19 months. Two studies specifically restricted enrollees to those within 3[72] or 6[71] months of injury while another restricted enrollment to individuals at least 3 months postinjury.[70] Several studies included participants with a wide range of time since injury. For instance, the Cicerone RCT included participants with injuries from 3 months to over 5 years prior to enrollment.

Studies rarely reported functional status at time of enrollment, either as an inclusion criterion or as a baseline characteristic. The Salazar RCT restricted enrollment to those with Rancho Los Amigos cognitive level of 7.[72] Other studies reported inclusion criteria suggesting that participants had been judged to need the level of treatment administered in the study,[70, 71] suggesting some threshold level of impairment. Other studies enrolled participants judged to have adequate potential to achieve productivity[76] or who had been unsuccessful in other rehabilitation programs.[79]

Primary studies typically failed to report many other variables believed to be related to recovery and rehabilitation response, such as measures of social support, comorbidities, concomitant treatments, prior employment, and compensation seeking status.

Methods of collecting outcome data also varied. Cicerone collected CIQ data self-reported by participants under supervision.[70] Other primary outcomes data were described as being obtained through interview, military records, or both,[72] and through structured interview questions.[71]

Productivity

Productivity outcomes are presented in Table 9. Overall strength of evidence and the individual strength of evidence component assessments for each outcome or comparison appear in Table 10. Because of the heterogeneity in comparisons across studies, SOE was assessed most often at the single study level. Only one eligible study assessing productivity compared the intervention to a no-treatment group. This small cohort study found no significant difference in the proportion gainfully employed at followup (50 percent versus 36 percent) at one timepoint somewhere between 6 and 24 months post-treatment. However, this study was likely

underpowered and did not adequately control for confounding. Thus it provided insufficient evidence about effectiveness.

Six studies assessed the comparative effectiveness for productivity outcomes between groups participating in different interventions. Two larger RCTs found no productivity differences between groups of patients participating in different treatment programs early in the postacute period.[71, 72] Vanderploeg et al. examined different approaches in four Veterans Affairs inpatient rehabilitation programs. A low strength of evidence demonstrated that the cognitive-didactic approach was no more effective than the functional-experiential approach during the earlier postacute phase in achieving productivity outcomes 1-year post-treatment in this military and veteran population with moderate to severe closed head injuries. Salazar et al. compared inpatient rehabilitation to home-based treatment.[72] A low strength of evidence demonstrated that a 6-week inpatient postacute rehabilitation program was no more effective than limited home-based rehabilitation during the early postacute period in achieving productivity outcomes 1-year post-treatment in this military population. Generally, it is recommended that SOE be downgraded to insufficient in evaluating equivalent results between comparison groups if evidence is too imprecise.[84] However, while this evidence in some cases is imprecise, we maintained our low SOE assessment because results were not grossly imprecise.

Cicerone et al. found that the group of chronically impaired civilians enrolled in the ICRP were significantly more productive immediately post-treatment than those who received standard treatment at that rehabilitation center (47 percent versus 21 percent).[70] However, no group differences existed at followup 6-months post-treatment, by which time both groups had improved rates of productivity (60 percent versus 50 percent). In summary, we found a low level of evidence that the ICRP resulted in earlier productivity than a conventional program in chronically impaired moderate to severe TBI survivors judged to need 4 months of intensive treatment. However, the group difference no longer existed at 6 months post-treatment, because the control group had significantly improved their rates of productivity.

We found insufficient evidence to conclude whether the INSURE program was more or less effective than standard rehabilitation in improving participation 2 years post-treatment.[76]

We also found insufficient evidence to conclude whether case management added to conventional programs resulted in significantly different rates of productivity compared to conventional rehabilitation alone at various followup timepoints.[73]

Community Integration

Integration CIQ outcomes are presented in Table 11. Overall strength of evidence and individual component assessments for each comparison appear in Table 12. Neither of the two studies that evaluated community integration with the CIQ found significant group differences in CIQ scores post-treatment (ICRP = 12.9, standard rehabilitation = 11.7 in RCT;[70] ICRP = 16.8, standard rehabilitation = 16.1, unadjusted in cohort study[61]). However, the authors suggest other indications of effectiveness. Specifically, a statistically significant improvement in the CIQ score for the ICRP group from baseline to the end of the program was reported in the RCT; however, mean differences between groups were not significantly different.[61] The cohort study detected a greater rate of clinically meaningful change in the ICRP group (52 percent of the ICRP group showed clinically significant improvement of 4.2 points compared to 31 percent of the standard rehabilitation group). While these indications of potential benefit may have value, the data provided a low level of evidence that participation in ICRP versus standard rehabilitation achieved equivalent improvements in CIQ. We assessed the SOE low because it was derived

from one moderately sized RCT with a moderate risk of bias. Results from the RCT were primarily used to assess SOE because the cohort study provided unadjusted results.

Secondary Outcomes

Table 13 summarizes findings for secondary outcomes in all eligible studies with a risk of bias assessment of low or moderate. Six studies assessed six measures considered secondary patient-centered outcomes.

Among studies that also provided primary outcomes, analyses of secondary patient-centered outcomes demonstrated patterns consistent with their primary outcomes. Vanderploeg et al. found no group differences in the DRS or on a measure of life satisfaction at 1 year post-treatment.[71] Cicerone et al. found no group differences in PQOL scores, despite noticing greater mean improvements in the ICRP group.[70] Greenwood identified no group differences on secondary outcomes, with the exception of a higher DRS score among the control group at 24 months post-treatment;[73] however, this measurement is likely biased due an attrition rate of nearly 50 percent. Cicerone et al. found that the standard rehabilitation group had significantly greater QCI scores than the ICRP group.[61]

Other studies that reported secondary outcomes showed some positive treatment effects. Bell et al. analyzed measures of productivity and community integration in their RCT of a telephone counseling and education program added to a conventional rehabilitation program compared to the conventional program alone.[81] Neither of these measures was considered a primary outcome for our review because authors used composite scores for productivity and community integration, inconsistent with our primary outcome criteria. No differences were found between the telephone intervention group and standard rehabilitation group in these composite measures of productivity and community integration. However, the authors identify an overall composite score as the primary outcome in the study, which demonstrated significant improvements among the telephone group. Additionally, this study provided individual scale scores for three secondary outcomes. The telephone group achieved higher adjusted mean scores in quality of life, as measured by the EuroQOL and the PQOL. No group differences were detected on the GOS-E. Powell et al. found median change scores on the BICRO-39 were significantly higher in an outreach group as compared to an information only group at 2 years post-treatment.[82]

Intervention Characteristics

Due to the heterogeneity of the studied interventions, our main findings from the primary studies pertain only to specific intervention characteristics. In general, interventions targeting the earlier postacute phase of recovery showed no significant group differences. Vanderploeg et al. compared two interventions of similar intensity.[71] Salazar et al. compared an intensive program to a substantially less intensive home program and found no group differences.[72] However, these results might reflect the limited degree of impairment experienced by participants.

The most frequent studied intervention targeted to TBI survivors with chronic impairments from their injuries is the comprehensive holistic day program. One cohort study found a higher proportion productive, but the difference was not significant.[77] One RCT demonstrated higher levels of productivity immediately post-treatment. However, comprehensive holistic day-treatment programs did not substantially or permanently improve outcomes when compared to standard multidisciplinary programs.[70]

Due to limited evidence, lack of clear findings about comparative effectiveness, and heterogeneity in populations, interventions, comparisons, and outcomes definitions, we could not assess the impact of program intensity or duration on effectiveness.

Injury Characteristics

Many of the conclusions previously identified for effectiveness and comparative effectiveness re-emerge when specific injury characteristics are considered. For example, many interventions enrolled only those with closed head injuries, and other interventions enrolled only those with severe TBI. Unfortunately, such studies do not allow for meaningful conclusions about which interventions may be most effective for specific injury types, recovery periods, or impairment types and levels, due to the heterogeneity of interventions and the limited findings of effectiveness.

The studies often provided scant or no details about injury characteristics for the enrolled populations, other than severity levels. Often, studies failed to provide cause of injury, area of brain injured, or details regarding sustained impairment.

A few studies reported on post hoc analyses of certain subgroups of patients when evaluating comparative effectiveness. Salazar et al. noticed significant improvements in the return-to-duty rate among more severely injured TBI survivors (those with loss of consciousness greater than 1 hour) enrolled in the in-hospital program versus the home program (80 percent versus 58 percent, p=.05).[72] Cicerone et al. placed more chronically impaired individuals in the ICRP program, some of whom had failed to resume functioning after completing previous postacute treatments.[61] These more impaired TBI survivors had higher mean change scores in the CIQ than those enrolled in the standard rehabilitation program. This may be an indication that individuals with more severe impairments are more likely to benefit from a program like the ICRP. The study conducted by Powell et al., restricted to those with severe TBI, found an improved BICRO-39 score among those enrolled in the outreach program versus the information-only program.[82] Not all analyses of more severely injured TBI survivors suggest group differences. Rattock et al. detected no differences in productivity across different treatment mixes delivered to severe TBI survivors.[79] However, lack of statistically significant differences in employment rates may have resulted from inadequate power.

Patient Characteristics

Studies were less likely to be restricted or analyzed based on specific patient characteristics. The two largest RCTs enrolled either only active-duty military personnel or a combination of active-duty military personnel and veterans.[71, 72] These two studies provided key findings to our main analysis that are most relevant to military and veteran populations.

Vanderploeg, et al. identified another important patient characteristic during post hoc exploratory analyses. Younger patients enrolled in the cognitive-didactic arm had significantly greater rates of return to work or school than those in the functional-experiential arm.

Table 8. Summary of study population characteristics (primary outcome studies with low of moderate risk of bias)

Characteristic	Mean (Range) *Unless Otherwise Noted*	Number of Studies Reporting
Total number of patients evaluated	870 (36 to 366)	8
Randomized trials, number of patients	680 (49 to 366)	4 [a,b,c,h]
Nonrandomized studies, number of patients	190 (36 to 59)	4 [d,e,f,h]
Age of subjects, years	31 (25 to 38)	8
Sex, male, % of patients	85 (68 to 94)	8
White race/ethnicity, % of patients	70 (69 to 75)	3 [a,b,c]
Married, % of patients	28 (25 to 35)	3 [a,b,c]
Education, years	13 (12 to 13)	4 [a,e,f,g]
Education, high school or greater, % of patients	94	1 [b]
Education, some college or greater, % of patients	42	1 [c]
Employment status, preinjury	91 (81 to 100)	7 [a,b,c,d,e,f,h]
TBI Severity, % mild (studies that included patients with minor TBI)	12 (11 to 13)	2 [a,e] *
Time postinjury (months)	12 (1.3 to 45)	7 [a,b,c,d,e,f]
Time postinjury (months), median	19 (1.3 to 45)	7
TBI etiology-motor vehicle accident, % of patients	63 (38 to 67)	4 [b,c,d,h]
TBI etiology-assault, % of patients	11 (5 to 19)	4 [b,c,d,h]
TBI etiology-fall, % of patients	15	2 [b,h] **
History of psychiatric illness/treatment, % of patients	19 (13 to 22)	2 [a,c]
History of alcohol and/or substance abuse, % of patients	31 (21 to 37)	2 [a,c]
Studies done in the United States, number of patients	705 (36 to 366)	7 [a,b,c,e,f,g]
Studies done outside the United States, number of patients	165	2 [d,h] †

a = Cicerone 2008; b = Vanderploeg 2008; c = Salazar 2000; d = Sarajuuri 2005; e = Cicerone 2004; f = Prigatano 1983; h = Rattok 2004; i = Greenwood 1994

* The remaining 4 studies included participants with only moderate to severe TBI.

** Sarajuuri 2005 combined fall and blunt object injury (33% of TBI).

† Finland and United Kingdom

Table 9. Productivity outcomes

Study Design Outcome and Description	Treatment Arms	% Working or Productive (n/N) Before Treatment	% Working or Productive (n/N) After Completion of Treatment	Treatment Vs. Control at Endpoint
Cicerone 2008[70] RCT Productive[a] post-treatment (16 wks)	Intensive cognitive rehabilitation	9% (3/34)	47% (16/34)	RR: 2.29 [1.08 to 4.84] P=0.03
	Standard neurorehabilitation	12% (4/34)	21% (7/34)	
Vanderploeg 2008[71] RCT RTW[b] at 1 yr post protocol treatment	Functional-experiential	NR	35% (58/164)	RR: 0.91 [0.69 to 1.20] P=0.50
	Cognitive-didactic	NR	39% (65/167)	
Salazar 2000[72] RCT RTW[c] in 12 mos post-treatment	Hospital	NR	90% (60/67)	RR: 0.95 [0.85 to 1.05] P=0.33
	Home	NR	94% (50/53)	
Salazar 2000[72] RCT Fitness for Duty in 12 mos post-treatment	Hospital	NR	73% (49/67)	RR: 1.11 [0.87 to 1.41] P=0.41
	Home	NR	66% (35/53)	
Greenwood 1994[73] RCT (Hospitals – not patients) At competitive work 6 mos post injury	Case management	100% (42/42)	24% (10/42)	RR: 0.84 [0.42 to 1.68] P=0.62
	Conventional rehabilitation	96% (54/56)	28% (15/53)	
Sarajuuri 2005[76] Prospective Cohort Productive[d] 2 yrs post-treatment	Comprehensive neurorehabilitation	5% (1/19)	89% (17/19)	RR: 1.63 [1.06 to 2.49] P=0.02
	Conventional rehabilitation	NR	55% (11/20)	

Table 9. Productivity outcomes (continued)

Study Design Outcome and Description	Treatment Arms	% Working or Productive (n/N) Before Treatment	% Working or Productive (n/N) After Completion of Treatment	Treatment Vs. Control at Endpoint
Rattok 1992[79] Prospective Cohort Productive[e] 9 mos post-treatment	Treatment Mix 1 (balanced package, including cognitive remediation and small group interpersonal communication training)	NR[f]	70% (16/23)	P=0.33 between all groups
	Treatment Mix 2 (similar to Mix 1 stressing small group inter-personal communication training but without cognitive remediation)	NR[f]	89% (16/18)	Treatment mix was unrelated to the number of patients attaining employment
	Treatment Mix 3 (emphasis on individualized cognitive remediation but without small group interpersonal communication training)	NR[f]	78% (14/18)	
Prigatano 1984[77] Prospective Cohort RTW[g] at followup (treatment was 6 mos)	Neuropsychological rehabilitation	NR	50% (9/18)	P=0.49
	Controls	NR	36% (5/14)[h]	

RR = risk ratio [95 percent confidence intervals]

[a] according to Vocational Integration Scale dichotomized into productive (supported, transitional or competitive) vs. nonproductive (unemployed or sheltered employment)

[b] current status of paid employment or school enrollment, either full or part time, not sheltered workshop.

[c] Work defined working either FT (≥35 hours/week) or PT (≤35 hours/week) in gainful military or civilian employment.

[d] defined as working, studying, or participating in volunteer activities

[e] productive employment

[f] all subjects in the study had "unsuccessful vocational rehabilitation" prior to study entry

[g] defined as gainfully employed or actively engaged in a realistic school program at time of followup.

[h] 17 controls total but 3 were excluded (lost to followup)

Table 10. Strength of evidence for productivity outcomes

Intervention; Outcome	Comparison	Study Type	n	Summary Statistics RR [95% CI]	Risk of Bias	Direct-ness	Precision	Consis-tency	Evidence Rating
Cicerone 2008[70] Post-treatment, 16 weeks	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	68	RR: 2.29 [1.08 to 4.84]	moderate*	direct	precise	NA	Low
Vanderploeg 2008[71] Post-treatment, 1 year	Functional-experiential vs. Cognitive-didactic	RCT	331	RR: 0.91 [0.69 to 1.20]	low	direct	imprecise	NA	Low
Salazar 2000[72] Post-treatment, 1 year	Hospital-based therapy vs. Home-based therapy	RCT	120	RR: 0.95 [0.85 to 1.05]	moderate	direct	precise	NA	Low
	Hospital-based therapy vs. Home-based therapy	RCT	120	RR: 1.11 [0.87 to 1.41]	moderate	direct	imprecise	NA	Low
Greenwood, 1994[73] Post-injury, 6 months	Case management vs. Conventional rehabilitation	RCT (Hospitals, not patients)	126	RR: 0.84 [0.42 to 1.68]	high	direct	imprecise	NA	Insufficient
Sarajuuri 2005[76] Post-treatment, 2 years	Comprehensive neurorehabilitation vs. Conventional rehabilitation	, prospective cohort	39	RR: 1.63 [1.06 to 2.49]	high	direct	precise	NA	Insufficient
Rattok 1992[79] Post-treatment, 9 months	Comparison of 3 “treatment mixes”	prospective cohort	59	-	high	direct	-	NA	Insufficient
Prigatano 1984[77] Post-treatment, ranged from 6 mo to 2 years	Neuropsychological rehabilitation vs. Control (untreated)	Prospective cohort/ retrospective control	32	RR: 1.40 [0.60 to 3.25]	high	direct	imprecise	NA	Insufficient

RR = risk ratio [95 percent confidence intervals]

* Moderate risk of bias indicates that the results are probably believable taking study limitations into consideration (low risk of bias would indicate that the results are believable taking study limitations into consideration and high risk of bias would indicate that the results are uncertain taking study limitations into consideration)

Note: This presents the assessment of the individual components of strength of evidence and the overall evidence rating. NA appears under consistency because only one study was available for each outcomes-comparison combination.

Table 11. Community integration questionnaire

Study Design Outcome Measurement	Treatment Arms	Score (SD), Before Treatment	Score (SD), After Completion of Treatment	Effect size (ES) [95%CI] for Treatment vs. Control; Comments
Cicerone 2008[70] RCT Self report under supervision	Intensive Cognitive Rehabilitation Program (ICRP) (n=34)	11.2 (3.4)	12.9 (3.4) P<0.05 versus before treatment	ES=0.30 [-0.18 to 0.78] No significant differences between groups but Intensive cognitive rehabilitation participants showed greater improvements on the CIQ
	Standard Neurorehabilitation Program (STD) (n=34)	12.1 (4.0)	11.7 (4.4)	
Cicerone 2004[61] Prospective Cohort Administered and scored according to original procedures (Willer, 1993)	Intensive Cognitive Rehabilitation Program (ICRP) (n=27)	11.6 (4.6)	16.8 (4.2) ES vs. before treatment 1.16 [0.59 to 1.74]	ES=0.14 [-0.38 to 0.67] 52% of ICRP participants showed clinically significant improvement compared with 31% of SRP participants (OR=2.41 [0.8 to 7.2]
	Standard Neurorehabilitation (SRP) (n=29)	13.7 (4.4)	16.1 (5.4) ES vs. before treatment 0.48 [-0.04 to 1.00]	The ICRP group exhibited over twice the magnitude of treatment effect on total CIQ than the participants receiving SRP (1.20 vs. 0.49).

OR = Odds ratio [95% confidence interval]

Table 12. Strength of evidence for the primary TBI studies: CIQ

Intervention; Assessment	Treatment Arms	Study Type	n	Summary Statistics [95% CI]	Risk of Bias	Directness	Precision	Consistency	Evidence Rating
Cicerone 2008[70] Post treatment, 16 weeks	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	68	ES = 0.30 [-0.18 to 0.78]	moderate**	direct	imprecise	NA	Low
Cicerone 2004[61] Post treatment, 16 weeks	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	Prospective Cohort	56	OR = 2.41 [0.8 to 7.2]†	high	direct	imprecise	NA	Insufficient

*ES = effect size (standardized mean difference), calculated by using Hedges' adjusted g,

** Medium risk of bias indicates that the results are probably believable taking study limitations into consideration (low risk of bias would indicate that the results are believable taking study limitations into consideration and high risk of bias would indicate that the results are uncertain taking study limitations into consideration)

†OR = odds ratio, participants achieving clinically significant improvement, treatment versus control.

Table 13. Overview of secondary outcomes results

Treatments; Study Design	Study Populations	Outcome Definition	Post-Treatment Assessment	Followup Post-Treatment Assessment
Intensive cognitive rehabilitation vs. Standard neurorehabilitation[70] RCT	68 American TBI patients (mild 13%), at least 3 months post-injury in a postacute brain injury rehabilitation center within a suburban rehabilitation hospital.	Perceived Quality of Life (PQOL)	↔	↔ 6 months post-treatment
Functional-experiential vs. Cognitive-didactic[71]	RCT 360 American Veterans Affairs inpatients (active duty or veteran) with non-penetrating TBI within the preceding 6 months.	Disability Rating Scale (DRS)	NR	↔ 1 year post-treatment
		Quality of Life	NR	↔ 1 year post-treatment
Telephone counseling vs. Standard rehabilitation alone[81] RCT	171 moderate to severe TBI patients discharged from acute care unit.	EuroQoL	NR	↑ 1 year post injury
		GOS-E	NR	↑ 1 year post injury
		PQOL	NR	↑ 1 year post injury
Outreach vs. Information[82]	112 TBI patients with long-term treatment goals amenable to intervention.	BICRO-39 change score	NR	↑ 2 years post allocation
Case management Versus Conventional rehabilitation [73] RCT (hospitals, not patients)	126 British TBI patients with closed head injury. Case-managed patients were more severely injured at study entry (Glasgow coma score and amnesia P<0.05 between groups).	GOS-E	↔ 6 months post injury	↔ 1 year post injury ↔ 2 years post injury
		DRS	NR	↓ 2 years post injury
Intensive cognitive rehabilitation vs. Standard neurorehabilitation[61]	57 chronically impaired TBI survivors	QCI	↑ post-treatment	

Key Question 3. What evidence exists to establish a minimum clinically important difference in community reintegration as measured by the Mayo-Portland Adaptability Inventory (MPAI-4) for postacute rehabilitation for TBI in adults?

Key Points

- We found no eligible studies that measured effectiveness using the MPAI.
- MCID does not appear to be established for the MPAI.
- MCID in CIQ scores is addressed in one eligible study.

Detailed Analysis

None of the eligible studies addressed MCID for the MPAI. Because we did not find studies assessing community integration with the MPAI, we evaluated MCID with respect to the CIQ. In their pilot study of the ICRP in which they evaluated the incidence of clinically significant changes in community integration, Cicerone and colleagues derived a ~~"r~~eliable change index" of 4.2 in total CIQ score (from psychometric data from a previous sample of TBI patients). The authors described the reliable change index that indicated whether individuals made positive change, no change, or negative change in community integration in a previous sample of TBI survivors. The authors cited the consistency of this MCID with another that was derived from a previous study.[61] However, the later RCT evaluating the ICRP did not mention a reliable change index or other attempts to assess MCID, nor did it explain the omission.[70]

Key Question 4. Are improvements in outcomes achieved via multidisciplinary postacute rehabilitation for TBI sustained over time?

Key Points

- Only two eligible studies with moderate or low risk of bias reported participation outcomes measured at post-treatment and followup intervals.
- A low level of evidence showed that statistically significant improvements immediately post-treatment in CIQ scores and community-based employment were sustained. However, these variables no longer differed between groups at 6 months.
- We found a low strength of evidence that rates of participation in competitive work achieved at 6 months post-treatment were sustained at 12 months post-treatment.[73]

Detailed Analysis

Two primary outcomes studies incorporated additional followup outcomes measurements for productivity.[70, 73] Table 14 presents the sustainability results for these studies. Cicerone et al. assessed community-based employment immediately post-treatment and again at 6 months post-treatment.[70] Improvements in both the ICRP and the standard rehabilitation groups were maintained at 6 months. Greenwood and colleagues assessed outcomes at 6, 12, and 24 months postinjury;[73] however, the 24-month measures were considered high risk of bias due to limited data. Both groups appeared to have maintained productivity outcomes from the 6-month postinjury measurement. Cicerone et al. also report a followup assessment of community integration.[70] Table 15 describes the sustainability results of this study. Table 16 presents

individual components and an overall SOE for each of these comparisons. The study conducted by Cicerone, et al., provides a low SOE that outcomes achieved at completion of the ICRP or standard rehabilitation were sustained at 6 months. Evidence was insufficient to conclude whether outcomes for case management or standard rehabilitation alone were maintained at followup.

Table 14. Sustainability of productivity outcomes

Study Outcome	Treatment Arms	Productive at Timepoint 1	Productive at Timepoint 2	Posttreament Vs. Followup
Cicerone 2008[70] Community-based employment[a]	Intensive cognitive rehabilitation	47% (16/34)	60% (18/30)	P=0.57
	Standard neurorehabilitation	21% (7/34)	50% (14/28)	P=0.10
Greenwood 1994[73] At competitive work	Case management	24% (10/42)	30% (9/30)	P=0.65
	Conventional rehabilitation	28% (15/53)	30% (14/47)	P=0.90

[a]Timepoint 1 – immediately post-treatment; Timepoint 2 – 6 months post-treatment.
[b] Timepoint 1 – 6 months postinjury; Timepoint 2 – 12 months postinjury.
RR = relative risk [95% confidence intervals].
Note: This table reports the outcomes from studies with followup measurements of productivity outcomes.

Table 15. Sustainability of community integration questionnaire score

Study Outcome Measurement	Treatment Arms	Score (SD), Timepoint 1[a]	Score (SD), Timepoint 2[a]	Sustainability of Treatment at Timepoint 1
Cicerone 2008[70]	Intensive Cognitive Rehabilitation Program (n = 34)	12.9 (3.4)	13.2 (4.3)	At the 6-month followup, scores remained significantly different from pretreatment (P = .02)
	Standard Neurorehabilitation Program (n = 34)	11.7 (4.4)	12.9 (4.4)	At the 6 month followup, participants showed improvement on CIQ scores from post-treatment (P = 0.04)

[a]Timepoint 1 – immediately post-treatment; Timepoint 2 – 6 months post-treatment.
Note: This table reports the outcomes from studies that with followup measurements of community integration outcomes.

Table 16. Strength of evidence for sustainability outcomes

Intervention Outcome Assessment	Treatment Arms	Study Type	n	Summary Statistics	Risk of Bias	Directness	Precision	Consistency	Evidence Rating
Cicerone 2008[70] Community-based employment 6 months post-treatment	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	58	RR: 1.22 [0.75 to 1.92]	moderate*	direct	imprecise	NA	Low
Cicerone 2008[70] CIQ 6 months post-treatment	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	58	ES: 0.07 [-0.41 to 0.54]	moderate*	direct	imprecise	NA	Low
Greenwood, 1994[73] Post-injury, 1 year	Case-management vs. Conventional rehabilitation	RCT (Hospitals, not patients)	77	RR: 1.01 [0.50 to 2.03]	moderate	direct	imprecise	NA	Low

RR = risk ratio [95 percent confidence intervals]

* Moderate risk of bias indicates that the results are probably believable taking study limitations into consideration (low risk of bias would indicate that the results are believable taking study limitations into consideration and high risk of bias would indicate that the results are uncertain taking study limitations into consideration)

Key Question 5. What adverse effects are associated with multidisciplinary postacute rehabilitation for TBI?

Key Points

Adverse events of postacute rehabilitation treatments are inadequately addressed in research. We identified one study that formally addressed adverse events.

Detailed Analysis

The single study that described adverse events did not appear to assess them in a systematic manner, and reported that no adverse events were observed.[71]

Summary and Discussion

Summary of Findings

This review sought to identify the most effective multidisciplinary postacute rehabilitation interventions for impairments from moderate to severe TBI in adults. The primary outcome of interest was participation in community life as indicated by productivity or measures of community integration. We searched and screened the literature for studies that assessed the effectiveness or comparative effectiveness of multidisciplinary rehabilitation for TBI in enhancing patient-centered outcomes relating to participation. We identified 16 studies assessing our prespecified primary outcomes or secondary patient-centered outcomes. We extracted data, assessed risk of bias for individual studies, qualitatively analyzed evidence relevant to each Key Question, and assessed the strength of the body of evidence for each comparison as insufficient, low, moderate, or high.

Characterizing Interventions (Key Question 1)

Multidisciplinary postacute rehabilitation programs for impairments from moderate to severe TBI varied widely in terms of populations targeted, setting, program intensity and duration, and timing of intervention. Clear categorization of all studied interventions was not possible. However, programs based upon the comprehensive holistic day treatment model of care are the most frequently studied. These programs maintained a similar approach and mode of delivery. Individuals were enrolled in and progressed through these structured intensive day-treatment programs in small cohort groups, receiving several hours of treatments per day, several days per week. Treatment was delivered largely through group sessions, while maintaining an emphasis on addressing individual needs. Areas of focus included self-awareness of impairments and compensatory approaches to retraining, with vocational rehabilitation as a key component.

Effectiveness and Comparative Effectiveness (Key Question 2)

Our review, like others, found the currently available evidence insufficient to draw conclusions about the effectiveness or ineffectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI. While we found stronger evidence on the comparative effectiveness of different approaches to multidisciplinary postacute rehabilitation, we identified few well-designed studies that addressed comparative effectiveness and we were unable to find robust evidence for the superiority of any one approach over another. Table 17 lists summary results for comparative effectiveness. Comparative effectiveness research on complex conditions and interventions lends itself to conclusions about specific populations and interventions:

We found that gainful employment or return to military fitness did not differ significantly at 1-year post-treatment between groups enrolled in a 6-week inpatient hospital treatment versus an 8-week limited home-based treatment (low SOE). Participants were active duty military patients with closed head injuries experiencing relatively mild impairment levels and treated within 3 months of injury.

We found that productivity did not differ significantly at 1-year post-treatment between closed head injury groups enrolled in functional-experiential versus cognitive didactic inpatient rehabilitation programs (low SOE). Both programs lasted an average of just over 1 month and were delivered in VA rehabilitation facilities. Participants began treatment within 6 months of injury.

We found that rates of return to community-based employment were higher immediately post-treatment among the group of TBI survivors with predominantly chronic impairments enrolled in the ICRP versus the group enrolled in standard rehabilitation (low SOE). These individuals were treated in civilian outpatient rehabilitation hospitals and judged to need 16 weeks of intensive treatment. The ICRP group did not achieve higher rates of community integration (low SOE).

We found that rates of return to community-based employment between these two groups equalized by 6-month post-treatment (rates in the standard rehabilitation group caught up with those of the ICRP group) (low SOE).

Effectiveness and comparative effectiveness conclusions of this review are highly specific to the populations and settings addressed by individual studies. On the face, various competing treatments appeared to produce similar effects, demonstrating no statistical differences between treatment groups 1 year after completion of multidisciplinary rehabilitation programs.

Two studies demonstrated equivalent participation results in comparison groups with regard to productivity; however, these equivalent results may be an embodiment of the context in which these studies were conducted. For instance, Salazar, et al. enrolled patients whose functional status was high enough to allow for randomization to home care.[72] Thus, the fact that this group experienced similar improvements to those randomized to inpatient rehabilitation may be specific to their low level of impairment. Indeed, the authors‘ post hoc subgroup analysis of those with more serious injuries found greater improvements from inpatient rehabilitation. A similar situation occurred in the Vanderploeg study, in which certain patient subgroups fared better with one rehabilitation approach versus the other as detected in post hoc analysis.[71] Similar findings relevant to a specific subgroup are evident with regard to the CIQ.[61] The prospective cohort study delivered the ICRP to a more chronically impaired group and achieved a greater rate of clinically significant improvement, suggesting that this approach might be better suited to these individuals. Although these programs achieved equivalent outcomes, the studies also indicated that perhaps different patient subgroups respond better to certain types of treatments.[61]In certain studies, the timing of outcome measurement was important. For example, when Cicerone et al. measured participation outcomes at *earlier* timepoints, results suggested greater improvements for the groups involved in a comprehensive holistic program compared to a traditional program.[70] This distinction could appear irrelevant since outcomes equalized within 6 months post-treatment in the single study that collected followup data.[70] However, given the financial and social impact of TBI on survivors and their families, earlier participation outcomes may be important to patients and families.

Table 17. Summary and strength of evidence of effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for TBI

Population	Intervention/Comparator	Outcome	Conclusion	SOE
Active-duty military personnel with moderate to severe closed head injury treated within 3 months of injury (Salazar 2000)[72]	Inpatient hospital rehabilitation program (8 weeks) vs. limited home treatment	Return to gainful employment at 1 year post-treatment	No difference between groups	Low (moderate risk of bias, single study)
		Fitness for military duty at 1 year post-treatment	No difference between groups	Low (moderate risk of bias, imprecise, single study)
Veterans or active duty military personnel with moderate to severe closed head injury treated within 6 months of injury (Vanderploeg 2008)[71]	Functional-experiential vs. Cognitive-didactic rehabilitation programs for varying durations	Return to gainful employment at 1-year post-treatment	No difference between groups	Low (low risk of bias, imprecise, single study)
Chronically impaired patients with primarily moderate to severe TBI (Cicerone 2008; Cicerone 2004)[61, 70]	Intensive cognitive rehabilitation (16 weeks) vs. standard rehabilitation (16 weeks)	Community-based employment at end of treatment	Statistically higher proportion Intensive cognitive rehabilitation group employed	Low (moderate risk of bias, single study)
		Community-based employment at 6 months post-treatment	No difference between groups	Low (moderate risk of bias, imprecise, single study)
		CIQ at end of treatment	No difference between groups	Low (moderate risk of bias, imprecise, consistent)
		CIQ at 6 months post-treatment	No difference between groups	Low (moderate risk of bias, imprecise, single study)

SOE – strength of evidence.
Note: This table presents a summary of the findings for this systematic review.

Minimum Clinically Important Differences (Key Question 3)

We identified no evidence establishing minimum clinically important differences (MCIDs) for the MPAI. In their pilot study of the ICRP, Cicerone and colleagues derived a "reliable change index" of 4.2 of the total CIQ score to evaluate the incidence of clinically significant changes in community integration. The authors described the reliable change index as indicating whether individuals made positive change, no change, or negative change in community integration in a previous sample of TBI survivors, essentially an MCID concept.[61] However, the later RCT evaluating the ICRP did not mention a reliable change index or any attempts to determine the incidence of clinically significant changes, nor did it explain the omission.[70]

Maintenance of Outcomes (Key Question 4)

Very few eligible studies conducted followup assessments to determine maintenance of rehabilitation gains. The two studies that evaluated followup outcomes yielded highly specific conclusions:

We found a low strength of evidence that improvements in return to community-based employment and CIQ scores were sustained at 6 months post-treatment.[70]

We found a low strength of evidence that rates of participation in competitive work achieved at 6 months post-treatment appear to be sustained at 12 months post-treatment.[73]

Adverse Events (Key Question 5)

The single study that mentioned adverse events does not appear to have assessed them in a systematic manner, reporting that no adverse events were observed.[71]

Comparison With Previous Systematic Reviews

Our review found the currently available evidence on the comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI in adults limited, as other reviews have suggested.[38, 39] Conclusions from these reviews report insufficient or low levels of evidence about multidisciplinary rehabilitation programs for moderate to severe TBI. However, these conclusions are inconsistent with those of some previous systematic reviews that suggested more robust evidence of effectiveness.[14, 37, 40, 42, 85] However, these contrasting reviews differed from ours methodologically in important ways, such as by addressing research on the ABI population (which may include studies that enrolled primarily stroke patients), and by applying more lenient inclusion criteria with respect to study design or less rigorous assessments of SOE. The reviews conducted by groups specializing in systematic reviews apply a more rigorous level of scrutiny to the evidence base than has been previously applied to the literature on this topic. More rigorous scrutiny of the evidence tends to result in more conservative assessments about effectiveness.

Limitations of the Evidence

Strength of Evidence

In many ways, the results of this review are unsatisfactory. Problems with synthesizing evidence arise from the complexity of sustained TBI impairments and the interventions to

rehabilitate them. This complexity makes it challenging to achieve SOE assessments higher than low. Systematic review methodology requires the assessment of SOE at the outcome level. The specificity of the comparisons for this topic means that often, single studies were the basis for drawing conclusions and assessing SOE. Several factors impede high SOE assessments on complex interventions. First, heterogeneity among populations, interventions, and outcomes makes pooling of data impossible. Further, inconsistency in selection of outcomes as well as timing and method of outcome measurement complicates the ability to group studies for grading and interpretation. In addition to the limited number of studies within a comparison, formidable obstacles to obtaining a SOE on this topic include small sample sizes, and the difficultly in achieving a "low risk of bias" for individual studies evaluating complex interventions.

Risk of Bias

Risk of bias presented a major challenge in drawing conclusions about effectiveness. In order to earn an overall low risk of bias assessment, a body of evidence should include several well designed studies, RCTs and prospective cohort studies, of sufficient sample sizes that study similar interventions and controls in similar populations with consistent patterns across consistent outcomes measures. Further, the individual studies must have a low risk of bias. Risk of bias increases when treatment and control groups are not comparable; participants, providers, and outcomes assessors are not blinded; interventions are not well defined or implemented; outcomes measures do not have strong psychometric properties, appropriate statistical analysis is not conducted; confounding variables are not controlled for; estimates are not adjusted for multiple comparisons; and for indications of possible reporting bias.

For this topic, blinding may be the greatest hurdle. Double blinding is typically impossible in rehabilitation research, but outcome evaluators can and should be blinded. Risk of bias is higher without adequate blinding of participants, providers, and outcomes assessors. This risk is especially heightened when intervention outcomes are assessed via subjective self-report measures, which are common in rehabilitation research.

The aforementioned inadequacy of intervention definitions detracts from the internal validity of these studies. Further, the inadequate treatment definitions were often accompanied by a lack of information about measures to insure effective implementation. We looked for reports of staff training, references to treatment manuals documenting treatment components and/or algorithms, and fidelity checks assessing whether interventions were effectively implemented. The studies we reviewed rarely addressed these issues. Lastly, several outcome-related issues contribute to the higher risk of bias for individual studies on this topic.

The primary outcomes we selected appeared to have acceptable psychometric properties, but often failed to identify MCIDs. Additionally, many studies tested the effect of their interventions on many different outcome scales. While some studies identified their primary outcomes, very few adjusted estimates for multiple comparisons or provided justification for not doing so. Failure to use a Bonferroni correction or other appropriate adjustment technique when multiple comparisons are made can result in accepting statistically significant results when they occurred by chance.

Study design also affects risk of bias during SOE assessment. We recognize a difficult paradox with regard to studying postacute multidisciplinary rehabilitation for moderate to severe TBI. That is, the complexity of the topic adds significant challenge to the design, conduct, and expense of RCTs (compared to pharmaceutical intervention studies), and the resources and incentives (i.e. Federal Drug Administration approval) for conducting these trials is not well

established. Yet, given the potential for selection bias and the high number of confounding and effect-modifying variables, RCTs are a superior methodology for studying the impact of these interventions. The cohort studies we reviewed typically failed to adequately select controls and/or adjust for differences between groups.

Applicability

The studies evaluated for this review may be applicable to the specific populations targeted by the examined interventions (e.g. military populations, those with significant disabilities, without other psychiatric diagnoses, chronically impaired, etc.) and the time periods in which they were studied. Even then, many of the interventions and control conditions seemed to be embodiments of their local rehabilitation systems, making replicability in other contexts challenging. This is especially evident in studies in military and VA health systems, in which rehabilitation may differ markedly from that available in civilian facilities. Because rehabilitation for TBI is a rapidly evolving field, studies conducted in the 1990s may not be applicable to the conditions in which rehabilitation is conducted today. Additionally, most studies excluded individuals with substance abuse or psychiatric diagnoses, both of which are common in the TBI population.[86] Inconsistent insurance coverage for rehabilitation services[10] may limit applicability of these results. Moreover, TBI disproportionately affects males, those aged 15-24, and those with lower socioeconomic status,[11] groups known to have lower rates of health insurance. Knowledge of which treatments are most effective is less likely to benefit those who lack insurance coverage to receive the services.

Selected Primary Outcomes

The outcomes selected for this review reflect current views on the importance of participation as an outcome of rehabilitation. However, given the complexity of this condition, arguments can be made for the importance of other outcomes despite small changes in participation measures. Some rehabilitation programs may have specific goals related to maintaining function or preventing deterioration of functional status. To maintain or prevent deterioration in participation outcomes may also be important goals of rehabilitation. Cicerone et al. re-analyzed data from previous studies and found that preventing deterioration in these outcomes may have substantial impact.[20] Other patient-centered outcomes such as reduced burden of care or need for supervision may be meaningful without changes in participation measures. Other reviews have considered a wider array of outcomes than those selected here. The recent IOM review considered the outcomes of cognitive functioning, quality of life, and functional status, and reached conclusions similar to ours, and concluded that the evidence on multimodal cognitive rehabilitation was not informative.[38]

Clinical Implications

Our inability to draw broader and more meaningful conclusions is of limited value to providers and payers seeking to identify the best possible care for those experiencing impairments from moderate to severe TBI. Ultimately, the available evidence provided little information about the overall effectiveness or comparative effectiveness of postacute multidisciplinary rehabilitation for adults with for moderate to severe TBI. However, our failure to draw broad conclusions must not be misunderstood to be evidence of ineffectiveness. This topic, like many other complex topics, merely lacks high quality conclusive evidence of

effectiveness or ineffectiveness from rigorously conducted systematic reviews. This type of evidence is a high bar currently met by only a small portion of medical interventions (and an even smaller portion of rehabilitation interventions). The limited evidence on this topic stems from the complexity of the condition and treatments resulting in limited available research, and from limitations within that research to answer salient research questions about what works for which patients. In light of the attention dedicated to this topic as demonstrated by the number of recent reviews and media stories, future research to better establish the evidence base for rehabilitation interventions for the TBI population is of utmost importance.

Future Research

Many systematic reviews have synthesized existing evidence for effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI in adults. Past reviews have had different focal points and eligibility criteria. The recently conducted IOM review of cognitive rehabilitation for TBI impairments was not able to draw conclusions about the effectiveness or comparative effectiveness of comprehensive multimodal programs for those with moderate to severe injuries, (the section of that review overlapping this review). Despite many reviews, research gaps remain. Additional comparative effectiveness reviews cannot satisfy these gaps until more high quality studies are completed. A followup study and report outlining the future research needs for this topic is forthcoming. Collaborative efforts among payers, providers, and other decisionmakers will enhance the value of future efforts. Conceptual work to overcome the shortcomings of current research may be the highest priority. Formal evidence synthesis efforts should aim to identify combinations of patient groups and rehabilitation approaches most likely to achieve success. Effectiveness trials can then be conducted for these high-priority subgroups and interventions. Future effectiveness and comparative effectiveness studies need to address the shortcomings of the currently available literature.

Conceptual work could assist an advancing knowledge in the field by making comparative effectiveness research more useful. For example, the development and consistent use of standardized assessments of TBI impairments could foster consistent reporting in research. The Interagency Workgroup on Demographics and Clinical Assessment has recently provided recommendations to achieve this standardization. Standardization would enable researchers to better define impairment domains and levels of impairment, which is critical to understanding which interventions work best for which patients. Additionally, as with many postacute rehabilitation topics, the taxonomy of treatment is underdeveloped.[87] Future research should work across all relevant disciplines to advance the development and consistent use of a taxonomy for rehabilitation interventions. This taxonomy would enhance patients‘ understanding of rehabilitation programs and enable more informed decisionmaking. The recent effort to develop unique taxonomies relevant to spinal cord injury rehabilitation could inform similar efforts specific to TBI rehabilitation.[88]

Future evidence synthesis efforts could address questions relevant to the current state of the research on this topic. For example, realist reviews are well suited to complex interventions (characterized as programs in which effects are dependent on context and implementation).[89] Realist reviews seek to provide an explanatory analysis discerning what works for whom and under what circumstances. This information can help strengthen understanding of programs and inform efficient and effective implementation.[89] Although realist reviews cannot achieve the goal of comparative effectiveness reviews, which is to identify what works and what does not, they can generate information that spurs hypotheses from which to design comparative effectiveness studies.

Future effectiveness and comparative effectiveness studies should aim to decrease risk of bias in individual studies and to expand sample sizes. Given the complexity of TBI and the interventions to address persistent impairments, and the heterogeneity common in these patients, the most valuable studies may those that aim to answer the question of which programs work for which impairments and types of patients or injuries. RCTs could be designed to address these questions. However, additional small RCTs alone may not move the field forward toward a substantially stronger evidence base. The construction of a sufficient evidence base will require

reconsideration of common methodological practices that have weakened RCT evidence, including 1) the specificity of populations studied, interventions compared, and outcomes used to measure effectiveness, and 2) small sample sizes. Large RCTs may be able to address these issues and thus provide stronger evidence. Larger sample sizes in RCTs that collect and report data elements relevant to patients, injuries, and interventions would allow for statistical adjustment of key confounding variables and may provide sufficient power to explore subgroup differences in treatment response. The expanded CONSORT statement provides guidance on reporting for RCTs evaluating nonpharmacological treatments.[90] Resulting data could then be used to statistically control for the many confounding variables inherent to this complex condition and interventions. However, specific alternatives to RCTs have been proposed as better suited to provide higher quality comparative effectiveness evidence with these complex topics. For example, the practice-based evidence approach[91] may help overcome certain shortcomings of the available research, also in part by allowing for studies with larger sample sizes.

The addition of high quality prospective cohort studies—if conducted on a broader scale—could also add valuable information about specific interventions and subgroups of TBI survivors. Therefore, several steps should be taken to correct common methodological flaws and to address unanswered questions. First, research on TBI rehabilitation must be appropriately powered to detect differences between treatment groups. Constructing research studies with adequate numbers in relevant subgroups or with sample sizes large enough to adjust for these differences would allow more meaningful results and conclusions. Cohort studies should carefully select comparison groups as similar as possible to the treatment group.

Both future RCTs and prospective cohort studies should address other methodological issues that currently detract from the current body of evidence. The adequacy of treatment definitions varied widely across studies. While some studies provided substantial details about their interventions, we would like to see references to treatment manuals (i.e. manualized interventions) that provide a resource for determining specific treatment components and content, including: (1) the ~~h~~how and why" of what is implemented for specific patients; (2) treatment progress; and (3) injury or impairment characteristics. Adequately defining the intervention would also assist in promoting the effective implementation of the interventions and control conditions and enable studies to evaluate the importance of intervention characteristics. Adherence or fidelity checks for the treatment and control conditions would verify the effective implementation of the compared interventions. Attention to these intervention definition and implementation issues would reduce risk of bias for intervention studies and enhance replicability of successful programs. While blinding of participants and providers may not be feasible, outcome assessors can and should be blinded. A lower risk of bias related to outcomes in these intervention studies could be achieved through a priori selection of primary patient-centered outcomes; a limited number of outcomes scales and comparisons; use of consistent and appropriate psychometrically justifiable outcomes scales; the establishment of minimum clinically important differences in these scales; and the adjustment for multiple comparisons. All of this would help create a stronger evidence base.

The TBI Model Systems programs.[92] may offer a venue for conducting rigorously designed comparative effectiveness studies, but are not without limitations (e.g., limited resources, systems not designed for intervention research). Future research should continue to explore comparative effectiveness by comparing interventions implemented in different TBI model systems locations. Secondary analysis of individual patient data could reveal patterns among patient, injury, and rehabilitation characteristics that are associated with improved outcomes.

However, systems that capture the necessary intervention level information may not yet exist. Large RCTs and prospective cohort designs with appropriate controls would best move the field forward.

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Acronyms and Abbreviations

ABI	acquired brain injury
ABIER	Evidence-based Review of Moderate to Severe Acquired Brain Injury Report
AHRQ	Association for Health Care Research and Quality
BIRCO-39	Brain Injury Community Rehabilitation Outcome-39
CENTRAL	Cochrane Central Register of Controlled Trials
CHART	Craig Handicap Assessment and Report Technique
CHART-SF	Craig Handicap Assessment and Report Technique - Short Form
CIQ	Community Reintegration Questionnaire
DRS	Disability Rating Scale
ECRI	Emergency Care Research Institute
EGOS-E	Extended Glasgow Outcome Score
EuroQoL	European Quality of Life Scale
GCS	Glasgow Coma Score
ICF	International Classification of Function, Disability and Health
ICRP	Intensive Cognitive Rehabilitation Program
ICTRP	International Controlled Trials Registry Platform
IOM	Institute of Medicine
KQ	Key Questions
MCID	minimum clinically important difference
MPAI	Mayo-Portland Assessment Inventory
NIAF	Newcastle Independence Assessment From
NIH	National Institutes of Health
NR	Not Reported
PEDro	Physiotherapy Evidence Database
PICOTS	Population, Intervention, Comparator, Outcome, Timing , Setting
PQOL	Perceived Quality of Life Scale
QCIQ	Quality of Community Integration Questionnaire
QOLI	Quality of Life Inventory
RCT	Randomized Controlled Trial
RR	Risk ratio
RTW	Return to work
SOE	Strength of Evidence
SWLS	Satisfaction with Life Scale
TBI	Traumatic Brain Injury
TEP	technical expert panel
VA	Veterans Affairs
WHO	World Health Organization

Appendix A. Search Strategy

Ovid MEDLINE Search Strategy

1 Epidemiologic studies/
2 exp case control studies/
3 exp cohort studies/
4 Case control.tw.
5 (cohort adj (study or studies)).tw.
6 Cohort analy$.tw.
7 (Follow up adj (study or studies)).tw.
8 (observational adj (study or studies)).tw.
9 Longitudinal.tw.
10 randomized controlled trial/
11 clinical trial/
12 clinical trial, phase i.pt.
13 clinical trial, phase ii.pt.
14 clinical trial, phase iii.pt.
15 clinical trial, phase iv.pt.
16 controlled clinical trial.pt.
17 randomized controlled trial.pt.
18 multicenter study.pt.
19 clinical trial.pt.
20 or/1-19
21 Craniocerebral Trauma/
22 exp Brain Injuries/
23 Cerebrovascular Trauma/
24 brain injur*.ti,ab.
25 head injur*.ti,ab.
26 tbi.ti,ab.
27 or/21-26
28 20 and 27
29 Rehabilitation/
30 rehab*.ti,ab.
31 neurorehabilitation.ti,ab.
32 29 or 30 or 31
33 28 and 32
34 limit 33 to "all child (0 to 18 years)"
35 limit 34 to "all adult (19 plus years)"
36 33 not 34
37 35 or 36
38 limit 37 to (addresses or autobiography or bibliography or biography or case reports or clinical conference or congresses or dictionary or directory or in vitro or interactive tutorial or interview or lectures or legal cases or legislation or news or newspaper article or patient education handout or periodical index or portraits or video-audio media or webcasts)
39 37 not 38
40 limit 39 to yr="1980 -Current"

PsycINFO Search Strategy

1 epidemiologic studies.mp.
2 case control.mp.
3 exp Longitudinal Studies/
4 (cohort adj (study or studies)).tw.

5 Cohort analy$.tw.
6 (Follow up adj (study or studies)).tw.
7 (observational adj (study or studies)).tw.
8 longitudinal.mp.
9 randomized controlled trial.mp.
10 clinical trial.mp. or exp Clinical Trials/
11 controlled clinical trial.mp.
12 phase i clinical trial.mp.
13 phase ii clinical trial.mp.
14 phase iii clinical trial.mp.
15 phase iv clinical trial.mp.
16 multicenter study.mp.
17 or/1-16
18 exp Traumatic Brain Injury/ or exp Head Injuries/ or craniocerebral trauma.mp.
19 brain injur*.mp.
20 exp Cerebrovascular Accidents/ or cerebrovascular trauma.mp.
21 head injur*.mp.
22 tbi.mp.
23 or/18-22
24 17 and 23
25 exp Rehabilitation/ or exp Neuropsychological Rehabilitation/ or rehabilitation.mp.
26 rehab*.mp.
27 exp Neurorehabilitation/ or neurorehabilitation.mp.
28 or/25-27
29 24 and 28
30 limit 29 to (100 childhood <birth to age 12 yrs> or 120 neonatal <birth to age 1 mo> or 140 infancy <age 2 to 23 mo> or 160 preschool age <age 2 to 5 yrs> or 180 school age <age 6 to 12 yrs> or 200 adolescence <age 13 to 17 yrs>)
31 limit 30 to ("300 adulthood <age 18 yrs and older>" or 320 young adulthood <age 18 to 29 yrs> or 340 thirties <age 30 to 39 yrs> or 360 middle age <age 40 to 64 yrs> or "380 aged <age 65 yrs and older>" or "390 very old <age 85 yrs and older>")
32 29 not 30
33 31 or 32
34 limit 33 to yr="1980 -Current"

Cochrane Central Register of Controlled Trials Search Strategy

1 traumatic brain injur* and rehab*

PEDro Search Strategy

1 traumatic brain injur* AND rehab*

Appendix B. Risk of Bias

Appendix B. Table 1. Risk of Bias for Individual Studies

Study	Study design	Overall Risk of Bias Assessment	Comments
Cicerone, 2008[1]	RCT	Moderate	Possible contamination via same professionals delivering treatment and control interventions; minimally clinically important difference in CIQ not specified *a priori*; subjective self-report scale used for primary outcome measurement; no adjustment for multiple comparisons.
Vanderploeg, 2008[2]	RCT	Low	Well-designed study; no adjustment for multiple comparisons.
Salazar, 2000[3]	RCT	Moderate	Outcome assessors not blinded; intervention implementation judged partially adequate; primary outcomes self-report; no adjustment for multiple comparisons.
Greenwood, 1994[4]	RCT	Moderate	Group randomization; moderate attrition at 6-month time point, high attrition at 12-month time point; no adjustment for multiple comparisons. Outcomes at 24 months considered high risk of bias due to high attrition and not used.
Ponsford, 2006[5]	Cohort	High	Potential selection bias, retrospective control group; intervention definition and implementation partially adequate; no adjustment for multiple comparisons, many outcomes assessed including several scales and subscales; potential reporting bias.
Sarajuuri, 2005[6]	Cohort	Moderate	Potential selection bias; confounding not appropriately addressed.
Prigatano, 1994[7]	Cohort	High	Potential selection bias, retrospective control group; outcome assessors not blinded; intervention implementation partially adequate; inconsistent outcomes measurement across groups; confounding not adequately addressed.
Rattok, 1992[8]	Cohort	Moderate	Possible contamination via same professionals delivering treatment and control interventions; blinding of outcomes assessors not reported; no adjustment for multiple comparisons.

Prigatano, 1984[9]	Cohort	Moderate	Potential selection bias, retrospective control group; inadequate intervention implementation; inconsistent outcomes measurement across groups; confounding not adequately addressed.
Hashimoto, 2006[10]	Cohort	High	Potential selection bias; blinding of outcomes assessors not reported, inadequate intervention definition; treatment group provided varying levels of treatment intensity, but comparisons are for entire group to a no treatment group; subjective self-report scale used for primary outcome measurement; minimally clinically important difference in CIQ not specified *a priori*; confounding not adequately addressed; no adjustment for multiple comparisons, many outcomes assessed including several scales and subscales.
Cicerone, 2004[11]	Cohort	Moderate	Selection bias; intervention definition and implementation partially adequate scale used for primary outcome measurement; confounding not adequately for multiple comparisons.
Willer, 1999[12]	Cohort	High	Potential selection bias; inadequate intervention definition; intervention implementation partially adequate; subjective self-report scale used for primary outcome measurement; minimally clinically important difference in CIQ not specified *a priori*; insufficient statistical analysis; confounding not adequately addressed; no adjustment for multiple comparisons.
Bell, 2005[13]	RCT	Moderate	Well-designed study; composite outcome measures challenging to interpret; no adjustment for multiple comparisons.
Powell, 2002[14]	RCT	Moderate	Minimally clinically important difference in BICRO-39 not specified *a priori*; subjective self-report scale used for primary outcome measurement; no adjustment for multiple comparisons.
Thomas, 2004[15]	Cohort	High	Potential selection bias; subjective self-report scale used for primary outcome measurement; minimally clinically important difference not specified *a priori*; insufficient statistical analysis; confounding not adequately addressed; no adjustment for multiple comparisons.
Semlyen, 1998[16]	Cohort	High	Potential selection bias; inadequate intervention definition; intervention implementation partially adequate; subjective self-report scale used for primary outcome measurement; minimally clinically important difference not specified *a priori*; insufficient statistical analysis; confounding not adequately addressed; no adjustment for multiple comparisons.

Appendix B. Table 2. Risk of Bias Assessment Form for RCTs

Author _____ ***Year*** _____ **PMID** _____ **Reviewer** _____

Question	Response	Criteria	Justification
	Internal Validity		
1. Was the method of randomization adequate?	Yes ☐	Method used should produce comparable groups.	
	No ☐	Pseudo randomization (ie. alternate allocation, by days of week, etc) or randomization approach cannot be determined	
	Uncertain ☐	Randomization method unclear	
2. Was allocation concealment adequate?	Yes ☐	Method used to conceal the allocation sequence could not have been foreseen in advance of, or during, enrolment.	
	No ☐	No concealment	
	Uncertain ☐	Could not be ascertained.	
3. Were outcome assessors blinded?	Yes ☐	Yes	
	No ☐	No	
	Uncertain ☐	Could not be ascertained.	
4a. Is the level of detail in describing the treatment intervention adequate?	Yes ☐	Treatment intervention described based upon model or theory, specific intervention components adequately described, interventions documented in manuals or other documentation.	
	Partially ☐	Some of the above features.	
	No ☐	None of the above features.	
4b. Is the level of detail in describing the control intervention adequate?	Yes ☐	Active control intervention described based upon model or theory, specific intervention components adequately described, interventions documented in manuals or other documentation. Passive control adequately described.	
	Partially ☐	Some of the above features.	
	No ☐	None of the above features.	

5. Are interventions assessed using valid and reliable measures, implemented consistently across all study participants?	Yes	☐	Implementation accompanied by staff training and fidelity checks, consistency across groups in treatment features not studied.	
	Partially	☐	Implementation accompanied by some of above features.	
	No	☐	No training or fidelity checks.	
6. Are outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Yes	☐	Measure valid and reliable (i.e. objective measures, well validated scale, provider report)	
	Partially	☐	Some of the above features (partially validated scale)	
	No	☐	None of the above features. (self-report, scales with lower validity, reliability)	
7. Were incomplete outcome data adequately addressed?	Yes	☐	Balanced across groups and/or imputed using appropriate methods.	
	No	☐	High attrition or differential loss; no imputations or inappropriate imputations for missing data.	
	Uncertain	☐	Could not be ascertained.	
8. Are reports of the study free of suggestion of selective outcome reporting?	Yes	☐	All prespecified outcomes reported.	
	No	☐	Not all prespecified outcomes reported, subscales reported not prespecified, outcomes reported incompletely.	
	Uncertain	☐	Could not be ascertained.	
9. Is the study free from additional sources of bias?	Yes	☐		
	No	☐		
	Uncertain	☐		
	Overall Assessment			
Overall Risk of Bias assessment	Low	☐	Results are believable taking study limitations into consideration	
	Moderate	☐	Results are probably believable taking study limitations into consideration	
	High	☐	Results are uncertain taking study limitations into consideration	

Appendix B. Table 3. Risk of Bias Assessment Form for Observational Studies

Author _____ ***Year*** _____ **PMID** _____ **Reviewer** _____

Question	Response	Criteria	Justification
	Internal Validity		
1. Is the study design prospective, retrospective, or mixed?	Prospective ☐	Outcome has not occurred at the time the study is initiated and information is collected over time to assess relationships with the outcome.	
	Mixed ☐	Case-control or cohort studies in which one group is studied prospectively and the other retrospectively.	
	Retrospective ☐	Analyzes data from past records.	
2a. Are inclusion/exclusion criteria clearly stated (i.e., severity, time since injury, pre-existing conditions, comorbidities, prior tbi)	Yes ☐		
	Partially ☐	Some, but not all, criteria stated or some not clearly stated.	
	No ☐		
2b. TBI severity inclusion criteria measured using valid and reliable measures and appropriate cut points for mod/sev TBI?	Yes ☐	e.g., GCS<13; LOC> 30 minutes; AOC >24 hours; PTA>1 day; AISS>2; positive imaging	
	No ☐		
	Uncertain ☐	Could not be ascertained.	
2c. Did the study apply inclusion/exclusion criteria uniformly to all comparison groups of the study?	Yes ☐		
	Partially ☐	Some criteria applied to all arms	
	No ☐		
2d. Is the selection of the comparison group appropriate, after taking into consideration feasibility and ethical considerations?	Yes ☐	Groups selected from same source (e.g., community or hospital) to reduce baseline differences between groups. For case-control studies, cases should have met case definition if they had the outcome.	
	No ☐		
	Uncertain ☐	Could not be ascertained.	

3. Were outcome assessors blinded?	Yes ☐	Yes	
	No ☐	No	
	Uncertain ☐	Could not be ascertained.	
4a. Is the level of detail in describing the treatment intervention adequate?	Yes ☐	Treatment intervention described based upon model or theory, specific intervention components adequately described, interventions documented in manuals or other documentation.	
	Partially ☐	Some of the above features.	
	No ☐	None of the above features.	
4b. Is the level of detail in describing the control intervention adequate?	Yes ☐	Intervention described based upon model or theory, specific intervention components adequately described, interventions documented in manuals or other documentation.	
	Partially ☐	Some of the above features.	
	No ☐	None of the above features.	
5. Are interventions assessed using valid and reliable measures, implemented consistently across all study participants?	Yes ☐	Implementation accompanied by staff training and supervision, checks of adherence/fidelity; consistency across groups in treatment features not studied.	
	Partially ☐	Implementation accompanied by some of above features.	
	No ☐	Implementation accompanied by none of above features.	
6. Are outcomes assessed using valid and reliable measures, implemented consistently across all study participants?	Yes ☐	Measure valid and reliable (i.e. objective measures, well validated scale, provider report); consistent implementation across groups.	
	Partially ☐	Some of the above features (partially validated scale)	
	No ☐	None of the above features. (self-report, scales with lower validity, reliability); in consistent implementation across groups	
	Uncertain ☐	Could not be ascertained.	

7a. Was attrition from all groups less than 20 percent?	Yes	☐		
	No	☐		
	Uncertain	☐	Could not be ascertained (i.e. retrospective designs where eligible at baseline could not be determined)	
7b. Did attrition differ between groups by less than 20 percent?	Yes	☐		
	No	☐		
	Uncertain	☐	Could not be ascertained (i.e. retrospective designs where eligible at baseline could not be determined)	
7c. In cases of high attrition or differential attrition, is the impact assessed (e.g. through sensitivity analysis or other adjustment method)?	Yes	☐		
	No	☐		
	Uncertain	☐	Could not be ascertained (i.e. retrospective designs where eligible at baseline could not be determined)	
	NA	☐	Not considered high or case-control study	
8. Were the important confounding and effect modifying variables taken into account in the design and/or analysis (e.g. through matching, stratification, interaction terms, multivariate analysis, or other statistical adjustment)?	Yes	☐		
	Partially	☐	Some variables taken into account or adjustment achieved to some extent	
	No	☐	Not accounted for or not identified.	
	Uncertain	☐	Could not be ascertained	
9. Are the statistical methods used to assess the primary outcomes appropriate to the data?	Yes	☐	Statistical techniques used must be appropriate to the data and take into account issues such as controlling for dose-response, small sample size, clustering, rare outcomes, and multiple comparisons. In normally distributed data the standard error, standard deviation, or confidence intervals should be reported. In non-normally distributed data, inter-quartile range should be reported.	

	Partially ☐		
	No ☐		
	Uncertain ☐	Could not be ascertained	
10. Are reports of the study free of suggestion of selective outcome reporting?	Yes ☐		
	No ☐	Not all prespecified outcomes reported, subscales not prespecified reported, outcomes reported incompletely.	
	Uncertain ☐	Could not be ascertained.	
11. Is the study free from additional sources of bias?	Yes ☐		
	No ☐		
	Uncertain ☐		
	Overall Assessment		
Overall Risk of Bias assessment	Low ☐	Results are believable taking study limitations into consideration	
	Moderate ☐	Results are probably believable taking study limitations into consideration	
	High ☐	Results are uncertain taking study limitations into consideration	

Appendix C. Excluded Studies

1. Altman IM, Swick S, Parrot D, et al. Effectiveness of community-based rehabilitation after traumatic brain injury for 489 program completers compared with those precipitously discharged. Archives of Physical Medicine & Rehabilitation. 2010 Nov;91(11):1697-704. 21044714. *Not eligible study design*
2. Anderson SI, Wilson CL, McDowell IP, et al. Late rehabilitation for closed head injury: a follow-up study of patients 1 year from time of discharge. Brain Injury. 1996 Feb;10(2):115-24. 8696311. *No comparison group*
3. Ashley MJ, Persel CS, Clark MC, et al. Long-term follow-up of post-acute traumatic brain injury rehabilitation: a statistical analysis to test for stability and predictability of outcome. Brain Injury. 1997 Sep;11(9):677-90. 9376835. *Not intervention study*
4. Ashley MJ, Persel CS, Lehr RP, Jr., et al. Post-acute rehabilitation outcome: relationship to case-management techniques and strategy. Journal of Insurance Medicine (Seattle). 1994;26(3):348-54. 10150511. *Not eligible study design*
5. Backhaus SL, Ibarra SL, Klyce D, et al. Brain injury coping skills group: a preventative intervention for patients with brain injury and their caregivers.[Erratum appears in Arch Phys Med Rehabil. 2010 Nov;91(11):1793]. Archives of Physical Medicine & Rehabilitation. 2010 Jun;91(6):840-8. 20510972. *No primary or secondary outcomes*
6. Bateman A, Culpan FJ, Pickering AD, et al. The effect of aerobic training on rehabilitation outcomes after recent severe brain injury: a randomized controlled evaluation. Archives of Physical Medicine & Rehabilitation. 2001 Feb;82(2):174-82. 11239307. *No primary or secondary outcomes*
7. Bell KR, Brockway JA, Hart T, et al. Scheduled telephone intervention for traumatic brain injury: a multicenter randomized controlled trial. Archives of Physical Medicine & Rehabilitation. 2011 Oct;92(10):1552-60. 21963122. *Not 75% Moderate/Severe TBI*
8. Benge JF, Caroselli JS, Reed K, et al. Changes in supervision needs following participation in a residential post-acute brain injury rehabilitation programme. Brain Injury. 2010;24(6):844-50. 20377342. *Not eligible comparison group*
9. Bornhofen C, McDonald S. Comparing strategies for treating emotion perception deficits in traumatic brain injury. Journal of Head Trauma Rehabilitation. 2008 Mar-Apr;23(2):103-15. 18362764. *Impairment-specific intervention*
10. Bornhofen C, McDonald S. Treating deficits in emotion perception following traumatic brain injury. Neuropsychological Rehabilitation. 2008 Jan;18(1):22-44. 17852760. *Impairment-specific intervention*
11. Bourgeois MS, Lenius K, Turkstra L, et al. The effects of cognitive teletherapy on reported everyday memory behaviours of persons with chronic traumatic brain injury. Brain Injury. 2007 Nov;21(12):1245-57. 18236200. *Not 75% moderate/severe TBI*
12. Bowen A, Tennant A, Neumann V, et al. Neuropsychological rehabilitation for traumatic brain injury: do carers benefit? Brain Injury. 2001 Jan;15(1):29-38. 11201312. *No primary or secondary outcomes*
13. Braunling-McMorrow D, Dollinger SJ, Gould M, et al. Outcomes of post-acute rehabilitation for persons with brain injury. Brain Injury. 2010;24(7-8):928-38. 20545448. *No comparison group*
14. Brooks N. The effectiveness of post-acute rehabilitation. Brain Injury. 1991 Apr-Jun;5(2):103-9. 1873599. *No original data*
15. Burke WH, Wesolowski MD, Guth ML. Comprehensive head injury rehabilitation: an outcome evaluation. Brain Injury. 1988 Oct-Dec;2(4):313-22. 3203177. *No comparison group*
16. Bush BA, Novack TA, Malec JF, et al. Validation of a model for evaluating outcome after traumatic brain injury. Archives of Physical Medicine & Rehabilitation. 2003 Dec;84(12):1803-7. 14669187. *No comparison group*
17. Cannon XL, Zhu WS, Poon Chetwyn CCCSW. Does Intensive Rehabilitation Improve Functional Outcome In Patients with Traumatic Brain Injury (TBI). Preliminary Results of a Prospective Randomized Controlled Trial. Journal of Neurotrauma. 1998(1):85. CN-00689851. *No primary or secondary outcomes*

18. Carnevale GJ, Anselmi V, Busichio K, et al. Changes in ratings of caregiver burden following a community-based behavior management program for persons with traumatic brain injury. The Journal of head trauma rehabilitation. 2002(2):83-95. CN-00378995. *Not 75% moderate/severe TBI*

19. Carnevale GJ, Anselmi V, Johnston MV, et al. A natural setting behavior management program for persons with acquired brain injury: a randomized controlled trial. Archives of physical medicine and rehabilitation. 2006(10):1289-97. CN-00568342. *No primary or secondary outcomes*
20. Cattelani R, Roberti R, Lombardi F. Adverse effects of apathy and neurobehavioral deficits on the community integration of traumatic brain injury subjects. European journal of physical & rehabilitation medicine. 2008 Sep;44(3):245-51. 18762734. *Not intervention study*
21. Cattelani R, Tanzi F, Lombardi F, et al. Competitive re-employment after severe traumatic brain injury: clinical, cognitive and behavioural predictive variables. Brain Injury. 2002 Jan;16(1):51-64. 11796099. *Not intervention study*
22. Cattelani R, Zettin M, Zoccolotti P. Rehabilitation treatments for adults with behavioral and psychosocial disorders following acquired brain injury: a systematic review. Neuropsychology Review. 2010 Mar;20(1):52-85. 20143264. *No original data*
23. Chang Zj LP. Rehabilitation and acupuncture treatment for patients with traumatic brain injury. Chinese Journal of Medical Device. 2005(5):38-9. CN-00784100. *No primary or secondary outcomes*
24. Chard SE. Community neurorehabilitation: a synthesis of current evidence and future research directions. NeuroRx. 2006 Oct;3(4):525-34. 17012066. *No original data*
25. Chen SH, Thomas JD, Glueckauf RL, et al. The effectiveness of computer-assisted cognitive rehabilitation for persons with traumatic brain injury. Brain Injury. 1997 Mar;11(3):197-209. 9058001. *No primary or secondary outcomes*
26. Chesnut RM, Carney N, Maynard H, et al. Summary report: evidence for the effectiveness of rehabilitation for persons with traumatic brain injury. The Journal of Head Trauma Rehabilitation 1999;14(2):176-188. 1999. *No original data*
27. Choi JH, Jakob M, Stapf C, et al. Multimodal early rehabilitation and predictors of outcome in survivors of severe traumatic brain injury. Journal of Trauma-Injury Infection & Critical Care. 2008 Nov;65(5):1028-35. 19001970. *No comparison group*
28. Cicerone KD, Azulay J, Trott C. Methodological quality of research on cognitive rehabilitation after traumatic brain injury. Archives of Physical Medicine & Rehabilitation. 2009 Nov;90(11 Suppl):S52-9. 19892075. *No original data*
29. Cicerone KD, Dahlberg C, Kalmar K, et al. Evidence-based cognitive rehabilitation: recommendations for clinical practice. Archives of Physical Medicine & Rehabilitation. 2000 Dec;81(12):1596-615. 11128897. *No original data*
30. Cicerone KD, Dahlberg C, Malec JF, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 1998 through 2002. Archives of Physical Medicine & Rehabilitation. 2005 Aug;86(8):1681-92. 16084827. *No original data*
31. Cicerone KD, Langenbahn DM, Braden C, et al. Evidence-based cognitive rehabilitation: updated review of the literature from 2003 through 2008. Archives of Physical Medicine & Rehabilitation. 2011 Apr;92(4):519-30. 21440699. *No original data*
32. Cifu DX, Kreutzer JS, Kolakowsky-Hayner SA, et al. The relationship between therapy intensity and rehabilitative outcomes after traumatic brain injury: a multicenter analysis. Archives of Physical Medicine & Rehabilitation. 2003 Oct;84(10):1441-8. 14586910. *No primary or secondary outcomes*
33. Coetzer R, Rushe R. Post-acute rehabilitation following traumatic brain injury: are both early and later improved outcomes possible? International Journal of Rehabilitation Research. 2005 Dec;28(4):361-3. 16319563. *No comparison group*
34. Constantinidou F, Thomas RD, Robinson L. Benefits of categorization training in patients with traumatic brain injury during post-acute rehabilitation: additional evidence from a randomized controlled trial. Journal of Head Trauma Rehabilitation. 2008 Sep-Oct;23(5):312-28. 18815508. *Impairment-specific intervention*
35. Cope DN, Cole JR, Hall KM, et al. Brain injury: analysis of outcome in a post-acute rehabilitation system. Part 2: Subanalyses. Brain Injury. 1991 Apr-Jun;5(2):127-39. 1908341. *No comparison group*
36. Cope DN, Cole JR, Hall KM, et al. Brain injury: analysis of outcome in a post-acute rehabilitation system. Part 1: General analysis. Brain Injury. 1991 Apr-Jun;5(2):111-25. 1873600. *No comparison group*

37. Cusick CP, Gerhart KA, Mellick D, et al. Evaluation of the home and community-based services brain injury Medicaid Waiver Programme in Colorado. Brain Injury. 2003 Nov;17(11):931-45. 14514446. *Not eligible study design*
38. Dahlberg CA, Cusick CP, Hawley LA, et al. Treatment efficacy of social communication skills training after traumatic brain injury: a randomized treatment and deferred treatment controlled trial. Archives of Physical Medicine & Rehabilitation. 2007 Dec;88(12):1561-73. 18047870. *Impairment-specific intervention*
39. Dawson DR. A multidsciplinary community-based rehabilitation program improved social functioning in severe traumatic brain injury. ACP Journal Club. 2002(1):22. CN-00477567. *No original data*
40. Devitt R, Colantonio A, Dawson D, et al. Prediction of long-term occupational performance outcomes for adults after moderate to severe traumatic brain injury. Disability & Rehabilitation. 2006 May 15;28(9):547-59. 16690584. *Not intervention study*
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Appendix D. Secondary Outcomes

Appendix D. Table 1. Secondary outcomes

Study, Design; Instrument	Treatment Arms	Outcome Before Treatment	Outcome After Completion of Treatment	Treatment vs. Control; Comments
Cicerone 2008,[1] RCT **Perceived Quality of Life (PQOL)** post treatment (16 weeks)	Intensive Cognitive Rehabilitation Program (ICRP) (n=34)	59.0 (21.7)	66.8 (17.5) P<0.05 versus before treatment	ES=0.26 [-0.22 to 0.74] No significant differences between groups but Intensive cognitive rehabilitation participants showed greater improvements on the PQOL
	Standard Neurorehabilitation Program (STD) (n=34)	61.2 (16.5)	62.2 (17.2)	
Vanderploeg 2008,[2] RCT **Disability Rating Scale (DRS)** 1 year post protocol treatment	Functional-experimental (n=150)	NR	8.2 (5.3)	ES=0.12 [-0.11 to 0.34] No significant differences between groups (P=0.29)
	Cognitive-didactic (n=152)	NR	7.6 (4.8)	
Vanderploeg 2008,[2] RCT **Quality of Life (satisfied with life- yes/no)** 1 year post protocol treatment	Functional-experimental (n=124)	NR	65% (81/124)	RR = 1.06 [0.88 to 1.28] No significant differences between groups (P=0.53)
	Cognitive-didactic (n=130)	NR	62% (80/130)	
Powell 2002,[14] RCT **Brain injury community rehabilitation outcome-39 (BICRO-39)** 27 weeks post treatment	Outreach (n=35 of 54 randomized)	Median (range) 15.3 (8 to 22.3)	% improving 80.0 (28/35) Median change (range) 2.5 (-1.7 to 6.2)	RR = 1.14 [0.88 to 1.49] Total BICRO-39 change score (summed across the six scales) was significantly greater in the outreach group than in the information group (mean ranks: outreach 43.2, information 33.4; *U*=517, p=0.05).
	Information (n=40 of 56 randomized)	Median (range) 12.9 (8.8 to 25.7)	% improving 70.0 (28/40) Median change (range) 0.9 (-4.1 to 6.8)	
Bell 2005[13]	Telephone	NR	Adjusted mean	Treatment effect=0.10 (0.02-0.19)

Study, Design; Instrument	Treatment Arms	Outcome Before Treatment	Outcome After Completion of Treatment	Treatment vs. Control; Comments
RCT			0.78	
	Standard	NR	Adjusted mean 0.67	
EuroQoL				
Bell 2005[13] **RCT**	Telephone	NR	Adjusted mean 6.58	Treatment effect=0.40 (-0.05-0.84)
	Standard	NR	Adjusted mean 6.19	
GOS-E				
Bell 2005[13] **RCT**	Telephone	NR	Adjusted mean 78.9	Treatment effect=8.8 (1.7-15.9)
	Standard	NR	Adjusted mean 70.1	
PQoL				
Cicerone 2004[11]	Intensive Cognitive Rehabilitation Program (ICRP) (n=34)	NR	27.1 (4.6)	Standard treatment group reported higher QCI scores (P<.01)
QCI	Standard Neurorehabilitation Program (STD) (n=34)	NR	29.7 (4.4)	
Thomas 2004[15]	Potential Unlimited Program	35.36 (8.80)	Stage 1 42.57 (11.08) Posttreatment 38.26 (10.56) 6-month followup 46.14 (12.22) 2-year followup 50.00 (13.95)	Only significant difference between groups at 6-month followup.
	No treatment	38.63 (21.97)	Stage 1 39.63 (19.66) Posttreatment 39.00 (18.88) 6-month followup 20.25 (14.73) 2-year followup 41.83 (10.36)	
Semlyen 1998[16] quasi-experimental (CCT)	Multidisciplinary rehabilitation service (n=33)	Group differences in change 8 wk to 12 wk 4.00 (p<0.001)†	Group differences in change 6 mo to 12 mo 3.82 (p<0.01)†	The multidisciplinary rehabilitation service group showed significant gains throughout the rehabilitation period, the single discipline approach group did not.
Newcastle Independence	Single discipline approach	Group differences in change	Group differences in change	

Study, Design; Instrument	Treatment Arms	Outcome Before Treatment	Outcome After Completion of Treatment	Treatment vs. Control; Comments
Assessment Form (NIAF) 6-12 months post treatment (rehab period)	(n=18)	8 wk to 12 wk 2.30 (p<0.05)†	6 mo to 12 mo 1.05 (p NS)	
Greenwood 1994[4] GOS-E	Case-management (N=53 at entry)	NR	6 months posttreatment 5.3 (1.7) N=48 12 months posttreatment 5.5 (1.6) N=37 24 months posttreatment 5.6 (1.5) N=21	No group differences.
	Control (N=65 at entry)	NR	6 months posttreatment 5.8 (1.5) N=59 12 months posttreatment 6.2 (1.4) N=55 24 months posttreatment 6.3 (1.2) N=29	
Greenwood 1994[4] GOS-E	Case-management (N=53 at entry)	NR	24 months posttreatment 2.0 (2.4) N=19	Case managed have significantly worse DRS scores. (p<0.05)
	Control (N=65 at entry)	NR	24 months posttreatment 0.6 (1.7) N=29	

* Based on Cohen's "Rules-of-Thumb" standardized mean difference effect size are as follows: small = 0.20; medium = 0.50; and large = 0.80. ** 25th and 75th quartiles. † For within group differences between means at each time point

ES = effect size; NS = not statistically significant; RR = Risk ratio [95% confidence interval]

Note: This table presents the results of studies that assessed a secondary outcome.

Appendix E. Evidence Tables

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Bell, 2005[13] **Moderate to Severe TBI**	**Telephone Counseling** **Theory/Model:** Modeled after validated telephone interventions in chronic care, smoking cessation, depression **Program Type:** Post-rehabilitation telephone contact **Setting:** Patient home **Delivery:** Scheduled phone calls with individualized mail supplements	**Description:** Scheduled phone calls made "research care manager to randomly allocated post-rehabilitation discharge patients. Calls were comprised of 3 basic elements: Follow-up of previously stated concerns, patient or family member stated current concerns, research care manager determined level of intervention in response to patient's concern. **Coordination:** NR **Disciplines:** NR **Components:** Giving information, mentoring, goal-setting, reassurance, modeling problem-solving, referral to community resources, triaging to regional or tertiary center if local resources unavailable **Therapy hours/week:** 30-45 minutes, weeks 2, 4 and months 2, 3, 5, 7, and 9 post-rehabiltation **Duration:** 9 months **Total therapy hours:** NR **Manualized:** Yes, described in detail in previous publication **Staff Training:** NR **Fidelity Checks:** NR	**Bell, et al, 2005 [**15895327**]** **Moderate to Severe TBI**	**Telephone Counseling** **Theory/Model:** Modeled after validated telephone interventions in chronic care, smoking cessation, depression **Program Type:** Post-rehabilitation telephone contact **Setting:** Patient home **Delivery:** Scheduled phone calls with individualized mail supplements

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Cicerone, 2004[11] **Study design** Prospective Cohort **Sample size** 57 **Location** Edison, NJ **Setting** Community-based, postacute outpatient brain injury rehabilitation program **Interventions** • Intensive cognitive rehabilitation group (ICRP) (n=27) • (Control) Standard neurorehabilitation (SRP) (n=29) **Primary outcomes** CIQ	**Inclusion criteria** • medically stable • independent in basic self-care skills • cognitive ability to participate in treatment • medical documentation TBI • 18 or older • adequate language expression and comprehension **Exclusion criteria** • current substance use or psychiatric disturbance precluding effective treatment • no available family member or person to participate in program	**Age (years±SD)** • ICRP 38±10.6 • SRP 37±12.0 **Gender (% male)** • ICRP 63% • SRP 79% **Race/ethnicity** NR **Education (years±SD)** • ICRP 13.2±1.7 • SRP 13.0±2.2 **Employment status (% competitively employed)** • ICRP 96 • SRP 97 **Income** NR **Marital status** NR **Military/Veteran** NR **Insurance status** NR **Prior TBI** NR **Preexisting psychiatric conditions** NR	**Severity (% moderate/severe)** • ICRP 89% • SRP 90% **Severity definition** NR **Time since injury (months±SD)** • ICRP 33.9±4.8 • SRP 4.8±9.5 **TBI etiology** NR **Area of brain injured** NR **Other injury characteristics** NR	**Comorbidities** Psychiatric comorbidities not described, although subjects identified with current substance use or psychiatric disturbance that would preclude effective treatment for their cognitive deficits were not admitted. Psychiatric subjects were guided to the intensive cognitive group. **Compensation seeking** NR **Acute rehabilitation history** NR **Concomitant treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Cicerone, 2008[1] **Study design** RCT **Sample size** 68 **Location** Edison, NJ **Setting** Postacute brain injury rehabilitation center in suburban hospital **Interventions** • Intensive cognitive rehabilitation (ICRP) • Standard neurorehabilitation (STD) **Primayr Outcomes** • CIQ • Vocational Integration Scale (community-based employment) **Secondary Outcomes** • Perceived Quality of Life scale (PQOL)	**Inclusion Criteria:** • Medical documentation of TBI based on primary source within 24 hours of injury • At least 3 months postinjury • 18-62 years of age • Adequate language expression and comprehension (English) • Judged to require at least 4 months comprehensive treatment • Clinically appropriate for either arm of treatment • Capable of attending treatment 3 days/week • Capable of giving informed consent **Exclusion Criteria:** • Active psychiatric illness, substance abuse, or pain that may prevent compliance with treatment	**Age (years, SD)** ICRP: 39 (±11.) STD: 35 (±12.4) **Gender (% male):** 68% **Race/ethnicity:** 75% white, 10% black, 12% Hispanic, 3% Asian **Education:** (HS or <, some college, college grad) **Employment status:** 79% employed, 4% unemployed, 2% homemaker, 13% student, 2% retired **Income:** NR **Marital status(% married):** 35% **Military/Veteran status:** NR **Insurance status:** NR **Prior TBI:** 4% **Preexixting psychiatric conditions:** psychiatric illness 13% substance abuse 21%	**Severity** Mild: 13% ModerateI: 24% SevereI: 59% **Severity Definition:** Any combination of initial Glasgow Coma Scale score, duration of unconsciousness, duration of post-traumatic amnesia, and positive neuroimaging available from primary medical records. **Time since injury (mos mean, (std dev.))** ICRP=49.6 (±76.5) STD=37.0 (±58.2) **TBI Etiology** NR **Brain area injured** NR **Other injury characteristics:** NR	**Comorbidities:** NR **Compensation seeking status:** NR **Acute rehabilitation history (% inpatient rehab)** ICRP: 77% STD: 85% **Concomitant Treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics

Greenwood, 1994[4]
 	
Study design
prospective controlled unmatched nonrandomized study
 	
Sample size
126 (outcomes for 118)
 	
Location
four district general hospitals and two university teaching hospitals with neurosurgical units
 	
Setting
London and environs
 	
Interventions
• case managed (CM) (n=56)
• control (n=70)
 	
Secondary outcomes
• DRS
• GOS
	Inclusion criteria
	• closed head injury
	• aged 16-60
	• been in coma for 6 hours or had a PTA > 48 hours
	• care giver was resident in district
	• informed consent
	
	Exclusion criteria
	• received hospital treatment for drug or alcohol misuse
	• aged 16-60
	• psychiatric disturbance, or a disorder of the central nervous system during the previous year
	• no fixed abode or if follow up unlikely
		Age (years±SD)
		• CM 31.6±14.4
		• control 30.7±14.0
		
		Gender (% male)
		• CM 69.6
		• control 75.7
		
		Race/ethnicity
		NR
		
		Education
		NR
		
		Employment status (%)
		• CM 100
		• control 96
		
		Income
		NR
		
		Marital status
		NR
		
		Military/Veteran
		NR
		
		Insurance status
		NR
		
		Prior TBI
		NR
		
		Preexisting psychiatric conditions
		alcohol intake at injury (%)
		• CM 36
		• control 37
			Severity definition
			“severely head injured patients”
			
			Severity
			GCS (mean±SD)
			• CM 5.5±2.6
			• control 6.6±3.0
			
			Duration of PTA (days±SD)
			• CM 64.9±97.5
			• control 40.8±75.0
			
			Time since injury
			NR
			
			TBI etiology (%)
			traffic accident/assault/fall/other
			• CM
			  ○ traffic accident 60
			  ○ assault 16
			  ○ fall 18
			  ○ other 5
			• control
			  ○ traffic accident 63
			  ○ assault 14
			  ○ fall 16
			  ○ other 7
			
			Area of brain injured
			NR
			
			MRI/imaging findings
			NR
			
			Other injury characteristics
			days unconscious (mean±SD)
			• CM 11.3±13.5
			• control 4.6±7.5
				Comorbidities
				• respiratory
				  ○ CM 47
				  ○ control 21
				• conservative management
				  ○ CM 16
				  ○ control 31
				• tracheostomy
				  ○ CM 32
				  ○ control 16
				
				Compensation seeking (%)
				• 6 months
				  ○ CM 2
				  ○ control 2
				• 12 months
				  ○ CM 0
				  ○ control 6
				• 24 months
				  ○ CM 17
				  ○ control 4
				
				Acute rehabilitation history
				NR
				
				Concomitant treatment
				NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics

Hashimoto 2006[10]
 	
Study design
prospective, nonrandomized controlled trial
 	
Sample size
37
 	
Location
Kanagawa Prefecture, Japan
 	
Setting
Kanagawa Rehabilitation Hospital
 	
Interventions
• comprehensive day treatment program (n=25)
• control (outpatients with TBI) (n=12)
 	
Primary outcomes
• return to work
• FIM/FAM
• CIQ
	Inclusion criteria
	• near independence in Activities of Daily Living (ADL) irrespective of ability to walk or wheelchair use
	• the goal of returning to work or school
	• having no place they were required to visit frequently except for outpatient clinic
	
	Exclusion criteria
	NR
		Age (years±SD)
		• intervention 26.6±9.7
		• control 28.7±10.9
		
		Gender (% male)
		• intervention 72
		• control NR
		
		Race/ethnicity
		NR
		
		Education
		NR
		
		Employment status (% competitively employed)
		• intervention 60
		• control NR
		
		Income
		NR
		
		Marital status
		NR
		
		Military/Veteran
		NR
		
		Insurance status
		NR
		
		Prior TBI
		NR
		
		Pre-existing psychiatric conditions
		NR
			Severity definition
			GCS ≤ 8
			
			Severity (%)
			• intervention 76.0
			• control 83.3
			
			Duration of PTA
			NR
			
			Time since injury (days±SD)
			• intervention 527.3±512.6
			• control 487.6±125.9
			
			TBI etiology (%)
			• intervention
			  ○ auto accident 20
			  ○ pedestrian/auto 20
			  ○ bike/auto 36
			  ○ cerebral aneurysm 8
			  ○ glioma 4
			  ○ fall 8
			  ○ work accident 4
			• control NR
			
			Area of brain injured
			• intervention
			  ○ diffuse brain injury 64
			  ○ diffuse brain injury + right acute subdural hematoma 20
			  ○ right acute subdural hematoma 4
			  ○ Sub arachnoid hemorrhage 8
			  ○ diffuse brain injury + contusion 4
			• control NR
			
			MRI/imaging findings
			NR
				Comorbidities
				NR
				
				Compensation seeking
				NR
				
				Acute rehabilitation history
				NR
				
				Concomitant treatment
				NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Ponsford, 2006[5] **Study design** Controlled, individually matched cohort trial **Sample size** 77 **Location** Melbourne, Australia **Setting** Rehabilitation center **Interventions** • Community based rehabilitation (n=77) • Control (n=77) **Primary outcomes** Return to work	**Inclusion criteria** Moderate to severe TBI patients **Exclusion criteria** NR	**Age (years±SD)** • Community based 35.43±16.65 • Control 33.78±15.41 **Gender (% male)** • Community based 73 • Control 73 **Race/ethnicity** NR **Education (years±SD)** • Community based 11.56±2.42 • Control 11.15±2.54 **Employment status (% competitively employed)** • Community based 66 • Control 70 **Income** NR **Marital status (% single)** • Community based 63 • Control 61 **Military/Veteran** NR **Insurance status** NR **Prior TBI** NR **Preexisting psychiatric conditions** NR	**Severity (mean GCS±SD)** • Community based 8.22±4.37 • Control 7.76±4.13 **Severity definition** GCS **Time since injury (years)** NR **TBI Etiology** NR **Area of brain injured** NR **Other injury characteristics** NR	**Comorbidities** NR **Compensation seeking** NR **Acute rehabilitation history** NR **Concomitant treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Powell, 2002[14] **Study design:** RCT **Sample size** 94 **Location** London, England **Setting** Community-based **Study design:** RCT **Interventions:** • Outreach • Information **Primary Outcomes** • none **Secondary Outcomes** • BICRO-39 • **Intermediate Outcomes** • BICRO-39 • FIM + FAM	**Time since injury (yrs mean, (std dev.)):** Outreach=4.0±4.9, Information=2.7±3.6 **Inclusion Criteria:** • Age 16-65 • Severe TBI between 3 months and 20 years previously • No other neurological conditions • Reside within 1 hour travel time of hospital • Long-term treatment goals amenable with intervention **Exclusion Criteria** NR	**Age (years, SD)** Outreach=34±11, Information=35±10 **Gender (% male):** 76% **Race/ethnicity** NR **Education** NR **Employment status** NR **Income** NR **Marital status** NR **Military/Veteran status** NR **Insurance status** NR **Prior TBI** NR **Psychiatric conditions** NR	**Severity** Mild: 1% Moderate: 0% Severe: 99% **Severity Definition:** Severe: PTA >1day Mild: PTA <= 1 hour **TBI Etiology** NR **Brain area injured** NR **Other injury characteristics:** NR	**Comorbidities** NR **Compensation seeking status** NR **Social support:** NR **Acute rehabilitation history:** community or post-rehab discharge **Concomitant Treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics

Prigatano, 1984[9]
 	
Study design
retrospective, controlled cohort study
 	
Sample size
18
 	
Location
Oklahoma City, Oklahoma
 	
Setting
Neuropsychological rehabilitation program
 	
Interventions
• Psychotherapeutic (n=18)
• Control (n=18)
 	
Primary outcomes
Return to work
	Inclusion criteria
	NR
	
	Exclusion criteria
	NR
		Age (years±SD)
		• Neuropsychologic 26.1±8.3
		• Control NR
		
		Gender (% male)
		• Neuropsychologic 83.3
		• Control NR
		
		Race/ethnicity
		NR
		
		Education (%)
		• Neuropsychologic
		  ○ ≤ 12 years 61.1
		  ○ > 12 years 38.9
		• Control NR
		
		Employment status (% competitively employed)
		• Neuropsychologic 72.2
		• Control NR
		
		Income
		NR
		
		Marital status
		NR
		
		Military/Veteran (%)
		• Neuropsychologic 5.6
		• Control NR
		
		Insurance status
		NR
		
		Prior TBI
		NR
		
		Preexisting psychiatric conditions
		NR
			Severity (% moderate/severe)
			NR
			
			Severity Definition
			Russell-Neurenger Average Impairment Rating
			
			Time since injury (months)
			• Neuropsychologic 21.6
			• Control NR
			
			TBI etiology
			“Severe closed head injury”
			
			Area of brain injured (%)
			• Neuropsychologic
			  ○ Severe cerebral contusion 61.1
			  ○ Brain stem contusion 5.6
			  ○ Severe cerebral contusion + brain stem contusion 33.3
			• Control NR
			
			Other injury characteristics (%)
			• Neuropsychologic
			  ○ Post traumatic seizure disorder 16.7
			  ○ Residual paresis 66.7
			  ○ Residual signs of aphasia and/or dysarthria 33.3
			  ○ “Virtually all . . . had cerebral contusions and/or brain stem contusion”
			• Control NR
				Comorbidities
				NR
				
				Compensation seeking
				NR
				
				Acute rehabilitation history
				NR
				
				Concomitant treatment
				NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics

Prigatano, 1994[7]
 	
Study design
Matched control, prospective cohort
 	
Sample size
79 (outcomes for 76)
 	
Location
Phoenix, Arizona
 	
Setting
Work Re-entry Program of the Adult Day Hospital for Neurological Rehabilitation at Saint Joseph's Hospital
 	
Interventions
• Neuropsychological rehab (n=41, outcomes for 38)
• Historic controls (n=38)
 	
Primary outcomes
Return to work
	Inclusion criteria
	• Primary diagnosis of craniocerebral trauma or TBI
	• By end of study, ≥ 15 months elapsed since injury
	• Admitted to study 2-55 months from injury
	• All subjects considered potentially able to return to work/school
	
	Exclusion criteria
	NR
		Age (years±SD)
		• Neuropsychological rehab 29.6±12.7
		• Historic controls (28.7±12.2
		
		Gender (% male)
		• Neuropsychological rehab 68.4
		• Historic controls 71.1
		
		Race/ethnicity
		NR
		
		Education (years±SD)
		• Neuropsychological rehab 13.6±2.3
		• Historic controls 12.0±1.2
		
		Employment status (% competitively employed)
		• Neuropsychological rehab 78.0
		• Historic controls NR
		
		Income
		NR
		
		Marital status
		NR
		
		Military/Veteran
		NR
		
		Insurance status
		NR
		
		Prior TBI
		NR
		
		Preexisting psychiatric conditions
		NR
			Severity (mean±SD)
			• Neuropsychological rehab 8.08±2.7
			• Historic controls (n=38) 8.03±2.8
			
			Severity definition
			GCS
			
			Time since injury (months±SD)
			• Neuropsychological rehab 43.3±16.1
			• Historic controls 33.5±8.7
			
			TBI etiology
			NR
			
			Area of brain injured
			NR
			
			Other injury characteristics (%)
			• Neuropsychological rehab
			  ○ CT/MRI findings of contusion and/or hematoma 87.7
			  ○ Skull fracture/no hematoma 4.9
			  ○ Loss of consciousness 7.3
			• Historic controls NR
				Comorbidities
				NR
				
				Compensation seeking
				NR
				
				Acute rehabilitation history
				NR
				
				Concomitant treatment
				NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Rattok, 1992[8] **Study design** 3 group comparison **Sample size** 59 **Location** New York, NY Metropolitan Area **Setting** Outpatient rehabilitation center **Interventions** • Treatment 1 (Balanced) • Treatment 2 (Interpersonal) • Treatment 3 (Individualized) **Primary outcomes** • Cognitive performance measures • Behavioral Competence Index (BCI) • Vocational	**Inclusion Criteria** • Diagnosis of TBI, ≥1hr coma • Diagnosis of cerebral anoxia, ≥12hr coma • ≥1 year post-injury • Neurological stability • Unsuccessful vocational or educational rehabilitation prior to entry into program • Residence in New York metropolitan area for duration of study • Age, 18-55 • Command of English • Partial independence in basic activities of self-care, ambulation, and continence • Minimum IQ of 80 on WAIS • Minimum motivation for rehabilitation • Basic level of social appropriateness and manageability in therapeutic or training environment **Exclusion criteria** • History or present psychiatric complications • History of drug or alcohol abuse • History of sociopathy • Inability to communicate	**Age (median years)** • Treatment 1: 26.8 • Treatment 2: 27.1 • Treatment 3:28.5 **Gender (% male)** • Treatment 1: 65% • Treatment 2: 89% • Treatment 3: 61% **Race/ethnicity (%)** NR **Education (median years)** • Treatment 1: 14.3 • Treatment 2: 13.5 • Treatment 3: 14.6 **Employment status (% competitively employed)** NR **Income** NR **Marital status (%)** NR **Military/Veteran** NR **Insurance status** NR **Prior TBI (%)** NR	**Severity definition** Severe=Coma of ≥1hr or cerebral anoxia of ≥12hrs **Severity (Days in coma)** • Treatment 1: 34.3 • Treatment 2: 38.9 • Treatment 3: 36.9 **Time since injury (median months)** • Treatment 1: 32 • Treatment 2: 33.8 • Treatment 3: 40.2 **TBI etiology** 95% acceleration/deceleration concussion; 5% cerebral anoxia **MRI/imaging findings** NR **Other injury characteristics (%)** • NR	**Prior psychiatric conditions (%)** • NR **Comorbidities (%)** • NR **Compensation seeking** NR **Acute rehabilitation history** "Unsuccessful"

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Salazar, 2000[3] **Study design:** RCT **Sample size** 120 **Location:** Washington, D.C. **Setting** US Military medical referral center **Interventions:** • Intensive, interdisciplinary, in-hospital cognitive rehabilitation program (Hospital)) (n=xx) • Limited home rehabilitation program with telephone support from psychiatric nurse (Home) (n=xx) **Primary Outcomes** • Return to work • Fitness for military duty Secondary Outcomes • none	**Inclusion Criteria:** • Moderate-to-severe closed head injury • Head injury within 3 months of randomization • Rancho Los Amigos cognitive level of 7 • Active duty military member; not pending separation • Accompanied home setting with at least 1 responsible adult available • Ability to independently ambulate • No prior severe TBI or other severe diability that would preclude return to active duty after study treatment **Exclusion Criteria:** • Mild TBI	**Age:** Hospital=25, 6.63; Home=26,6.22 **Gender(% male):** Hospital: 93% Home: 96% **Race/ethnicity(% white)** Hosptial: 69% Home: 70% **Education (% some college):** Hosptial: 41% Home=44% **Employment status:** NR **Income:** NR **Marital status (% married)** Hospital:30% Home=34% yes **Military/Veteran status(% active military):** 100% **Insurance status (% military coverage):** 100% **Prior TBI** Hospital: 11% Home: 18% **Psychiatric conditions(% posibive diagnosis)** Hospital=19% Home=25%	**Severity** **Severity Definition** Glasgow Coma Score≤13; or posttraumatic amnesia≥24 hours; or focal cerebral contusion or hemorrhage on computed tomography or MRI **Time since injury (mean days, SD)** Hospital: 38 (23.6) Home: 39 (33.2) **Etiology** MVC Hospital:49% Home: 72% Assault: Hospital: 27% Home: 9% Unknown: Hospital: 24% Home: 19% **Area of brain injured:** cerebrum; computed tomography or MRI **Other injury characteristics** Closed: 100%	**Comorbidities:** Headaches, violent behavior, aggressive behavior, seizures, major depression **Compensation seeking status:** NR **Social support:** Accompanied home setting with at least 1 responsible adult available **Acute rehabilitation history:** NR **Concomitant Treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Sarajuuri, 2005[6] **Study design** Prospective Cohort **Sample size** 39 **Location** Helsinki, Finland **Setting** Nationwide Rehabilitation Center & Neurosurgery Department within academic medical center hospital **Interventions** • Comprehensive (T) (n=19) • Conventional (C) (n=20) **Primary Outcome** Status of productivity	**Inclusion Criteria** • Independence in daily life and only slight physical disabilities • 16 to 55 years of age • completed compulsory education • adequate potential to achieve productivity **Exclusion Criteria** • significant psychiatric history • alcohol or drug abuse • previous brain injury • another malignant disease **Population (n)** T: 19 C: 20	**Age (at injury; years, SD)** T: 30.5 (±10.6) C: 29.5 (±11.0) **Gender (% male)** T: 84% C: 85% **Race/ethnicity** NR **Education (years, SD)** T: 11.3 (±2.0) C: 12.2 (±2.9) **Employment status (preinjury; % employed or stydying preinjury)** T: 84% C: 85% **Income** NR **Marital status** NR **Military/Veteran** NR **nsurance status** NR **Prior TBI** NR, but prior TBI is excluded **Preexixting psychiatric conditions** NR, but significant psychiatric history excluded	**Severity (admission GCS; mean, SD, range)** T: 7.9 (2.7) (4-14) C: 8.2 (2.5) (3-13) **Severity Definition:** NR **Time since injury (month,SD)** T: 84% C: 85% **TBI Etiology (% by mechanism)** MVC/bike/pedestrian T: 63% C: 55% Assault T: 5% C: 5% Other(fall, hit by) T: 26% C: 40% Unknown T: 5% C: 0% **Area of brain injured:** NR **Other Injury characteristics** Contusion/hematoma T: 79% C: 80% Diffuse axonal injury T: 42% C: 25% Severe intracranial pressure T: 37% C: 25% Craniotomy T: 21% C: 25%	**Comorbidities:** NR **Compensation seeking** NR **Acute rehabilitation history** OT T: 32% C: NR PT T: 47% C: NR SLP T: 26% C: NR NP T: 37% C: NR **Concomitant Treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Semlyen, 1998[16] **Study design** Prospective Cohort **Sample size** 51 **Location:** Newcastle upon Tyne, UK **Setting** Regional rehabilitation centre **Interventions:** • Coordinated, multidisciplinary rehabilitation • Single-discipline rehabilitation **Primary Outcomes** • None • **Secondary Outcomes** • Newcastle Independence Assessment Form-Research (NIAF-R) **Intermediate Outcomes** • Barthel Index • FIM	**Inclusion Criteria:** • Initial Glasgow Coma Scale score≤8 for at least 6 hours • Between 16-65 years • Identifiable primary consenter • Resides in Northern Regional Health Authority • Surgically stable and able to be discharged from neurosurgical unit within 4 weeks of injury **Exclusion Criteria:** • Previous drug or alcohol misuse • Premorbid neurologic history	**Age (at injury; years, SD)** Treatment: 36(13) Control: 30(12) **Gender (% male)** Treatment: 85% Control: 84% **Race/ethnicity:** NR **Education:** NR **Employment status:** NR **Income** "majority in both groups in lower-middle SES" **Marital status:** NR **Military/Veteran status:** NR **Insurance status:** NR **Prior TBI:** NR **Psychiatric conditions:** NR	**Severity** **Severe:** 100% **Severity Definition** Severe: GCS Score ≤8 for at least 6 hours **Time since injury (mean days, SD)** Treatment: 49.37 (29.62) Control: 17.94 (13.6) **TBI Etiology** MVC Treatment: 69.8% Control: 44.6% Falls Treatment: 18.2% Control:33.3% Assault Treatment: 9.1% Control: 22.2% Self-harm Treatment: Control: 3% **Brain area injured:** NR **Other injury characteristics** NR	**Comorbidities:** NR **Compensation seeking status:** NR **Acute rehabilitation history:** NR **Concomitant Treatment** NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Thomas, 2004[15] **Study design** Matched comparison **Sample size** 22 **Location** Australia **Setting** Community, Outward Bound course, patient home **Interventions** • 3-stage Outward Bound program (PUP) • Matched controls **Primary outcomes** • Quality of Life Inventory (QOLI)	**Inclusion Criteria** • Self-selected volunteers • ABI • Past or present client of NSW Brain Injury Rehabilitation Programme **Exclusion criteria** • NR	**Age (mean years±SD)** • PUP 31.54±10.37 • Controls 38.38±12.14 **Gender (% male)** • PUP NR • Control NR **Race/ethnicity (%)** • PUP NR • Control NR **Education (mean years±SD)** • Intensive therapy 13.2±1.9 • Standard therapy 12.5±1.2 **Employment status (% competitively employed)** • PUP "Most not working/studying" • Control "Most not working/studying" **Income** NR **Marital status (%)** • PUP NR • Control NR **Military/Veteran** NR **Insurance status** NR **Prior TBI (%)** • PUP NR • Control NR	**Severity definition** Mild=PTA 5-60 minutes Severe=PTA 1-7 days Very Severe=PTA 7-28 days Extremely Severe=PTA>28 days **Severity (%)** • PUP ○ Mild 2 ○ Severe 1 ○ Very Severe 2 ○ Extremely Severe 8 • Control ○ Mild 2 ○ Severe 3 ○ Very Severe 0 ○ Extremely Severe 3 **Time since injury (mean years±SD)** • PUP ○ 5.99±4.54 • Control ○ 4.97±2.28 **TBI etiology** NR **MRI/imaging findings** NR **Other injury characteristics (%)** • NR	**Prior psychiatric conditions (%)** • NR **Comorbidities (%)** prior substance abuse • NR **Compensation seeking** NR **Acute rehabilitation history (%)** All participants in PUP and control were current or past clients of New South Wales Brain Injury Rehabilitation Programme

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics

Vanderploeg, 2008[2]
 	
Study design RCT, Multicenter
 	
Sample size 366
 	
Location Minneapolis, Palo Alto, Richmond, Tampa
 	
Setting VA acute inpatient TBI rehab programs
 	
Interventions
• Cognitive-didactic (CD) rehab therapy (n=184)
• Functional-experiential (FE) (n=182)
 	
Primary Outcomes
• Return to work
 	
Secondary Outcomes
• Disability Rating Scale score
• Functional independence in living
	Inclusion Criteria: (1) moderate-to-severe nonpenetrating TBI within the preceding 6 months, manifested by a postresuscitation Glasgow Coma Scale score of 12 or less, or coma of 12 hours or more, or PTA of 24 hours or more, and/or focal cerebral contusion or hemorrhage on CT or MRI; (2) RLAS cognitive level of 5 to 7 at time of randomization; (3) age 18 years or older; (4) active duty military member or veteran; and (6) anticipated length of needed acute interdisciplinary TBI rehabilitation of 30 days or more
	
	Exclusion Criteria: (1) history of prior inpatient acute rehabilitation for the current TBI and (2) history of a prior moderate to severe TBI or other preinjury severe neurologic or psychiatric condition, such as psychosis, stroke, multiple sclerosis, or spinal cord injury
		Age (at injury; years, SD)
		CD 33.2 (±13.5)
		FE 31.7 (±12.9)
		
		Gender (% male)
		CD: 92% FE:95%
		
		Race/ethnicity
		Hispanic
		CD: 10% FE:11%
		White
		CD: 68% FE:69%
		Black
		CD: 20% FE:18%
		Other
		CD: 12% FE:12%
		
		Education (% post high school)
		CD: 34% FE:37%
		
		Employment status: (% working or in school)
		CD: 86% FE:89%
		
		Income: NR
		
		Marital status (% married)
		CD: 25.6% FE: 25.1%
		
		Military/Veteran status (% what?)
		CD: 58.4% FE:67.8%
		
		Insurance status: NR
		
		Prior TBI (% "prior head injury")
		CD: 7.2% FE: 7.2%
		
		Pre-existing psychiatric conditions: NR
			Severity NR, but moderate/severe inclusion criteria
			
			Severity Definition: NR
			
			Time since injury:
			• CD 48.9±28.5 (n = 180) days
			• FE 51.1±29.8 (n = 180) days
			
			TBI Etiology:
			MVC
			CD: 68% FE:66%
			Assault
			CD: 10% FE:8%
			
			Area of brain injured: NR
			
			Injury characteristics:
			• CD
			  ○ Motor vehicular 122/180 (67.8%)
			  ○ Fall 21/180 (11.7%)
			  ○ Blunt object 15/180 (8.3%)
			  ○ Sports/training accident 5/180 (2.8%)
			  ○ Indeterminant 17/180 (9.4%)
			• FE
			  ○ Motor vehicular 119/180 (66.1%)
			  ○ Fall 29/180 (16.1%)
			  ○ Blunt object 9/180 (5.0%)
			  ○ Sports/training accident 6/180 (3.3%)
			  ○ Indeterminant 17/180 (9.4%)
				Comorbidities: NR
				
				Compensation seeking status: NR
				
				Acute rehabilitation history: NR
				
				Concomitant Treatment NR

Appendix E. Table 1. Evidence table of multidisciplinary postacute rehabilitation for moderate to severe TBI studies

Study Description	Inclusion/Exclusion Criteria	Demographic/ Preinjury Characteristics	TBI Characteristics	Postinjury Characteristics
Willer, 1999[12] **Study design** Case controlled study using a matched design in a before-and-after trial **Sample size** 46 **Location** Ontario, Canada **Setting** Postacute residential rehabilitation program or home-based subjects **Interventions** • Residential-based postacute rehabilitation (RBPR) (n=23) • Control (n=23) **Primary outcomes** CIQ	**Inclusion criteria** Individuals with brain injury who had not undergone treatment in this community-based program **Exclusion criteria** NR	**Age (years±SD)** • RBPR 33.42±11.31 • Control 34.76±10.72 **Gender (% male)** • RBPR 87 • Control 87 **Race/ethnicity** NR **Education (%)** • RBPR ○ < HS 26.0 ○ Completed HS 43.5 ○ > HS 30.4 • Control ○ < HS 26.0 ○ Completed HS 34.8 ○ > HS 39.1 **Employment status** NR **Income** NR **Marital status** NR **Military/Veteran** NR **Insurance status** NR **Prior TBI** NR **Preexisting psychiatric conditions** • RBPR: 30.4% were recruited from psychiatric hospitals • Control NR	**Severity (% moderate/severe)** All subjects were considered severe TBI **Severity Definition (HALS disability score±SD)** • RBPR 20.39±6.02 • Control 20.30±6.09 **Time since injury (years±SD)** • RBPR 3.05±2.98 • Control 4.66±4.66 **TBI etiology (%)** • RBPR ○ Vehicular related 95.7 ○ Assault 4.3 • Control ○ Vehicular related 95.7 ○ Assault 4.3 **Area of brain injured** NR **Other injury characteristics** Closed brain injury ○	**Comorbidities** NR **Compensation seeking** NR **Acute rehabilitation history** NR **Concomitant treatment** NR

Appendix E. Table 2. Intervention Characteristics

Study Target Population	Intervention Arm	Intervention Description and Implementation
Bell, 2005[13] **Moderate to Severe TBI**	**Telephone Counseling** **Theory/Model:** Modeled after validated telephone interventions in chronic care, smoking cessation, depression **Program Type:** Post-rehabilitation telephone contact **Setting:** Patient home **Delivery:** Scheduled phone calls with individualized mail supplements	**Description:** Scheduled phone calls made "research care manager to randomly allocated post-rehabilitation discharge patients. Calls were comprised of 3 basic elements: Follow-up of previously stated concerns, patient or family member stated current concerns, research care manager determined level of intervention in response to patient's concern. **Coordination:** NR **Disciplines:** NR **Components:** Giving information, mentoring, goal-setting, reassurance, modeling problem-solving, referral to community resources, triaging to regional or tertiary center if local resources unavailable **Therapy hours/week:** 30-45 minutes, weeks 2, 4 and months 2, 3, 5, 7, and 9 post-rehabiltation **Duration:** 9 months **Total therapy hours:** NR **Manualized:** Yes, described in detail in previous publication **Staff Training:** NR **Fidelity Checks:** NR
	Standard Follow-up **Theory/Model:** NR **Program Type:** Recommendations of the acute rehabilitation team with no compliance checks **Setting:** Patient home **Delivery:** N/A	**Description:** Patient given recommendations from acute care team then not contacted until 1 year follow-up **Coordination:** NR **Disciplines: primarily** NR **Components:** NR **Therapy hours/week:** NR **Duration:** 1 year **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Study Target Population	Intervention Arm	Intervention Description and Implementation
Cicerone, 2004 [11] **Chronic Moderate to Severe TBI**	**Intensive Cognitive Rehabilitation Program (ICRP)** **Theory/Model:** Holistic neuropsychological rehabilitation (Ben-Yishay and Gold 1990) **Program Type:** Community-based day treatment program **Setting:** Suburban postacute brain injury rehabilitation center (US) **Delivery:** Peer groups progress through program together.	**Description:** 'Individual and group cognitive remediation with an emphasis on increasing awareness and developing compensations for cognitive deficits, small-group treatment for interpersonal and pragmatic communication skills, individual and/or group psychotherapy, family support, and therapeutic work trials and placement to facilitate educational or vocational readiness.' **Coordination:** NR **Disciplines:** NP, VT,; PT, OT if necessary **Components:** Cognitive group - 6 hrs/wk; individual cognitive remediation - 3 hrs/wk; communication and interpersonal skills group - 3 hrs/wk; applied skills group - 1 hr/wk; additional tailored therapies - variable/wk; therapeutic work trials – 1 day/wk; family involvement. **Therapy hours/week:** 15 hrs/wk **Duration:** 16 weeks **Total therapy hours:** 240 hours. **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Standard Rehabilitation Program (SRP) **Theory/Model:** 'conventional program' **Program Type:** Community-based day treatment program **Setting:** Postacute brain injury rehabilitation center (Suburban US) **Delivery:** Individuals progress through tailored treatments	**Description:** Treatment content and duration tailored to individual. **Coordination:** monitored by staff NP throughout course of treatment **Disciplines: primarily** NP, PT, OT, SLP; could also include RT, VT, E psychologic counseling **Components:** Tailored, typical patterns NR **Therapy hours/week:** 15 hrs/ wk initially, adjusted individually to range of 12 to 24 hr/ wk. **Duration:** 3.9 mo (mean) **Total therapy hours:** variable **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Study Target Population	Intervention Arm	Intervention Description and Implementation
Cicerone, 2008[1] **Chronic Moderate to Severe TBI**	**Intensive Cognitive Rehabilitation Program (ICRP)** **Theory/Model:** Berquist 1994; Holistic neuropsychological rehabilitation (Ben-Yishay and Gold 1990) **Program Type:** Day treatment program **Setting:** Suburban postacute brain injury rehabilitation center (US) **Delivery:** Peer groups progress through program together.	**Description: Integrated treatments for c**ognitive deficits, interpersonal and behavioral difficultings, functional skills within therapeutic environment. Meta-cognition, emotional regulation, compensatory approaches emphasized. Weeks grouped by themes. **Coordination:** **Disciplines:** NP, primary therapist **Components:** Cognitive group - 6 hrs/wk; communication and interpersonal skills group - 3 hrs/wk; life skills group - 2 hr/wk; individual therapy - 3 hrs/wk, individual NP treatment 1 hr/wk. **Therapy hours/week:** 15 hr/wk **Duration:** 16 weeks **Total therapy hours:** 240 **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** Yes
	Standard Neurorehabilitation Program (STD) **Theory/Model:** Comprehensive , interdisciplinary day treamtment program (Malec 1996 Berquist 1994 **Program Setting/Type:** Day treatment program **Setting:** Postacute brain injury rehabilitation center (Suburban US) **Delivery:** Individuals progress through tailored treatments	**Description:** Individual, discipline-specific therapies targeting specific deficit areas designed to be responsive to stage and rate of recovery after TBI. Restorative strategies. **Coordination:** Followed by NP. **Disciplines:** NP**,** Psych, PT, OT, SLP, RT, VT, EC **Components:** Amounts and combinations of therapies varied. Most participants: individual NP treatment – 1 hr/wk; Participants could receive psychological counseling – 1 hr/wk, RT, VT, or educational counseling – 1 hr/wk; group therapy limited to 3 hrs/wk **Therapy hours/week:** 15 **Duration:** 16 weeks **Total therapy hours:** 240. **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** Yes

Appendix E. Table 2. Intervention Characteristics

Study Target Population	Intervention Arm	Intervention Description and Implementation
Greenwood, 1994[4] **Severe TBI**	**Case Management** **Theory/Model:** Case management model established by authors in previous papers; "assertive" or "clinical" case management elements developed by Holloway for mentally ill **Program Type:** Pro-active case management **Setting:** 4 general hospitals and 2 university teaching hospitals **Delivery:** Home-based outreach	**Description:** Early (within 7 days of injury) case management program which served as facilitator rather than therapeutic role, recruiting services for patient from a variety of agencies. **Coordination:** Case manager **Disciplines:** Physiotherapy, occupational therapy, speech therapy, psychology, social work **Components:** Determining patient needs and recruiting services based on these needs **Therapy hours/week:** NR **Duration:** NR; outcomes reported at 6, 12, and 24 months **Total therapy hours:** NR **Manualized:** Yes, described in detail in previous publication **Staff Training:** NR **Fidelity Checks:** NR
	Control **Theory/Model:** NR **Program Type:** Standard rehabilitation **Setting:** 4 general hospitals and 2 university teaching hospitals **Delivery:** N/A	**Description:** Patient given standard rehabilitation without case management **Coordination:** NR **Disciplines:** Physiotherapy, occupational therapy, speech therapy, psychology, social work **Components:** NR **Therapy hours/week:** NR **Duration:** NR, outcomes reported at 6, 12, and 24 months **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Hashimoto, 2006[10] **Moderate to Severe TBI comprehensive treatment of varying intensities**	**Comprehensive Day Treatment program** **Theory/Model:** Positivist-behavioral **Program Type:** Comprehensive **Setting:** Rehabilitation hospital **Delivery:** Group	**Description:** Group sessions focusing on enhancing individual's quality of life by teaching useful and effective behaviors and by redesigning patient's environment to help achieve goals. **Coordination:** All staff members **Disciplines:** Physical, social work, psychology, speech, vocational, "gymnastics," occupational, welfare **Components:** **Therapy hours/week:** 4 sessions/day for total of 4hrs/day for 6 months **Duration:** 6 months **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Comprehensive Day Treatment program **Theory/Model:** Positivist-behavioral **Program Type:** Comprehensive **Setting:** Rehabilitation hospital **Delivery:** Group	**Description:** Group sessions focusing on enhancing individual's quality of life by teaching useful and effective behaviors and by redesigning patient's environment to help achieve goals. **Coordination:** All staff members **Disciplines:** Physical, social work, psychology, speech, vocational, "gymnastics," occupational, welfare **Components:** N/A **Therapy hours/week:** 4 sessions for total of 2 hrs/day, twice weekly **Duration:** 4 months **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Comprehensive Day Treatment program **Theory/Model:** Positivist-behavioral **Program Type:** Comprehensive **Setting:** Rehabilitation hospital **Delivery:** Group	**Description:** Group sessions focusing on enhancing individual's quality of life by teaching useful and effective behaviors and by redesigning patient's environment to help achieve goals. **Coordination:** All staff members **Disciplines:** Physical, social work, psychology, speech, vocational, "gymnastics," occupational, welfare **Components:** Giving information, mentoring, goal-setting, reassurance, modeling problem-solving, referral to community resources, triaging to regional or tertiary center if local resources unavailable **Therapy hours/week:** 4 sessions for total of 2 hrs/day, twice weekly **Duration:** 3 months **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
Comprehensive Day Treatment program **Theory/Model:** Positivist-behavioral **Program Type:** Comprehensive **Setting:** Rehabilitation hospital **Delivery:** Group	**Description:** Group sessions focusing on enhancing individual's quality of life by teaching useful and effective behaviors and by redesigning patient's environment to help achieve goals. **Coordination:** All staff members **Disciplines:** Physical, social work, psychology, speech, vocational, "gymnastics," occupational, welfare **Components:** N/A **Therapy hours/week:** 4 sessions for total of 2 hrs/day, twice weekly **Duration:** 4 months **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Ponsford, 2006[5] **Postacute moderate to severe TBI**	**Community-based therapy programme (CT)** **Theory/Model:** NR **Program Type:** Community-based group therapy **Setting:** Epworth Rehabilitation Programme (Australia) **Delivery:** Tailored to individaul	**Description:** Access and conduct therapy in the home, workplace or community setting with active involvement of TBI individual, relatives and other s. **Coordination:** NR **Disciplines:** several disciplines; referrals made to local services; a significan number of patient do attend regular physiotherapy sessions at the rehabilitation center.. **Components:** Identification of important roles, goal setting, assessment of strengths and weaknesses, impairments and disabilities to be overcome to achieve goals. Therapies delivered in relevant setting. **Therapy hours/week:** NR, but most patients seen by a given therapist once a week or less **Duration:** NR **Total therapy hours:** NR. **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Hospital-based outpatient rehabilitation (historical) **Theory/Model:** NR **Program Type:** Hospital-based outpatient **Setting:** Epworth Rehabilitation Programme (Australia) **Delivery:** Tailored to individual	**Description:** Group social communication skills training to improve pragmatic language skills, social behaviors and cognitive abilities**.** **Coordination:** NR **Disciplines:** NR **Components:** domain specific therapies and group sessions, visits to home, work, shopping, domestic activities. **Therapy hours/week:** NR **Duration:** NR **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Powell, 2002[14] **Chronic Severe TBI**	**Outreach** **Theory/Model:** NR **Program Type:** Multidisciplinary Outreach **Setting:** Homes or community settings – organized through Homerton Hospital (London) **Delivery:** Tailored to individual	**Description:** a goal planning framework for delivering rehabilitation through individualized retraining delivered through community –based services. **Coordination:** led by a clinical NP **Disciplines:** OT, PT, S:P, psych, SW **Components::** Individual sessions, 2/week **Therapy hours/week:** 2-6 hours/week **Duration:** 6-12 weeks for goal setting/assessment; After initial assessment period, individuals seen for 27.3(sd=19.1) weeks for treatment **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Information **Theory/Model:** NR **Program Type:** Information **Setting:** Home - organized through Homerton Hospital (London) **Delivery:** Home visit & Standard booklet	**Description:** One home visit by therapist who gave patient specially collated booklet listing resources and highlighting those relevant to patient's needs. **Coordination:** NR **Disciplines:** team therapist **Components:** Individual session, education **Therapy hours/week:** 0 **Duration:** 1 visit **Total therapy hours:** 1 **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Prigatano, 1984[9] **Chronic Severe Closed Head Injury Patients**	**Neuropsychological Rehabilitation Program (NRP)** **Theory/Model:** Milieu based programs (Ben-Yishay 1982, Rosenbaum et al., 1978) **Program Type:** Hospital-based outpatient **Setting:** Presbyterian Hospital (Oklahoma City, US) **Delivery:** Peer groups progress through treatments	**Description:** Intensive, coordinated treatment emphasizing awareness and acceptance of impairments; cognitive retraining of select residual deficits and the development of compensatory skills. **Coordination:** NR **Disciplines:** NP, SLP, OT, PT, psychologist **Components:** Small group and individual sessions **Therapy hours/week:** 24 **Duration:** 6 mo. **Total therapy hours:** 576 **Manualized:** Yes **Staff Training:** NR **Fidelity Checks:** NR
	Untreated	
Prigatano, 1994[7] **Chronic Moderate to Severe TBI with adequate potential to return to work**	**Neuropsychological Rehabilitation Program (NRP)** **Theory/Model:** Intensive holistic cognitive rehabilitation/milieu program **(**Ben-Yishay et al., 1985) Neuropsychological rehabilitation (Ben-Yishay, et al., 1987) **Program Type:** Work Re-entry program **Setting:** Adult Day Hospital for Neurological Rehabilitation, Saint Joseph's Medical Center (Phoenix, AZ) **Delivery:** Peer groups progress through treatment	**Description:** A series of interdisciplinary therapies embedded in a milieu program thet emphasizes a holistic approach. Teadching patienst to be part of a small communityencouraging cooperation and responsibility. Simulated natural setting. Individual learns along with othes. TBI patients who underwent a specialty rehabilitation program; after 6-8 weeks of therapy, patients were integrated into 15-20 hours of work per week **Coordination:** NR **Disciplines:** PT, OR, SPL, cognitive therapy **Components:** individual therapies depending upon needs, individual psychotherapy, daily group psychotherapy, 'simulated' community interaction, protected work trial. **Therapy hours/week:** 24 **Duration:** 6 mo. **Total therapy hours:** approximately 576 **Manualized:** No **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

	Untreated (historical)	
Rattok, 1992[8] **Cognitive remediation**	**Treatment 1 - Balanced** **Theory/Model:** Ben-Yishay **Program Type:** Balanced **Setting:** Outpatient rehabilitation center **Delivery:** Small group	**Description:** Balanced package that included training to alleviate attentional disorders, individualized cognitive remediation, small-group interpersonal communication exercises, therapeutic community activities, and personal counseling functions. Remediative cognitive training included. **Coordination:** NR **Disciplines:** NR **Components:** Individual and small-group counseling **Therapy hours/week:** 5hr/day, 4 days/week **Duration:** 20 weeks **Total therapy hours:** 200 **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Treatment 2 - Interpersonal **Theory/Model:** Ben-Yishay **Program Type:** Small-group, interpersonal **Setting:** Outpatient rehabilitation center **Delivery:** Small group	**Description:** Training in attention, community activities, and personal counseling; no individualized counseling; emphasis on small-group interpersonal exercises **Coordination:** NR **Disciplines:** NR **Components:** Group work **Therapy hours/week:** 5hr/day, 4 days/week **Duration:** 20 weeks **Total therapy hours:** 200 **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Salazar, 2000[3] Moderate to Severe Closed head injury among active duty military personnel	**Inpatient Cognitive Rehabilitation** **Theory/Model:** Milieu-oriented approach modified to fit military framework (Prigatano 1994 Prigatano 1989); intergrated work therapy (Ben-Yishay 1987, Burke 1988) **Setting:** minimum care hospital ward, Walter Reed Army Medical Center (Washington, DC) **Delivery:** Peer groups progress through treatmen	**Description:** In a military milieu, physical fitness training and group and individual cognitive, speech, occupational, and coping skills therapies conducted with integrated work therapy coordinated to simulate patient's previous work or military specialty **Coordination:** Physiatrist **Disciplines:** Neuropsychology, occupational therapy, speech pathology, physical therapy, neurological and psychiatric consultation **Components:** Group and individual **Therapy hours/week:** NR **Duration:** 6 wks. **Total therapy hours:** NR **Manualized:** Yes **Staff Training:** NR **Fidelity Checks:** Intermittent reviews and continuing education
	Home rehabilitation **Theory/Model:** NR **Program Type:** Home-based postacute rehabilitation **Setting:** Home **Delivery:** Visits and phone calls from psychiatric nurse.	**Description:** Patients received TBI education and individual counseling from a psychiatric nurse and were given educational materials and recommended strategies for enhancing cognitive and organizational skills. included **Disciplines:** psychiatric nurse **Components: Trained to in various home number and** card games; encouragement to read and watch news programs, resumed daily physical exercise at their own pace. **Therapy hours/week:** .5 h/wk **Duration weeds:** 8 weeks **Total therapy hours:** NR **Manualized:** Yes **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Sarajuuri, 2005[6] **Chronic Moderate to Severe TBI**	**INSURE Program** **Theory/Model:** Neuropsychologic rehabilitation and psychotherapy (Ben-Yishay 1987 ; Ben-Yishay 1985 Christensen 1992, Prigatano 1986) **Program Type:** Residential Neuropsychologic rehabilitation **Setting:** Kapyla Rehabilitation Centre (Helsinki, Finland) **Delivery:** Peer groups progress through treatment	**Description:** Postacute, interdisciplinary, 6-week, inpatient neuropsychologic rehabilitation and psychotherapy. Therapeutic alliance is emphasized. Compensatory techniques, **Coordination:** NR **Disciplines:** NP, neurologist, rehabilitation nurse, SW, SPL, OT, PT **Components:** Cognitive group – 2 session/wk, pragmatic group – 1 session/wk, pictures of self group – 1 session/ wk, quality of life group – 1 session/ wk, sport, relaxation, and jogging group – 1 session/ wk; 2-day seminar with participation from family, employers, public health professionals to plan remaining 2 wks of program; supported and individually tailored vocational interventions. **Therapy hours/week:** 37.5 **Duration weeks:** 6 weeks **Total therapy hours:** 225 **Manualized:** Yes **Staff Training:** NR **Fidelity Checks:** NR
	Conventional Rehabilitation **Theory/Model:** NR **Program Type:** As referred by physician **Setting:** Recruited from Department of Neurosurgery, Helsinki University Central Hospital, Level 1 Trauma Center **Delivery:** As referred by physician	**Description:** Conventional clinical care and rehabilitation in local healthcare system. Rehabilitation services individually tailored and delivered in an unstructured and nonsystematic way. **Coordination:** NR **Disciplines:** Such as PR, PR SLP, NP and psychotherapy **Components:** NR **Therapy hours/week:** NR **Duration:** NR **Program total therapy hours:** NR **Manualized:** No **Staff Training:** No **Fidelity Checks:** No

Appendix E. Table 2. Intervention Characteristics

Semlyen, 1998[16] **Postacute Severe TBI**	**Multidisciplinary rehabilitation** **Theory/Model:** NR **Program Type:** Residential Neuropsychologic rehabilitation **Setting:** Hunters Moor Regional Rehabilitation Centre (Newcastle upon Tyne, UK) **Delivery:** Coordinated, multidisciplinary rehabilitation delivered individually	**Description:** Coordinated multidisciplinary approach that could include Inpatient, outpatient or home-based services delivered by multidisciplinary team with TBI specialization and coordinated patient goal setting with patient, team, and family members. Weekly review of goals. **Coordination:** NR **Disciplines:** nursing, PT, SLP, OT, clinical psychology, rehabilitation medicine, counseling, social work **Components:** individualized, daily **Therapy hours/week:** NR **Duration:** 201.0±144.12 (mean days±SD); **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR
	Single discipline approach **Theory/Model:** NR **Program Type:** variable **Setting:** settings other than Hunters Moor Regional Rehabilitation Centre (Newcastle upon Tyne, UK) **Delivery:** variable, but independatn for each Individual	**Description**: Less coordinated, single discipline approaches including inpatient and outpatient rehabilitation and could be only physiotherapy delivered for 1 hour once a week or several therapies providing input several times a week. **Coordination:** NR **Disciplines:** NR **Components**: variable **Total therapy hours/week:** NR **Program Duration:** 111.80±175.17 (mean days±SD) **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Thomas, 2004[15] **Adjustment to Acquired Brain Injury**	**Potential Unlimited Program (PUP)** **Theory/Model:** Simpson, 1996; Understanding, Re-integrating identity, acceptance, restructuring **Program Type:** Outward Bound **Setting:** Community, Outward Bound course (Australia), patient home **Delivery:** Mixed	**Description:** Three stage program consisting of 1)Group fundraising, 2)9-day Outward Bound "Discovery" course adapted to accommodate patients' needs, 3)Follow-up group work to transfer insights from program to key areas of psychosocial functioning **Coordination:** NR **Disciplines:** NR **Components:** Goal setting, group work, physical activities **Therapy hours/week:** Stage 1 = NR, Stage 2= 9 days, Stage 3 = 2 hours every other week for 3-4 months **Duration:** NR **Total therapy hours:** NR **Manualized:** Outward Bound portion (Stage 2) **Staff Training:** NR **Fidelity Checks:** NR
	Control **Theory/Model:** NR **Program Type:** NR **Setting:** NR **Delivery:** N/A	**Description:** Matched patients who had expressed initial interest in the PUP but were unable to participate **Coordination:** NR **Disciplines:** NR **Components:** NR **Therapy hours/week:** NR **Duration:** Assessments taken at same time points as PUP group **Total therapy hours:** NR **Manualized:** NR **Staff Training:** NR **Fidelity Checks:** NR

Appendix E. Table 2. Intervention Characteristics

Vanderploeg, 2008[2] **Postacute Moderate to Severe TBI in veterans or active duty military personnel**]	**Cognitive didactic treatments inpatient TBI rehabilitation** **Theory/Model: Cognitive-didactic treatments** (Sohlberg & Mateer 1986, 1989, 2001) **Program Type:** Residential postacute rehabilitation center **Setting:** Four VA inpatient postacute rehabilitation centers **Delivery:** Individual in person	**Description:** Emphasized explicit learning in an environment permitting and encouraging errors to assist clients to develop cognitive self-awareness. Targeting specific cognitive processes. Targeted 4 cognitive domains (attention, memory, executive function, and pragmatic communication) using trial-and-error learning approach to address patient self-awareness. Directly rehabilitating the cognitive deficits that underlie most functional TBI deficits to result in a generalized functional improvement. **Coordination:** Physiatrist **Disciplines:** Rehabilitation nurses, PT, PR, rehabilitation counseling, patient and family education, psychologic or SW support services, Occupational therapy, physical therapy, speech/cognitive/language therapy, neuropsychology **Components:** 7.5-15 hrs/wk cognitive didactic treatment integrated into essential CARF standard of care interdisciplinary rehabilitation. Memory notebooks. **Therapy hours/week:** 21.5-30 hrs/wk **Duration:** 32.2(±12.2) days **Total therapy hours:** NR; continued until clinically judged ready for discharge or 60 days **Manualized:** No **Staff Training:** Yes **Fidelity Checks:** Yes
	Functional-experiential treatments within inpatient TBI rehabilitation **Theory/Model:** Functional treatment concepts (Giles1993, 1999, 2006; Hartley 1995) **Program Type:** Residential postacute rehabilitation center **Setting:** Four VA inpatient acute rehabilitation centers **Delivery:** Groups in natural settings	**Description:** Real life performance situations and common tasks to remediate or compensate forfucntional deficits Learning-by-doing functional daily activities using an errorless treatment strategy incorporating therapist direction and structure to complete components of gradually more complex tasks; did not entail explicit awareness or learning, but rather emphasized mothor and other forms of implicit learning. **Coordination:** Physiatrist **Disciplines:** Occupational therapy, physical therapy, speech/cognitive/language therapy, neuropsychology **Rehab Goals:** To use real-life performance situations and common tasks to remediate or compensate for functional deficits **Components:** 7.5-15 hrs/wk functional-experimental treatment integrated into essential CARF standard of care interdisciplinary rehabilitation. Memory notebooks. **Therapy hours/week:** 21.5-30 hrs/wk **Duration:** 33.3(±13.6) mean (std dev) days **Total therapy hours:** NR; continued until clinically judged for discharge or until 60 days **Manualized:** No **Staff Training:** Yes **Fidelity Checks:** Yes

Appendix E. Table 2. Intervention Characteristics

Willer, 1999[12] Postacute severe brain injury with multiple disabilities	**Community-based residential rehabilitation** **Theory/Model:** Cognitive rehabilitation and community readaptation (Fryer 1987) **Program Type:** Residential postacute rehabilitation program **Setting:** homelike residential (Canada) **Delivery:** Individuals	**Description:** TBI subjects who received postacute, community and residential-based rehabilitation **Coordination:** NP **Disciplines: MD, PT, OT, SPL,** paraprofessionals **Components:** NR **Therapy hours/week:** NR **Duration:** ≥ 1 year (up to 3 years) **Total therapy hours:** NR **Manualized:** No **Staff Training:** Yes **Fidelity Checks:** No
	Home-based rehabilitation services **Theory/Model:** NA **Program Type:** varies **Setting:** Home and outpatient sevices **Delivery:** Individuals	**Description:** A highly variable range of home-based or outpatient services. **Coordination:** NR **Disciplines:** occupational and physical therapists, neuropsychology, case management , and nursing services **Components:** NR **Total therapy hours/week:** NR **Program Duration:** ≥ 1 year (up to 3) **Total therapy hours:** NR **Manualized:** No **Staff Training:** Yes **Fidelity Checks:** No

Appendix F. References to Appendixes

1. Cicerone KD, Mott T, Azulay J, et al. A randomized controlled trial of holistic neuropsychologic rehabilitation after traumatic brain injury. Archives of Physical Medicine & Rehabilitation. 2008 Dec;89(12):2239-49. PMID 19061735.
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