

## *Comparative Effectiveness Research Review Disposition of Comments Report*

**Research Review Title:** *Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults*

Draft review available for public comment from January 9, 2012 to February 9, 2012.

**Research Review Citation:** Brasure M, Lamberty G, Sayer N, Nelson N, MacDonald R, Ouellette J, Tacklind J, Grove M, Rutks I, Kane R, Wilt T. Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults. Comparative Effectiveness Review No. 72. (Prepared by the University of Minnesota Evidence-based Practice Center under Contract No. HHS A 290-2007-10064-I.) AHRQ Publication No. 12-EHC101-EF. Rockville, MD: Agency for Healthcare Research and Quality. June 2012. [www.effectivehealthcare.ahrq.gov/reports/final.cfm](http://www.effectivehealthcare.ahrq.gov/reports/final.cfm).

### **Comments to Research Review**

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Comments on draft reviews and the authors' responses to the comments are posted for public viewing on the EHC Program Web site approximately 3 months after the final research review is published. Comments are not edited for spelling, grammar, or other content errors. Each comment is listed with the name and affiliation of the commentator, if this information is provided. Commentators are not required to provide their names or affiliations in order to submit suggestions or comments.

The tables below include the responses by the authors of the review to each comment that was submitted for this draft review. The responses to comments in this disposition report are those of the authors, who are responsible for its contents, and do not necessarily represent the views of the Agency for Healthcare Research and Quality.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Introduction	The Introduction is effective in defining the issues to be addressed and in establishing the focus of the review	Thank You.
Peer Reviewer #2	Introduction	The introduction outlines the topic population and goals fine. The only thing I might add is a comment on the incredible heterogeneity of injuries in this population (in terms of brain tissue damaged AND in terms of co-morbidities sustained during an injury)	Added text in 'Sustained impairments from Moderate to Severe TBI' section of Introduction to emphasize heterogeneity.
Peer Reviewer #3	Introduction	Well written	Thank You.
Peer Reviewer #4	Introduction	An appropriate introduction to the state of the art of the field of TBI (post-acute) rehabilitation that lays out the objectives of the review.	Thank You.
Peer Reviewer #5	Introduction	n/a	n/a
Peer Reviewer #6	Introduction	well described	Thank You.
Peer Reviewer #7	Introduction	The introduction provided an adequate rationale for the particular focus on the post-acute phase of rehabilitation for individuals with TBI.  Figure 2 provides readers with a clear understanding of where and how each of the key questions fit given the larger rehabilitation process.	Thank You.
Peer Reviewer #7	Introduction	I could have benefited from an introduction to "minimum clinically important differences", which is presented later (Q4) but which seems to be a very important problem with this body of research.	Added text and references to ES and Introduction to introduce MCID.
Peer Reviewer #7	Introduction	On page iii of the ES, stakeholders are mentioned, but then I did not find an explicit description of who the stakeholders are/were. If they are individuals with TBI, researchers and clinicians, then that should be made explicit in the introduction.	Reworded report text to say 'public comments' instead of using term stakeholders. Stakeholders in the AHRQ text box refers to patients, families, providers, payers, and other decision makers.
Peer Reviewer #8	Introduction	Fair- it does not include in reference work by the Norwich group in the UK- Dr Turner Stokes	The Cochrane review described in the report Introduction (Focus of Review section) is the most recent Turner-Stokes review. Added a sentence to explicitly address this review in the ES.

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Peer Reviewer #8	Introduction	The term postacute could be confusing as it is used by clinicians and responsible parties in different ways I would consider a more explicit definition of time frame	Our technical expert panel recommended that we not define 'postacute' using a specific timeframe.
Peer Reviewer #9	Introduction	General: Introduction is thorough and generally well-written, although some clarifications are needed (see below). Page ES-2, L21-22: This sentence is misleading. Reads as though everyone recovers to baseline after mild TBI. Most studies suggest up to 20% have persistent deficits.	Deleted text to avoid potential misunderstanding. Mild TBI is not the focus of this review.
Peer Reviewer #9	Introduction	Page ES-3, L 44-48: Shouldn't this statement be qualified to acknowledge that reliance on RCT's only has been criticized as overly narrow and not reflective of real-world interventions. Evidence grading systems such as GRADE and the recently-updated AAN evidence review model have incorporated changes to reflect these concerns.	The advantages and disadvantages regarding decisions about which study designs to include in systematic reviews is beyond the scope of this review. Added text to describe why our review expanded inclusion criteria to prospective cohort studies.
Peer Reviewer #9	Introduction	Page 9, L 43-45: The last sentence in the Topic Refinement section states, "...our review evaluates the evidence of effectiveness for multidisciplinary postacute rehabilitation for moderate to severe TBI in adults." This statement over-generalizes the scope of the review and may lead some to misinterpret the findings and implications. A more accurate and transparent statement would be, "Our review evaluates the evidence of effectiveness for multidisciplinary postacute rehabilitation for moderate to severe TBI in adults as determined by measures of community integration."	Revised text to specifically mention primary outcomes.
Peer Reviewer #10	Introduction	Adequate	Thank You.
Peer Reviewer #11	Introduction	Nice introduction...lays the groundwork for the paper.	Thank You.
Peer Reviewer #12	Introduction	there is a thorough review presented of the background literature and challenges to the field, including definitions, heterogeneity, complexity and limited research. While on P2 long-term disability after severe TBI is acknowledged, it is not discussed or incorporated in outcomes, such as remediation of targeted deficits, maintenance versus deterioration as a treatment goal or reduction in burden of care. Bath in this section and ES2-3, the long term perils of severe TBI are noted, but the focus remains on productivity and return to pre-injury levels, neither of which may be optimal outcome measures for post-acute care. ICF participation appears to be selected without adequate foundation	We selected the primary outcomes of productivity and community integration. These are justifiable primary outcomes according to the literature and recommendations from our technical expert panel. Other reviews that addressed a broader array of outcomes reached similar conclusions. Text was added to the Discussion (Limitations to the Evidence section) to describe this.

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Peer Reviewer #12	Introduction	Also, the idea that all agree that as time of injury increases, recovery slows and scope of impairment narrows (P3) is not accurate. As the chronic disease model of TBI indicates, numerous complications frequently ensue, broadening the impairments experienced by the individual. thus reduced lifespan, health, productivity and increased quality of life issues.	Deleted text to avoid misunderstanding.
Peer Reviewer #12	Introduction	Additionally, there is a significant misstatement (P5) regarding TRICARE policy on cognitive rehabilitation (see TRICARE Policy Manual as reference) that further increases risk for adverse impact from the (mis)use of this report by funding entities.	Deleted text to avoid misunderstanding.
Peer Reviewer #12	Introduction	Lastly, selection of the MPAI-4 alone (P6) appears questionable given the long history of the CIQ in the TBI Model Systems and other research programs. However, it is noted that the CIQ was later addressed.	We selected one outcome measure on which to investigate how MCID was addressed in eligible studies. When no eligible studies used the MPAI-4, we discussed how MCID was addressed in eligible studies using CIQ.
Peer Reviewer #13	Introduction	Page 5 of 164 lines 42-64: I had to read this a few times to follow the points. just wondering if it could be written slightly differently.	Reworded text to clarify.
Peer Reviewer #13	Introduction	page 11 of 164 line 47: it may be useful to similarly characterize the basis of the conclusions drawn by Cicerone in order to complete the contrast. i.e. The conclusions of the ECRI and IOM reviews are drawn heavily from RCT data where as the conclusions of the Cicerone study are drawn significantly from....	Added text to explain different findings.
Peer Reviewer #13	Introduction	page 36 line 10- it may be useful to clearly point out the CDC/NCHS data specifically exclude military and other federal TBI. if interested you can find current DoD numbers for TBI at <a href="http://www.dvbic.org/TBI-Numbers.aspx">http://www.dvbic.org/TBI-Numbers.aspx</a>	Added text to Introduction and ES to clarify.
Peer Reviewer #14	Introduction	Introduction gives a good overview of the condition and its treatment, the rationale for the key questions, and an awareness of the prior systematic reviews on the topic. Given that such a small literature has been reviewed so extensively, it is not clear what unique contributions this review hoped to make to the field. Is it to address potential methodological limitations in prior reviews, or to contribute another review with simply a different set of inclusion criteria? A slightly more explicit purpose statement would be helpful.	Added more explicit purpose statement to Introduction and ES.
Peer Reviewer #14	Introduction	It appears to be explained later in the methods, but on pg 2, li 50-54 the authors should give a brief (even parenthetical) example of an impairment-specific therapy that was excluded from the report.	Added example to text.

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Susan Connors, President/CEO Brain Injury Association of America	Introduction	<p>A traumatic brain injury is not an event or an outcome. It is the start of a lifelong disease causative and disease-accelerative process involving the central nervous, autonomic nervous, endocrine and immune systems that result in chronic respiratory conditions, widespread infections, neurologic disorders and psychiatric diseases as well as musculoskeletal, bowel, bladder and sexual dysfunction.<sup>1</sup> BIAA believes it is critically important for the authors to acknowledge the disease-causative and disease-accelerative nature of TBI in their final report.</p> <p><sup>1</sup> Masel BE and DeWitt DS. J of Neurotrauma. August 2010, 27(8): 1529-1540.</p>	<p>Discussion of the IOM review on long-lasting impairments in the Introduction discusses many of these issues. Added text and reference to Masel &amp; DeWitt, 2010.</p>
Susan H. Connors President/CEO Brain Injury Association of America	Introduction	<p>Individuals who sustain brain injuries require access to expert trauma care, specialized acute and postacute rehabilitation, lifelong disease management and individualized services and supports in order to live healthy, independent and satisfying lives. TBI Model Systems researchers conservatively estimate that 125,000 Americans over the age of 15 survive a moderate or severe TBI each year, but only 16,000 of these patients receive acute rehabilitation and as many as 60,000-70,000 are discharged home from the hospital.<sup>2,3</sup> The lack of access to care—particularly postacute rehabilitation—stems from inconsistent coverage policies and often unscrupulous payment practices of public and private health plans. The failure to provide postacute rehabilitation of appropriate scope, intensity, timing and duration results in higher levels of disability, an increased reliance on pharmacological interventions, greater durable medical equipment needs and higher long-term care costs, to say nothing of the burden on families.<sup>4</sup> Because access to care is so problematic for patients with brain injury, BIAA is compelled to alert the authors to statements that we believe further undermine access to care. For example, the notion that TBI recovery is complete after one year or even a few years is a myth arising from the neurophysiological metabolic normalization that occurs in the first year after injury. This normalization paves the way for the development of new neural structures and ultimately restoration of physical, cognitive and behavioral function many years following the injury. Consistently, public and private payers invoke this “plateau myth” to deny treatment, even when patients continue to demonstrate gains. Perpetuation of the myth in this report will merely compound the problem of access to care. BIAA urges the authors to strike the sentence found on page 2, “Some argue that neurologic recovery is complete at 1 year, while others believe recovery spans 2 or more years.” Similarly, BIAA suggests the authors clarify or contextualize the statement, “All agree that as time since injury increases, recovery slows, and the scope of impairments narrows” [also on page 2]. It is true that individuals who sustain brain injuries and their families learn to live with a “new normal” and tend to self-report less impairment as time goes by, but the statement is misleading given the disease-causative and disease-accelerative nature of TBI.</p> <p><sup>2</sup> Cuthbert JP, Corrigan, JD, Harrison-Felix C, Coronado V, Dijkers, MP, Heinemann AW, Whiteneck GG. Factors that predict acute hospitalization discharge dispositions</p>	<p>Inconsistent reimbursement policies and the potential access issues are addressed in the Introduction and Discussion.</p> <p>Discussion of spontaneous recovery in Introduction revised to reflect current evidence on long-lasting outcomes of TBI.</p>

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Commentator & Affiliation	Section	Comment	Response
		<p>for adults with moderate to severe traumatic brain injury. Arch Phys Med Rehabil 2011;92:721-30.</p> <p><sup>3</sup> Corrigan JD, Cuthbert JP, Whiteneck GG, Dijkers MP, Coronado V, Heinemann AW, Harrison-Felix C, Graham, JE. (2012) Representatives of the traumatic brain injury model systems national database. J Head Trauma Rehabilitation. doi:10.1097/HTR.0b013e3182238cdd.</p> <p><sup>4</sup> Ashley MJ, Braunling-McMorrow D, Connors S, Gordon W, Trudel T. Traumatic Brain Injury in the United States: A Call for Public/Private Cooperation. Retrieved from <a href="http://www.biausa.org/biaa-position-papers.htm">http://www.biausa.org/biaa-position-papers.htm</a> on January 31, 2012.</p>	
Susan H. Connors President/CEO Brain Injury Association of America	Introduction	The authors properly note the absence of research on scope, timing, intensity and duration of treatment (i.e., dose/response studies). BIAA appreciates this observation as we believe it is time—in fact past time—for researchers and clinicians to conceptualize and implement a disease management approach to brain injury care over the lifespan. Thus, we agree that one intention of rehabilitation is to restore, not accommodate for, lost function, but we also recognize that some individuals require rehabilitation to maintain or prevent deterioration of function throughout their lives. We encourage the authors to add maintenance of function and prevention of deterioration in their discussion on page 4.	Added text regarding the importance of outcomes other than participation to Discussion section.
Susan H. Connors President/CEO Brain Injury Association of America	Introduction	<p>In light of the difficulty patients encounter in accessing care and because of the importance of the topic and the prestige associated with AHRQ reports, BIAA suggests the authors delete the following statement [found on page 5]: “Tricare {sic} 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.” We are concerned about the statement because it mischaracterizes TRICARE’s Policy Manual,<sup>11</sup> which states: “Cognitive rehabilitation strategies may be incorporated into comprehensive brain injury rehabilitation programs and may be covered when cognitive rehabilitation is not billed as a separate service.” This policy was in place before the ECRI study was conducted and is still in place today. Furthermore, as the authors know, ECRI’s work was denounced as a “misuse of science”<sup>12</sup> so it would seem unwise to call attention to it in this report.</p> <p><sup>11</sup> TRICARE Policy Manual 6010.57-M, February 1, 2008, Chapter 7, Section 18.1 Rehabilitation – General. Retrieved from <a href="http://manuals.tricare.osd.mil/DisplayManual.aspx?SeriesId=T3TPM">http://manuals.tricare.osd.mil/DisplayManual.aspx?SeriesId=T3TPM</a> on January 26, 2012.</p> <p><sup>12</sup> Miller TC and Zwerdling D. Pentagon Plan</p>	<p>While the ECRI study was called a “misuse of science” by one individual, our review of the study did not agree with that assessment and feel mentioning this study provides context for our review. The recently completed IOM review reached conclusions similar to that of the ECRI study.</p> <p>Reworded text regarding TRICARE to avoid potential misunderstanding.</p>

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Susan H. Connors President/CEO Brain Injury Association of America	Introduction	BIAA recognizes the statement on page 5, "Persistent decisional dilemmas about postacute rehabilitation for TBI do not stem from a lack of relevant systematic reviews" is intended to lay the groundwork for the authors' comments on weaknesses in methodology [see pages 49-50] and the futility of additional systematic reviews until the weaknesses are overcome [see page 52], but it is very likely that the statement will be quoted out of context so we recommend its revision or deletion.	Reworded text to avoid misunderstanding. However, it is important to highlight the many attempts to synthesize the evidence on this topic.
Peer Reviewer #1	Methods	The methodology is well outlined. Although clearly explained, the arbitrary selection of 6-months post injury outlined in Topic Refinement remains of concern. An overlap with the IOM systematic review does not entirely stand as appropriate justification nor does it mitigate the impact the narrowed scope has on the data abstracted.	We did not use a 6-months postinjury inclusion criterion. Added text to Methods (Topic Refinement section) to clarify.
Peer Reviewer #1	Methods	The Search Strategy, Inclusion/Exclusion Criteria and Grading of the Evidence are clearly outlined.	Thank You.
Peer Reviewer #2	Methods	In general, this section is fine. One might argue whether limiting studies to only participation measures is justified. I understand the importance of societal level outcomes, but there may be benefits at the activity or even impairment level which might be clinically important but not addressed in this report. In addition, of the three ICF levels - participation is by far the most difficult to define and measure. Search strategies are stringent - but clear. Definitions are fine.	The recent IOM review addressed a broader array of outcomes and reached similar conclusions. Text was added to the Discussion (Limitations to the Evidence section) to discuss the potential importance of other outcomes variables and refer to the IOM review.
Peer Reviewer #3	Methods	Given the nature of the studies done on the topic, the inclusion criteria were justifiable. However, particularly in cases of severe brain injury, a review of evidence for reduction in caregiver burden might be appropriate.  The authors followed customary guidelines for a review of this type.	Text was added to the Discussion (Limitations to the Evidence section) to discuss the potential importance of other outcomes variables and to refer to the recent IOM review that did address other outcomes and reached similar conclusions.
Peer Reviewer #4	Methods	Yes, this review has considered appropriate literature based on relevant inclusion and exclusion criteria and using well-accepted scientific methods/review criteria.	Thank You.
Peer Reviewer #5	Methods	Inclusion/exclusion criteria are appropriate and search strategies are logical. Definitions are appropriate. Statistical methods appear appropriate but I am not an expert in this area.	Thank You.
Peer Reviewer #6	Methods	All the above seem appropriately described and defined.	Thank You.

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Peer Reviewer #7	Methods	In general, the methods were described clearly and with transparency. The search strategies were logical and it was clear how the exclusion criteria limited the numbers of studies reviewed. Related to that is the decision to exclude studies that had < 75% TBI participants: while the rationale is made explicit, one could certainly argue for a different number, such as a simple majority. This makes me wonder how many studies would have been included if this criteria had been lowered to 51%? It would be worth knowing what this would have been and if it would have added substantially to the number of studies included.	Because our nominated topic asked about the effectiveness of rehabilitation for TBI and moderate to severe TBI impairments and recovery may be different than that for stroke or mild TBI, it was important that we were able to trust that individual study results were a reflection of this condition. We refer to a recent Cochrane review in the Introduction that evaluates the effectiveness of multidisciplinary rehabilitation for ABI.
Peer Reviewer #7	Methods	I applaud the focus on participation outcomes, however given that there are so many factors or variables that could potentially affect ones productivity (e.g., not having bus fare to get to work), would it not be wise to have also considered 'activity' level outcomes, i.e., outcomes that perhaps were more closer related to the intervention? Were activity outcomes reported and just included in this review?	Text was added to the Discussion (Limitations to the Evidence section) to discuss the potential importance of other outcomes variables and to refer to the recent IOM review that did address other outcomes and reached similar conclusions.  The scales selected to measure community integration contain items that measure activities. Most outcomes that we considered intermediate were primarily specific neuropsychological performance measures. Others included specific measures of behavioral health status. If we identified outcome measures that we did not prespecify, but they appeared to capture how an individual integrated in a community setting or represented a global assessment, we kept those measures and considered them secondary outcomes.
Peer Reviewer #8	Methods	Frankly still a bit confused by the inclusion criteria and exclusion criteria between studies and how we looked at patterns comparing initial injury and function at the time of the intervention as well as time since injury	Added text to Results section to better describe inclusion and exclusion criteria of primary studies.

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Peer Reviewer #9	Methods	General: Only 10% of studies with full-text review met eligibility criteria. This raises questions regarding the appropriateness of inclusion/exclusion criteria.	Full text review is required when the title and abstract, if available, provide insufficient information to determine if a study identified in the initial search is eligible. Many studies provided few details in their abstracts and therefore required full text review. We do not consider this rate an indication of the appropriateness of the eligibility criteria. Eligibility criteria were determined appropriate scientifically and <i>a priori</i> .
Peer Reviewer #9	Methods	Page v, lines 46-48: If the measures selected to determine effectiveness lacked psychometric capacity to identify MCID, couldn't one conclude that the metric selected (participation scales) was not appropriate, rather than concluding the evidence for rehab effectiveness is insufficient?	While MCID is an important consideration in interpreting study results, the lack of MCID did not directly factor into strength of evidence assessments (i.e. Insufficient strength of evidence assessments was not the result of inattention to MCID).
Peer Reviewer #9	Methods	Page ES-8, L 56: Need some description of PICOTS.	Deleted text containing 'PICOTS'.
Peer Reviewer #9	Methods	Page 10, L 27 (Inclusion Criteria): The review, by definition, focuses on treatment outcomes in persons with "moderate to severe TBI." However, there is little attention to subjects' level of function at the time of enrollment in the trial. Complicating matters further, the length of time from injury ranged from 1 to 46 months suggesting that subjects differed dramatically in the degree of recovery they had sustained in cognitive-behavioral function at the time they were exposed to holistic rehabilitation. Consequently, one can infer that the potential to benefit from the treatment was not equivalent across subjects or studies. This issue was raised during the TEP teleconferences, yet, the review does not appear to address this concern. To use an analogy, if one were investigating the effectiveness of acyclovir for treatment of memory disturbance after herpes encephalitis, and included subjects' with prodromal symptoms as well as others with fulminant disease, and still others who were exposed toward the end of the active disease process, the effect of the memory treatment would be swamped by the stage of the disease. Similar issues concerning sample heterogeneity have been raised to account for the "failure" of many neuroprotective drug trials in TBI.	Added text to Results section describing the extent of reporting of functional status in individual studies.  Length of time since injury varied dramatically across and sometimes within studies. We did not pool studies and therefore did not make conclusions across studies composed of individuals with different times since injury. Conclusions were drawn from studies that included individuals with varying degrees of time since injury.
Peer Reviewer #9	Methods	In my view, the review could be improved by reporting on whether each study included established criteria for level of function (or degree of disability) at the time of enrollment and for those that did, what strata were included (table 8 would be a logical place to include these data).	Added text to Results section to better describe inclusion and exclusion criteria of primary studies.

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Peer Reviewer #9	Methods	If treatment effectiveness was considered in the context of subjects' level of function, degree of disability or length of time post-injury at enrollment, this would increase precision and might influence the conclusions. At a minimum, I would like to see some discussion of this issue in the Discussion section.	Agreed, added text to Discussion section addressing this issue.
Peer Reviewer #10	Methods	See attachment. Given the heterogeneity of the patients, the treatment programs, and the outcome measures used, I believe that a traditional evidence based review methodology is unlikely to deliver useful conclusions. These methods were developed for much "tidier" medical domains.	Added text to the Discussion section about the value of a 'realist' review on this topic.
Peer Reviewer #11	Methods	Inclusion criteria may be too strict as only 16/178 articles were included, but it maintains the focus of the paper. Does it make sense to repeat and expand criteria to include more mild cases (from the 75% mod/sev rule)??	<p>Full text review is required when the title and abstract, if available, provide insufficient information to determine if a study identified in the initial search is eligible. Many studies provided insufficient details in their abstracts and therefore required full text review. We do not consider this rate an indication of the appropriateness of the eligibility criteria. Eligibility criteria were determined appropriate scientifically and <i>a priori</i>.</p> <p>Because the review topic asked about the effectiveness of rehabilitation for TBI and moderate to severe TBI impairments and recovery may be different than that for stroke or mild TBI, it was important that we were able to trust that individual study results were a reflection of this condition. We refer to a recent Cochrane review in the Introduction that evaluates the effectiveness of multidisciplinary rehabilitation for ABI.</p>

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Peer Reviewer #12	Methods	Inclusion criteria appear narrow given the aforementioned complexity/heterogeneity of the topic and historic low research funding, as well as the pressing need of providing some type of clinician, funder and consumer guidance. Given the nature of this topic, it was refreshing to see inclusion of some observational studies. With the limited outcomes selected P11-13, the exclusion of impairment specific interventions and lack of focus on maintenance of function and reduced burden of care are of concern. Data synthesis indicates only a few of the 16 studies were utilized to address the majority of questions. this needs to be made far more explicit throughout, including in summary and abstract documents, as otherwise this is quite misleading and further raises risk of misuse and harm to persons with TBI in need of postacute care. The MCID (ES3 and methods) has been subject to some controversy within the field, and pros/cons of this approach were not addressed.	<p>Inclusion criteria were initially developed a priori and were meant to identify a set of studies that answered scientifically important questions. Criteria were expanded once it became apparent that so few studies were available. IOM review which included a few more studies in the section relevant to this review reached similar conclusions. The focus on participation measures made this review unique for a topic with many existing and current systematic reviews.</p> <p>Text was added to the Discussion (Limitations to the Evidence section) to discuss the potential importance of other outcomes variables and to refer to the recent IOM review that did address other outcomes and reached similar conclusions.</p> <p>Added text to describe pros/cons of MCID.</p>
Peer Reviewer #13	Methods	The methods seem appropriate.	Thank You.
Peer Reviewer #14	Methods	The authors clearly described their methods and the rationale they used for their approach. This was critical given the diversity of inclusion/exclusion criteria used in the previously published systematic reviews on the topic and will account for the variations in results and conclusions across the reviews. In this study, the key decisions on patient diagnosis, patient centered outcomes, study designs, and risk of bias were adequately justified and their consequences appropriately discussed.	Thank You.
Peer Reviewer #14	Methods	Key Question 3 addresses the minimum clinically important differences for outcome measures. The authors should clarify in the methods that they only looked to see if this was reported within the context of the 8 studies they examined to answer the other effectiveness questions and did not conduct a separate search to look for other studies that established the MCID for their primary TBI outcomes more generally (if true).	Added text in methods section to clarify.

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Susan H. Connors President/CEO Brain Injury Association of America	Methods	<p>Throughout the report, the authors acknowledge the heterogeneity and complexity of TBI, rehabilitation interventions and outcomes measures. They note the significant number of variables and the difficulty in isolating the variables with respect to sustained impairments and treatment programs/approaches. The authors discuss the impossibility of double blinding in rehabilitation research and speak to the challenges in designing, conducting and paying for randomized controlled trials. The authors recognize conclusions about effectiveness and comparative effectiveness cannot be achieved by additional systematic reviews until the weaknesses in methodology are resolved and the gaps in research addressed. While BIAA appreciates affirmation of these facts, it is regrettable that AHRQ's investigation did not add more to the body of knowledge in our field. In our March 2011 comments to AHRQ concerning the key questions to be addressed in this project, BIAA urged investigators to include all of the reliable evidence<sup>5</sup> that is available. We did so because we anticipated the exclusion of much of the published research in brain injury would yield nominal results. In those comments, we recommended investigators consider the National Service Framework, an approach developed in the United Kingdom for extracting evidence from studies that are not randomized controlled trials.<sup>6</sup> While BIAA was pleased to see the authors included prospective cohort studies, we are dismayed that a comprehensive search strategy for TBI rehabilitation spanning 30 years would produce only 1,616 studies and deeply troubled that only 16 studies were useable. That means conclusions about the efficacy of postacute rehabilitation were formed based on less than 1 percent of the literature!</p> <p><sup>5</sup> 32 CFR 199.2 defines "reliable evidence" as (i) Well controlled studies of clinically meaningful endpoints published in refereed medical literature; (ii) Published formal technology assessments; (iii) Published reports of national professional medical associations; (iv) Published national medical policy organization positions; and (v) Published reports of national expert opinion organizations.</p> <p><sup>6</sup> Turner-Stokes L, et al. Generating the evidence base for the national service framework for the long term conditions: a new typology. <i>Clinical Medicine</i> 2006;6(1): 91-97.</p>	<p>Given the complexity and heterogeneity of the condition and interventions, it was critically important to include only studies where results were believable. Also given that spontaneous recovery occurs without agreement to its time frame, only controlled studies could achieve a risk of bias assessment that could provide evidence useful for drawing conclusions.</p> <p>Disappointed with the lack of available studies, we explored expanding eligibility <i>post hoc</i> to include retrospective controlled cohort studies. Unfortunately, risk of bias among these studies was high and results were not believable. Therefore, we concluded that expanding eligibility would not improve the ability to draw conclusions from the literature. This decision is validated by examining the recent IOM review that included many different study designs, however still failed to be able to draw conclusions about the effectiveness of multimodal postacute rehabilitation programs.</p> <p>It is inaccurate to say that our conclusions were drawn based upon 1 percent of the literature. Our review utilized a comprehensive search strategy because there is a relatively poor fit between indexing and this topic, terminology used is inconsistent making reliance on key words challenging, and we made a conscious decision to maximize recall at the expense of precision to ensure that we identified all of the relevant literature through a thorough screening process.</p>

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Peer Reviewer #1	Results	The Results are detailed and well presented. The tables and associated references are well organized. The Study details are appropriately descriptive, highlighting the relevant data and characteristics. The breadth of the references seems appropriate and inclusive. The key points are comprehensive in their summary of the reviewed and assessed data.	Thank You.
Peer Reviewer #2	Results	I am not aware of other studies which might be included and meet the I/E criteria. Detail is adequate. There are several important issues mentioned in the discussion. One is the "black box" of rehabilitation treatment - this is an area that plagues our field. The authors do a good job in trying to characterize the studies as much as the source documents allow them to. Again - you cannot overemphasize the "insufficient data to conclude" vs "ineffective" issue. This is particularly true in an environment of looking for drastic cuts in medical expenditures.	Reworded text in Discussion to emphasize the "insufficient data to conclude" vs "ineffective" issue.  Added text to Discussion section to emphasize issues around treatment definition.
Peer Reviewer #3	Results	ample figures and tables. Detail is sufficient	Thank You.
Peer Reviewer #4	Results	Yes the detail is appropriate. I am quite familiar with this literature and this review described the studies in the appropriate manner. One issue that was not fully explained however was the importance of the time of the research and the context of when it was performed (i.e., research in the 1980 and 1990's health systems for rehabilitation is not particularly relevant to healthcare for rehabilitation in the 2010's) and the nature of the health care organization that performed it (i.e., the Salazar and Vanderploug articles are performed in the VA system, which is significantly different than the private or academic sector systems.	Added text to Discussion section to elaborate on applicability.
Peer Reviewer #5	Results	Detail is appropriate and the authors do a nice job of covering the included articles. The tables are very good and provide an adequate amount of information except the means of collecting follow up data is not described.	Added text to the Results section to describe how outcomes data collected.
Peer Reviewer #6	Results	One can get lost in the the large amount of details and the way in which each question is addressed separately. The summary sections, however, provided a nice compilation of findings and are much easier to read/access. Of course, this all depends on the reader and the specific information the reader is after.	Thank You.
Peer Reviewer #7	Results	Given the transparency of the methods and the explicit inclusion/exclusion criteria, the results stand on their own. The tables are well organized, and easy to follow and understand. To my knowledge no studies were overlooked.	Thank You.
Peer Reviewer #8	Results	the tables are well presented but the data is difficult to compare i.e. populations	Added text to results section to emphasize heterogeneity of populations.
Peer Reviewer #9	Results	Page ES-6, Figure A: This figure is confusing. For example, starting from "Adults with sustained impairments..." leads to "Intermediate Outcomes" but this box doesn't lead anywhere else. And how does one enter the pathway that connects "Multidisciplinary Post-acute Rehab," "Primary PCO," and "Sustainability of Health Outcome?" The conceptual framework is not apparent	Revised analytical model. It appears that pieces were lost during transition to review version.

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Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #9	Results	Page ES-13, L 15-18: How can one have a TBI "with no acquired brain injury?"	They can't. Thank you for pointing out this error. We have deleted the inaccurate text
Peer Reviewer #9	Results	Page ES-17, L 7-17: This statement implies that there was no MCID for the ICRP using the CIQ. However, the "RCI" is a robust index of change indicating that differences are above chance level and not attributable to practice effects. Not clear why this finding was discounted.	We did not mean to discount this evidence of MCID for the CIQ. We have reworded the text in the ES and the report text to avoid this perception.
Peer Reviewer #10	Results	The results follow reasonably well from the methodologic decisions but the methodologic decisions largely guarantee a non-useful set of results.	Methodological decisions were made to insure appropriate scientific evidence base from which to draw conclusions to key questions. IOM review with broader inclusion criteria reached similar conclusions for comprehensive multimodal cognitive rehabilitation for moderate to severe TBI.
Peer Reviewer #11	Results	Results were laid out well and explained adequately.	Thank You.
Peer Reviewer #12	Results	The results section is well detailed and studies are very well described and compiled in a readily accessible manner through various tables. P22-31 demonstrates the extreme diversity of approaches, populations, time periods, etc. which is extremely limiting for this review and should be better highlighted in summary documents. The comments regarding inclusion are addressed previously.	Added text to describe the diversity of populations and interventions in included studies.
Peer Reviewer #13	Results	in table C of the ExSumm and table 7 of the body for Key Question 2 it would be very helpful for me if you listed the Author/date of the studies to help keep them straight.	Added study author and year to these tables.
Peer Reviewer #14	Results	The authors explicitly state only a qualitative synthesis of results was possible secondary to the heterogeneity of the PICOTS in the included studies, so the omission of statistical methods was appropriate.  The organization of the results section with key points and summary tables by key question facilitated presentation of the findings. Additional detail is available in the Appendices for those with specific questions, but these details do not disrupt the flow of the main report.	Thank You.
Peer Reviewer #1	Discussion	The Discussion Section appropriately highlights the limitations and challenges in conducting Level I research in this field/topic. It appropriately cautions on the impact of small RCTs in the area and appropriately cautions misinterpretation of the paucity of data's impact on the overall assessment.	Thank You.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #1	Discussion	Recommendations regarding TBI Model Systems are sound, but do not surmount these issues and should not be held in such esteem in the recommendations on Future research.	Revised text in ES and Discussion section of full report to suggest TBI models systems as viable sources, but have limitations as well.
Peer Reviewer #2	Discussion	the nature of the conclusion don't lend themselves to many implications. But I think the authors do as good a job as they can with limited conclusions. The issue of the heterogeneity of the TBI population I think should be given greater emphasis. This is important because it makes the target population difficult to define (literally there IS NO typical TBI) and makes doing high quality research extremely difficult and expensive because such larger sample sizes are required. Although the Models Systems represents a venue for research - they are grossly underfunded and could only address the effectiveness questions at hand with a great increase in support.	Added text to emphasize heterogeneity in Results and Discussion sections of ES and full report.  Revised text in ES and Discussion section of full report to suggest TBI models systems as viable sources, but have limitations as well.
Peer Reviewer #3	Discussion	The conclusions are essentially that there is insufficient evidence to support post-acute TBI rehabilitation, or one approach over another. Again, more emphasis should be placed on the fact that this is not the same as saying there is evidence for ineffectiveness. Specific recommendations for research design should be included.	Reworded text to indicate insufficient evidence is not the same as evidence of ineffectiveness.
Peer Reviewer #4	Discussion	Essentially, the authors could not make any conclusions given the paucity of studies and the variability of the literature/findings. These limitations are well described.	Thank You.
Peer Reviewer #5	Discussion	Implications are clearly stated but there is not a sufficient description of how the outcome data is obtained in the studies (is the data collected via phone vs. inperson clinical evaluation by rehab professional??). Future research section is clear.	Added text to Results section describing how outcomes data was obtained from study participants.
Peer Reviewer #6	Discussion	Yes and yes! In my view the Future Directions section is clearly and concisely written. It carefully lays out the limitations of current state of research and the need for future research to allow clinicians to determine the appropriate (effective) treatment interventions for a particular patient.	Thank You.
Peer Reviewer #7	Discussion	Is the future research section clear and easily translated into new research? I think the authors could provide a more detailed list of recommendations for future research given the number and kinds of issues/concerns with the literature reviewed. For example, simply stating at the end that the TBI Model systems is where this work could be done, does not go far enough. NIDRR has limited funds. I would like to see the authors take this opportunity to identify other agencies that indeed could be funding this kind of research. Agencies such as IES, NIH, VA, DOD, HRSA should also be funding this kind of work, given the size of the population with TBI (1.7 million) and estimated loss in productivity (\$60 billion).  In general, I was disappointed in the limited number of recommendations and in the cursory manner in which these critical problems were linked or connected to tangible steps for moving the field ahead (pgs 55-56).	Thank you for your concerns about the future research needs on this topic. We have added some text to the Discussion section of the ES and full report to address these concerns and mentioned the subsequent project that aims to refine future research needs relevant to this topic.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #8	Discussion	Conclusions are difficult to interpret and reflect concerns with population Care needs to be taken to reinforce the limitations of these conclusions especially when it comes to acute inpatient rehabilitation of such patients as it is typically delivered in the US Terms used continue to add to the lack of clarity ie time frame in this section	Added text to emphasize heterogeneity in Results and Discussion sections of ES and full report.  Enhanced descriptions of the time-frames addressed in original studies in terms of time since injury in the Results section.
Peer Reviewer #9	Discussion	Page ES-8, L 10 and Page 14, L 18-20: The absence of an objective method for establishing risk of bias (e.g., weighting variables, establishing a cut-off for number of criteria judged adequate to justify mild, moderate or high risk rating) seems a major shortcoming given the significance of this factor in deriving SOE. This seems to set a low bar for a critical component of CER. Not sure what can be done about this at this point but, as a reader, this compromises the impact of the review. It is also awkwardly juxtaposed against the high bar set for research design.	Added text to justify risk of bias assessment methodology using guidance from AHRQ. AHRQ guidance recommends against using risk of bias assessments that incorporate scoring.
Peer Reviewer #9	Discussion	Page ES-22, L 13-14: What are the implications suggested?	Reworded text to clarify meaning.
Peer Reviewer #10	Discussion	The limitations are enormous and very complex. I don't think the authors of the report, being largely new to the domain, are in a position to fully know what they are or to be able to articulate them.	Added text to further emphasize the limitations of this review and available research.
Peer Reviewer #11	Discussion	Discussion section read well. May consider additional/specific recommendations for future areas of research based on this review.	Added text to the Discussion section of the ES and full report to further address future research needs and mentioned the subsequent project that aims to refine future research needs relevant to this topic.
Peer Reviewer #12	Discussion	the summary in particular P48 must indicate the limited number of studies used to address the respective questions at hand, providing a context for the reader. P51 use of the term conclusive evidence should be elaborated to avoid misuse and misunderstanding by the reader. P52 while acknowledging that this review is unsatisfactory, the authors avoid addressing or proposing With the continued low civilian funding, minimal severe TBI research, lack of RCTS and small sample sizes (none of which will change any time soon), it could be many years and millions of affected individual lives before a review using such limited criteria has any meaningful impact other than to fuel the fires of those denying treatment due to 'lack of evidence'. Brief discussion for the 'lack of evidence' of much of what we do in medicine and the difference between evidence-based (rare) versus best practices (common) based treatment should be noted, given the potential for misuse of this report to deny access to care. P53 discussion of the need for detailed definitions and implementation of training are well stated and a needed priority for the field.	Added text to describe the limited number of studies used in drawing conclusions.  Reworded text to avoid misunderstanding of 'conclusive evidence'.  Added text to Discussion section addressing that the topic may benefit from other types of reviews.

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Peer Reviewer #13	Discussion	Risk of Bias assessment was surely a challenge but seems to have been quite well addressed and executed. Kudos.	Thank You.
Peer Reviewer #14	Discussion	The Summary and Discussion Chapter is succinctly focused on the key points of the review. Table 17 is an especially helpful summary linking findings to strength of evidence.	Thank You.
Peer Reviewer #14	Discussion	The comparison of this report to other systematic reviews was critical. A large number of prior systematic reviews on TBI were cited by the authors in proportion to only the 8 studies they included to evaluate effectiveness and comparative effectiveness in this review. This shows the large discrepancy between the need for evidence on rehabilitation and the available research. The large number of systematic reviews with differing conclusions will only add to the confusion, not decrease it, so I applaud the authors for highlighting how the variations in primary research and systematic review methods account for the differing findings.	Thank You.
Peer Reviewer #14	Discussion	The authors were very explicit in describing their use of strength of evidence when assessing (comparative) effectiveness. Therefore it is critically important that they included the caution that insufficient or low strength of evidence for effectiveness is not equivalent to ineffectiveness. Given the use of prior systematic reviews by payers, I recommend the authors' cautionary statement be placed in bold and/or underlined in the final version if possible. It also warrants inclusion in the Executive Summary and perhaps the Abstract if word limits allow.	Cautionary statement placed in bold in ES, full report, and Abstract.
Peer Reviewer #14	Discussion	<p>Future research is an especially important subsection of the report given the authors' conclusions. I offer two comments for their consideration:</p> <p>The discussion of outcomes in the last paragraph on pg 55 describes a problem that is common to many conditions/impairments in the musculoskeletal and neuromuscular fields and has been challenging to solve. The authors could comment on their use of work by the TBI Common Data Elements Outcomes Workgroup led by NINDS and if this type of effort could move the field in the direction advised.</p> <p>The trajectory of improvement is discussed in the first paragraph on pg 56. The timing of treatment benefits is specifically mentioned, and the length of time benefits are sustained could be cited as well since this was reported earlier in the report. Within this topic the timing, frequency and duration of treatment, including "boosters" after the initial course of treatment has concluded are closely related questions asked about how to maximize the benefit of treatment.</p>	<p>Added text to the Discussion section addressing the Common Data Elements Outcomes Workgroup</p> <p>Added text to describe how improved definitions would allow this type of future research. Also incorporated specific question into followup Future Research Needs project.</p>

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Susan H. Connors President/CEO Brain Injury Association of America	Discussion	We believe their conclusion as shown below, particularly the bold portion, should be included in the report's structured abstract and executive summary: "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...However, <b>our failure to draw broad conclusions must not be misunderstood to be evidence of ineffectiveness</b> ... 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 failure to directly and emphatically state in the abstract and the executive summary that a lack of evidence is not proof of ineffectiveness does a great disservice to millions of individuals who sustain brain injuries each year.	This statement was previously included in the ES and full report. A similar cautionary statement has been added to the Abstract. These cautionary statements have been placed in bold to highlight their importance.
Susan H. Connors President/CEO Brain Injury Association of America	Discussion	BIAA agrees that the TBI Model Systems "offer a valuable venue for conducting rigorously designed intervention studies," but we also know that large randomized controlled trials and well-coordinated prospective cohort designs with appropriate controls are expensive and require far greater resources than are presently allocated to the Model Systems. Consequently, it is somewhat misleading when the authors note on page 24 of the executive summary, that "both the research quality and funding are increasing" and conclude "therefore the body of evidence should strengthen with time."	Deleted statement to avoid misunderstanding
Susan H. Connors President/CEO Brain Injury Association of America	Discussion	During the last 30 years, scientists and neurosurgeons have found more and better ways to save the lives of the millions of Americans who sustain brain injuries each year, while payers and policymakers have used lack of evidence <sup>9, 10</sup> to deny those same individuals access to the postacute rehabilitation and disease management systems they need to live healthy and productive lives. Perhaps the authors would find greater satisfaction with this investigation if they concluded with a more compelling statement about the urgency of addressing TBI research and funding gaps. Certainly BIAA would be more satisfied.  <sup>9</sup> NIH. 1989. <i>Interagency Head Injury Task Force Report</i> . Available from Brain Injury Association of America. <sup>10</sup> Rehabilitation of Persons With Traumatic Brain Injury. NIH Consens Statement Online 1998 Oct 26-28; [cited 2012, January 26]; 16(1): 1-41.	Agree. Added text to emphasize need for future research on this topic.

Commentator & Affiliation	Section	Comment	Response
Susan H. Connors President/CEO Brain Injury Association of America	Discussion	In several places in the report, the authors refer to expert opinion to describe what is known in the TBI field. On page 22 of the executive summary, the authors indicate “For example, the practice-based evidence approach may help overcome certain shortcomings of the available research...” BIAA strongly supports the development of medical treatment guidelines for postacute rehabilitation of moderate and severe TBI that would be applicable for both civilian and military populations. We believe the desperately-needed taxonomy of TBI impairments and interventions should be created as part of the guidelines development process so that patients and payers can understand treatments and objectively compare options and prices. Accordingly, we urge the authors to expound on this suggestion and to do so forcefully in their final report.	Added text to emphasize the importance of the development of a taxonomy in the Discussion section of the ES and full report.
Susan H. Connors President/CEO Brain Injury Association of America	Discussion	BIAA supports the call for additional research to enhance the evidence base of postacute brain injury rehabilitation interventions. This evidence-base is critical for all stakeholders, including patients, providers, insurers and policymakers. In pursuing the evidence base, however, we urge AHRQ and the authors of the paper not to engage in an over-reliance on sources of information that might in fact “bias” our understanding and mislead people with TBI and their families, policymakers, insurers, clinicians and others. This potential for bias might seem benign if it were only a matter of academic debates and the prestige of competing research paradigms. The policy and insurer communities, however, are often influenced by the outcomes of these debates and, as a result, real people may either benefit or suffer. Access to high quality medically necessary care for TBI patients must be our guide.	Our methodology was cautious not to use studies with results that may not be believable in drawing conclusions. Any conclusions drawn are from studies that were felt to have a low or moderate risk of bias.
Peter C. Esselman, MD, Chair Health Policy and Legislation Committee & Elliot J. Roth, MD Chair Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation (AAPM&R)	Discussion	As with the IOM research, the Academy also advocates for future RCT and prospective cohort studies to include the formal assessment of adverse effects. Although one of the sixteen studies included assessment for adverse effects, it failed to assess them in a systematic manner. However, it is important to note that no treatment-related harms were found in this comparative effectiveness report.	Revised text to report that no adverse effects were observed when adverse events were reported.

Commentator & Affiliation	Section	Comment	Response
Peter C. Esselman, MD, Chair Health Policy and Legislation Committee & Elliot J. Roth, MD Chair Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation (AAPM&R)	Discussion	Moreover, despite the lack of evidence found during this review, the group did pinpoint key research questions that still lack answers. AAPM&R strongly supports the recommendation for more research in this area, specifically within the TBI Model Systems programs, which as a venue, "should continue to explore comparative effectiveness by comparing interventions implemented in different TBI model systems locations." The TBI Model Systems are a valuable source of non-proprietary longitudinal data on what happens to people with brain injury. They are a key source of evidence-based medicine and serve as a "proving ground" for future researchers. They are also well-positioned to use large scale RCTs and prospective cohort designs with appropriate controls (as recommended by AHRQ) to move the field forward, in collaboration with other relevant agencies including the National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC).	Future research needs section enhanced and reference made to subsequent report outlining future research needs in more detail.
Peer Reviewer #1	General	This report systematically evaluates several clinically relevant questions regarding the post acute rehabilitation for patients having suffered traumatic brain injury.	Thank You.
Peer Reviewer #1	General	The questions posed, appropriately highlight the challenges faced clinically. Additionally, they reflect the paucity of available data in guiding outcomes based on treatment algorithms.	Thank You.
Peer Reviewer #1	General	The target population and audience are clearly defined and appropriate to the scope and associated questions.	Thank You.
Peer Reviewer #2	General	Overall the report makes a great effort to answer question in an area where the research is often lacking. The authors need to make sure that the message of "insufficient evidence" rather than "ineffective" clear in any summary of the report. The clinical meaningfulness is limited due to lack of solid conclusions. Probably the most importance aspect is setting a research direction for the future. the key questions are explicit and appropriate for this topic.	Cautionary statements about insufficient evidence versus evidence of ineffectiveness have been added to the Abstract, ES, and full report. They have been place in bold text to emphasize their importance.  Future research needs section enhanced and reference made to subsequent report outlining future research needs in more detail.
Peer Reviewer #3	General	The report is clinically meaningful in that it honestly reflects the state of research on the topic: there is insufficient research and it is not possible to compare treatment strategies. It is important to address how this review might be interpreted; lack of evidence is not tantamount to evidence of ineffectiveness.	Cautionary statements about insufficient evidence versus evidence of ineffectiveness have been added to the Abstract, ES, and full report. They have been place in bold text to emphasize their importance.

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Peer Reviewer #4	General	This is a comprehensive review of the limited (16 reviewable studies) literature on post-acute rehabilitation of moderate-severe TBI, that provides a good context and summary of this limited body of knowledge, but is unable to draw any conclusions.	Thank You.
Peer Reviewer #5	General	This is a very good review of the available literature of post-TBI rehabilitation. However the term holistic day treatment plans is somewhat confusing as this has a connotation of an outpatient rehabilitation program (at least to this reviewer). The key questions are appropriate and this topic is clinically meaningful.	Added text to clarify inpatient vs. outpatient programs. However, the holistic model seemed to be cited as a model in a couple of inpatient program studies.
Peer Reviewer #6	General	The report highlights the challenge faced by clinicians in determining the appropriate intervention strategy for patients with TBI. Evidence regarding one approach versus another is limited, as pointed out in this report.	Thank You.
Peer Reviewer #7	General	The report provides important information about the evidence (or lack thereof) about the effectiveness of comprehensive, multidisciplinary rehabilitation for those with traumatic brain injury (TBI) in the post-acute phase of recovery. The authors described the targeted population thoroughly and succinctly. By limiting the review to this particular phase of rehabilitation, it allowed the authors to provide readers with a thorough review of the small amount of the evidence that met their criteria.  The five questions are appropriate and relevant given the targeted population and phase of rehabilitation. I appreciate that the authors included other measures of participation once it was clear that question 3 could be answered as it was stated (albeit a priori).	Thank You.
Peer Reviewer #8	General	The authors have done a fair amount deal of work and are to be congratulated. Some concerns remain-The review does not adequately characterize the subjects being considered for studies at the time of the rehabilitation intervention It also mixes and matches inpatient and outpatient rehabilitation interventions and does not provide a good look at acute immediately after injury inpatient rehabilitation	Added text to describe the populations included in the individual studies.  Acute rehabilitation, or rehabilitation that occurs immediately post injury, was beyond the scope of this review. The nominator of this topic did not feel that early rehabilitation lacked sufficient evidence of effectiveness and was most concerned with programs treating individuals farther from their injuries.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #9	General	My general impression is that methodology employed in conducting the review, while mechanically sound, set the bar for establishing effectiveness so high that the outcome (i.e., inconclusive to low SOE) was pre-destined. Requiring studies to concurrently meet so many difficult-to-achieve qualifications (e.g., controlling for selection bias in community-based clinic samples, requiring use of outcome measures with pre-established MCID's and a-priori specification). The methodologic benchmarks utilized in the review represent ideals and do not reflect the quotidian realities of post-acute, community-based rehabilitation.	Inclusion criteria did require that studies were controlled (although we did not make specific exclusions based upon how studies addressed selection bias). Inclusion criteria did not require use of MCID.  We included study designs that would best produce believable results and agree that these designs are underutilized in this field. Text in Discussion section addresses concern that studies may not be indicative of commonly utilized populations and programs.
Peer Reviewer #10	General	Not clinically meaningful. Too much of the literature is excluded and the included literature is analyzed in too rigid a fashion.	Added text to describe recent IOM review with broader inclusion criteria and similar conclusions for related effectiveness questions.
Peer Reviewer #10	General	I have had the opportunity to review the report entitled " <i>Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury</i> ," and provide the following comments. As someone who provided some methodological consultation along the way, I'll discuss some of the "big picture context" that affects what the report can say and, indeed, the overall utility of the approach of structured evidence based review in this domain. Researchers and clinical experts in brain injury are well aware of the limited rigorous evidence that speaks to the efficacy and effectiveness of various forms of brain injury rehabilitation. Given a very limited evidence base, one might rightly question the utility of performing a structured evidence based review, since the benefits of such a review are most clear when there is a large volume of evidence of varying quality and conclusions.	Added text to present a more explicit purpose statement.
Peer Reviewer #10	General	One rationale given for such reviews in this "evidence landscape" is to highlight the methodological limitations that result in insufficient evidence so that future researchers can do things differently. Unfortunately, most of the reasons for the limited quality of evidence are known to current researchers but cannot easily be remedied because of major conceptual barriers (e.g., lack of a validated taxonomy of treatment active ingredients) or financial constraints (e.g., lack of funding of the scale required to do large trials of complex interventions).	Further attention to these methodological problems could have an impact on future research efforts including enhanced collaboration and additional funding.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #10	General	Secondly, reviewers often note that “absence of evidence is not evidence of absence” and, therefore, that failure to find clear efficacy or effectiveness data doesn’t mean that treatments are ineffective and doesn’t necessarily mean that they shouldn’t be paid for until we have the evidence. This, however, is disingenuous. Many reviews, including this one, are funded by entities that are seeking to influence health policy and ultimately payment policy. And many payers adopt the stance that the burden of proof is on the field to show efficacy, not shared between the field and the payer, to support the services that are the “best guess” for efficacy in a climate of uncertainty.	We have specifically included text describing that many treatments are not evidence-based, in terms of evidence obtained from CERs. Without this level of evidence, many decision makers must rely on lower quality evidence, such as consensus or expert opinion. However, it is beyond the scope of this report to make recommendations to decision makers.
Peer Reviewer #10	General	Thus, from the beginning of my involvement in this effort, I have been concerned about the ability of this report to help patients and caregivers, who are ultimately the potential beneficiaries of service. I’m afraid that a review of the report confirms that it offers them very little. To begin with, it was clear that the staff responsible for conducting the study had very limited knowledge of the field or its clinical or research realities. One of the supposed virtues of structured evidence based reviews is their objectivity, and organizers of such reviews may worry that inclusion of content experts will bias the results. But, as noted above, in a field where the interventions are complex, the available outcome measures are many, and the research designs are primarily not RCTs, it is very difficult for “generic” evidence based reviewers to adequately appreciate the analytic options. Despite the coaching of content experts during the planning stages, the authors of the report adopted a very traditional review medical evidence frame, which involved a number of problematic decisions:	Added text to Discussion section discussing the advantages of other types of reviews for this topic and to establish the difference between those types of reviews and a comparative effectiveness review, which has a standard methodology.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #10	General	<p><i>Standard design and outcome requirements:</i> The authors selected participation and self reported outcomes as the outcomes of interest. This lends itself to a structured review because all of the studies can be interpreted in a parallel fashion and we can examine the size of their impact in a similar fashion. This makes perfect sense when there is a clear-cut medical entity (e.g., atherosclerotic vascular disease), which has its effects on a narrow range of outcomes (e.g., patency of arteries, survival of heart muscle tissue, contractile properties of the heart). Medical researchers strive to develop ever improving treatments for maximizing those same outcomes and it is therefore logical to ask, “How well does angioplasty restore arterial patency as compared to a statin drug?” But most interdisciplinary brain injury rehabilitation programs develop in response to a cadre of patients with many perceived unmet needs, and they design themselves around whatever needs that can realistically hope to meet. Thus, there is no group of rehabilitation clinical researchers striving to develop “multidisciplinary treatment programs to maximize performance on the MPAI.” In other words, one could contrast a “standard clinical service” to which relatively homogeneous patients with the target problem are referred (and are not referred to it if they have some other problem) to an “individualized clinical service” that accepts a high proportion of heterogeneous patients referred to it with a range of problems and asks, “Given the resources we have and the range of problems this person has, what specific problems do we have the most potential to address?” This may turn out to be access to driving for one patient, dating skills for another, interpersonal friction at work with another, etc. While one would hope that these programs, in the aggregate, have an impact on extremely large scale outcomes like participation, without paying attention to their more focused goals it’s difficult to know whether failure to demonstrate a treatment impact reflects unrealistic measurement expectations or actual treatment ineffectiveness. Consider the following thought experiment: if one asked a bunch of researchers working on treatments for atherosclerotic vascular disease, “What outcome measures would be sensitive to the impact of your treatment?”, one would likely get widespread endorsement of one or more of the outcomes mentioned above. If one asked the leaders of all of the programs analyzed here, to nominate one or more measures that they would predict to be sensitive to the impact of their program, it seems quite unlikely that a consensus would have formed around the specific narrow set of outcome measures that the authors required.</p>	<p>Patient-centered outcomes are the most valuable outcomes in comparative effectiveness research. While attaining short-term goals of rehabilitation interventions is also important, rehabilitation should ultimately make an important impact on individual’s lives.</p> <p>Additionally, based upon the recent IOM review, it is clear that the inclusion of a broader set of outcomes and study designs would not have permitted more meaningful conclusions.</p>

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #10	General	The adoption of this standard set of requirements, as noted by the authors, resulted in the exclusion of the vast majority of the available literature. One might be satisfied by this if one believes that the remaining literature is completely uninformative. But in the early design stages, the authors reached the decision to exclude all of the treatments that were pursuing more focused aims, in favor of those that were pursuing (or were perceived to be pursuing) global participation aims. But no one knows of a treatment that directly enhances participation. So even treatment programs that “target participation” do so through painstakingly addressing many building blocks such as mood, social skills, fatigue, cognitive impairments, transportation obstacles, etc. Failing to understand these more focused treatments also fails to understand the active ingredients that are aggregated into the macro programs the authors studied.	Inclusion criteria developed to capture a set of studies most likely to lead to believable results to key questions.
Peer Reviewer #10	General	<i>Multidisciplinary rehabilitation vs. nothing?</i> Many individuals with neurocognitive impairments will consume some kind of resources no matter what. Consider a client who is unemployed, depressed, has pain complaints, and gets into interpersonal conflicts after a brain injury. We could imagine that such an individual either receives multidisciplinary rehabilitation or contentedly receives nothing. Or, more plausibly, we could imagine that such an individual might receive multidisciplinary rehabilitation or some combination of unemployment/disability payments and services, frequent presentations to her primary care physician for miscellaneous somatic complaints, periodic crisis intervention in the mental health system, family intervention at the expense of family members' work hours, and/or “services” from the criminal justice system. In a very real way, then, the relevant comparison is the outcomes and costs of multidisciplinary rehabilitation vs. <i>the other systems and resources that will be invoked without it</i> . This highlights the consequences of the failure of partnership of payers and policy makers with providers and researchers. A different perspective would commit to providing resources to individuals with needs and asking about the most cost-effective arrangement of those resources.	Understanding and estimating the societal costs of supporting those with impairments from moderate to severe TBI is important information that would add to the significance of research on this topic.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #10	General	<p><i>Efficacy or Comparative Effectiveness:</i> It might be argued that comparative effectiveness research is premature before basic efficacy and effectiveness has been firmly established. The authors note that many of the studies they reviewed compared two different models of treatment and found negligible differences in outcome. In the absence of firm efficacy data, however, we don't know whether this means that both programs are similarly effective or both programs are similarly ineffective. Since most multidisciplinary treatment programs include a certain amount of tailoring to individual patient problems, and deal with practical realities of patients' lives, the commonalities between treatment models may be larger than the philosophical differences between them. And when one uses relatively global outcome measures to compare them, this is less likely to reveal the modest differences that may exist, which may be more in the way of how patients solve problems than whether or not they do so. The reason for this premature jump to comparative effectiveness trials, presumably, is that institutions are already offering and charging for some form of postacute service and it seems unethical and/or poor business to suddenly decide not to treat half of the people who are currently being treated. But this highlights all the more the need for a partnership between payers and researchers in the efforts to optimize the services provided. Related to this, it would be helpful to highlight more obviously which studies are truly efficacy/effectiveness studies (with a no-treatment group, wait list control group, etc.) and which are comparative effectiveness studies, and then to note this conceptual and methodological problem more overtly in the discussion.</p>	<p>Ethical considerations likely make comparative effectiveness studies on this topic more feasible. Discussion addresses the potential to address effectiveness may be feasible in chronic patients by using waitlist controls.</p> <p>Added text to Discussion section to elaborate on subgroups addressed in eligible studies.</p>

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #10	General	In summary, this report addresses a very narrow question: What is the evidence from specific kinds of studies, that multidisciplinary rehabilitation, as grossly characterized, positively affects productivity as measured in very specific ways? Or worse, What is the evidence from specific kinds of studies that a particular form of multidisciplinary rehabilitation positively affects participation <i>more than another form</i> as measured in very specific ways? The questions that would actually be useful to answer are quite different. What kinds of benefits (and harms) are experienced by patients participating in various forms of multidisciplinary rehabilitation? What outcomes appear to be most affected by such programs for which patients? What elements of such programs appear to have impact for what potential outcomes? Until we have the methods to wring useful information out of the majority of studies, rather than exclude the majority of studies from analysis, I believe we will know very little about the impact of multidisciplinary rehabilitation treatment. As written, this report has plenty to say about the problems that emerge in the world of clinical research and very little to say about the treatments that were the subject of the study.	<p>This is an important point. The challenges presented in this review highlight the poor fit in applying methods for comparative effectiveness reviews to complex conditions. While data were being analyzed for this review, we explored other approaches to reviewing evidence on complex conditions. However, they did not seem applicable at that point in the process. Future research attempting to synthesize evidence on multidisciplinary programs should explore other approaches, such as realist reviews. The suggested key questions would nicely fit that approach. Added text to the discussion of the ES and full report to address this idea.</p> <p>Also added text to the Discussion section addressing these types of questions.</p>
Peer Reviewer #11	General	Nice review and helps to lay the groundwork for future studies...could be a little more specific in this area, but I don't think that is the primary purpose of this paper. Page 23, there is a spelling mistake in the second paragraph (rehabilitation treatments)	Future research needs section enhanced and reference made to subsequent report outlining future research needs in more detail.
Peer Reviewer #12	General	this report articulates the key questions clearly, as well as the population definition and limitations in type of treatment selected for examination, although some of the studies included (outdoor adventure and telephonic) appear to contradict the proposed focus.	Thank You.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #12	General	<p>The report is marginally clinically meaningful, and unfortunately could produce significant unintended negative consequences for persons who may benefit from or be in need of post-acute rehabilitation services due to the wording of findings and the failure to clearly state that this is a review of 16 heterogeneous studies (8 or fewer used in some instances) reflecting approximately 1% or less of the published peer-reviewed literature. Overall, there are fundamental issues in that the authors seemingly have minimal contextual knowledge of post-acute rehabilitation, as is evident is assumptions stated regarding theoretical goals (return to work or pre-injury levels) rather than current pragmatics of post-acute rehabilitation addressing what had been acute rehabilitation issues decades ago, personal and community ADL's and reducing burden of care and supervision needs, particularly with the severe TBI population.</p>	<p>It is inaccurate to say that our conclusions were drawn based upon 1 percent of the literature. Our review utilized a comprehensive search strategy because there is a relatively poor fit between indexing and this topic, terminology used is inconsistent making reliance on key words challenging, and we made a conscious decision to maximize recall at the expense of precision to ensure that we identified all of the relevant literature through a thorough screening process.</p> <p>Methodological decisions were made to insure appropriate scientific evidence base from which to draw conclusions to key questions. IOM review with broader inclusion criteria reached similar conclusions for comprehensive multimodal cognitive rehabilitation for moderate to severe TBI.</p>

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #12	General	The authors fail to address the critical outcomes of reduced burden of care and the maintenance value of post-acute rehabilitation warranted by the numerous clinical and research articles noting the deterioration of individuals post-TBI and the importance of viewing this condition in a chronic disease model. Further, the sample selection criteria appear both restrictive and limiting to provide a foundation for a meaningful review of this intervention area, whose complexity is extremely high and whose research funding is extremely low.	<p>Reduced burden of care and the maintenance value of rehabilitation are important outcomes of TBI rehabilitation. Burden of care outcomes would likely have been included as secondary outcomes if otherwise eligible studies reported those outcomes. Maintenance of outcomes is more difficult to address, but we have added text to the Discussion to describe these potential benefits of rehabilitation.</p> <p>Methodological decisions were made to insure appropriate scientific evidence base from which to draw conclusions to key questions. IOM review with broader inclusion criteria reached similar conclusions for comprehensive multimodal cognitive rehabilitation for moderate to severe TBI.</p>
Peer Reviewer #12	General	Statements indicating increased funding for research have no substantiation for the civilian, post-acute, moderate to severe TBI world. Such funding is largely Defense Department driven with a predominantly mild TBI population and little attention or focus on issues relevant to this review. While this report is a much needed step, the lack of contextual knowledge, restrictive review criteria and language choices describing analyses and conclusion fails to either answer key questions appropriately.	Deleted text to avoid potential misunderstanding.
Peer Reviewer #12	General	Many readers may assume an absence of evidence (by these criteria based on 16 studies) is evidence of absence, and the paper fails to speak strongly enough on this point and the major self-imposed limitations of both the outcome criteria examined and limitations excluding 99+% of the studies. The review is neither contextualized nor conclusive, and needs to reflect more critically on its own shortcomings in the abstract and summary as well as the body of the report.	This is a literature review. We are constrained by the limitations of the literature
Peer Reviewer #13	General	<p>Thank you for the opportunity to review this CER. It is quite valuable to know where we stand with the evidence on this topic even if it is limited.</p> <p>There are important recommendations relating to standardized research and clinical outcome metrics that should impact research funding guidance to drive improvements in future similar efforts. However, the level of available evidence is not likely to have significant impact on current clinical practice patterns or system level policy.</p>	We have made methodological recommendations but they are directed at future research.

Source: <http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1141>

Published Online: April 2012

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #14	General	Although the report findings cannot be immediately translated into patient care, the authors have presented a well written and thoughtfully presented review of the literature with recommendations for future research that can improve patient outcomes.	Thank You.
Peer Reviewer #14	General	The definitions of productivity and community integration, the primary outcomes selected for this review, are defined on page 4 of the introduction but are used earlier in the report. Definitions also should be included in the Executive Summary, ES-3, li 17.	Added definitions to ES; and first occurrence in report.
Peer Reviewer #14	General	A few minor editorial comments: Search for the occurrence of double periods at end of sentences and replace. A few I noticed were pg ES-8, li 16, 34, pg 1, li 34  pg 5, li 6 phases no pases  pg 52 li 57 a word likely is missing. Perhaps the line should read “requires an assessment” ?  I believe aneurysm is preferred to aneurism, but only one spelling should be used. Both appear in the report.	Corrected. Thank You.
Susan H. Connors President/CEO Brain Injury Association of America	General	we would like to applaud the decision by AHRQ to focus attention on the effectiveness and comparative effectiveness of multidisciplinary postacute rehabilitation for moderate to severe traumatic brain injury (TBI). Individuals with TBI and their families are depending on increased support for research and the expansion and improvement of evidence-based practices to enhance access to medically necessary health care. We support many of the findings and conclusions in the draft report. However, there are several findings that we recommend be modified. We also recommend improvements in the way in which the findings are communicated.	Thank You.
Susan H. Connors President/CEO Brain Injury Association of America	General	BIAA strongly disagrees with the decision not to include all reliable evidence consistent with the well accepted Hierarchy of Evidence. However, given the decision to only include so-called “high quality conclusive evidence” (RCT and cohort studies that meet very strict criteria), we believe that it is incumbent on the authors to modify the title, the structured abstract, the executive summary, and the text to reflect the limited focus of the report. We recommend that the title of the report be modified as follows: “ <i>Review of Sixteen Studies of Multidisciplinary Postacute Rehabilitation for Moderate to Severe Brain Injury.</i> ” In addition, the structured abstract should indicate that “High quality conclusive evidence from rigorously conducted reviews is a high bar currently met by only a small portion of medical interventions (and even smaller portion of rehabilitation interventions)” [see page 51 of the paper]. All statements in the executive summary and in the report related to the “available evidence” [see page 51 and ES 23-24] should be modified to indicate that the authors are referring to available evidence from 16 studies.	Due to the heterogeneous nature of the interventions, comparisons, and outcomes used across all studies that met inclusion criteria – most conclusions were drawn specifically from one particular study.

Source: <http://effectivehealthcare.ahrq.gov/search-for-guides-reviews-and-reports/?pageaction=displayproduct&productID=1141>

Published Online: April 2012

Commentator & Affiliation	Section	Comment	Response
Susan H. Connors President/CEO Brain Injury Association of America	General	<p>We also recommend that the following statements of limitations be included in the abstract, executive summary and text. These statements of limitations are derived from the recent Institute of Medicine reports on essential health benefits and cognitive rehabilitation.<sup>7, 8</sup></p> <p><input type="checkbox"/> Despite the scarcity of conclusive high quality evidence, we support the ongoing use of promising practices/approaches while improvements are made in the standardization, design, and conduct of research studies.</p> <p><input type="checkbox"/> Policy should facilitate the application of techniques based on best available evidence with the proviso that objectively measurable functional goals are articulated and tracked and treatment continues so long as it is medically necessary.</p> <p><input type="checkbox"/> Conclusions based on the limited evidence regarding effectiveness of postacute rehabilitation do not indicate that the effectiveness of particular interventions are limited.</p> <p><input type="checkbox"/> Limitations of the evidence do not rule out meaningful benefit.</p> <p><sup>7</sup> IOM (Institute of Medicine). 2011. <i>Essential Health Benefits: Balancing Coverage and Cost</i>. Washington, DC: The National Academies Press.<sup>7</sup></p> <p><sup>8</sup> IOM (Institute of Medicine). 2011. <i>Cognitive Rehabilitation Therapy for Traumatic Brain Injury: Evaluating the Evidence</i>. Washington, DC: The National Academies Press.</p>	<p>Our study was separate from the IOM study and has limitations relevant to the objectives of this particular research. Although our objectives were similar, the report and our charge from our supporting agency are not identical to that of the IOM.</p> <p>However, similar statements are included in our report.</p> <p>Abstracts for reports have word limitations that prevent extensive lists of limitations.</p> <p>We do, however, refer to the IOM report in our report.</p>
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p>We recommend that the comparative effectiveness reviews (CER) include expanded research assessments on the following five categories:</p> <ol style="list-style-type: none"> <li>1. Interventions for individuals diagnosed with a mild TBI</li> <li>2. The use of cognitive assistive devices in TBI rehabilitation</li> <li>3. Interventions for individuals with a TBI 65 years and older as a unique study group</li> <li>4. Public and private payer challenges in provision of needed, comprehensive TBI rehabilitation</li> <li>5. Individuals with a TBI and one or more co-morbid disability</li> </ol> <p>We are providing research supported rationales for the inclusion of each of these recommendations within the AHRQ report. The full reference list for the cited supporting research is found at the end of this document.</p>	<p>1 &amp; 2 represent important research questions, but were unfortunately outside the scope of this review and have a separate set of scientific evidence.</p> <p>3 &amp; 5 were covered by our review, however none of the eligible studies examined these subgroups of patients specifically.</p> <p>4 – is a difficult question to address in a CER, but we do address these issues in the Introduction highlighted the need for an evidence base.</p>

Commentator & Affiliation	Section	Comment	Response
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p><b>1. Interventions for individuals diagnosed with a mild TBI:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> 80% of all TBIs are mild, 10% of which will result in disability (Kraus &amp; Sorenson, 1994).</li> <li><input type="checkbox"/> Observable permanent damage occurs to the brain structure after “mild” trauma (Jane, Steward, &amp; Gennarelli, 1985). <input type="checkbox"/> The presence of acute neuropsychological and physical deficits acquired from a mild TBI may be maintained long after symptoms resolve (Macciocchi et al., 1996; Mcree et al., 2003).</li> <li><input type="checkbox"/> College students who sustained asymptomatic mild TBIs were abnormally prone to mental inefficiency when physiologically stressed (Gronwall, 1989).</li> <li><input type="checkbox"/> Sport-related concussions resulted in cognition and balance impairments on repeated examinations (Macciocchi et al., 1996; Mcree et al., 2003).</li> <li><input type="checkbox"/> TBIs categorized by mild severity are not uniform in symptoms. Many may require treatments effective for other severities. (Saatman et al., 2008).</li> </ul>	While we agree that this is an important issue, this topic has a separate set of research and was beyond the scope of this review. See the recent IOM review for comprehensive assessment of effectiveness of cognitive rehabilitation for mild TBI.
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p><b>2. The use of cognitive assistive devices in TBI rehabilitation:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> Cognitive prosthetic systems can achieve significant increase in function, self confidence, and problem-solving ability after an initially poor prognosis of recovery (Cole et al., 1994). <input type="checkbox"/> External memory aids are effective tools that compensate for prospective memory impairment following a TBI and aid in completing daily life tasks (Dowds et al., 2011).</li> <li><input type="checkbox"/> Clinicians may not implement aids because of inexperience with technology, and patients’ effective use may be limited by little systematic training (Hart et al., 2004; Sohlberg et al., 2007).</li> </ul>	While we agree that this is an important issue, this topic has a separate set of research and was beyond the scope of this review.
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p><b>3. Interventions for individuals with a TBI 65 years and older as a unique study group:</b></p> <ul style="list-style-type: none"> <li><input type="checkbox"/> 20% of individuals with a TBI are over 65 years of age, 73% of which had a medical condition before injury compared to 28% of younger adults (Thompson, McCormick, &amp; Kagan, 2006).</li> <li><input type="checkbox"/> When compared to younger patients, these older individuals with a TBI have twice the mortality rate, poorer functioning with less severe TBI, longer rehabilitation periods, and worsening prognosis related to poorer neuronal reserve and quality (Chua, Ng, Yap, &amp; Bok, 2007).</li> </ul>	This subgroup of patients was covered by our review; however none of the eligible studies examined these subgroups of patients specifically.

Commentator & Affiliation	Section	Comment	Response
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p><b>4. Public and private payer challenges in provision of needed, comprehensive TBI rehabilitation:</b></p> <p><input type="checkbox"/> There are Medicaid waivers that support community based long term care for individuals with a TBI which have long service provision wait lists. In States without these waivers, individuals with a TBI are placed in often medically not necessary nursing homes instead of receiving community based services (Katz, Zasler, &amp; Zafonte, 2007).</p> <p><input type="checkbox"/> With poor guidance, it is difficult to find the appropriate resources or navigate the points of entry into publicly funded systems, which are often fragmented and poorly coordinated. Points of entry often have artificial barriers defined by narrow eligibility criteria (Katz et al., 2007).</p> <p><input type="checkbox"/> Cognitive and behavioral problems may not fit characteristics of original medical rehabilitation qualifications and thus payers may not cover these types of services (Katz et al. 2007).</p>	This is a difficult question to address in a CER, but we do address these issues in the Introduction highlighting the need for an evidence base.
Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.	General	<p><b>5. Individuals with a TBI and one or more co-morbid disability:</b></p> <p><input type="checkbox"/> 56.3% of individuals with a TBI are on Medicaid. This creates large economic burdens, particularly when it is compounded with concomitant psychiatric disability (Wei, Sambamoorthi, Crystal, &amp; Findley, 2005).</p> <p><input type="checkbox"/> Psychiatric and psychosocial difficulties are often preexisting conditions in individuals with a TBI and may become comorbidities following injury (Katz et al., 2007).</p> <p><input type="checkbox"/> There is a lack of understanding on the economic impact of diagnosed comorbidities in the TBI population on Medicaid, and the extent to which appropriate treatment is received for these conditions. (Wei et al., 2005).</p>	This subgroup of patients was covered by our review questions, however none of the eligible studies examined these subgroups of patients specifically.

Commentator & Affiliation	Section	Comment	Response
<p>Eileen Elias, M.Ed. Director Disability Service Center Senior Policy Advisor for Disability and Mental Health TBI Resource Optimization Center (ROC) and its Advisory Group, JBS International, Inc.</p>	<p>General</p>	<p>The importance of the research endeavor initiated by the AHRQ draft report is recognized by many TBI experts. The following comments regarding the need for additional comparative effectiveness research on TBI treatment and rehabilitation are from three members of the TBI ROC advisory group.</p> <p><i>Richard V. Briggs, Jr., Major, U.S.A.F. Retired Veterans Program, Manager Brain Injury Association of Michigan</i></p> <p><input type="checkbox"/> "In working with our returning combatants with TBI every day, I do see the need for this program to be successful, to be completed quickly, and to be implemented precisely. Our heroes are not getting the level of care they need and deserve, and this effort may prove to be the key to getting them that very specialized care".</p> <p><i>Joe Cannelongo C.E.O., AdvoCare Group</i></p> <p><input type="checkbox"/> "Visual perceptual remediation services can be very significant in enhancing recovery and in developing coping skills".</p> <p><i>Pamela Gonzalez Manager of Quality and Research, American Academy of Physical Medicine and Rehabilitation</i></p> <p><input type="checkbox"/> "There is a need for more research in this area due to the difficulty in studying demonstrated benefits of one approach over another including defining key research questions, allowing room for evidence of all classes, determining that no harm is being inflicted by a treatment, and detailing that a lack of evidence is not proof that a treatment is ineffective".</p> <p><input type="checkbox"/> "AAPM&amp;R largely support the findings of AHRQ in reference to the efficacy of a holistic approach to postacute brain injury rehabilitation". Again, we thank you for the effort of AHRQ's staff to create the "Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury in Adults" report. We appreciate the special attention on TBI and share the views expressed in the report.</p>	<p>Thank You.</p>
<p>Peter C. Esselman, MD, Chair Health Policy and Legislation Committee &amp; Elliot J. Roth, MD Chair Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation (AAPM&amp;R)</p>	<p>General</p>	<p>The Academy believes that with some modifications to the federal research agenda, and with adequate funding, we can establish more evidence to drive effective treatments in postacute care for the 1.7 million people each year who sustain brain injuries and are fighting to return to meaningful and productive lives. AAPM&amp;R would like to echo AHRQ's conclusion that the need for more research in this area is made more challenging due to the difficulty in studying demonstrated benefits of one approach over another. Specifically the Academy supports the conclusion that, "further research should address methodological flaws common in these studies and further address effectiveness research questions." The Academy further agrees that "failure to draw broad conclusions must not be understood to be evidence of ineffectiveness". In light of this finding, it is important that our patients have access to postacute rehabilitation that is pragmatic, based on consensus guidelines, and that is associated with good programmatic outcomes, while the body of research evidence is further developed.</p>	<p>Agreed.</p>

Commentator & Affiliation	Section	Comment	Response
Peter C. Esselman, MD, Chair Health Policy and Legislation Committee & Elliot J. Roth, MD Chair Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation (AAPM&R)	General	<p>The preliminary outcome of this study showing that additional research is needed regarding the effectiveness of TBI postacute rehabilitation is aligned with recent publications of the Institute of Medicine of the National Academies (IOM). Both reports addressed treatment for TBI. The first study, released on October 7, 2012, titled “Essential Health Benefits – Balancing Coverage and Cost,” detailed recommendations to the Department of Health and Human Services (HHS) regarding the criteria and methods for determining and updating the essential health benefits package as mandated through the health care reform law (PPACA). As part of the medical necessity portion of the report, IOM allows for the use of the hierarchy of evidence, which includes, but is not limited to Class I research, case studies, cohort studies, and professional consensus. Specifically, IOM expresses that accepting other classifications of evidence is appropriate when Class I research does not or cannot exist for the treatment of a specific condition or disease process. This encouraging finding was echoed in the AHRQ study in which cohort studies were utilized in addition to randomized control trials (RCTs). The Academy supports this approach when rehabilitation does not fit neatly into a RCT methodology. AAPM&amp;R further encourages additional research to broaden its scope to include high quality cohort studies that specifically utilize practice-based evidence and professional consensus. On October 11, 2011, IOM released a second report, this time to the Department of Defense (DOD) titled, “Cognitive Rehabilitation Therapy (CRT) for Traumatic Brain Injury: Evaluating the Evidence.” Cognitive rehabilitation therapy is one component of a comprehensive rehabilitation package. In the report, IOM experts expressed support for “the ongoing use of CRT for people suffering from a TBI while improvements are made in the standardization, design, and conduct of studies, adding, “CRT interventions are promising approaches, but further development and assessment of this therapy is required.” <b>The Academy recognizes the similarities in outcomes of both the AHRQ study and the IOM study and applauds DOD’s assertion that access to these treatments should remain available while additional research is conducted.</b></p>	Agreed.

Commentator & Affiliation	Section	Comment	Response
Peter C. Esselman, MD, Chair Health Policy and Legislation Committee & Elliot J. Roth, MD Chair Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation (AAPM&R)	General	In conclusion, AAPM&R largely supports the findings of AHRQ in reference to the efficacy of a holistic approach to postacute brain injury rehabilitation. There is additional work to be done in this area including: <ul style="list-style-type: none"> <li><input type="checkbox"/> Defining key research questions</li> <li><input type="checkbox"/> Allowing room for multiple classes of evidence</li> <li><input type="checkbox"/> Determining that no harm is being inflicted by a treatment, and</li> <li><input type="checkbox"/> Detailing that a lack of evidence is not proof that a treatment is ineffective</li> </ul> The Academy believes that by mobilizing federal research agencies and setting priorities in this direction, we are one step further towards understanding the best rehabilitation strategies to improve outcomes in postacute rehabilitation, including decreased dependence on long term care due to severe, chronic disability. AAPM&R appreciates the opportunity to comment on Multidisciplinary Postacute Rehabilitation for Moderate to Severe Traumatic Brain Injury (TBI) in Adults. If there are questions concerning the Academy's comments, please contact Sarah D'Orsie, Manager of Government Affairs, (202)349-4277 (SD'Orsie@aapmr.org.)	This work will be continued with the subsequent Future Research Needs project.
R. Scott Ward, PT, PhD President American Physical Therapy Association (APTA)	General	Recommendation 1 (Heterogeneity of TBI population): APTA appreciates the need to look at the efficacy of postacute rehabilitation in the traumatic brain injury patient, but does have concerns about the heterogeneity of this patient population. The ability to generalize the findings of this analysis to traumatic brain injury population may have inherent flaws given the vast differences in these patients which include the severity of their injury, co-morbid conditions, pre-morbid functioning, substance abuse, psychiatric problems, and various environmental factors.	Added text to the Introduction emphasizing the heterogeneity.
R. Scott Ward, PT, PhD President American Physical Therapy Association (APTA)	General	Recommendation 2 (Inclusion of other outcome tools): In previous comments, APTA suggested that AHRQ consider secondary outcomes in its key question comments on this research topic. APTA specifically suggested the inclusion of gait speed as measured through the Functional Gait Assessment (FGA), the High Level Mobility Assessment Tool (HiMAT), or the Six Minute Walk Test. APTA recognizes that, with brain injury and the continuum of injury severity, target outcomes are accordingly diverse – as are the impairments, activity limitations, and participation restrictions with which patients present. Therefore, the use of other valid and reliable tests to measure important determinants of functional outcomes would be beneficial.	The suggested outcomes are not patient-centered outcomes of comprehensive rehabilitation programs. While improving these measures is important, the goal of our review is to determine whether programs improve more global measures.

Commentator & Affiliation	Section	Comment	Response
R. Scott Ward, PT, PhD President American Physical Therapy Association (APTA)	General	Recommendation 3 (Methodology limitations): APTA appreciates the rigorous methodology of this review which include randomized controlled trials; however, we feel that the methodology poses limitations by excluding relevant research. Rehabilitation consists of multiple component interventions that are difficult to study in a randomized controlled trial (RCT) approach, while also being highly challenging for patients or therapists to be blinded to such interventions. This makes study of the area quite complex. APTA emphasizes that any identified shortage in randomized controlled trials or perceived lack in quality evidence represents an opportunity for AHRQ to pursue further investigations. The value of these interventions should not automatically be assumed inconsequential, but rather simply understudied. APTA applauds AHRQ in recommending a consistent use of taxonomies such as the ICF to better communicate and standardize the various domains of functioning that may impact the individual with TBI.	Prospective observational studies were included. Inclusion of other research designs was explored; however, high risk of bias in these study designs prevented believability of results of those studies.
Public Reviewer #1	General	REDACTED	
Peer Reviewer #1	Clarity and Usability	This report is well structured in its systematic assessment of this clinically relevant and timely topic. The essential goals, strategies and conclusions, with appropriate limitations, are clearly presented. The Conclusions however are best suited for researchers in the field and will undoubtedly serve to inform and guide essential areas of focus in this area. The conclusions however should have limited clinical impact due to the narrowed scope of interest, the many limitations posed and the inability to use data/outcomes, etc... to effectively assess the current strategies.	Put her on the FRNs panel
Peer Reviewer #2	Clarity and Usability	Very well written, clear and concise. the conclusions can be used to inform further research but not policy in my opinion. this needs to be made very clear in any iteration of the report including executive summary or abstract.	Emphasized the limitations of conclusions to decision-makers and the point that insufficient evidence is not evidence of ineffectiveness.
Peer Reviewer #3	Clarity and Usability	The report is clear and well organized. However, it should not be used to inform policy or practice (or funding decisions) other than, perhaps, to fund further clearer research on this topic	Thank You.
Peer Reviewer #4	Clarity and Usability	This report is well-structured and organized. There are no meaningful findings that can be used to inform policy (other than "we need more research in this area).	Thank You.
Peer Reviewer #5	Clarity and Usability	Overall report is well structured and organized. Main points are clearly presented and the limitations of the research data are adequately presented. Studies did not include patients with common comorbid problems such as psychiatric diagnosis and substance abuse. This should be more effectively reiterated in the results and the future studies section.	Thank You.

Commentator & Affiliation	Section	Comment	Response
Peer Reviewer #6	Clarity and Usability	I found the summary sections to be a bit easier to follow. These were clearly written and provided a nice framework. The other very detailed sections are nice sources for reference and further background information as needed by the reader.	Thank You.
Peer Reviewer #7	Clarity and Usability	Is the report well structured and organized? YES Are the main points clearly presented? YES Can the conclusions be used to inform policy and/or practice decisions? NO, given that there is such limited amount of evidence.	Thank You.
Peer Reviewer #8	Clarity and Usability	organization has no concerns	Thank You.
Peer Reviewer #9	Clarity and Usability	The Executive Summary is well-organized but the body of the report is difficult to follow. I had to repeatedly go forward and/or backward in the manuscript to access the information I needed to fully grasp the material I was currently reading. I know this structure is conventional but it is also very clunky.	Thank You. Template not always clearest way to present information. Sorry.
Peer Reviewer #10	Clarity and Usability	The report is clear, but it doesn't provide much in the way of useful information because of its narrow focus.	Thank You.
Peer Reviewer #11	Clarity and Usability	Discussion section read well. May consider additional/specific recommendations for future areas of research based on this review.	Expanded Future Research Needs Section and referred to subsequent project on Future Research Needs.
Peer Reviewer #12	Clarity and Usability	The report is very well structured and organized with clarity and supported by detailed tables that complement the text. The conclusion cannot be used to inform policy and/or practice decisions, as is indicated by the authors of the report themselves in their acknowledgement of the report as unsatisfactory P52.	Thank You.
Peer Reviewer #13	Clarity and Usability	The report is very clearly written and well organized. Key points are clearly stated and well supported by the accompanying synthesis and analysis.	Thank You.
Peer Reviewer #14	Clarity and Usability	The report is well written and main points are clearly and effectively presented. Report conclusions follow from results and are presented within the context of the many other systematic reviews that have been conducted on this topic.	Thank You.