

AHRQ Comparative Effectiveness Review Surveillance Program

CER #25: Traumatic Brain Injury and Depression

Original Release Date: April, 2011

Surveillance Report: March, 2012

Surveillance Report: November, 2012

Surveillance Report: August, 2014

Summary of Key Findings from Surveillance Reports:

- All conclusions for KQ1-6 are still considered valid
- New significant safety concerns were identified including warnings about contraindications for one medication
- Several new studies were identified, including imaging studies aimed at linking neural changes to depression, studies examining patient factors associated with prevalence of depression, a study assessing markers to predict treatment response, and several studies on non-pharmacological treatment modalities

Signal Assessment: The signals examined in this surveillance assessment suggest that the original CER is likely up to date.

Authors:

Maya O'Neil
Shammarie Mathis
Ryan McKenna
Johanna Anderson
Kelly Vander Ley
Karli Kondo
Mark Helfand

Conflict of Interest:

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

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Reviewers

Nancy Temkin, PhD
Professor of Biostatistics and Neurological Surgery
University of Washington
Seattle, WA

James Chesnutt, MD
Pediatrics, Orthopedics & Rehabilitation, and Family Medicine
Oregon Health & Science University
Portland, OR

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Introduction

The purpose of the surveillance process for the EPC Program is to decide if and when a systematic review is in need of updating. Approximately 25 systematic reviews are selected for surveillance annually based on popularity, use in obtaining continuing medical education certificates, potential impact for changing the field, and use in clinical practice guidelines.

Comparative Effectiveness Review (CER) #25 titled “Traumatic Brain Injury and Depression” was published in April, 2011.¹ Previous surveillance assessments were conducted in March, 2012 and November, 2012². In November, 2012 the CER’s priority for updating was low. The CER was again selected for surveillance assessment based on popularity, potential impact, and other measures of use collected as of June, 2013.³

The key questions for the original CER are as follows:

- **Key Question 1.** What is the prevalence of depression after traumatic brain injury, and does the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury or other patient factors influence the probability of developing clinical depression?
- **Key Question 2.** When should patients who suffer traumatic brain injury be screened for depression, with what tools, and in what setting?
- **Key Question 3.** Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, post-traumatic stress disorder (PTSD), substance abuse, and major psychiatric disorders?
- **Key Question 4.** What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing psychotropic medications, individual/group psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine, neuromodulation therapies, and other therapies?
- **Key Question 5.** Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?
- **Key Question 6.** Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, preexisting mental health status or medical conditions, functional status, and social support?

Our surveillance assessment began in April, 2014. We conducted an electronic search for literature published since the most recent surveillance report search date. After completing a scan of this literature to identify evidence potentially related to the key questions in this CER, we contacted experts involved in the original CER to request their opinions as to whether the conclusions had changed.

Methods

Prior Surveillance

Surveillance reports for the original CER were released in March, 2012 and November, 2012. Information across these two reports included a search for relevant literature published between October 20, 2010 and October 31, 2012, expert opinion, and a search of FDA reports. The findings from these reports are included in our assessment.

Literature Searches

We conducted a limited literature search covering November 1, 2012 to January 30, 2014, using the identical search strategy used for the original report¹ and searching for studies published since the end date of the most recent surveillance search. This search included the same ten journals selected for the prior surveillance assessments. This process included selecting journals from among the top 10 journals from relevant specialty subject areas (Appendix A) and among those most highly represented among the references for the original report (Appendix B). The included journals were five high-profile general medical interest journals (New England Journal of Medicine, Lancet, JAMA, British Medical Journal, and Annals of Internal Medicine), and five specialty journals (American Journal of Psychiatry, Brain Injury, Journal of Neuropsychiatry and Clinical Neuroscience, Archives of Physical Medical Rehabilitation, and Journal of Head Trauma Rehabilitation). The search strategy is reported in Appendix C.

Study Selection

Using the same inclusion and exclusion criteria as the original CER (see Appendix D), one investigator reviewed the titles and abstracts of the high-impact journal search results (see Appendix E).

Expert Opinion

We shared the conclusions of the original report and the newly identified studies with eight experts in the field (original peer reviewers and technical expert panel members (TEP) to request their assessment of the need to update the report and their recommendations of any relevant new studies. Two subject matter experts responded to our request. Appendix F shows the form that the experts were asked to complete.

Horizon Scanning High-Impact Potential

The AHRQ Healthcare Horizon Scanning System identifies emerging health care technologies and innovations with the potential to impact health care for AHRQ's 14 priority conditions.⁴ We reviewed the Depression and Other Mental Health Disorders section to identify new potentially high-impact interventions related to the key questions in this CER. Potentially high impact interventions were considered in the final assessment of the need to update.

FDA Black Box Warnings

We searched the FDA MedWatch online database website for black box warnings relevant to the key questions in this CER.

Check for Qualitative Signals

The authors of the original CER conducted qualitative synthesis of data on prevalence, harms and outcomes of depression after Traumatic Brain Injury (TBI). We compared the conclusions of the included abstracts to the conclusions of the original CER and surveillance reports, and assessed expert opinions to identify qualitative signals to update.

Compilation of Findings and Conclusions

For this assessment we constructed a summary table (Appendix G) that includes the key questions, the conclusions from the original and most recent surveillance assessment, the findings of the new literature search, and the expert assessments that pertained to each key question. Because we did not find any FDA black box warnings relevant to the key questions in this CER, we did not include a column for this in the summary table. We categorized whether the conclusions need updating using a 3-category scheme:

- Original conclusion is still valid and this portion of the CER is likely not in need of updating
- Original conclusion is possibly out of date and this portion of the CER may need updating
- Original conclusion is out of date.

We considered the following factors when making our assessments:

- If we found no new evidence or only confirmatory evidence and all responding experts assessed the CER conclusion as still valid, we classified the CER conclusion as likely not in need of updating.
- If we found some new evidence that might change the CER conclusion, and /or a minority of responding experts assessed the CER conclusion as having new evidence that might change the conclusion, then we classified the CER conclusion as possibly out of date.
- If we found new evidence that rendered the CER conclusion out of date or no longer applicable, we classified the CER conclusion as out of date. Recognizing that our literature searches were limited, we reserved this category only for situations where a limited search would produce prima facie evidence that a conclusion was out of date, such as the withdrawal of a drug or surgical device from the market, a black box warning from FDA, etc.

Signal Assessment for Updating

We used the following considerations in our assessment of the need to update this CER:

- **Strong signal:** A report is considered to have a strong signal for updating if new evidence is identified that clearly renders conclusions from the original report out of date, such as the addition or removal of a drug or device from the market or a new FDA boxed warning.
- **Medium signal:** A report is considered to have a medium signal for updating when new evidence is identified which may change the conclusions from the original report. This may occur when abstract review and expert assessment indicates that some conclusions from the original report may be out of date, or when it is unclear from abstract review how new evidence may impact the findings from the original report. In this case, full-text review and data abstraction may be needed to more clearly classify a signal.
- **Weak signal:** A report is considered to have a weak signal for updating if little or no new evidence is identified that would change the conclusions from the original report. This may occur when little to no new evidence is identified, or when some new evidence is identified but it is clear from abstract review and expert assessment that the new evidence is unlikely to change the conclusions of the original report.

Results

Prior Surveillance

The most recent previous surveillance report² found that all conclusions for KQ1-6 were still valid. The most recent previous surveillance report found new significant safety concerns including warnings about contraindications for one medication. Several new studies were identified in the most recent previous

surveillance report, including imaging studies aimed at linking neural changes to depression, studies examining patient factors associated with prevalence of depression, a study assessing markers to predict treatment response, and several studies on non-pharmacological treatment modalities.

Literature Search

The literature search identified 15 titles (Appendix E) published in the selected high priority journals since the last surveillance search. Upon abstract review, 13 articles were rejected because they did not meet the original CER inclusion criteria (see Appendix D). The remaining 2 abstracts⁵⁻⁶ were examined for potential to change the results of the original review.

Horizon Scanning

None of the topics in the horizon scanning report for Priority Area 05: Depression and Other Mental Health Disorders overlapped with the key questions in the original CER.⁷ Thus, we did not identify new interventions with high-impact potential for this topic.

FDA Black Box Warnings

We did not find any FDA black box warnings relevant to the key questions in this CER.

Expert Opinion

We shared the conclusions of the original report with eight experts in the field (original peer reviewers and TEP members) to request their assessment of the need to update the report and their recommendations of any relevant new studies. Two subject matter experts responded. The two experts were in agreement that all the conclusions were up to date.

Identifying Qualitative Signals

Appendix G shows the original key questions, the conclusions of the original report and the most recent surveillance report, the results of the literature search, the experts' assessments, and the recommendations of the Scientific Resource Center (SRC) regarding the need for update.

Signal Assessment for Updating

In general, the new studies we identified reflected the conclusions of the original CER. There were no new high-impact potential interventions for this report based on horizon scanning data, and no FDA boxed warnings were identified since the original report was published. The SRC recommendation based on literature published since the original report, FDA boxed warnings, horizon scanning, and expert assessment is that the original conclusions for all key questions in the original report are still valid and the original report does not need updating. The signal to update this report is weak, suggesting that the conclusions in the original CER are likely up to date.

References

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5. Rao V, Mielke M, Xu X, et al. Diffusion tensor imaging atlas-based analyses in major depression after mild traumatic brain injury. *The Journal of Neuropsychiatry & Clinical Neurosciences*, 2012; 24(3): 309-315.
6. Van der Horn HJ, Spikman JM, Jacobs B, et al. Postconcussive complaints, anxiety, and depression related to vocational outcome in minor to severe traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 2013; 94(5): 867-874.
7. ECRI Institute. AHRQ Healthcare Horizon Scanning System Potential High-Impact Interventions: Priority Area 05: Depression and Other Mental Health Disorders. Rockville, MD: Agency for Healthcare Research and Quality. December 2013.
<http://effectivehealthcare.ahrq.gov/index.cfm/who-is-involved-in-the-effective-health-care-program1/ahrq-horizon-scanning-system/>.

Appendices

Appendix A: Top 10 Journals

Appendix B: Most Cited Journals from Original Systematic Review

Appendix C: Original Search Strategy

Appendix D: Inclusion and Exclusion Criteria from Original Systematic Review

Appendix E: Literature Search Results

Appendix F: Questionnaire Matrix Sent to Expert Reviewers

Appendix G: Summary Table

Appendix A. Top 10 Journals

In the Journal Citation Reports database, the science and social science sections were searched by subject area discipline(s) for each surveillance reports topic area. For each subject area discipline the list was constructed by selecting the top 10 journals from the 5 year citation impact factor average list. Selected citations were downloaded in .csv format.

Behavioral Sciences:

1. Behavioral & Brain Sciences
2. Trends in Cognitive Sciences
3. Neuroscience & Biobehavioral Reviews
4. Advances in the Study of Behavior
5. Cognitive, Affective, & Behavioral Neuroscience
6. Frontiers in Behavioral Neuroscience
7. Cortex
8. Autism Research
9. Neuropsychologia
10. Biological Psychology

Rehabilitation:

1. The Journal of Head Trauma Rehabilitation
2. Research in Autism Spectrum Disorders
3. Exceptional Children
4. Journal of Fluency Disorders
5. American Journal of Speech-Language Pathology
6. Journal of Speech Language and Hearing Research
7. Research in Developmental Disabilities
8. American Journal on Intellectual and Developmental Disabilities
9. Journal of Occupational Rehabilitation
10. Journal of Learning Disabilities – US

Psychiatry:

1. Archives of Gen Psychiatry
2. The American Journal of Psychiatry
3. Molecular Psychiatry
4. Biological Psychiatry
5. Schizophrenia Bulletin
6. Neuropsychopharmacology
7. Journal of the American Academy of Child Psychiatry
8. The British Journal of Psychiatry
9. Journal of Psychiatry & Neuroscience
10. World Psychiatry

Top 10 General Medical:

1. New England Journal of Medicine
2. Lancet
3. Journal of the American Medical Association
4. PLoS Medicine
5. Annals of Internal Medicine
6. British Medical Journal
7. Archives of Internal Medicine
8. Canadian Medical Association Journal
9. Cochrane Database of Systematic Reviews
10. BMC Medicine

Psychology:

1. Annual Review of Psychology
2. Psychological Bulletin
3. Annual Review of Clinical Psychology
4. Psychological Review
5. Social Cognitive and Affective Neuroscience
6. Journal of Child Psychology and Psychiatry
7. Psychological Medicine
8. Psychotherapy and Psychosomatics
9. Cognitive Psychology
10. Health Psychology

Appendix B. Most Cited Journals from Original Systematic Review

Journal	Citations
Brain Injury	30
The Journal of Head Trauma Rehabilitation	13
The Journal of Neuropsychiatry and Clinical Neurosciences	11
Archives of Physical Medicine and Rehabilitation	8
The American Journal of Psychiatry	6
Archives of General Psychiatry	4
Journal of Affective Disorders	4
Journal of Clinical and Experimental Neuropsychology	3
The Journal of Nervous and Mental Disease	3
Journal of Neurology, Neurosurgery & Psychiatry	3
Journal of Neurotrauma	3
The American Journal of Geriatric Psychiatry	2
Journal of the American Medical Association	2
New England Journal of Medicine	2
Neuropsychology	2

Appendix C. Original Search Strategy

Top Journals used for surveillance of this topic:

- Annals of Internal Medicine
- British Medical Journal
- Journal of the American Medical Association
- Lancet
- New England Journal of Medicine
- American Journal of Psychiatry
- Archives of Physical Medicine and Rehabilitation
- Brain Injury
- Journal of Head Trauma and Rehabilitation
- Journal of Neuropsychiatry and Clinical Neurosciences

Medline via PubMed Searched January 30th 2014 Rose Relevo

Original Search from previous Report	<pre> ((((((((((((((((depressive[Title/Abstract]) OR depression[Title/Abstract]) OR depressed[Title/Abstract]) OR sadness[Title/Abstract]) OR sad[Title/Abstract]) OR hopelessness[Title/Abstract]) OR suicidal[Title/Abstract]) OR suicide[Title/Abstract]) OR mood[Title/Abstract])) OR (("Depressive Disorder"[Mesh] OR "Depression"[Mesh] OR "Mental Disorders"[Mesh:noexp])) AND (((((((depressive[Title/Abstract]) OR depression[Title/Abstract]) OR depressed[Title/Abstract]) OR sadness[Title/Abstract] OR sad[Title/Abstract]) OR hopelessness[Title/Abstract]) OR suicidal[Title/Abstract] OR suicide[Title/Abstract]) OR mood[Title/Abstract])) AND ((((((((TBI[Title/Abstract]) OR head injuries[Title/Abstract]) OR head injury[Title/Abstract]) OR traumatic brain injury[Title/Abstract]) OR traumatic brain injuries[Title/Abstract]) OR neurotrauma[Title/Abstract]) OR diffuse axonal injury[Title/Abstract]) OR brain trauma[Title/Abstract]) OR head trauma[Title/Abstract])) OR (((((((("Brain Concussion"[Mesh] OR "Brain Injuries"[Mesh:noexp]) OR "Brain Hemorrhage, Traumatic"[Mesh]) OR "Epilepsy, Post-Traumatic"[Mesh]) OR "Head Injuries, Closed"[Mesh]) OR "Head Injuries, Penetrating"[Mesh]) OR "Intracranial Hemorrhage, Traumatic"[Mesh]) OR "Craniocerebral Trauma"[Mesh]) OR "Diffuse Axonal Injury"[Mesh])))) AND Humans[Mesh] AND English[lang])) NOT (((((((("Case Reports"[Publication Type]) OR "Letter"[Publication Type]) OR "Comment"[Publication Type]) OR "Editorial"[Publication Type]) OR "Practice Guideline"[Publication Type]) </pre>
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	OR "News"[Publication Type]) OR "Review"[Publication Type])) AND Humans[Mesh] AND English[lang]))
AND	
Journal Limits	((((((((((("Annals of internal medicine"[Journal]) OR "British medical journal"[Journal]) OR "British medical journal (Clinical research ed.)"[Journal]) OR "BMJ (Clinical research ed.)"[Journal])) OR "Journal of the American Medical Association"[Journal]) OR "JAMA"[Journal]) OR "Lancet"[Journal]) OR "The New England journal of medicine"[Journal]) OR "The American journal of psychiatry"[Journal]) OR (Archives of physical medicine[Journal] AND rehabilitation[Journal])) OR Brain injury : [BI]) OR (journal of head trauma[Journal] AND rehabilitation[Journal])) OR (journal of neuropsychiatry[Journal] AND clinical neurosciences[Journal])
AND	
Date Limits	("2012/10/01"[Date - Entrez] : "2014/01/30"[Date - Entrez])
N=15	

Appendix D. Inclusion and Exclusion Criteria from Original Systematic Review

Our inclusion/exclusion criteria were developed in consultation with the Technical Expert Panel (TEP). Criteria are summarized below.

Category	Criteria
Study population	Adults age ≥ 16 years old
Study settings and geography	Developed nations: United States, Canada, United Kingdom, Western Europe, Japan, Australia, New Zealand, Israel, South America
Publication languages	English only
Admissible evidence (study design and other criteria)	<u>Admissible designs</u> Randomized controlled trials, cohorts with comparison, case-control, and case series ($n \geq 50$) <u>Other criteria</u> <ul style="list-style-type: none">• Original research studies that provide sufficient detail regarding methods and results to enable use and adjustment of the data and results• Patient populations must include participants that have been diagnosed with depression following a traumatic brain injury received in adulthood• Studies must address one or more of the following for depression after traumatic brain injury:<ul style="list-style-type: none">○ Treatment modality○ Symptom management approach○ Short- and long-term outcomes and quality of life• Relevant outcomes must be able to be abstracted from data presented in the papers

*Note: Original inclusion/exclusion criteria extracted from Effective Health Care Program, CER #25, *Traumatic Brain Injury and Depression*, pps. 8-9.

We limited the review to studies published in developed countries to better approximate the United States health care system in terms of access to screening and treatment services. We did not have translation services available to us to review non-English papers, and our TEP agreed that the vast majority if not all of the relevant literature would be published in English. Furthermore, this review is intended to inform U.S. health care, and most research in this population is published in studies. Empirical evidence on the potential for bias created by excluding non-English studies also suggests little effect. All study designs except individual case reports were included in order to be inclusive and identify all possible prevalence, screening, and treatment studies. The decision to require at least 50 participants in each study was made in concert with our TEP, and resulted in the exclusion of only 36 studies, of which one was a randomized controlled trial. The adult trauma population is defined at the Level I trauma center as 16 years old or older. Short- and long-term outcomes in traumatic brain injury in children are pathologically distinct from the adult

population. We chose to limit this study to the adult population of traumatic brain injury and outcomes associated with depression. In order to ascertain prevalence and to further assess potential modifiers of likelihood of being depressed, it was important that studies use an acceptable means of diagnosing depression. We accepted a structured clinical interview or any validated diagnostic tool, excluding for these questions any studies that relied only on self-report of depressed status or that did not describe their approach to depression diagnosis.

Additional criteria:

In order to answer KQ1, studies had to provide some measure of prevalence. We excluded studies that did not provide prevalence data (e.g., for which only mean depression scores were available).

In order to answer KQ2, studies had to provide data that allowed prevalence to be assessed in accordance with a specific timeframe, setting, or tool (or some combination of these). Studies that did not provide any information about when depression screening took place relative to injury were excluded from the weighted average for depression prevalence calculations for specific time points.

In order to answer KQ3, we required that studies present data on comorbid psychiatric conditions within the depressed population separately from the nondepressed population, as our intent was not to measure these conditions in the general TBI population but to explain their specific relationship to depression.

This review focused on the prevalence of diagnosed depression in populations that had sustained a documented traumatic brain injury, and on the treatment of those populations. We excluded studies of individuals with penetrating head injuries because penetrating injury, such as gunshot wounds, create specific and severe tissue damage along the course of the injury as well as associated bleeding and inflammation. The mechanism of injury associated with blunt force trauma to the head more often leads to a diffuse pattern of injury that may affect the entirety of the brain. Although long-term outcomes may be similar in some penetrating head injury cases, our focus on the more global nature of blunt-force trauma and its consequences lead us to exclude studies of penetrating head injuries from this review.

Appendix E. Literature Search Results

1. Bryan CJ, Clemans TA, Hernandez AM, et al. Loss of consciousness, depression, posttraumatic stress disorder, and suicide risk among deployed military personnel with mild traumatic brain injury. *The Journal of Head Trauma Rehabilitation*, 2013; 28(1): 13-20.
2. Cantor JB, Bushnik T, Cicerone K, et al. Insomnia, fatigue, and sleepiness in the first 2 years after traumatic brain injury: an NIDRR TBI model system module study. *The Journal of Head Trauma Rehabilitation*, 2012; 27(6): E1-14.
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4. Failla MD, Burkhardt JN, Miller MA, et al. Variants of SLC6A4 in depression risk following severe TBI. *Brain Injury, Informa Healthcare*, 2013; 27(6): 696-706.
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13. Van der Horn HJ, Spikman JM, Jacobs B, et al. Postconcussive complaints, anxiety, and depression related to vocational outcome in minor to severe traumatic brain injury. *Archives of Physical Medicine and Rehabilitation*, 2013; 94(5): 867-874.
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15. Wong GK, Ngai K, Lam SW, et al. Validity of the Montreal Cognitive Assessment for traumatic brain injury patients with intracranial haemorrhage. *Brain Injury, Informa Healthcare*, 2013; 27(4): 394-398.

Appendix F. Questionnaire Matrix Sent to Expert Reviewers

Surveillance and Identification of Triggers for Updating Systematic Reviews for the EHC Program

Title: Traumatic Brain Injury and Depression

Conclusions From CER Executive Summary	Is this conclusion almost certainly still supported by the evidence?	Has there been new evidence that may change this conclusion?	Do Not Know
Key Question 1: What is the prevalence of depression after traumatic brain injury, and does the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury or other patient factors influence the probability of developing clinical depression?			
Prevalence of depression after TBI (SOE Moderate): <i>Findings:</i> Prevalence ranged from 12.2 to 76.7 percent, weighted average was 31 percent. Depression was more common among those with TBI than normal comparison groups. <i>Future research needs:</i> resources to identify and follow large cohorts of varied injury severity and mechanisms over time.	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:	<input type="checkbox"/> Yes <input type="checkbox"/> No New Evidence:	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:
	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:	<input type="checkbox"/> Yes <input type="checkbox"/> No New Evidence:	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:
Severity of the injury, area of the brain injured, and other patient factors influencing probability of depression (No SOE reported): Too few high quality studies to make valid estimates.	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:	<input type="checkbox"/> Yes <input type="checkbox"/> No New Evidence:	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:
	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:	<input type="checkbox"/> Yes <input type="checkbox"/> No New Evidence:	<input type="checkbox"/> Yes <input type="checkbox"/> No Please explain:
Key Question 2: When should patients who suffer traumatic brain injury be screened for depression, with what tools, and in what setting?			
Studies selecting time and setting of	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No

screening (SOE Low): Cross-sectional literature with short follow-up intervals does not indicate clear findings.	Please explain:	New Evidence:	Please explain:
Key Question 3: Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, post-traumatic stress disorder (PTSD), substance abuse, and major psychiatric disorders?			
Concomitant psychiatric/behavioral conditions (No SOE reported): Very few studies. Eight to 93 percent of depressed participants had one or more concomitant conditions.	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Please explain:	New Evidence:	Please explain:
Key Question 4: What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing psychotropic medications, individual/group psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine, neuromodulation therapies, and other therapies?			
Psychotropic medications (No SOE reported): Few studies.	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Please explain:	New Evidence:	Please explain:
Key Question 5: Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?			
No studies.	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Please explain:	New Evidence:	Please explain:
Key Question 6: Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, preexisting mental health status or medical conditions, functional status, and social support?			
No studies.	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No	<input type="checkbox"/> Yes <input type="checkbox"/> No
	Please explain:	New Evidence:	Please explain:

Are there new data that could inform the key questions that might not be addressed in the conclusions?

Appendix G. Summary Table

Conclusions From CER Executive Summary	Conclusion from the Most Recent Previous Surveillance Report (http://effectivehealthcare.ahrq.gov/ehc/products/77/1513/depression-brain-injury-surveillance-130524.pdf)	SRC Literature Analysis	Expert Opinion	SRC Conclusion
Key Question 1: What is the prevalence of depression after traumatic brain injury, and does the area of the brain injured, the severity of the injury, the mechanism or context of injury, or time to recognition of the traumatic brain injury or other patient factors influence the probability of developing clinical depression?				
The prevalence of [depression among individuals with] traumatic brain injury is approximately 30 percent across multiple time points up to and beyond a year. Based on structured clinical interviews, on average 27 percent met criteria for depression 3 to 6 months from injury; 32 percent at 6 to 12 months; and 33 percent beyond 12 months.	Original conclusion is still valid and this portion of the original report does not need updating.	Two studies ^{5,6} yielded similar results and do not have the potential to significantly change original report findings.	No new evidence that would change conclusions; experts noted that recent studies provide similar prevalence estimates.	Original conclusion is still valid and this portion of the original report does not need updating.
Data are sparse to assess whether severity of injury influences risk of depression.	Original conclusion is still valid and this portion of the original report does not need updating.	One study ⁶ on gender and TBI severity does not have the potential to significantly change original report and previous surveillance report findings.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Stratification of prevalence by explanatory factors such as age, gender, area of brain injured, or mechanism of injury is not possible within the current body of literature.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
History of alcohol and substance abuse increase risk. Pain, involvement in litigation related to the injury, and perceived stress have been reported as risk factors	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions; experts noted that PTSD may be associated with higher	Original conclusion is still valid and this portion of the original report does not need updating.

among those entering rehabilitation care and in prospective cohorts			rates of depression in Veterans with TBI history.	
Imaging research about the areas of the brain injured and the relationship to depression risk yields inconsistent results. In aggregate for all those with TBI, onset of major depression within 3 months of injury has been reported to be sevenfold as common (95 percent CI: 1.36 to 43.48) among those with abnormal CT scans after injury compared with normal imaging.	Original conclusion is still valid and this portion of the original report does not need updating.	One study ⁵ of 14 patients undergoing diffusion tensor imaging does not have the potential to significantly change original report and previous surveillance report findings.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Key Question 2: When should patients who suffer traumatic brain injury be screened for depression, with what tools, and in what setting?				
Prevalence of depression is high at multiple time points after TBI. No evidence provides a basis for targeting screening to one timeframe over another.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions	Original conclusion is still valid and this portion of the original report does not need updating.
The literature is insufficient to determine whether tools for detecting depression that have been validated in other populations can accurately identify depression in individuals with TBIs.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions	Original conclusion is still valid and this portion of the original report does not need updating.
The literature does not support any one tool over the others.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Key Question 3: Among individuals with TBI and depression, what is the prevalence of concomitant psychiatric/behavioral conditions, including anxiety disorders, post-traumatic stress disorder (PTSD), substance abuse, and major psychiatric disorders?				
When conditions were reported individually, anxiety disorder	Original conclusion is still valid and this portion of the original	No new studies identified.	No new evidence that would change	Original conclusion is still valid and this

was most prevalent and affected from 31 to 61 percent of study participants in four papers.	report does not need updating.		conclusions.	portion of the original report does not need updating.
PTSD, a major anxiety disorder, was observed in 37 percent of depressed patients and in no patients without depression.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Panic disorder was seen in 15 percent of patients with major depression, but not measured in those without depression.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Consideration of potential for coexisting psychiatric conditions is warranted.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Key Question 4: What are the outcomes (short and long term, including harm) of treatment for depression among traumatic brain injury patients utilizing psychotropic medications, individual/group psychotherapy, neuropsychological rehabilitation, community-based rehabilitation, complementary and alternative medicine, neuromodulation therapies, and other therapies?				
Only two publications addressed treatment for individuals diagnosed with depression after a traumatic brain injury: Both were studies of antidepressant efficacy (one a controlled trial of sertraline and one an open-label trial of citalopram). The sertraline trial showed no significant effect compared with placebo, and the citalopram study did not show improvement in a majority of participants.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions.	Original conclusion is still valid and this portion of the original report does not need updating.
Key Question 5: Where head-to-head comparisons are available, which treatment modalities are equivalent or superior with respect to benefits, short- and long-term risks, quality of life, or costs of care?				
No head-to-head trials were identified that compared the effectiveness of two or more	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions	Original conclusion is still valid and this portion of the

modalities for treating depression that follows TBI. Such studies are needed.				original report does not need updating.
Key Question 6: Are the short- and long-term outcomes of treatment for depression after TBI modified by individual characteristics, such as age, preexisting mental health status or medical conditions, functional status, and social support?				
No studies were identified that assessed the impact of demographic or other potentially modifying characteristics on treatment effectiveness. Future research needs to address this issue.	Original conclusion is still valid and this portion of the original report does not need updating.	No new studies identified.	No new evidence that would change conclusions	Original conclusion is still valid and this portion of the original report does not need updating.

Legend: TBI = traumatic brain injury.