Draft Comparative Effectiveness Review

Number XX

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

Prepared for:
Agency for Healthcare Research and Quality
U.S. Department of Health and Human Services
540 Gaither Road
Rockville, MD 20850
www.ahrq.gov

Contract No.

Prepared by:

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AHRQ Publication No. xx-EHCxxx
<Month Year>

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Financial Disclosure Statement

None of the investigators has any affiliations or financial involvement that conflicts with the material presented in this report.

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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 e-mail 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 e-mail to epc@ahrq.hhs.gov.

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Acknowledgments

The authors gratefully acknowledge the following individuals for their contributions to this project:

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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 was 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 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 one-year posttreatment. 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 posttreatment because the standard rehabilitation group made significant progress during the followup period. Gains made during rehabilitation appear to be sustained at follow-ups 6-months to 1-year posttreatment. 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 limited regarding effectiveness or comparative effectiveness of multidisciplinary postacute rehabilitation. The evidence is insufficient to assess effectiveness. Comparative effectiveness studies do not demonstrate clear benefits of one approach over another in terms of productivity or community integration. Further research should address methodological flaws common in these studies and further address effectiveness research questions.

Contents

Executive Summary ES-1

Introduction 1
Background 1
Definition and Severity of Traumatic Brain Injury 1
Sustained Impairments from Moderate to Severe TBI 2
Spontaneous Recovery 2
Treatment for Moderate to Severe TBI 2
Multi Disciplinary Postacute Rehabilitation 3
Outcomes of Postacute Rehabilitation 3
Decisional Delimmas 4
Focus of Review 5

Methods 9
Topic Refinement 9
Search Strategy 9
Triage and Screening 10
Inclusion Criteria 10
Data Extraction 13
Risk of Bias 13
Data Synthesis 14
Grading the Evidence 14
Assessing Applicability 15

Results 16
Previous Systematic Reviews 16
Description of Eligible Studies 17
Key Question 1. How have studies characterized multidisciplinary postacute rehabilitation for TBI in adults? 21
Key Points 21
Detailed Analysis 21
Key Question 2. What is the effectiveness and comparative effectiveness of miltidisciplinary postacute rehabilitation for TBI? 27
Key Points 27
Detailed Analysis 27
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? 41
Key Points 41
Detailed Analysis 41
Key Question 4. Are improvements in outcomes achieved via multidisciplinary postacute rehabilitation for TBI sustained over time? 41
Key Points 41
Detailed Analysis 41

Key Question 5. What adverse effects are assocaited with multidisciplinary postacute rehabilitation for TBI? 44
Key Points 44
Detailed Analysis 44

Summary and Discussion 45
Summary of Findings 45
Characterizing Interventions (KQ1) 45
Efficacy and Effectiveness (KQ2) 45
Minimum Clinicaly Important Differences (KQ3) 49
Maintenance of Outcomes (KQ4) 49
Adverse Events (KQ5) 49
Comparison to Previous Systematic Reviews 49
Limitations for the Evidence 49
Strength of Evidence 50
Risk of Bias 50
Applicability 50
Clinical Implications 51

Future Research 52

References 54

Acronyms and Abbreviations 59

Tables

Table A/1. Criteria used to classify TBI severity ES-2, 1
Table 2. Primary outcomes scale descriptions 12
Table 3. Exclusion criteria 13
Table 4. Secondary outcomes measures descriptions 19
Table 5. Overview of included trials 20
Table B/6. Summary of implementation characteristics ES-10, 25
Table C/7. Overview of primary outcomes with strength of evidence ES-14, 28
Table 8. Summary of study population characteristics (graded primary outcome studies 34
Table 9. Productivity outcomes 35
Table 10. Strength of evidence for productivity outcomes 37
Table 11. Community integration questionnaire 38
Table 12. Strength of evidence for the primary TBI studies 38
Table 13. Secondary outcomes 39
Table 14. Sustainability of productivity outcomes 42
Table 15. Sustainability of community integration outcome questionaire score 42
Table 16. Strength of evidence for sustainability outcomes 43
Table 17. Summary and strength of evidence of effectiveness and comparative effectiveness 47

Figures

Figure 1 International Classification of Function, Disability and Health 4
Figure 2. Analytic Framework ES-5, 8

Figure 3 Literature Flow Diagram ……..……..…….18

Appendixes

Appendix A. Search Strategy
Appendix B. Data Collection Forms
Appendix C. List of Studies Undergoing Full Text Review
Appendix D. Intermediate Outcomes Assessed
Appendix E. Evidence Tables

Effective Health Care

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

Executive Summary

The Effective Health 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. Ahrq.gov/reports/final.cfm

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. Between 2002 and 2006, approximately 1.7 million TBIs were recorded annually,[2] with 1.37 million treated and released from emergency departments; 275,000 hospitalized; and 50,000 deaths each year.[2] Additional TBIs are treated in primary care settings and in Federal, military, and Veterans Affairs hospitals. 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.[3]

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, with standard criteria including 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 1).[4]

The GCS is the most widely used scale to determine injury severity. However, this score can be inaccurate when certain acute interventions such as intubation are used, and some research suggests that loss of consciousness and post-traumatic amnesia may better predict functional status. Therefore, other measures are also used.[5]

Table A. Criteria used to classify TBI severity[6]

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

Most TBIs are mild injuries from which people recovery fully in a relatively short time. 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.[4] 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.[6] Deficits resulting from penetrating head injuries may be similar to those observed in stroke patients.[7] More common, however, are closed head injuries from which diffuse brain damage can result, leading to a variety of impairments unique to the individual.[7] 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.[8] Some long lasting impairments may not become apparent until well after the injury. By one estimate, 2 percent of the U.S. population lives with TBI-related disabilities, presumably from moderate to severe TBI.[9]

Patients with moderate to severe TBI are typically treated first in acute medical settings for a duration that varies according to injury severity, impairment level, other injuries, patient age, and specific patient and healthcare system characteristics. Once the patient is medically stable, postacute rehabilitation may occur (or in some instances, intensive rehabilitation occurs in a subacute setting).

Postacute rehabilitation addresses sustained impairments across physical, cognitive, and affective/behavioral domains. Rehabilitation programs strive to restore an individual's functioning and participation to preinjury levels. During the 1970s and 80s, research emerged suggesting that domain-specific training may be insufficient to rehabilitate those with damage to the frontal lobe.[10] Spurred by these findings, clinicians began to adopt holistic approaches to TBI rehabilitation, including vocational and neurobehavioral interventions that incorporate arranged work trials.[10] The current preferred approach is multidisciplinary, with treatments (including 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.[11]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. While there appears to be a general understanding that comprehensive programs comprise many professionals working as a team, it is difficult to find program descriptions that specify percentages or doses of the various available therapies. This is in part because an individual's sustained impairments may largely determine the composition, intensity, and duration of rehabilitation.

To determine whether rehabilitation programs have met the goal of restoring TBI survivors to previous or newly defined roles, it is important to address patient-centered outcomes, which are those valued by patients.[12] To identify these outcomes, we looked to the International Classification of Functioning Disability and Health's (ICF) participation domain.[13] Participation as demonstrated by productivity and community integration are obvious indicators of progress for survivors attempting to reclaim meaningful lives after debilitating injuries.

However, patient-centered outcomes can be subjective and are often measured with scales. Unfortunately, clinical interpretation of the scales used to assess community integration is not straightforward. It is critical to identify the level of change in a particular scale score that equates to a meaningful life improvement for patients and their families. Understanding this meaningful level of change, often called the minimum clinically important difference (MCID), is key to evaluating effectiveness and comparative effectiveness.

Scope and Key Questions

Although experts in the field believe comprehensive multidisciplinary postacute rehabilitation to be the best approach for addressing impairments from moderate to severe TBI, access is problematic. Inconsistent health insurance reimbursement policies prevent some patients from receiving rehabilitation.[7, 14] 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.

The uncertainty does not reflect insufficient efforts to synthesize evidence, but rather inconsistency of the conclusions. Dozens of related systematic reviews have been conducted, with conflicting results. Differences in conclusions across reviews reflect methodological decisions about populations, outcomes, and included study designs. For instance, reviews by Cicerone et al.[15-18] are widely cited as demonstrating the effectiveness of cognitive rehabilitation. However, reviews by ECRI and the Institute of Medicine report insufficient evidence to determine the effectiveness or comparative effectiveness of cognitive rehabilitation for TBI.[19, 20] The conclusions of the ECRI and IOM reviews are drawn heavily from RCT data.

Another issue leading to inconsistent findings of reviews relates to outcomes. Many previous reviews appeared to base determinations of effectiveness on any outcome measures used in original studies. Unfortunately, many outcomes measures used in primary research are not patient-centered, and thus do not reflect the impact of rehabilitation on the lives of those suffering TBI impairments. Therefore, our review emphasizes selected patient-centered participation outcomes of productivity and community integration.

In addition, many treatments target specific functional difficulties, and thus intervention programs often enroll both TBI patients and those with non-traumatic brain injuries (primarily from stroke and aneurism). However, stroke patients differ distinctly from TBI survivors. Further, evidence suggests that TBI patients achieve greater functional outcomes when matched on age and demographic characteristics.[21] Therefore, we specifically address the TBI population and include only in which at least 75 percent of the subjects have impairments from moderate to severe TBI.

Finally, our review includes prospective cohort studies as opposed to restricting eligibility to randomized controlled trials (RCTs). Our full report provides a detailed description of this systematic review.[22] We address the following key questions:

Question 1

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

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?

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?

Question 4

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

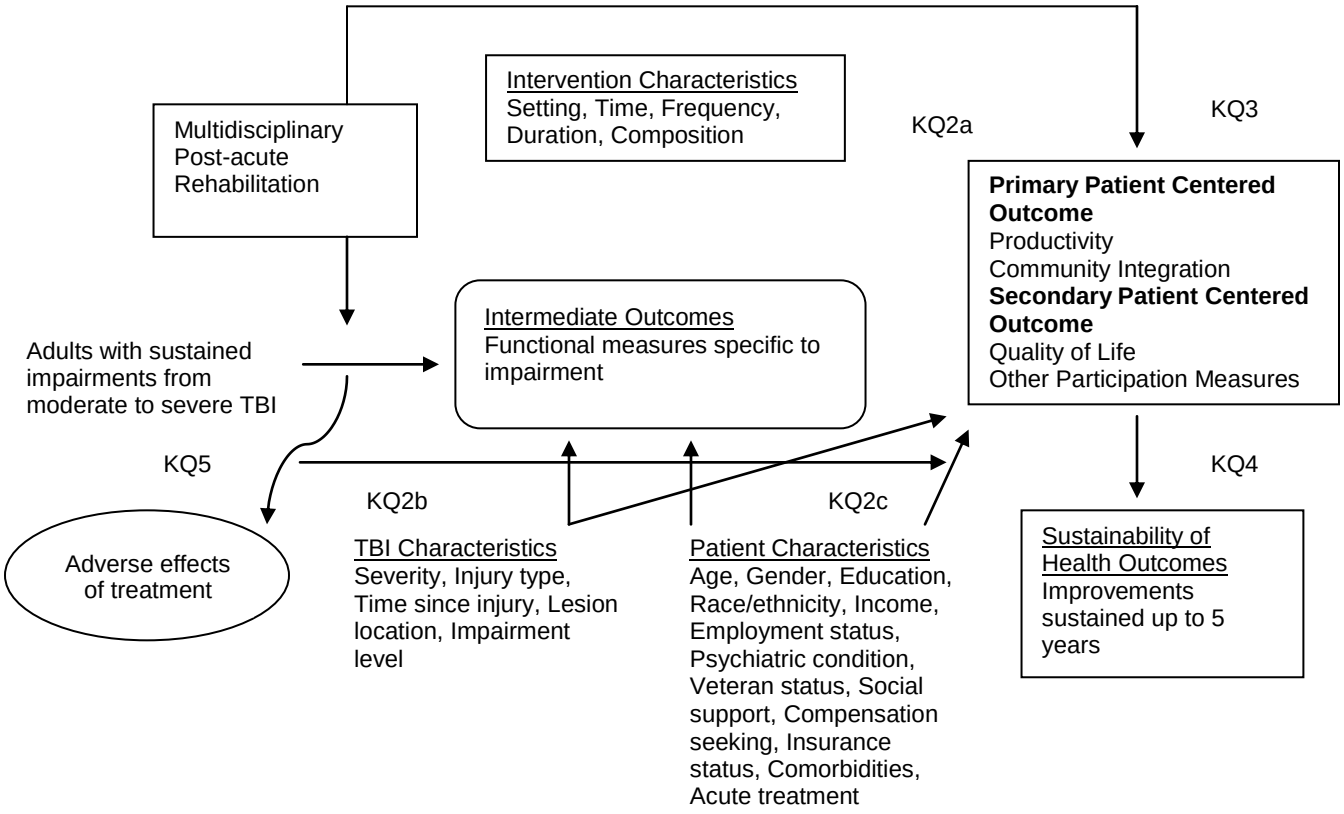
Question 5

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

We address these key questions in the context of our analytical framework (Figure A). This framework greatly simplifies the complex process navigated by those with sustained impairments from moderate to severe TBI. For instance, spontaneous recovery (most marked immediately following injury) may occur simultaneously with rehabilitation, complicating efforts to distinguish natural improvements from those due to treatment.[7] 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 back to their previous roles in society, or as close thereto as possible.

Figure A. Analytic framework for multidisciplinary postacute rehabilitation for traumatic brain injury in adults



Methods

Our full report provides a detailed methodology.[22]

Topic Refinement and Review Protocol

Our final key questions were determined after several iterations of the original publically nominated topic of rehabilitation for TBI. We recruited Key Informants representing several 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 key questions for comments from stakeholders, and recruited a panel of technical experts in the field. This panel recommended we further refine the key questions to focus on comprehensive or multidisciplinary programs, and identified participation outcomes as most relevant to evaluating the effectiveness of these programs.

Literature Search Strategy

We developed a comprehensive search strategy consisting of a combination of controlled vocabulary relevant to each bibliographic database (such as MeSH for MEDLINE) and natural language terms for two concepts (rehabilitation and traumatic brain injury). We used filters for study design when possible. We searched the following bibliographic databases from 1980 to August of 2011:

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

We searched for randomized controlled trials (RCTs) and prospective cohort studies. We supplemented this search with backwards citations searches of relevant systematic reviews.

Two investigators independently reviewed each citation, and full text when deemed necessary, to determine eligibility. 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)
- No original data
- No full text available in English
- Pediatric population only
- Less than 75 percent patients with moderate to severe TBI
- No intervention studied
- Not been studied in the post-acute stage
- Only included impairment-specific intervention
- No comparison group (i.e. case series)
- No relevant comparison
- No outcomes of interest for this review reported
- Study design flaws, such as retrospective study design

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

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[23] by adding items to capture potential risk of bias specific to this topic, such as that associated with intervention definition and implementation, and the outcomes measures used to assess effectiveness. We obtained these additional items from the RTI Observational Studies Risk of Bias and Precision Item Bank.[24] 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 assesse risk of biasof eligible studies that evaluated rehabilitation effectiveness with a primary outcome. Summary scores of low, moderate, or high were assigned by investigators based on their judgment about the collective risk of bias created by the assessments of the individual items and the magnitude of potential 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 the Effective Health Care Program.[25] Studies with a high risk of bias were not included when determining SOE. We evaluated strength of evidence based on four required domains (risk of bias, consistency, directness, and precision). Two investigators worked independently to qualitatively rate each component and overall strength of evidence. Overall assessments reflected the investigators' subjective assessment and relied heavily on their in-depth knowledge of each study, as well as assessments for 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 of the studies according to the PICOTS format. To assess applicability, we reviewed 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.[26]

Results

Results of Literature Searches

We searched four bibliographic databases (Ovid MEDLINE, PschINFO, Cochrane CENTRAL Register of Controlled Trials and PEDro) through August of 2011 and identified 1,616 unique references. Review of titles and abstracts identified 166 references meriting full text review. Hand searching identified 12 references meriting full text review, for a total of 178 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 no intervention, no primary or secondary outcome, ineligible study design, and not 75 percent moderate to severe TBI population. The full report includes the literature flow diagram, outcomes, evidence, strength of evidence tables, and risk of bias assessment forms and results.[22]

Key Question 1.Characterizing the Interventions

All 16 studies were used to characterize 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, with more recent studies providing improved 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 of intervention; 3) methods of intervention delivery; 4) models of care used to develop the intervention; and 5) intensity and duration of 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.[27-30] Six studies compared new models of care being delivered by their institution or agency to the standard care typically delivered.[31-36] Five studies compared different models of care.[27, 37-40] Two studies examined an additional component added to a standard program.[41, 42]

Most of the programs addressed TBI survivors whose impairments were chronic or had lasted more than 6 months postinjury. However, three interventions addressed patients earlier in the postacute period, within 6 months of injury.[35, 39, 40] Two interventions began in the earlier postacute period and continued to the chronic stage.[41, 42] Other programs addressed survivors of severe injuries[35, 36, 42] or military populations.[39, 40]

Programs typically engaged a similar variety of disciplines, and included 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.[27-29, 31, 32, 34, 38, 39] These interventions 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,[34, 39] and a single program addressed TBI survivors earlier in the postacute period.[39] Despite their many similarities, interventions based on this model of care varied in duration of treatment from 6 weeks to 6 months.

Other programs described outreach to TBI survivors;[37] community-based care;[33] specific approaches to remediation of skills;[40] multidisciplinary programs without mentioning a specific model;[35] residential communities of TBI survivors;[36] and an outdoor experiential education program.[30] Specific components of multidisciplinary programs that were studied included case management[42] and telephone counseling.[41]

Table B: Summary of Implementation Characteristics

Author, year location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
Bell 2005[41] 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[31], **2008**[32] 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[42] UK	Early Postacute through Chronic Severe	Case management		Home	Individuals	NR	NR
Hashimoto 2006[27] 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
Ponsford 2006[33] 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[37] UK	Chronic Severe	Outreach	NR	Home or community	Individuals	2-6 hrs/wk 27 wks (mean)	54-162
		Information	NR	Home	Individuals	1 hr 1 session	1
Prigatano 1984[28], **1994**[29] United States	Chronic Moderate to Severe	Neuropsychological rehabilitation	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	24 hrs/wk 6 mos	576
Rattok 1992[38] 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
Salazar 2000[39] United States	Active duty military Early postacute Moderate to severe Mild impairments	Inpatient Cognitive Rehabilitation	Holistic Day Treatment	Residential	Small groups	NR 6 wks	NR
	Active duty military Early postacute Moderate to severe	Home rehabilitation	NR-	Home	Individuals	.5 hr/wk 8 wks;	4

Author, year location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
	Mild impairments						
Sarajuuri, 2005[34] Finland	Chronic Moderate to Severe	Comprehensive neurorehabilitation	Holistic Day Treatment	Residential	Small groups	37.5 hrs/wk 6 wks	225
Semlyen 1998[35] UK	Early postacute Severe	Multidisciplinary rehabilitation	NR	Residential	Individuals	NR	NR
Thomas 2004[30] 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[40] United States	Active-duty military, veterans Early postacute Moderate to Severe	Cognitive didactic	Cognitive-didactic	Residential	Individuals	7.5-15 hrs/wk 32 days (mean)	NR
		Functional-experiential	Functional treatment concepts	Residential	Small groups	21.5-30 hrs/wk 33 days (mean)	NR
Willer 1999[36]	Chronic Severe Multiple disabiites	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. More detailed descriptions can be found in the appendix to the full report.

Key Question 2. Efficacy and Comparative Effectiveness

Of the 16 eligible studies, 12 assessed a primary outcome and eight assessed secondary outcomes. Of the 12 assessing primary outcomes, four were judged to have a high risk of bias, and thus excluded from analysis,[27, 29, 33, 36]leaving eight studies (four RCTs and four cohort studies) used to grade evidence on primary outcomes. Of these eight studies, one was rated low risk of bias, and seven were rated moderate risk of bias.

Sample sizes 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 (with no acquired brain injury) often included only closed head injuries. Median time since injury varied widely between studies, from 1 to 45 months with a median of 19 months. Two studies specifically restricted enrollees to those within 3[39] or 6[40] months of injury. Table C presents a summary of results and strength of evidence grades for all primary outcomes studies.

Productivity The heterogeneity in populations and comparisons across studies precluded an overall summary SOE for productivity, as SOE is calculated for each comparison. Only one of the eligible studies assessing a primary outcome compared the intervention to a no-treatment group.[28] This small cohort study found no significant differences in return to work between groups at a timepoint between 6 and 24 months posttreatment. However, this study was likely underpowered and did not use current accepted methodology to adequately control for confounding; thus it provides insufficient evidence about effectiveness.

Six studies assessed the comparative effectiveness of two interventions with respect to productivity outcomes.[32, 34, 38-40, 42] Two larger RCTs found no productivity differences soon after injury between groups of patients who received different treatments.[39, 40] Another single-center RCT found that a 4-month Intensive Cognitive Rehabilitation Program (ICRP) compared to standard treatment at that outpatient rehabilitation center resulted in a moderate effect size end-of-treatment increase in productivity for chronically impaired civilian survivors of 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.[32] This difference disappeared at the 6-month posttreatment 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 provides a low strength of evidence that for the described population, the ICRP improved productivity over and above that of standard rehabilitation immediately posttreatment, but differences were not maintained by 6 months posttreatment. We graded this evidence 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 CIQ found significant group differences in CIQ scores posttreatment (ICRP=12.9, standard rehabilitation=11.7 in RCT[32]; ICRP=16.8, standard rehabilitation=16.1, unadjusted in cohort study[31]), despite differences in mean change in the CIQ scores between groups enrolled in the cohort study.[31] The cohort study also

provided analysis of clinically meaningful change in CIQ scores between groups. Fifty-two percent of the ICRP group showed clinically significant improvement (of 4.2 points) compared to only 31 percent of the standard rehabilitation group. This indicates that ICRP participants were 2.5 times more likely than standard program participants to achieve a clinically significant improvement in CIQ score. Unfortunately, these trends were not repeated in the RCT. The data provide a low level of evidence that participation in ICRP versus standard rehabilitation did not improve community integration. We graded this evidence low because it was derived from one moderately sized RCT with a moderate risk of bias. Results from the RCT were primarily used to grade strength of evidence because the cohort study provided unadjusted results.

Table C: Overview of primary outcomes for multidisciplinary postacute rehabilitation for TBI with Strength of Evidence (SOE)

Treatments; Study design	Study populations	Outcome definition	Post-treatment assessment	Followup post-treatment assessment
Intensive cognitive rehabilitation versus Standard neurorehabilitation Study 1 RCT[32] Study 2 non-RCT[31]	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	↑↑ 16 weeks (Study 1) Low (SOE)	↔ 6 months (Study 1) Low SOE
		Community Integration Questionnaire	↔ 16 weeks (Study 1 and Study 2) Low SOE	↔ 6 months (Study 1) Low SOE
Functional-experiential versus Cognitive-didactic[40] 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*) Low SOE
Hospital treatment versus Home treatment[39] 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 [42] 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 versus Conventional rehabilitation[34] 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
Neuropyschological rehabilitation	35 American closed head injury outpatients in a neuropsychological rehabilitation program compared to similar	Gainfully employed or		↔ Unclear, following 6

versus Controls[28] Non-RCT	head injury controls. Mean age 25, Male 86%.	actively engaged in a realistic school program	not reported	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)[38] 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
* 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.

Key Question 3. Minimally Clinically Important Differences

We identified no evidence establishing minimum clinically important differences (MCIDs) for the MPAI. Because we found no studies evaluating 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 described the reliable change index that indicates whether individuals made positive change, no change, or negative change in community integration in a previous sample of TBI survivors. The authors also mentioned the consistency of this RCT with a previous study.[31] However, the later RCT evaluating the ICRP did not mention a reliable change index or attempts to determine the incidence of a MCID.[32]

Key Question 4. Sustainability of Intervention Effectiveness

Two primary outcomes studies incorporated followup outcome measurements.[32, 42] Table D presents the results for these studies. These data provide a low strength of evidence that outcomes achieved during rehabilitation did not deteriorate between timepoints studied. We assessed the strength of evidence as low for these comparisons because they were each derived from one moderately sized RCT with a moderate risk of bias.

Table D: Sustainability of Improvements in Productivity and Community Integration

Study Outcome	Outcome	Treatment Arms	% or Score After Completion of Treatment	% or Score at Follow up, timepoint 1*	Posttreament vs. Followup
Cicerone 2008[32]	Community-based employment	Intensive cognitive rehabilitation	47% (16/34)	60% (18/30)	P=0.57
		Standard neurorehabilitation	21% (7/34)	50% (14/28)	P=0.10
	CIQ	Intensive Cognitive Rehabilitation Program (n=34)	12.9 (3.4)	13.2 (4.3)	NR, but followup score still different from pretreatment
		Standard Neurorehabilitation Program (n=34)	11.7 (4.4)	12.9 (4.4)	P=0.04
Greenwood 1994[42]	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

RR = relative risk [95% confidence intervals].
Note: This table presents the results measuring sustainability of improvements from rehabilitation.

Key Question 5. Adverse Events

The single study that mentioned adverse events did not appear to assess them in a systematic manner; reporting that no adverse events were observed.[40]

Discussion

Key Findings and Strength of Evidence

The evidence we reviewed emphasized the complexity of traumatic brain injuries and the interventions to rehabilitate individuals suffering from associated sustained impairments. Studies of multidisciplinary postacute rehabilitation often fail to define interventions sufficiently. Newer studies provide more useful definitions than those published prior to 2000.

Our review, like others, found the currently available evidence insufficient to draw meaningful conclusions about the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury in adults. Specifically, we found insufficient evidence to assess effectiveness, and identified few well-designed studies to address comparative effectiveness.

Unfortunately, the current research on effectiveness and comparative effectiveness is not designed to permit needed conclusions about whether or which interventions contribute or not to improved participation outcomes. Table E summarizes findings regarding effectiveness and comparative effectiveness. This single cohort study that examined a 6-month comprehensive holistic day treatment program was underpowered, and rated to have a moderate risk of bias, thereby warranting an insufficient strength of evidence. 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. A low level of evidence suggests that ICRP may lead to earlier productivity as compared to standard rehabilitation. However, this study also provided a low strength of evidence that rates of productivity between groups were not significantly different at 6 months posttreatment.

Conducting and synthesizing research on this topic is impeded by the complexity of the condition of moderate to severe TBI, 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 RCTs in achieving the high strength of evidence required for conclusions about effectiveness.

Table E: 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[39]	Inpatient hospital rehabilitation program (8 weeks) vs. limited home treatment	Return to gainful employment at 1 year posttreatment	No difference between groups	Low (moderate risk of bias, single study)
		Fitness for military duty at 1 year posttreatment	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[40]	Functional-experiential vs. Cognitive-didactic rehabilitation programs for varying durations	Return to gainful employment at 1-year posttreatment	No difference between groups	Low (moderate/low risk of bias, imprecise, single study)
Chronically impaired patients with primarily moderate to severe TBI[31, 32]	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 posttreatment	No difference between groups	Low (moderate risk of bias, single study)
		CIQ at end of treatment	No difference between groups	Low (medium risk of bias, imprecise, consistent)
		CIQ at 6 months posttreatment	No difference between groups	Low (medium risk of bias, single study)
Severe TBI patients at least 6 months postinjury[28]	Comprehensive day neurorehabilitation program (6 months) vs. No Treatment	Participation in gainful employment at one timepoint measured between 6 and 24 months posttreatment	No difference between groups	Insufficient (high risk of bias, inprecise, single study)
TBI patients who were independent in daily life and had only slight physical disabilities [34]	Comprehensive neurorehabilitation vs Conventional rehabilitation	Working, studying, or participating in volunteer activities	Statistically higher proportion neurorehabilitation group working, studying, or participating in volunteer activities	Insufficient (high risk of bias, single study)
Primarily chronically	Case-management vs.	Competitive work at 6	No difference between	Insufficient

Population	Intervention/Comparator	Outcome	Conclusion	SOE
impaired patients with moderate to severe TBI[42]	conventional neurorehabilitation	months posttreatment	groups	(high, imprecise, single study)
		Competitive work at 1 year posttreatment	No difference between groups	Insufficient (high risk of bias, imprecise, single study)
		Competitive work at 2 years posttreatment	No difference between groups	Insufficient (high risk of bias, imprecise, single study)
Severe TBI patients at least 1 year post injury[38]	Treatment Mix 1 vs. Treatment Mix 2 vs. Treatment Mix 3	Productive employment at 9 months posttreatment	No difference between groups	Insufficient (high risk of bias, imprecise, single study)

SOE – strength of evidence.
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, without other psychiatric diagnoses, chronically impaired, etc.). Even then, many of the interventions and control conditions seemed to be embodiments of their local rehabilitation systems, making replicability in other contexts challenging. Additionally, most studies excluded individuals with substance abuse or psychiatric diagnoses, both of which are common in the TBI population.[43] The policy issue of inconsistent insurance coverage for rehabilitation services[7] has implications for the applicability of these results. Moreover, TBI disproportionately affects males, those ages 15 to 24, and those with lower socioeconomic status[8], 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 the evidence relevant to the effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury in adults, research gaps remain. Additional systematic reviews cannot satisfy these gaps until additional high quality studies are completed. Studies designed specifically to overcome the shortcomings of current research may be the highest priority. Effectiveness research, for which a no-treatment control group is needed, 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.

Evidence is needed from RCTs and well-designed cohort studies 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. The construction of a sufficient 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 to this complex condition and relevant interventions when randomization does not achieve balanced groups. Additionally, alternative approaches proposed as better suited for studying comparative effectiveness on complex topics may be more feasible and should be explored. For example, the practice-based evidence approach [44] may help overcome certain shortcomings of the available research, in part by allowing for studies with much larger sample sizes.

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 surround the selection of the comparison group. 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. Adequately defining the intervention and ensuring the effective implementation of the interventions and controls would reduce risk of bias. Finally, a lower risk of bias related to outcomes in these intervention studies could be achieved through selecting *a priori* primary patient-centered outcomes; limiting the number of outcomes scales and comparisons; using consistent and appropriate psychometrically justifiable outcomes scales; establishing minimum clinically important differences in these scales; and adjusting for multiple comparisons. All of this would help create a stronger evidence base.

Furthermore, conceptual work could assist an advancing knowledge in the field. For example, the development and consistent use of taxonomies of TBI impairments and treatments could foster consistent reporting in research. The ICF presents a useful taxonomy of impairments and outcomes domains. This enables researchers to report impairment domains and levels of impairment, which is critical to understanding which interventions work best for which patients. However, as with many postacute rehabilitation topics, the taxonomy of treatment is underdeveloped.[45] Future research should advance the development and consistent use of a taxonomy of interventions.

Aside from methodological improvements and enhancing the groundwork from which to improve intervention studies, several additional research questions should be addressed with intervention studies. 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, longer-term followup data on patient-centered outcomes measures should be collected. The most frequently studied programs used the comprehensive holistic day-treatment model of care. Given the support for this approach in the TBI community, additional studies comparing this approach to standard rehabilitation programs should be undertaken. Because recent work has recommended certain outcomes for use in research on these topics,[46] future studies should incorporate these measures into their intervention research. The MPAI appears most promising for this topic. Finally, given the heterogeneity at many levels of this topic, a better understanding of which patients best benefit from which interventions would advance the field significantly.

The TBI Model Systems programs offer necessary settings and populations for conducting patient-centered outcomes research on rehabilitation topics.[47] The quality of intervention studies conducted in these venues could be improved by incorporating methods for documenting specific intervention components and steps in determining the course of treatment.

Conclusions

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. High quality conclusive evidence from rigorously conducted systematic reviews is a high bar currently met by only small portion of medical interventions (and an even smaller portion of rehabilitation interventions). The insufficiency of the evidence on this topic likely stems from the complexity of the condition and treatments resulting in limited available research. However, both the research quality and funding are increasing; therefore the body of evidence should strengthen dramatically with time.

Internet Citation

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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 are treated in primary care settings and in Federal, military, and Veterans Affairs hospitals. Incidence is highest among children, adolescents, and young adults, but hospitalization and death occur most often among those age 75 and older.[3] 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.[3, 4]

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.[5] The GCS is the most widely used scale to determine injury severity. However, GCS has significant limitations.. For example, it is used at several time points, and studies of TBI do not always clearly report which GCS measurement time point was used to assess severity. Additionally, GCS may not be the most accurate determinant of severity. In cases where certain acute interventions are used, the GCS score can be inaccurate.[6] Some experts have begun to support the use of other measures for severity based on research suggesting that loss of consciousness and post-traumatic amnesia may better predict functional status.[6] 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[3]

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

Note: This table describes the predominant ways in which TBI severity is assessed.

Sustained Impairments from Moderate to Severe TBI

Moderate to severe injuries 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.[5] The Institute of Medicine 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.[3] By one estimate, 2 percent of the U.S. population lives with TBI-related disabilities, presumably from moderate to severe TBI.[7]

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;[3] these injuries are associated with long-term unemployment and deficits similar to those observed in stroke patients.[8] Closed head injuries, which are more common, result in diffuse brain damage leading to impairments unique to the individual.[8] Evidence suggests that long-lasting effects of moderate to severe TBI include cognitive deficits, psychiatric outcomes (depressive and aggressive behaviors, post traumatic stress disorder in military populations, and psychoses), and social functioning (unemployment and diminished social relationships).[9] Specifically, sustained *physical* impairments may reduce endurance, cause headaches and seizures, and affect muscle tone, vision, hearing, smell, taste, and speech.[10] Sustained *cognitive* deficits may affect memory, attention, judgment, communication, planning, and spatial orientation.[10] Sustained *affective/behavioral* impairments include changes in mood, behavior, or personality that manifest as impulsiveness, passivity, agitation, loss of empathy, or emotional lability.[8] The constellation of impairments following moderate to severe TBI can impede function and societal participation for months or years after injury.[8]

Spontaneous Recovery

Controversy persists around the period and extent of spontaneous recovery after moderate to severe TBI. Recovery from physical impairments is thought to occur most quickly immediately after injury, while the bulk of neurologic recovery occurs during the first 6 months. Experts differ about the probable maximum duration of recovery. Some argue that neurologic recovery is complete at 1 year, while others believe recovery spans 2 or more years. All agree that as time since injury increases, recovery slows, and the scope of impairments narrows.[8] However, certain psychiatric outcomes may become more apparent several years postinjury.[9]

Treatment for moderate to severe Traumatic Brain Injury

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 rehabilitation may occur. Those with multiple long-lasting impairments might participate in impairment-specific therapies. These impairment-specific therapies are not addressed in this report. 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. Rehabilitation programs strive to restore an individual's functioning and participation to preinjury levels. During the 1970s and 80s, research emerged suggesting that domain-specific training may be insufficient to rehabilitate those with damage to the frontal lobe.[11] Spurred by these findings, clinicians began to adopt holistic approaches to TBI rehabilitation, including vocational and neurobehavioral interventions that incorporate arranged work trials.[11] 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.[12]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. The "program" is often variable and seen as a function of specific patients' presumed needs.

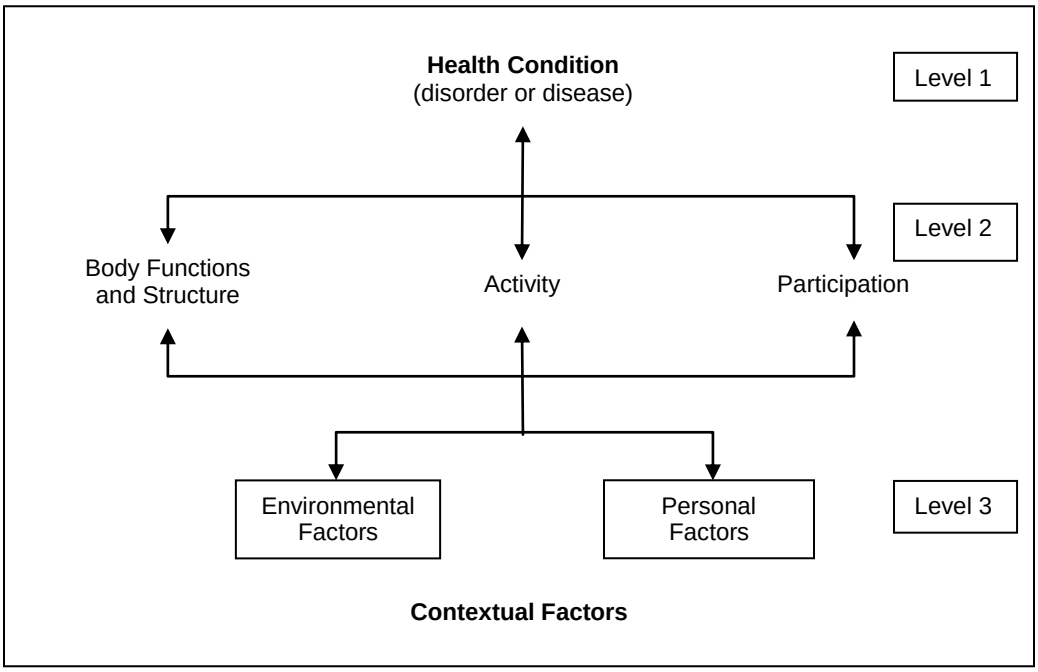
Multidisciplinary rehabilitation programs for brain injury lack a clear and consistent taxonomy.[12] Malec and Basford describe four types of programs: neurobehavioral, residential community reintegration, comprehensive (holistic) day treatment, and outpatient community reentry. Neurobehavioral programs provide behavioral interventions for patients with significant behavioral disturbances.[13] 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.[13] Outpatient community reintegration programs offer circumscribed rehabilitation treatments and vocational and social reintegration.[13] 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.[13]

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.[14] Outcomes for the rehabilitation of moderate to severe TBI impairments likely reflect the participation domain of the International Classification of Function, Disability, and Health (ICF) framework, created to classify and assess function and disability associated with health conditions.[15] 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.

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.[16] 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.[16] Several scales are available for assessing community reintegration in the brain injury population. However, interpreting whether scale score changes are meaningful presents a challenge. It is critical to identify the level of change in a particular scale score that equates to a meaningful life improvement for patients and their families. Adequately evaluating effectiveness and comparative effectiveness hinges on adequately understanding this meaningful level of change, often called the minimum clinically important difference (MCID).

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 relatively short time frame during which research on this condition has occurred, 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 prevent some patients from receiving rehabilitation. Lack of coverage may be a problem of particular concern for those in the very chronic pases of recovery or who need specific types of rehabilitation, such as cognitive rehabilitation.[8, 17] 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. Tricare attributed their decision not to cover certain cognitive rehabilitation treatments to the results of a systematic review of effectiveness and comparative effectiveness commissioned by the Department of Defense.[18] Lack of conclusive evidence for effectiveness has also confounded ongoing efforts to advocate for appropriate care coverage.

Focus of Review

Persistent decisional dilemmas about postacute rehabilitation for TBI do not stem from a lack of relevant systematic reviews. Dozens of 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[19]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.[12] The first version of the Cochrane review was supplemented with one comparing study eligibility criteria.[20]
- 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.[21] Doig et al. compared day hospital versus home-based rehabilitation settings for brain injury.[22] Evans and Brewis evaluated the efficacy of community-based rehabilitation programs.[23]
- 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[24-26] of cognitive rehabilitation effectiveness for brain injury.[27] The Institute of Medicine very recently released the prepublication version of their comprehensive evidence review of cognitive rehabilitation for TBI (sponsored by the Department of Defense).[28] While not quite as recent, the controversial [18] 2009 Emergency Care Research Institute (ECRI) review[29] on cognitive rehabilitation for traumatic brain injury (also sponsored by the Department of Defense) provides context for the renewed and lasting interest in determining effectiveness via systematic review. Finally, Cattelani reviewed treatments for behavioral impairments after acquired brain injury.[30]
- Vocational rehabilitation, often incorporated into multidisciplinary postacute rehabilitation, was reviewed by Fadyl et al.[31]
- Several recently completed systematic reviews have similarly focused on community integration.[32, 33] 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.[34]

- Other highly relevant ABIER reports have evaluated the efficacy of various models of care, one on cognitive interventions, and one on communication interventions. [34]

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 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-traumatic brain injury patients. However, the non-traumatic brain injury 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.[35] 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). Additionally, clearly defined primary outcomes are necessary to ensure quality in a systematic review.[36] Inadequately defined outcomes can result in unreliable conclusions, especially when an abundance of outcomes measures are used in individual studies. Previous systematic reviews have not always prespecified primary outcomes, and may suffer from bias created by multiple comparisons.[37] 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 studies that employ high quality observational designs as opposed to restricting eligibility to randomized controlled trials. 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?

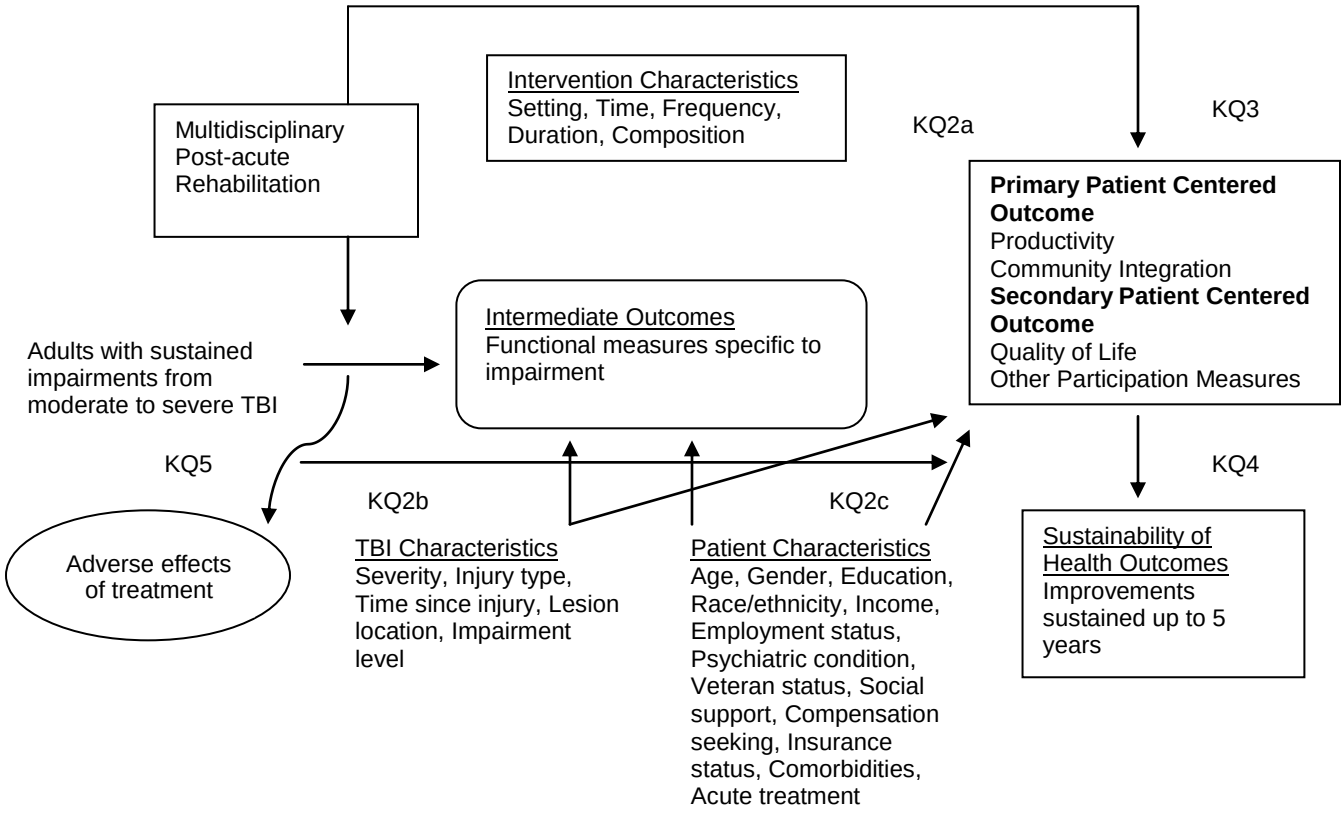
Key Question 4

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?

Figure 2. Analytic framework for multidisciplinary postacute rehabilitation for traumatic brain injury in adults



Methods

Topic Refinement

The initial topic of rehabilitation for traumatic brain injury 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.[8] Additionally, any impairments sustained after mild TBI tend to differ from those related to moderate to severe TBI.[3] Key informants also argued against an arbitrary 6-month cut off, emphasizing that rehabilitation timing is unique to each injury. They suggested a more meaningful clinical designation, such as postacute. 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.

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 present. 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.[38]

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 appears in Appendix A. We adapted the strategy to conform to controlled vocabulary and indexing used in the other bibliographic databases. We will update the literature search while the draft report is under public/peer review.

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)
- 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)

We prioritized return to work or productivity as the most relevant outcome. The most appropriate outcomes measurement scale for the population addressed in this review is the MPAI (current version, MPAI-4). The MPAI was developed to evaluate rehabilitation programs specifically for the postacute brain injury population.[39]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.[40] This group also cited the utility of this measure in evaluating progress in rehabilitation. The Craig Handicap Assessment and Reporting Technique (CHART) is another promising measure of community integration for the postacute TBI population. The CHART addresses the ICF's participation domain and has been tested in TBI populations.[41] This scale is available both in the full version and as a short form (SF). The CHART-SF has been suggested as a core measure of social participation by the TBI Common Data Elements Outcomes Workgroup.[40] The last scale selected as a primary outcome measure is the Community Integration Questionnaire (CIQ). This scale was developed for and has been used extensively in traumatic brain injury populations and within the TBI model systems programs.[42]. Table 2 describes these primary outcomes scales in more detail.

We did not prespecify all secondary outcomes. Instead, we chose to include studies with scales that incorporated community integration or quality and/or satisfaction with life. Scales we expected to include were the Disability Rating Scale (DRS) and the Satisfaction with Life Scale (SWLS). We identified other scales during the screening process. We examined any scale used in a study and that potentially met our secondary outcome criteria. If the scale appeared to contain components that addressed community integration or quality of life, and was designed for people in community settings, we considered it a secondary outcome.

We deemed outcomes as not patient-centered if they did not directly relate to life participation, or encompass indicators of resumption to previous roles in the family and community or quality of life. We recorded the scales and the frequencies of their use in included studies, as well as in studies excluded for lacking a primary or secondary outcome measure.

We also included observational studies because rehabilitation intervention RCTs can present ethical and operational challenges. We considered only studies controlled with 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 3.

Table 2. Primary Outcome Scale Descriptions

Primary outcomes	Definition	Scoring
Community Integration Questionnaire (CIQ)[43]	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)[44-46]	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 rangefrom 0-600 with higher scores indicating less handicap and greater social participation.
Craig Handicap Assessment and Reporting Technique (CHART)[47]	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 rangefrom 0-500 with a higher score indicating less handicap and greater social participation.
Mayo-Portland Adaptability Inventory (MPAI-4)[48]	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 the primary outcomes selected for this review.

Table 3. 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 KQ 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

We developed risk of bias assessment forms specifically for this project. For RCTs, we modified the Cochrane Risk of Bias tool[49]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[50] 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,[51] 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 observational studies from the RTI Observational Studies Risk of Bias and Precision Item Bank.[50] 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 observational 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 precludes 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 with only 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 eligible studies for each primary outcome or comparison using methods developed by the Agency for Healthcare Research and Quality and the Effective Health Care Program.[52] 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, medium, or high.
2. Consistency (the degree of similarity in the effect sizes (i.e., same direction of effect) of the included studies). Consistency is rated consistent, inconsistent or unknown/not applicable (e.g., a single study was evaluated).
3. Directness (reflecting a single, direct link between the intervention of interest and the outcome). Directness can either be direct or indirect.
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.

Two investigators worked independently to qualitatively rate each component and overall strength of evidence. Disagreements were reconciled through discussion between 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.[53]

Results

Our bibliographic database searches, conducted through August of 2011, identified 1,616 unique references:

- 1,157 from Ovid MEDLINE
- 300 from PschINFO
- 142 from Cochrane CENTRAL Register of Controlled Trials
- ….17 from PEDro

Triage of titles and abstracts identified 166 references meriting comprehensive screening. Backward citation searches of relevant systematic reviews identified an additional 12 references, for a total of 178 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 studies undergoing full text screening, eligibility or exclusion reason 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 or quality of life. We identified over 50 additional scales or measures used in the 16 eligible studies that we considered intermediate outcomes. These measures are listed in Appendix D, Table 1. These measures were considered intermediate for several reasons: some captured outcomes specific to interventions, such as attention or memory; some measured domain-specific outcomes such as aggressive behavior or depressive symptoms; and others were broader measures of global functioning were best suited to rehabilitation environments and failed to capture participation at the community level.

Descriptions of these secondary patient-centered outcomes appear in Table 4. These scales included the Disability Rating Scale (DRS); the Extended Glasgow Outcome Scale (GOS-E); the EuroQOL (presumably the 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).

Table 5 lists eligible studies with primary and secondary outcomes assessed. Each study assessing a primary outcome was evaluated for risk of bias. The overall risk of bias assessments are documented in Table 4. 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 questions or PICOTS 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[54] and an RCT,[55] 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.[56] 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.[57] 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.[58] Ponsford et al. compared cohorts participating in a community-based postacute rehabilitation program to a group of those participating in the center-based program it replaced.[59] Hashimoto et al. compared a day treatment program to controls not participating in the program.[60] Sarajuuri et al. compared a cohort of moderate to severe TBI survivors enrolled in an intensive inpatient program to those receiving standard care.[61] Prigatano et al. conducted two cohort studies comparing neuropsychological rehabilitation to nonparticipants.[62, 63] Rattock et al. studied three treatment mixes for comparative effectiveness.[64] Willer et al. evaluated the comparative effectiveness of a residential rehabilitation program to standard care.[65]

Four studies assessed only secondary outcomes, two RCTs and two observational 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.[66] Powell conducted an RCT to compare an outreach program to an information-only intervention.[67] Thomas evaluated the effectiveness of an outdoor experiential education program adapted to TBI survivors with chronic impairments.[68] Semlyen et al. compared the effectiveness of a coordinated multidisciplinary program provided at a regional rehabilitation center to care provided by other facilities.[69]

Figure 3. Literature Flow Diagram for Multidisciplinary Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults

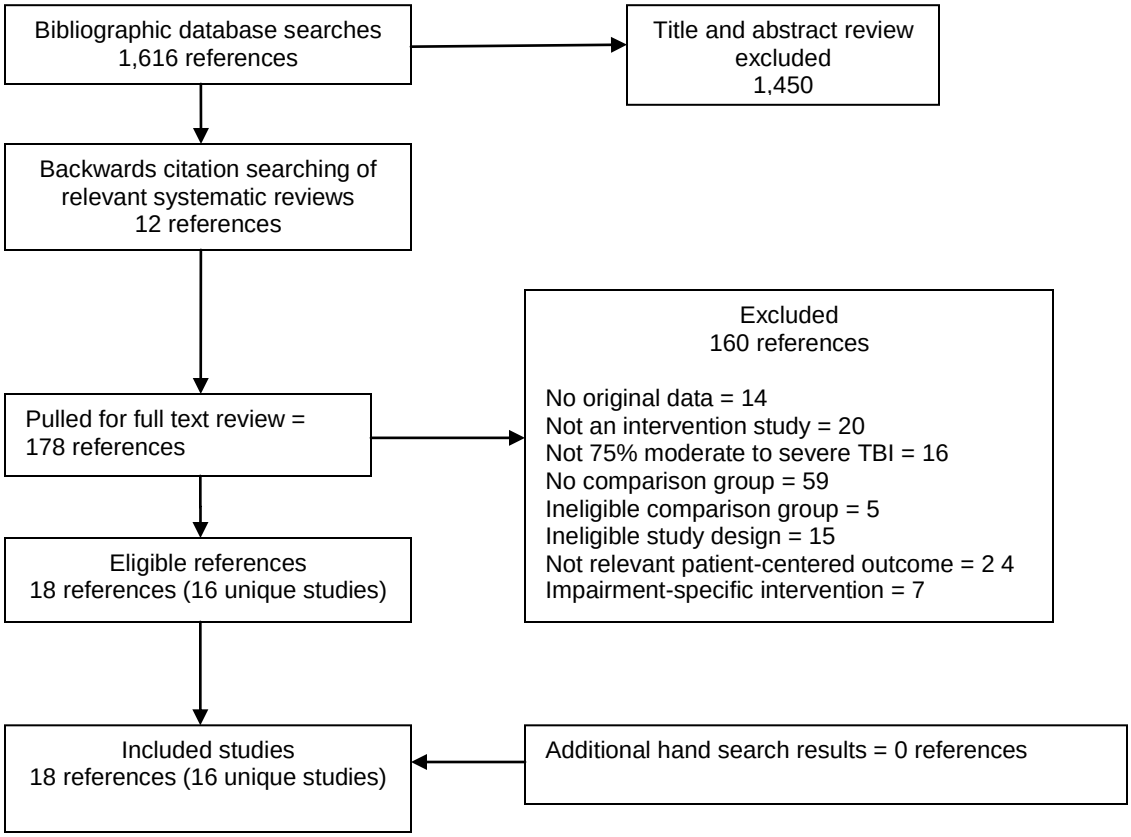


Table 4. Secondary Outcomes Measures Descriptions

Secondary outcomes	Definition	Scoring
Brain Injury Community Rehabilitation Outcome-39 (BICRO-39)[70]	A proxy or patient-reported 39-item questionnaire assessing problems of brain-injured subjects living in the community. Eight domains include 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)[71]	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)[72]	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[40]	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)[69]	A clinician-reported 55-item measure of global functional independence designed to measure recovery from acute rehabilitation to 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' perception 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)[54]	15 question tool designed to evaluate participants' satisfaction with their functioning after cognitive rehabilitation and complement the Community Integration Questionnaire, this measure queries 2 types of satisfaction: (1) individuals' subjective satisfaction with their level of community integration (QCI; 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 (QCOG; 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)[73]	Clinical validation of the Quality of Life Inventory. A measure of life satisfaction for use in treatment planning and outcome assessment. The QOLI assesses an individual's 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 scores are summed to determine an overall current quality of life for each individual. Higher scores indicate a higher overall quality of life

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[55]	RCT	✓	✓			PQoL	Moderate
Vanderploeg 2008[56]	RCT	✓				DRS	Low
Salazar 2000[57]	RCT	✓					Moderate
Greenwood 1994[58]	RCT	✓				DRS, GOS-E	Moderate
Ponsford 2006[59]	Cohort	✓		✓	✓		High
Sarajuuri 2005[61]	Cohort	✓					Moderate
Prigatano 1994[63]	Cohort	✓					High
Rattok 1992[64]	Cohort	✓					Moderate
Prigatano 1984[62]	Cohort	✓					Moderate
Hashimoto 2006[60]	Cohort		✓				High
Cicerone 2004[54]	Cohort		✓			QCI	Moderate
Willer 1999[65]	Cohort		✓				High
Bell 2005[66]	RCT					GOS-E, EuroQol, MPQoL	NA
Powell 2002[67]	RCT					BICRO-39	NA
Thomas 2004[68]	Cohort					QOLI	NA
Semlyen 1998[69]	Cohort					NIAF-R	NA
Total number of studies eligible		9	4	1	1	8	
Less High Risk of Bias		2	2	1	1	NA	
Studies used to evaluate SOE		7	2	0	0	NA	

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 graded 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. Generally, definitions appeared to improve over time, with more recent studies providing more detailed definitions. Table 6 provides a summary of various intervention characteristics. 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, 60, 62, 63, 68] Six studies compared new models of care delivered by their institution or agency to a standard care typically delivered to that community.[54, 55, 59, 61, 65, 69] Five studies compared different models of care where the interventions varied by setting, intensity or approach.[56, 57, 64, 67] Two studies examined an additional component added to a standard program.[58, 66]

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.[56, 57, 69] Two interventions began earlier in the postacute period and continued to the chronic stage.[58, 66] Other programs specifically addressed survivors of severe injuries[58, 65, 69] or military populations.[56, 57]

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.[54, 55, 57, 60-64] 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.[57, 61] A single program citing this model of care addressed TBI survivors in the early postacute period, within 3 months from injury.[57] 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;[67] community-based care;[59] specific approaches to remediation of skills;[56] multidisciplinary programs without mentioning a specific model;[69] residential communities of TBI survivors;[65] and an outdoor experiential education program.[68] Specific components of programs that were studied included case management[58] and telephone counseling.[66]

Program Characteristics

Several postacute multidisciplinary rehabilitation programs were studied.[54-57, 59-65, 67-69] Three programs compared the effectiveness of programs delivered to TBI survivors earlier in the postacute period.[56, 57, 69] Vanderploeg et al. compared two inpatient approaches to rehabilitate TBI survivors within 6 months of injury. 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. 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 services provided by the local rehabilitation center. 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 and colleagues)[57] addressed chronic impairments of moderate to severe TBI.[54, 55, 60-64] Of these, all but one[61]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 center.[54, 55] 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.[62, 63] 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.[62] The later study described a similar intervention called a "work reentry 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.[60] 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.[64] 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. This 6-week inpatient program (called INSURE) was conducted in Finland for select groups of patients with TBI.[61] 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 studies reflected additional models or theories. Thomas evaluated an outdoor experiential education program adapted to brain injury survivors with chronic impairments. 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 theories on which their programs were based.[59, 65, 67] Ponsford et al. evaluated a program change from center-based outpatient rehabilitation to community-based services.[59] 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.[67] 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. 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.[58, 66] Both of these programs offered services beginning earlier in the postacute period that continued through the chronic period of recovery. Bell studied a telephone intervention.[66] 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.[58] 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. Six studies reported a manual or other detailed documentation with thorough intervention content.[58Prigatano, 1984 #2139Salazar, 2000 #2140Sarajuuri, 2005 #2142Thomas, 2004 #2179, 66] Two studies reported staff training prior to beginning of the study.[56, 65] Two studies described efforts to ensure fidelity to treatment protocol.[55, 56]

Table 6. Summary of Implementation Characteristics

Study location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
Bell 2005[66] 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[54], 2008[55] 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[58] UK	Early Postacute through Chronic Severe	Case management		Home	Individuals	NR	NR
Hashimoto 2006[60] 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[59] 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[67] 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[62], 1994[63] United States	Chronic Moderate to Severe	Neuropsychological rehabilitation	Holistic Day Treatment	Outpatient rehabilitation center	Small groups	24 hrs/wk 6 mos	576
Rattok 1992[64] 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
Salazar 2000[57] United States	Active duty military Early postacute Moderate to severe Mild impairments	Inpatient Cognitive Rehabilitation	Holistic Day Treatment	Residential	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	Chronic	Comprehensive	Holistic Day	Residential	Small groups	37.5 hrs/wk	225

Study location	Target Population	Intervention Studied	Model of Care	Setting	Delivery	Intensity Duration	Total Therapy Hours
2005[61] Finland	Moderate to Severe	neurorehabilitation	Treatment			6 wks	
Semlyen 1998[69] UK	Early postacute Severe	Multidisciplinary rehabilitation	NR	Residential	Individuals	NR	NR
Thomas 2004[68] 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[56] United States	Active-duty military, veterans Early postacute Moderate to Severe	Cognitive didactic	Cognitive-didactic	Residential	Individuals	7.5-15 hrs/wk 32 days (mean)	NR
		Functional-experiential	Functional treatment concepts	Residential	Small groups	21.5-30 hrs/wk 33 days (mean)	NR
Willer 1999[65] 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 observational 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 posttreatment.
- 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 posttreatment 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 posttreatment 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 posttreatment in a civilian population. However, group differences were no longer significant at 6 months posttreatment.

Table 7. Overview of primary outcomes for multidisciplinary postacute rehabilitation for TBI 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[55] Study 2 non-RCT[54]	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	↑↑ 16 weeks (Study 1) Low strength of evidence (SOE)	↔ 6 months (Study 1) Low SOE
		Community Integration Questionnaire	↔ 16 weeks (Study 1 and Study 2) Low SOE	↔ 6 months (Study 1) Low SOE
Functional-experiential versus Cognitive-didactic[56] 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[57] 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 [58] 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[61] 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
Neuropyschological rehabilitation versus Controls[62] 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	59 American TBI (open or closed) patients that had been			

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)[64] Non-RCT	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 observational studies). Two of the cohort studies were evaluated to have a high risk of bias and thus excluded from analysis.[59, 63] One observational study assessed MPAI-3 and the CHART-SF. However, this study was evaluated as having a high risk of bias,[59] 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 observational studies were evaluated as having a high risk of bias and excluded,[60, 65] leaving two studies for analysis (one RCT and one observational study).[54, 55] Of the eight studies graded to analyze primary outcomes, one was rated low risk of bias,[56] and eight were rated moderate risk of bias[54, 55, 57, 58, 61, 62, 64] 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,[54-57, 62, 64] one in the United Kingdom,[58] and one in Finland.[61] Subjects were predominantly male (85 percent) and young relative to the adult population of the United States (mean age of 31). Studies less often reported other demographic statistics. Median time since injury varied widely between studies, from 1 to 45 months with a median of 19 months. Two studies specifically restricted enrollees to those within 3[57] or 6[56] months of injury.

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 observational study found no significant difference in the proportion gainfully employed at followup (50 percent versus 36 percent) at one time point somewhere between 6 and 24 months posttreatment. 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.[56, 57] 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 posttreatment 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 posttreatment in a military population.

Cicerone et al. found that the group of chronically impaired civilians enrolled in the ICRP were significantly more productive immediately posttreatment than those who received standard treatment at that rehabilitation center (47 percent versus 21 percent).[55] However, no group differences existed at followup 6-months posttreatment, 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 posttreatment, because the control group had significantly improved their rates of productivity.

We found insufficient evidence that those participating in the INSURE program had higher rates of productivity (work or volunteer activities), but not in employment alone, 2 years posttreatment than those in the standard program.[61]

We found insufficient evidence that case management when added to conventional programs resulted in significantly different rates of productivity at various followup timepoints.[58]

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 posttreatment,(ICRP=12.9, standard rehabilitation=11.7 in RCT,[55] ICRP=16.8, standard rehabilitation=16.1, unadjusted in cohort study[54]) despite differences in mean change in the CIQ scores between groups enrolled in the cohort study.[54] The cohort study also provided analysis of clinically meaningful change in CIQ scores between groups. Fifty-two percent of the ICRP group showed clinically significant improvement (of 4.2 points) compared to only 31 percent of the standard rehabilitation group. This indicates that ICRP participants were 2.5 times more likely than standard program participants to achieve a clinically significant improvement in CIQ score. Unfortunately, these trends were not repeated in the RCT. Therefore, the data provide a low level of evidence that the ICRP versus standard rehabilitation did not improve community integration. This evidence was graded low because it was derived from one moderately sized RCT and one moderately sized observational study, each with a moderate risk of bias. Results from the RCT were weighted more heavily in assessing strength of evidence because the cohort study provided unadjusted results and contained selection bias.

Secondary Outcomes

Table 13 summarizes findings for secondary outcomes in all eligible studies. Eight studies assessed eight 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 posttreatment.[56] Cicerone et al. found no group differences in PQOL scores, despite noticing greater mean improvements in the ICRP group.[55] Greenwood identified no group differences on secondary outcomes, with the exception of a higher DRS score among the control group at 24 months posttreatment;[58] however, this measurement is likely biased due an attrition rate of nearly 50 percent. Cicerone et al. found that the standard rehabilitation group has significantly greater QCI scores than the ICRP group.[54]

Other studies of 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.[66] 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 did demonstrate 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. find median change scores on the BICRO-39 significantly higher in an outreach group as compared to an information only group at 2 years posttreatment.[67] Thomas detected only one significant difference in QOLI scores from measurements at four timepoints.[68] Semlyen et al. found greater improvements in NIAF scores among the multidisciplinary treatment group than the TBI patients receiving the single-discipline treatments.[69]

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.[56] Salazar et al. compared an intensive program to a substantially less intensive home program and found no group differences.[57] 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 were not significant.[62] 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.[55]

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 messages previously identified for effectiveness and comparative effectiveness reemerge 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* analysis 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).[57] 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.[54] 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.[67] 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.[64] However, lack of statistical 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. Both of the two largest RCTs enrolled either only active-duty military personnel or a combination of active-duty military personnel and veterans.[56, 57] 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 analysis. 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 (graded primary outcome studies)

Characteristic	Mean (range) *Unless otherwise noted*	Number of trials 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]
Non-randomized studies, number of patients	190 (36 to 59)	4 [d,e,f,h]
Age of subjects, years	31 (25 to 38)	8
Gender, 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[55] 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[56] 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[57] 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[57] 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[58] 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[61] 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)	
Rattok 1992[64] 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)	

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
Prigatano 1984[62] Prospective Cohort RTW[g] at followup (treatment was 6 mos)	Neuropyschological 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	Directness	Precision	Consistency	Evidence rating
Cicerone 2008[55] 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[56] 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[57] 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	precise	NA	Low
Greenwood, 1994[58] 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[61] Post treatment, 2 years	Comprehensive neurorehabilitation vs. Conventional rehabilitation	Non-RCT, prospective cohort	39	RR: 1.63 [1.06 to 2.49]	high	direct	precise	NA	Insufficient
Rattok 1992[64] Post treatment, 9 months	Comparison of 3 “treatment mixes”	Non-RCT, prospective cohort	59	-	high	direct	-	NA	Insufficient
Prigatano 1984[62] Post treatment, ranged from 6 mo to 2 years	Neuropsychological rehabilitation vs. Control (untreated)	Non-RCT, 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 table 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[55] 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[54] 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 ration [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[55] 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[54] 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[55] 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 posttreatment
Functional-experiential Vs. Cognitive-didactic[56]	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 posttreatment
		Quality of Life	NR	↔ 1 year posttreatment
Telephone counseling vs. Standard rehabilitation alone[66] 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[67]	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 [58] 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[54]	57 chronically impaired TBI survivors	QCI	↑ posttreatment	

Treatments; Study design	Study populations	Outcome definition	Post-treatment assessment	Followup post-treatment assessment
Potential Unlimited Programmes (PUPs) vs. no treatment[68]	22 moderate to severe TBI patients with chronic impairements..	QOLI	↔ Completion stage 2	↔ Completion stage 3 ↑ 6 months posttreatment ↔ 2 years posttreatment
Multidisciplinary rehabilitation service vs. single discipline approach[69]	51 severe TBI patients within four weeks of injury.	NIAF	↑ 6-12 months post	

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 efficacy 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

We identified no studies that addressed the minimum clinically important differences (MCIDs) for the MPAI. Because we did not find studies assessing community integration with the MPAI, we evaluated 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 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 mention the consistency of this RCT with a previous study.[54] However, the later RCT evaluating the ICRP did not mention a reliable change index or other attempts to determine MCID, and provided no explanation for the omission.[55]

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 posttreatment and followup intervals.
- A low level of evidence showed that statistically significant improvements immediately posttreatment 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 posttreatment appear to be sustained at 12 months posttreatment.[58]

Detailed Analysis

Two primary outcomes studies incorporated followup outcomes measurements for productivity.[55, 58] Table 14 presents the sustainability results for these studies. Cicerone and colleagues assess outcomes immediately posttreatment and again at 6 months posttreatment.[55] Table 15 describes the sustainability results of this study. Greenwood and colleagues assess outcomes at various points during and after treatment. Table 16 presents individual components and overall assessment of strength of evidence for each of these comparisons. The study conducted by Cicerone, et al., provides a low strength of evidence that outcomes achieved at the end of treatment were sustained at 6-month followup.

Table 14. Sustainability of Productivity Outcomes

Study Outcome	Treatment Arms	Productive at timepoint 1	Productive at timepoint 2	Posttreament vs. Followup
Cicerone 2008[55] 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[58] 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 posttreatment; Timepoint 2 – 6 months posttreatment.
[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[55]	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 posttreatment; Timepoint 2 – 6 months posttreatment.
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[55] Community-based employment 6 months posttreatment	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	58	RR: 1.22 [CI = 0.75 to 1.92]	moderate*	direct	imprecise	NA	Low
Cicerone 2008[55] CIQ 6 months posttreatment	Intensive cognitive rehabilitation vs. Standard neurorehabilitation	RCT	58	ES: 0.07 [-0.41 to 0.54]	moderate*	direct	imprecise	NA	Low
Greenwood, 1994[58] 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, reported that no adverse events were observed.[56]

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. Originally, our intent was to provide information to inform decisions about reimbursement policy and treatment. 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 traumatic brain injury 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, assessed the strength of the body of evidence for each comparison as insufficient, low, moderate, or high, and qualitatively analyzed evidence relevant to each key question.

Characterizing Interventions (KQ 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 (KQ 2)

We were unable to draw broad conclusions about effectiveness or comparative effectiveness. Table 17 lists summary results for effectiveness and comparative effectiveness. Comparative effectiveness research on complex conditions and interventions lends itself to conclusions about specific populations and interventions:

- We found insufficient evidence assessing effectiveness for productivity (gainful employment or school program) with neuropsychological rehabilitation for closed head injury patients with chronic impairments (followups measured between 6 and 24 months posttreatment).
- We found a low strength of evidence that gainful employment or return to military fitness did not differ significantly at 1-year posttreatment between an 6-week inpatient hospital treatment and a 8-week limited home-based treatment. Participants were active duty military patients with closed head injuries experiencing relatively mild impairment levels and treated within 3 months of injury.
- We found a low strength of evidence that productivity did not differ significantly at 1-year posttreatment between closed head injury participants of functional-experiential programs and cognitive didactic inpatient rehabilitation programs. 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 a low strength of evidence that moderate to severe TBI survivors with chronic impairments judged to need 16 weeks of intensive treatment enrolled in an Integrated Cognitive Rehabilitation Program (ICRP) achieved higher rates of return to community-based employment, but not higher rates of community integration, than participants of standard rehabilitation immediately posttreatment.
    - We found a low strength of evidence that rates of return to community-based employment between these two groups equalized by 6-month posttreatment (rates in the standard rehabilitation group caught up with those of the ICRP group).

Effectiveness and comparative effectiveness conclusions of this review are highly specific to the populations and setting 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. However, in certain studies, the timing of outcome measurement was important. For example, when Cicerone et al. measured participation outcomes at *earlier* time points, results suggested greater improvements for the groups involved in a comprehensive holistic program compared to a traditional program.[55] This distinction could appear irrelevant since outcomes equalized within 6 months posttreatment in the single study that collected followup data.[55] However, given the financial and social impact of TBI on survivors and their families, earlier participation outcomes should be a priority.

Table 17. 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[57]	Inpatient hospital rehabilitation program (8 weeks) vs. limited home treatment	Return to gainful employment at 1 year posttreatment	No difference between groups	Low (moderate risk of bias, single study)
		Fitness for military duty at 1 year posttreatment	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[56]	Functional-experiential vs. Cognitive-didactic rehabilitation programs for varying durations	Return to gainful employment at 1-year posttreatment	No difference between groups	Low (moderate/low risk of bias, imprecise, single study)
Chronically impaired patients with primarily moderate to severe TBI[54, 55]	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 posttreatment	No difference between groups	Low (moderate risk of bias, single study)
		CIQ at end of treatment	No difference between groups	Low (medium risk of bias, imprecise, consistent)
		CIQ at 6 months posttreatment	No difference between groups	Low (medium risk of bias, single study)
Severe TBI patients at least 6 months postinjury[62]	Comprehensive day neurorehabilitation program (6 months) vs. No Treatment	Participation in gainful employment at one timepoint measured between 6 and 24 months posttreatment	No difference between groups	Insufficient (high risk of bias, inprecise, single study)
TBI patients who were independent in daily life and had only slight physical disabilities [61]	Comprehensive neurorehabilitation vs Conventional rehabilitation	Working, studying, or participating in volunteer activities	Statistically higher proportion neurorehabilitation group working, studying, or participating in volunteer activities	Insufficient (high risk of bias, single study)
Primarily chronically impaired patients with	Case-management vs. conventional neurorehabilitation	Competitive work at 6 months posttreatment	No difference between groups	Insufficient (high, imprecise, single study)

Population	Intervention/Comparator	Outcome	Conclusion	SOE
moderate to severe TBI[58]		Competitive work at 1 year posttreatment	No difference between groups	Insufficient (high risk of bias, imprecise, single study)
		Competitive work at 2 years posttreatment	No difference between groups	Insufficient (high risk of bias, imprecise, single study)
Severe TBI patients at least 1 year post injury[64]	Treatment Mix 1 vs. Treatment Mix 2 vs. Treatment Mix 3	Productive employment at 9 months posttreatment	No difference between groups	Insufficient (high 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 (KQ 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 chance 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. The authors mentioned the consistency of this RCT with a previous study.[54] 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 offer an explanation for the omission.[55]

Maintenance of Outcomes (KQ 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 posttreatment.[55]
- We found a low strength of evidence that rates of participation in competitive work achieved at 6 months posttreatment appear to be sustained at 12 months posttreatment.[58]

Adverse Events (KQ 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.[56]

Comparison to Previous Systematic Review

Our review, like some others, found the currently available evidence insufficient to draw broad conclusions about the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury in adults. However, our conclusions are inconsistent with those of some previous systematic reviews. Reviews that reported evidence of effectiveness differed from ours methodologically. Several addressed the acquired brain injury population, which may include additional evidence from primarily stroke studies. Others did not prespecify certain outcomes, and instead based their conclusions on any outcomes measured and reported in primary research. Many outcomes used in primary research are not patient-centered. Therefore systematic review conclusions based upon these results may not translate to meaningful improvements in patients' lives.

Limitations to the Evidence

Strength of Evidence

In many ways, the results of this review are unsatisfactory. Problems for synthesizing evidence arise from the complexity of sustained TBI impairments and the interventions to rehabilitate them. This complexity makes it challenging to achieve strength of evidence grades above low. Systematic review methodology requires and the assessment of SOE at the

comparison level. The specificity of the comparisons for this topic means that often, single studies are the basis of results in conclusions and strength of evidence assessments about effectiveness or comparative effectiveness. Several factors impede standard systematic review methodology from reaching a high strength of evidence on this topic. 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 grouping studies for grading and interpretation. In addition to the limited number of studies within a comparison, formidable obstacles to obtaining a high strength of evidence for studies 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 for individual studies. The best way for a body of evidence to achieve a low overall risk of bias assessment is to have several well-conducted RCTs assessing similar interventions and controls in similar populations with consistent patterns across a set of outcomes (that are also defined and measured consistently). Blinding may be the greatest hurdle. Double blinding is typically impossible in rehabilitation research, but outcomes 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.

TBI rehabilitation intervention studies frequently failed to adjust for multiple comparisons. Often, studies test the effect of their interventions on many outcomes. In analysis, comparing all scale scores as well as subscale scores is not uncommon. While some studies do identify primary outcomes, very few appropriately adjust estimates for multiple comparisons, or provide justification for not making these adjustments. Failure to use a Bonferroni correction or other appropriate adjustment technique can result in accepting statistically significant results when they may have occurred by chance.

Study design also affects risk of bias. We recognize a difficult paradox in 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). Yet, given the potential selection bias and the high number of confounding and effect-modifying variables, RCTs are the 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.

The inadequacy of intervention definitions mentioned previously deters from the internal validity of these studies. Further, the inadequate treatment definitions were often accompanied by inadequate demonstration of effective implementation. We looked for reports of staff training, use of treatment or intervention manuals, and fidelity checks to assess whether interventions were effectively implemented. The studies we reviewed rarely addressed these issues. Lastly, several outcomes-related issues contribute to the higher risk of bias for individual studies on this topic. Inadequate attention to meaningful differences in outcomes scales also increases risk of bias at the individual study level.

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.). Even then, many of the interventions and control conditions seemed to be embodiments of their local rehabilitation systems, making replicability in other contexts challenging. Additionally, most studies excluded individuals with substance abuse or psychiatric diagnoses, both of which are common in the TBI population.[74] The policy issue of inconsistent insurance coverage for rehabilitation services[8] has implications for the applicability of these results. Moreover, TBI disproportionately affects males, those ages 15-24, and those with lower socioeconomic status[9], groups traditionally 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.

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. High quality conclusive evidence from rigorously conducted systematic reviews is a high bar currently met by only a small portion of medical interventions (and an even smaller portion of rehabilitation interventions). The insufficiency of the evidence on this topic stems from the complexity of the condition and treatments, and the limited available research. However, both the research quality and funding for research on this topic are increasing; therefore the body of evidence should strengthen dramatically with time.

Future Research

Many systematic reviews have attempted to synthesize existing evidence for effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury in adults. Past reviews have had different focal points and eligibility criteria. Recent rigorously conducted reviews of postacute multidisciplinary rehabilitation that focused on TBI populations (as opposed to ABI patients) failed to draw overall conclusions about rehabilitation effectiveness based on patient-centered outcomes. Yet, research gaps remain, and additional systematic reviews cannot satisfy these gaps until additional high quality studies are completed. Future studies need to address the shortcomings of the currently available literature.

Evidence is needed from future RCTs regarding which programs work for which impairments and types of patients or injuries. However, additional small-scale 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 would allow for the collection of all data relevant to patients, injuries, and interventions. 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 for providing higher quality comparative effectiveness evidence with these complex topics. For example, the practice-based evidence approach[75] 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. Observational 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. While blinding of participants and providers may not be feasible, outcomes assessors can and should be blinded. Adequately defining the intervention and ensuring the effective implementation of the interventions and controls would reduce risk of bias related to the intervention. Finally, 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.

Furthermore, many topic-specific questions of clinical importance have not yet been adequately addressed by research. For example, current evidence does not allow for meaningful conclusions about timing of treatment benefits. Studies 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. In addition, the consistent use of a clear taxonomy of TBI impairments and interventions would allow future research to address interventions specific to particular impairment types, and better answer questions about which interventions work best for which patients.

The TBI Model Systems programs offer a valuable venue for conducting rigorously designed intervention studies.[76] Future research should continue to explore comparative effectiveness by comparing interventions implemented in different TBI model systems locations. Large scale 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