Comparative Effectiveness Review
Number 72

Effective Health Care Program

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

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

Effective Health Care Program

The Effective Health Care Program was initiated in 2005 to provide valid evidence about the comparative effectiveness of different medical interventions. The object is to help consumers, health care providers, and others in making informed choices among treatment alternatives. Through its Comparative Effectiveness Reviews, the program supports systematic appraisals of existing scientific evidence regarding treatments for high-priority health conditions. It also promotes and generates new scientific evidence by identifying gaps in existing scientific evidence and supporting new research. The program puts special emphasis on translating findings into a variety of useful formats for different stakeholders, including consumers.

The full report and this summary are available at **www.effectivehealthcare.ahrq.gov/reports/final.cfm**.

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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.

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

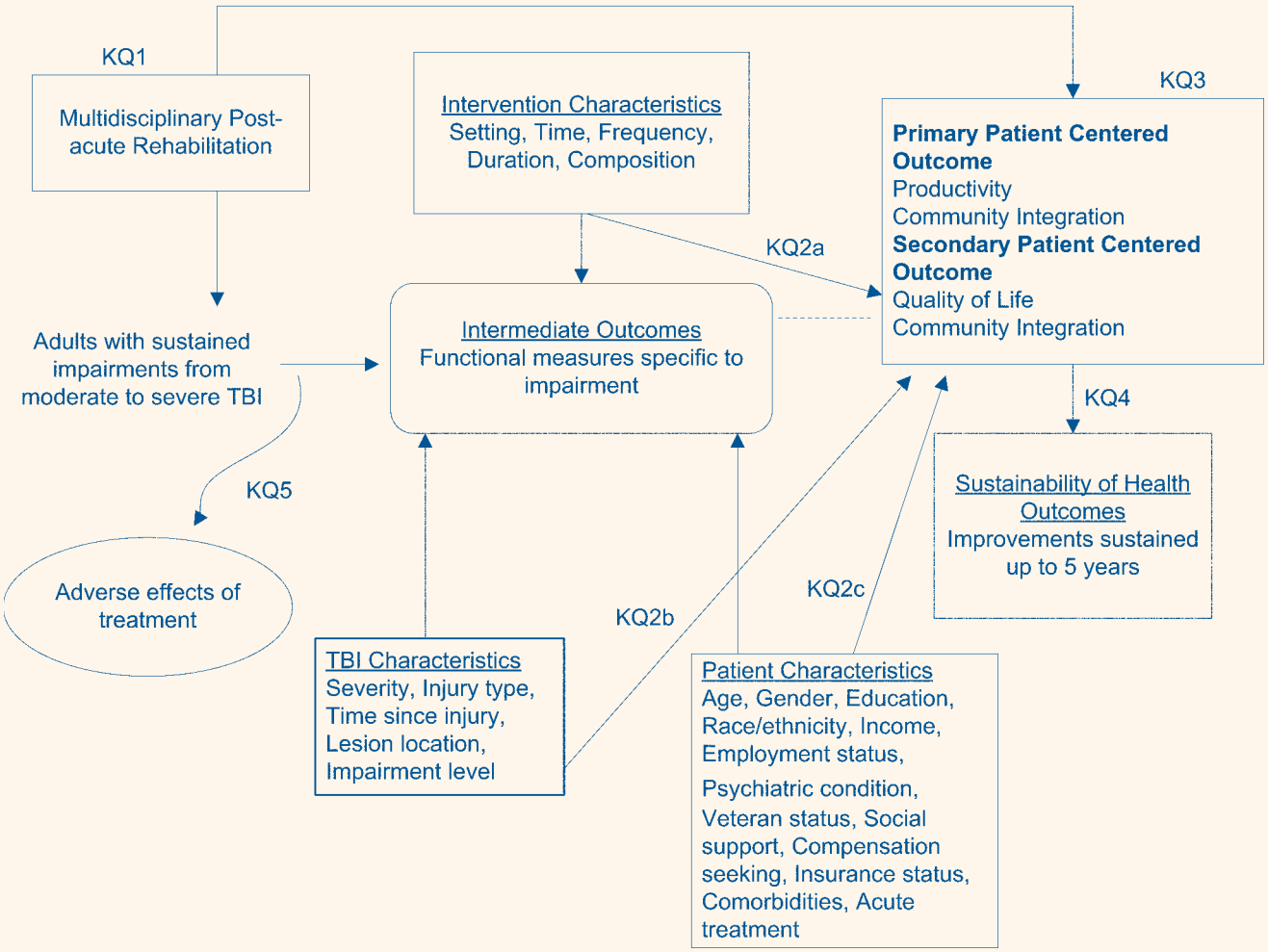
We developed a comprehensive search strategy consisting of a combination of controlled vocabulary and natural language terms for each bibliographic database (such as MeSH for MEDLINE), for two concepts (rehabilitation and TBI). We used filters for study design when possible. We searched the following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

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



KQ = Key Question; TBI = traumatic brain injury

- 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]

Table B. Summary of postacute rehabilitation programs studied (continued)	
Program Characteristics	**Studies Reporting**
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 342 or 643 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% 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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