VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE MANAGEMENT OF CONCUSSION-MILD TRAUMATIC BRAIN INJURY

Department of Veterans Affairs

Department of Defense

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor**.**

Version 2.0 – 2016

Prepared by:

The Management of Concussion-mild Traumatic Brain Injury Working Group

With support from:

The Office of Quality, Safety and Value, VA, Washington, DC
&
Office of Evidence Based Practice, U.S. Army Medical Command

Version 2.0 – 2016

Based on evidence reviewed through March 2015

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I. Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Working Group (EBPWG) was established and first chartered in 2004, with a mission to advise the "…Health Executive Council on the use of clinical and epidemiological evidence to improve the health of the population across the Veterans Health Administration (VHA) and Military Health System," by facilitating the development of clinical practice guidelines (CPG) for the VA and DoD populations.[1] This CPG is intended to provide primary care providers/patient aligned care teams (PACT) and other healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with a history of mild traumatic brain injury (mTBI).

In 2009, the VA and DoD published a CPG for the Management of Concussion-mild Traumatic Brain Injury (2009 mTBI CPG), which was based on evidence reviewed through 2008. Since the release of that guideline, research has expanded the general knowledge and understanding of mTBI. Recognition of the complex nature of this condition has led to the adoption of new strategies to manage and treat individuals with a history of mTBI.

Consequently, the process to update the 2009 mTBI CPG was initiated in 2014. The updated CPG includes evidence-based information on the management of patients with a history of mTBI. The CPG is primarily intended to assist primary care providers in the management of all aspects of patient care, including, but not limited to, diagnosis, assessment, treatment and follow-up. However, this CPG may be used by all healthcare providers. The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being. This CPG guides providers in the care of patients with a history of mTBI along the management pathways that are supported by evidence. The expected outcomes of successful implementation of this guideline are to:

- Assess the patient's condition and determine the best treatment method
- Optimize the clinical management to improve symptoms and functioning, adherence to treatment, recovery, well-being, and quality of life outcomes
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care

II. Background

A traumatic brain injury (TBI) is defined as a traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force and is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:[2,3]

- Any period of loss of or a decreased level of consciousness
- Any loss of memory for events immediately before or after the injury (posttraumatic amnesia)
- Any alteration in mental state at the time of the injury (e.g., confusion, disorientation, slowed thinking, alteration of consciousness/mental state)
- Neurological deficits (e.g., weakness, loss of balance, change in vision, praxis, paresis/plegia, sensory loss, aphasia) that may or may not be transient
- Intracranial lesion

External forces may include any of the following events: the head being struck by an object, the head striking an object, the brain undergoing an acceleration/deceleration movement without direct external trauma to the head, a foreign body penetrating the brain, forces generated from events such as a blast or explosion, or other forces.

The above criteria define the event of a TBI. Not all individuals exposed to an external force will sustain a TBI, but any person who has a history of such an event with immediate manifestation of any of the above signs and symptoms can be said to have had a TBI. For more details about mechanisms of brain injury, see Appendix C: Mechanism of Injury.

The Centers for Disease Control and Prevention (CDC) estimate that approximately 2.2 million emergency department visits and 50,000 deaths occur annually due to TBI.[2] In the 2014 CDC Report to Congress "Traumatic Brain Injury In the United States: Epidemiology and Rehabilitation," according to data from the DoD, 235,046 Service Members (or 4.2% of the 5,603,720 who served in the Army, Air Force, Navy, and Marine Corps) were diagnosed with a TBI between 2000 and 2011.[2] Similarly, the Defense and Veterans Brain Injury Center (DVBIC) estimates that over 1.7 million people sustain a TBI every year in the United States.[4] Of these injuries, approximately 84% are classified as mTBI.

To determine the TBI severity, clinicians should use the criteria displayed in **Table 1** below.

Table 1. Classification of TBI Severity [3]

(If a patient meets criteria in more than one category of severity, the higher severity level is assigned)			
Criteria	**Mild**	**Moderate**	**Severe**
Structural imaging	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0-30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/ mental state (AOC)*	up to 24 hours	>24 hours; severity based on other criteria	
Posttraumatic amnesia (PTA)	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (GCS) (best available score in first 24 hours)**	13-15	9-12	<9

*Alteration of mental status must be immediately related to the trauma to the head. Typical symptoms would be looking and feeling dazed and uncertain of what is happening, confusion, and difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event.
**In April 2015, the DoD released a memorandum recommending against the use of GCS scores to diagnose TBI. See the memorandum for additional information.[3]

A. Terminology Conventions within this CPG

This CPG focuses only on mild TBI (mTBI or concussion). Within this CPG, the terms "mTBI" and "concussion" are used interchangeably. Patients are also referred to as "patients with a history of mTBI" denoting patients that have been diagnosed with a TBI of mild severity. The use of the phrase "patients with mTBI," although widely used in clinical practice, is discouraged in this document because the accepted clinical case definition of mTBI refers only to those symptoms and signs that occur in the immediate injury period, and thus should never be used in present tense to refer to ongoing symptoms that persist and are attributed to the TBI injury event after the immediate period.

The Work Group acknowledges that there is not standard terminology regarding the periods following mTBI; however, the following construct of terms is used within this CPG and was arrived at by Work Group consensus. The terms used within this CPG to delineate post-injury periods following mTBI are outlined below:

- **Immediate period** refers to 0-7 days post-injury
- **Acute period** refers to 1-6 weeks post-injury
- **Post-acute period** refers to 7-12 weeks post-injury
- **Chronic** refers to >12 weeks post-injury

B. Additional Educational Materials and Resources

For additional information on mTBI, there are several topic-specific resources published and offered by the Defense Centers of Excellence (DCoE), Office of the Surgeon General (OTSG), and DVBIC that pertain to the content described in this CPG. These resources may offer additional information about numerous topics in the care and management of patients with a history of mTBI. See the OTSG Army Toolkit[1] and

[1] See the OTSG Army Toolkit here: http://www.cs.amedd.army.mil/borden/Portlet.aspx?ID=065de2f7-81c4-4f9d-9c85-75fe59dbae13

the DVBIC educational materials and publications list[2] for more details. The Work Group has not reviewed the scientific content or quality of any of those materials, and is not in a position to endorse them.

[2] See the DVBIC patient and provider educational materials here: http://dvbic.dcoe.mil/resources, and the DVBIC publications list here: http://dvbic.dcoe.mil/research/browse/dvbic-publications

III. About this Clinical Practice Guideline

This guideline represents a significant step toward improving the treatment and management of patients with a history of mTBI, who present for care in the VA and DoD. As with other CPGs, challenges remain, including the need to develop effective strategies for guideline implementation and to evaluate the effect of guideline adherence on clinical outcomes. This guideline is intended for VA and DoD healthcare providers including physicians, nurse practitioners, physician assistants, psychologists, social workers, nurses, speech-language pathologists, occupational therapists, physical therapists, and others involved in the primary care of Service Members or Veterans who have a history of suspected or diagnosed mTBI.

This CPG is not intended to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for a patient and are subject to change as scientific knowledge and technology advances and patterns evolve. This CPG is based on evidence reviewed through March 2015, and is intended to provide a general guide to best practices. The guideline can assist care providers, but the use of a CPG must always be considered as a recommendation, within the context of a provider's clinical judgment, for the care of an individual.

A. Methods

The current document is an update to the 2009 mTBI CPG. The methodology used in developing the 2016 CPG follows the *Guideline for Guidelines*,[1] an internal document of the VA and DoD EBPWG. The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. This document provides information regarding the process of developing guidelines, including the identification and assembly of the Guideline Champions (Champions) and other subject matter experts from within the VA and DoD, known as the Work Group, and ultimately, the development and publication of an updated mTBI CPG.

The Champions and Work Group for this CPG were charged with developing evidence-based clinical practice recommendations, as well as writing and publishing a guideline document to be used by providers within the VA/DoD healthcare system. Specifically, the Champions and the Work Group members for this guideline were responsible for identifying the key questions (KQs) of the greatest clinical relevance, importance, and interest for the management of patients with a history of mTBI. The amount of new scientific evidence that had accumulated since the previous version of the CPG was also taken into consideration in the identification of the KQs. The Champions and the Work Group also provide direction on inclusion and exclusion criteria for the evidence review and assessed the level of quality of the evidence. In addition, the Champions assisted in:

- Identifying appropriate disciplines of individuals to be included as part of the Work Group
- Directing and coordinating the Work Group
- Participating throughout the guideline development and review processes

The VA Office of Quality, Safety and Value, in collaboration with the Office of Evidence Based Practice, U.S. Army Medical Command, the proponent for CPGs for the DoD, identified three clinical leaders, Dr. David X. Cifu from the VA and Colonel Geoffrey G. Grammer, MD and Colonel Lisa A. Teegarden, PsyD from the DoD, as Champions for the 2016 CPG.

The Lewin Team (Team), including The Lewin Group, Duty First Consulting, ECRI Institute, and Sigma Health Consulting, LLC, was contracted by the VA and DoD to support the development of this CPG and conduct the evidence review. The team held the first conference call in December 2014, with participation from the contracting officer's representative (COR), leaders from the VA Office of Quality, Safety and Value and the DoD Office of Evidence Based Practice, and the Champions. During this call, the project team discussed the scope of the guideline initiative, the roles and responsibilities of the Champions, the project timeline, and the approach for developing and prioritizing specific research questions on which to base a systematic review about the management of mTBI. The group also identified a list of clinical specialties and areas of expertise that are important and relevant to the management of mTBI, from which Work Group members were recruited. The specialties and clinical areas of interest included: blind rehabilitation, family medicine, occupational therapy (OT), language neurology, nursing, pharmacy, physical medicine and rehabilitation (PM&R), physical therapy (PT), polytrauma care, primary care, psychiatry, psychology, and speech-language pathology.

The guideline development process for the 2016 CPG update consisted of the following steps:

1. Formulating and prioritizing KQs for the systematic review
2. Conducting the systematic review
3. Convening a face-to-face meeting with the CPG Champions and Work Group members
4. Drafting and submitting a final CPG about the management of mTBI to the VA/DoD EBPWG

Appendix A: Guideline Development Methodology provides a detailed description of each of these tasks.

a. Reconciling 2009 CPG Recommendations

Evidence-based CPGs should be current, which typically requires revisions based on new evidence or as scheduled subject to time-based expirations. For example, the U.S. Preventive Services Task Force (USPSTF) has a process for refining or otherwise updating its recommendations pertaining to preventive services.[5] Further, the inclusion criteria for the National Guideline Clearinghouse specify that a guideline must have been developed, reviewed, or revised within the past five years.

The mTBI Guideline Work Group focused largely on developing new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. In addition to those new and updated recommendations, the Guideline Work Group considered the current applicability of other recommendations that were included in the previous 2009 mTBI CPG, subject to evolving practice in today's environment.

A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE, UK).[6,7] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated. In brief, the categories took into account whether or not the evidence that related to a recommendation was systematically reviewed as part of the update, the degree to which the recommendation was modified, and the degree to which a recommendation is relevant in the current patient care environment and inside the scope of the CPG. Additional information regarding these categories and their definitions can be found in Appendix A:Guideline Development Methodology. The categories for the recommendations

included in the 2016 version of the guideline are noted in the Recommendations. The categories for the recommendations from the 2009 mTBI CPG are noted in Appendix E: 2009 Recommendation Categorization.

Because the 2009 mTBI CPG was developed using an evidence-rating method (USPSTF method) differing from the methodology currently used (GRADE method), the CPG Work Group recognized the need to accommodate the transition in evidence rating systems from the 2009 mTBI CPG to the current CPG. In order to report the strength of all recommendations using a consistent format (i.e., the GRADE system) the CPG Work Group converted the USPSTF strengths of the recommendation accompanying the carryover recommendations from the 2009 guideline to the GRADE system. As such, the CPG Work Group considered the strength of the evidence cited for each recommendation in the 2009 mTBI CPG as well as harms and benefits, values and preferences, and other implications, where appropriate. The CPG Work Group referred to the available evidence as summarized in the body of the 2009 mTBI CPG and did not assess the evidence review systematically that was conducted for the 2009 mTBI CPG. In some instances, selected peer-reviewed literature published since the 2009 mTBI CPG was considered along with the evidence base used for that CPG. When newer literature was considered in converting the strength of the recommendation from the USPSTF to GRADE system, it is referenced in the discussion of the corresponding recommendation, as well as in Appendix D: Evidence Table.

The CPG Work Group recognizes that, while there are practical reasons for incorporating findings from a previous systematic review, previous recommendations, or recent peer-reviewed publications into an updated CPG, doing so does not involve an original, comprehensive systematic review and, therefore, may introduce bias.[8] In contrast, the recommendations labeled as “Reviewed” were based on a new or an updated systematic review of the literature.

b. Peer Review Process

The CPG was developed through an iterative process in which the Work Group produced multiple drafts of the CPG. The process for developing the initial draft is described in more detail in Drafting and Submitting the Final Clinical Practice Guideline.

Once a near-final draft of the guideline was agreed upon by the Champions and Work Group members, the draft was sent out for peer review and comment. The draft was posted on a wiki website for a period of 14 business days. The peer reviewers comprised individuals working within the VA and DoD health systems as well as experts from relevant outside organizations designated by the Work Group members. The VA and DoD Leadership reached out to both the internal and external peer reviewers to solicit their feedback on the CPG. Organizations designated by the Work Group who were contacted to participate in the peer review included the following:

- Defense and Veterans Brain Injury Center
- IHC Family Practice Center
- National Center for Medical Rehabilitation Research
- University of North Carolina, Department of Rehabilitation Research
- University of Utah, Rehabilitation and Wellness Clinic

Reviewers were provided a hyperlink to the wiki website where the draft CPG was posted. All reviewer feedback was posted in tabular form on the wiki site, along with the name of the reviewer, for transparency. All feedback from the peer reviewers was discussed and considered by the Work Group. Modifications made throughout the CPG development process were made in accordance with the evidence.

B. Conflict of Interest

At the start of this guideline development process and at other key points throughout, the project team was required to submit disclosure statements to reveal any areas of potential conflict of interest in the past two years, including verbal affirmations of no conflict of interest at regular meetings. The project team was also subject to random web-based surveillance (e.g., ProPublica). If there was a positive (yes) conflict of interest response (actual or potential), then action was taken by the co-chairs and evidence-based practice program office, based on the level and extent of involvement, to mitigate the conflict of interest. Actions ranged from restricting participation and/or voting on sections related to a conflict, to removal from the Work Group. Recusal was determined by the individual, co-chairs, and the Office of Evidence Based Practice.

Noted conflict of interest disclosures:

- COL Sidney Hinds II, MD, has previously served on the National Football League (NFL) Head Trauma Advisory Board; however, over 12 months has elapsed since this engagement.
- Scott McDonald, PhD, is involved in TBI research that is funded by the VA and by General Dynamics.

The above disclosures were brought forward by the individuals and evaluated by VA/DoD leadership. Given the nature of the disclosures, the Work Group members were authorized to continue work on the CPG in an unrestricted capacity.

C. Scope of this CPG

This CPG is designed to assist providers in managing or co-managing patients with a history of mTBI. Moreover, the patient population of interest for this CPG is adults who are eligible for care in the VHA and DoD healthcare delivery systems. It includes Veterans as well as deployed and non-deployed active duty Service Members, and National Guard and Reserve components. This CPG does not address the following populations:

- Individuals in the immediate period (within seven days) following mTBI
- Individuals with moderate or severe TBI
- Children or adolescents

D. Highlighted Features of this CPG

The 2016 edition of the VA/DoD CPG for the Management of Concussion-mTBI is the first update to the original CPG. It provides best practice recommendations for the care of patients with a history of mTBI. While screening for and addressing co-occurring mental disorders is considered good clinical practice, specific guidance on management of co-occurring mental health conditions is beyond the scope of this

CPG. Interested readers are referred to related VA/DoD CPGs (e.g., Posttraumatic Stress Disorder [PTSD][3], Major Depressive Disorder [MDD][4] , Bipolar Disorder[5], Suicide Risk[6]). A particular strength of this CPG is the multidisciplinary stakeholder involvement from its inception, ensuring representation from the broad spectrum of clinicians engaged in the management of patients with a history of mTBI.

The literature review encompassed studies published between 2008 and March 2015, was systematic, based on specific inclusion/exclusion criteria (see Appendix A: Guideline Development Methodology), and targeted 10 KQs focusing on the means by which the delivery of healthcare could be optimized for patients with a history of mTBI. The selected KQs were prioritized from many possible KQs. Due to resource constraints, a review of the evidence in all aspects of care for patients with a history of mTBI was not feasible for the update to this CPG.

The framework for recommendations used in this CPG considered factors beyond the strength of the evidence, including balancing desired outcomes with potential harms of treatment, equity of resource availability, and the potential for variation in provider and patient values and preferences. Applicability of the evidence to VA/DoD populations was also taken into consideration.

Additionally, several components of this CPG offer further guidance for providers on the clinical management of patients with a history of mTBI. The evidence synthesis for this CPG found a lack of randomized clinical trials (RCTs) for treatment of symptoms in patients with a history of mTBI. As such, Appendix B: Clinical Symptom Management offers symptom-based clinical guidance and best practices that have been reviewed by the experts assembled to produce this CPG. However, this material is set apart from the body of the CPG, as it is based on expert consensus and common clinical practice. A set of algorithms also accompanies the guideline to provide an overview of the recommendations in the context of the flow of clinician decision making and to assist with training providers. The algorithm may be used to help facilitate translation of guideline recommendations into effective practice.

E. Patient-centered Care

Guidelines encourage providers to use a patient-centered approach. Regardless of setting or availability of professional expertise, any patient in the healthcare system may be offered the interventions recommended in this guideline and found to be appropriate to the patient's specific condition according to the clinician's clinical judgment and patient values and preferences.

Treatment and care should take into account a patient's needs and preferences. Good communication between healthcare professionals and the patient is essential. Information provided to patients by health professionals should be supported by evidence and be tailored to the patient's needs. The information that patients are given about treatment and care should be culturally appropriate (including

[3] See the VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Reaction. Available at: http://www.healthquality.va.gov/guidelines/mh/ptsd/index.asp

[4] See the VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/mdd/index.asp

[5] See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults. Available at: http://www.healthquality.va.gov/guidelines/mh/bd/index.asp

[6] See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide. Available at: http://www.healthquality.va.gov/guidelines/mh/srb/index.asp

care in a military setting) and available to people who do not speak or read English or who have limited literacy skills. Information should also be accessible to people with additional needs such as physical, sensory or learning disabilities.

Care of Veterans and Service Members in transition between facilities, services, or from the DoD healthcare system to the VA healthcare system should have a transition plan and be managed according to best practice with emphasis on continuity of care. Healthcare teams should work jointly to provide assessment and services to patients within this transitioning population. Management should be reviewed throughout the transition process, and there should be clarity between providers to ensure continuity of care. Providers can use programs and mechanisms put in place within VA/DoD to assist with transitions such as DVBIC's Recovery Support Specialist (RSS) program, or the Lead Coordinator Initiative for those who require a care plan and/or case manager. Rehabilitation therapists with expertise in mTBI should also be competent in military/Veteran culture and should understand the important role of developing a therapeutic alliance with the patient.

F. Implementation

This CPG and associated algorithms were designed to be adapted by individual healthcare providers with consideration of local needs and resources. The algorithms serve as tools to prompt providers to consider key decision points in the course of an episode of care. Within the body of the CPG, the recommendations offer evidence-based guidance for the care of patients with a history of mTBI. Appendix B: Clinical Symptom Management also offers users of the CPG a symptom-based clinical guide to best practices that have been reviewed by the Work Group. It should be noted that this material is set apart from the body of the CPG because it is based on expert consensus and common clinical practice. In addition, a clinician summary, clinician pocket card, and patient guide were developed to accompany this CPG to facilitate use of the content.

This CPG represents current clinical practice as of the date of publication. It is important to note, however, that scientific evidence often evolves and may result in the need to update this guideline. New technology and more research will improve patient care in the future. The CPG can assist in identifying priority areas for research and to inform optimal allocation of resources. Future studies examining the results of CPG implementation may lead to the development of new evidence particularly relevant to clinical practice.

IV. Guideline Working Group

Guideline Working Group*	
Department of Veterans Affairs	***Department of Defense***
David X. Cifu, MD (Co-Chair)	**COL Geoffrey G. Grammer, MD (Co-Chair)**
Jennifer Burton, DPT	**COL Lisa Teegarden, PsyD (Co-Chair)**
Mary Dameron, MSN, RN, CRRN, CCM, CBIS	Amy O. Bowles, MD
Blessen C. Eapen, MD	Megan Chilson, PharmD
Robin A. Hurley, MD, FANPA	Thomas J. DeGraba, MD
Scott D. McDonald, PhD	CDR Josh L. Duckworth, MD
Linda M. Picon, MCD, CCC-SLP	CDR Jeffrey Feinberg, MD, MPH, FAAFP
Ronald G. Riechers, II, MD	Louis M. French, PsyD
Kathryn Tortorice, PharmD, BCPS	COL Sidney R. Hinds II, MD
Linda Van Horn, MSN, BSN, CFNP	Charles W. Hoge, MD
Deborah Voydetich, OTR/L, SCLV	Timothy Lacy, MD
	James Sall, PhD, FNP-BC
	Major Derrick F. Varner, PhD, DFAAPA
Office of Quality, Safety and Value Veterans Health Administration	***Office of Evidence Based Practice U.S. Army Medical Command***
Eric Rodgers, PhD, FNP, BC Rene Sutton, BS, HCA	Ernest Degenhardt, COL USA (Ret.) RN, MSN, ANP/FNP, BC Corinne K. B. Devlin, MSN, RN, FNP-BC James Sall, PhD, FNP-BC
Lewin Group	***ECRI Institute***
Cliff Goodman, PhD Christine Jones, MS, MPH Erin Gardner, BS Nicolas Stettler, MD, MSCE	James Reston, PhD Kristen D'Anci, PhD Amy Tsou, MD
Sigma Health Consulting, LLC	***Duty First Consulting***
Fran Murphy, MD, MPH	Anita Ramanathan, BA

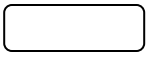
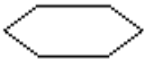
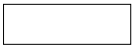
*Additional contributor contact information is available in Appendix F: Participants List.

V. Algorithms

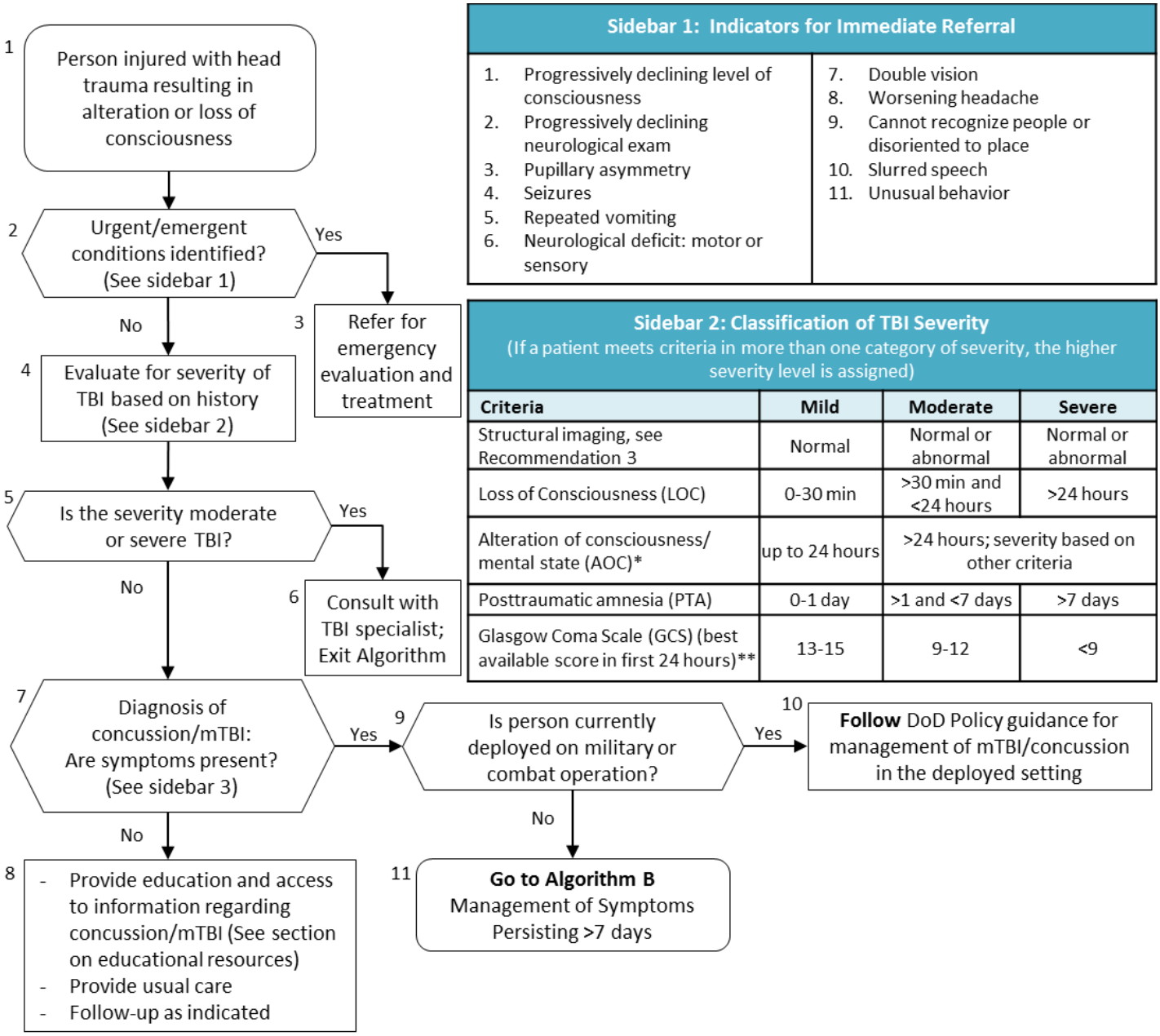
This CPG includes an algorithm that is designed to facilitate clinical decision making for the management of mTBI. The use of the algorithm format as a way to represent patient management was chosen based on the understanding that such a format can allow for efficient diagnostic and therapeutic decision making, and has the potential to change patterns of resource use. The algorithm format allows the provider to follow a linear approach in assessing the critical information needed at the major decision points in the clinical process, and includes:

- An ordered sequence of steps of care
- Recommended observations and examinations
- Decisions to be considered
- Actions to be taken

A clinical algorithm diagrams a guideline into a step-by-step decision tree. Standardized symbols are used to display each step in the algorithm, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[9]

	Rounded rectangles represent a clinical state or condition.
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered Yes or No.
	Rectangles represent an action in the process of care.

A. Module A: Initial Presentation (>7 Days Post-injury)



Sidebar 1: Indicators for Immediate Referral

1. Progressively declining level of consciousness
2. Progressively declining neurological exam
3. Pupillary asymmetry
4. Seizures
5. Repeated vomiting
6. Neurological deficit: motor or sensory
7. Double vision
8. Worsening headache
9. Cannot recognize people or disoriented to place
10. Slurred speech
11. Unusual behavior

Sidebar 2: Classification of TBI Severity

(If a patient meets criteria in more than one category of severity, the higher severity level is assigned)

Criteria	Mild	Moderate	Severe
Structural imaging, see Recommendation 3	Normal	Normal or abnormal	Normal or abnormal
Loss of Consciousness (LOC)	0-30 min	>30 min and <24 hours	>24 hours
Alteration of consciousness/ mental state (AOC)*	up to 24 hours	>24 hours; severity based on other criteria	
Posttraumatic amnesia (PTA)	0-1 day	>1 and <7 days	>7 days
Glasgow Coma Scale (GCS) (best available score in first 24 hours)**	13-15	9-12	<9

Sidebar 3: Possible Post-mTBI Related Symptoms***

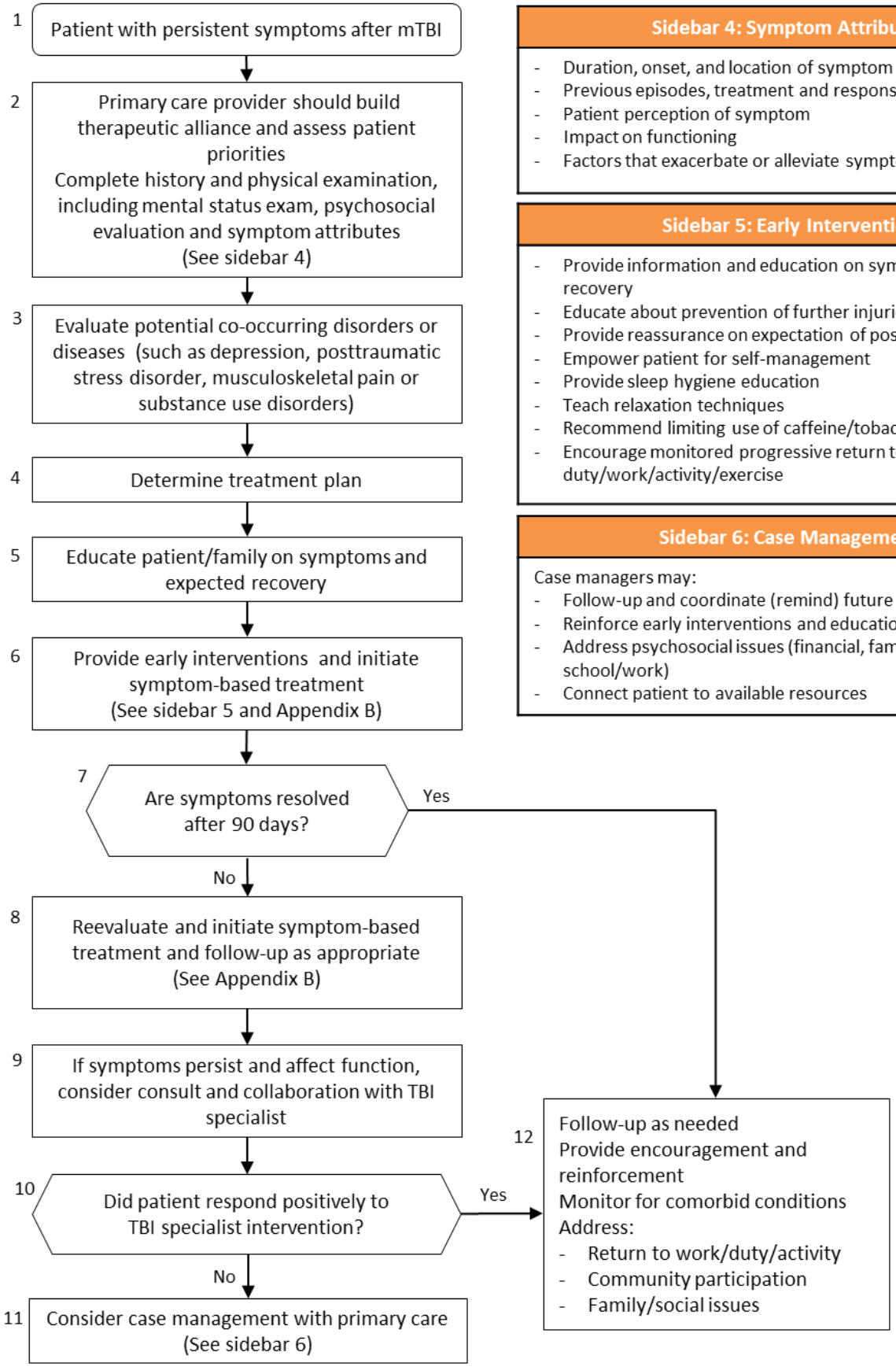
Physical Symptoms:	Cognitive Symptoms:	Behavior/Emotional Symptoms:
Headache, dizziness, balance disorders, nausea, fatigue, sleep disturbance, blurred vision, sensitivity to light, hearing difficulties/loss, tinnitus, sensitivity to noise, seizure, transient neurological abnormalities, numbness, tingling	Problems with attention, concentration, memory, speed of processing, judgment, executive control	Depression, anxiety, agitation, irritability, impulsivity, aggression

*Alteration of mental status must be immediately related to the trauma to the head. Typical symptoms would be: looking and feeling dazed and uncertain of what is happening, confusion, difficulty thinking clearly or responding appropriately to mental status questions, and being unable to describe events immediately before or after the trauma event.

**In April 2015, the DoD released a memorandum recommending against the use of GCS scores to diagnose TBI. See the memorandum for additional information.

***Symptoms that may develop within 30 days post injury.

B. Module B: Management of Symptoms Persisting >7 days



VI. Recommendations

Recommendation	Strength*	Category†
A. Diagnosis and Assessment		
1. We suggest using the terms "history of mild traumatic brain injury (mTBI)" or "concussion" and to refrain from using the terms "brain damage" or "patients with mTBI" in communication with patients and the public.	Weak for	Not Reviewed, Amended
2. We recommend evaluating individuals who present with symptoms or complaints potentially related to brain injury at initial presentation.	Strong for	Not Reviewed, Amended
3. Excluding patients with indicators for immediate referral, for patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we suggest ***against*** using the following tests to establish the diagnosis of mTBI or direct the care of patients with a history of mTBI: a. Neuroimaging b. Serum biomarkers, including S100 calcium-binding protein B (S100-B), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal esterase L1 (UCH-L1), neuron specific enolase (NSE), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) peptide c. Electroencephalogram (EEG)	Weak against	Reviewed, New-replaced
4. We recommend ***against*** performing comprehensive neuropsychological/ cognitive testing during the first 30 days following mTBI. For patients with symptoms persisting after 30 days, see Recommendation 17.	Strong against	Not Reviewed, Amended
5. For patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we recommend ***against*** using the following tests in ***routine*** diagnosis and care of patients with symptoms attributed to mTBI: a. Comprehensive and focused neuropsychological testing, including Automated Neuropsychological Assessment Metrics (ANAM), Neuro-Cognitive Assessment Tool (NCAT), or Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)	Strong against	Reviewed, New-replaced
6. For patients with new symptoms that develop more than 30 days after mTBI, we suggest a focused diagnostic work-up specific to those symptoms only.	Weak for	Not Reviewed, Amended
B. Co-occurring Conditions		
7. We recommend assessing patients with symptoms attributed to mTBI for psychiatric symptoms and comorbid psychiatric disorders including major depressive disorder (MDD), posttraumatic stress disorder (PTSD), substance use disorders (SUD) and suicidality. Consult appropriate VA/DoD clinical practice guidelines.	Strong for	Not Reviewed, Amended
C. Treatment		
8. We suggest considering, and offering as appropriate, a primary care, symptom-driven approach in the evaluation and management of patients with a history of mTBI and persistent symptoms.	Weak for	Not Reviewed, Amended
a. Effect of mTBI Etiology on Treatment Options and Outcomes		
9. We recommend ***not*** adjusting treatment strategy based on mechanism of injury.	Strong against	Reviewed, New-added
10. We recommend ***not*** adjusting outcome prognosis based on mechanism of injury.	Strong against	Reviewed, New-added

Recommendation	Strength*	Category†
b. Headache		
11. We suggest that the treatment of headaches should be individualized and tailored to the clinical features and patient preferences. The treatment may include: a. Headache education including topics such as stimulus control, use of caffeine/tobacco/alcohol and other stimulants b. Non-pharmacologic interventions such as sleep hygiene education, dietary modification, physical therapy (PT), relaxation and modification of the environment (for specific components for each symptom, see Appendix B: Clinical Symptom Management) c. Pharmacologic interventions as appropriate both for acute pain and prevention of headache attacks	Weak for	Reviewed, New-replaced
c. Dizziness and Disequilibrium		
12. In individuals with a history of mTBI who present with functional impairments due to dizziness, disequilibrium, and spatial disorientation symptoms, we suggest that clinicians offer a short-term trial of specific vestibular, visual, and proprioceptive therapeutic exercise to assess the individual's responsiveness to treatment. Refer to occupational therapy (OT), physical therapy (PT) or other vestibular trained care provider as appropriate. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***.	Weak for	Reviewed, Amended
d. Tinnitus		
13. There is no evidence to suggest for or against the use of any particular modality for the treatment of tinnitus after mTBI.	N/A	Reviewed, New-added
e. Visual Symptoms		
14. There is no evidence to suggest for or against the use of any particular modality for the treatment of visual symptoms such as diplopia, accommodation or convergence disorder, visual tracking deficits and/or photophobia after mTBI.	N/A	Reviewed, New-added
f. Sleep Disturbance		
15. We suggest that treatment of sleep disturbance be individualized and tailored to the clinical features and patient preferences, including the assessment of sleep patterns, sleep hygiene, diet, physical activities and sleep environment. The treatment may include, in order of preference: a. Sleep education including education about sleep hygiene, stimulus control, use of caffeine/tobacco/alcohol and other stimulants b. Non-pharmacologic interventions such as cognitive behavioral therapy specific for insomnia (CBTi), dietary modification, physical activity, relaxation and modification of the sleep environment (for specific components for each symptoms see Appendix B: Clinical Symptom Management) c. Pharmacologic interventions as appropriate to aid in sleep initiation and sleep maintenance	Weak for	Reviewed, Amended
g. Behavioral Symptoms		
16. We recommend that the presence of psychological or behavioral symptoms following mTBI should be evaluated and managed according to existing evidence-based clinical practice guidelines, and based upon individual factors and the nature and severity of symptoms.	Strong for	Reviewed, Amended

Recommendation	Strength*	Category†
h. Cognitive Symptoms		
17. We suggest that patients with a history of mTBI who report cognitive symptoms that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms (e.g., sleep disturbance, headache) be referred as appropriate for a structured cognitive assessment or neuropsychological assessment to determine functional limitations and guide treatment.	Weak for	Not Reviewed, Amended
18. We suggest that individuals with a history of mTBI who present with symptoms related to memory, attention or executive function problems that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. We suggest considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***.	Weak for	Reviewed, New-replaced
19. We suggest ***against*** offering medications, supplements, nutraceuticals or herbal medicines for ameliorating the neurocognitive effects attributed to mTBI.	Weak against	Not Reviewed, Amended
D. Setting of Care		
20. We suggest ***against routine*** referral to specialty care in the majority of patients with a history of mTBI.	Weak against	Reviewed, Amended
21. If the patient's symptoms do not resolve within 30-90 days and are refractory to initial treatment in primary care and significantly impact activities of daily living (ADLs), we suggest consultation and collaboration with a locally designated TBI or other applicable specialist.	Weak for	Reviewed, Amended
22. For patients with persistent symptoms that have been refractory to initial psychoeducation and treatment, we suggest referral to case managers within the primary care setting to provide additional psychoeducation, case coordination and support.	Weak for	Reviewed, Amended
23. There is insufficient evidence to recommend for or against the use of interdisciplinary/multidisciplinary teams in the management of patients with chronic symptoms attributed to mTBI.	N/A	Reviewed, New-replaced

*For additional information, please refer to Grading Recommendations.
†For additional information, please refer to Recommendation Categorization and Appendix E: 2009 Recommendation Categorization.

A. Diagnosis and Assessment

Recommendation

1. We suggest using the terms “history of mild traumatic brain injury (mTBI)” or “concussion” and to refrain from using the terms “brain damage” or “patients with mTBI” in communication with patients and the public.
   (Weak For| Not Reviewed, Amended)

Discussion

Within this guideline, the terms concussion and mTBI are used interchangeably. The use of the term concussion or history of mild TBI may be preferred when communicating with the patient, indicating a transient condition, avoiding the use of the terms "brain damage" or "brain injury" that may inadvertently reinforce misattribution of symptoms or insecurities about recovery. The patient who is told he or she has "brain damage" based on vague symptoms or complaints and no clear indication of significant head trauma may develop a long-term perception of disability that may be difficult to reverse.[10] The terms “concussion” and “mTBI” will be used throughout this document as a convention. Also, patients should not be referred to as “mTBI patients” or “patients with mTBI” as this implies that the mTBI (the injury itself, clinically defined only by immediate symptoms/signs at the time of injury) is continuing currently.

Recommendation

2. We recommend evaluating individuals who present with symptoms or complaints potentially related to brain injury at initial presentation.
   (Strong For| Not Reviewed, Amended)

Discussion

A thorough history and physical examination are the basis of any clinical diagnosis. Currently, the diagnosis of mTBI is based on clinical criteria obtained during a history and physical exam (see Algorithms for definition). Symptoms associated with mTBI are identified while conducting the history of present illness. The signs and symptoms associated with mTBI are evaluated through physical examination and history and are treated in accordance with this guideline. This recommendation was not reviewed in the recent literature review; however, the strength of this recommendation is strong. The content of the 2009 mTBI CPG was reviewed and generally accepted as current best practice. The Work Group recognized primary care providers should consider, as appropriate during each encounter, the following physical findings, signs and symptoms (“red flags”) that may indicate a neurologic condition that requires urgent specialty consultation (e.g., consultation with neurology, neuro-surgical):

- Progressively declining level of consciousness
- Progressively declining neurological exam
- Pupillary asymmetry
- Seizures
- Repeated vomiting
- Neurological deficit: motor or sensory
- Double vision
- Worsening headache
- Cannot recognize people or disoriented to place
- Slurred speech
- Unusual behavior

Evaluating individuals in military operational settings who are exposed to potentially concussive events (e.g., blast, motor vehicle accidents, blow to the head) while in theater is strongly encouraged as soon as possible after exposure.

Detecting mTBI close to the time of injury is best for providing optimal care and potentially preventing persisting symptoms. DoDI 6490.11 mandates that all Service Members exposed to a potentially concussive event be screened for TBI using the Military Acute Concussion Evaluation (MACE), and be required to rest for 24 hours regardless of results.[11] The MACE assesses neurological status and history to help the evaluation after an mTBI, queries for symptoms, and briefly assesses cognitive functioning. However, studies have shown inconclusive results with regard to the validity of the MACE as a clinical evaluation tool to assess for cognitive function acutely following concussion in military settings,[12] with particularly low sensitivity and specificity when administered more than 12 hours after injury.[13] Since implementation of the DoDI 6490.11 requirements, there has been an increase in the number of mTBIs identified and the number of patients who received early treatment.[11] TBI evaluation is also included in post-deployment screening efforts upon return from deployment to combat zones to facilitate identification of those individuals exposed to concussive events who were not evaluated in theater at the time of the event.

The Post-Deployment Health Assessment (PDHA) uses two questions to screen for TBI regarding exposure to an injury event and experiencing an associated alteration of consciousness. However, screening months to years following an injury event for mTBI can result in adverse effects including misdiagnosis, inflated symptom reporting and symptom misattribution; in addition, there is no evidence base to support this practice.[14,15]

Recommendation

3. Excluding patients with indicators for immediate referral, for patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we suggest ***against*** using the following tests to establish the diagnosis of mTBI or direct the care of patients with a history of mTBI:
   a. Neuroimaging
   b. Serum biomarkers, including S100 calcium-binding protein B (S100-B), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal esterase L1 (UCH-L1), neuron specific enolase (NSE), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) peptide
   c. Electroencephalogram (EEG)

   (Weak Against | Reviewed, New-replaced)

Discussion

The diagnosis of mTBI is a clinical diagnosis which, in many cases, relies on history alone. Conceptually, a confirmatory objective test that could provide a definitive diagnosis of mTBI that could be used to direct treatment and/or predict outcomes would be desirable. Unfortunately, at this time, evidence does not support the use of any laboratory, imaging, or physiological test for these purposes.

There are several studies that evaluate the use of computerized tomography (CT) scan or magnetic resonance imaging (MRI) within the first week after the concussive incident.[16,17] These studies fall beyond the scope of this CPG, which is focused on patients seen in primary care with symptoms persisting a week after the concussive incident. Of note, however, the study by Kim et al. found that subjects with mTBI and abnormal MRIs

within the first week were more likely to have a symptom duration of greater than two weeks.[16] Consequently, the evidence does not support obtaining an MRI beyond the first week, but if one was completed during the first week and was abnormal, a longer duration of symptoms might be anticipated.

While many advanced neuroimaging techniques show promise in the diagnosis of mTBI, there is no evidence to support routine use in this population later than seven days after the event. A meta-analysis of MRI diffusion tensor imaging (DTI) in the post-concussion population (time since injury of three days to eight years) showed fractional anisotropy (FA) reduction in several brain regions that have been associated with brain injury.[18] However, many of the studies had significant methodological problems, particularly problems with selection of control groups that adequately control for potential confounders. In a military cross-sectional study with the same FA findings (and the same methodological problems with control selection), only 40% of post-concussion patients had abnormalities on DTI, making sensitivity inadequate for routine use at this time.[19] In addition, these studies have not linked DTI findings with clinical presentation or outcomes.

There is emerging literature about serum biomarkers, and much of the investigation has surrounded the acute phase with a number of good candidate proteins. In the post-acute period (greater than seven days), however, there is little information. In a single pilot study, serum levels of the AMPAR peptide were found to be significantly different between non-concussed controls and concussed athletes one to two weeks following concussion.[20] While there was some correlation between AMPAR levels and baseline cognitive testing performance, there is inadequate data at this time to suggest that the use of this proposed biomarker would affect clinical management or outcomes.

There are no studies to support the use of EEG in routine post-concussion care.

In conclusion, the current evidence does not support the routine use of laboratory, imaging or physiologic testing in the management of a patient more than seven days following concussion. There does not appear to be any benefits from these tests at the present time and clinicians should consider weighing the risk of unnecessary testing in terms of communication considerations, management of patient expectations, and utilization of resources. Future research should include long-term outcomes with a particular focus on how these test results can help clinical decision making.

Recommendation

4. We recommend ***against*** performing comprehensive neuropsychological/cognitive testing during the first 30 days following mTBI. For patients with symptoms persisting after 30 days, see Recommendation 17.
   (Strong Against | Not Reviewed, New-replaced)

Discussion

The Work Group reviewed, and strongly agreed with, the 2009 mTBI CPG recommendation against the use of comprehensive cognitive testing, including neuropsychological testing, in the first 30 days after concussion/mTBI and strongly. The supporting literature was not addressed in the updated systematic review; however, the existing literature from the 2009 CPG (all of which was from pre-2002) was reviewed. The literature utilized in the 2009 mTBI CPG was from a systematic review from 2005 [21] and three meta-analyses [22-24] that included research articles published prior to 2002. This literature stated that cognitive deficits after mTBI usually only persist for a few hours or days (rarely up to 30 days or beyond). These deficits were noted to be in the domains of memory,

complex attention or working memory, and speed of mental and motor processing; however, these deficits usually resolved rapidly. Beyond the initial week to 30 days after concussion, there is no clear correlation between an individual's self-report of cognitive-related symptoms and findings from formal testing.

The recommendation is made "strong against" based on a high confidence in the existing literature and clinical consensus, the harms from early formal testing (e.g., limits ability to formally test again for six or more months, reinforces the impaired status of the individual when rapid and full cognitive recovery is likely), the relatively high use of resources involved in formal neuropsychological testing, and the significant variability in preferences (for both individuals with a history of mTBI and clinical providers) for the use and specific type of formal neuropsychological testing.

Recommendation

5. For patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we recommend ***against*** using the following tests in routine diagnosis and care of patients with symptoms attributed to mTBI:
    a. Comprehensive and focused neuropsychological testing, including Automated Neuropsychological Assessment Metrics (ANAM), Neuro-Cognitive Assessment Tool (NCAT), or Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT).

    (Strong Against | Reviewed, Amended)

Discussion

Following the immediate period (more than seven days post-concussive incident), there is insufficient evidence for recommending routine (i.e., performed for all patients) cognitive or neuropsychological testing for the diagnosis of mTBI compared to diagnosis based on history and physical only. Although there are consistent findings of cognitive deficits especially in the first 48 hours after injury, well-controlled, long-term natural history studies after concussion injuries are lacking, and the diagnostic utility of information on cognitive functioning in the post-acute period is not clear.[25] Pape et al. performed a systematic review of 13 diagnostic accuracy studies of neurocognitive and psychological tests in the diagnosis of mTBI.[26] Across studies, encompassing both acute and post-acute concussion/mTBI, sensitivity ranged from 13-92%, specificity ranged from 72-99%, and correct classification (which is influenced by base rate of mTBI) ranged from 3-96%.[26] However, the research methods employed by the majority of the 13 studies reviewed were likely to provide biased, under- or overestimates of true diagnostic accuracy. Similarly, although there may be some clinical utility in comparing baseline neuropsychological functioning to post-injury functioning, a review of the literature indicated that there is insufficient evidence for this strategy as an aid to diagnose concussion/mTBI in the post-acute period.[27]

In the post-acute period after mTBI, there is insufficient evidence for recommending routine (i.e., performed for all patients) cognitive or neuropsychological testing to guide treatment decisions and to improve outcomes compared to routine primary care. Individuals presenting for care with complaints potentially related to mTBI may or may not present with cognitive symptoms. As discussed in more detail in other areas of this CPG (see section on Cognitive Symptoms), cognitive and neuropsychological testing may be indicated for symptomatic patients in specific situations, such as baseline assessment in preparation for cognitive rehabilitation [28] and identifying emotional or motivational factors that could impact treatment planning.[29,30]

The Work Group has high confidence in this recommendation, which is based principally on a lack of evidence for the routine use of comprehensive and focused neuropsychological testing in the diagnosis and care of patients with symptoms attributed to mTBI. In addition, the Work Group felt the potential harms of routine testing outweigh the potential benefits in the post-acute period. Potential harms include unnecessary appointments for the patient, promotion of negative illness expectations, and increased utilization of clinical resources that could be applied elsewhere. No literature was reviewed concerning patient values and preferences; however, the Work Group considered that some patients would prefer to receive testing in order to validate their symptoms (or receive reassurance as to their overall well-being) whereas others would prefer to minimize the number of appointments and procedures received. In addition to the aforementioned implications on resource management and acceptability, the Work Group identified the potential for stigma and the availability of testing infrastructure as a potentially limiting factor.

Future research to improve the diagnostic accuracy of tests for mTBI in the post-acute period is needed. Identification of interactions between cognitive, behavioral, and emotional factors as well as clinical and demographic factors may improve diagnostic and prognostic models. In addition, Pape et al. emphasized that the clinical utility of prior research on the diagnostic accuracy of cognitive and neuropsychological tests for concussion/mTBI has been limited by the lack of a standardized and well-defined case definition of mTBI.[26] Future studies will have to be designed in a way that acknowledges the lack of validation of existing case definitions.

Recommendation

6. For patients with new symptoms that develop more than 30 days after mTBI, we suggest a focused diagnostic work-up specific to those symptoms only.
   (Weak For | Not Reviewed, Amended)

Discussion

It is important to recognize that the majority of individuals who sustain a single concussion recover within hours to days without residual deficits. Post-concussion symptoms are nonspecific (e.g., headache, nausea, dizziness, fatigue, irritability, concentration problems), which makes it very difficult to definitively attribute symptoms to the concussive injury, particularly as the time since the event lengthens. In addition, there is little evidence to suggest that treatment interventions should be different when symptoms are attributed to concussion versus a different etiology.[31] Consequently, symptom-focused evaluation and treatment is recommended, particularly when the time since injury is greater than 30 days.

The vast majority of patients who develop symptoms after concussion will do so immediately. In some cases, analogous to the acute trauma setting where initial events (e.g., life-threatening injury) may take precedence over other injuries (e.g., ankle sprain), patients may not notice some symptoms until later. However, with patients that are initially asymptomatic and develop new symptoms 30 days or more following concussion, these symptoms are unlikely to be the result of the concussion and the work-up and management should not focus on the initial concussion.[31]

B. Co-occurring Conditions

Recommendation

7. We recommend assessing patients with symptoms attributed to mTBI for psychiatric symptoms and comorbid psychiatric disorders including major depressive disorder (MDD), posttraumatic stress disorder (PTSD), substance use disorders (SUD) and suicidality. Consult appropriate VA/DoD clinical practice guidelines.
   (Strong For | Not Reviewed, Amended)

Discussion

Depression, anxiety and irritability are common co-occurring behavioral symptoms of mTBI. When behavioral symptoms are reported, they should be treated in accordance with treatment/management recommendations within this guideline (see Appendix B: Clinical Symptom Management) or other VA/DoD CPGs. The relationship between mTBI and comorbid psychiatric conditions, most notably PTSD, MDD and SUD is controversial and complex.[15,32-39] There is evidence, however, that suggests comorbid depression or other mental disorders are associated with higher rates of persistent post-concussive symptoms and poorer outcomes following concussion. For these reasons, it is prudent to assess for comorbid psychiatric conditions and treat in accordance with existing VA/DoD CPGs for the Management of PTSD,[7] MDD,[8] SUD,[9] and patients at risk for suicide.[10]

The overall quality of the evidence for this recommendation is high, and the Work Group felt strongly that it is important to recommend assessment and specific treatment for comorbid psychiatric conditions in accordance with existing VA/DoD CPGs. The benefit of early diagnosis and treatment of behavioral health symptoms or disorders clearly outweighs the harms; it increases the likelihood symptoms will respond favorably to treatment thereby alleviating the distress of the patient. In addition, given the demand on behavioral health resources within the VA and DoD, initiating treatment for behavioral symptoms within a primary care setting helps to ensure access to care standards for behavioral health services. Assessment in primary care is also an important component of management of chronic multisymptom conditions, of which persistent post-concussion symptoms meet the definition. (See the VA/DoD CPG for the Management of Chronic Multisymptom Illness [CMI][11])

For additional clinical guidance, please see Appendix B: Co-occurring Conditions.

C. Treatment

In both the military and civilian populations, over 80% of diagnosed TBIs are categorized as mild and have been associated with multiple clinical signs and symptoms.[40,41] In conjunction with a spectrum of possible clinical

[7] See the VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Reaction. Available at: http://www.healthquality.va.gov/guidelines/mh/ptsd/index.asp
[8] See the VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/mdd/index.asp
[9] See the VA/DoD Clinical Practice Guideline for Management of Substance Use Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/sud/index.asp
[10] See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide. Available at: http://www.healthquality.va.gov/guidelines/mh/srb/index.asp
[11] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

presentations, a variety of clinical outcomes have also been observed in patients following a concussive event.[42]

Recommendation

8. We suggest considering, and offering as appropriate, a primary care, symptom-driven approach in the evaluation and management of patients with a history of mTBI and persistent symptoms.
   (Weak For | Not Reviewed, Amended)

Discussion

Individuals who have had a concussive event at some point in the past may continue to have persistent and potentially chronic symptoms, although it is often difficult to determine the exact etiology of these symptoms. Persistent post-concussive symptoms often involve multiple physiological domains (e.g., psychological symptoms, neurological symptoms, neuroendocrine symptoms). There is currently insufficient evidence regarding the long-term sequelae of concussive events. Some of a patient's experiences may possibly be the result of neurological injury that is not well detected by the tools available at this time. Therefore, it may be difficult to determine which symptoms are the result of the original event and which are not.

Some presenting symptoms may be attributed to the mTBI event by both providers and patients, even though the contribution of the original event to current symptoms is uncertain. This can place the patient into a category in which all of his or her symptoms are considered "mTBI symptoms." This attribution, and potential misattribution, of symptoms to mTBI can potentially place the patient at risk. When such a patient becomes "a TBI patient," providers may continue to view all of his or her symptoms through that prism. Unfortunately, some of the very programs that are intended to help patients with a history of mTBI may have the unintended consequence of reinforcing the concept that all of his or her symptoms are mTBI-related.[43,44] When this happens, the patient may consider himself/herself as a "lifelong" mTBI patient. Patients may subsequently be subjected to (or request) repeated evaluations that are unlikely to be helpful and are potentially harmful (e.g., needless exposure to radiation). Furthermore, attributing all symptoms to mTBI may bias providers who could miss important chronic or acute symptoms that may be more accurately associated with other conditions.

These patients are best managed within the primary care system. Rather than reinforce mTBI as the "cause" of the patient's problems, the primary care provider should use an approach to care that is consistent with the treatment of chronic, multisymptom conditions. The provider should use a collaborative step-care approach that builds on the principles of treatment for other chronic conditions, including CMI (see the VA/DoD CPG for the Management of CMI[12]) in the development of a comprehensive and personalized treatment plan. Building a solid therapeutic patient-provider alliance is essential to the proper management of patients with a history of mTBI. Symptoms should be acknowledged, not labeled as psychogenic, with an emphasis on reinforcing normalcy and wellness rather than impairment and self-labeling. Regularly scheduled appointments in primary care, rather than as-needed appointments, are recommended. Primary care providers should protect patients from unnecessary tests or consultations that could potentially put them at risk (e.g., from medication interactions prescribed from different providers) or lead to more negative illness expectations. Specialty consultation should be used if clinically indicated, but the use of specialty referrals should be conducted in a

[12] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

prudent and judicious fashion. This symptom-driven approach based in primary care validates the patient's experience, minimizes misattribution and labeling, maintains vigilance regarding new symptoms that may arise, helps avoid needless evaluations, and reduces the use of expensive and labor intensive specialty consultation and evaluations.

a. Effect of mTBI Etiology on Treatment Options and Outcomes

The leading causes of concussion include falls, motor vehicle accidents, being struck by or against an object, sports injury, and assaults. Blast exposure is another mechanism of mTBI injury, though it is uncertain to what extent the injury effects are due to primary blast exposure versus secondary or tertiary injuries from flying debris or being thrown into a hard object. Typically, TBI resulting from blast exposure represents a threat to military personnel only.

Recommendations

9. We recommend ***not*** adjusting treatment strategy based on mechanism of injury.
   (Strong Against | Reviewed, New-added)

10. We recommend ***not*** adjusting outcome prognosis based on mechanism of injury.
    (Strong Against | Reviewed, New-added)

Discussion

At the higher energy states associated with moderate and severe TBI, primary blast injury has been identified as a distinct, complex, and dynamic process, which results in unique tissue-level pathology.[45,46] However, unique effects associated with blast or other mechanisms of injury at lower energy states, consistent with concussive injury, are unknown. In the absence of an identified mechanism of injury and associated pathophysiology, treatment and prognosis are based on clinical assessment at this time. To date, assessments of mTBI symptoms as well as other health outcomes have demonstrated no significant clinical variance based on mechanism of injury.

In the systematic evidence review for the current mTBI CPG, none of the studies identified were specifically designed to evaluate mechanisms of injury or effectiveness of treatment as related to mechanism of injury. Given the limited evidence base and lack of evidence to suggest a difference in mTBI symptoms, therapy should not be modified based on mechanism of injury at this time. An increased proportion of patients with a history of mTBI associated with acceleration/deceleration brain injury may have anosmia, and an increased percentage of those with blast-associated mTBI may have hearing loss, which suggests a benefit for selective screening in these populations. Also, screening for psychological reaction and need for support may be warranted in those patients for whom assault is the underlying etiology.

Future research may investigate mechanism-specific physiologic response and may examine pathophysiology for which specific treatment and predictive outcome measures may be of value. Additional research is needed to improve diagnostic criteria and develop neuroprotective therapies before specific treatment recommendations or prognostic models can be developed based on individual mechanisms of injury.

See Appendix C: Mechanism of Injury for additional information.

b. Headache

Recommendation

11. We suggest that the treatment of headaches should be individualized and tailored to the clinical features and patient preferences. The treatment may include:
    a. Headache education including topics such as stimulus control, use of caffeine/tobacco/alcohol and other stimulants
    b. Non-pharmacologic interventions such as sleep hygiene education, dietary modification, physical therapy (PT), relaxation and modification of the environment (for specific components for each symptom, see Appendix B: Clinical Symptom Management)
    c. Pharmacologic interventions as appropriate both for acute pain and prevention of headache attacks

    (Weak For| Reviewed, Replaced)

Discussion

Headaches are common physical symptoms after mTBI occurring in 30-90% of individuals following TBI (mild, moderate, or severe).[47,48] *The International Classification of Headache Disorders- 2nd edition* defines posttraumatic headaches as secondary headache disorders that start within seven days after head trauma.[49] Posttraumatic headaches are commonly classified as migraine headaches, tension-type headaches, mixed tension/migraine headaches or cervicogenic headaches. The normal recovery of posttraumatic headaches following concussion is usually rapid (hours to days) with most headaches resolving within three months. However, in some cases, headaches may last longer and are referred to as persistent posttraumatic headaches.[50]

The overall evidence for the treatment of posttraumatic headaches neither supports nor refutes the effectiveness of current management strategies and the clinician must use best clinical judgment in treating headaches while weighing benefits and possible risks.

Clinical consideration for the management of posttraumatic headaches should begin with a detailed headache history, including headache location, severity, intensity, frequency, and associated symptoms (e.g., nausea, vomiting, photophobia) and physical examination with a focused neurological and musculoskeletal (including cervical spine) examination. Headache phenotype (e.g., migraines, tension type, cervicogenic headache, mixed headache) should be diagnosed and a treatment plan should be initiated. Headache management should take a patient-centered approach with the treatment program individualized and tailored to meet the needs and clinical presentation of the patient. Comorbid symptoms (e.g., dizziness, vision impairment, cognitive impairment, tinnitus) and conditions (e.g., PTSD, depression) should also be assessed and considered prior to initiation of the treatment program. Treatment considerations may include both non-pharmacologic and pharmacologic management options. Non-pharmacologic management may include education on lifestyle modifications, PT, integrative medicine techniques (e.g., acupuncture, relaxation therapy, mindfulness training), biofeedback and cognitive behavioral therapy (CBT).

Pharmacologic management for acute headache may include nonsteroidal anti-inflammatory drugs (NSAIDs), aspirin or acetaminophen. The use of the triptan class of medication (e.g., sumatriptan) for migraine-type headaches may be efficacious. For chronic daily headaches the use of prophylactic medications (e.g., topiramate) may be considered. (See Appendix B: Clinical Symptom Management for pharmacologic management options.) In the acute phase of management of posttraumatic headaches, narcotic analgesics

should be avoided, if possible. Also, special consideration is recommended for the assessment of medication-overuse headaches. Patients with posttraumatic headaches that are refractory to treatment should be referred to a physical medicine and rehabilitation physician, neurologist or brain injury specialist for further assessment. Further research is needed to address headache management after mTBI.

For additional clinical guidance, please see Appendix B: Headache.

c. Dizziness and Disequilibrium

Dizziness and disequilibrium are common symptoms/signs of many diagnoses, including mTBI. Dizziness was reported in one study as occurring in 26% of soldiers immediately after a deployment-related concussion, but only in 5% of all soldiers after returning from deployment. It is not clear to what degree this symptom was directly due to the previous mTBI in these soldiers. Dizziness is one of the most common symptoms in primary care.[51,52]

Recommendation

12. In individuals with a history of mTBI who present with functional impairments due to dizziness, disequilibrium, and spatial disorientation symptoms, we suggest that clinicians offer a short-term trial of specific vestibular, visual, and proprioceptive therapeutic exercise to assess the individual's responsiveness to treatment. Refer to occupational therapy (OT), physical therapy (PT) or other vestibular trained care provider as appropriate. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***.
    (Weak For| Reviewed, New-added)

Discussion

In the acute stage, mTBI may cause dizziness.[53-55] Subjective reports of dizziness correlate with objective testing only during the first week after the concussion/mTBI.[56] Mild TBI may cause coordination deficits of the lower extremities (imbalance) and/or upper extremities (dysmetria).[57-59] Cognitive distractions or performance of dual tasks are sensitive provocative tests for detection of imbalance and coordination deficits in the acute stage of mTBI.[57,59] Adjusting for age, gender, educational and employment status, patients with a history of mTBI who had a skull fracture, dizziness, and/or headache were at increased risk of developing persistent symptoms at one month.[60]

Although there is efficacy of vestibular and balance rehabilitation programs in patients with vestibular disorders in general, such as following acoustic neuroma resection or unexplained dizziness treated in primary care settings, there is no evidence that any specific program improves post-mTBI related symptoms.[61-63] One uncontrolled case series reported that preliminary vestibular rehabilitation or graded exercise improved posttraumatic dizziness symptoms in some patients.[54] In one randomized trial, Naguib and Madian found that a group of individuals with a history of TBI (all levels of severity) participating in a vestibular rehabilitation program immediately after the head trauma demonstrated significantly shorter recovery time than patients receiving a medication (betahistine) alone, with faster recovery in those with milder brain injury.[64]

Given the lack of evidence specific to vestibular rehabilitation in the mTBI population, it is unknown if the benefits of implementing a specific vestibular program, guided by a qualified vestibular rehabilitation therapist, could outweigh potential harms in certain patients (harms could include loss of patient's time and resources to attend a course of therapy without significant improvement or heightening negative perceptions of one's health

status). The purpose of such a trial would be to assess whether a particular patient benefits from vestibular rehabilitation techniques, as suggested. From case observations, one to two sessions can be sufficient for some patients, while others may benefit from more sessions. To minimize the potential negative effects of protracted, ineffective treatment, we suggest goal-based, functional re-assessment to determine treatment responsiveness. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***. Consideration should be given to patient preferences. Options should be presented clearly, such as whether participation will be primarily in a clinical setting with an adjunct home exercise program, or primarily focus on a home exercise program with infrequent follow-ups to manage and direct patient progress. While a brief trial of vestibular therapy may be considered, a symptom-based approach per other guidelines may be also considered. See related VA/DoD CPGs (e.g., PTSD[13], MDD[14] , Bipolar Disorder[15], Patients at Risk for Suicide[16], CMI[17]). Future controlled research is recommended on vestibular rehabilitation exercises in patients with a history of mTBI. Rigorous research should be conducted to define the types of dizziness in this patient population that will respond positively to specific vestibular rehabilitation.

For additional clinical guidance, please see Appendix B: Dizziness and Disequilibrium.

d. Tinnitus

Tinnitus is a common problem among the Operation Iraqi Freedom (OIF), Operation Enduring Freedom (OEF) and Operation New Dawn (OND) Veterans and Service Members who have sustained an mTBI.[65] A retrospective study published in 2012 reported that 75.7% of the Veterans with a history of mTBI reported tinnitus.[66] Tinnitus can occur as a direct consequence of mTBI, but can also occur from other causes such as a side effect from medications used to treat other common symptoms associated with mTBI.[67]

Recommendation

13. There is no evidence to suggest for or against the use of any particular modality for the treatment of tinnitus after mTBI.
    (N/A | Reviewed, New-added)

Discussion

As a guide to treatment, there is no evidence to support or refute differentiating tinnitus after mTBI from tinnitus from other etiologies. However, in a patient with functionally limiting symptoms, the Work Group suggests considering a short-term trial of tinnitus management (e.g., white noise generator, biofeedback, hypnosis, relaxation therapy) to assess the individual's responsiveness to treatment. Refer to an audiologist as appropriate. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***.

[13]See the VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Reaction. Available at: http://www.healthquality.va.gov/guidelines/mh/ptsd/index.asp

[14]See the VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/mdd/index.asp

[15]See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults. Available at: http://www.healthquality.va.gov/guidelines/mh/bd/index.asp

[16]See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide. Available at: http://www.healthquality.va.gov/guidelines/mh/srb/index.asp

[17] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

The literature search identified one prospective study of tinnitus after TBI conducted by Henry et al. that found no significant improvement in tinnitus after six sessions of telephone counseling over six months.[68] Confidence in the quality of the study is very low. The benefits and harms or burden are balanced with some variation of patient values and preferences. The purpose of such a trial would be to assess whether a particular patient benefits from tinnitus management techniques, as suggested. From case observations, one to two sessions can be sufficient for some patients, while others may benefit from more sessions. To minimize the potential negative effects of protracted, ineffective treatment, we suggest goal-based, functional re-assessment to determine treatment responsiveness.

Acute audiologic symptoms, including altered acuity, tinnitus and sensitivity to noise, occur in up to three-quarters of all individuals who sustain a concussion. The vast majority of those symptoms resolve within a month, unless there is significant or permanent injury to the eardrum. Audiologic symptoms may be related to concurrent injury to ear structure or other related medical conditions; assessment should be done to rule out these causes. The guideline panel advises performing an otologic examination, reviewing medications for ototoxicity and referring to audiology for hearing assessment if no other apparent cause if found. The Work Group acknowledges a paucity of literature on the difference between tinnitus from mTBI versus tinnitus from any other etiology and urges that head-to-head comparison trials be conducted.

e. Visual Symptoms

Recommendation

14. There is no evidence to suggest for or against the use of any particular modality for the treatment of visual symptoms such as diplopia, accommodation or convergence disorder, visual tracking deficits and/or photophobia after mTBI.
    (N/A | Reviewed, New-added)

Discussion

Visual dysfunction is a common complaint following mTBI,[69-71] manifested by problems with near visual acuity, an accommodation dysfunction, eye movement and ocular alignment disorders, and photophobia/glare sensitivity. Non-resolving vision disorders have a significant impact on functional performance and quality of life. Common vision complaints may include problems with reading print and electronic media, as well as changes to visual habits such as using a cell phone/texting, driving, visual gaming and participating in sports.

Limited evidence exists to demonstrate that vision rehabilitation reduces or eliminates functionally-limiting vision symptoms following mTBI. However, in a patient with functionally limiting symptoms, we suggest considering a short-term trial of specific visual rehabilitation to assess the individual's responsiveness to treatment. Consider a referral to optometry, ophthalmology, neuro-ophthalmology, neurology, and/or a vision rehabilitation team. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged***. Only one study among patients with a history of mTBI (with data reported in three separate publications) met inclusion criteria for the systematic review update for this CPG.[72-74] Although results of this study concluded that oculomotor training improved reading rate and reading grade level efficiency, the overall quality rating for the evidence was very low due to serious study design limitations (non-randomized, patients-blinded, crossover study), a small number of patients (n=12), and a short length of follow-up (treatment effects measured at seven weeks). Despite the lack of evidence to support vision rehabilitation care in patients with a history of mTBI, clinicians may consider a brief trial of an individualized vision therapy program while taking into

consideration potential harms (e.g., utilizing patient's time and resources to attend therapy with the possibility of completing the intervention without significant improvement, fostering negative illness expectations). The purpose of such a trial would be to assess whether a particular patient benefits from visual rehabilitation techniques, as suggested. From case observations, one to two sessions can be sufficient for some patients, while others may benefit from more sessions. To minimize the potential negative effects of protracted, ineffective treatment, we suggest goal-based, functional re-assessment to determine treatment responsiveness. Further research is needed to provide evidence on effective treatment interventions for visual dysfunction following mTBI.

For additional clinical guidance, please see Appendix B: Visual Symptoms.

f. Sleep Disturbance

Sleep disturbances can occur in approximately 30% of patients following mTBI.[75] These disturbances can include the following: (1) Persistent difficulty falling asleep or staying asleep despite the opportunity, (2) Delayed sleep phase syndrome, and (3) Irregular sleep-wake pattern. Sleep apnea, depression, pain, and other conditions may contribute to the overall poor quality of sleep. Pharmacologic treatment of sleep disturbance following mTBI may be complex. For all pharmacologic interventions, providers should weigh the risk-benefit profiles, including toxicity and abuse potential.

Recommendation

15. We suggest that treatment of sleep disturbance be individualized and tailored to the clinical features and patient preferences, including the assessment of sleep patterns, sleep hygiene, diet, physical activities and sleep environment. The treatment may include, in order of preference:
    a. Sleep education including education about sleep hygiene, stimulus control, use of caffeine/tobacco/ alcohol and other stimulants
    b. Non-pharmacologic interventions such as cognitive behavioral therapy specific for insomnia (CBTi), dietary modification, physical activity, relaxation and modification of the sleep environment (for specific components for each symptoms see Appendix B: Clinical Symptom Management)
    c. Pharmacologic interventions as appropriate to aid in sleep initiation and sleep maintenance

    (Weak For| Reviewed, Amended)

Discussion

There is no available literature demonstrating that sleep dysfunction after mTBI should be treated any differently than sleep dysfunction from other causes. A small study of 24 patients evaluated the use of acupuncture or a control intervention in the management of insomnia after mTBI.[76] Insomnia, as measured by the Insomnia Severity Index (ISI), and sleep time did not clinically improve.

Treatment of sleep disorders among patients with a history of mTBI can include both non-pharmacologic and pharmacologic therapy. The aim of sleep management is to establish a regular, normalized sleep-wake pattern. Non-pharmacologic therapies such as CBT and sleep hygiene may be employed. Tools used with CBT may include sleep education, stimulus control, sleep restriction, as well as methods to deal with stress, all with a goal of empowering the patient to manage his or her sleep dysfunction, especially in relation to comorbid conditions (e.g., circadian rhythm shift, restless leg syndrome, periodic limb movement disorder, rapid eye movement [REM] sleep behavior disorder).[77] CBT has proven efficacious in the treatment of sleep disorders as

demonstrated in a meta-analysis of behavioral therapies for insomnia that reported CBT improved subjective sleep quality and decreased subjective wake time during the night.[78]

Pharmacologic therapy for sleep dysfunction may include either prescription or over-the-counter (OTC) medications. The aim of therapy should be to use medications that will not produce dependency and have minimal adverse effects for patients with a history of mTBI. Medications should be used on a short-term basis only and may include trazodone, mirtazapine, and tricyclic antidepressants (e.g., amitriptyline). The use of benzodiazepines should be avoided in patients with a history of mTBI due to potential development of dependency and worsening of other persistent symptoms such as cognitive changes and decision making ability, as well as a high likelihood to worsen comorbid health conditions if present (particularly depression or PTSD).

For additional clinical guidance, please see Appendix B: Sleep Disturbance.

g. Behavioral Symptoms

Although the rates, intensity, and types of psychiatric symptoms following mTBI remain unclear, some evidence exists for the association of mental disorders, such as MDD or PTSD, with reduced recovery after concussion injury. Behavioral symptoms can also emerge following trauma due to direct or indirect effects of trauma. Commonly reported diagnostic groups include mood, anxiety, substance misuse, and trauma- and stress-related disorders, such as PTSD.[79-82]

Recommendation

16. We recommend that the presence of psychological or behavioral symptoms following mTBI should be evaluated and managed according to existing evidence-based clinical practice guidelines, and based upon individual factors and the nature and severity of symptoms.
    (Strong For | Reviewed, Amended)

Discussion

The emergence of psychiatric symptoms after mTBI can depend on many factors, including pre-injury psychosocial function and/or pre-existing mental illness, genetic predisposition to psychiatric illness, injury factors, and post-injury psychosocial factors. The nature and severity of symptoms (including any presence of suicidal ideation or threats to others), as ascertained in a thorough medical history, is necessary to choose appropriate treatments. Given the association of depression, PTSD, and other mental health problems with a history of mTBI and other injuries, it is recommended to assess for these conditions and consult related VA/DoD CPGs (e.g., PTSD[18], MDD[19] , Bipolar Disorder[20], Patients at Risk for Suicide[21], CMI[22]).

[18]See the VA/DoD Clinical Practice Guideline for Management of Posttraumatic Stress Disorder and Acute Stress Reaction. Available at: http://www.healthquality.va.gov/guidelines/mh/ptsd/index.asp

[19]See the VA/DoD Clinical Practice Guideline for Management of Major Depressive Disorder. Available at: http://www.healthquality.va.gov/guidelines/mh/mdd/index.asp

[20]See the VA/DoD Clinical Practice Guideline for Management of Bipolar Disorder in Adults. Available at: http://www.healthquality.va.gov/guidelines/mh/bd/index.asp

[21]See the VA/DoD Clinical Practice Guideline for Assessment and Management of Patients at Risk for Suicide. Available at: http://www.healthquality.va.gov/guidelines/mh/srb/index.asp

[22] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

The standard of care for psychological and behavioral symptoms following mTBI includes both psychotherapeutic and pharmacologic treatment modalities. In the 2009 mTBI CPG, there was stronger evidence for psychotherapies.[83-85] There has been some evidence demonstrating the effectiveness of CBT for treatment of PTSD, decreased cognitive skills, and depression in this population. However, there is no strong evidence for any specific therapy for irritability and other behavioral symptoms (such as impulsivity) following mTBI. To date, there are no medications specifically approved by the U.S. Food and Drug Administration (FDA) for treatment of post-mTBI psychiatric/behavioral symptoms. Since the 2009 mTBI CPG, there have been two randomized double-blind controlled clinical trials of medications specifically targeting behavioral symptoms after brain injuries. However, both studies included patients with moderate and severe brain injuries as well as mild and may only be marginally relevant to the patient population of interest.[86,87] Thus, although there are few studies involving specific populations with a history of mTBI, there is a broader body of evidence supporting the use of psychotherapy or pharmacologic interventions for mental disorders. Clinicians are encouraged to consult relevant CPGs for these conditions, taking into consideration the underlying diagnoses, patient preferences, comorbidities, and available treatment modalities.

h. Cognitive Symptoms

Recommendation

17. We suggest that patients with a history of mTBI who report cognitive symptoms that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms (e.g., sleep disturbance, headache) be referred as appropriate for a structured cognitive assessment or neuropsychological assessment to determine functional limitations and guide treatment.
    (Weak For | Not Reviewed, Amended)

Discussion

After 30 days post-injury, the use of formal neuropsychological testing should be reserved for specific diagnostic or management questions (e.g., What factors are contributing to the cognitive symptoms reported?, Are there behavioral deficits that are causing cognitive limitations or preventing clinical response to interventions?). Testing should be tailored to the specific questions being asked, the characteristics of the individual with the history of concussion, and to the skills, training and preferences of the neuropsychologist providing the assessment. Individuals who present with persistent complaints of cognitive-related symptoms (e.g., subjective memory deficits), despite normal cognitive skills on neuropsychological and functional assessments, should be provided psychoeducation and managed by primary care with a focus on health management (e.g., diet, exercise, mindfulness, general medical care), preventing and/or managing conditions that may affect cognition (e.g., depression, PTSD, insomnia, substance use), and use strategies for the long-term management of individuals with non-specific symptoms that persist for a number of months (e.g., VA/DoD CPG for the Management of CMI[23]).[22,88]

[23] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

Recommendation

18. We suggest that individuals with a history of mTBI who present with symptoms related to memory, attention or executive function problems that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. We suggest considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). **A *prolonged course of therapy in the absence of patient improvement is strongly discouraged*.** **(Weak For| Reviewed, New-replaced)**

Discussion

Although initial complaints of impaired memory, attention and executive function are common immediately following mTBI, the vast majority of individuals recover within a few hours to days.[22-24] However, a small number report new, persistent or worsening cognitive symptoms weeks, months or sometimes years post-injury.[22,88-90] This subgroup often presents with pre-morbid or comorbid conditions, such as depression, anxiety, poor health, chronic pain, negative self-beliefs and expectations, poor psychosocial support or other limited coping resources, or are involved in litigation or disability processes.[22,88,90] When considering referral to cognitive rehabilitation therapists with expertise in TBI rehabilitation (e.g., speech-language pathology, neuropsychology, OT) for a trial of cognitive rehabilitation treatment, coexisting factors that may decrease cognitive functioning (e.g., sleep difficulties, mental health concerns) must be considered. Conditions that have not been treated should be addressed by primary care providers or referred to the appropriate specialist for intervention when initiating cognitive treatment.

Cognitive-related difficulties can be treated symptomatically in some cases, regardless of the etiology of the symptom. Early in the treatment process, it is recommended to provide individuals with psychoeducation, supportive stress management and/or cognitive behavioral interventions to enhance recovery, in concert with optimizing the individual's overall health condition (e.g., sleep hygiene, pain management, dizziness management) and comorbid conditions (e.g., PTSD, MDD, anxiety disorder, SUD). If cognitive testing is done, it should emphasize focused assessment of functional limitations to guide interventions, and should be based on the skills, training and preferences of the treating clinician (e.g., psychologist, occupational therapist, speech-language pathologist). A comprehensive, holistic approach that integrates cognitive, emotional and interpersonal skills, focuses on metacognitive strategy training (thinking about thinking), and compensatory aids to improve planning, organization and participation in daily activities, such as work, school and household management tasks, are some strategies that have been used.

While evidence for the effectiveness of targeted cognitive rehabilitation in the moderate-to-severe TBI population has been well established,[91] there is limited evidence supporting a specific cognitive practice and dosage standard for mTBI. One systematic review [92] and three RCTs [93-95] were published since the last review of the literature and met inclusion criteria for the systematic review that informed this CPG. The overall quality rating for the current evidence was low for reported neuropsychologic or functional outcomes. Upcoming publications may provide additional information on this topic.

In the absence of strong scientific evidence and given that the potential harms (e.g., excessive resource use, over-emphasis on illness and disability) are probably no greater than the benefits; a weak recommendation was

made to consider a trial of cognitive rehabilitation focused on time-limited, measurable goals related to reducing activity limitations and improving activity participation. The purpose of such a trial would be to assess whether a particular patient benefits from strategy training and memory compensation techniques, as suggested. From case observations, one to two sessions can be sufficient for some patients, while others may benefit from more sessions. To minimize the potential negative effects of protracted, ineffective treatment, we suggest goal-based, functional re-assessment to determine treatment responsiveness. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged.*** If used, selection of the components and goals of the cognitive rehabilitation trial should be based on the integration of best available current evidence with clinical expertise and judgment, and should aim to reflect patient/family preferences, values, needs, abilities and interests.[96]

For additional clinical guidance, please see Appendix B: Cognitive Symptoms.

Recommendation

19. We suggest ***against*** offering medications, supplements, nutraceuticals or herbal medicines for ameliorating the neurocognitive effects attributed to mTBI.
    (Weak Against| Not Reviewed, Amended)

Discussion

Psychotropic medications have been used in treating cognitive issues related to other conditions, such as attention deficit hyperactivity disorder (ADHD) and dementia. For individuals with cognitive dysfunction after mTBI, atomoxetine, a non-stimulant ADHD medication,[97] and bromocriptine [98] have not been shown to be effective. Cholinergic agonists have been used for Alzheimer's patients to improve cognition and have been studied in TBI. Both rivastigmine [99] and donepezil [100,101] have been shown to be minimally effective in moderate to severe TBI, but are not recommended for mTBI. Lisdexamfetamine, a stimulant medication used for ADHD, was studied in a small group of only moderate to severe TBI patients with only mild improvement reported.[102] All of these studies have been small and some have significant methodological flaws. Additionally, the literature utilized in the 2009 mTBI CPG was from studies that were either small and poorly controlled or had mixed samples of injury severity. While some of these studies did include patients with a history of mTBI, the majority of subjects were diagnosed with moderate to severe TBI and those diagnosed with mTBI did not undergo a subgroup analysis. No medication has received approval from the FDA for the treatment of any mTBI-related cognitive dysfunction. Predominately with the stimulant class of medications, both substance abuse and diversion are potential concerns, with rates in the adult ADHD population ranging between 5-35%.[103]

Supplements, nutraceuticals and herbal treatments have not been studied in any controlled studies in patients with a history of mTBI.

The recommendation has a strength of "weak against" based on a low confidence in the existing literature and the risk of the harms from medication (e.g., side effects, medication interactions, polypharmacy) and supplements, nutraceuticals or herbal usage (e.g., side effects, interactions with medications, non-regulated products, variable strength and purity). There is also a relatively high use of resources associated with these agents and significant variability in preferences (for both patients and clinical providers) for both the use and specific type of agents recommended.

D. Setting of Care

Recommendation

20. We suggest ***against routine*** referral to specialty care in the majority of patients with a history of mTBI. **(Weak Against | Reviewed, Amended)**

Discussion

The diagnosis of mTBI is a clinical diagnosis, relying predominantly on patient history. Primary care providers can–and should–take a careful history, evaluate potential mTBI-related symptoms, and treat as appropriate. However, providers should also be cognizant of the risks of assuming that symptoms that present months or years after mTBI are directly attributable to the mTBI. Primary care providers are encouraged to utilize all techniques applicable to other chronic conditions (see the VA/DoD CPG for the Management of CMI[24]) and only make referrals judiciously as clinically indicated.

Confidence in the quality of the evidence for this recommendation was low.[46,92,104] The balance of positive outcomes or benefits slightly outweighs harms/burden to the patient in the primary care setting. There is some variation in patient values and preferences and the Work Group speculated that some patients may desire a more comprehensive interdisciplinary intervention (e.g., physical therapist, occupational therapist, clinical psychologist, pain medicine and rehabilitation medicine physician), evaluation and follow-up in addition to primary care. However, if primary care providers establish an alliance, build confidence with the patient, and also help the patient to understand potential risks of unnecessary referrals, this may not be necessary.

Recommendation

21. If the patient's symptoms do not resolve within 30-90 days and are refractory to initial treatment in primary care and significantly impact activities of daily living (ADLs), we suggest consultation and collaboration with a locally designated TBI or other applicable specialist. **(Weak For | Reviewed, Amended)**

Discussion

Consultation and collaboration with a TBI specialist may be considered if symptoms are refractory to treatment. However, it is best if care remains coordinated and managed in the primary care setting.[104] Patients should be asked about the impact of their symptoms on their daily function. Patients with a history of mTBI are typically independent in basic ADLs (e.g., grooming, bathing, dressing, toileting, mobility). However, a small minority of patients may present with problems performing instrumental ADLs (IADLs). These problems may impact independent functioning in tasks such as driving, home management, childcare, financial management, and performance at work or school.

Patients with symptoms should be asked open-ended questions to allow them to describe their difficulties and their impact on activity participation (e.g., What changes have you noticed due to symptom[s] in your work/school/home performance since your injury?). Presenting patients with symptom checklists is not recommended; however, these lists may be useful in documenting symptoms and symptom intensity.

[24] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

Consultation and collaboration with a TBI specialist may be considered when the patient's persistent symptoms significantly impact ADLs or IADLs. Confidence in the quality of evidence is very low based on a lack of current literature indicating improved outcomes in the TBI specialty setting versus ongoing symptom management in the primary care setting. Additional research is needed to evaluate patient symptom management outcomes in the TBI specialty care setting.

TBI specialist services may be provided in an outpatient treatment setting based on the individual needs of the patient. Symptom management under the direction of primary care with support of a TBI specialist may incorporate an interdisciplinary team setting that includes several subspecialties. A treatment plan is developed based on comprehensive evaluations and patient/family goals.

Local TBI subspecialties to consider for referral may include:

- Audiology/Vestibular – strategies for management for tinnitus, hearing loss, and vertigo
- Optometry/Ophthalmology – strategies for management for visual impairments
- Physical Therapy – strategies for management of gait/mobility impairments, vertigo, or pain
- Speech-Language Pathology – assessment of and strategies for management of cognitive deficits and cognitive/social communication
- Occupational Therapy – assessment and strategies for management of cognitive deficits and impact on everyday activities/IADLs
- Psychology/Neuropsychology – assessment and management of cognitive deficits of mental health or behavioral problems

However, it is unknown if the benefits outweigh the harms or burden of involving TBI specialists in patient symptom management or interventions to improve performance of ADLs. Increasing the number of specialists involved in care, even if optimally coordinated, increases the likelihood of differences in clinical opinions, conflicting patient education messages, or potential for risks such as medication interactions. Patient preferences and values should be considered when designing treatment plans. Other implications to consider include the lack of availability of TBI specialists and TBI programs in certain areas, as well as differences in how healthcare systems define a "TBI specialist." This may present issues in resource use, equity, acceptability, feasibility, and subgroup considerations. Lessons from the VA/DoD CMI CPG are particularly pertinent to this discussion (see the VA/DoD CPG for the Management of CMI[25]).

Recommendation

22. For patients with persistent symptoms that have been refractory to initial psychoeducation and treatment, we suggest referral to case managers within the primary care setting to provide additional psychoeducation, case coordination and support.
    (Weak For | Reviewed, Amended)

[25] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

Discussion

Individuals presenting with persistent symptoms should be considered for referral to case management, particularly in the primary care setting. Whether the individual has recently returned from deployment or combat, or is a Veteran who has sustained non-combat related head trauma, the need for a collaborative and coordinated approach to comprehensive care is important.

Case managers serve multiple functions:

- Complete an in-depth assessment of functional status and coordinate treatment resources
- Ensure that the patient is screened for social service needs and behavioral health problems
- Assure that referrals are coordinated and made as appropriate to the responsible discipline
- Ensure that the patient and family have received appropriate education
- Participate in setting short- and long-term goals
- Assist in the process of moving between facilities and levels of care
- Monitor patient progress
- Coordinate and collaborate with the multidisciplinary team

The recommendation for care/case coordination and incorporating psychoeducation for patients with persistent symptoms to improve clinical outcomes is based largely on research conducted by Bell et al.,[104] which only included relatively acute patients. Participants in the study who received active case management telephone follow-up with psychoeducation over the course of three months immediately following injury reported fewer symptoms at six months post-injury than those in the control group. Confidence in the quality of evidence is low and is based on the findings of a single study, the fact that the intervention was conducted solely by phone, and the relative acuity of the injury. The benefit of care/case management at greater than 6-12 months post-injury is unknown. Given the low risk and relative availability of care/case management in the military and VA settings, the benefits of care/case coordination slightly outweigh the harms or burdens. Patient values and preferences were noted to be similar with patients generally accepting of case management services incorporated in an interdisciplinary team approach. Effective case management services decrease the excessive use of resources through improved symptom management. Subgroup considerations include variability of skill of case managers and collaboration with the interdisciplinary or primary care teams.

Case managers should complete a comprehensive psychosocial assessment of the patient and the patient's family. It may be necessary or beneficial to meet with other members of the patient's support system (e.g., family, caregiver) and/or invite the patient to ask them to accompany him or her to an appointment. Case managers should collaborate with the treatment team, the patient, and the patient's family to develop a treatment plan that emphasizes the psychosocial needs of the patient. In collaboration with the treatment team, case managers should prepare and document a detailed treatment plan in the medical record describing follow-up care and services required.

Recommendation

23. There is insufficient evidence to recommend for or against the use of interdisciplinary/multidisciplinary teams in the management of patients with chronic symptoms attributed to mTBI.
    (N/A | Reviewed, New-replaced)

Discussion

The overall quality of evidence was very low for studies comparing multidisciplinary interventions (e.g., physical therapist, occupational therapist, clinical psychologist, pain medicine and rehabilitation medicine physician) versus usual care that was managed by a general practitioner. The evidence showed no significant difference in outcomes (TBI symptoms, fuction, quality of life, community integration) when using a multidisciplinary intervention versus usual care. However, Snell et al. found that a multidisciplinary intervention team approach was associated with significantly fewer mood disorder symptoms reported on the general health questionnaire (GHQ) at six months in participants with pre-injury psychiatric difficulties.[92] Additionally, Browne et al. found that patients who received a multidisciplinary intervention reported significantly greater pain relief compared to controls after controlling for age, gender and injury severity.[37] There is no current evidence to support that patients who initiate treatment for symptoms attributed to a history of mTBI should receive care solely in a primary care or multidisciplinary setting. Furthermore, no evidence examined patients with refractory symptoms who have failed initial treatment for symptoms attributed to a history of mTBI in primary care.

While the Work Group agreed that patients with a history of mTBI and subsequent symptoms are best treated within the primary care setting, the Work Group also recognized that primary care providers are often overwhelmed with a high volume of patient care encounters, and that some primary care settings may not be structured optimally to support management of chronic symptoms. This could challenge providers to assess, diagnose and provide recommended education. In addition to scheduling more regular primary care appointments for patients with chronic health conditions, such as persistent post-concussive symptoms, integrated behavioral health consultants and other specialists (e.g., nurse case managers) within the primary care setting are resources that can assist primary care providers. The Work Group recommends more research in this area.

VII. Knowledge Gaps and Recommended Research

During the development of the 2016 version of the CPG, the Work Group identified the following areas for conducting future research:

A. Diagnosis and Assessment

- Long-term outcome studies with a focus on the role of laboratory, imaging or physiologic testing in the management of and clinical decision making with a patient more than seven days following concussion
- Research to improve the diagnostic accuracy of tests for concussion/mTBI in the post-acute period
- Studies that acknowledge the lack of validation of existing case definitions of mTBI and examine diagnostic accuracy of cognitive and neuropsychological tests for concussion/mTBI
- Examine mechanism-specific physiologic response and associated pathophysiology for which specific treatment and predictive outcome measures may be of value

B. Treatment

- Studies of neuroprotective therapies to produce specific treatment recommendations or prognostic models based on individual mechanisms of injury
- Studies to address headache management specific to patients with a history of mTBI
- Controlled research to examine vestibular rehabilitation exercises in patients with a history of mTBI; define types of dizziness in this patient population that will respond positively to specific vestibular rehabilitation
- Head-to-head comparison trials on the difference between tinnitus from mTBI versus tinnitus from any other etiology
- Examine effective treatment interventions for visual dysfunction following mTBI

C. Care Delivery

- The role of interdisciplinary/multidisciplinary teams in the management of patients with chronic or persistent symptoms attributed to a history of mTBI
- The efficacy of stepped collaborative care models of treatment delivered in primary care settings

Appendix A: Guideline Development Methodology

A. Developing the Scope and Key Questions

The CPG Champions, along with the Work Group, were tasked with identifying key evidence questions to guide the systematic review of the literature on mTBI. These questions, which were developed in consultation with the Lewin team, addressed clinical topics of the highest priority for the VA and DoD populations. The KQs follow the population, intervention, comparison, outcome, timing and setting (PICOTS) framework for evidence questions, as established by the Agency for Healthcare Research and Quality (AHRQ). **Table A-1** provides a brief overview of the PICOTS typology.

Table A-1. PICOTS [105]

P	Patients, Population, or Problem	A description of the patients of interest. It includes the condition(s), populations or sub-populations, disease severity or stage, co-occurring conditions, and other patient characteristics or demographics.
I	Intervention or Exposure	Refers to the specific treatments or approaches used with the patient or population. It includes doses, frequency, methods of administering treatments, etc.
C	Comparison	Describes the interventions or care that is being compared with the intervention(s) of interest described above. It includes alternatives such as placebo, drugs, surgery, lifestyle changes, standard of care, etc.
O	Outcome	Describes the specific results of interest. Outcomes can include short, intermediate, and long-term outcomes, or specific results such as quality of life, complications, mortality, morbidity, etc.
(T)	Timing, if applicable	Describes the duration of time that is of interest for the particular patient intervention and outcome, benefit, or harm to occur (or not occur).
(S)	Setting, of applicable	Describes the setting or context of interest. Setting can be a location (such as primary, specialty, or inpatient care).

The Champions and evidence review team carried out several iterations of this process, each time narrowing the scope of the CPG and the literature review by prioritizing the topics of interest. Due to resource constraints, all developed KQs were not able to be included in the systematic evidence review. Thus, the Champions and Work Group determined which questions were of highest priority, and those were included in the review. **Table A-2** contains the final set of KQs used to guide the systematic review for this CPG.

a. Population(s)

The KQs are specific to adult patients aged 18 years or older with mTBI or a history of mTBI treated in any VA/DoD clinical setting. However, evidence from studies of patients with this condition managed outside the VA system were also included. The literature search did not include patients within seven days post-injury. Injury types considered included: blast, coup, contra-coup, direct trauma, acceleration/deceleration injury (whiplash).

b. Interventions

The diagnostic measures of interest included: neuroimaging (DTI, MRI, single photon emission computed tomography [SPECT]), electrophysiologic imaging, EEG, gait testing, balance testing, biomarkers, effort/validity testing, focused neurologic exam, Continuous Performance Task (CPT), neuropsychologic testing, visual, hearing, smell, eye tracking or oculomotor tests.

Interventions to treat common symptoms of mTBI included: specialized vestibular rehabilitation exercises (including visual, proprioceptive, and balance exercises), headache rehabilitation, medications, mind-body interventions, integrative medicine interventions, PT and other professionally-supervised exercises, sleep hygiene interventions, cognitive rehabilitation (e.g., brain training), CBT (various delivery methods), CBTi, white noise generator, repetitive transcranial magnetic stimulation (rTMS), visual /ocular rehabilitation.

c. Outcomes

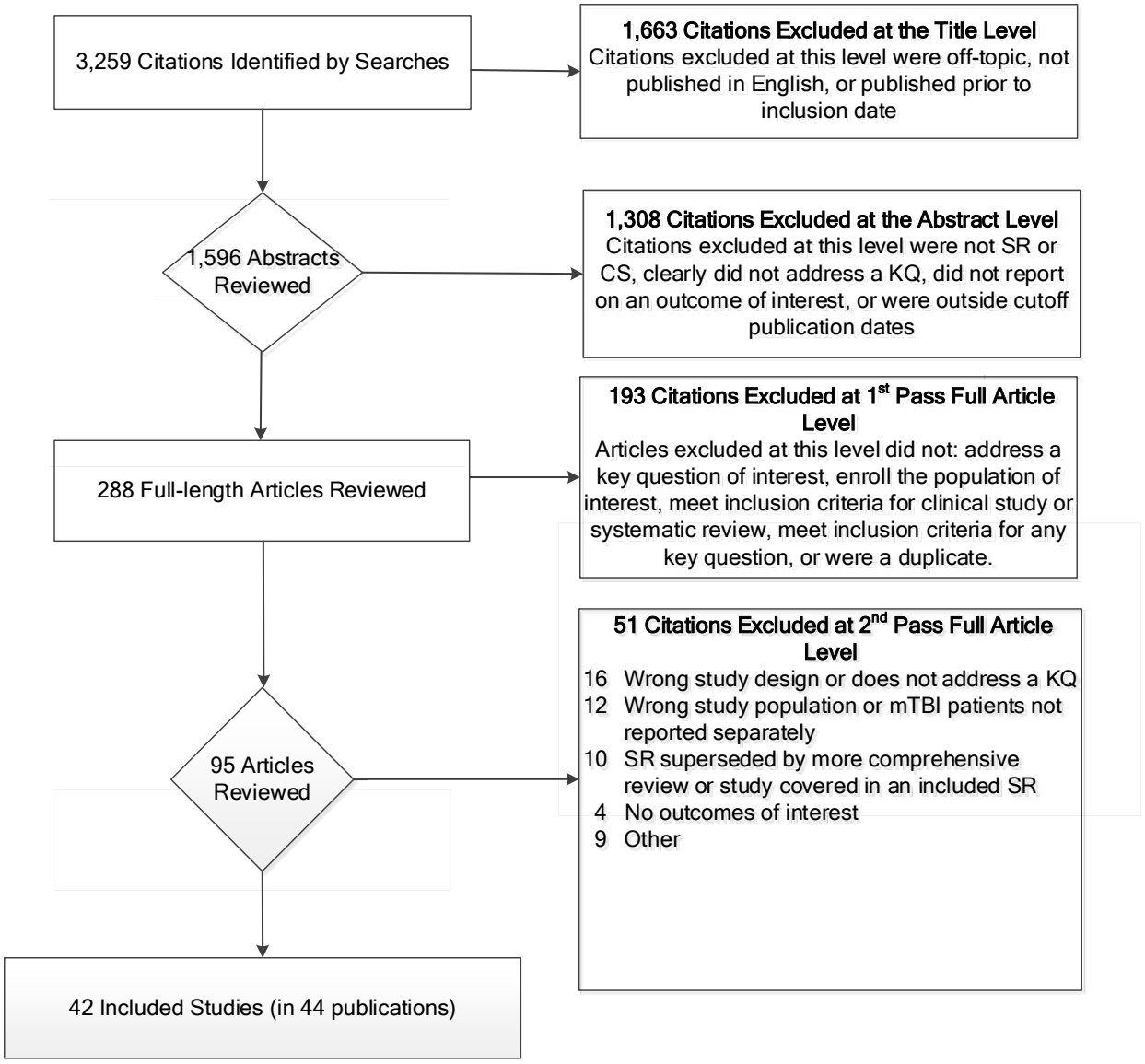
Outcomes of interest included: presence or intensity of symptoms attributed to mTBI; functional status; functional status predictive value for outcomes, or predictive value versus a gold standard; quality of life; severity of dizziness as measured by the Dizziness Handicap Inventory (DHI), Balance Error Scoring System (BESS) test, Berg Balance Scale (BBS), or other validated tests; severity of headache as measured by visual analog scales, the Oswestry Pain Scale, or other validated tools; safety/ adverse events; functional attention, concentration, or memory, as measured by validated tools; severity of irritability, as reported by patient or family, using a validated tool; severity of insomnia, as measured by the Pittsburgh Sleep Quality Index, the Epworth Sleepiness Scale, or other validated tools; severity of tinnitus, as measured by a standardized tinnitus questionnaire; and symptoms of visual impairment, such as diplopia, visual tracking deficits, or photophobia.

B. Conducting the Systematic Review

Extensive literature searches identified 3,259 citations potentially addressing the KQs of interest to this evidence review. Of those, 1,663 were excluded upon title review for clearly not meeting inclusion criteria (e.g., not pertinent to the topic, not published in English, published prior to study inclusion publication date, not a full-length article). Overall, 1,596 abstracts were reviewed with 1,308 of those being excluded for the following reasons: not a systematic review or clinical study, did not address a KQ of interest to this review, did not enroll a population of interest, or published prior to January 2008. A total of 288 full-length articles were reviewed. Of those, 193 were excluded at a first pass review for the following reasons: not addressing a KQ of interest, not enrolling the population of interest, not meeting inclusion criteria for clinical study or systematic review, not meeting inclusion criteria for any KQ, or being a duplicate. A total of 95 full-length articles were thought to address one or more KQs and were further reviewed. Of these, 51 were ultimately excluded for the reasons detailed in **Figure A-1**.

Overall, 42 studies (in 44 publications) addressed one or more of the KQs and were considered as evidence in the review. **Table A-2** indicates the number of studies that addressed each of the questions.

Figure A-1. Study Flow Diagram



mTBI: Mild traumatic brain injury
KQ: Key question
SR: Systematic review
CS: Controlled studies

Table A-2. Evidence Base for Key Questions

Number of Question	Question	Number of Studies & Type of Studies
1	a) For adults with acute mTBI, is there a single specialized diagnostic test, or set of tests, that improve accuracy of diagnosis, treatment decisions, and outcomes compared with routine primary care? b) Is there a single or set of specialized tests that improve the accuracy of diagnosis, treatment decisions and outcomes in post-acute period?	7 systematic reviews and 11 diagnostic studies
2	In adults with mTBI, what is the evidence that the mechanism of injury influences treatment effectiveness and outcomes?	6 prognostic cohort studies
3	In adults with mTBI and chronic symptoms attributed to mTBI, does the setting of care or model of care impact outcomes?	1 systematic review and 3 RCTs
4	For adults with mTBI and vestibular origin of dizziness, do specialized vestibular rehabilitation exercises improve symptoms at 3 months or more after initiation of the exercises?	1 RCT
5	For adults with headaches after a mTBI, what is the evidence that any intervention is effective and safe for improving symptoms (measured using standardized tools) or functional status (measured using standardized tools) at 3 months or more after initiation of the intervention?	2 systematic reviews and 2 RCTs
6	a) In adults with mTBI and post-concussive symptoms of impaired attention, concentration and/or memory, what is the evidence that automated (computer based) cognitive rehabilitation has equal or superior efficacy compared to clinician-based services in improving chronic symptoms at 3 months or more after initiation of the intervention? b) What is the comparative effectiveness of comprehensive neuropsychologic rehabilitation versus targeted cognitive rehabilitation in improving chronic symptoms at 3 months or more after initiation of the intervention?	1 systematic review and 3 RCTs
7	In adults with mTBI and behavioral dyscontrol (irritability), what is the safety and effectiveness of cognitive behavioral therapy (CBT) or pharmacotherapy as compared to usual care in improving symptoms as measured by patient or family report, at 3 months or more after initiation of CBT?	2 RCTs
8	In adults with mTBI and sleep disturbance, what is the safety and effectiveness of sleep hygiene interventions when compared to each other or to pharmacotherapy in improving outcomes at 3 months or more after initiation of the intervention?	1 RCT
9	In adults with mTBI and persistent tinnitus, what is the comparative effectiveness and safety of tinnitus interventions, such as white noise generators, medications, transcranial magnetic stimulation (rTMS), or other interventions on reducing symptoms when compared to stress management strategies as measured using standardized tinnitus questionnaires, at 3 months or more after initiation of intervention?	1 prospective cohort study
10	In adults with mTBI and post-concussive visual symptoms such as diplopia, visual tracking deficits and/or photophobia, does visual rehabilitation improve symptoms at 3 months or more after initiation of rehabilitation?	1 non-randomized crossover study (in 3 publications)
		42 Studies

d. Criteria for Study Inclusion/Exclusion

i. General Criteria

- Clinical studies or systematic reviews published on or after January 1, 2008. If multiple systematic reviews addressed a KQ, we selected the most recent and/or comprehensive review.

Clinical studies published subsequent to relevant systematic reviews were used to supplement the evidence base.

- Studies must have been published in English.
- Publication must be a full clinical study or systematic review; abstracts alone were not included. Similarly, letters, editorials, and other publications that are not full-length, clinical studies were not accepted as evidence.
- Studies enrolled adults 18 years or older. In studies that mixed adults and children, at least 80% of the enrolled patients had to be 18 years or older.
- Studies must have enrolled ≥10 patients per treatment arm.
- Study must have reported on an outcome of interest.
- Study must have enrolled a patient population in which the most prevalent diagnosis is mTBI, with identifiable data for the population of interest (i.e., patients with a history of mTBI should be identifiable in the dataset). Studies that did not report separate data for mTBI were included only in the absence of other studies meeting this criterion, and only if the remaining patients in the study had moderate or severe TBI (not stroke). However, studies including at least 80% of patients with a history of mTBI were not required to report separate data for patients with a history of mTBI.

ii. Key Question-Specific Criteria

- For KQ 1a, studies must have focused on use of specialized diagnostic approaches used at less than seven days following injury (acute period). For KQ 1b, studies must have focused on use of specialized diagnostic approaches at least seven days after the time of injury (post-acute period). Studies must have compared specialized diagnostic approaches to no test or usual care. For assessment of diagnostic accuracy, diagnostic cohort studies that compared a diagnostic test(s) to a reference standard within the same patient were acceptable.
- For KQ 2, non-randomized trials, cohort studies, case-controlled studies, and other observational studies were accepted as evidence in addition to RCTs and systematic reviews. Assessments must have been made at least seven days after the time of injury.
- For KQ 3, study must have been a systematic review of RCTs or an RCT. If insufficient evidence met this criterion, then controlled observational studies were considered as evidence for this question. Assessments must have been made at least seven days after the time of injury.
- For KQs 4–10, study must have been a systematic review of RCTs or an RCT. If insufficient evidence met this criterion, then controlled observational studies were considered as evidence for these questions. The minimum follow-up was three months.

e. Literature Search Strategy

ECRI Institute information specialists searched the following databases for relevant information. Search terms and strategies for the bibliographic databases appear below.

Table A-3. Resources Searched

Name	Date Limits	Platform/Provider
Agency for Healthcare Research and Quality (AHRQ)	2008 – March 2015	U.S. Department of Health & Human Services
CINAHL	2008 – March 2015	EBSCO Host
Cochrane Library	2008 – March 2015	John Wiley & Sons, Ltd.
Embase (Excerpta Medica)	2008 - March 2015	Elsevier
Healthcare Standards (HCS)	2008 – March 2015	ECRI Institute
Medline	2008 – March 2015	OVID Technologies, Inc.
National Guideline Clearinghouse (NGC)	2008 – March 2015	Agency for Healthcare Research and Quality (AHRQ)
National Institute for Health and Care Excellence (NICE)	2008 – March 2015	National Institute for Health and Care Excellence
PsycINFO	2008 – March 2015	OVID Technologies, Inc.
PubMed (In-process, Publisher, and PubMedNotMeSH records)	2008 – March 2015	National Library of Medicine (NLM)
TRIP	2008 – March 2015	TRIP (Jon Brassey and Dr. Chris Price)

i. Key question-specific search strategies

The strategies below are presented in Embase.com and OVID syntaxes. Embase.com was used to search for unique EMBASE (EMTREE) records. OVID was used to simultaneously search Medline (MeSH) and PsycINFO. Similar strategies were used to search CINAHL and PubMed, as well as the ancillary databases listed above.

Specific search strings were used to capture studies based on the KQs identified by the mTBI Working Group. Unique strategies were structured for each question and pertain to diagnostic methods, mechanisms of injury, care settings, dizziness, headaches, impaired concentration and memory, behavioral problems, sleep disturbance, tinnitus, and vision impairment. These search results were further refined to capture specific study designs, publication types, date ranges, patient populations, English language studies, and to exclude out-of-scope citations.

Table A-4. Topic-specific Search Terms

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
Patient Population		
Traumatic Brain Injury	**EMBASE** brain concussion brain injury concussion head injury post concussion syndrome traumatic brain injury **MeSH** brain concussion brain hemorrhage, traumatic brain injuries brain stem hemorrhage, traumatic coma, post-head injury craniocerebral trauma diffuse axonal injury intracranial hemorrhage, traumatic post-concussion syndrome subarachnoid hemorrhage, traumatic **PsycINFO** brain concussion brain damage head injuries traumatic brain injury **CINAHL** brain concussion brain injuries head injuries intracranial hemorrhage right hemisphere injuries left hemisphere injuries postconcussion syndrome	brain concuss* damage head injur* mtbi post* postconcuss* trauma*
KQ1 For adults with acute mTBI a. Is there a single specialized diagnostic test, or set of tests, that improve accuracy of diagnosis, treatment decisions, and outcomes compared with routine primary care? b. Is there a single or set of specialized tests that improve the accuracy of diagnosis, treatment decisions and outcomes in post-acute period?	**EMBASE** agnosia anosmia balance disorder balance impairment brain mapping biological marker brain electrophysiology brain injury assessment brain radiography brain scintiscanning brain tomography computer assisted tomography computer assisted emission tomography diagnostic imaging diffusion tensor imaging echoencephalography electroencephalography	agnosia anosmia assess* biological marker* biomarker* brain map* calcium binding protein* computed tomograph* decision* diagnos* diagnostic imag* diffuse tensor diffusion tensor effort test* elecroenceph* encephalog* evaluat*

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	electrophysiological procedures electrophysiology exercise test functional magnetic resonance imaging gait gait disorder low resolution brain electromagnetic tomography magnetoencephalography multimodal imaging neurologic examination neuropsychological test neuroradiology nuclear magnetic resonance imaging odor recognition test physical examination positron emission tomography protein s 100 protein s100B radiography single photon emission computed tomography smelling disorder spiral computer assisted tomography tomography **MeSH** agnosia biological markers brain mapping techniques diagnosis, differential diagnostic imaging diagnostic techniques, neurological diagnostic texts, routine diffusion magnetic resonance imaging diffusion tensor imaging echoencephalography electroencephalography electrophysiology gait gait disorders, neurologic image processing, computer assisted imaging, three-dimensional magnetic resonance imaging magnetic resonance spectroscopy magnetoencephalography multimodal imaging neuroimaging neurologic examination neuropsychological tests neuroradiography	exam* fmri functional magnetic* imag* magnetic resonance magnetoenceph* neuroimag* neuroradiograph* olfact* PET physical positron emission s100 s100b scinisc* single photon emission smell* SPECT SPECT-CT test* tomograph*

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	olfaction disorders physical examination positron-emission tomography postural balance s100 calcium binding protein beta subunit s100 proteins smell spectroscopy tomography, emission computed, single photon tomography, spiral computed tomography, x-ray computed **PsycINFO** Agnosia anosmia behavioral assessment biological markers differential diagnosis encephalography equilibrium functional magnetic resonance imaging gait magnetic resonance imaging neuroimaging neuropsychological assessment olfactory perception physical examination positron emission spectroscopy positron emission tomography stereotaxic atlas tomography **CINAHL** agnosia anosmia balance, postural biological markers brain mapping calcium binding proteins diagnostic imaging digital imaging electrophysiology electroencephalography eye movement measurements eye movements gait gait disorders, neurologic imaging, three-dimensional magnetic resonance imaging magnetic resonance spectroscopy	

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	multidetector computed tomography neurologic examination neuropsychological tests neuroradiography oculomotor muscles oculomotor nerve oculomotor nerve disease olfaction disorders physical examination smell spectroscopy tomography, emission computed tomography, emission-computed, single-photon tomography, spiral computed tomography, x-ray computed	
KQ2 In adults with mTBI, what is the evidence that the mechanism of injury influences treatment effectiveness and outcomes?	**EMBASE** acceleration blast injury contrecoup injury deceleration traffic accident whiplash injury **MeSH** acceleration accidents, traffic blast injuries contrecoup injury deceleration explosions whiplash injuries **PsycINFO** military deployment motor traffic accidents whiplash **CINAHL** acceleration (mechanics) accidents, traffic blast injuries whiplash injuries	accelerat* accident* decelerat* blast* bomb* car car accident* cause* coup contrecoup decelerat* deploy* explosi* injur* mechanism* non-deploy* nondeplo* traffic traffic accident* un-deploy* undeploy* type* whiplash
KQ3 In adults with mTBI and chronic symptoms attributed to mTBI, does the setting of care or model of care impact outcomes? a. What is the comparative effectiveness of primary care with case management versus an interdisciplinary team model on symptom reduction and improvements in quality of life, satisfaction and functional status following mTBI?	**EMBASE** ambulatory care case management case manager community hospital day hospital emergency health service emergency ward general hospital general practice general practitioner	ambulatory care case manag* center* clinic clinics collaborativ* consult consultation cooperativ* department* doctor* emergency

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
b. What is the evidence that certain subpopulations of patients with mTBI benefit from integrated multidisciplinary team approaches and what are the criteria for referral? c. Do outcomes differ based on setting of post-acute (i.e., greater than seven days) management approaches such as inpatient/outpatient primary/specialty?	health care facility health center hospital outpatient care outpatient department primary health care primary medical care private hospital public hospital rapid response team rehabilitation center rehabilitation hospital residential care residential home team nursing teamwork tertiary care center **MeSH** ambulatory care ambulatory care facilities case management emergency service, hospital family practice hospitals hospitals, veterans inpatient nursing, team outpatients outpatient clinics, hospital patient handoff patient care team primary health care referral and consultation residential treatment tertiary care centers trauma centers **PsycINFO** case management clinics emergency services hospitalized patients hospitals interdisciplinary treatment approach outpatient treatment outpatients primary health care professional consultation professional referral residential care institutions self managing work teams	family general hospital* inpatient integrat* interdisciplin* location* multidisciplin* nurs* outpatient patient physician* practice practitioner* primary professional refer referral residential setting* specialist specialty team* tertiary treatment* unit units veteran* ward*

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	walk in clinics work teams teams **CINAHL** ambulatory care facilities case management case managers community health centers emergency service hospitals hospitals, veterans inpatients multidisciplinary care team nurse-managed centers outpatients outpatient service physicians, family primary health care referral and consultation residential care residential facilities rural health centers team nursing teamwork	
KQ4 For adults with mTBI and vestibular origin of dizziness, do specialized vestibular rehabilitation exercises improve symptoms at 3 months or more after initiation of the exercises?	**EMBASE** balance disorder balance impairment dizziness kinesiotherapy physiotherapy vertigo vestibular disorder vestibular function vestibular test vestibular testing equipment **MeSH** dizziness exercise therapy physical therapy modalities postural balance vertigo vestibular diseases vestibular function tests **PsycINFO** equilibrium exercise labyrinth diseases physical therapy vertigo vestibular apparatus **CINAHL** balance, postural	balance balance error scoring system berg balance scale canalith continuous performance test dizziness handicap inventory test deficit disorder* dizz* exercise* epley equilibrium impair* labyrinth liberatory loss maneuver* problem* screen* semont symptom test* therap* treat* vertigo vestibular

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	balance training, physical dizziness physical therapy therapeutic exercise vertigo vestibular diseases vestibular functional tests	
KQ5 For adults with headaches after a mTBI, what is the evidence that any intervention is effective and safe for improving symptoms (measured using standardized tools) or functional status (measured using standardized tools) at 3 months or more after initiation of the intervention??	**EMBASE** functional assessment functional status glasgow outcome scale headache measurement migraine oswestry disability index questionnaire rating scale severity of illness index **MeSH** glasgow coma scale glasgow outcome scale headache headache disorders migraine disorders pain measurement post-traumatic headache psychometrics questionnaires severity of illness index **PsycINFO** headache migraine headache questionnaires rating scales severity (disorders) **CINAHL** behavior rating scales functional status headache headache, primary headache, secondary questionnaires scales severity of illness indexes structured questionnaires tension headache ways of coping questionnaires	glasgow headache* measure* index* migraine* oswestry pain questionnaire rating scale* rivermead scale* severity severity of illness

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
KQ6 In adults with mTBI and post-concussive symptoms of impaired attention, concentration and/or memory: a. What is the evidence that automated (computer based) cognitive rehabilitation has equal or superior efficacy compared to clinician-based services in improving chronic symptoms at 3 months or more after initiation of the intervention? b. What is the comparative effectiveness of comprehensive neuropsychologic rehabilitation versus targeted cognitive rehabilitation in improving chronic symptoms at 3 months or more after initiation of the intervention?	**EMBASE** attention attention deficit disorder computer assisted therapy concentration loss group therapy memory memory assessment memory disorder mental concentration cognitive rehabilitation cognitive therapy support group psychotherapy **MeSH** attention attention deficit disorder attention deficit disorder with hyperactivity cognitive therapy computer user training memory memory disorders psychotherapy psychotherapy, brief psychotherapy, group self-help groups therapy, computer assisted **PsycINFO** attention attention deficit disorder attention deficit disorder with hyperactivity brief psychotherapy cognitive behavior therapy cognitive rehabilitation concentration computer assisted therapy group counseling group psychotherapy individual psychotherapy memory memory disorders psychotherapy support groups **CINAHL** attention attention deficit hyperactivity disorder cognitive therapy memory disorders psychotherapy psychotherapy, brief psychotherapy, group rehabilitation, cognitive support groups therapy, computer assisted	attention brief* cognitive behav* cognitive rehab* cognitive therap* comprehensive computer* concentration focused group* individual* memories memory psychiatr* psychol* psychotherap* short* support group* targeted

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
KQ7 In adults with mTBI and behavioral dyscontrol (irritability), what is the safety and effectiveness of cognitive behavioral therapy (CBT) or pharmacotherapy as compared to usual care in improving symptoms as measured by patient or family report, at 3 months or more after initiation of CBT?	**EMBASE** antidepressant agent anxiolytic agent anxiolytic agent tranquilizer behavior behavior disorder caregiver caregiver burden cognitive behavioral stress management cognitive therapy cognitive rehabilitation domestic violence dysfunctional therapy emotional abuse emotional stress extended family family family assessment family conflict family coping family functioning family interaction family life family stress group therapy hypnotic sedative agent mental instability neuroleptic agent patient assessment patient attitude partner violence psychopharmacology psychotherapy psychotrauma sedative agent support group violence **MeSH** anti-anxiety agents antidepressive agents antipsychotic agents behavioral control behavioral symptoms brief psychotherapy cognitive therapy dangerous behavior drug therapy family family conflict "hypnotics and sedatives" individual psychotherapy nuclear family patient satisfaction	irrational irritabl* medicat* neuroleptic* partner* pharmacother* psychopharmacol* psychotherap* sedativ* spouse* support* targeted tranquiliz* uncontrol* unpredictab* unsafe unstable violen* wife wives

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	psychopharmacology psychotherapy psychotherapy, brief psychotherapy, group self-help groups tranquilizing agents **PsycINFO** aggressive behavior antidepressant drugs antipsychotic agents behavior problems brief psychotherapy cognitive behavior therapy cognitive rehabilitation dangerousness family family conflict family crises family intervention family members family relations family therapy group counseling group psychotherapy 'hypnotics and sedatives' individual psychotherapy minor tranquilizers neuroleptic drugs psychopharmacology sedatives self destructive behavior self injurious behavior self report tranquilizing drugs support groups violence **CINAHL** aggression antianxiety agents antidepressive agents antipsychotic agents behavioral changes cognitive therapy domestic violence dysfunctional family family family attitudes family relations 'hypnotics and sedatives' intimate partner violence nuclear family psychopharmacology psychotherapy	

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	psychotherapy, brief psychotherapy, group rehabilitation, cognitive risk taking behaviors self-injurious behavior social behavior disorders support groups tranquilizing agents verbal abuse violence	
KQ8 In adults with mTBI and sleep disturbance, what is the safety and effectiveness of sleep hygiene interventions when compared to each other or to pharmacotherapy in improving outcomes at 3 months or more after initiation of the intervention?	**EMBASE** acupressure acupuncture alternative medicine central sleep apnea syndrome circadian rhythm sleep disorder cognitive rehabilitation cognitive therapy diphenhydramine dream dreaming eszopiclone herbaceous agent herbal medicine holistic care hypnotic sedative agent insomnia insomnia severity index integrative medicine nightmare parasomnia prazosin reiki relaxation training rem sleep deprivation sedative agent sleep sleep arousal disorder sleep disorder sleep disorder assessment sleep disordered breathing sleep therapy unpleasant dream vivid dream yoga zolpidem tartrate **MeSH** acupressure acupuncture acupuncture therapy analgesics complementary medicine diphenhydramine	acupressure acupuncture alternative ambien benadryl apnea* circadian cognitive behavior* cognitive processing therap* cognitive rehab* cognitive therap* complementary diphenhydramine dream* drug* epworth sleepiness scale eszopiclone exercis* holistic* hygiene hypnotic* insomnia* lunesta nightmare* parasomnia* pittsburgh sleep quality index prazosin reiki relax* sedat* sleep* yoga zolpidem

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	dreams circadian rhythm cognitive therapy complementary therapies diphenhydramine drug therapy glasgow outcome scale holistic health hypnotics and sedatives medicine, chinese traditional prazosin prescription drugs psychotropic drugs relaxation therapy rem sleep parasomnias sleep sleep apnea sleep apnea, central sleep apnea, obstructive sleep apnea syndromes sleep arousal disorders sleep deprivation sleep disorders, circadian rhythm sleep disorders, intrinsic sleep initiation and maintenance disorders sleep-wake transition disorders sleep initiation and maintenance disorders therapeutic touch **PsycINFO** acupuncture alternative medicine cognitive behavior therapy cognitive rehabilitation diphenhydramine dream analysis dream content dream recall dreaming drug therapy holistic health hypnotic drugs insomnia lucid dreaming medicinal herbs and plants nightmares prescription drugs relaxation therapy rem dreams sleep disorders sleep onset sleep-wake cycle	

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	sleep treatment sleep-wake cycle yoga **CINAHL** alternative health facilities alternative therapies cognitive therapy diphenhydramine drugs, prescription eszopiclone holistic care holistic health holistic nursing hypnotics and sedatives insomnia meditation rehabilitation, cognitive relaxation techniques sleep arousal disorders sleep disorders, circadian rhythm sleep disorders, intrinsic sleep-wake transition disorders Zolpidem	
KQ9 In adults with mTBI and persistent tinnitus, what is the comparative effectiveness and safety of tinnitus interventions, such as white noise generators, medications, transcranial magnetic stimulation (rTMS), or other interventions on reducing symptoms when compared to stress management strategies as measured using standardized tinnitus questionnaires, at 3 months or more after initiation of intervention?	**EMBASE** alternative medicine auditory rehabilitation cochlea implant cochlear implantation cognitive behavioral stress management cognitive rehabilitation cognitive therapy functional assessment functional status glasgow outcome scale hearing aid psychotropic agent questionnaire rating scale severity of illness index transcranial magnetic stimulation transcranial magnetic stimulation system tinnitus white noise **MeSH** acoustic stimulation behavior therapy cochlear implantation cochlear implants cognitive therapy complementary therapies glasgow outcome scale hearing aids meditation mindfulness perceptual masking	acoustic* alternative auditory cochlear cognitive behavior* cognitive processing therap* cognitive rehab* cognitive therap* complementary drug* evoked hearing aid* magnetic* measure* medicat* meditat* mindful* noise generator index* psychotropic* questionnaire* rehab* scale* severity of illness sound generator* stress* tinnitus transcranial white noise

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
	psychotropic drugs questionnaires therapeutic use severity of illness index transcranial magnetic stimulation stress, psychological tinnitus **PsycINFO** acoustics auditory evoked potentials auditory perception auditory stimulation behavior therapy cochlear implants cognitive behavior therapy cognitive rehabilitation functional analysis disability evaluation hearing aids measurement meditation mindfullness questionnaires rating scales severity (disorders) stress stress management tinnitus transcranial magnetic stimulation white noise **CINAHL** acoustic stimulation auditory perception auditory diseases, central auditory neuropathy behavior rating scales evoked potentials, auditory, brainstem cochlear implant functional status hearing aids magnetic therapy meditation mindfulness questionnaires scales severity of illness indexes stress management structured questionnaires tinnitus tinnitus retraining therapy ways of coping questionnaires	

Concept	Controlled Vocabulary	Keywords/PubMed Concepts
KQ10 In adults with mTBI and post-concussive visual symptoms such as diplopia, visual tracking deficits and/or photophobia, does visual rehabilitation improve symptoms at 3 months or more after initiation of rehabilitation?	**EMBASE** abnormal vision diplopia photosensitivity vision test visual disorder visual impairment **MeSH** diplopia photosensitivity disorders vision disorders vision tests **PsycINFO** vision disorders **CINAHL** diplopia photosensitivity disorders visual perception vision disorders vision screening vision, subnormal vision tests	blur* deficien* deficit* diplopia disorder* double* double vision eye eyes eyesight impair* ocular oculo* photophobia photosensitiv* rehab* sensitiv* therap* track* train* vision visual* sight

OVID Conventions:

* (within or following a term) = truncation character (wildcard)

.ab. = limit to abstract

ADJn = search terms within a specified number (*n*) of words from each other in any order

exp/ = "explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)

.mp. = combined search fields (default if no fields are specified)

.pt. = publication type

.ti. = limit to title

.ti,ab. = limit to title and abstract fields

Table A-5. Medline/PsycINFO Search Strategies Presented in OVID Syntax

Set #	Concept	Search Statement
1	**Mild Traumatic Brain Injury**	exp brain concussion/ or exp brain damage/ or exp brain injuries/ or exp brain hemorrhage, traumatic/ or exp brain stem hemorrhage, traumatic/ or exp coma, post-head injury/ or exp craniocerebral trauma/ or exp intracranial hemorrhage, traumatic/ or exp post-concussion syndrome/ or exp subarachnoid hemorrhage, traumatic/ or exp traumatic brain injury/ or ((brain or head) adj1 (concuss* or damage* or injur* or trauma*)).ti,ab. or (post* adj1 concuss*).ti,ab. or mtbi.ti,ab. or postconcuss*.ti,ab.
2	**KQ1** **Diagnostic Assessments/Tests/Procedures**	exp agnosia/ or exp anosmia/ or exp biological markers/ or exp brain mapping/ or exp diagnostic imaging/ or exp diagnostic techniques, neurological/ or exp diagnostic texts, routine/ or exp diffusion magnetic resonance imaging/ or exp diffusion tensor imaging/ or exp echoencephalography/ or exp electroencephalography/ or exp electrophysiology/ or exp encephalography/ or exp functional magnetic resonance imaging/ or exp gait/ or exp gait disorders, neurologic/ or exp image processing, computer assisted/ or exp imaging, three-dimensional/ or exp magnetic resonance imaging/ or exp magnetic resonance spectroscopy/ or exp magnetoencephalography/ or exp multimodal imaging/ or exp neuroimaging/ or exp neurologic examination/ or exp neuropsychological assessment/ or exp neuropsychological tests/ or exp neuroradiography/ or exp olfaction disorders/ or exp olfactory perception/ or exp positron emission/ or exp positron emission tomography/ or exp positron-emission tomography/ or exp postural balance/ or exp s100 calcium binding protein beta subunit/ or exp s100 proteins/ or exp smell/ or exp spectroscopy/ or exp stereotaxic atlas/ or exp tomography/ or exp tomography, emission computed, single photon/ or exp tomography, spiral computed/ or exp tomography, x-ray computed/ or (agnosia or anosmia or biological marker* or biomarker* or brain map* or calcium binding protein* or computed tomograph* or diagnostic imag* or diffuse tensor or diffusion tensor or echoenceph* or effort test* or elecroenceph* or encephalogr* or functional magnetic or fmri or magnetic resonance or magnetoenceph* or neuroimag* or neuroradiograph* or PET or positron emission or s100 or s100b or scinisc* or single photon emission or SPECT or SPECT-CT or tomograph*).ti,ab. or (diagnos* adj2 decision*).ti,ab. or ((electrophysiolog* or gait or neurolog* or neuropsych* or olfact* or physical* or smell*) adj1 (assess* or diagnos* or evaluat* or exam* or test*)).ti,ab.
3	**KQ2** **Mechanism of Injury**	exp acceleration/ or exp accidents, traffic/ or exp blast injuries/ or exp contrecoup injury/ or exp deceleration/ or exp explosions/ or exp military deployment/ or exp motor traffic accidents/ or exp whiplash/ or exp whiplash injuries/ or (accelerat* or accident* or blast* or bomb* or car accident* or coup or contrecoup or decelerat* or deploy* or explosi* or non-deploy* or nondeploy* or traffic accident* or un-deploy* or undeplo* or whiplash).ti,ab. or (injur* adj2 (cause* or mechanism* or type*)).ti,ab.
4	**KQ3** **Care Settings**	exp ambulatory care/ or exp ambulatory care facilities/ or exp case management/ or exp clinics/ or exp emergency service, hospital/ or exp emergency services/ or exp family practice/ or exp hospitalized patients/ or exp hospitals/ or exp hospitals, veterans/ or exp inpatient/ or exp interdisciplinary treatment approach/ or exp nursing, team/ or exp outpatient clinics, hospital/ or exp outpatient treatment/ or exp outpatients/ or exp patient care team/ or exp patient handoff/ or exp primary health care/ or exp professional consultation/ or exp professional referral/ or exp "referral and consultation"/ or exp residential care institutions/ or exp residential treatment/ or exp self managing work teams/ or exp teams/ or exp tertiary care centers/ or exp trauma centers/ or exp walk in clinics/ or exp work teams/ or (team* adj1 (care or collaborat* or cooperativ* or integrat* or interdisciplin* or multidisciplin* or nurs* or treatment*)).ti,ab. or (case adj1 manag*).ti,ab. or ((treatment or care) adj1 (location* or setting*)).ti,ab. or ((ambulatory or emergency or inpatient* or

Set #	Concept	Search Statement
		outpatient* or primary or residential or tertiary or veteran*) adj1 (center* or clinic or clinics or department* or hospital* or location* or setting* or unit or units or ward*)).ti,ab. or ((patient or professional or specialist or specialty) adj1 (consult or consultation or refer or referral)).ti,ab. or ((primary or family) adj1 (care or doctor* or physician* or practitioner*)).ti,ab.
5	**KQ4** **Dizziness/Vestibular Rehabilitation**	((exp dizziness/ or exp equilibrium/ or exp labyrinth diseases/ or exp postural balance/ or exp vertigo/ or exp vestibular diseases/) and (exp exercise/ or exp exercise therapy/ or exp physical therapy/ or exp physical therapy modalities/ or exp vestibular apparatus/ or exp vestibular function tests/)) or ((balanc* or canalith or dizz* or epley or equlibrium or labyrinth or liberatory or semont or vertigo or vestibular) adj1 (deficit* or disorder* or exercis* or impair* or loss* or maneuver* or problem* or screen* or symptom* or test* or therap* or treat*)).ti,ab or (balance error scoring system or berg balance scale or continuous performance test or dizziness handicap inventory).ti,ab.
6	**KQ5** **Headache**	((exp headache/ or exp headache disorders/ or exp migraine disorders/ or exp migraine headache/ or exp post-traumatic headache/) and (exp glasgow coma scale/ or exp glasgow outcome scale/ or exp pain measurement/ or psychometrics/ or exp questionnaires/ or exp rating scales/ or exp "severity (disorders)"/ or exp severity of illness index/)) or ((headache* or migraine*) adj1 (glasgow or measure* or index* or oswestry or questionnaire* or rivermead or rating scale* or scale* or severity of illness)).ti,ab.
7	**KQ6** **Attention/Concentration/ Memory Impairment**	((exp attention/ or exp attention deficit disorder/ or exp attention deficit disorder with hyperactivity/ or exp concentration/ or exp memory/ or exp memory disorders/) and (exp brief psychotherapy/ or exp cognitive behavior therapy/ or exp cognitive rehabilitation/ or exp cognitive therapy/ or exp computer assisted therapy/ or exp computer user training/ or exp group counseling/ or exp group psychotherapy/ or exp individual psychotherapy/ or exp psychotherapy/ or exp psychotherapy, brief/ or exp psychotherapy, group/ or exp self-help groups/ or exp support groups/ or exp therapy, computer assisted/)) or ((attention or concentration or memories or memory).ti,ab. and ((brief* or comprehensive or computer* or focused or group* or individual* or short* or targeted) adj1 (cognitive behav* or cognitive therap* or cognitive rehab* or psychol* or psychotherap* or psychiatric*))).ti,ab.
8	**KQ7** **Behavioral Problems**	((exp aggressive behavior/ or exp behavior problems/ or exp behavioral control/ or exp behavioral symptoms/ or exp dangerous behavior/ or exp dangerousness/ or exp self destructive behavior/ or exp self injurious behavior/ or exp self report/ or exp violence/) and (exp anti-anxiety agents/ or exp antidepressant drugs/ or exp antidepressive agents/ or exp antipsychotic agents/ or exp brief psychotherapy/ or exp cognitive therapy/ or exp cognitive behavior therapy/ or exp cognitive rehabilitation/ or exp drug therapy/ or exp family/ or exp family conflict/ or exp family crises/ or exp family intervention/ or exp family members/ or exp family relations/ or exp family therapy/ or exp group counseling/ or exp group psychotherapy/ or exp 'hypnotics and sedatives'/ or exp individual psychotherapy/ or exp neuroleptic drugs/ or exp nuclear family/ or exp psychopharmacology/ or exp psychotherapy/ or exp psychotherapy, brief/ or exp sedatives/ or exp self-help groups/ or exp support groups/ or exp tranquilizing agents/ or exp tranquilizing drugs)) or ((abus* or aggress* or anger or angry or conflict* or danger* or destruct* or discontrol* or distress* or erratic* or instability or irrational* or irrit* or uncontrol* or unpredict* or unsafe or unstable or violen*) adj1 (antianxiety or antidepress* or antipsychotic* or care giver or caregiver* or child* or cognitive behav* or cognitive rehab* or cognitive therap* or domestic or drug therap* or family or families or group therap* or husband or partner* or medicat* or neuroleptic* or psychiatr* or psychol* or psychopharmacol* or psychotherap* or sedative* or spouse* or support group* or tranquiliz* or wife or wives)).ti,ab

Set #	Concept	Search Statement
9	**KQ8** **Sleep Disturbance**	((exp circadian rhythm/ or exp insomnia/ or exp rem sleep behavior disorder/ or exp rem sleep parasomnias/ or exp sleep/ or exp sleep apnea/ or exp sleep apnea, central/ or exp sleep apnea, obstructive/ or exp sleep apnea syndromes/ or exp sleep arousal disorders/ or exp sleep deprivation/ or exp sleep disorders/ or exp sleep disorders, circadian rhythm/ or exp sleep disorders, intrinsic/ or exp "sleep initiation and maintenance disorders"/ or exp sleep onset/ or exp sleep wake cycle/ or exp sleep-wake transition disorders) and (exp acupressure/ or exp acupuncture/ or exp acupuncture therapy/ or exp alternative medicine/ or exp analgesics/ or exp cognitive behavior therapy/ or exp cognitive rehabilitation/ or exp cognitive therapy/ or exp complementary medicine/ or exp complementary therapies/ or exp diphenhydramine/ or exp dream analysis/ or exp dream content/ or exp dream recall/ or exp dreaming/ or exp dreams/ or exp drug therapy/ or exp glasgow outcome scale/ or exp holistic health/ or exp hypnotic drugs/ or exp "hypnotics and sedatives"/ or exp lucid dreaming/ or exp "medicinal herbs and plants"/ or exp medicine, chinese traditional/ or exp nightmares/ or exp prazosin/ or exp prescription drugs/ or exp relaxation therapy/ or exp rem dreams/ or exp sleep treatment/ or exp therapeutic touch/ or exp yoga/)) or ((apnea* or circadian or insomnia* or parasomnia* or sleep*) adj3 (acupressure or acupuncture or alternative or ambien or apnea* or benadryl or circadian or cognitive behavior* or cognitive processing therap* or cognitive rehab* or cognitive therap* or complementary or diphenhydramine or dream* or drug* or eszopiclone or exercis* or holistic* or hygiene or hypnotic* or lunesta or nightmare* or prazosin or reiki or relax* or sedat* or yoga or zolpidem)).ti,ab. or (epworth sleepiness scale or pittsburgh sleep quality index).mp.
10	**KQ9** **Tinnitus**	((exp tinnitus/) and (exp acoustic stimulation/ or exp acoustics/ or exp auditory evoked potentials/ or exp auditory perception/ or exp auditory stimulation/ or exp behavior therapy/ or exp cochlear implantation/ or exp cochlear implants/ or exp cognitive behavior therapy/ or exp cognitive rehabilitation/ or exp cognitive therapy/ or exp complementary therapies/ or exp functional analysis/ or exp glasgow outcome scale/ or exp hearing aids/ or exp measurement/ or exp meditation/ or exp mindfulness/ or exp perceptual masking/ or exp psychotropic drugs/ or exp questionnaires/ or exp rating scales/ or exp "severity (disorders)"/ or exp severity of illness index/ or exp stress management/ or exp stress, psychological/ or exp transcranial magnetic stimulation/ or exp white noise/)) or ((tinnitus) adj3 (acoustic* or alternative or auditory or cochlear or cognitive behavior* or cognitive processing therap* or cognitive rehab* or cognitive therap* complementary or drug* or evoked or hearing aid* or magnetic* or measure* or medicat* or meditat* or mindful* or noise generator or index* or psychotropic* or questionnaire* or rehab* or scale* or severity of illness or sound generator* or stress* or transcranial or white noise)).ti,ab.
11	**KQ10** **Visual Symptoms**	exp diplopia/ or exp photosensitivity disorders/ or exp vision disorders/ or exp vision tests/ or (diplopia or double vision or photophobia or photosensitiv*).ti,ab. or ((eye or eyes or eyesight or ocular or oculo* or vision or visual* or sight) adj3 (blur* or deficien* or deficit* or diplopia or disorder* or double* or impair* or photosensitiv* or rehab* or sensitiv* or track* or train* or therap*)).ti,ab.
12	**Combine Key Questions**	2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11
13	**Combine mTBI set and Key Questions**	1 and 12
14	**Remove unwanted study designs/publication types/patient populations**	13 not ((authored book or autobiography or biography or book or case reports or comment or conference* or dissertation abstract edited book or editorial or encyclopedia or lectures or letter or news or note or proceeding or video-audio media or webcasts).pt. or (bibliography or chapter or column/opinion or comment/reply or dissertation or editorial or encyclopedia entry or letter or obituary or review-book).dt. or (adolescen* or antenatal or babies or baby or

Set #	Concept	Search Statement
		birth or child* or infan* or kid or kids or neonat* or newborn* or paediatric* or pediatric* or perinatal or prenatal or teen* or toddler* or young* or youth*).ti.)
15	**Limit to specific study designs/publication types/patient populations**	14 and (clinical trials as topic/ or crossover studies/ or doubleblind method/ or meta-analysis as topic/ or random allocation/ or randomized controlled trials as topic/ or single-blind method/ or (clinical trial or controlled clinical trial or meta-analysis or randomized controlled trial or review).pt. or (ACTRN* or cross over or crossover or ISRTCN or latin square or meta analy* or meta-analy* or metaanal* or randomized or randomized controlled trial* or placebo* or systematic review*).mp. or ((doubl* or singl* or trebl* or tripl*) adj2 (blind* or mask* or sham*)).mp. or (evidence or random* or systematic*).ti. or (NCT* not NCT).mp.)
16	**Limit to English language**	limit 15 to english language
17	**Limit to humans**	Limit 16 to humans
18	**Apply date limits**	Limit 17 to "2008-current"
19	**Final set**	Remove duplicates

EMBASE Conventions:

* (within or following a term) = truncation character (wildcard)

:ab = limit to abstract

:ab,ti = limit to abstract and title

NEAR/n = search terms within a specified number (*n*) of words from each other in any order

/exp = "explodes" controlled vocabulary term (e.g., expands search to all more specific related terms in the vocabulary's hierarchy)

:it. = limit to publication type

:ti. = limit to title

Table A-6. EMBASE Search Strategies Conducted Using EMTREE Syntax

Set #	Concept	Search Statement
1	**Mild Traumatic Brain Injury**	'brain concussion'/exp OR 'brain injury'/exp OR concussion/exp OR 'head injury'/exp OR 'post concussion syndrome'/exp OR 'traumatic brain injury'/exp OR (brain OR head) NEAR/1 (concuss* OR damage* OR injur* OR trauma*) OR post* NEAR/1 concuss* OR mtbi:ab,ti OR postconcuss*:ab,ti
2	**KQ1** **Diagnostic Assessments/Tests/Procedures**	agnosia/exp OR anosmia/exp OR 'balance disorder'/exp OR 'balance impairment'/exp OR 'biological marker'/exp OR 'brain electrophysiology'/exp OR 'brain injury assessment'/exp OR 'brain mapping'/exp OR 'brain radiography'/exp OR 'brain scintiscanning'/exp OR 'brain tomography'/exp OR 'computer assisted emission tomography'/exp OR 'computer assisted tomography'/exp OR 'computer tomography'/exp OR 'diagnostic imaging'/exp OR 'diffusion tensor imaging'/exp OR 'echoencephalography'/exp OR 'electroencephalography'/exp OR 'electrophysiological procedures'/exp OR electrophysiology/exp OR 'exercise test'/exp OR 'eye movement'/exp OR 'functional magnetic resonance imaging'/exp OR gait/exp OR 'gait disorder'/exp OR 'low resolution brain electromagnetic tomography'/exp OR 'magnetoencephalography'/exp OR 'multimodal imaging'/exp OR 'neurologic examination'/exp OR 'neuropsychological test'/exp OR 'neuroradiology'/exp OR 'nuclear magnetic resonance imaging'/exp OR 'odor recognition test'/exp OR 'physical examination'/exp OR 'positron emission tomography'/exp OR 'protein S 100'/exp OR 'protein S100B'/exp OR 'radiography'/exp OR 'single photon emission computer tomography'/exp OR 'smelling disorder'/exp OR 'spiral computer assisted tomography'/exp OR 'tomography'/exp OR (agnosia OR anosmia OR 'biological marker' OR 'biological markers' OR biomarker* OR 'brain map' OR 'brain mapping' OR 'computed tomography' OR 'diagnostic imaging' OR 'diffuse tensor' OR 'diffusion tensor' OR echoenceph* OR elecroenceph* OR encephalogr* OR 'functional magnetic' OR fmri OR 'magnetic resonance' OR magnetoenceph* OR neuroimag* OR neuroradiograph* OR PET OR 'positron emission' OR scinisc* OR 'single photon emission' or s100 OR s100b OR SPECT OR SPECT-CT OR tomograph*):ab,ti OR (diagnos* NEAR/2 decision*):ab,ti OR ((equilibrium OR gait OR neurolog* OR neurophysiol* OR neuropsych* OR olfact* OR physical* OR smell*) NEAR/1 (assess* OR diagnos* OR evaluat* OR exam* OR test*)):ab,ti OR 'calcium binding' NEAR/1 protein* OR effort NEAR/1 test* OR symptom* NEAR/1 valid*
3	**KQ2** **Mechanism of Injury**	'acceleration'/exp OR 'blast injury'/exp OR 'contrecoup injury'/exp OR 'deceleration'/exp OR 'traffic accident'/exp OR 'whiplash injury'/exp OR accelerat*:ab,ti OR decelerat*:ab,ti OR blast*:ab,ti OR bomb*:ab,ti OR coup:ab,ti OR contrecoup:ab,ti OR deploy*:ab,ti OR explosi*:ab,ti OR nondeploy*:ab,ti OR whiplash:ab,ti OR undeploy*:ab,ti OR (car OR traffic) NEAR/1 (injur*) OR (cause* OR mechanism* OR type*) NEAR/2 (injur*)
4	**KQ3** **Care Settings**	'ambulatory care'/exp OR 'case management'/exp or 'case manager'/exp OR 'community hospital'/exp OR 'day hospital'/exp OR 'emergency health service'/exp OR 'emergency ward'/exp OR 'general hospital'/exp OR 'general practice'/exp OR 'general practitioner'/exp OR 'health care facility'/exp OR 'health center'/exp OR 'hospital'/exp OR 'outpatient care'/exp OR 'outpatient department'/exp OR 'primary health care'/exp OR 'primary medical care'/exp OR 'private hospital'/exp OR 'public hospital'/exp OR 'rapid response team'/exp OR 'rehabilitation center'/exp OR 'rehabilitation hospital'/exp OR 'residential care'/exp OR 'residential home'/exp OR 'team nursing'/exp OR teamwork/exp OR 'tertiary care center'/exp OR (team* NEAR/1 (care OR collaborat* OR cooperativ* OR integrat* OR interdisciplin* OR multidisciplin* OR nurs* OR treatment*)):ab,ti OR (case NEAR/1 manag*):ab,ti or ((treatment OR care) NEAR/1 (location* OR setting*)):ab,ti or ((ambulatory

Set #	Concept	Search Statement
		OR emergency OR inpatient* OR outpatient* OR primary OR residential OR tertiary OR veteran*) NEAR/1 (center* OR clinic OR clinics OR department* OR hospital* OR location* OR setting* OR unit OR units OR ward*)):ab,ti or ((patient OR professional OR specialist OR specialty) NEAR/1 (consult OR consultation OR refer OR referral)):ab,ti or ((primary OR family) NEAR/1 (care OR doctor* OR physician* OR practitioner*)):ab,ti
5	**KQ4** **Dizziness/Vestibular Rehabilitation**	'balance disorder'/exp OR 'balance impairment'/exp OR dizziness/exp OR kinesiotherapy/exp OR physiotherapy/exp OR vertigo/exp OR 'vestibular disorder'/exp OR 'vestibular function'/exp OR 'vestibular test'/exp OR 'vestibular testing equipment'/exp OR ((balanc* OR canalith OR dizz* OR epley OR equlibrium OR labyrinth OR liberatory OR semont OR vertigo OR vestibular) NEAR/1 (deficit* or disorder* or exercis* or impair* or loss* or maneuver* or problem* or screen* or symptom* or test* or therap* or treat*)):ab,ti OR ('continuous performance test' or 'balance error scoring system' or 'berg balance scale' or 'dizziness handicap inventory'):ab,ti
6	**KQ5** **Headache**	headache/exp OR migraine/exp AND ('glasgow outcome scale'/exp OR measurement/exp OR 'oswestry disability index'/exp OR questionnaire/exp OR 'rating scale'/exp OR 'severity of illness index'/exp) OR (headache*:ab,ti OR migraine*:ab,ti AND (glasgow:ab,ti OR measure*:ab,ti PR index*:ab,ti OR oswestry:ab,ti OR questionnaire*:ab,ti OR 'rating scale':ab,ti OR rivermead:ab,ti OR scale*:ab,ti OR 'severity of illness':ab,ti))
7	**KQ6** **Attention/Concentration/Memory Impairment**	attention/exp OR 'attention deficit disorder'/exp OR 'concentration loss'/exp OR memory/exp OR 'memory assessment'/exp OR 'memory disorder'/exp OR 'mental concentration'/exp AND ('cognitive rehabilitation'/exp OR 'cognitive therapy'/exp OR 'computer assisted therapy'/exp OR 'group therapy'/exp OR psychotherapy/exp OR 'support group'/exp) OR (attention OR concentration OR memories OR memory AND (brief* OR comprehensive OR computer* OR focused OR group* OR individual* OR short* OR targeted) NEAR/1 ('cognitive behavior' OR 'cognitive behaviour' OR 'cognitive behavioral' OR 'cognitive behavioural' OR 'cognitive rehabilitation' OR 'cognitive therapy' OR psychol* OR psychotherap* OR psychiatric*))
8	**KQ7** **Behavioral Problems**	behavior/exp OR 'behavior disorder'/exp OR 'domestic violence'/exp OR 'emotional abuse'/exp OR 'emotional stress'/exp OR 'family conflict'/exp OR 'family stress'/exp OR 'mental instability'/exp OR 'partner violence'/exp OR psychotrauma/exp OR violence/exp AND ('antidepressant agent'/exp OR 'anxiolytic agent'/exp OR 'anxiolytic agent tranquilizer'/exp OR caregiver/exp OR 'caregiver burden'/exp OR 'cognitive behavioral stress management'/exp OR 'cognitive rehabilitation'/exp OR 'cognitive therapy'/exp OR 'dysfunctional therapy'/exp OR 'extended family'/exp OR family/exp OR 'family assessment'/exp OR 'family coping'/exp OR 'family functioning'/exp OR 'family interaction'/exp OR 'family life'/exp OR 'group therapy'/exp OR 'hypnotic sedative agent'/exp OR 'neuroleptic agent'/exp OR 'patient assessment'/exp OR 'patient attitude'/exp OR 'psychopharmacology'/exp OR 'psychotherapy'/exp OR 'sedative agent'/exp OR 'support group'/exp) OR ((abus* OR aggress* OR anger OR angry OR conflict* OR danger* OR destruct* or discontrol* OR distress* OR erratic OR instability OR irrational* OR irrit* OR uncontrol* OR unpredict* OR unsafe OR unstable OR violen*) NEAR/1 (antianxiety OR antidepress* OR antipsychotic* OR 'care giver' OR caregiver* OR 'cognitive behavior' OR 'cognitive behaviour' OR 'cognitive behavioral' OR 'cognitive behavioural' OR 'cognitive therapy' OR 'cognitive rehabilitation' OR domestic OR 'drug therapy' OR families OR family OR medicat* OR 'group therapy' OR husband* OR neuroleptic* OR partner* OR psychiatr* OR psycholog* OR psychopharmacol* OR psychother* OR sedative* OR spouse* OR 'support group' OR tranquiliz* OR wife OR wives)):ab,ti

Set #	Concept	Search Statement
9	**KQ8** **Sleep Disturbance**	(sleep/exp OR 'circadian rhythm sleep disorder'/exp OR insomnia/exp OR 'REM sleep deprivation'/exp OR 'sleep disorder'/exp OR 'sleep arousal disorder'/exp OR 'sleep disorder assessment'/exp OR 'sleep disordered breathing'/exp OR parasomnia/exp AND (acupressure/exp OR acupuncture/exp OR 'alternative medicine'/exp OR 'central sleep apnea syndrome'/exp OR 'cognitive rehabilitation'/exp OR 'cognitive therapy'/exp OR diphenhydramine/exp OR dream/exp OR dreaming/exp OR eszopiclone/exp OR 'herbaceous agent'/exp OR 'herbal medicine'/exp OR 'holistic care'/exp OR 'hypnotic sedative agent'/exp OR 'insomnia severity index'/exp OR 'integrative medicine'/exp OR nightmare/exp OR prazosin/exp OR reiki/exp OR 'relaxation training'/exp OR 'sedative agent'/exp OR 'sleep disorder assessment'/exp OR 'sleep therapy'/exp OR 'unpleasant dream'/exp OR 'vivid dream'/exp OR yoga/exp OR 'zolpidem tartrate'/exp)) OR ((apnea* OR circadian OR insomnia* OR parasomnia* OR sleep*) NEAR/3 (acupressure OR acupuncture OR alternative OR ambien OR benadryl OR circadian OR cognitive OR complementary OR diphenhydramine OR dream* OR drug* OR eszopiclone OR exercis* OR holistic* OR hygiene OR hypnotic* OR lunesta OR nightmare* OR prazosin OR reiki OR relax* OR sedat* OR yoga OR zolpidem)):ab,ti OR epworth sleepiness scale OR pittsburgh sleep quality index
10	**KQ9** **Tinnitus**	tinnitus/exp AND ('alternative medicine'/exp OR 'auditory rehabilitation'/exp OR 'cochlea implant'/exp OR 'cochlear implantation'/exp OR 'cognitive behavioral stress management'/exp OR 'cognitive rehabilitation'/exp OR 'cognitive therapy'/exp OR 'functional assessment'/exp OR 'functional status'/exp OR 'glasgow outcome scale'/exp OR 'hearing aid'/exp OR 'psychotropic agent'/exp OR questionnaire/exp OR 'rating scale'/exp OR 'severity of illness index'/exp OR 'stress management'/exp OR 'transcranial magnetic stimulation'/exp OR 'transcranial magnetic stimulation system'/exp OR 'white noise'/exp) OR (tinnitus NEAR/1 (acoustic OR alternative OR auditory OR cochlear OR cognitive OR complementary OR drug* OR evoked OR 'hearing aid' OR magnetic OR medicat* OR meditat* OR mindful* OR 'noise generator' OR index* OR psychotropic OR questionnaire* OR rehab* OR scale* OR 'severity of illness' OR 'sound generator' OR stress* OR transcranial OR 'white noise')):ab,ti
11	**KQ10** **Visual Symptoms**	'abnormal vision'/exp OR diplopia/exp OR photosensitivity/exp OR 'vision test'/exp OR 'visual disorder'/exp OR 'visual impairment'/exp OR diplopia:ab,ti OR 'double vision':ab,ti OR photophobia:ab,ti OR photosensitiv*:ab,ti OR ((eye OR eyes OR eyesight OR ocular OR oculo* OR vision or visual* OR sight*) NEAR/3 (blur* OR deficien* OR deficit* OR diplopia or disorder* OR double* OR impair* OR photosensitiv* OR rehab* OR sensitiv* OR track* OR train* OR therap*)):ab,ti
12	**Combine Key Questions**	#2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11
13	**Combine mTBI set and Key Questions**	#1 AND #12
14	**Apply limits** **(English language/humans/2008-2015)**	#13 AND [humans]/lim AND [english]/lim AND [2008-2015]/py
15	**Remove unwanted study designs/publication types/patient populations**	#14 NOT ('case study/exp' OR 'case report/exp' OR 'conference abstract':it OR 'conference paper':it OR 'conference review':it OR editorial:it OR letter:it OR note:it)
16	**Selected study designs/publication types**	'crossover procedure'/exp OR 'double blind procedure'/exp OR 'meta analysis'/exp OR placebo/exp OR randomization/exp OR 'randomized controlled trial'/exp OR 'single blind procedure'/exp OR 'systematic review'/exp OR actrn*:ab,ti OR 'clinical trial':ab,ti OR 'controlled clinical trial':ab,ti OR 'cross over':ab,ti OR crossover:ab,ti OR isrtcn:ab,ti OR 'latin

Set #	Concept	Search Statement
		square':ab,ti OR metaanaly*:ab,ti OR placebo*:ab,ti OR randomized:ab,ti OR (doubl* OR singl* OR trebl* OR tripl*) NEAR/2 (blind* OR mask* OR sham*) OR 'randomized controlled' NEAR/1 trial* OR systematic NEAR/1 review* OR meta* NEAR/1 analy* OR evidence:ti OR random*:ti OR systematic*:ti OR (nct* NOT nct)
17	**Combine results with selected study designs/publication types**	#15 AND #16
18	**Limit to Embase results**	#17 AND [embase]/lim
19	**Omit Medline Results**	#18 NOT [medline]/lim

C. Convening the Face-to-face Meeting

In consultation with the Contracting Officer's Representative (COR), the Champions, and the Work Group, the Lewin Team convened a three and a half day face-to-face meeting of the CPG Champions and Work Group members on June 29 – July 2, 2015. These experts were gathered to develop and draft the clinical recommendations for an update to the 2009 mTBI CPG. Lewin presented findings from the evidence review of KQs 1-10 in order to facilitate and inform the process.

Under the direction of the Champions, the Work Group members were charged with interpreting the results of the evidence review, and asked to review, assess, and categorize recommendations from the 2009 mTBI CPG. The members also developed new clinical practice recommendations not present in the 2009 mTBI CPG, based on the 2015 evidence review. The subject matter experts were divided into three smaller subgroups at this meeting.

As the Work Group members drafted clinical practice recommendations, they also assigned a grade for each recommendation based on a modified GRADE and USPSTF methodology. Each recommendation was graded by assessing the quality of the overall evidence base, the associated benefits and harms, the variation in values and preferences, and other implications of the recommendation.

D. Grading Recommendations

This CPG uses the GRADE methodology to assess the quality of the evidence base and assign a grade for the strength of each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: [106]

- Balance of desirable and undesirable outcomes
- Confidence in the quality of the evidence
- Values and preferences
- Other implications, as appropriate, include:
    - Resource Use
    - Equity
    - Acceptability
    - Feasibility

- Subgroup considerations

The following sections further describe each domain.

Balance of desirable and undesirable outcomes refers to the size of anticipated benefits (e.g., increased longevity, reduction in morbid event, resolution of symptoms, improved quality of life [QoL], decreased resource use) and harms (e.g., decreased longevity, immediate serious complications, adverse event, impaired quality of life, increased resource use, inconvenience/hassle) relative to each other. This domain is based on the understanding that the majority of clinicians will offer patients therapeutic or preventive measures as long as the advantages of the intervention exceed the risks and adverse effects. The certainty or uncertainty of the clinician about the risk-benefit balance will greatly influence the strength of the recommendation.

Some of the discussion questions that fall under this domain include:

- Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa?
- Are the desirable anticipated effects large?
- Are the undesirable anticipated effects small?
- Are the desirable effects large relative to undesirable effects?

Confidence in the quality of the evidence reflects the quality of the evidence base and the certainty in that evidence. This second domain reflects the methodological quality of the studies for each outcome variable. In general, the strength of recommendation follows the level of evidence, but not always, as other domains may increase or decrease the strength. The evidence review used for the development of recommendations for mTBI, conducted by ECRI, assessed the confidence in the quality of the evidence base and assigned a rate of "High," "Moderate," "Low," or "Very Low."

The elements that go into the confidence in the quality of the evidence include:

- Is there high or moderate quality evidence that answers this question?
- What is the overall certainty of this evidence?

Values and preferences is an overarching term that includes patients' perspectives, beliefs, expectations, and goals for health and life. More precisely, it refers to the processes that individuals use in considering the potential benefits, harms, costs, limitations, and inconvenience of the therapeutic or preventive measures in relation to one another. For some, the term "values" has the closest connotation to these processes. For others, the connotation of "preferences" best captures the notion of choice. In general, values and preferences increase the strength of the recommendation when there is high concordance and decrease it when there is great variability. In a situation in which the balance of benefits and risks are uncertain, eliciting the values and preferences of patients and empowering them and their surrogates to make decisions consistent with their goals of care becomes even more important. A recommendation can be described as having "similar values," "some variation," or "large variation" in typical values and preferences between patients and the larger populations of interest.

Some of the discussion questions that fall under the purview of values and preferences include:

- Are you confident about the typical values and preferences and are they similar across the target population?
- What are the patient's values and preferences?
- Are the assumed or identified relative values similar across the target population?

Other implications consider the practicality of the recommendation, including resources use, equity, acceptability, feasibility and subgroup considerations. Resource use is related to the uncertainty around the cost-effectiveness of a therapeutic or preventive measure. For example statin use in the frail elderly and others with multiple comorbidities may not be effective and depending on the societal benchmark for willingness to pay, may not be a good use of resources. Equity, acceptability, feasibility and subgroup considerations require similar judgments around the practically of the recommendation.

The framework below was used by the Work Group to guide discussions on each domain.

Table A-7. Evidence to Recommendation Framework

Decision Domain	Judgment
Balance of desirable and undesirable outcomes	
▪ Given the best estimate of typical values and preferences, are you confident that the benefits outweigh the harms and burden or vice versa? ▪ Are the desirable anticipated effects large? ▪ Are the undesirable anticipated effects small? ▪ Are the desirable effects large relative to undesirable effects?	▪ Benefits outweigh harms/burden ▪ Benefits slightly outweigh harms/burden ▪ Benefits and harms/burden are balanced ▪ Harms/burden slightly outweigh benefits ▪ Harms/burden outweigh benefits
Confidence in the quality of the evidence	
▪ Is there high or moderate quality evidence that answers this question? ▪ What is the overall certainty of this evidence?	▪ High ▪ Moderate ▪ Low ▪ Very low
Values and preferences	
▪ Are you confident about the typical values and preferences and are they similar across the target population? ▪ What are the patient's values and preferences? ▪ Are the assumed or identified relative values similar across the target population?	▪ Similar values ▪ Some variation ▪ Large variation
Other implications (e.g., resource use, equity, acceptability, feasibility, subgroup considerations)	
▪ Are the resources worth the expected net benefit from the recommendation? ▪ What are the costs per resource unit? ▪ Is this intervention generally available? ▪ Is this intervention and its effects worth withdrawing or not allocating resources from other interventions? ▪ Is there lots of variability in resource requirements across settings?	Various considerations

The strength of a recommendation is defined as the extent to which one can be confident that the desirable effects of an intervention outweigh its undesirable effects and is based on the framework above, which combines the four domains.[106] GRADE methodology does not allow for recommendations to be made based on expert opinion alone. While strong recommendations are usually based on high or moderate confidence in the estimates of effect (quality of the evidence) there may be instances where strong recommendations are warranted even when the quality of evidence is low.[107] In these types of instances where the balance of desirable and undesirable outcomes and values and preferences played large roles in determining the strength of a recommendation, this is explained in the discussion section for the recommendation.

The GRADE of a recommendation is based on the following elements:

- Four decision domains used to determine the strength and direction (described above)
- Relative strength (Strong or Weak)
- Direction (For or Against)

The relative strength of the recommendation is based on a binary scale, "Strong" or "Weak." A strong recommendation indicates that the Work Group is highly confident that desirable outcomes outweigh undesirable outcomes. If the Work Group is less confident of the balance between desirable and undesirable outcomes, they present a weak recommendation.

Similarly, a recommendation for a therapy or preventive measure indicates that the desirable consequences outweigh the undesirable consequences. A recommendation against a therapy or preventive measure indicates that the undesirable consequences outweigh the desirable consequences.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong For (or "We recommend offering this option …")
- Weak For (or "We suggest offering this option …")
- Weak Against (or "We suggest not offering this option …")
- Strong Against (or "We recommend against offering this option …")

Note that weak (For or Against) recommendations may also be termed "Conditional," "Discretionary," or "Qualified." Recommendations may be conditional based upon patient values and preferences, the resources available, or the setting in which the intervention will be implemented. Recommendations may be at the discretion of the patient and clinician or they may be qualified with an explanation about the issues that would lead decisions to vary.

E. Recommendation Categorization

a. Recommendation Categories and Definitions

For use in the 2016 mTBI CPG, a set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE, UK).[6,7] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated. The categories and definitions can be found in **Table A-8**.

Table A-8. Recommendation Categories and Definitions

Evidence Reviewed*	Recommendation Category*	Definition*
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG and has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed based on review of the evidence
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from the previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from the previous CPG that has been removed because it was deemed out of scope for the updated CPG

*Adapted from the NICE guideline manual (2012)[6] and Garcia et al. (2014)[7]

b. Categorizing Recommendations with an Updated Review of the Evidence

Recommendations were first categorized by whether or not they were based on an updated review of the evidence. If evidence had been reviewed, recommendations were categorized as “New-added,” “New-replaced,” “Not changed,” “Amended,” or “Deleted.”

“Reviewed, New-added” recommendations were original, new recommendations that were not in the 2009 mTBI CPG. “Reviewed, New-replaced” recommendations were in the previous version of the guideline, but were modified to align with the updated review of the evidence. These recommendations could have also included clinically significant changes to the previous version. Recommendations categorized as “Reviewed, Not changed” were carried forward from the previous version of the CPG unchanged.

To maintain consistency between 2009 recommendations, which were developed using the USPSTF methodology, and 2016 recommendations, which were developed using the GRADE methodology, it was necessary to modify the 2009 recommendations to include verbiage to signify the strength of the recommendation (e.g., “We recommend,” “We suggest”). Because the 2009 recommendations inherently needed to be modified at least slightly to include this language, the “Not changed” category was not used. For recommendations carried forward to the updated CPG with review of the evidence and slightly modified wording, the “Reviewed, Amended” recommendation category was used. This allowed for the wording of the recommendation to reflect GRADE methodology as well as for any other non-substantive (i.e., not clinically meaningful) language changes deemed necessary.

Recommendations could have also been designated “Reviewed, Deleted.” These were recommendations from the previous version of the CPG that were not brought forward to the updated guideline after review of the evidence. This occurred if the evidence supporting the recommendations was out of date, to the extent that

there was no longer any basis to recommend a particular course of care and/or new evidence suggests a shift in care, rendering recommendations in the previous version of the guideline obsolete.

c. Categorizing Recommendations without an Updated Review of the Evidence

There were also cases in which it was necessary to carry forward recommendations from the previous version of the CPG without a systematic review of the evidence. Due to time and budget constraints, the update of the mTBI CPG could not review all available evidence on management of mTBI, but instead focused its KQs on areas of new or updated scientific research or areas that were not previously covered in the CPG.

For areas of research that have not changed, and for which recommendations made in the previous version of the guideline were still relevant, recommendations could have been carried forward to the updated guideline without an updated systematic review of the evidence. These recommendations were categorized as "Not reviewed." If evidence had not been reviewed, recommendations could have been categorized as "Not changed," Amended," or "Deleted."

"Not reviewed, Not changed" recommendations refer to recommendations from the previous version of the mTBI CPG that were carried forward unchanged to the updated version. The category of "Not reviewed, Amended" was used to designate recommendations which were modified from the 2009 CPG with the updated GRADE language, as explained above.

Recommendations could also have been categorized as "Not reviewed, Deleted" if they were determined to be out of scope. A recommendation was out of scope if it pertained to a topic (e.g., population, care setting, treatment, condition) outside of the scope for the updated CPG as defined by the Work Group.

The categories for the recommendations included in the 2016 version of the guideline are noted in the Recommendations. The categories for the recommendations from the 2009 mTBI CPG are noted in Appendix D.

F. Drafting and Submitting the Final CPG

Following the face-to-face meeting, the Champions and Work Group members were given writing assignments to craft discussion sections to support each of the new recommendations and/or to update discussion sections from the 2009 mTBI CPG to support the amended "carried forward" recommendations. The Work Group also considered tables, appendices, and other sections from the 2009 mTBI CPG for inclusion in the update. During this time, the Champions and Work Group also made additional revisions to the algorithms, as necessary.

After developing the initial draft of the updated CPG, an iterative review process was used to solicit feedback on and make revisions to the CPG. Once they were developed, the first two drafts of the CPG were posted on a wiki website for a period of 14-20 business days for internal review and comment by the Work Group. All feedback submitted during each review period was reviewed and discussed by the Work Group and appropriate revisions were made to the CPG.

Draft 3 of the CPG was made available for peer review and comment. This process is described in Peer Review Process. After revisions were made based on the feedback received during the peer review and comment period, the Champions presented the CPG to the EBPWG for their approval. Changes were made based on feedback from the EBPWG and the guideline was finalized.

The Work Group also produced a set of guideline toolkit materials which included a provider summary, pocketcards, and a patient summary. The final 2016 mTBI CPG was submitted to the EBPWG in January 2016.

Appendix B: Clinical Symptom Management

A. Appendix Contents

This appendix includes options for treatment of co-occurring conditions and a selected list of physical symptoms that are most common in patients presenting with symptoms following a concussion/mTBI. The options were formulated based on consensus of clinical experts. The evidence synthesis for this CPG found a lack of RCTs for treatment of symptoms in patients with a history of mTBI. As such, the approach to symptom management is based on common clinical practice.

B. Introduction

Emergence of neuropsychiatric post-concussive symptoms after mTBI can depend on many factors including pre-injury psychosocial function and/or pre-existing illnesses/conditions, genetic predisposition to neuropsychiatric disorders, injury factors, and post-injury psychosocial and health factors. The nature and severity of symptoms, as ascertained in a thorough medical history, is necessary to choose appropriate treatments. To date, a comprehensive treatment plan that addresses both psychosocial and pharmacologic interventions is recommended by experts in the field, as there is a paucity of strong evidence specifically targeting this population.

There is a complex relationship among concussion/mTBI symptoms (e.g., headache, sleep disturbances, cognition, mood) and it is clinically reasonable to expect that alleviating/improving one symptom may lead to improvement in other symptom clusters. The presence of comorbid psychiatric problems such as MDD, anxiety disorders, PTSD or SUD–whether or not these are regarded as etiologically related to the mTBI–should be treated aggressively using appropriate psychotherapeutic and pharmacologic interventions.

There are no specific FDA approved pharmaceutical agents for the treatment of any post-concussive neurological or psychiatric symptoms emerging after mTBI. Experts in the field recommend using published CPGs for other neuropsychiatric conditions as a reference, as well as the general guidance from the fields of neuropsychiatry and behavioral neurology. See guidance such as:

- VA/DoD Clinical Practice Guidelines Homepage - www.healthquality.va.gov

- VA National Center for PTSD: Traumatic Brain Injury and PTSD - http://www.ptsd.va.gov/professional/co-occurring/traumatic-brain-injury-ptsd.asp
- Defense Center of Excellence (DCoE) Resource Catalog - http://www.dcoe.mil/PsychologicalHealth/Resources.aspx
- VA Health Services Research and Development: Evidence-based Synthesis Program - www.hsrd.research.va.gov/publications/esp/

However, this committee did not review and cannot endorse the accuracy or clinical utility of any such guidance that is available.

Treatments are symptom based and not based on the historical traumatic event. While there is little empirical evidence, some experts prescribe medications for attention, irritability, sleep, agitation, anxiety, stress, mood disturbances, headaches, and symptoms of impaired balance/dizziness. Sound clinical judgment with a thorough clinical history, targeted physical exam, and any needed laboratory testing appropriate to the condition are always prudent before prescribing any medication. Following recommended dosing guidelines is prudent as well.

Table B-1. General Considerations in Using Medication for Treatment of Symptoms after Brain Injury

▪ Avoid medications that lower the seizure threshold (e.g., bupropion, traditional antipsychotic medications) or those that can cause confusion (e.g., lithium, benzodiazepines, anticholinergic agents).
▪ Before prescribing medications, rule out social factors (e.g., abuse, neglect, caregiver conflict, environmental issues).
▪ Unless side effects prevail, give full therapeutic trials at maximal tolerated doses before discontinuing a medication trial. Under-treatment is common.
▪ Patients with a history of TBI can be more sensitive to side effects. Watch closely for toxicity and drug-drug interactions. Assess regularly for side effects.
▪ Limit quantities of medications with high risk for suicide as the suicide rate is higher in this population.
▪ Educate patients and family/care givers to avoid the use of alcohol with the medications.
▪ Minimize caffeine and avoid herbal or diet supplements such as “energy” products as some contain agents that cross-react with the psychiatric medications and lead to a hypertensive crisis.

C. Co-occurring Conditions

a. Clinical Guidance

- Assess individuals in a primary care setting. Typical screening instruments are the Patient Health Questionnaire (PHQ-2 or PHQ-9), the Generalized Anxiety Disorder Scale (GAD-2 or GAD-7), and the primary care PTSD screener or PTSD Checklist (PCL). While these instruments do not diagnose individuals with MDD, anxiety, or PTSD, they serve to identify individuals who require further assessment.
- If a patient’s psychiatric history is too complex to clearly diagnose a comorbid psychiatric diagnosis, consider consulting with, or referring to, a behavioral health provider. For individuals who present with an existing psychiatric diagnosis, refer to behavioral health services for further follow-up/treatment if indicated.
- Evaluation of patients with persistent symptoms following concussion/mTBI should include assessment for suicidal ideation and homicidal ideation.

- Patients with persistent symptoms following concussion/mTBI should be re-evaluated for psychiatric symptoms and comorbid psychiatric disorders.
- In patients with persistent post-concussive symptoms, which have been refractory to treatment, consideration should be given to other factors that may be contributing, including psychiatric disorders, lack of psychosocial support, negative illness expectations, and compensation/ litigation. However, clinicians should be very careful with any communications with patients regarding possible attributions of physical symptoms to any of these causes, and should follow clinical guidelines for management of persistent unexplained symptoms. (See the VA/DoD CPG for the Management of CMI[26])
- Referral of patients with persistent behavioral symptoms to mental health specialty should be considered.

D. Headache

a. Background

Posttraumatic headaches occur acutely in up to 90% of all individuals who sustain a concussion. Of note, amongst Veterans who have sustained a concussion, headaches are one of the most common persisting complaints and are often rated as moderate severity or higher.[108] Posttraumatic headaches usually develop within seven days of head trauma and can resolve within three months (acute posttraumatic headache) or persist for longer than three months (chronic posttraumatic headache). The inclusion of neck trauma is important to acknowledge because the most frequent forms of civilian head trauma also cause injury to the cervical spinal column, spinal cord and neck musculature. Individuals who sustain head and neck injury can have headaches in which the pain originates from both the head and the neck. In addition, cervicogenic headaches may require specific types of treatment dedicated to the cervical spine.

Although posttraumatic headaches represent a unique category of headache, they often share features of other types of headaches. Characterization of the predominant clinical phenotype in posttraumatic headaches is critical to establishing appropriate management as the pharmacologic and non-pharmacologic strategies parallel those used in clinical practice to manage primary headache disorders. The three most common patterns of posttraumatic headaches are:

1. Tension-type headaches, including cervicogenic component
2. Migraine headaches, or
3. Mixed migraine and tension-type headaches

[26] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

Table B-2. Criteria for Characterizing Posttraumatic Headaches as Tension-like (Including Cervicogenic) or Migraine-like Based upon Headache Features

Headache Feature	Headache Type	
	Tension-like (including cervicogenic pain)	Migraine-like
Pain Intensity	Usually mild-moderate	Often severe or debilitating
Pain Character	Dull, aching, or band like pressure Sharp pain may be present, but is not predominant	Throbbing or pulsatile, can also be sharp/stabbing or electric-like
Duration	Usually less than 4 hours	Can last longer than 4 hours
Phono- or photo-phobia	One but not both may be present	One, or both usually present
Able to carry out routine activities/work	Usually; of note, cervicogenic headaches may be triggered by work environment/posture	Usually not, or with a decreased level of participation, often worsened with physical exertion
Location	Bilateral frontal, retro-orbital, temporal, cervical and occipital, or holocephalic	Often unilateral and may vary in location among episodes
Nausea or malaise	Not present	Usually present
Palpable muscle tenderness or contraction	Pericranial muscles including temporalis, masseter, pterygoid, posterior neck muscle, sternocleidomastoid, splenius or trapezius Decreased cervical range of motion may also be present in those with cervicogenic headaches	Localized muscle tenderness is not typical, muscle tenderness may be present with long duration headaches

b. Assessment

i. History and Physical Examination

Acute assessment focuses on determining if an individual has intracranial pathology as a consequence of the brain injury or an alternate cause of the headaches. Good clinical history is critical to establishing the underlying headache type as well as identifying red flags. Historical red flags for headaches include systemic symptoms (fever, weight loss), atypical onset (abrupt or split second onset, awakening patient from sleep due to headache), or focal neurologic symptoms. The appropriate examination of the posttraumatic headache patient includes musculoskeletal assessment of the head and neck and cranial nerve examination, including test of olfaction, funduscopic evaluation, measurement of pupil size and reaction to light, and observation of eye movements. The examination also evaluates muscle strength and tone, gait and upper and lower extremity coordination. Warning signs of intracranial pathology that will require neurosurgical intervention include drowsiness, impaired motor function (hemiparesis or hemi-ataxia), unsteady gait or inability to stand, vomiting with or without head pain, headache with valsalva maneuvers such as coughing, papilledema or pupil asymmetry of size or reactivity to light. Patients with warning signs of intracranial pathology need to have additional assessment including intracranial imaging.

As indicated in **Table B-2**, focal muscle contraction can be identified in some individuals with tension-type headaches or cervicogenic pain. A thorough neck exam including cervical range of motion should also be performed.

ii. Medication Review

Medication review is a critical part of the assessment of patients with posttraumatic headaches. Chronic use (particularly daily) of NSAIDs or acetaminophen (alone or combined with caffeine), may lead to medication

overuse or rebound headaches. Rebound headaches can occur with migraine or tension headaches. Headaches associated with medication overuse are typically tension-like in character. Treatment of medication overuse headaches requires that patients stop daily use of acute headache medication treatment. This will invariably lead to withdrawal symptoms that could include rebound headaches, and patients can fall into a pattern of continued medication overuse to avoid rebound headaches. When patients are caught in a pattern of medication overuse, they are usually refractory to preventive medications. In most cases, headaches improve after an analgesic washout period. When rebound headaches occur as a result of OTC medications, initial management can safely begin in primary care; however, if patients have rebound headaches secondary to prescription agents (especially opiates or butalbital containing preparations), these patients should be managed in a specialty care setting such as neurology or pain management. Additionally, particular caution is required for individuals who have frequent headaches and who state that headaches respond only to opioid medications. Such individuals should be directed to a pain clinic or headache specialist.

iii. Sleep History

Sleep deprivation can cause or exacerbate headaches in addition to several other post-concussive symptoms. Also, certain sleep disorders such as obstructive sleep apnea can cause morning headaches which have features of tension headaches. It is important to gather a good sleep history from the patient including details of the sleep-wake cycles, nocturnal awakenings (nightmares or parasomnias), snoring or sleep-disordered breathing. Basic sleep hygiene counseling can be beneficial for headache patients with symptoms of sleep apnea and specialty referral should be considered.

c. Treatment

Selection of pharmacologic and non-pharmacologic treatments for posttraumatic headaches is based upon the character of the headaches. Patients who have mixed migraine/tension-like headaches may need treatment for both headache types. Based upon currently available information, most individuals with mTBI will have improvement in their headaches during the first three months of treatment. Initial pharmacologic treatment of uncomplicated posttraumatic headaches can begin in primary care using the guidance in **Table B-3** and **Table B-4**. Consider referring patients who do not respond to treatments to headache specialists or pain treatment programs. It is important to maintain a positive outlook and to encourage active patient ownership and involvement in the care plan. It is also important to recognize comorbid conditions, especially sleep disorders, anxiety disorders, PTSD, and depression. Treatment of these conditions may also improve headache.

i. Posttraumatic Headaches with Tension Features

Episodic tension-type headaches may or may not require specific interventions. When the pain severity is such that the patient desires intervention, pharmacologic and non-pharmacologic interventions should be considered. Pharmacologic therapies to consider include acetaminophen and NSAIDs which are often trialed OTC by patients prior to being seen. Prescription options for treatment of posttraumatic headaches with tension features include prescription-strength NSAIDs and combination medications. Combination medications typically are comprised of aspirin, acetaminophen, caffeine and a sedative drug in a single medication. Combination drugs may be more effective than NSAIDs or acetaminophen alone. These drugs should not be used more than two days a week due to side effect concerns and the potential for dependency. When using any medications, caution must be taken to avoid overuse and subsequent rebound headaches. As such, patients may achieve better pain relief if medication treatment is coupled with non-pharmacologic modalities such as relaxation training, biofeedback and PT. Physical therapy may provide musculoskeletal interventions to address

cervicogenic components of headache including joint/soft tissue mobilization, cervical joint proprioception training, cervical strengthening, ergonomic/postural assessments, and functional dry needling. Regardless of the treatment modality, pain treatment is more likely to be successful if the intervention starts at the onset of a headache rather than waiting for the headache pain to escalate. Patients who experience more than three tension headaches per week may benefit from prophylactic therapy designed to prevent tension headaches. Pharmacologic considerations for prevention of tension headaches include tricyclic antidepressants, propranolol, anticonvulsants (topiramate) or tizanidine. Poorly controlled tension headaches can also indicate that attention should be directed to physical or psychological factors that may be triggering the headaches.

ii. Posttraumatic Headaches with Migrainous Features

Medical treatment of migraine headaches includes strategies for acute interventions and headache prevention. Many patients with migraines can be effectively treated with various acute headache medications and non-pharmacologic strategies. Patients need to be aware of factors that can trigger migraines and avoid those that trigger their headaches. Headache risk factors and triggers include sleep disruption, delaying meals, stress, and, for some people, specific foods, beverages or odors. Non-pharmacologic treatments are often adjunctive to acute treatment. They may be effective and may eliminate the need for pharmacologic interventions, especially when utilized early in the evolution of a migraine. Non-pharmacologic treatments commonly employed are relaxation, biofeedback, visualization, extracranial pressure, and thermal therapies. Regular exercise and maintaining consistent sleep and meal schedules are important parts of the overall treatment regimen but are more effective as preventive than as abortive treatments.

Effective acute treatment requires that patients recognize their specific personal warning signs (aura) of an impending headache. A migraine headache often begins with mild to moderate pain that may be similar to the pain of a tension-type headache. As the migraine progresses, the headache includes the typical migraine features such as throbbing pain, nausea and phono- or photophobia. Acute treatment is more likely to succeed if medication is taken as soon as the patient recognizes the warning signs. Potential abortive therapies for migraine are listed in **Table B-3**.

It is important that acute migraine treatment be used prudently to avoid inducing headaches due to medication overuse or rebound and to educate patients that acute migraine medication treatment be limited to three treatments a week or less on a regular basis. A headache diary including frequency and medication history use may be useful in detecting medication overuse.

Interventions to reduce headache frequency should be considered when migraine headaches occur more than once a week or any of the following criteria exist:

a. Headache attacks that are disabling despite aggressive acute interventions
b. Patient's desire to reduce frequency of acute attacks
c. Headaches compromise work attendance, societal integration or daily life

Selection of appropriate prophylactic therapies needs to take into account the patient's comorbidities and attempts should be made to address multiple symptoms with one medication. Careful consideration should also be given to potential drug-drug interactions. Potential treatment considerations for headache prophylaxis are listed in **Table B-4**.

Table B-3. Abortive Migraine Pharmacotherapy*

*Medications are listed in alphabetical order, not by preference

** Periodic reevaluation of the need for and efficacy of the therapies listed is strongly encouraged

Dosing Recommendations: Abortive Migraine Medications**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
NSAIDs			
Ibuprofen	Usual Dose: 400-600 mg; 3-4 times daily Maximum Dose: 3200 mg daily	▪ GI effects ▪ Dizziness ▪ Vertigo ▪ Bleeding related risks	▪ Rebound headache may occur with continuous use ▪ Potential renal impairment with long-term use ▪ Associated with an increased risk of cardiovascular thrombotic events (stroke and MI) ▪ Caution in patients with history of GI ulcers or abdominal complications ▪ Limit to no more than 12 days of the month to prevent rebound headache
Ketorolac injection	IM: Inject 30-60 mg as a single dose Limit use to 5 days		
Naproxen	Initial Dose: 750 mg daily Titration Dose: Additional 250-500 mg may be given Maximum Dose: 1250 mg daily		
Serotonin 5-HT Receptor Agonist			
Rizatriptan	Initial Dose: 5-10 mg at onset of headache, may repeat in 2 hrs Maximum Dose: 30 mg daily	▪ Dizziness ▪ Somnolence ▪ Nausea	▪ Use with caution in patients with history of cardiac events ▪ Serious cardiac events, including MI, have been reported (tablet and nasal formulations) ▪ Risk of serotonin syndrome when used concomitantly with other serotonergic drugs ▪ Limit to no more than 12 days of the month to prevent rebound headache
Sumatriptan	**Oral** Initial Dose: 50-100 mg at onset of headache, may repeat in 2 hrs Maximum Dose: 200 mg daily	▪ Dizziness ▪ Vertigo ▪ Tingling ▪ Hypertension ▪ Injection site reactions	
	Intranasal Initial Dose: 10 mg spray in 1 nostril at onset of headache, may repeat in 2 hrs Maximum Dose: 40 mg daily		
	Sub-cutaneous Initial Dose: 6 mg SubQ at onset of headache, may repeat in 1 hr Maximum Dose: 12 mg daily		
	Transdermal Initial Dose: Apply 1 patch (6.5 mg) at onset of headache, may repeat in 2 hrs Maximum Dose: 2 patches daily		

Dosing Recommendations: Abortive Migraine Medications**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
Zolmitriptan	**Oral** Initial Dose: 1.25-2.5 mg at onset of headache, may repeat in 2 hrs Titration Dose: 5 mg at onset of headache, may repeat in 2 hrs Maximum Dose: 10 mg daily	▪ Unusual taste (nasal formulation) ▪ Paresthesia ▪ Hyperesthesia ▪ Dizziness	
	Intranasal Initial Dose: 2.5-5 mg spray in 1 nostril at onset of headache, may repeat in 2 hrs Maximum dose: 10 mg daily		
Other			
Butalbital/ Acetaminophen/ Caffeine	Usual Dose: 1-2 tablets every 4 hrs as needed Maximum Dose: 6 tablets per day	▪ Dizziness ▪ Sedation ▪ GI effects ▪ Intoxicated feeling	▪ These agents should only be used as third line therapies due to dependence risk, high risk of rebound headache and sedation ▪ Patient selection is key when using these agents ▪ Use when serotonin 5-HT receptor agonist is contraindicated ▪ Rebound headache with overuse ▪ Acetaminophen may cause severe hepatotoxicity ▪ Monitor total acetaminophen consumption ▪ Use caution with aspirin in patients with history of GI ulcers or abdominal complications
Butalbital/Aspirin/ Caffeine	Usual Dose: 1-2 capsules every 4 hrs as needed Maximum Dose: 6 capsules daily		
Acetaminophen/ Isometheptene/ Dichloralphenazone	Initial Dose: 2 capsules at onset of headache Titration Dose: 1 capsule every hr until relief is obtained Maximum Dose: 5 capsules/ 12 hrs	▪ Dizziness	▪ Acetaminophen may cause severe hepatotoxicity ▪ Monitor total acetaminophen consumption ▪ Limit to no more than 12 days of the month to prevent rebound headache

Dosing Recommendations: Abortive Migraine Medications**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
OTC			
Acetaminophen	**Regular Strength** Usual Dose: 650 mg every 4-6 hrs as needed Maximum dose: 3250 mg daily (for OTC use) **Extra Strength** Usual Dose: 1000 mg every 6 hrs as needed Maximum dose: 3000 mg daily (for OTC use)	▪ Liver impairment ▪ Skin rash	▪ Risk of hepatotoxicity with acetaminophen containing products ▪ Tinnitus with aspirin containing products ▪ May increase maximum dose to 4000 mg per day with provider supervision ▪ Limit to no more than 15 days of the month to prevent rebound headache
Acetaminophen/ Aspirin/ Caffeine (Excedrin Extra Strength)	Usual Dose: 2 tablets once daily Maximum Dose: 2 tablets per day	▪ Liver impairment ▪ GI related effects ▪ Bleeding related risks	
Aspirin	Usual Dose: 325-650 mg every 4-6 hrs as needed Maximum Dose: 4000 mg daily	▪ GI related effects ▪ Bleeding related risks ▪ Renal impairment	
Antiemetic agents			
Prochlorperazine	Usual Dose: 5-10 mg 3-4 times daily Maximum Dose: 40 mg daily	▪ Drowsiness ▪ Agitation ▪ Constipation	▪ Use with caution in patients with severe cardiovascular disease ▪ Extrapyramidal effects with long-term use
Promethazine (Oral, IM, Rectal)	Usual Dose: 12.5-25 mg every 4-6 hrs as needed	▪ Drowsiness ▪ Constipation ▪ Xerostomia	▪ Extrapyramidal effects with long-term use ▪ May cause photosensitivity

Note: Refer to product prescribing insert for more information regarding use restrictions, dose modification, dosing in special populations (e.g., renal or liver impairment, advanced age, pregnancy), drug-drug interactions, and other warnings and precautions.

Abbreviations: GI: gastrointestinal; hrs: hours; IM: intramuscular; mg: milligram; MI: myocardial infarction; NSAIDs: nonsteroidal anti-inflammatory drugs; OTC: over-the-counter; SubQ: sub-cutaneous

Table B-4. Prophylactic Migraine Pharmacotherapy*

*Medications are listed in alphabetical order, not by preference

** Periodic reevaluation of the need for and efficacy of the therapies listed is strongly encouraged

Dosing Recommendations: Prophylactic Migraine Medications** It may take up to 3 months for patients to receive the full benefit of prophylactic therapies.			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
Anti-Convulsants			
Gabapentin	Initial Dose: 100-300 mg at bedtime Titration Dose: 100-300 mg every 5 days as necessary/tolerated on a TID schedule Maximum Dose: 2400 mg daily	▪ Dizziness ▪ Somnolence ▪ Weight gain	▪ Dual benefits of gabapentin (neuropathic pain, seizure disorder, diabetic neuropathy)
Topiramate	Initial Dose: 25 mg once daily Titration Dose: Increase weekly by 25 mg daily Maximum Dose: 100 mg daily	▪ Paresthesia ▪ Nausea ▪ Anorexia ▪ Sedation ▪ Ataxia ▪ Dizziness	▪ May worsen cognitive dysfunction ▪ May cause renal stones
Divalproex sodium products	**Extended Release** Initial Dose: 500 mg once daily Titration Dose: Increase after 7 days to 1000 mg daily, adjust dose based on patient response Maximum Dose: 1000 mg daily **Immediate Release** Initial Dose: 250 mg twice daily Titration Dose: Increase by 250 mg per day every week; adjust dose based on patient response Maximum Dose: 1000 mg daily	▪ Weight gain ▪ Tremor ▪ Liver toxicity ▪ Nausea ▪ Asthenia ▪ Dizziness ▪ Somnolence ▪ Diplopia	▪ Association with teratogenicity (neural tube defects); caution in women of childbearing potential ▪ Evaluate for drug interactions
Beta-Blockers			
Propranolol	**Immediate Release** Initial Dose: 80 mg per day divided every 6 to 8 hours Titration Dose: Increase by 20-40 mg per dose every 3-4 weeks Maximum Dose: 160-240 mg per day given in divided doses **Long-Acting** Initial Dose: 80 mg once daily Effective Dose Range: 160-240 mg daily	▪ Fatigue ▪ Exercise intolerance ▪ Bradycardia	▪ May mask signs and symptoms of hypoglycemia ▪ Avoid withdrawal of agent abruptly to avoid cardiac related events

Dosing Recommendations: Prophylactic Migraine Medications** It may take up to 3 months for patients to receive the full benefit of prophylactic therapies.			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
Alpha-Blockers			
Prazosin	Initial Dose: 1 mg at bedtime Titration Dose: Increase dose weekly to 4 mg, 6 mg, 8 mg, 10 mg Maximum Dose: 10 mg at bedtime	▪ Dizziness ▪ Palpitations	▪ Evaluate for orthostatic hypotension and syncope ▪ May offer additional benefit in patients with nightmares and PTSD
Tricyclic Antidepressants			
Amitriptyline	Initial Dose: 10-25 mg at bedtime Titration Dose: Increase at weekly increments of 10-25 mg daily Maximum Dose: 150 mg daily	▪ Weight gain ▪ Xerostomia ▪ Sedation ▪ Agitation	▪ Monitor for suicidality ▪ Multiple drug interactions ▪ Caution in patients with a history of cardiovascular disease ▪ Avoid abrupt discontinuation
Desipramine	Initial Dose: 10-25 mg at bedtime Titration Dose: Increase at weekly increments of 10-25 mg daily Maximum Dose: 150 mg daily		
Nortriptyline	Initial Dose: 10 mg at bedtime Titration Dose: Increase at weekly increments of 10-25 mg daily Maximum Dose: 50-100 mg daily		
Vitamins/Supplements			
Magnesium oxide	Usual Dose: 600 mg daily Maximum Dose: 800 mg daily	▪ Diarrhea	▪ Administer at least 2 hrs apart from other medications ▪ Assess for drug interactions ▪ Take with food
Vitamin B2 (Riboflavin)	Usual Dose: 400 mg daily	▪ Discoloration of urine	▪ Protect storage bottle from light

Note: Refer to product prescribing insert for more information regarding use restrictions, dose modification, dosing in special populations (e.g., renal or liver impairment, advanced age, pregnancy), drug-drug interactions and adverse events.

Abbreviations: GI: gastrointestinal; hrs: hours; mg: milligram; PTSD: posttraumatic stress disorder; TID: three times daily

E. Dizziness and Disequilibrium

a. Background

Dizziness and disequilibrium is one of the most common symptoms in primary care, and may also result from mTBI. Dizziness and disequilibrium due to various causes can be broadly organized into the following disorders: inner ear disorders (peripheral vestibular disorders), central nervous system disorders, psychological disorders, musculoskeletal disorders, and idiopathic disorders (one of the most common forms of dizziness).

Table B-5. Criteria for Categorization and Referral for Dizziness and Disequilibrium After mTBI [109,110]

#	Possible Diagnosis	Symptoms	Duration/Provocation	Referral
Inner Ear Disorders (Peripheral Vestibular Disorders)				
1	Benign paroxysmal positional vertigo (BPPV)	▪ Vertigo ▪ Lightheadedness ▪ Nausea	▪ Spells that last for seconds to minutes and are associated with changes in head position ▪ Nystagmus, often with a torsional component, usually observed when symptomatic	▪ Canalithic repositioning maneuver ▪ PT
2	Labyrinthine concussion	▪ Vertigo with movement ▪ Disequilibrium ▪ Oscillopsia with head movements ▪ Nausea and vomiting (acute)	▪ History of event, symptoms improved since event but remain problematic ▪ Mostly related to fast head movements/turns	▪ ENT Specialist ▪ PT
3	Posttraumatic endolymphatic hydrops	▪ Vertigo ▪ Disequilibrium ▪ Aural fullness ▪ Tinnitus	▪ Spontaneous, episodic spells that can last for hours	▪ ENT
4	Perilymphatic fistula	▪ Loud tinnitus ▪ Hearing loss ▪ Vertigo	▪ Onset related to an event ▪ Increase in abdominal pressure can elicit symptoms	▪ ENT
5	Bilateral labyrinthine dysfunction	▪ Disequilibrium ▪ Vertigo and oscillopsia if lesions asymmetrical	▪ Related to one or more events, induced by head movements, difficulty with postural control in the dark or on uneven surfaces	▪ ENT ▪ PT
Central Disorders				
6	Migraine-induced vestibulopathy	▪ Motion sensitivity ▪ Disequilibrium ▪ Headache ▪ Vertigo	▪ Movement induced spells of vertigo that usually last for minutes to 1 hour, usually close temporal relationship with headache	▪ See Appendix B: Headache ▪ PT
7	Visual dysfunction	▪ Dizziness ▪ Disequilibrium ▪ Blurred vision ▪ Diplopia ▪ Impaired visual-spatial orientation ▪ Eye hand incoordination	▪ Difficulties with balance on uneven, conforming terrain ▪ Dizziness with increased environmental stimulation ▪ Squinting/closing one eye during activities ▪ Difficulty standing in midline or noted head tilt	▪ Ophthalmology ▪ Optometry ▪ Vision Rehabilitation

#	Possible Diagnosis	Symptoms	Duration/Provocation	Referral
			▪ Reading difficulties ▪ Sensitivity to light	
Psychological Disorders				
8	Depression, anxiety, somatic symptom disorder	▪ Lightheadedness ▪ Floating ▪ Rocking ▪ Vague/bizarre accounts	▪ May be related to event but could report chronic history, symptoms can be induced by eye movements with head still	▪ Psychiatry ▪ Psychology ▪ PT
Musculoskeletal Disorders				
9	Flexion-extension, rotation, cervical injury (cervicogenic)	▪ Disequilibrium ▪ Lightheadedness ▪ Neck pain	▪ Onset with event ▪ Symptoms coincide with movement of cervical spine	▪ Physiatry ▪ PT
Uncommon Central Disorders				
10	Vertebral-basilar insufficiency related to occipitoatlantal instability	▪ Nausea and vomiting ▪ Vertigo ▪ Visual hallucinations/loss ▪ Visual field deficit ▪ Numbness/weakness ▪ Ataxia ▪ Drop attacks ▪ Diplopia ▪ Headaches	▪ Related to an event ▪ Usually symptoms induced by cervical extension and rotation	▪ Neurology ▪ Neurosurgery
Other				
11	Temporal bone fracture	▪ Conductive hearing loss ▪ Vertigo ▪ Disequilibrium ▪ Nausea and vomiting ▪ Oscillopsia	▪ Onset with event ▪ Will follow the course of labyrinthine concussion	▪ ENT ▪ PT
12	Idiopathic	▪ Non-specific dizziness and many other related symptoms	▪ One of the most common symptoms in primary care, and most common reason for dizziness	▪ Generally best to treat in primary care setting and minimize referrals, unless clinically indicated

Abbreviations: ENT: ear, nose and throat specialist; PT: physical therapy

b. *Assessment*

i. Physical Examination

Defining how the patient characterizes dizziness (e.g., vertigo, lightheadedness, syncope, disequilibrium, confusion), describes the temporal pattern (e.g., seconds, minutes, hours, days), and provokes symptoms (e.g., rolling over in bed, bending over, head movement) may provide valuable information in establishing a working differential diagnosis. Primary care assessment for vestibular disturbance should be done before referring for further vestibular examination and exercise. Once initial primary care assessment is complete and other causes are eliminated (e.g., vertebral basilar insufficiency, orthostatic hypotension, polypharmacy), refer to vestibular rehabilitation specialist for trial intervention sessions.

Observation and patient interview are key elements to the exam and often guide the clinician in determining the plan of care. Evaluation should include a thorough neurologic examination and the following functions and structures: orthostatics, vision (acuity, monocular confrontation fields, pupils, eye movements, nystagmus), auditory (hearing screen, otoscopic exam), sensory (sharp, light touch, proprioception, vibration), motor (power, coordination), cervical, and vestibular (dynamic acuity, positional testing). Evaluation of functional activities should include sitting and standing balance (Romberg with eyes open/closed, single leg stance), transfers (supine↔sit, sit↔stand) and gait (walking, tandem walking, and turning).

ii. Medication Review

A detailed medication history is warranted. Numerous medications include dizziness as a potential side effect. The following classes of medication can cause or aggravate dizziness: stimulants, benzodiazepines, tricyclics, monoamine oxidase inhibitors, tetracyclics, neuroleptics, anticonvulsants, selective serotonin agonists, beta blockers and cholinesterase inhibitors. The temporal relationship to the onset of dizziness and the initiation/dosing of these medications should be investigated.

c. Treatment

i. Pharmacologic Treatment

Initiating vestibular suppressants for dizziness may delay central compensation or promote counterproductive compensation.[111,112] Vestibular suppressants might be helpful during the acute period of several vestibular disorders but have not been shown to be effective in chronic dizziness after concussion.[113] Medications should only be considered if symptoms are severe enough to significantly limit functional activities. Trials should be brief and optimally less than a week. It is important to be particularly careful regarding dosing and titration due to the effects on arousal and memory as well as the potential addictive qualities of these medications.[114] First-line medication choice would be meclizine, followed by scopolamine and dimenhydrinate, depending upon symptom presentation. Pharmacotherapy with clonazepam, diazepam or lorazepam is discouraged due to the sedating and addictive qualities of those agents.

ii. Non-Pharmacologic Treatment

Non-pharmacologic interventions for posttraumatic dizziness may be useful as an alternative to pharmacotherapies, although the effectiveness of such interventions is not fully established with concussion/mTBI.[115] Efficacy of vestibular and balance rehabilitation has been shown in different populations with vestibular disorders.[61-63] Patients with vestibular disorders who received customized programs showed greater improvement than those who received generic exercises.[62] Studies utilizing vestibular exercises have shown up to an 85% success rate in reducing symptoms and improving function in the population with peripheral vestibular disorders.[62,116]

With mTBI, recovery of vestibular lesions is often limited or protracted due to the coexistence of central or psychological disorders.[56] Evidence is limited regarding the benefits patients with a history of mTBI participating in specific vestibular exercises.

Knowledge of the canalith repositioning procedures for the treatment of benign paroxysmal positional vertigo (BPPV) would be beneficial for primary care physicians.[117] In addition, patients with history and clinical examination consistent with BPPV may also be sent to a vestibular rehabilitation therapist for further specialized

BPPV assessment and treatment with guided follow-up, should symptoms not fully resolve after one trial of canalithic repositioning maneuver.

In cases of persistent dizziness and disequilibrium, a qualified vestibular rehabilitation therapist may also be utilized to execute a more comprehensive vestibular/balance evaluation and treatment program. The types of specialized assessment tools, maneuvers and exercises to treat dizziness and disequilibrium are beyond the scope of this guideline. Patients with central and psychological disorders need a coordinated team effort to address the underlying impairments in order to maximize the outcome of vestibular rehabilitation.

If an individual appears to be at fall risk due to symptoms of dizziness and disequilibrium, referral for home evaluation for adaptive equipment should also be considered as a compensatory strategy to limit further injury.

The OTSG Army Toolkit as well as DVBIC may also provide guidance regarding symptoms of dizziness and vestibular rehabilitation. These additional resources are mentioned to provide assistance to primary care providers; however, it should be noted that information contained in these documents was not reviewed. (See Additional Educational Materials and Resources.)

F. Visual Symptoms

a. Background

Vision difficulties, including sensitivity to light, eye fatigue, difficulty focusing and/or blurry vision occur acutely in some individuals who sustain an mTBI. The vast majority of vision difficulties resolve within minutes or hours, with some individuals experiencing symptoms for longer. Therefore, targeted treatments aimed at symptom management during the early period when these symptoms are occurring are usually effective. If, over time, visual problems persist and impact daily function, a referral to optometry, ophthalmology, neuro-ophthalmology, neurology, and/or vision rehabilitation team is indicated.

Primary care providers need to be keenly aware of potential reasons for an urgent referral to an eye care provider in cases of vision loss or decline, diplopia, abnormal pupils, abnormal external eye exam, abnormal visual behavior (e.g., unexpectedly bumping into things), abnormal eye movements (e.g., nystagmus) or acute ocular symptoms (e.g., evidence of trauma, severe eye pain, flashes and/or floaters, severe photophobia).

b. Assessment and Treatment

In response to persistent vision problems the primary care provider should inquire about how the vision impairment has been impacting the patient's daily functioning, by asking questions such as "how have your vision problems impacted school or work such as reading and/or using a computer?" If functional impairments are evident, proceed with a basic eye/vision exam which should include visual acuity (distant and near), monocular confrontational fields, pupils (size/equality/response), eye movements, external exam (direct illumination of anterior segment) and a check for nystagmus (primary position and gaze evoked). A slit lamp exam can be helpful, if available.

All current medications should be evaluated as they may be the cause of the visual dysfunction. Drugs to be aware of that may be associated with vision problems include antihistamines, anticholinergics, digitalis derivatives, antimalarial drugs, corticosteroids, erectile dysfunction drugs, phenothiazines, chlorpromazine, indomethacin and others. Other comorbidities may also be contributing factors or the source of the vision dysfunction, such as migraines, sleep disturbances, chronic pain, mood disorders and PTSD.

If the vision problem is impacting function over time, consider a referral to a specialist trained in oculomotor rehabilitation care (e.g., a polytrauma blind rehabilitation outpatient specialist, low vision therapist, occupational therapist) to complete a vision screen and functional assessment. If indicated, an eye care provider can complete a comprehensive vision assessment and together with the rehabilitation team can develop a treatment intervention to address the individual's visual complaints and functional deficits.

The types of specialized vision rehabilitation assessment tools and interventions (e.g., vision exercises) to address visual dysfunction related to mTBI are beyond the scope of this guideline. Patients will need a coordinated team effort to address the underlying impairments in order to maximize the outcome of vision rehabilitation.

Refer to DCoE Clinical Recommendations for clinical algorithm, functional vision questions, yellow and red flags for referral to a specialist and additional guidance on how to manage vision deficits following mTBI.

G. Fatigue

a. Background

Fatigue is the third most common symptom reported after mTBI, and is also one of the most common symptoms in other primary care populations. It can be due to a primary effect related to central nervous system dysfunction or a secondary effect of common coexisting disorders in mTBI such as depression or sleep disturbances, or any number of other reasons. Medications, substance use and lifestyle may also contribute to fatigue.[118,119]

b. Assessment and Treatment

A detailed history of pre/post-injury level of physical activity, cognitive function and mental health is important to determine the effects of fatigue in temporal relation to the injury. The ability to maintain a job is often a good measure of the impact of this symptom. Several outcome measures exist for fatigue, and many have been studied in other populations. Common measures in TBI include the Multidimensional Assessment of Fatigue (MAF), Fatigue Impact Scale (FIS) or Fatigue Assessment Instrument (FAI). However, there is no specific scale recommended for mTBI. Laboratory tests to rule out other medical conditions affecting fatigue may be considered. Current pharmacotherapy and supplement use must be reviewed to eliminate the contribution of these agents to fatigue.

Education is important in the treatment of fatigue. Educational efforts should be focused on factors contributing to fatigue, importance of well-balanced meals, promotion of sleep hygiene and encouragement of regular exercise. Exercise routines should be individualized to maximize benefit and promote a proper ratio of activity and rest. Scheduling of exercise may need to be addressed depending upon when the patient is at his or her best. CBT and PT can be tried to decrease fatigue level and improve functional performance in patients with a history of mTBI.

H. Sleep Disturbance

Pharmacologic treatment of sleep disturbance following mTBI may be complex. For all pharmacologic interventions, providers should weigh the risk-benefit profiles, including toxicity and abuse potential.

Table B-6. Dosing Recommendations for Sleep Agents*

*Medications listed in alphabetical order, not by preference

** Periodic reevaluation of the need for and efficacy of the therapies listed is strongly encouraged

Dosing Recommendations: Sleep Agents**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
Alpha-Blockers			
Prazosin	Initial Dose: 1 mg at bedtime Titration Dose: Increase dose weekly to 4 mg, 6 mg, 8 mg, 10 mg Maximum Dose: 10 mg at bedtime	▪ Dizziness ▪ Palpitations ▪ Orthostasis	▪ For patients with nightmares associated with PTSD ▪ Evaluate for orthostatic hypotension and syncope
Hypnotics			
Eszopiclone	Initial Dose: 1 mg before bedtime Maximum Dose: 3 mg before bedtime	▪ Headache ▪ Drowsiness ▪ Abnormal dreams ▪ Memory impairment ▪ Disorientation ▪ Unpleasant taste (specifically with eszopiclone)	▪ Not indicated for long-term use ▪ Sleep walking effects ▪ Short-term amnesia ▪ Abnormal behavior ▪ Recommend taking immediately before bedtime ▪ Zaleplon has a very short half-life of about 1 hr; as a result, it may be more effective for patients who have difficulty with sleep onset and sleep latency ▪ Patients using eszopiclone or zolpidem should be advised to refrain from driving or other activities that require mental alertness the day after taking the drug
Zaleplon	Initial Dose: 10 mg immediately at bedtime Low body weight: 5 mg Titration Dose: Less than 65 years: 20 mg		
Zolpidem	**Immediate Release** Initial Dose: Females: 5 mg before bedtime; Males: 5-10 mg before bedtime Maximum Dose: 10 mg before bedtime		
	Extended Release Initial Dose: Females: 6.25 mg before bedtime; Males: 6.25-12.5 mg before bedtime Maximum Dose: 12.5 mg before bedtime		

Dosing Recommendations: Sleep Agents**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
SSRIs/Antidepressants			
Trazodone	Usual Dose: 50-100 mg at bedtime Maximum Dose: 200 mg at bedtime	▪ Sedation ▪ Headache ▪ Xerostomia ▪ Dizziness ▪ Priapism (specifically with trazodone)	▪ Risk of serotonin syndrome when used concomitantly with other serotonergic drugs ▪ Monitor for suicidality ▪ May lower seizure threshold ▪ May use for patients with comorbid conditions such as depression,*** pain or headaches
Amitriptyline	Initial Dose: 25 mg at bedtime Maximum Dose: 150 mg		
Doxepin	Initial Dose: 3 mg taken within 30 minutes of bedtime Maximum Dose: 6 mg	▪ Somnolence	▪ Monitor for suicidality ▪ May lower seizure threshold ▪ May use for patients with comorbid conditions such as depression,*** pain or headaches
Mirtazapine	Initial Dose: 15 mg at bedtime Maximum Dose: 45 mg at bedtime	▪ Somnolence ▪ Nausea ▪ Dizziness ▪ Increased appetite ▪ Weight gain	▪ Degree of sedation is moderate to high relative to other antidepressants ▪ Monitor for suicidality ▪ May lower seizure threshold
Melatonin receptor agonists			
Ramelteon	Initial Dose: 8 mg taken within 30 minutes of bedtime Maximum Dose: 8 mg per day	▪ Somnolence ▪ Dizziness ▪ Nausea ▪ Fatigue ▪ Headache ▪ Hallucinations have been reported in some patients	▪ Do not use in combination with fluvoxamine ▪ Use caution in patients taking other CYP1A2-inhibiting drugs
Orexin receptor antagonists			
Suvorexant	Initial Dose: 10 mg taken within 30 minutes of bedtime Maximum Dose: 20 mg	▪ Somnolence ▪ Headache ▪ Dizziness	▪ CNS depression impairing physical and mental capabilities ▪ Significant drug interactions exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy

Note: Refer to product prescribing insert for more information regarding use restrictions, dose modification, dosing in special populations (e.g., renal or liver impairment, advanced age, pregnancy), drug-drug interactions and adverse events.
Abbreviations: CNS: central nervous system; hr: hour; mg: milligram; PTSD: posttraumatic stress disorder; SSRIs: selective serotonin re-uptake inhibitors
***Doses used for depression are higher than those recommended for sleep. Additionally, if a patient has comorbid depression and cannot sleep, then a wider range of antidepressants can be considered (SSRIs/serotonin–norepinephrine reuptake inhibitors [SNRIs]) as treating depression often improves sleep.

I. Cognitive Symptoms

a. Clinical Guidance

- Cognitive complaints (e.g., forgetting appointments or medication schedules, losing items more than expected or usual) should be followed up with a comprehensive patient history and, if they persist after 30 to 90 days, a functional cognitive assessment.
- A comprehensive evaluation that includes reliable and valid tools, self-report and ecologically-relevant measures requiring higher levels of sustained effort or similar to the everyday environments of the individual may help determine clinical indications for treatment, need for referral to other rehabilitation specialists and/or a treatment plan based on functional needs.[120]
- Education should be an integral part of the management process. Clinicians should use principles of risk communication to provide reassurance, promote normalization and minimize the perception of disability. Cautious risk communication also will help reduce the perception of neurologically-based deficits and guide treatment based on symptoms and functional needs. Education should include information about the potential effects of coexisting conditions and medication side effects on cognition.
- Motivational interviewing techniques may help with identifying activity limitations and setting meaningful goals, as well as promoting active patient engagement in the treatment process.[121]
- Goal attainment scaling (GAS) for rehabilitation may facilitate setting measurable and term-limited goals that are individualized to the unique situation and needs of the patient.[122,123] GAS may help clinicians develop goals that are based on gradual improvements in activity participation, thus setting positive and realistic expectations of treatment.
- Referrals for clinician-directed interventions, whether in individual or group settings, are suggested over self-directed computer-based programs and exercises. Computer-based interventions and the selective use of mobile applications (e.g., Concussion Coach) may be considered when used by clinicians in support of a comprehensive treatment approach focused on symptom management and real-world benefit.
    - Compensatory strategy training can involve adaptive strategies such as environmental modifications to facilitate attention, as well as establishing and practicing new techniques to support daily functioning, work and school activities.
    - Cognitive AT may range from a wrist watch with an alarm function, to a multi-function device (e.g., smartphone, tablet). Familiar and readily available devices are preferred over customized devices.
    - Successful long-term utilization of strategies and devices requires specialized evaluation to select the appropriate technique or device (for the person and the situation) and sufficient practice in real-life contexts.
    - Techniques that promote self-reflection and self-regulation during therapeutic treatment trials are suggested to support generalization of treatment gains to community-based activities leading to functional independence.
- Cognitive rehabilitation requires patient and family engagement and often collaboration with other rehabilitation team members (e.g., OT, PT, vocational rehabilitation, recreational therapy, speech-language pathology). Collaboration with mental health professionals, particularly for patients with

associated or comorbid mental health issues, may help reduce distress, improve emotional functioning and facilitate improvement in functional outcomes.[85]

J. Persistent Pain

(See also discussion of Headache)

a. Background

Approximately 40-50% of patients with a history of mTBI may experience chronic pain.[48] Pain management is similar to patients without a history of mTBI. However, in a patient with a history of mTBI, the complaint of chronic pain is sometimes interwoven with comorbid conditions such as sleep disorders, anxiety, MDD, or PTSD.

b. Assessment

Assessing patients for pain and its underlying causes is an essential component of the clinical work-up. It is important to attribute symptoms correctly and to identify and treat any comorbid conditions. If medication is being considered, it is essential to establish the underlying cause prior to prescribing and to clearly define the goals of therapy.

c. Treatment

Pain management is a priority and all patients presenting with a history of mTBI and complaints of pain should be assessed. The underlying cause of the pain should be determined and treated. The use of non-pharmacologic therapies should be considered. Rehabilitation therapies may be beneficial for the management of pain in patients with a history of or who have sustained mTBI. The use of opioid agents in chronic pain conditions should be avoided until other avenues of pain control have been given appropriate treatment trials.

Providers may also consult the VA/DoD CPG for the Management of CMI[27] or the VA/DoD CPG for Opioid Therapy for Chronic Pain[28] for additional strategies to manage persistent pain.

K. Hearing Difficulties

a. Background

Hearing difficulties, including altered acuity and sensitivity to noise, occur acutely in the majority of individuals who sustain a blast-related mTBI.[66] Symptoms are either decreased auditory acuity or sensitivity to noise. The vast majority of symptoms resolve within a month, unless there is significant or permanent injury to the ear drum. Aggressive, targeted treatments aimed at symptom management (e.g., reassurance, pain management, controlling environmental noise, white noise generators) in the early treatment period are usually effective. True abnormalities in central auditory acuity or processing are extremely rare with mTBI. Other causes of problems are also extremely rare and often not related directly to the concussion injury. Pre-injury hearing deficits are common and need to be ruled out.

[27] See the VA/DoD Clinical Practice Guideline for Management of Chronic Multisymptom Illness. Available at: http://www.healthquality.va.gov/guidelines/mr/cmi/index.asp

[28] See the VA/DoD Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. Available at: http://www.healthquality.va.gov/guidelines/pain/cot/index.asp

b. Assessment and treatment

1. Perform an otologic examination.
2. Review medications for ototoxicity.
3. Refer to audiology for hearing assessment if no other apparent cause is found.

L. Smell (Olfactory Deficits)

a. Background

Posttraumatic olfactory deficits (anosmia) are not common in individuals who sustain an mTBI.[124] The vast majority of cases resolve within a six month period. Treatments have limited effect and are usually aimed at flavoring/spicing food to enhance taste and providing specific safety education (e.g., particular attention to working smoke detectors for patients who may not smell smoke). Other causes are also extremely rare and often not related directly to the concussion injury. Depression, common among those with persistent symptoms following mTBI, has been associated with perceptual biases in olfaction that may drive patient complaints of changes in smell and taste.[125] Pre-injury causes of anosmia need to be ruled out.[52]

b. Assessment and treatment

1. Perform a nasal and oropharyngeal examination. Screen for depression.
2. Refer to ear, nose and throat specialist (ENT) for further evaluation, if needed.
3. If neurologic status is stable and there are no objective findings, reassurance and monitoring are appropriate.
4. For depressed patients, treatment with psychotherapy may improve olfaction.[126]
5. Increase spicing of foods (+/- dietary referral). Monitor weight. Provide specific safety education.

M. Nausea

a. Background

Occasionally, posttraumatic nausea occurs acutely after mTBI, most often in combination with dizziness, as a secondary effect of medications (pain), or due to an exacerbation of underlying gastroesophageal reflux disease (GERD)/gastrointestinal (GI) dysfunction. This symptom may also be associated with psychological stressors.

b. Assessment and treatment

1. Define triggers and patterns of nausea. Refer to **Table B-5** as appropriate.
2. Assess medication lists for agents that may cause or worsen GI symptoms.
3. The initial focus should be on the rapid management of dizziness and return to activity. Formal assessment should be limited.

N. Changes in Appetite

While changes in appetite can occur, these are not a primary effect from mTBI but rather are the result of secondary issues. When a change in appetite is noted, it may be related to mood, medications, smell, or other factors and will likely resolve as these factors are addressed.

O. Numbness

Numbness following mTBI in the absence of peripheral nerve injury is atypical and may be associated with psychological stressors. A sensory examination may be performed to assess the symptom.

Appendix C: Mechanism of Injury

Figure C-1. DoD TBI Diagnoses from 2002-2009 [127]

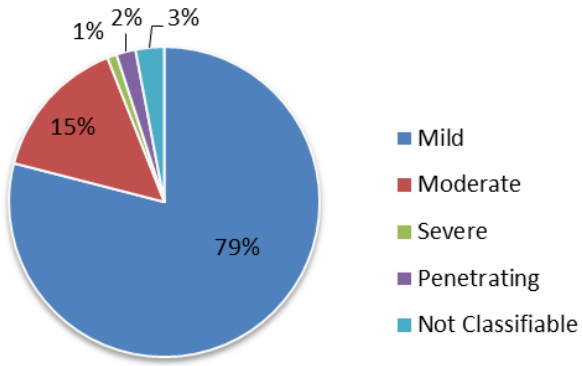
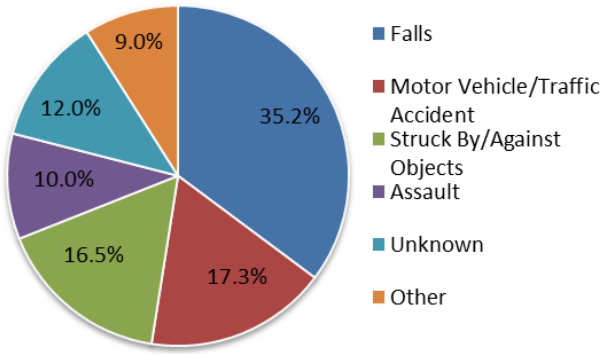


Figure C-2. Leading Causes of mTBI [127]



In both blast and non-blast etiologies, primary injury can involve neurons, neuroglia, and vascular structures.[128] A multitude of diffuse and dynamic processes also can contribute to secondary injury to include hypoxia and hypotension. The result of this secondary process is the release of inflammatory cytokines, initiation of an excitotoxic cascade, development of cerebral edema, and apoptotic signaling. The effects of free radical oxygen species, excitatory amino acids, and fluctuations in ion gradients such as calcium, alterations in neurotransmitters such as glutamate, receptor activation, lipid peroxidation, and mitochondrial uncoupling all result in increased neurologic injury. While the extent of such processes may be limited within the mTBI spectrum, the disturbances in brain metabolism and network connectivity associated with mTBI are related more to the complex cascade of ionic, metabolic and physiologic events rather than to structural injury or damage. The unique molecular activation and intracellular processes associated with individual mTBI etiologies require continued investigation. In addition, the effect of these physiologic responses needs to be studied over a variety of acute, sub-acute, and chronic time points in order to identify the underlying pathophysiology associated with mTBI and its association with the development of chronic neurodegenerative changes in a subpopulation of at-risk individuals.

An individual blast produces a complex mechanical profile consisting of a primary shock wave, followed immediately by a period of negative pressure, generation of a supersonic blast wind, and a delayed period of dissipating elevated pressure. However, depending on multiple blast and environmental variables this profile is quickly modified. Primary blast injury originates from early time point interactions between the blast-induced shock wave and the regional parenchyma and extra parenchymal tissues. This may result in a diffuse traumatic injury which precedes the onset of any linear or rotational acceleration injury. Passage of the shock wave through the tissues generates a combination of mechanical stresses which engage the neurons, glial cells, extracellular matrix, vascular structures, and cerebrospinal fluid-containing structures. These forces include spalling, shearing, mean and deviatoric stress, pressure, and volumetric tension. Secondary blast injury is related to objects which are displaced by the blast overpressure and blast wind. Secondary injuries may include a combination of both penetrating and blunt trauma. Tertiary blast injury occurs when an individual is thrown by the blast, sustaining blunt trauma such as a closed brain injury. Quaternary blast injuries, such as burns, chemical exposure, and asphyxia are directly related to the blast, but cannot be classified as a primary, secondary, or tertiary injury. Physical effects of the primary blast on an individual depend not only on blast

characteristics but also on the physical relationship to the blast, such as the distance from the blast and exposure in an open environment versus an enclosed structure.

While isolated head trauma does occur, often mTBI blast-related mechanisms of TBI are associated with multi-system polytrauma and complicated by factors known to exacerbate secondary injury such as hypotension, hypoxia, and hypothermia, and primary blast effects on an individual likely do not often occur in the absence of secondary or tertiary blast effects, due to the narrower radius of primary blast dispersion compared with more widespread dispersion of blast fragment. The neurometabolic cascade following TBI is diverse and dynamic. The contribution of any particular physiologic response varies based on the magnitude of the forces involved, environmental features, and an individual's unique characteristics at the time of the event. Potential modifiers include, but are not limited to, genetic profile and epigenetic response to blast or non-blast stimulus, a history of previous TBI, general medical conditions, sleep deprivation, increased levels of stress hormone, and nutritional and hydration status.

Non-blast injuries are associated with focal, multifocal, and diffuse injury. Coup/contracoup injury is the result of a mismatch in brain and skull movement. When the skull moves faster than the brain, the brain will strike the inner table of the calvarium causing a focal contusion, then, after the skull and brain have stopped their initial direction of movement, the brain may rebound in the opposite direction and impact the calvarium a second time. The orbitofrontal and anterior temporal lobes are most often affected as these are the most common sites of impact from motor vehicle accidents and sports-related injuries. The secondary effects of an acceleration/deceleration injury include edema and hemorrhage. Depending on the individual forces transmitted during an event, white matter injury through axonal stretch may play a prominent role in the pathology and clinical sequelae associated with both blast and non-blast mechanisms of TBI. With increased energy transfer, acceleration/deceleration is the primary etiology associated with diffuse axonal injury (DAI) and can occur as a primary mechanism of injury in closed brain injury or as a secondary force associated with blast exposure. A complex interrelationship exists between impact location, linear and rotational acceleration and concussion as a primary or secondary effect of acceleration/deceleration forces. To what extent the addition of shock wave propagation plays in modulation of biomechanical properties and what, if any, distinct physiologic effects are generated from the cumulative effects of blast plus acceleration, rather than either primary mechanism of injury in isolation, is currently unknown.

In the systematic evidence review for the current mTBI CPG, six prognostic cohort studies were reviewed specifically as they related to either the treatment or outcome prognostication of mTBI. Four of the studies evaluated blast versus non-blast cohorts; however, none of the studies were specifically designed to evaluate mechanisms of injury or effectiveness of treatment. Treatment was not controlled for, nor was it reported in any of the included studies. Cooper et al. included blast versus non-blast mechanism of injury as part of a multivariable analysis in an attempt to identify prognostic variables of outcome.[129] The study was limited in that it did not control for treatment, diagnosis was based on a retrospective self-report, it included a significantly heterogeneous population and the time from injury was delayed with an average time from injury of 354 (+/-457) days. However, even with this heterogeneous population, the mechanism of injury, blast versus non-blast and time from injury combined accounted for only 1.4% of variance and was not a statistically significant predictor of neurocognitive outcome. MacDonald et al. evaluated outcomes between combat-associated blast and non-blast mTBI using the Glasgow Outcome Scale (GOS) at six and 12 months from injury and found no significant difference between the two cohorts.[36] This study is severely limited in that the blast-

exposed cohort has no objective validation of overpressure exposure, and environmental data such as mounted versus dismounted exposure, direct versus shielded exposure, explosive device, and distance from exposure are not provided. MacDonald et al. did report that the non-blast TBI group had significantly more olfactory deficits which would be consistent with a primary axonal stretch injury such as acceleration/deceleration etiology.[36] Belanger et al. evaluated the reported symptoms between patients who had sustained blast and non-blast mechanism of mTBI using a Neurobehavioral Symptom Inventory (NSI).[33] While there were limitations in retrospective data collection, subjective event reporting, and a significant variance in time from injury between the two groups (mean blast exposure time since injury was 11.9 months and mean time from injury for non-blast TBI was 25.9 months), the study found no significant effect regarding mechanism of injury on the NSI score. The study did note that hearing difficulties were the only significant symptoms difference between the groups with more severe hearing difficulty in the blast group. Cooper et al. examined the relationship between combat stress and post-concussive symptoms and found that there was no association between the mechanism of injury, blast versus non-blast, and the observed differences in post-concussive symptoms.[34] Belanger et al. found no difference in neurocognitive testing in patients with blast versus non-blast mechanisms at a mean time of 1021 days from injury.[32] Finally, Lingsma et al. evaluated the performance of existing mTBI prognostic models in a prospective, unselected population of patients with non-blast, closed head-associated mechanisms of mTBI injury, to include assaults, motor vehicle accidents, and falls.[35] In a 21 variable univariate and multivariable proportional odds regression model with three and six month Glasgow Outcome Score, Extended (GOS-E) as ordinal outcomes, the study found that, in univariate analyses, assault was more predictive of a worse outcome and in multivariable analyses assault was also associated with a worse outcome where falls and motor vehicle accident did not vary.

Given the limited evidence base and lack of evidence to suggest a difference in mTBI symptoms, therapy and outcomes should not be modified based on mechanism of injury at this time.

Appendix D: Evidence Table

Recommendation	2009 Grade[29]	Evidence[30]	Strength of Recommendation[31]	Recommendation Category[32]
1. We suggest using the terms "history of mild traumatic brain injury (mTBI)" or "concussion" and to refrain from using the terms "brain damage" or "patients with mTBI" in communication with patients and the public.	None	**Additional References:** [10]	Weak for	Not Reviewed, Amended
2. We recommend evaluating individuals who present with symptoms or complaints potentially related to brain injury at initial presentation.	None	**Additional References:** [12,14,15]	Strong for	Not Reviewed, Amended
3. Excluding patients with indicators for immediate referral, for patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we suggest against using the following tests to establish the diagnosis of mTBI or direct the care of patients with a history of mTBI: a. Neuroimaging b. Serum biomarkers, including S100 calcium-binding protein B (S100-B), glial fibrillary acidic protein (GFAP), ubiquitin carboxyl-terminal esterase L1 (UCH-L1), neuron specific enolase (NSE), and α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor (AMPAR) peptide c. Electroencephalogram (EEG)	None, I	[16-20] **Additional References:** [130]	Weak against	Reviewed, New-replaced
4. We recommend ***against*** performing comprehensive neuropsychological/ cognitive testing during the first 30 days following mTBI. For patients with symptoms persisting after 30 days, see Recommendation 17.	D	**Additional References:** [21-24]	Strong against	Not Reviewed, Amended

[29] The 2009 VA/DoD mTBI CPG used the U.S. Preventive Services Task Force (USPSTF) evidence grading system (http://www.uspreventiveservicestaskforce.org). Inclusion of more than one 2009 Grade indicates that more than one 2009 CPG recommendation is covered under the 2016 recommendation.

[30] The evidence column indicates studies that support each recommendation. For new recommendations, developed by the 2016 guideline Work Group, the literature cited corresponds directly to the 2015 evidence review. For recommendations that have been carried over from the 2009 VA/DoD mTBI CPG, slight modifications were made to the language in order to better reflect the current evidence and/or the change in grading system used for assigning the strength of each recommendation (USPSTF to GRADE). For these "modified" recommendations, the evidence column indicates "additional evidence," which can refer to either 1) studies that support the recommendation and which were identified through the 2015 evidence review, or 2) relevant studies that support the recommendation, but which were not systematically identified through a literature review.

[31] Refer to the Grading Recommendations section for more information on how the strength of the recommendation was determined using GRADE methodology.

[32] Refer to the Recommendation Categorization section for more information on the description of the categorization process and the definition of each category.

Recommendation	2009 Grade[29]	Evidence[30]	Strength of Recommendation[31]	Recommendation Category[32]
5. For patients identified by post-deployment screening or who present to care with symptoms or complaints potentially related to brain injury, we recommend ***against*** using the following tests in ***routine*** diagnosis and care of patients with symptoms attributed to mTBI: a. Comprehensive and focused neuropsychological testing, including Automated Neuropsychological Assessment Metrics (ANAM), Neuro-Cognitive Assessment Tool (NCAT), or Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT)	None	[25-30]	Strong against	Reviewed, New-replaced
6. For patients with new symptoms that develop more than 30 days after mTBI, we suggest a focused diagnostic work-up specific to those symptoms only.	None	**Additional References:** [31]	Weak for	Not Reviewed, Amended
7. We recommend assessing patients with symptoms attributed to mTBI for psychiatric symptoms and comorbid psychiatric disorders including major depressive disorder (MDD), posttraumatic stress disorder (PTSD), substance use disorders (SUD) and suicidality. Consult appropriate VA/DoD clinical practice guidelines.	None	**Additional References:** [15,32-39]	Strong for	Not Reviewed, Amended
8. We suggest considering, and offering as appropriate, a primary care, symptom-driven approach in the evaluation and management of patients with a history of mTBI and persistent symptoms.	None, C	**Additional References:** [43,44]	Weak for	Not Reviewed, Amended
9. We recommend ***not*** adjusting treatment strategy based on mechanism of injury.	--	[45,46]	Strong against	Reviewed, New-added
10. We recommend ***not*** adjusting outcome prognosis based on mechanism of injury.	--	[45,46]	Strong against	Reviewed, New-added
11. We suggest that the treatment of headaches should be individualized and tailored to the clinical features and patient preferences. The treatment may include: a. Headache education including topics such as stimulus control, use of caffeine/tobacco/alcohol and other stimulants b. Non-pharmacologic interventions such as sleep hygiene education, dietary modification, physical therapy (PT), relaxation and modification of the environment (for specific components for each symptom, see Appendix B: Clinical Symptom Management) c. Pharmacologic interventions as appropriate both for acute pain and prevention of headache attacks	None	[47,49,50]	Weak for	Reviewed, New-replaced

Recommendation	2009 Grade[29]	Evidence[30]	Strength of Recommendation[31]	Recommendation Category[32]
12. In individuals with a history of mTBI who present with functional impairments due to dizziness, disequilibrium, and spatial disorientation symptoms, we suggest that clinicians offer a short-term trial of specific vestibular, visual, and proprioceptive therapeutic exercise to assess the individual's responsiveness to treatment. Refer to occupational therapy (OT), physical therapy (PT) or other vestibular trained care provider as appropriate. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged.***	None	[53-64]	Weak for	Reviewed, Amended
13. There is no evidence to suggest for or against the use of any particular modality for the treatment of tinnitus after mTBI.	--	[68]	N/A	Reviewed, New-added
14. There is no evidence to suggest for or against the use of any particular modality for the treatment of visual symptoms such as diplopia, accommodation or convergence disorder, visual tracking deficits and/or photophobia after mTBI.	--	[72-74] **Additional References:** [69-71]	N/A	Reviewed, New-added
15. We suggest that treatment of sleep disturbance be individualized and tailored to the clinical features and patient preferences, including the assessment of sleep patterns, sleep hygiene, diet, physical activities and sleep environment. The treatment may include, in order of preference: a. Sleep education including education about sleep hygiene, stimulus control, use of caffeine/tobacco/alcohol and other stimulants b. Non-pharmacologic interventions such as cognitive behavioral therapy specific for insomnia (CBTi), dietary modification, physical activity, relaxation and modification of the sleep environment (for specific components for each symptoms see Appendix B: Clinical Symptom Management) c. Pharmacologic interventions as appropriate to aid in sleep initiation and sleep maintenance	None	[76] **Additional References:** [77,78]	Weak for	Reviewed, Amended
16. We recommend that the presence of psychological or behavioral symptoms following mTBI should be evaluated and managed according to existing evidence-based clinical practice guidelines, and based upon individual factors and the nature and severity of symptoms.	A, I	[83-87]	Strong for	Reviewed, Amended

Recommendation	2009 Grade[29]	Evidence[30]	Strength of Recommendation[31]	Recommendation Category[32]
17. We suggest that patients with a history of mTBI who report cognitive symptoms that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms (e.g., sleep disturbance, headache) be referred as appropriate for a structured cognitive assessment or neuropsychological assessment to determine functional limitations and guide treatment.	B	**Additional References:** [22,88]	Weak for	Not Reviewed, Amended
18. We suggest that individuals with a history of mTBI who present with symptoms related to memory, attention or executive function problems that do not resolve within 30-90 days and have been refractory to treatment for associated symptoms should be referred as appropriate to cognitive rehabilitation therapists with expertise in TBI rehabilitation. We suggest considering a short-term trial of cognitive rehabilitation treatment to assess the individual patient responsiveness to strategy training, including instruction and practice on use of memory aids, such as cognitive assistive technologies (AT). **A *prolonged course of therapy in the absence of patient improvement is strongly discouraged.***	C	[92-95] **Additional References:** [22,88-91]	Weak for	Reviewed, New-replaced
19. We suggest ***against*** offering medications, supplements, nutraceuticals or herbal medicines for ameliorating the neurocognitive effects attributed to mTBI.	None	**Additional References:** [97-103]	Weak against	Not Reviewed, Amended
20. We suggest ***against routine*** referral to specialty care in the majority of patients with a history of mTBI.	None	[46,92,104]	Weak against	Reviewed, Amended
21. If the patient's symptoms do not resolve within 30-90 days and are refractory to initial treatment in primary care and significantly impact activities of daily living (ADLs), we suggest consultation and collaboration with a locally designated TBI or other applicable specialist.	None	[104]	Weak for	Reviewed, Amended
22. For patients with persistent symptoms that have been refractory to initial psychoeducation and treatment, we suggest referral to case managers within the primary care setting to provide additional psychoeducation, case coordination and support.	None	[104]	Weak for	Reviewed, Amended
23. There is insufficient evidence to recommend for or against the use of interdisciplinary/multidisciplinary teams in the management of patients with chronic symptoms attributed to mTBI.	None	[37,92]	N/A	Reviewed, New-replaced

Appendix E: 2009 Recommendation Categorization

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
A-2	The following physical findings, signs and symptoms ("Red Flags") may indicate an acute neurologic condition that requires urgent specialty consultation (neurology, neuro-surgical): a. Altered consciousness b. Progressively declining neurological examination c. Pupillary asymmetry d. Seizures e. Repeated vomiting f. Double vision g. Worsening headache h. Cannot recognize people or is disoriented to place i. Behaves unusually or seems confused and irritable j. Slurred speech k. Unsteady on feet l. Weakness or numbness in arms/legs	-	Not Reviewed, Deleted	-
A-3	A diagnosis of mTBI should be made when there is an injury to the head as a result of blunt trauma, acceleration or deceleration forces or exposure to blast that result in one or more of the following conditions: a. Any period of observed or self-reported: i. Transient confusion, disorientation, or impaired consciousness ii. Dysfunction of memory immediately before or after the time of injury iii. Loss of consciousness (LOC) lasting less than 30 minutes. b. Observed signs of neurological or neuropsychological dysfunction, such as: i. Headache, dizziness, irritability, fatigue or poor concentration, when identified soon after injury, can be used to support the diagnosis of mild TBI, but cannot be used to	-	Not Reviewed, Deleted	-

[33] The 2009 Recommendation Text column contains the wording of each recommendation from the 2009 mTBI CPG.

[34] The 2009 VA/DoD mTBI CPG used the U.S. Preventive Services Task Force (USPSTF) evidence grading system (http://www.uspreventiveservicestaskforce.org). The strength of recommendations were rated as follows: A- a strong recommendation that the clinicians provide the intervention to eligible patients; B- a recommendation that clinicians provide (the service) to eligible patients; C- no recommendation for or against the routine provision of the intervention is made; D- recommendation is made against routinely providing the intervention; I- the conclusion is that the evidence is insufficient to recommend for or against routinely providing the intervention.

[35] The Category column indicates the way in which each 2009 mTBI CPG recommendation was updated. See Recommendation Categorization for more information.

[36] For recommendations that were carried forward to the 2016 mTBI CPG, this column indicates the new recommendation(s) to which they correspond.

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
	make the diagnosis in the absence of loss of consciousness or altered consciousness.			
A-3	The severity of TBI must be defined by the acute injury characteristics and not by the severity of symptoms at random points after trauma.	-	Not Reviewed, Deleted	-
A-5	Management of Service Members presenting for care immediately after a brain injury (within 7 days) during military combat or ongoing operation should follow guidelines for acute management published by DoD. (See: Recommendations for acute management of concussion/mTBI in the deployed setting, Defense and Veterans Brain Injury Center Consensus August, 2008) (This guidance is not included in this evidence-based guideline.)	-	Not Reviewed, Deleted	-
A-6	Management of non-deployed Service Members, Veterans, or civilian patients presenting for care immediately after a brain injury (within 7 days) should follow guidelines for acute management. (See Recommendations for acute management in guideline published by the American College of Emergency Medicine and the Center for Disease Control and Prevention (ACEP/CDC, 2008) (These protocols and guidance are not included in this evidence-based guideline.)	-	Not Reviewed, Deleted	-
A-6	Service Members or Veterans identified by post deployment screening or who present with symptoms should be assessed and diagnosed according to Algorithm A – Initial Presentation. The initial evaluation and management will then follow the recommendations in Algorithm B – Management of Symptoms.	-	Reviewed, New-replaced	Recommendation 5
A-6	Patients who continue to complain of concussion/mTBI-related symptoms beyond 4 to 6 weeks after treatment has been initiated, should have the assessment for these chronic symptoms repeated and should be managed using Algorithm C – Follow-up Persistent Symptoms.	-	Not Reviewed, Deleted	-
A-6	Patients who continue to have persistent symptoms despite treatment for persistent symptoms (Algorithm C) beyond 2 years post-injury do not require repeated assessment for these chronic symptoms and should be conservatively managed using a simple symptom-based approach.	-	Not Reviewed, Amended	Recommendation 8
A-6	Patients with symptoms that develop more than 30 days after a concussion should have a focused diagnostic work-up specific to those symptoms only. These symptoms are highly unlikely to be the result of the concussion and therefore the work-up and management should not focus on the initial concussion.	-	Not Reviewed, Amended	Recommendation 6
A-7	Persons who complain about somatic, cognitive or behavioral difficulties after concussion/mTBI should be assessed and treated symptomatically regardless of the elapsed time from injury.	-	Not Reviewed, Deleted	-
A-7	The assessment of an individual with persistent concussion /mTBI related symptoms should be directed to the specific nature of the symptoms regardless of their etiology.	-	Not Reviewed, Deleted	-

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
A-7	The management of an individual who has sustained a documented concussion/mTBI and has persistent physical, cognitive and behavioral symptoms after one month should not differ based on the specific underlying etiology of their symptoms (i.e., concussion vs. pain, concussion vs. stress disorder).	-	Not Reviewed, Deleted	-
A-7	In communication with patients and the public, this guideline recommends using the term concussion or history of mild-TBI and to refrain from using the term 'brain damage.'	-	Not Reviewed, Amended	Recommendation 1
A-8	Individuals who sustain a concussion/mTBI and are asymptomatic should be reassured about recovery and advised about precautionary measures to prevent future brain injury.	-	Not Reviewed, Deleted	-
A-8	Patients should be provided with written contact information and be advised to contact their healthcare provider for follow-up if their condition deteriorates or they develop symptoms.	-	Not Reviewed, Deleted	-
A-8	Individuals who sustain a concussion/mTBI and are asymptomatic should be screened for comorbid mental health disorders (MDD, PTSD, and SUD) and dangerousness.	-	Not Reviewed, Amended	Recommendation 7
B-2	Individuals who are presumed to have symptoms related to concussion/mTBI or who are identified as positive for mTBI on the initial screening should receive specific assessment of their symptoms.	-	Not Reviewed, Amended	Recommendation 6
B-2	Medical history should include the following: a. Obtaining detailed information on the patient's symptoms and health concerns. b. Obtaining detailed information of the injury event including mechanism of injury, duration and severity of alteration of consciousness, immediate symptoms, symptom course and prior treatment c. Screening for pre-morbid conditions, potential co-occurring conditions or other psychosocial risk factors, such as substance use disorders that may exacerbate or maintain current symptom presentation (using standardized screening tools such as, PHQ-2, Audit-C, PTSD screen) d. Evaluating signs and symptoms indicating potential for neurosurgical emergencies that require immediate referrals e. Assessing of danger to self or others.	-	Not Reviewed, Deleted	-
B-2	Patient's experiences should be validated by allowing adequate time for building a provider-patient alliance and applying a risk communication approach.	-	Not Reviewed, Deleted	-

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-2	The physical examination of the person sustaining a concussion/mTBI should focus on the following: a. A focused neurologic examination, including a Mental Status Examination (MSE), cranial nerve testing, extremity tone testing, deep tendon reflexes, strength, sensation, and postural stability (Romberg's Test, dynamic standing) b. A focused vision examination including gross acuity, eye movement, binocular function and visual fields/attention testing c. A focused musculoskeletal examination of the head and neck, including range of motion of the neck and jaw, and focal tenderness and referred pain.	-	Not Reviewed, Deleted	-
B-2	The following physical findings, signs and symptoms ("Red Flags") may indicate an acute neurologic condition that requires urgent specialty consultation (neurology, neuro-surgical): a. Altered consciousness b. Progressively declining neurological examination c. Pupillary asymmetry d. Seizures e. Repeated vomiting f. Double vision g. Worsening headache h. Cannot recognize people or is disoriented to place i. Behaves unusually or seems confused and irritable j. Slurred speech k. Unsteady on feet l. Weakness or numbness in arms/legs.	-	Not Reviewed, Deleted	-
B-2	Laboratory testing is not necessary to confirm or manage symptoms associated with concussion/mTBI.	-	Reviewed, New-replaced	Recommendation 3
B-2	Laboratory testing may be considered for evaluating other non-TBI causes of the symptoms presented.	-	Reviewed, New-replaced	Recommendation 3
B-2	There is insufficient evidence to support the use of serum biomarkers for concussion/mTBI in clinical practice.	I	Reviewed, New-replaced	Recommendation 3
B-2	A patient who presents with any signs or symptoms that may indicate an acute neurologic condition that requires urgent intervention should be referred for evaluation that may include neuroimaging studies.	-	Not Reviewed, Deleted	-

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-2	Neuroimaging is not recommended in patients who sustained a concussion/mTBI beyond the emergency phase (72 hours post-injury) except if the condition deteriorates or red flags are noted.	-	Reviewed, Amended	Recommendation 3
B-2	The management of a patient who has sustained multiple concussions should be similar to the management for a single concussion/mTBI.	I	Not Reviewed, Deleted	-
B-2	The patient with multiple concussions and his/her family should be educated to create a positive expectation of recovery.	I	Not Reviewed, Deleted	-
B-3	Self-reported symptomatology is an appropriate assessment of the patient's condition in concussion/mTBI when the history is consistent with having sustained an injury event and having a subsequent alteration in consciousness.	[SR = C]	Not Reviewed, Amended	Recommendation 8
B-3	Assessment of the patient with concussion/mTBI should include detailed questioning about the frequency, intensity and nature of symptoms the patient experiences, and their impact on the patient's social and occupational functioning.	-	Not Reviewed, Deleted	-
B-3	Assessment should include a review of all prescribed medications and over-the-counter supplements for possible causative or exacerbating influences. These should include caffeine, tobacco and other stimulants, such as energy drinks.	-	Not Reviewed, Deleted	-
B-3	The patient who sustained a concussion/mTBI should be assessed for sleep patterns and sleep hygiene.	-	Reviewed, Amended	Recommendation 15
B-3	If the patient's symptoms significantly impact daily activities (such as child care, safe driving), a referral to rehabilitation specialists for a functional evaluation and treatment should be considered.	-	Reviewed, Amended	Recommendation 21
B-5	Develop and document a summary of the patient's problems.	-	Not Reviewed, Deleted	-
B-5	Develop a potential treatment plan that includes severity and urgency for treatment interventions.	-	Not Reviewed, Deleted	-
B-5	Discuss with the patient the general concept of concussion sequelae, treatment options and associated risk/benefits and prognosis of illness to determine the patient's preferences.	-	Not Reviewed, Deleted	-
B-5	Emphasizing good prognosis and empowering the patient for self-management.	-	Not Reviewed, Deleted	-
B-5	Implement the treatment plan and follow up.	-	Not Reviewed, Deleted	-
B-5	Referral to specialty care is not required in the majority of patients with concussion/mTBI, if their symptoms resolve in the early post-acute recovery period as expected.	-	Reviewed, Amended	Recommendation 20

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-5	Treatment should be coordinated and may include consultation with rehabilitation therapists, pharmacy, collaborative mental health, and social support.	-	Reviewed, New-replaced	Recommendation 23
B-6	Patients who sustain a concussion/mTBI should be provided with information and education about concussion/mTBI symptoms and recovery patterns as soon as possible after the injury. Education should be provided in printed material combined with verbal review and consist of: a. Symptoms and expected outcome b. Normalizing symptoms (education that current symptoms are expected and common after injury event) c. Reassurance about expected positive recovery d. Techniques to manage stress (e.g., sleep education, relaxation techniques; minimize consumption of alcohol, caffeine and other stimulants).	a.[SR = A] b.[SR = A] c.[SR = A] d.[SR = B]	Not Reviewed, Deleted	-
B-6	Information and education should also be offered to the patient's family, friends, employers, and/or significant others.	-	Not Reviewed, Deleted	-
B-6	Symptomatic management should include tailored education about the specific signs and symptoms that the patient presents and the recommended treatment.	-	Not Reviewed, Deleted	-
B-6	Patients should be provided with written contact information and be advised to contact their healthcare provider for follow-up if their condition deteriorates or if symptoms persist for more than 4-6 weeks.	[SR = B]	Not Reviewed, Deleted	-
B-7	Provide early intervention maximizing the use of non-pharmacological therapies: a. Review sleep patterns and hygiene and provide sleep education including education about excess use of caffeine/tobacco/alcohol and other stimulants b. Recommend graded aerobic exercise with close monitoring.	-	Reviewed, Amended	Recommendation 15
B-7	Immediately following any concussion/mTBI, individuals who present with post-injury symptoms should have a period of rest to avoid sustaining another concussion and to facilitate a prompt recovery.	-	Not Reviewed, Deleted	-
B-7	Individuals with concussion/mTBI should be encouraged to expediently return to normal activity (work, school, duty, leisure) at their maximal capacity.	-	Not Reviewed, Deleted	-
B-7	In individuals who report symptoms of fatigue, consideration should be given to a graded return to work/activity.	-	Not Reviewed, Deleted	-
B-7	In instances where there is high risk for injury and/or the possibility of duty-specific tasks that cannot be safely or competently completed, an assessment of the symptoms and necessary needs for accommodations should be conducted through a focused interview and examination of the patient.	-	Not Reviewed, Deleted	-

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-7	If a person's normal activity involves significant physical activity, exertional testing can be conducted that includes stressing the body.	-	Not Reviewed, Deleted	-
B-7	If exertional testing results in a return of symptoms, a monitored progressive return to normal activity as tolerated should be recommended.	-	Not Reviewed, Deleted	-
B-7	Individually based work duty restriction should apply if: a. There is a duty specific task that cannot be safely or competently completed based on symptoms b. The work/duty environment cannot be adapted to the patient's symptom-based limitation c. The deficits cannot be accommodated d. Symptoms reoccur	-	Not Reviewed, Deleted	-
B-8	Initial treatment of physical complaints of a patient with concussion/mTBI should be based upon a thorough evaluation, individual factors and symptom presentation.	-	Not Reviewed, Deleted	-
B-8	The evaluation should include: a. Establishing a thorough medical history, completing a physical examination, and review of the medical record (for specific components for each symptoms see Table B-2 Physical Symptoms-Assessment) b. Minimizing low yield diagnostic testing c. Identifying treatable causes (conditions) for patient's symptoms d. Referring for further evaluation as appropriate	-	Not Reviewed, Deleted	-
B-8	The treatment should include: a. Non-pharmacological interventions such as sleep hygiene education, physical therapy, relaxation and modification of the environment b. Use of medications to relieve pain, enable sleep, relaxation and stress reduction	-	Reviewed, Amended	Recommendation 15
B-8	A consultation or referral to specialists for further assessment should occur when: a. Symptoms cannot be linked to a concussion event (suspicion of another diagnosis) b. An atypical symptom pattern or course is present c. Findings indicate an acute neurologic condition that requires urgent neurologic/neuro-surgical intervention d. There are other major co-morbid conditions requiring special evaluation	-	Reviewed, New-replaced	Recommendation 20 Recommendation 21
B-8	All individuals who sustain a concussion/mTBI should be provided with information and education about concussion/mTBI symptoms and recovery patterns as soon as possible after the injury.	[SR = A]	Not Reviewed, Deleted	-

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-8	A patient sustaining a concussion/mTBI should be evaluated for cognitive difficulties using a focused clinical interview.	[SR = C]	Not Reviewed, Deleted	-
B-8	Comprehensive neuropsychological/cognitive testing is not recommended during the first 30 days post injury.	[SR = D]	Not Reviewed, Amended	Recommendation 4
B-8	If a pre-injury neurocognitive baseline was established in an individual case, then a post injury comparison may be completed by a psychologist but should be determined using reliable tools and test-retest stability should be ensured.	[SR = B]	Reviewed, Deleted	-
B-8	Patients with concussion/mTBI should be screened for psychiatric symptoms and co-morbid psychiatric disorders (Depression, Post Traumatic Stress, and Substance Use).	-	Not Reviewed, Amended	Recommendation 7
B-8	Treatment of psychiatric/behavioral symptoms following concussion/mTBI should be based upon individual factors and nature and severity of symptom presentation, and include both psychotherapeutic and pharmacological treatment modalities.	psycho-therapeutic [SR = A] pharma-cological [SR = I]	Reviewed, Amended	Recommendation 16
B-8	Individuals who sustain a concussion/mTBI and present with anxiety symptoms and/or irritability should be provided reassurance regarding recovery and offered a several week trial of pharmacologic agents.	[SR = I]	Not Reviewed, Deleted	-
B-8	Medication for ameliorating the neurocognitive effects attributed to concussion/mTBI is not recommended.	-	Not Reviewed, Amended	Recommendation 19
B-8	Treatment of concussion/mTBI should be symptom-specific.	-	Not Reviewed, Amended	Recommendation 8
B-8	Medications may be considered for headaches, musculoskeletal pain, depression/anxiety, sleep disturbances, chronic fatigue or poor emotional control or lability.	-	Reviewed, New-replaced	Recommendation 11 Recommendation 15
B-8	Appropriate and aggressive pain management strategies should be employed.	-	Reviewed, Deleted	

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
B-8	When prescribing any medication for patients who have sustained a concussion/mTBI, the following should be considered: a. Review and minimize all medication and over-the-counter supplements that may exacerbate or maintain symptoms b. Use caution when initiating new pharmacologic interventions to avoid the sedating properties that may have an impact upon a person's attention, cognition, and motor performance. c. Recognize the risk of overdose with therapy of many medication classes (e.g., tricyclics). Initial quantities dispensed should reflect this concern. d. Initiate therapy with the lowest effective dose, allow adequate time for any drug trials, and titrate dosage slowly based on tolerability and clinical response. e. Document and inform all those who are treating the person of current medications and any medication changes	-	Not Reviewed, Deleted	
B-8	There is no contraindication for return to aerobic, fitness and therapeutic activities after concussion/mTBI. Non-contact, aerobic and recreational activities should be encouraged within the limits of the patient's symptoms to improve physical, cognitive and behavioral complaints and symptoms after concussion/mTBI.	[SR = B]	Not Reviewed, Deleted	
B-8	Specific vestibular, visual, and proprioceptive therapeutic exercise is recommended for dizziness, disequilibrium, and spatial disorientation impairments after concussion/mTBI.	-	Reviewed, Amended	Recommendation 12
B-8	Specific therapeutic exercise is recommended for acute focal musculoskeletal impairments after concussion/mTBI.	-	Not Reviewed, Deleted	
B-8	Complementary-alternative medicine treatments may be considered as adjunctive treatments or when requested by individuals with concussion/mTBI.	[SR = I]	Not Reviewed, Deleted	
B-9	All patients should be followed up in 4 – 6 weeks to confirm resolution of symptoms and address any concerns the patient may have.	-	Not Reviewed, Deleted	
B-9	Follow-up after the initial interventions is recommended in all patients to determine patient status. The assessment will determine the following course of treatment: a. Patient recovers from acute symptoms – provide contact information with instructions for available follow-up if needed. b. Patient demonstrates partial improvement (e.g., less frequent headaches, resolution of physical symptoms, but no improvement in sleep) – consider augmentation or adjustment of the current intervention and follow-up within 4-6 weeks. c. Patient does not improve or status worsens – Focus should be given to other factors including psychiatric, psychosocial support, and compensatory/litigation. Referral to a specialty provider should be considered	-	Not Reviewed, Deleted	

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
C-2	Follow-up after the initial interventions is recommended in all patients with concussion/mTBI to determine patient status and the course of treatment	-	Not Reviewed, Deleted	
C-2	Evaluation of patients with persistent symptoms following concussion/mTBI should include assessment for dangerousness to self or others.	-	Not Reviewed, Amended	Recommendation 7
C-2	In assessment of patients with persistent symptoms, focus should be given to other factors including psychiatric, psychosocial support, and compensation/litigation issues and a comprehensive psychosocial evaluation should be obtained, to include: a. Support systems (e.g., family, vocational) b. Mental health history for pre-morbid conditions which may impact current care c. Co-occurring conditions (e.g., chronic pain, mood disorders, stress disorder, personality disorder) d. Substance use disorder (e.g., alcohol, prescription misuse, illicit drugs, caffeine) e. Secondary gain issues (e.g., compensation, litigation) f. Unemployment or/change in job status g. Other issues (e.g., financial/housing/legal)	-	Not Reviewed, Amended	Recommendation 7
C-3	Assessment of the patient with concussion/mTBI should include a detailed history regarding potential pre-injury, peri-injury, or post-injury risk factors for poorer outcomes. These risk factors include: a. Pre-injury: older age, female gender, low socio-economic status, low education or lower levels of intellectual functioning, poorer coping abilities or less resiliency, pre-existing mental health conditions (e.g., depression, anxiety, PTSD, substance use disorders). b. Peri-injury: lower levels of or less available social support. c. Post-injury: injury-related litigation or compensation, comorbid mental health conditions or chronic pain, lower levels of or less available social support	-	Not Reviewed, Deleted	
C-3	Any substance abuse and/or intoxication at the time of injury should be documented.	-	Not Reviewed, Amended	Recommendation 7
C-3	Establish and document if the patient with concussion/mTBI experienced headaches, dizziness, or nausea in the hours immediately following the injury.	-	Not Reviewed, Deleted	
C-3	Symptom exaggeration or compensation seeking should not influence the clinical care rendered, and doing so can be counter-therapeutic and negatively impact the quality of care.	-	Not Reviewed, Deleted	
C-3	Focus of the provider-patient interaction should be on the development of a therapeutic alliance.	[SR=C]	Not Reviewed, Deleted	

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
C-3	For clinical treatment purposes the use of post-concussion syndrome, post-concussive syndrome (PCS) or post-concussion disorder (PCD) as a diagnosis is not recommended. The unique individual pattern of symptoms should be documented and be the focus of treatment.	-	Not Reviewed, Deleted	
C-4	Patients with persistent symptoms following concussion/mTBI should be re-evaluated for psychiatric symptoms and co-morbid psychiatric disorders.	-	Not Reviewed, Amended	Recommendation 7
C-4	Treatment of psychiatric symptoms following concussion/mTBI beyond the acute phase should still be based on individual factors and nature and severity of symptom presentation, including psychotherapeutic and pharmacologic treatment modalities.	psycho-therapeutic [SR = A] pharma-cologic [SR = I]	Reviewed, Amended	Recommendation 16
C-4	In patients with persistent post-concussive symptoms, which have been refractory to treatment, consideration should be given to other factors including psychiatric disorders, lack of psychosocial support, and compensation/litigation.	-	Not Reviewed, Amended	Recommendation 7
C-5	A consultation or referral to specialists should occur in a patient with concussion/mTBI who complains of persistent or chronic symptoms when: a. An atypical pattern or course (worsening or variable symptom presentation) is demonstrated b. The patient is experiencing difficulties in return to pre-injury activity (work/duty/school) c. Problems emerge in the role of the patient in family or social life	-	Reviewed, Amended	Recommendation 21
C-5	Patients with multiple problems may benefit from an inter-disciplinary approach to include occupational therapy, recreation therapy, social work, psychology and/or psychiatry, neurology, ENT, ophthalmology or audiology, based on individual symptoms. The patient's provider should remain involved in the patient's care.	-	Reviewed, New-replaced	Recommendation 23
C-5	Referral to mental health specialty of patients with persistent behavioral symptoms should be considered.	-	Reviewed, Amended	Recommendation 21
C-6	Patients who are refractory to treatment of physical symptoms in the initial care setting should be referred to specialty care for further evaluation and management.	-	Reviewed, Amended	Recommendation 21
C-6	Patients who have cognitive symptoms that do not resolve or have been refractory to treatment should be considered for referral for neuropsychological assessment. The evaluation may assist in clarifying appropriate treatment options based on individual patient characteristics and conditions.	[SR = B]	Not Reviewed, Amended	Recommendation 17

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
C-6	Neuropsychological testing should only be conducted with reliable and standardized tools by trained evaluators, under controlled conditions, and findings interpreted by trained clinicians.	[SR = C]	Not Reviewed, Deleted	
C-6	Individuals who present with memory, attention, and/or executive function problems which did not respond to initial treatment (e.g., reassurance, sleep education, or pain management) may be considered for referral to cognitive rehabilitation therapists with expertise in TBI rehabilitation (e.g., speech-language pathology, neuropsychology, or occupational therapy) for compensatory training; and/or instruction and practice on use of external memory aids such as a PDA.	[SR = C]	Reviewed, New-replaced	Recommendation 18
C-7	Patients with persistent symptoms following concussion/mTBI may be considered for case management.	-	Reviewed, Amended	Recommendation 22
C-7	Case managers should complete a comprehensive psychosocial assessment of the patient and the patient's family. It may be necessary or beneficial to meet with other members of the patient's support system (family, care giver) and/or invite the patient to ask them to come to an appointment together with the patient.	-	Not Reviewed, Deleted	
C-7	Case managers should collaborate with the treatment team, the patient, and the patient's family in developing a treatment plan that emphasizes the psychosocial needs of the patient.	-	Not Reviewed, Deleted	
C-7	Case managers (in collaboration with the treatment team) should prepare and document a detailed treatment plan in the medical record describing follow-up care and services required.	-	Not Reviewed, Deleted	
C-7	Case managers who provide care in the clinical setting should communicate and coordinate with other potential care coordinators that provide care for the patient (such as a VHA social worker liaison or military social worker at the referring Military Treatment Facility, Patient Treatment Advocate [PTA]).	-	Not Reviewed, Deleted	
C-7	Case managers may provide assistance to the patient and family who are transferred to another facility (e.g., a polytrauma rehabilitation center).	-	Not Reviewed, Deleted	

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
C-7	Case management may serve as the main point of contact for the patient and family. This may include the following: a. Provide the patient with contact information including after-hours calls b. Maintain frequent contact by phone to remind about or facilitate an appointment c. Facilitate access to supportive services to the patient and family d. Serve as a liaison for the patient's family and as an advocate for the patient and the patient's family e. Provide easy-to-understand information in writing for the patient and the patient's family	-	Not Reviewed, Deleted	
C-7	All members of the treatment team should be involved in patient education as part of their interaction with the patient experiencing persistent symptoms.	-	Not Reviewed, Deleted	
C-7	Educational interventions should generally include information and a description of the specific procedures and events the patient will experience at the various phases of treatment and continue throughout the continuum of care.	-	Not Reviewed, Deleted	
C-7	General supportive counseling (e.g., eliciting and validating the patient's anxieties, fears, and concerns) may also be helpful. Open-ended questioning, active listening techniques, eliciting anticipation of future stressors, encouraging the patient to ask questions, and eliciting and encouraging utilization of the patient's social support resources are important strategies regardless of whether information-giving or coping skills training interventions are being used.	-	Not Reviewed, Deleted	
C-7	Educational interventions may also include coping techniques for symptom management, such as patient education handouts and helpful tips.	-	Not Reviewed, Deleted	
C-7	As with other chronic conditions, the focus of the management of patients with persistent symptoms following concussion/mTBI should shift to the psychological and social impacts on the patient.	-	Not Reviewed, Deleted	
C-7	The clinician should consider having the spouse or partner accompany the patient with concussion/mTBI to a consultation, to help them better understand the condition and provide an opportunity to discuss any coping difficulties.	-	Not Reviewed, Deleted	
C-7	Family members should be encouraged to consider joining a support group to provide education, advice and opportunities to exchange coping strategies for dealing with the day-to-day difficulties of living with an individual with persistent symptoms following concussion/mTBI.	-	Not Reviewed, Deleted	

2009 CPG Section	2009 CPG Recommendation Text[33]	2009 Grade[34]	Category[35]	2016 Recommendation[36]
C-7	Vocational interventions for the patient with persistent symptoms following concussion/ mTBI may include modifications such as: a. Modification of the length of the work day b. Gradual work re-entry (e.g., starting at 2 days/week and expanding to 3 days/week) c. Additional time for task completion d. Change of job e. Environmental modifications (e.g., quieter work environment; enhanced level of supervision)	-	Not Reviewed, Deleted	
C-7	Patients who have not successfully resumed pre-injury work duties following injury should be referred for a vocational evaluation by clinical specialists with expertise in assessing and treating concussion/mTBI.	-	Not Reviewed, Deleted	
C-7	For patients with persistent symptoms following concussion/mTBI, return to full work/duty in the jobs they have previously performed may not be possible. Patients may need to proceed through medical or disability evaluation processes. This process should follow national and local regulations and is beyond the scope of the guideline.	-	Not Reviewed, Deleted	
C-7	A referral to a structured program that promotes community integration may be considered for individuals with residual persistent post-concussive symptoms that impede return to pre-injury participation in customary roles.	-	Not Reviewed, Deleted	
C-8	Scheduled follow-up visits are recommended. The amount of time between visits will vary depending on a number of factors, including the following: a. Quality of the provider/patient relationship i. Distress of the patient ii. Need for refinement of the treatment plan or additional support iii. Presence or absence of psychosocial stressors. b. Severity of the symptoms i. Initially, a follow-up at two to three weeks would be appropriate ii. As soon as the patient is doing well, then follow-up every 3 to 4 months would be recommended iii. Telephone follow-up may be sufficient to evaluate resolution of symptoms and reinforce education c. For concussion/mTBI patients with complicated histories, comorbidities, and lack of social support consider case management	-	Not Reviewed, Deleted	
C-8	Continually re-evaluate the patient for worsening of chronic symptoms or presence of new symptoms suggestive of other diagnoses.	-	Not Reviewed, Amended	Recommendation 7

Appendix F: Participants List

Amy O. Bowles, MD Chief, Brain Injury Rehabilitation Service San Antonio Military Medical Center Fort Sam Houston, TX	**Jennifer Burton, DPT** Physical Therapy Clinician George E. Whalen Veterans Affairs Medical Center Salt Lake City, UT
Megan Chilson, PharmD Clinical Pharmacist Department of Pharmacy William Beaumont AMC El Paso, TX	**David X. Cifu, MD (Co-Chair)** Senior TBI Specialist, National Director of PM&R Program Office Cabinet-appointed member, Senior Executive Staff Department of Veterans Affairs Chairman and Herman J. Flax, M.D. Professor, Department of PM&R Founding Director, Center for Rehabilitation Sciences and Engineering, Virginia Commonwealth University Richmond, VA
Mary Dameron, MSN, RN, CRRN, CCM, CBIS RN Case Manager McGuire VA Medical Center Richmond, VA	**Thomas J. DeGraba, MD** Deputy Director, Chief of Medical Operations National Intrepid Center of Excellence (NICoE) Walter Reed National Military Medical Center Bethesda, MD
Ernest Degenhardt, COL USA (Ret.), MSN, RN, ANP, FNP Former Chief, Office of Evidence Based Practice Clinical Performance Directorate U.S. Army Medical Command Fort Sam Houston, TX	**Corinne K.B. Devlin MSN, RN, FNP-BC** Chief, Office of Evidence Based Practice Clinical Performance Directorate U.S. Army Medical Command Fort Sam Houston, TX
CDR Josh L. Duckworth, MD Assistant Professor, Department of Neurology F. Edward Hébert School of Medicine Uniformed Services University of the Health Sciences Bethesda, MD	**Blessen C. Eapen, MD** Section Chief, Polytrauma Rehabilitation Center Brain Injury Medicine/Polytrauma Fellowship Program Director South Texas Veterans Health Care System San Antonio, TX
CDR Jeffrey Feinberg, MD, MPH, FAAFP Staff Family Physician Department Head Family Medicine Naval Hospital Camp Pendleton Oceanside, CA	**Louis M. French, PsyD** Deputy Director for Operations National Intrepid Center of Excellence (NICoE), Walter Reed National Military Medical Center Bethesda, MD
COL Geoffrey G. Grammer, MD (Co-Chair) Chief, Department of Research National Intrepid Center of Excellence (NICoE) Walter Reed National Military Medical Center Bethesda, MD	**COL Sidney R. Hinds II, MD** National Director, Defense and Veterans Brain Injury Center (DVBIC) Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE) Silver Spring, MD
Charles W. Hoge, MD Senior Scientist, Walter Reed Army Institute of Research Neuropsychiatry Consultant, Office of the Army Surgeon General	**Robin A. Hurley, MD, FANPA** Associate Chief of Staff, Research and Academic Affairs Salisbury VAMC Professor, Wake Forest School of Medicine Departments of Psychiatry and Radiology

Attending Psychiatrist, Walter Reed National Military Medical Center Bethesda, MD	Richmond, VA
Timothy Lacy, MD Tri-Service Work Flow Team BH Lead Contract Support (EHRTS) Defense Health Headquarters Office of the Chief Information Officer Silver Spring, MD	**Scott D. McDonald, PhD** Co-Director, VA VISN-6 MIRECC Advanced Fellowship Program (Richmond) Research Neuropsychologist Affiliate Assistant Professor, Virginia Commonwealth University, Departments of PM&R and Psychology Hunter Holmes McGuire VA Medical Center Richmond, VA
Linda M. Picon, MCD, CCC-SLP Speech-Language Pathologist VA Senior Consultant/TBI Liaison, Defense Centers of Excellence Rehabilitation and Prosthetic Services, VA Central Office Washington, DC	**Ronald G. Riechers, II, MD** Chief, Department of Neurology Medical Director, Polytrauma Team Louis Stokes Cleveland VA Medical Center Assistant Professor, Department of Neurology Case Western Reserve University Cleveland, OH
M. Eric Rodgers, PhD, FNP, BC Director, VA/DoD Evidence-Based CPG Program Office of Quality, Safety & Value (10A4B) Department of Veterans Affairs Veterans Health Administration - Virtual Glendale, CO	**James Sall, PhD, FNP-BC** Primary Care Chronic Disease Clinical Practice Guideline Coordinator, U.S. Army Medical Command Quality Management Division, Office of Evidence Based Practice JBSA Fort Sam Houston, TX
Rene M. Sutton, BS, HCA Educational Program Specialist, VA/DoD Evidence-Based CPG Program Office of Quality, Safety and Value Department of Veterans Affairs Washington, DC	**COL Lisa Teegarden, PsyD (Co-Chair)** Chief, Department of Psychology Walter Reed National Military Medical Center Bethesda, MD
Kathryn Tortorice, PharmD, BCPS National PBM Clinical Pharmacy Program Manager, Neurology and Solid Organ Transplant Chair, National Drug File Support Group National Pharmacy Benefits Management Services, Department of Veterans Affairs Hines, IL	**Linda Van Horn, MSN, BSN, CFNP** Polytrauma Coordinator New Mexico VA Health Care System Farmington, NM
Major Derrick F. Varner, PhD, DFAAPA Clinical Coordinator, Interservice PA Program Graduate School, Academy of Health Sciences JBSA Fort Sam Houston, TX	**Deborah Voydetich, OTR/L, SCLV** Occupational Therapy Discipline Lead Blind Rehabilitation Planning Specialist Minneapolis VA Health Care System Minneapolis, MN

Appendix G: Acronym List

Abbreviation	Definition
ACEM	American College of Emergency Medicine
ADHD	Attention deficit hyperactivity disorder
ADLs	Activities of daily living
AOC	Alteration of consciousness
AHRQ	Agency for Healthcare Research and Quality
AMPAR	α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor peptide
ANAM	Automated Neuropsychological Assessment Metrics
AT	Assistive technologies
BPPV	Benign paroxysmal positional vertigo
CBT	Cognitive behavioral therapy
CBTi	Cognitive behavioral therapy specific for insomnia
CCBT	Computer-based cognitive behavioral therapy
CDC	Centers for Disease Control and Prevention
CMI	Chronic multisymptom illness
COR	Contracting Officer's Representative
CPG	Clinical practice guideline
CT	Computerized tomography
DAI	Diffuse axonal injury
DCoE	Defense Centers of Excellence
DoD	Department of Defense
DTI	Diffusion tensor imaging
DVBIC	Defense and Veterans Brain Injury Center
EBPWG	Evidence-Based Practice Working Group
EEG	Electroencephalogram
ENT	Ear, nose and throat
FA	Fractional anisotropy
FAI	Fatigue Assessment Instrument
FDA	Food and Drug Administration
FIS	Fatigue Impact Scale
GCS	Glasgow Coma Scale
GAD-2 or GAD-7	Generalized Anxiety Disorder Scale
GFAP	Glial fibrillary acidic protein
GI	Gastrointestinal
GOS-E	Glasgow Outcome Score, Extended
HTA	Health technology assessment
IADLs	Instrumental ADLs
IM	Intramuscular
ImPACT	Immediate Post-Concussion Assessment and Cognitive Testing

Abbreviation	Definition
KQ	Key question
LOC	Loss of consciousness
MACE	Military Acute Concussion Evaluation
MAF	Multidimensional Assessment of Fatigue
MDD	Major depressive disorder
MI	Myocardial infarction
mTBI	Mild traumatic brain injury
MRI	Magnetic resonance imaging
MSE	Mental Status Examination
NCAT	Neuro-Cognitive Assessment Tool
NFL	National Football League
NICE	National Institute for Health and Care Excellence
NSAIDs	Nonsteroidal anti-inflammatory drugs
NSE	Neuron specific enolase
NSI	Neurobehavioral Symptom Inventory
OEF	Operation Enduring Freedom
OIF	Operation Iraqi Freedom
OND	Operation New Dawn
OT	Occupational therapy
OTC	Over-the-counter
OTSG	Office of the Surgeon General
PACT	Providers/patient aligned care team
PCD	Post-concussion disorder
PCL	PTSD Checklist
PCS	Post-concussive syndrome
PDHA	Post-Deployment Health Assessment
PHQ-2 or PHQ-9	Patient Health Questionnaire
PICOTS	Population, Intervention, Comparison, Outcome, Timing and Setting
PT	Physical therapy
PTA	Posttraumatic amnesia
PTSD	Posttraumatic stress disorder
RCT	Randomized controlled trial
RSS	Recovery Support Specialist Program (DVBIC)
rTMS	Repetitive transcranial magnetic stimulation
S100-B	S100 calcium-binding protein B
SNRI	Serotonin-norepinephrine reuptake inhibitor
SPECT	Single photon emission computed tomography
SSRI	Selective serotonin reuptake inhibitor
SUD	Substance use disorder
TBI	Traumatic brain injury

Abbreviation	Definition
TMS	Transcranial magnetic stimulation
UCH-L1	Ubiquitin carboxyl-terminal esterase L1
USPSTF	U.S. Preventive Services Task Force
VA	Department of Veterans Affairs
VHA	Veterans Health Administration

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