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

Department of Veterans Affairs

Department of Defense

Clinician Summary

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 – 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

The full text of the CPG is availaible at the following link to provide more details about the evidence and the method used to develop the recommendations: http://www.healthquality.va.gov/guidelines/rehab/mtbi/index.asp. In addition to this clinician summary and the full text of the CPG, the Work Group also developed a pocket card for provider use and a patient information sheet also availaible at the link provided above.

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 in the full CPG.

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 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.

III. 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

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

[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

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.

IV. Guideline Working Group

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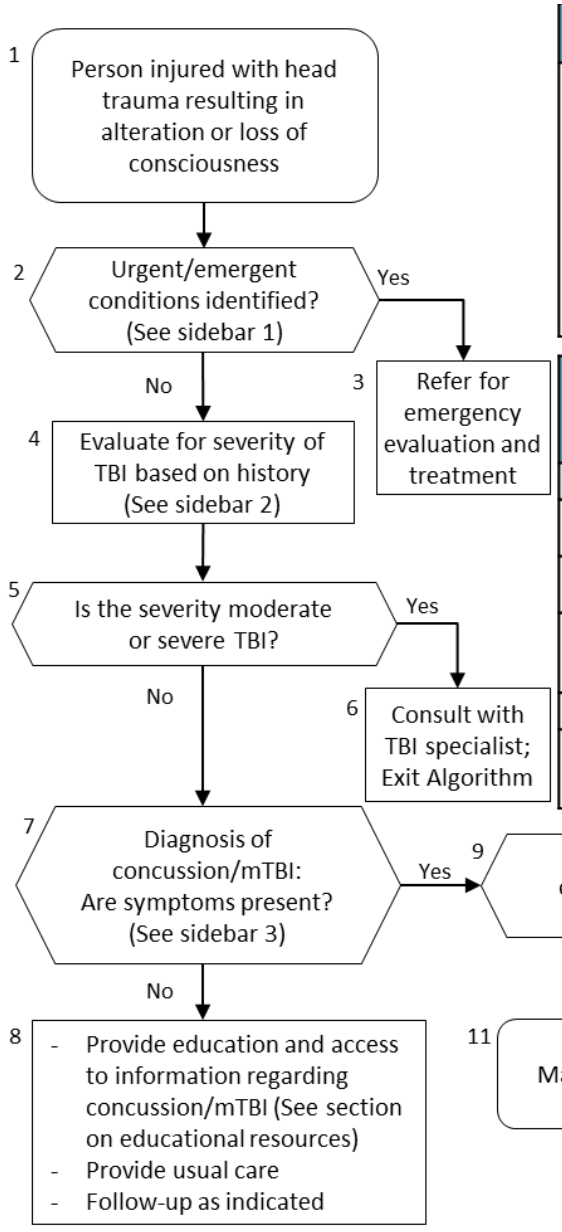
V. Algorithms

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***

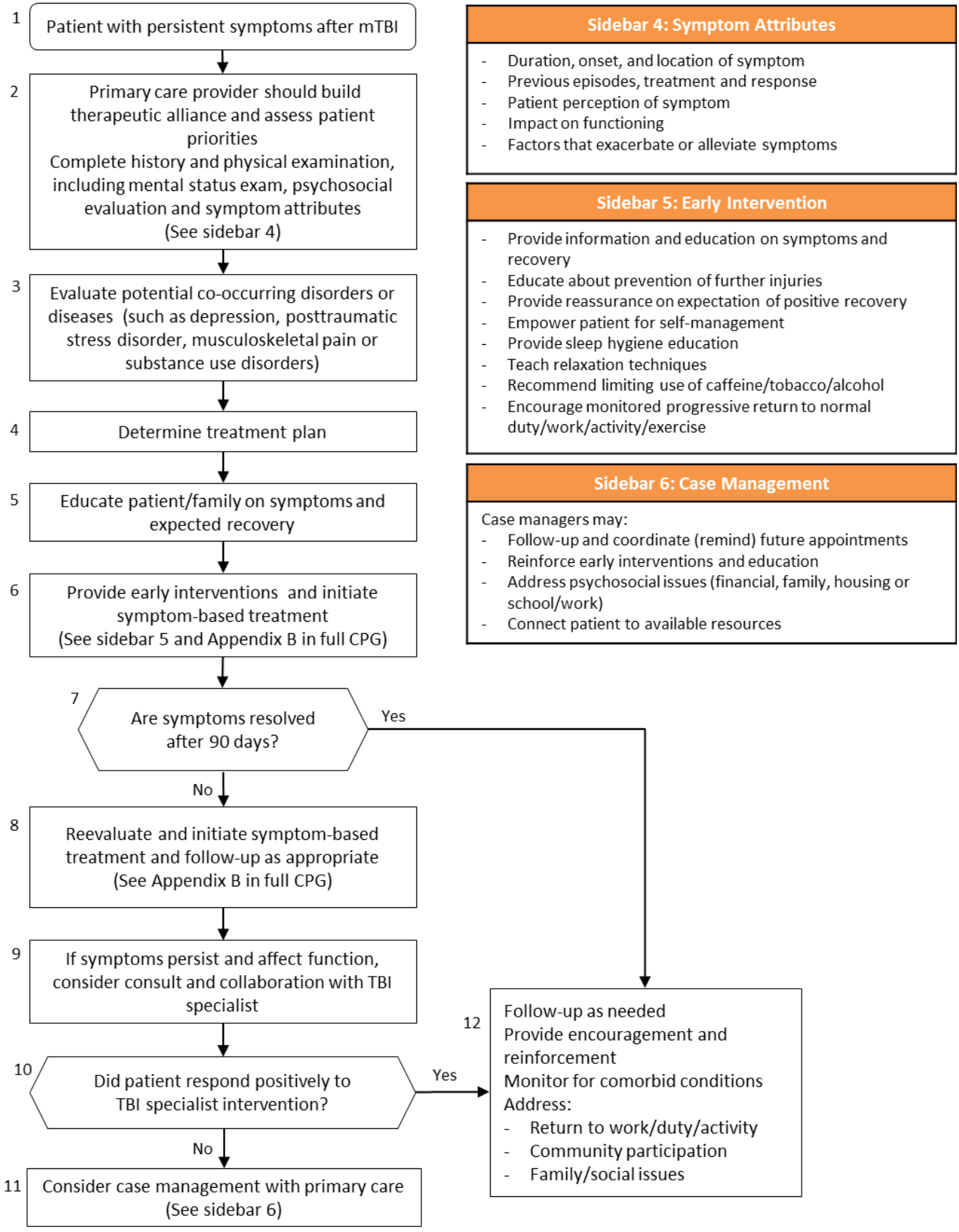
Physical Symptoms:	Cognitive Symptoms:	Behavior/Emotional Symptoms:
Headache, dizziness, balance disorders, nausea, fatigue, sleep disturbance, blurred vision, sensitivity to light, hearing difficulties/loss, tinnitus, sensitivity to noise, seizure, transient neurological abnormalities, numbness, tingling	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 in full CPG or the section on Headache) 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 symptom see Appendix B in full CPG or the section on Sleep Disturbance) 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 About Grading Recommendations.
†For additional information, please refer to About Recommendation Categorization.

VII. Diagnosis of mTBI

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. 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.

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 Chronic Multisymptom Illness [CMI][3]) and only make referrals judiciously as clinically indicated.

Conceptually, a confirmatory objective test would be desirable to have definitive diagnosis of mTBI and could direct treatment, and/or predict outcomes. Unfortunately, at this time, evidence does not support the use of any laboratory, imaging, or physiological test for these purposes. 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, managing patient expectations, and utilization of resources.

A. Effect of mTBI Etiology on Management 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.

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.[5,6] 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.

[3] 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

VIII. Behavioral Health Co-occurring Conditions

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 or other VA/DoD CPGs. The relationship between mTBI and comorbid psychiatric conditions, most notably PTSD, MDD and SUD, is controversial and complex.[7-15] 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,[4] MDD,[5] SUD,[6] and patients at risk for suicide.[7]

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 pharmaceutical agents that are approved by the U.S. Food and Drug Administration (FDA) 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

[4] 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

[5] 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

[6] 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

[7] 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

- 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.

A. Clinical Guidance for Screening of Behavioral Health Co-occurring Conditions

- 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[8])
- Referral of patients with persistent behavioral symptoms to mental health specialty should be considered.

For more details about the management of behavioral health symptoms, see applicable sections within this document.

[8] 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

IX. Clinical Symptom Management

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.[16,17] In conjunction with a spectrum of possible clinical presentations, a variety of clinical outcomes have also been observed in patients following a concussive event.[18] 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.

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.[19] 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.[19]

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.

Figure 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/caregivers 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.

The sections below include options for treatment of co-occurring conditions and a selected list of symptoms that are most common in patients presenting with symptoms following a concussion/mTBI. Some of the options were formulated based on consensus of clinical experts. The evidence synthesis for this CPG found a lack of randomized clinical trials for treatment of symptoms in patients with history of mTBI. As a result, some of the approaches to symptom management outlined below are based on standard clinical care, while some are evidence-based; both have been merged for this summary to facilitate use in the field. In contrast, the Recommendations listed earlier in this document have all been reviewed or developed based on published evidence. For more details regarding evidence and methodology, please review the full text of the mTBI CPG.

A. Headache

Headaches are common physical symptoms after mTBI occurring in 30-90% of individuals following TBI (mild, moderate, or severe).[20,21] *The International Classification of Headache Disorders- 2nd edition* defines posttraumatic headaches as secondary headache disorders that start within seven days after head trauma.[22] 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.[23]

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.[24] 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.

a. Assessment

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

Table 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

i. History and physical examination

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.

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 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 nonsteroidal anti-inflammatory drugs (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 over-the-counter (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.

b. Treatment

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.

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.

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 3** and **Table 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.

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 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. 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. Posttraumatic headaches, which 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.

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 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:

- Headache attacks that are disabling despite aggressive acute interventions
- Patient's desire to reduce frequency of acute attacks
- 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 4**.

Table 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		

Dosing Recommendations: Abortive Migraine Medications**			
Drug Category	**Usual Dose Range**	**Adverse Drug Events**	**Comments/Cautions**
	Transdermal Initial Dose: Apply 1 patch (6.5 mg) at onset of headache, may repeat in 2 hrs Maximum Dose: 2 patches daily		
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 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

B. Dizziness and Disequilibrium

Dizziness and disequilibrium are common symptoms/signs of many diagnoses, including mTBI. In the acute stage, mTBI may cause dizziness.[25-27] Subjective reports of dizziness correlate with objective testing only during the first week after the concussion/mTBI.[28] Mild TBI may cause coordination deficits of the lower extremities (imbalance) and/or upper extremities (dysmetria).[29-31] Cognitive distractions or performance of dual tasks are sensitive provocative tests for detection of imbalance and coordination deficits in the acute stage of mTBI.[29,31] Adjusting for age, gender, educational and employment status, patients with a history of mTBI who had skull fracture, dizziness, and/or headache were at increased risk of developing persistent symptoms at one month.[32]

a. Assessment

Dizziness and disequilibrium due to various causes can be broadly organized into the following: 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 5. Criteria for Categorization and Referral for Dizziness and Disequilibrium After mTBI [33,34]

#	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 ▪ 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 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 ▪ Reading difficulties ▪ Sensitivity to light	▪ Ophthalmology ▪ Optometry ▪ Vision Rehabilitation

#	Possible Diagnosis	Symptoms	Duration/Provocation	Referral
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

i. History and 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.

b. Treatment

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.[35-37] 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. 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[9], MDD[10], Bipolar Disorder[11], Suicide Risk[12], CMI[13]).

[9] 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

[10] 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

[11] 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

[12] 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

[13] 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

i. 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.[38] Efficacy of vestibular and balance rehabilitation has been shown in different populations with vestibular disorders.[35-37] Patients with vestibular disorders who received customized programs showed greater improvement than those who received generic exercises.[36] 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.[36,39]

With mTBI, recovery of vestibular lesions is often limited or protracted due to the coexistence of central or psychological disorders.[28] 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.[40] 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.

ii. Pharmacologic treatment

Initiating vestibular suppressants for dizziness may delay central compensation or promote counterproductive compensation.[41,42] Vestibular suppressants might be helpful during the acute period of several vestibular disorders but have not been shown to be effective for chronic dizziness after concussion.[43] 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.[44] 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.

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 the section on Additional Educational Materials and Resources for more information.)

C. 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.[45] A retrospective study published in 2012 reported that 75.7% of the Veterans with a history of mTBI reported tinnitus.[46] 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.[47]

a. Assessment

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.

b. Treatment

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.*** 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.

D. Visual Symptoms

Visual dysfunction is a common complaint following mTBI,[48-50] 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.

a. Assessment

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.

i. Medication review

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.

b. Treatment

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.

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. 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. ***A prolonged course of therapy in the absence of patient improvement is strongly discouraged.***

i. Referral

If visual problems persist over time and impact daily function, a referral to optometry, ophthalmology, neuro-ophthalmology, neurology and/or a 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). 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.

E. Sleep Disturbance

a. Assessment

Sleep disturbances can occur in approximately 30% of patients following mTBI.[51] 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.

b. Treatment

There is no available literature demonstrating that sleep dysfunction after mTBI should be treated any differently than sleep dysfunction from other causes. 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).[52] 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.[53]

Pharmacologic therapy for sleep dysfunction may include either prescription or 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) (**Table 6**). 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).

Table 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.

F. 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.[54-57]

a. Assessment

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 ideations 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 and consult related VA/DoD CPGs (e.g., PTSD[14], MDD[15] , Bipolar Disorder[16], Suicide Risk[17], CMI[18]). (See section on Behavioral Health Co-occurring Conditions.)

b. Treatment

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.[58-60] 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 FDA for treatment of post-mTBI psychiatric/behavioral symptoms. Clinicians are encouraged to consult relevant CPGs for these conditions, taking into consideration the underlying diagnoses, patient preferences, comorbidities, and available treatment modalities.

G. Cognitive Symptoms

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.[61-63] However, a small number report new, persistent or worsening cognitive symptoms weeks, months or sometimes years post injury.[61,64-66] This subgroup often presents with pre-morbid or comorbid conditions, such as depression, anxiety, poor health, chronic pain, negative self-beliefs and expectations,

[14]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

[15]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

[16]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

[17]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

[18] 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

poor psychosocial support or other limited coping resources, or are involved in litigation or disability processes.[61,65,66] 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.

a. Assessment

Following the immediate period (after 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.[67]

Beyond the initial seven to 30 days after concussion, there is no clear correlation between an individual's self-report of cognitive-related symptoms and findings on formal testing. 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[19]).[61,66] After 30 days post-injury, the use of formal neuropsychological testing should be reserved to 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 on the skills, training and preferences of the neuropsychologist providing the assessment.

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. Cognitive and neuropsychological testing may be indicated for symptomatic patients in specific situations, such as baseline assessment in preparation for cognitive rehabilitation [68] and identifying emotional or motivational factors that could impact treatment planning.[69,70]

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

[19] 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

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.[71]

b. 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.

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.[72]

Education should be an integral part of the cognitive rehabilitation 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.[73]

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.[74,75] 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 assistive technologies 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.[60]

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 attention deficit hyperactivity disorder (ADHD) population ranging between 5-35%.[76] Supplements, nutraceuticals and herbal treatments have not been studied in any controlled studies in patients with a history of mTBI.

H. Fatigue

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.[77,78]

a. Assessment

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.

b. Treatment

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.

I. Persistent Pain

Approximately 40-50% of patients with a history of mTBI may experience chronic pain.[21] Pain management in patients with a history of mTBI 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.

(See also discussion of Headache)

a. 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.

b. 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[20] or the VA/DoD CPG for Opioid Therapy for Chronic Pain[21] for additional strategies to manage persistent pain.

J. Hearing Difficulties

Hearing difficulties, including altered acuity and sensitivity to noise, occur acutely in the majority of individuals who sustain a blast-related mTBI.[46]

a. Assessment

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. Providers should perform an otologic examination and review medications for ototoxicity. Refer to audiology for hearing assessment if no other apparent cause is found.

b. Treatment

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.

K. Smell (Olfactory Deficits)

Posttraumatic olfactory deficits (anosmia) are not common in individuals who sustain an mTBI.[79]

a. Assessment

The vast majority of cases resolve within a six month period. 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.[80] Pre-injury causes of anosmia need to be ruled out.[81] Perform a nasal and oropharyngeal examination. Screen for depression. Refer to an ear, nose and throat (ENT) specialist for further evaluation, if needed.

b. Treatment

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). For depressed patients, treatment with psychotherapy may improve olfaction.[82] If neurologic status is stable and there are no objective findings, reassurance and monitoring are appropriate. Providers may encourage an increase in the spicing of foods (dietary referral), monitor weight, and provide specific safety education.

[20] 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

[21] 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

L. Nausea

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.

a. Assessment

Define triggers and patterns of nausea. Refer to **Table 5** as appropriate. Providers may also assess medication lists for agents that may cause or worsen GI symptoms. The initial focus should be on the rapid management of dizziness and return to activity. Formal assessments should be limited.

M. 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.

N. 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.

X. Setting of Care

We suggest against routine referral to specialty care in the majority of patients with a history of mTBI. Some patients may request specialized consultation. 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.

A. Consideration of Referral

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.[83] 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.

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 and 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[22]).

B. Case Management

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.,[83] 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 less 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

[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

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.

C. Interdisciplinary/Multidisciplinary Teams

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.[84] Additionally, Browne et al. found that patients who received multidisciplinary intervention reported significantly greater pain relief compared to controls after controlling for age, gender and injury severity.[12] There is no current evidence to support that patients who initiate treatment for symptoms attributed to 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.

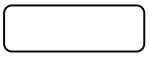
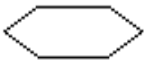
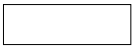
Appendix A: Methodology

A. About the 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.[85]

	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.

B. About Grading Recommendations

This CPG uses the GRADE (Grading of Recommendations Assessment, Development and Evaluation) 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: [86]

- 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 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.[86]

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 …")

Table A-1. 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

Decision Domain	Judgment
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

C. About Recommendation Categorization

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).[87,88] These categories, along with their corresponding definitions, were used to account for the various ways in which recommendations could have been updated from the 2009 version of the mTBI CPG. The categories and definitions can be found in **Table A-2**.

Table A-2. 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)[87] and Garcia et al. (2014)[88]

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