Evidence-based Practice Center Systematic Review Protocol

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

I. Background and Objectives for the Systematic Review

A traumatic brain injury (TBI) is an acquired (noncongenital) injury caused by sudden trauma to the brain.\(^1\) TBI is a significant public health issue in the United States, with an estimated 1.7 million TBIs recorded annually between 2002 and 2006.\(^2\) Of those injured each year, 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. Major causes of civilian 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). Further, TBI has been called the “signature wound” of modern-day military conflicts.\(^3\) As of July 2007, nearly 28,000 service members had sustained nonfatal injuries during the Global War on Terror.\(^4\) Blast incidents account for the majority of combat injuries, 60 percent of which result in TBI.\(^4\)

TBIs are categorized as mild, moderate, or severe according to acute injury characteristics that suggest the extent of damage to the brain. Injury severity is determined through one or more measures, including structural imaging findings, duration of loss of consciousness, duration of altered consciousness, duration of post-traumatic amnesia, the Glasgow Coma Scale score, or the Abbreviated Injury Severity Scale score (Table 1).\(^5\)

<table>
<thead>
<tr>
<th>Table 1. Traumatic brain injury severity levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria</td>
</tr>
<tr>
<td>Structural Imaging</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>Normal or abnormal</td>
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<tr>
<td>Normal or abnormal</td>
</tr>
<tr>
<td>Loss of Consciousness</td>
</tr>
<tr>
<td>&lt; 30 minutes</td>
</tr>
<tr>
<td>30 minutes to 24 hours</td>
</tr>
<tr>
<td>&gt;24 hours</td>
</tr>
<tr>
<td>Alteration of Consciousness/ Mental State*</td>
</tr>
<tr>
<td>A moment to 24 hours</td>
</tr>
<tr>
<td>&gt;24 hours</td>
</tr>
<tr>
<td>&gt;24 hours</td>
</tr>
<tr>
<td>Post-traumatic Amnesia</td>
</tr>
<tr>
<td>0–1 day</td>
</tr>
<tr>
<td>&gt;1 and &lt;7 days</td>
</tr>
<tr>
<td>&gt;7 days</td>
</tr>
<tr>
<td>Glasgow Coma Scale (best available score in 24 hours)</td>
</tr>
<tr>
<td>13–15</td>
</tr>
<tr>
<td>9–12</td>
</tr>
<tr>
<td>3–8</td>
</tr>
<tr>
<td>Abbreviated Injury Severity Scale</td>
</tr>
<tr>
<td>1–2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4–6</td>
</tr>
</tbody>
</table>

\(^*\)Table adapted from several sources.\(^5\)\(^7\)

More than 40 percent of people hospitalized with nonfatal TBIs develop associated long-term disabilities,\(^5\) some of which are physical, but the most enduring of which are cognitive and affective/behavioral. Sustained physical impairments may reduce endurance, cause headaches and seizures, and affect muscle tone, vision, hearing, smell, taste, and speech.\(^8\) Sustained cognitive deficits may affect memory, attention, judgment, communication, planning, and spatial orientation.\(^8\) Sustained affective/behavioral impairments include anxiety, depression, mood swings, impulsiveness, agitation, and social isolation.\(^8\) The incidence of TBI-related long-term disability increases with age, is higher among women, and occurs most often with TBIs from falls or firearms. By one estimate, 2 percent of the U.S. population lives with TBI-related disabilities.\(^9\)

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)
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Treatment for Traumatic Brain Injury

Patients with known TBI are typically first treated in acute medical settings for a duration that varies widely depending on injury severity, impairment level, other injuries, patient age, and other patient and healthcare system characteristics. If needed, intensive rehabilitation follows in an acute or subacute setting. Finally, once the patient is medically stable, postacute rehabilitation may occur.

Postacute rehabilitation is designed to address sustained impairments across physical, cognitive, and affective/behavioral domains. The preferred approach is multidisciplinary, with integrated rehabilitation and treatment of comorbidities from relevant disciplines. These programs differ in their components and may be described as multidisciplinary, interdisciplinary, neurobehavioral, comprehensive, integrated, or holistic. Once a recovering patient’s impairment severity and number of affected domains are lessened, rehabilitation may continue via specialized services such as those for long-term psychosocial disorders.

Postacute rehabilitation settings include long-term rehabilitation facilities, skilled nursing facilities, transitional living programs, outpatient clinics, and home- and community-based programs. Rehabilitation programs strive to restore an individual’s functioning to preinjury levels or as close thereto as possible.

Decisional Dilemma

While multidisciplinary postacute rehabilitation has been suggested as the more effective approach for addressing significant impairments from TBI, access may be complicated by lack of routine and/or full reimbursement from health insurers. Inconsistency in reimbursement policy may reflect uncertainty about which patients may benefit from specific rehabilitation programs. Likewise, efforts to advocate for appropriate care are confounded by uncertainty about which components of rehabilitation work best for different patients, injuries, impairments, and comorbidities.

An up-to-date evidence review will help identify areas of established effectiveness as well as areas needing further evaluation. This review will provide a synthesis of the evidence that may be used in developing guidelines for postacute TBI rehabilitation, as suggested in an amendment to the proposed FY 2012 National Defense Authorization Act.

Review Objectives and Contribution

Originally, the nominator of this topic requested a review that would broadly address the effectiveness of TBI postacute rehabilitation in all forms and for all ages and severity levels. Through subsequent research, discussions with key informants and technical experts, and public responses to our preliminary Key Questions (KQs), we learned that such a broad scope would not only be infeasible but would overlap current activities underway at the Institute of Medicine. Thus, this review will identify and evaluate the evidence of effectiveness of multidisciplinary postacute rehabilitation for moderate to severe TBI in adults.

Previous systematic reviews have addressed the effectiveness of postacute rehabilitation for the population with acquired brain injury (which combines patients who have TBI with those who have stroke and other brain injuries), specifically defined comprehensive programs, specific types of interventions, or specific outcome measurement instruments.

Source: www.effectivehealthcare.ahrq.gov
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A previous Agency for Healthcare Quality and Research (AHRQ) systematic review addressed TBI rehabilitation in adults, however, it did not focus on postacute rehabilitation, nor did it address the impact of timing, frequency, and duration of treatment, nor did it examine the comparative effectiveness of interventions. Finally, its scope was through 1997, after which many additional studies have been completed and published.

This review will enhance the knowledge and understanding of the evidence on postacute multidisciplinary rehabilitation for TBI by 1) focusing on moderate to severe traumatic brain injury in adults; 2) including a broad range of multidisciplinary programs; 3) characterizing multidisciplinary postacute rehabilitation programs; 4) evaluating effectiveness by program timing and composition; 5) addressing effectiveness for specific subgroups of patients and injuries; 6) evaluating the sustainability of rehabilitation outcomes; 7) assessing study quality and consistency and strength of evidence using standardized validated methods; and 8) identifying related adverse effects. Our a priori selection of primary outcomes and related instruments and our intention to address thresholds of clinically meaningful change further contributes to the field.

II. The Key Questions

Preliminary KQs for this topic were posted to the Effective Health Care Program Web site for public comment from February 7 to March 7, 2011. Commenters expressed concerns about our review, including that: 1) our report could affect reimbursement policies for TBI rehabilitation services; 2) such a broad scope would lead to inappropriate conclusions of effectiveness by intervention type; 3) restrictive inclusion criteria could exclude important research and expert opinion; 4) the review would be hampered by limited availability of studies and studies with inadequate data; and 5) our list of relevant outcome measures was too narrow. We revised the KQs and the PICOTS (population, intervention, comparator, outcomes, timing, and setting) criteria accordingly and developed a draft protocol that was used to facilitate discussions with a Technical Expert Panel (TEP) selected to provide topic-specific expertise. Discussions of the draft protocol were held in May 2011, after which we further revised the KQs and the PICOTS. Major changes involved limiting our scope to moderate and severe TBI in adults, focusing only on multidisciplinary postacute rehabilitation programs (the frequently suggested approach to TBI rehabilitation), and focusing on community reintegration as the primary outcome. The final KQs appear below.

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. Does effectiveness and comparative effectiveness vary by rehabilitation timing, setting, intensity, duration, or composition?

b. Does effectiveness and comparative effectiveness vary by injury characteristics?
c. Does effectiveness and comparative effectiveness vary by patient characteristics, preinjury or postinjury?

**Question 3**

What evidence exists to establish a minimally 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?

**PICOTS Criteria**

- **Population:**

  Our review will include adults with moderate to severe TBI (defined as age 16 and over, in order to include the population group in TBI Model Systems studies). Moderate to severe TBI will be defined by:

  - Abnormal imaging
  - Loss of consciousness for 30 minutes or more
  - Altered consciousness for more than 24 hours
  - Post-traumatic amnesia for greater than 1 day
  - A Glasgow Comma Scale score less than 13
  - An Abbreviated Injury Severity Scale score greater than 2

  Multidisciplinary postacute rehabilitation for moderate to severe TBI addresses impairments that differ from those associated with mild TBI. We will include studies that primarily enroll individuals with moderate to severe TBI and will exclude studies that primarily enroll individuals with mild TBI.

  We will attempt to address effectiveness by TBI etiology, impairment level, and comorbidities. We will examine differences in effectiveness by injury characteristics such as etiology, time since injury, lesion location, open versus closed wound, level of impairment, etcetera.

  We will also examine the association between intervention effectiveness and patient characteristics (preinjury and postinjury). Preinjury characteristics may include age, gender, education, race/ethnicity, income, vocational status, prior TBI, and psychiatric conditions (i.e., substance abuse, etc.). Postinjury patient characteristics may include social support, mental and
physical comorbidities, compensation seeking status, insurance status, and acute treatment factors.

● **Interventions:**

We will include studies of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury. We will classify interventions as multidisciplinary when they are delivered by two or more disciplines working in coordinated effort that is consistent with a recent systematic review of multidisciplinary rehabilitation for acquired brain injury.¹³

● **Comparators:**

We will consider all comparators, including wait list controls and postacute rehabilitation that is provided in different settings, of lower intensity, or has fewer or different components.

● **Outcomes:**

Community reintegration has been identified as the most clinically relevant outcome for postacute rehabilitation for moderate to severe TBI. The Mayo-Portland Adaptability inventory will be used to explore minimally clinically important differences because it was specifically developed for outcome measurement in brain injury during the postacute period.¹⁹ An a priori selection of operationalization and/or specific outcome measurement instruments for community reintegration includes:

- **Primary outcome — Community reintegration as measured by:**
  - Return to work/training/school
  - Mayo-Portland Adaptability Inventory (MPAI-4)
  - Community Integration Questionnaire (CIQ)
  - Craig Handicap Assessment and Reporting Technique Short Form (CHART-SF)
  - Craig Handicap Assessment and Reporting Technique (CHART)

- **Secondary Outcomes — Secondary outcomes data will be collected, although likely not graded, and may include:**
  - Quality of life
  - Disability Rating Scale (DRS)
  - Satisfaction with Life Scale (SWLS)

- **Intermediate Outcomes — Primarily functional measures specific to impairment (i.e., attention, gait) will be considered insufficient for inclusion.**

- **Adverse effects — All negative consequences directly related to treatment will be included.**
• **Timing:**

  We will include studies that record outcomes prior to the rehabilitation program and immediately following the intervention.

• **Setting:**

  We will include any setting in which multidisciplinary postacute rehabilitation is provided.
III. Analytical Framework

Figure 1. Provisional analytic framework for postacute rehabilitation for traumatic brain injury

(KQ 2)

Multidisciplinary Postacute Rehabilitation

Intermediate outcomes
- Functional measures specific to impairment (i.e., attention, gait)

(KQ 1)

Primary Health Outcome
- Community Reintegration

Secondary Health Outcome
- Quality of life
- Impairment level

(KQ 3)

Sustainability of Health Outcomes
- Improvements sustained up to 5 years beyond intervention

(KQ 4)

Adverse effects of treatment

TBI characteristics
- Severity
- Injury type
- Time since injury
- Lesion location
- Impairment level before postacute rehab

Patient characteristics
- Age
- Gender
- Education
- Race/ethnicity
- Income
- Employment status
- Psychiatric condition
- Veteran status
- Social support
- Compensation seeking
- Insurance status
- Comorbidities
- Acute treatment characteristics

(KQ 2a)

(KQ 2b)

(KQ 2c)

Adults with impairments from TBI after completion of acute medical and rehabilitative care

Source: www.effectivehealthcare.ahrq.gov
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Abbreviations: KQ = key question; TBI = traumatic brain injury.

IV. Methods

A. Criteria for Inclusion/Exclusion of Studies in the Review

All controlled trials and prospective comparative observational studies meeting PICOTS criteria with full text formally published in English will be included. 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.

B. Searching for the Evidence: Literature Search Strategies for Identification of Relevant Studies To Answer the Key Questions

We will identify evidence for this review by searching relevant bibliographic databases, as well as several sources commonly used to identify grey literature. Bibliographic database searching will utilize MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), PEDro, and PsycINFO to identify previous systematic reviews, randomized controlled trials and observational studies published from 1980 to the present. The last 30 years of studies are thought to contain programs and services most relevant to the topic today. The search process will be iterative, beginning with an initial precise search strategy run in Ovid MEDLINE to efficiently identify relevant studies to be screened, abstracted, and used to frame the analysis and draft summary tables. The initial concept analysis underlying the preliminary search strategy and the search strategy itself appear in Appendix A. The search will be progressively broadened by reducing concepts and expanding terminology per concept to maximize recall in Ovid MEDLINE and then adapted to the other databases. Bibliographic database searches will be supplemented with a backward and forward citation search of highly relevant documents. We will update the literature search while the draft report is under public/peer review.

Grey literature searching will include searches of trial registries, databases of funded research, and abstracts and conference proceedings. We will search ClinicalTrials.gov, the International Controlled Trials Registry Platform (ICTRP), and the NIH RePORTer database to identify relevant completed studies. These sources will be used to identify studies not previously found.

C. Data Abstraction and Data Management

We will review bibliographic database search results for previous systematic reviews and primary studies for relevance to the PICOTS criteria. The use of previous systematic reviews to replace the de novo process will be explored when relevant or partially relevant systematic reviews are identified and judged to be of fair or good quality by using modified AMSTAR criteria. Screening of primary studies identified in the bibliographic database searches against the inclusion criteria will occur in two stages: triage and screening. First, titles and abstracts will be reviewed by two independent investigators to exclude studies clearly off topic. Studies not excluded by both investigators during triage will undergo screening. Two independent investigators will review the abstracts and/or full text of the studies to determine if they meet the
inclusion criteria. Differences in screening decisions will be resolved by a third investigator. We will document the inclusion and exclusion status of each study and the reason for exclusion in the project library of citations relevant for screening. Studies meeting the inclusion criteria will be distributed among investigators for data abstraction. Two investigators will act as primary and secondary abstractors/evaluators for their assigned studies. Data fields to be abstracted will be determined for each KQ based upon proposed summary analysis. These fields will likely include 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. The primary abstractor/evaluator will abstract relevant data from studies meeting inclusion criteria into evidence tables. Evidence tables will be reviewed and verified for accuracy by the secondary abstractor/evaluator.

D. Assessment of Risk of Bias of Individual Studies

The primary and secondary abstractor/evaluator will independently assess the risk of bias of each eligible study by using tools specific to study design. For randomized controlled trials, the Cochrane Risk of Bias tool will be utilized. The seven domains included in this tool include sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other issues. The tool requires documentation of specific study methodology or conduct and judgment of risk of bias with respect to each domain. Risk of bias for each component is classified as high, uncertain, or low following guidance in the Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1.0. Summary scores for each individual study will be assessed as low, unclear, or high depending on the number of domains classified as low, uncertain, or high risk of bias. We will use the RTI Observational Studies Risk of Bias and Precision Item Bank to select items most relevant in assessing risk of bias for included observational studies. This item bank includes items on participant selection; intervention specification; outcome specification; allocation; attempts to balance allocation; contamination and binding; soundness of information on interventions/exposure and outcomes; followup equality; adequacy and completeness; comparability; effect modifiers and confounders; case-mix adjustment; intention-to-treat analysis; and appropriateness of analytic methods. The reviewer determines the overall risk of bias for each study—coded as yes, partial, or none—based on the criteria assessed and confidence that the results are believable given the study’s limitations. Investigators will consult to reconcile any discrepancies. When agreement cannot be reached through consultation, third party consultation will reconcile risk of bias summary judgements. randomized controlled trials and observational studies assessed with a high risk of bias will not be included in evidence synthesis for that outcome or comparison.

E. Data Synthesis

Evidence summary tables relevant to each KQ will be designed. Results will be qualitatively synthesized to arrive at conclusions regarding effectiveness. Precision will be evaluated at the individual study level by using the RTI Observational Studies Risk of Bias and Precision Item Bank precision items.
F. Grading the Evidence for Each Key Question

The overall strength of evidence for each primary outcome and comparison will be evaluated based on three required domains: 1) risk of bias (internal validity); 2) consistency (similarity of effect sizes of included studies); and 3) directness (single, direct link between intervention and outcome). Based on study design and conduct, risk of bias will be rated as low, medium, or high. Consistency will be rated as consistent, inconsistent, or unknown/not applicable (e.g. single study). Directness will be rated as either direct or indirect. Other factors that may be considered in assessing strength of evidence include dose-response relationship, the presence of confounders, strength of association, and publication bias.

Based on these factors, the overall evidence for each outcome will be rated 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.

An overall rating of high strength of evidence would imply that the included studies were randomized controlled trials with a low risk of bias and with consistent, direct, and precise domains.

G. Assessing Applicability

Applicability of studies will be determined according to the PICOTS format at the evidence level. Study characteristics that may affect 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.

V. References


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VI. Definition of Terms

Abbreviated Injury Severity Scale (AIS)—Measure used to classify the severity of traumatic brain injury based upon the extent of anatomical or structural damage. The scale ranges from 1 to 6 with 1–2 indicating mild injury, 3 indicating moderate injury, and 4–6 indicating severe injury.5

Glasgow Coma Scale (GCS)—Measure used to classify the severity of traumatic brain injury based upon eye opening, best motor response, and verbal response. The scale ranges from 3 to 15 with 13–15 indicating mild injury, 9–12 indicating moderate injury, and below 8 indicating severe injury.9

VII. Summary of Protocol Amendments

In the event of protocol amendments, the date of each amendment will be accompanied by a description of the change and the rationale.

VIII. Review of Key Questions

Key questions were reviewed and refined as needed with input from Key Informants. In addition, the key questions were posted for public comment and finalized by the EPC after review of the public comments.

IX. Key Informants

Key Informants were selected to provide input to the EPC in development of key research questions that will inform healthcare decisions, as well as in identifying high priority research gaps. Key Informants are the end users of research, including patients, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Key Informants will not be involved in analyzing the evidence or writing the report and will have the opportunity to review and comment on the draft report only through the public review mechanism.

Key Informants must have disclosed any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. The Task Order Officer and the EPC worked together to balance, manage, or mitigate any potential conflicts of interest identified.

X. Technical Experts
A Technical Expert Panel (TEP) will be selected to provide input on the Evidence Report. The TEP will be comprised of a multidisciplinary group of clinical, content, and methodological experts who will provide input in defining relevant study populations, interventions, comparisons, or outcomes, in refining the literature search strategy, and identifying particular studies or databases to search. The TEP also recommends approaches to specific issues as requested by the EPC. Study questions, design and/or methodological approaches will not necessarily represent the views of individual TEP members. TEP members will not perform analysis of any kind or contribute to the writing of the report. They may review and comment on the draft report only through the public review mechanism.

Technical Experts must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. The Task Order Officer and the EPC will work to balance, manage, or mitigate any potential conflicts of interest identified.

XI. Peer Reviewers

Peer reviewers will be invited to provide written comments on the draft report based on their clinical, content, or methodological expertise. Their written comments will be considered by the EPC in preparation of the final draft of the report. Peer reviewers do not participate in writing or editing of the final report. The synthesis of the scientific literature presented in the final report does not necessarily represent the views of individual reviewers. The dispositions of the peer review comments will be documented and published 3 months after the publication of the Evidence report.

Potential peer reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Invited Peer Reviewers may not have any financial conflict of interest greater than $10,000. Peer reviewers who disclose potential business or professional conflicts of interest may submit comments on draft reports through the public comment mechanism.
Appendix A. Search Strategy

Concept Analysis

Four concepts were identified as relevant to all key questions addressed in this review; therefore, one search strategy was used in multiple bibliographic databases. The concepts included 1) traumatic brain injury, 2) postacute, 3) multidisciplinary, and 4) rehabilitation. Appendix Table A-1 documents the concept analysis and identified terminology used in searching Ovid MEDLINE®. MeSH terms (or other terms relevant to the specific bibliographic database as determined by database thesaurus) and natural language text words (with truncation used as necessary) relating to each concept were aggregated with the OR operator. The search process is iterative. Concepts are combined with the AND operator to create a precise set of literature inclusive of all concepts for initial screening. Searching from primary studies will begin with a precise search to identify relevant studies efficiently and to gradually broaden the search by limiting the number of concepts and expanding the number of terms included in the search strategy to enhance recall. Limitations imposed on the Ovid MEDLINE® search (and other databases if available) will include human studies published in English. Search filters to enhance identification of trials and observational studies will be incorporated. A sample initial search strategy for primary studies appears below:

### Appendix Table A-1. Identification of search terms for relevant concepts

<table>
<thead>
<tr>
<th>Concept 1</th>
<th>Concept 2</th>
<th>Concept 3</th>
<th>Concept 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBI</td>
<td>postacute</td>
<td>multidisciplinary</td>
<td>rehabilitation</td>
</tr>
<tr>
<td>CRANIOCEREBRAL TRAUMA</td>
<td>Post acute.tw</td>
<td>Multi-disciplinary.tw</td>
<td>REHABILITATION.</td>
</tr>
<tr>
<td>&quot;traumatic brain injur$&quot;, ti, ab</td>
<td>Chronic.tw</td>
<td>Multidisciplinary.tw</td>
<td>RECOVERY OF</td>
</tr>
<tr>
<td>&quot;head injur$&quot;, ti, ab</td>
<td>Long-term.tw</td>
<td>Inter-disciplinary.tw</td>
<td>FUNCTION</td>
</tr>
<tr>
<td>MESH, natural language</td>
<td>Sustained.tw</td>
<td>Interdisciplinary.tw</td>
<td>rehab$.tw.</td>
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<tr>
<td></td>
<td>Disability$.tw</td>
<td>Comprehensive.tw</td>
<td>remediat$.tw.</td>
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<td></td>
<td></td>
<td>Integrated.tw</td>
<td>treat$.tw.</td>
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<td></td>
<td>Holistic.tw</td>
<td>intervention.tw.</td>
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<tr>
<td></td>
<td></td>
<td>Team.tw</td>
<td>train$.tw.</td>
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<tr>
<td></td>
<td></td>
<td>Coordinated.tw</td>
<td>cop$.tw.</td>
</tr>
</tbody>
</table>

Ovid MEDLINE Search Strategy for Primary Studies: First Iteration – Precise Search

1. exp CRANIOCEREBRAL TRAUMA/ (104599)
2. "traumatic brain injur$".mp. (11808)
3. "head injur$".mp. (18236)
4. 1 or 2 or 3 (109040)
5. exp REHABILITATION/ (125214)
6. exp RECOVERY OF FUNCTION/ (21182)
7. rehab$.mp. (97906)
8. remediat$.mp. (7920)
9. 5 or 6 or 7 or 8 (211915)
10. comprehensive.ti,ab. (97302)
11. multi-disciplinary.ti,ab. (2188)
12. multidisciplinary.ti,ab. (29958)
13. multimodal.ti,ab. (8464)

Source: [www.effectivehealthcare.ahrq.gov](http://www.effectivehealthcare.ahrq.gov)
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14 multi-modal.ti,ab. (799)
15 inter-disciplinary.ti,ab. (243)
16 interdisciplinary.ti,ab. (15017)
17 integrated.ti,ab. (88426)
18 holistic.ti,ab. (8151)
19 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 (239708)
20 4 and 9 and 19 (574)
21 limit 20 to "all child (0 to 18 years)" (204)
22 limit 21 to "all adult (19 plus years)" (146)
23 20 not 21 (370)
24 23 or 22 (516)
25 Epidemiologic studies/ (5008)
26 exp case control studies/ (504256)
27 exp cohort studies/ (1093654)
28 Case control.tw. (54710)
29 (cohort adj (study or studies)).tw. (52135)
30 Cohort analy$.tw. (2441)
31 (Follow up adj (study or studies)).tw. (31303)
32 (observational adj (study or studies)).tw. (26024)
33 Longitudinal.tw. (100244)
34 or/25-33 (1295736)
35 randomized controlled trial/ (306162)
36 clinical trial/ (462110)
37 clinical trial, phase i.pt. (11158)
38 clinical trial, phase ii.pt. (17717)
39 clinical trial, phase iii.pt. (6112)
40 clinical trial, phase iv.pt. (608)
41 controlled clinical trial.pt. (82354)
42 randomized controlled trial.pt. (306162)
43 multicenter study.pt. (130202)
44 clinical trial.pt. (462110)
45 or/35-44 (638585)
46 24 and 45 (36)
47 24 and 34 (142)
48 46 or 47 (154)