DEFENSE CENTERS OF EXCELLENCE
For Psychological Health & Traumatic Brain Injury

Co-occurring Conditions Toolkit: Mild Traumatic Brain Injury and Psychological Health

Concussion, Posttraumatic Stress, Depression, Chronic Pain, Headache, Substance Use Disorder

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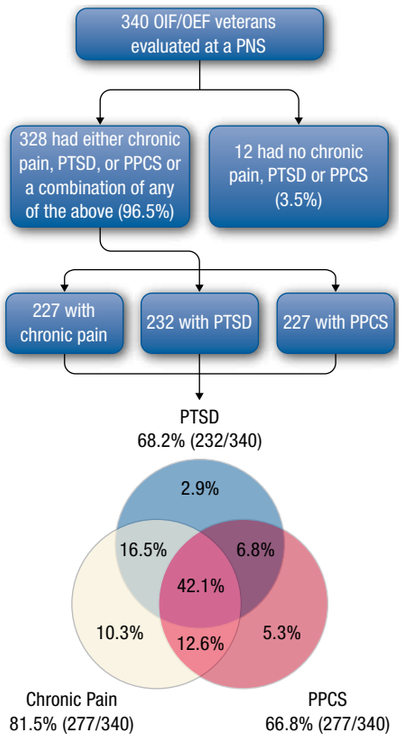
Background

In June 2009, the Department of Veterans Affairs (VA) held a consensus conference on concussion, posttraumatic stress disorder and pain, with the goals of providing a consensus recommendation on the treatment of veterans with these comorbid conditions. Based on reviewed literature and consensus opinions of Subject Matter Experts (SMEs) from the VA and Department of Defense (DoD), they determined that the treatments recommended in the VA/DoD Clinical Practice Guidelines (CPGs) are still recommended in the comorbid population. There was not evidence to suggest that the current CPGs were contraindicated. There are several excellent VA/DoD CPGs for use in the Continental United States (CONUS) that address concussion, posttraumatic stress disorder (PTSD), depression, chronic opioid therapy (COT) and substance use disorder (SUD). However, there are areas within these CPGs that are contradictory should a patient present with multiple conditions. This guide attempts to address these areas of conflict.

This toolkit does not educate on how to make these diagnoses, but rather, on how to further evaluate what conditions may be resulting in the presenting symptoms. It was developed to give guidance to primary care providers on the assessment and management of these patients, synthesizing the information of the above CPGs. Evidenced-based approaches to the management of co-occurring disorders are emerging but have not reached fruition. To that end, SMEs from the Defense Centers of Excellence for Psychological Health and Traumatic Brain Injury (DCoE), the Center for Deployment Psychology (CDP), the Center for the Study of Traumatic Stress (CSTS), the Defense and Veterans Brain Injury Center (DVBIC), the Deployment Health Clinical Center (DHCC), the National Center for Telehealth and Technology (T2) and the National Intrepid Center of Excellence (NICoE) gathered to provide expert opinion to address these gaps. As the science emerges, this toolkit will be revised to reflect the evidence.



The polytrauma clinical triad: Distribution of patients with chronic pain, posttraumatic stress disorder (PTSD), and persistent post-concussive symptoms (PPCS) in a sample of 340 Operation Iraqi Freedom/Operation Enduring Freedom (OIF/OEF) veterans evaluated at Department of Veterans Affairs Boston Polytrauma Network Site (PNS).

Lew et. al., Prevalence of chronic pain, posttraumatic stress disorder and persistent post-concussive symptoms in OIF/OEF veterans: Polytrauma clinical triad. JRRD, 2009, 46(6), 697-702.

Given the occurrence of co-occurring conditions, a holistic approach that works to incorporate all spheres of the patient's life is essential to include family and spiritual aspects. While medications can be very effective, this patient population is at high risk for polypharmacy which may lead to significant drug-drug interactions. Utilizing non-pharmacological approaches where indicated and appropriate is critical. Emerging research in the area of complimentary treatments in this population may indicate therapeutic alternatives in the near future.

Diagnostic criteria for the conditions are listed under the Provider Resources tab for reference. However, this guide is not intended to be used as a diagnostic tool. Rather, it is assumed that diagnoses have already been determined. Furthermore, this guide is designed to provide information and assist decision-making. It is not intended to define a standard of care and should not be construed as one. It should not be interpreted as prescribing an exclusive course of management and should not replace clinical judgment or consultation with a specialist when deemed appropriate. Every healthcare professional making use of this guide is responsible for evaluating the appropriateness of applying the recommendations in the clinical setting.

Case Vignette: Background

SGT King, a 23 y/o male, active duty US Army servicemember, presents to PCM for continued sleep problems, headaches and irritability. Relevant history includes injuries sustained in OIF two months ago, when the HUMVEE he was driving was hit by an IED. He reports a brief period (seconds to minutes) of loss of consciousness (LOC) followed by some confusion. He recalls his buddy who was in the passenger seat shaking him awake. The vehicle took enemy fire following the explosion during which five other members of his platoon were killed in action (KIA), including the same battle buddy. The other two members in the vehicle were dazed but no LOC. He was subsequently seen and treated in theater. Since this explosion, he reports headaches and dizziness for several days which have only moderately improved in frequency. He reports headaches two to three times/week with episodes of dizziness worsened by sleep deprivation. He reports frequent problems with staying asleep, mood, and concentration since then as well. This was his third concussion in nine months. Since returning home, he has had new marital problems and received some disciplinary actions from his supervisor.

Case Vignette: Treatment Analysis

His primary care provider initiated treatment with a seven day course of a triazolam 3mg, based on his primary complaint of sleep disturbance and scheduled a follow up visit in 14 days. Upon returning for follow up, SGT King, reported that the medication helped him to sleep through the night, but he discontinued its use after he could not wake up during a distressing nightmare. He felt increased anxiety for several days following this incident. He also noted that he was increasingly forgetful on the medication. At this time, the PTSD Check List (PCL) and Patient Health Questionnaire-9 (PHQ-9) were administered. SGT King reported a high degree of symptoms consistent with PTSD (PCL total=67), and moderate levels of depression (PHQ-9 total=10). Notably, SGT King's pattern of symptom endorsement included that he was extremely bothered (rating of 5 on 1-5 scale) by disturbing dreams of a stressful experience (item #3). Based upon further information gleaned during a more thorough clinical assessment, SGT King began a successful treatment regimen by his primary care provider for persistent symptoms following concussion, PTSD and depression.

The First Appointment

When seen initially in the primary care setting, the available appointment time is typically limited. Therefore, this section attempts to highlight areas that need to be addressed immediately. When seeing a post-deployment servicemember with a history of concussion and ongoing symptoms, a screening for potential co-occurring psychological health (PH) concerns should take place. In addition, several key areas of safety and symptoms should be addressed. General questions regarding the below topic areas should be followed up with specific questions to maximize clinical data.

1. Difficulty with sleep
2. Nightmares
3. Changes in mood (depression, anger, irritability)
4. Suicidal or homicidal ideation
5. Changes in cognitive function, attention
6. Chronic pain
7. New or worsening headaches
8. Violence
9. Substance use (alcohol, drugs, supplements)
10. Difficulties with relationships
11. Difficulties at work
12. Medications used (includes over-the-counter)

Suicidal and homicidal ideations are often associated with PTSD, SUD, and chronic pain and may certainly be seen at a higher prevalence in mild traumatic brain injury (TBI) when these disorders co-occur. Therefore, all patients where this guide would be used should routinely and carefully be evaluated for current suicidal and homicidal ideation, risk/protective factors, and past history of suicide attempts.

Given the time constraints of the primary care appointments, there will likely not be the time to assess for the etiology of all symptoms. However, inquiring about the function of these key areas is important for guiding treatment. For example, a servicemember who sees shadows move when frightened may be having symptoms reflective of hyperarousal from PTSD or may be displaying signs of a psychotic disorder. The assessment of perceptual abnormalities can be difficult, however obtaining the initial information to assess for safety and the need for immediate referral is possible.

There are no standard laboratory/neuroimaging studies or referrals that need to be ordered prior to the next visit unless clinically indicated (see table 1).

Table 1: The First Appointment

Clinical Concern	Action to Consider
Laboratory Studies	**Orders**
• Suspected SUD • Medications that require laboratory monitoring	• CBC, LFT's, chemistry, B12/folate • Studies dependent on medications
Neuroimaging Studies	**Orders**
• Focal neurological exam not previously evaluated and imaged • Severe worsening headaches (no prior imaging) • Significant altered mental status • New onset seizures • Threshold for imaging will be lower in the setting of acute concussion; Such criteria are, in addition to above, physical evidence of trauma above the clavicles, vomiting, age > 60, drug or alcohol intoxication, and coagulopathy	• Note: The decision between obtaining a CT and MRI is clinical and also based on availability as CT scans are typically easier to obtain than MRI; An MRI brain scan provides better evaluation of brain tissue while CT scan is preferable for suspected acute hemorrhage or skull fracture; If uncertain, consider specialty consultation; Retained fragments may affect imaging choice as MRI scans may be contraindicated
Referrals	**Clinic**
• Safety concerns (suicidal/homicidal ideations, active psychosis, SUD) • Significant clinical concerns (i.e., new focal neurological deficit, new onset seizures, severe PTSD, etc.)	• Note: Further clinical assessment should occur prior to these immediate specialty referrals • Examples: Behavioral Health Clinic, Neurology, Pain Clinic, Substance Abuse Program • Follow your hospital's procedures regarding management of acutely suicidal patients (i.e., line of sight monitoring, etc.)

Tips for Structuring the Clinical Interaction

Below are some general tips for ways to most effectively structure appointments with servicemembers with mild TBI and co-occurring PH problems. There is not a typical patient presentation as the pattern of symptoms vary widely depending on the conditions present. Some tailoring of the provider communication style will be important to maximize effective patient interaction. Common cognitive symptoms that may affect patient interactions include memory problems, slowed thought process, problems with organization, disinhibition and self-awareness. Thus, a longer appointment time is often required than most typical primary care appointments.

Communication

- Use short, simple sentences
- Minimize the amount that is said at one time
- Speak slowly and clearly
- Use the same words when repeating information
- Summarize key points throughout appointment
- Allow the individual extra time to respond

External Aids

- Use written notes either by or for the individual
- Use diagrams, drawings, checklists
- Set session agendas

Environment

- Meet with the individual more frequently, but for shorter therapy sessions
- Promote consistency by having a set meeting time and structure of the therapy activity
- Hold sessions at the individual's best time of day
- Be open to between session contact to assist individual in carrying-over information
- Plan for longer duration of treatment
- Minimize distractions in therapy and appointment environments

Kortte, KB, Briggs, F & Wegener, ST. (2005) Psychotherapy with Cognitively Impaired Adults. In GP Koocher, JC Norcross, & SS Hill, III (Eds.) The Psychologist's Desk Reference 2nd Edition (pp. 342-346), Oxford University Press.

How to Use this Guide

Purpose

The purpose of this guide is to help the primary care provider in the CONUS setting initiate appropriate symptom management when multiple diagnoses may be present, either resulting in resolution of symptoms or while awaiting specialty appointments. This guide does not replace clinical judgment or specialty consultation.

How to Use the Tables

Table 1

	SLEEP SYMPTOMS					4 Tool	5 Action Recommended
	Break-through pain	Fear of sleep due to nightmares	2 Difficulty with sleep due to anxiety symptoms	Difficulty with sleep due to depressive symptoms	Early AM/ night-time awakening (sleeplessness)		
Pain 1					✓	• Consider PHQ-2 • Consider Pain Scale • Assess for quality of sleep and significant snoring	• If either question in PHQ-2 scores ≥2, administer PHQ-9 to further assess for possible depression • If patient admits pain, clarify characteristics of any pain • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Headache	✓					• Pain Scale • Assess for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Post-traumatic Stress Disorder		3 ✓			✓	• PC-PTSD • Consider AUDIT-C and investigation of substance use given frequent co-occurrence • Assess for quality of sleep and significant snoring	• If PC-PTSD is positive on ≥2 items, administer PCL-5V to further assess for possible PTSD • If AUDIT-C (≥3F), (≥4M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-10 if suspicion of other substance are • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Depression			✓		✓	• PHQ-2 • Assess for quality of sleep and significant snoring	• If either question in PHQ-2 scores ≥2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Chronic Pain	✓			✓		• Pain Scale • Consider PHQ-2 • Consider AUDIT-C and investigation of substance use given frequent co-occurrence • Assess for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores ≥2, administer PHQ-9 to further assess for possible depression • If AUDIT-C (≥3F), (≥4M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-10 if suspicion of other substance are • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Acute Stress Disorder		✓	✓		✓	• PC-PTSD • Consider PHQ-2 • Assess for quality of sleep and significant snoring	• If PC-PTSD is positive on ≥2 items, administer Acute Stress Disorder (ASD) Scale to further assess for possible ASD • If either question in PHQ-2 scores ≥2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the Pittsburgh Sleep Quality Index
Substance Use Disorders				✓		• AUDIT-C and investigation of other substances • Consider FC-PTSD • Consider PHQ-2 • Consider Pain Scale	• If AUDIT-C (≥3F), (≥4M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-10 if suspicion of other substance are • If FC-PTSD is positive on ≥2 items, administer PCL-5V to further assess for possible PTSD • If either question in PHQ-2 scores ≥2, administer PHQ-9 to further assess for possible depression • If patient admits pain, clarify characteristics of any pain
ADDITIONAL FACTORS: Consider investigating for possible chronic/ family relations, work and career concerns, financial instability, exposures, etc. of stressors. SAFETY FACTORS: Anxiety, for suicidal/homicidal thoughts and potential abuse of medications; evaluate for risks during operation of heavy machinery and driving.						✓ – Frequently associated with diagnosis BLANK – Less likely to be associated with diagnosis Green text implies expert opinion as no guidance is given in CPGs	

Table 2

Primary Diagnosis Resulting in Symptom	6 Treatment Options: First Steps	Treatment Options: Second Steps
	Treatment approach for all conditions includes ruling out medication side effects as well as other diagnoses of sleep apnea. Utilization of assessment tools may assist with this. Table 1, Education of diagnosis as well as on emphasis on sleep hygiene, relaxation techniques and correction of circadian rhythm disruptions from travel are important initial steps.	Reassess for efficacy of initial intervention utilizing the same tools from First Steps.
Concussion	• If pain is present in disrupting sleep, medication and/or physical therapy to relieve pain • Consider referral to Neurology or Sleep Medicine if sleep issues persist after initial evaluation as needed • May consider non-benzodiazepine hypnotics (brief deactivation for 7-10 days)	• Follow up in 7-10 days, sooner if clinically indicated • Specialty care may prescribe medicine after stimulants if fatigue present despite resolution of sleep issues
Headache	• Adjust daytime Strategy as needed: – NSAIDs – Triptans – Triptans • Consider prophylactic medications if indicated for frequent headaches; consider agents that may be sedating (e.g., TCAs) • Have patient utilize headache diary to differentiate headaches aggravating triggers to headaches	• Follow up in 14-21 days, sooner if clinically indicated • Assess medication effects and consider dosage adjustment • Consider specialty consultation if headache management fails more than two prophylactic therapy attempts
Post-traumatic Stress Disorder	• Consider 5-7 days of sleep aid: – Benzodiazepines (brief to 5-7 days) (caution with history of substance) – Non-benzodiazepine hypnotic (brief to 7 days) – Antihistamines • Consider initiation of psychotherapy treatment of PTSD vs. referral for psychotherapy of PTSD: – TCAs and SSRIs – TCAs – Mirtazapine • Prazosin (specifically for nightmares limit dose-duration)	• Follow up in 7-10 days, sooner if clinically indicated • Refer to Behavioral Health for treatment of PTSD and sleep, especially if no significant improvement: – Cognitive Behavioral Therapy (CBT) regarding fear of going to sleep – Imagery Rehearsal Therapy for nightmares – Prolonged Exposure Therapy – Cognitive Processing Therapy – Stress Inoculation Training (SIT) – Eye Movement Desensitization and Reprocessing (EMDR)
Acute Stress	• Consider watchful waiting vs. initiation of medications for sleep disturbance vs. referral for psychotherapy for ASD • Consider initiation of medications for sleep disturbances: – Benzodiazepines (brief to 5-7 days) – Clinical hypnotic (brief to 5-7 days) – Propranolol (brief to 5-7 days) – Non-benzodiazepine hypnotics (brief to 5-7 days)	• Consider follow up in 7-10 days depending on symptom severity and functional impairment. At minimum, patient should be seen at 30 days for assessment of ASD and initiation of PTSD treatment if appropriate. For outpatient setting, monitor ASD symptoms for the development of PTSD using a validated measure of PTSD (e.g., PCL) • For patients with significant symptoms or full diagnosis of ASD, consider referral to Behavioral Health for treatment of sleep disturbance or ASD: – CBT regarding fear of going to sleep – Brief course of Exposure therapy – Brief course of CBT • Benzodiazepine prescription is not recommended for the management of ASD or for prevention of progression to PTSD
Depression	• Rule out primary sleep disorder as cause/trigger to mood disturbances, and treat if indicated • Consider watchful waiting vs. medication for depression vs. referral for treatment of depression: – Antidepressants – SSRIs – Serotonin/Norepinephrine Antagonist – Serotonin/Norepinephrine Reuptake Inhibitor – Serotonin/Norepinephrine Re-uptake Inhibitor	• Consider follow up in 4-6 weeks, sooner if clinically indicated • Discuss treatment options and patient's preference • Consider referral to Behavioral Health for treatment of depression
Chronic Pain	• If sleep apnea is present, pain control with medications, refer to a sleep specialist for appropriate apnea treatment • Consider medications for breakthrough pain with over-sedative if possible • Consider referral to PT/OT, and non-pharmacological treatments (biofeedback, acupuncture, etc.) • Consider use of TCAs, SNRIs, and anticonvulsants for chronic pain and sleep disturbance, and be cautious to help ensure single prescribing provider. In addition of use of antipsychotics to drug-to-drug interactions with provider discontinuation required by provider and patient (timing, dosage, pain relief and adverse effects)	• Follow up in 2-4 weeks to evaluate pain relief, sooner if clinically indicated • Close follow up as required • Refer to Pain Specialist as needed
Substance Use Disorder	• Consider baseline labs • Refer for substance abuse therapy (and detoxification, if needed) • Refer to community and peer support	• Follow up interval and frequency dependent on other treatments initiated during First Steps • Discuss treatment options and refer or channel decision regarding the treatment plan • Consider referral to Behavioral Health as recommended • Coordinate care with specialty clinic • Monitor and discuss problems/emerging needs through ongoing treatment plan updates • Recommend psychotherapy-assisted medication to patients with nicotine dependence; monitoring for potential drug-drug interactions

1. Identify table based on target symptom (sleep, mood, attention, chronic pain).
2. Identify characteristics of the symptom at the top of the table.
3. Determine probable etiology of the specific symptom. The ✓ "check mark -drawing" implies stronger association.
4. Consider assessment tools to assist with assessment and outcome monitoring.
5. Consider initial screening or assessment, and additional actions.
6. Consider initial treatment steps, as well as recommended follow up interval and treatment next steps.
7. If medications are considered, go to Appendix I to get information regarding potential effect of certain drugs on potential co-occurring disorders. Appendix I, Table II contains specific drug information (i.e., doses, side effects, safety warnings).
8. Appendix II contains patient education websites.
9. Appendix III contains provider resources, to include assessment tools and screening instruments.

Sleep

Table 1

Table 1: Sleep – Tool & Action Recommended

CO-OCCURING DISORDERS TO CONSIDER	Sleep Symptoms: Break-through pain	Fear of sleep due to nighttmares	Difficulty falling asleep due to ruminations	Difficulty with sleep due to withdrawal symptoms	Early AM/night-time awakening (unexplained)	Tool	Action Recommended
Concussion					✓	• Consider PHQ-2 • Consider Pain Scale • Assess for quality of sleep and significant snoring	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • If patient admits pain, clarify characteristics of any pain • Consider sleep questionnaire such as the PSQI
Headache	✓					• Pain Scale • Assess for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • Consider sleep questionnaire such as the PSQI
Posttraumatic Stress Disorder		✓	✓		✓	• PC-PTSD • Consider AUDIT-C and investigation of substance use given frequent co-occurrence • Assess for quality of sleep and significant snoring	• If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • Consider sleep questionnaire such as the PSQI
Acute Stress Disorder		✓	✓		✓	• PC-PTSD • Consider PHQ-2 • Assess for quality of sleep and significant snoring	• If PC-PTSD is positive on >2 items, administer Acute Stress Disorder (ASD) Scale to further assess for possible ASD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
Depression			✓		✓	• PHQ-2 • Assess for quality of sleep and significant snoring	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
Chronic Pain	✓			✓		• Pain Scale • Consider PHQ-2 • Consider AUDIT-C and investigation of substance use given frequent co-occurrence • Assess for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • Consider sleep questionnaire such as the PSQI
Substance Use Disorder				✓		• AUDIT-C and investigation of other substances • Consider PC-PTSD • Consider PHQ-2 • Consider Pain Scale	• If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • If patient admits pain, clarify characteristics of any pain

MODIFYING FACTORS: Consider investigating for possible stressful family relations, work and career concerns, financial concerns, excessive use of stimulants.

SAFETY FACTORS: Assess for suicidal/homocidal thoughts and potential abuse of medications; Evaluate for risk during operation of heavy machinery and driving.

✓ – Frequently associated with diagnosis

BLANK – Less likely to be associated with diagnosis

Green text implies expert opinion as no guidance is given in CPGs

PC-PTSD – Primary Care PTSD Screen

AUDIT C – Alcohol Use Disorders Identification Test

PHQ-2 – Patient Health Questionnaire (Depression) *the "2" is simply a more condensed depression screening than the "9"

PHQ-9 – Patient Health Questionnaire (Depression) *the "9" indicates that the tool is screening for depression specifically by looking at 9 DSM IV criteria – more comprehensive that then PHQ-2

DAST-20 – Drug Abuse Screening Test

PCL-M – PTSD Checklist – Military *the "M" signifies the military version of the screen

PSQI – Pittsburgh Sleep Quality Index

Sleep

Table 2

Table 2: Treatment Tips for Sleep Based on Potential Etiology

Primary Diagnosis Resulting in Symptom	Treatment Options: First Steps Initial treatment approach for all conditions includes ruling out medication side effects as well as other diagnoses such as sleep apnea. Utilization of assessment tools may assist with this (Table 1). Education of diagnosis as well as an emphasis on sleep hygiene, relaxation techniques and correction of circadian rhythm disruptions from travel are important initial steps.	Treatment Options: Second Steps Reassess for efficacy of initial intervention utilizing the same tools from First Steps.
Concussion	• If pain is present in disrupting sleep, medication and/or physical therapy to relieve pain • Assess for sleep disorders as these may occur secondary to TBI; Refer for sleep evaluation as needed • May consider non-benzodiazepine hypnotics (limit dose/duration to 7-10 days)	• Follow up in 7-10 days, sooner if clinically indicated • Specialty care may prescribe modafinil or other stimulants if fatigue present despite resolution of sleep issues
Headache	• Adjust abortive therapy as needed: – NSAIDs – Triptans – Anti-emetics • Consider prophylactic medications if indicated for frequent headaches; Consider agents that may be sedating (e.g., TCAs) • Have patient utilize headache diary in attempts to adjust aggravating triggers to headaches	• Follow up in 14-21 days, sooner if clinically indicated • Assess medication effects and consider dosage adjustment • Consider specialty consultation if headache management fails more than two prophylactic therapy attempts
Posttraumatic Stress Disorder	• Consider 5-7 days of sleep aid: – Benzodiazepines (limit to 5-7 days; Caution with history of concussion) – Non-benzodiazepine hypnotics (limit to 7 days) – Antihistamines • Consider initiation of psychotropic treatment of PTSD vs. referral for psychotherapy of PTSD: – SSRIs and SNRIs – TCAs – MAOIs – Prazosin (specifically for nightmares limit dose/duration)	• Follow up in 7-10 days, sooner if clinically indicated • Refer to Behavioral Health for treatment of PTSD and sleep, especially if no significant improvement: – Cognitive Behavioral Therapy (CBT) regarding fear of going to sleep – Imagery Rehearsal Therapy for nightmares – Prolonged Exposure Therapy – Cognitive Processing Therapy (CPT) – Stress Inoculation Training (SIT) – Eye Movement Desensitization and Reprocessing (EMDR)
Acute Stress Disorder	• Consider watchful waiting vs. initiation of medications for sleep disturbance vs. referral for psychotherapy for ASD • Medications for sleep disturbance/insomnia: – Benzodiazepines (limit to 5-7 days) – Chloral hydrate (limit to 5-7 days) – Propranolol (limit to 5-7 days) – Non-benzodiazepine hypnotics (limit to 5-7 days)	• Consider follow up in 7-14 days depending on symptom severity and functional impairment; At minimum, patient should be seen at 30 days post-event for assessment of progression to PTSD • For watchful waiting, monitor ASD symptoms for the development of PTSD using a validated measure of PTSD (e.g., PCL) • For individuals with significant symptoms or full diagnosis of ASD, consider referral to Behavioral Health for treatment of sleep disturbance or ASD: – CBT regarding fear of going to sleep – Brief course of Exposure Therapy – Brief course of CPT • Psychological Debriefing is not recommended for the reduction of ASD or for prevention of progression to PTSD
Depression	• Rule out primary sleep disorder as contributing to mood disturbance, and treat if indicated • Consider watchful waiting vs. medication for depression vs. referral for treatment of depression • Medications to consider: – SSRIs – Serotonin/Norepinephrine Antagonist – Norepinephrine/Dopamine Re-uptake Inhibitor – Serotonin/Norepinephrine Re-uptake Inhibitor	• Consider follow up in 3-4 weeks, sooner if clinically indicated • Discuss treatment options and patient's preference • Consider referral to Behavioral Health for treatment of depression
Chronic Pain	• If sleep apnea is present, use caution with medications; Refer to a sleep specialist for appropriate apnea treatment • Consider medications for breakthrough pain with non-narcotics if possible • Consider referral to PT/OT, and non-pharmacological treatments (biofeedback, acupuncture, etc.) • If narcotics are necessary: 1) recommend initiation of written contract for treatment with opioids to help ensure single prescribing provider; 2) addition of short-acting narcotics to titrate to optimal dose with precise documentation required by provider and patient (timing, dosage, pain relief and adverse effects)	• Follow up in 1-2 weeks to evaluate pain relief, sooner if clinically indicated • Close follow up is required • Refer to Pain Specialist as needed
Substance Use Disorder	• Consider baseline labs • Refer for substance abuse therapy (and detoxification if needed) • Refer to community and peer support	• Follow up interval and frequency dependent on other treatments initiated during First Steps • Discuss treatment options and arrive at shared decision regarding the treatment plan • Interdisciplinary approach is strongly recommended • Coordinate care with specialty clinics • Monitor and discuss problems/emerging needs through ongoing treatment plan updates • Recommend and offer nicotine cessation treatments to patients with nicotine dependence, monitoring for potential drug-drug interactions

Mood

Table 1

Table 1: Mood – Tool & Action Recommended

CO-OCCURING DISORDERS TO CONSIDER	Mood Symptoms (depressed mood is commonly seen in conjunction with all below): Emotional numbing	Irritability	Emotional fatigue	Physical fatigue	Lack of enjoyment in most daily activities	Distress with traumatic reminders	Impulsivity	Activities driven by medication needs	Hyperarousal	Tool	Action Recommended
Concussion		✓		✓			✓			• PHQ-2 • Assess for quality of sleep and significant snoring • Consider Pain Scale	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If patient admits pain, clarify characteristics of any pain
Headache			✓					✓		• Pain Scale • PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • if either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
Posttraumatic Stress Disorder	✓	✓	✓	✓	✓	✓			✓	• PC-PTSD • PHQ-2 • Consider assessment for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
Acute Stress Disorder	✓	✓	✓			✓			✓	• PC-PTSD • PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If PC-PTSD is positive on >2 items, administer Acute Stress Disorder Scale to further assess for possible ASD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
Depression		✓	✓	✓	✓					• PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
Chronic Pain					✓		✓	✓		• Pain Scale • PHQ-2 • Consider assessment for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
Substance Use Disorder		✓					✓	✓		• AUDIT-C and investigation of other substances • PHQ-2 • PC-PTSD • Consider assessment for quality of sleep and significant snoring • Consider Pain Scale	• If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • Consider sleep questionnaire such as the PSQI • If patient admits pain, clarify characteristics of any pain

MODIFYING FACTORS: Consider investigating for possible stressful family relations, work and career concerns, financial concerns, excessive use of stimulants.

SAFETY FACTORS: Assess for suicidal/homocidal thoughts and potential abuse of medications; Evaluate for risk during operation of heavy machinery and driving.

✓ – Frequently associated with diagnosis BLANK – Less likely to be associated with diagnosis

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Mood

Table 2

Table 2: Treatment Tips for Mood Based on Potential Etiology

Primary Diagnosis Resulting in Symptom	Treatment Options: First Steps Evaluate for existing or emerging medical conditions (e.g., hypo/hyperthyroidism, sleep disorder, etc.) that may cause mood symptoms and could exacerbate the below conditions. Evaluate for medication side effects that may cause mood disturbance (e.g., beta-blockers, etc.). Substance misuse should also be ruled out. Utilization of assessment tools may assist with identifying higher risk co-occurring conditions (Table 1). Evaluate for safety and suicide/homicide-risk.	Treatment Options: Second Steps Reassess for efficacy of initial intervention utilizing the same tools from First Steps.
Concussion	• Educate patient and family about symptoms and recovery patterns • Treatment for psychiatric/behavioral symptoms should be based upon individual factors and nature of severity of symptoms presentation; Assess for mood disorder vs. post-concussive fatigue • Mood changes in concussion often are exacerbated by overstimulation or even strong stimulation (e.g., bright lights, loud noises, other forms of stimulus overload), and may be treated by placing patient in quiet and non-demanding environment • Consider watchful waiting vs. referral to Behavioral Health treatment of mood disorder vs. initiation of medications for mood (e.g., SSRI, SNRIs, etc.)	• Follow up in 2-3 weeks, sooner if clinically indicated • Consider specialty referral to: – Cognitive rehabilitation – Behavioral Health – TBI specialist • Assess for co-occurring conditions
Headache	• Educate patient and family about symptoms; Mood disorders are often a comorbidity of chronic headaches • Treatment of primary headaches may help alleviate mood symptoms; Choosing headache prophylactic therapy that may also benefit mood symptoms	• Follow up in 2-3 weeks, sooner if clinically indicated • Assess for co-occurring conditions • Consider referral to Neurology for refractory headaches • Consider referral to Pain Specialist as needed • Consider referral to Behavioral Health for concurrent treatment depression
Posttraumatic Stress Disorder	• Educate patient and family about PTSD mood symptoms; Common mood symptoms in PTSD include trauma-related fear with anxious arousal, numbing of emotional response, and irritability/anger • Consider initiation of medication for PTSD – Initiate monotherapy with SSRIs or SNRIs (preferred) • Consider a referral to Behavioral Health in patients with PTSD; If PTSD is comorbid with depression, psychotherapeutic treatment of primary PTSD may result in improvement in depression; Consider referral to Behavioral Health early in course of treatment among individuals where PTSD is comorbid with other psychiatric conditions – Referral to Behavioral Health for psychotherapy for PTSD (e.g., Prolonged Exposure Therapy) or to address specific mood symptoms (e.g., anger management for irritability)	• Follow up in 3-4 weeks, sooner if clinically indicated • Consider adjunctive medications when treatment response is suboptimal after 8 weeks of monotherapy – Among atypical antipsychotics, risperidone and olanzapine are recommended; Quetiapine can be considered, although evidence to support its use is less conclusive; **Note: There is insufficient evidence to support the use of prazosin, anticonvulsants, or atypical or typical antipsychotics as monotherapy for PTSD** • Consider referral to Behavioral Health, if this was not previously done • A thorough assessment of mood symptoms and comorbid diagnoses is essential to effective treatment
Acute Stress Disorder	• Educate patient and family about ASD mood symptoms; Common mood symptoms in ASD include numbing of emotional response, and associated features such as irritability/anger • Consider watchful waiting (with appropriate patient education) vs. initiation of medications for ASD vs. referral to Behavioral Health for treatment – For watchful waiting, monitor ASD symptoms with a validated measure of PTSD (e.g., PCL) • Psychological Debriefing is not recommended for reduction of ASD or for prevention of progression to PTSD	• Follow up in 1-2 weeks, depending on symptom severity and functional impairment; At a minimum, patient should be seen at 30 days post-event for assessment of progression to PTSD • Consider referral to Behavioral Health for treatment
Depression	• Educate patient and family about symptoms of mood disorder and recovery patterns • Consider watchful waiting (with appropriate patient education) vs. initiation of treatment with either medications or with psychotherapy vs. referral to Behavioral Health for treatment	• Follow up in 3-4 weeks, sooner if clinically indicated • Adjust medications, if started • Consider referral to Behavioral Health if: – Failure to respond to treatment (e.g., 2 or more courses antidepressants) – Three months of treatment without improvement – Need for psychotherapy or combination psychotherapy and medication – Urgent or unstable psychiatric condition – Co-existing psychological or medical health condition that complicates treatment – History of suicide attempts or suicidal ideation – Concerns about adherence to treatment
Chronic Pain	• Education regarding relationship between chronic pain and mood disturbance; Depression lowers pain threshold and increases subjective 'suffering' induced by a given amount of pain • Consider watchful waiting (with appropriate patient education) vs. initiation of treatment with either medications or with psychotherapy vs. referral to Behavioral Health for treatment • Consider non-pharmacological treatments (e.g., PT/OT, biofeedback, acupuncture, etc.) vs. a short course of medications for pain treatment if required, utilizing non-narcotics as possible • Consider course of medications (e.g., SNRIs) that may help both depression and neuropathic pain • Consider initiation of treatment for depression by medications vs referral to Behavioral Health • Educate about potential adverse effects of opioids for pain (e.g., mood changes) and withdrawal	• Follow up in 1-3 weeks, sooner if clinically indicated • If chronic narcotics are required, recommend utilization of a pain contract to ensure a single prescribing provider with specialty involvement, both Pain Clinic and Behavioral Health • Re-examine for possible co-occurring psychological health diagnosis • As depression treatment improves there is usually a decrease in associated pain symptoms unless there are underlying comorbidities; Thus, both conditions should be aggressively treated • Referral to psychiatrist, psychologist or case manager may be indicated in cases of significant psychiatric comorbidity • Minimize adverse effects of pain medications by modifying the dose of medication during titration and/or rotating opioid agent
Substance Use Disorder	• Educate patient and family on adverse effects of substance use • Consider referral to Substance Specialty Clinic, vs. coordinating care with specialty clinics • Refer to community and peer support (e.g., AA/NA) • Monitor and discuss problems/emerging needs through ongoing treatment plan updates • Prioritize and address co-occurring medical and psychiatric conditions	• Follow up interval and frequency dependent on other treatments initiated during First Steps • Coordinate care with specialty clinics to include Pain Specialist • Interdisciplinary approach is strongly recommended • Recommend and offer nicotine cessation treatments to patients with nicotine dependence, monitoring for potential drug-drug interactions

Attention

Table 1

Table 1: Attention – Tool & Action Recommended

CO-OCCURING DISORDERS TO CONSIDER	Attention Symptoms									Tool	Action Recommended
		Re-experiences intrusive memories	Emotional numbing	Distracting pain	Difficulty multitasking	Worsens with emotional distress	Worsens with fatigue (physical or emotional)	Dissociative episodes	Worsens as withdrawal symptoms occur		
	Concussion				✓		✓			• PHQ-2 • Assess for quality of sleep and significant snoring • Consider Pain Scale	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If patient admits pain, clarify characteristics of any pain
	Headache			✓			✓			• Pain Scale • Assess for quality of sleep and significant snoring • PHQ-2	• If patient admits pain, clarify characteristics of any pain • Consider sleep questionnaire such as the PSQI • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression
	Posttraumatic Stress Disorder	✓	✓		✓	✓		✓		• PC-PTSD • Assess for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
	Acute Stress Disorder	✓	✓		✓	✓		✓		• PC-PTSD • PHQ-2 • Assess for quality of sleep and significant snoring	• If PC-PTSD is positive on >2 items, administer Acute Stress Disorder Scale to further assess for possible ASD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Depression		✓		✓	✓				• PHQ-2 • Assess for quality of sleep and significant snoring	• If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Chronic Pain			✓			✓			• Pain Scale • PHQ-2 • Assess for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
	Substance Use Disorder					✓	✓	✓	✓	• AUDIT-C and investigation of other substances • PHQ-2 • Assess for quality of sleep and significant snoring • PC-PTSD • Consider Pain Scale	• If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • If patient admits pain, clarify characteristics of any pain

✓ – Frequently associated with diagnosis BLANK – Less likely to be associated with diagnosis

Green text implies expert opinion as no guidance is given in CPGs

Attention

Table 2

Table 2: Treatment Tips for Attention Based on Potential Etiology

Primary Diagnosis Resulting in Symptom	Treatment Options: First Steps Initial treatment approach for all conditions includes evaluating for medications that may impair cognition (e.g., narcotics, sleeping aids, etc.) as well as other diagnoses (e.g., sleep disturbance). Substance misuse should also be ruled out. Utilization of assessment tools may assist with this (Table 1).	Treatment Options: Second Steps Reassess for efficacy of initial intervention utilizing the same tools from First Steps.
Concussion	• Educate patient and family about symptoms and recovery patterns • Treatment for psychiatric/behavioral symptoms should be based upon individual factors and nature of severity of symptoms presentation • Patients should be encouraged to implement life-style changes including exercise, nutritious diet, relaxation training, scheduling leisure activities and pacing to improve treatment outcome • Use caution with medications that may cause sedation or confusion (e.g., hyponotics and anxiolytics)	• Follow up in 2-3 weeks, sooner if clinically indicated • Consider referral for cognitive rehabilitation • Re-examine for possible co-occurring psychological health diagnosis • Medications to treat fatigue which may affect attention (in specialty care after ruling out sleep disturbance): – Modafinil – Methylphenidate – Amantadine
Headache	• Educate patient and family about the frequently existing relationship between chronic headaches and mood disorders that can impact attention • Have patient utilize headache diary in attempt to identify and adjust aggravating triggers to headaches • Carefully review medications as many prophylactic medications may affect attention/concentration (e.g., beta-blockers, antiepileptics, TCAs, etc.) • Treatment of headaches and any co-occurring mood disorder should improve attention/concentration	• Follow up in 2-3 weeks, sooner if clinically indicated • Re-examine for possible co-occurring psychological health diagnosis • Consider Neurology referral
Posttraumatic Stress Disorder	• Educate patient and family about PTSD symptoms such as poor attention and other memory/cognitive problems • Memory, concentration and attention difficulties may be due to anxiety or preoccupation with thoughts related to PTSD • Consider initiation of medications for PTSD vs referral for specialized Behavioral Health care; Treatment of this underlying disorder should improve attention/concentration	• Follow up in 3-4 weeks, sooner if clinically indicated • Consider referral to Behavioral Health for treatment of PTSD • Re-examine for possible co-occurring psychological health diagnosis
Acute Stress Disorder	• Educate patient and family about ASD symptoms such as dissociation; Create an expectation of recovery • Psychological Debriefing is not recommended for the reduction of ASD or for prevention of progression to PTSD • There is insufficient evidence to recommend use of a pharmacological agent to prevent PTSD • Consider initiation of medications for ASD vs referral for Behavioral Health care; Treatment of the underlying disorder (ASD) should improve attention/concentration	• Consider follow up in 1-2 weeks minimum, sooner if clinically indicated; Patient needs to be seen 30 days post-event for assessment of progression to PTSD • Consider referral to Behavioral Health for treatment of ASD • Re-examine for possible co-occurring psychological health diagnosis
Depression	• Educate patient and family about depression symptoms to include poor concentration, attention and a motivation • Consider initiation of medications for depression vs referral for Behavioral Health care • As depression improves with treatment, there is a corresponding increase in cognitive/attention functioning	• Consider follow up in 3-4 weeks, sooner if clinically indicated • Adjust medications if started • Consider referral to Behavioral Health for treatment of depression • Re-examine for possible co-occurring psychological health diagnosis
Chronic Pain	• Carefully examine relationship between symptoms and timing of medication doses • Consider medications for breakthrough pain with non-narcotics if possible • Consider referral to PT/OT and non-pharmacological treatments (e.g., biofeedback, acupuncture, etc.) • If narcotics are necessary, 1) recommend initiation of written contract for treatment with opioids to help ensure single prescribing provider; 2) addition of short-acting narcotics to titrate to optimal dose with precise documentation required by provider and patient (timing, dosage, pain relief, and adverse effects) • Once the pain is managed appropriately, cognitive functioning, including attention will improve. No additional treatment is recommended	• Consider follow up in 1-2 weeks, sooner if clinically indicated • Close follow up is required • Referral to Pain Specialist as needed • Re-examine for possible co-occurring psychological health diagnosis
Substance Use Disorder	• Educate patient and family on adverse effects of substance use • Consider baseline labs • Address co-occurring medical and psychological conditions • Refer for substance abuse therapy (and detoxification if needed) • Refer to community and peer support	• Follow up interval and frequency dependent on other treatments initiated during First Steps • Coordinate care with specialty clinics • Interdisciplinary approach is strongly recommended • Recommend and offer nicotine cessation treatments to patients with nicotine dependence, monitoring for potential drug-drug interactions

Chronic Pain

Table 1

Table 1: Chronic Pain – Tool & Action Recommended

Chronic Pain Symptoms							Tool	Action Recommended
		Neuropathic	Musculoskeletal	Diffuse pain (entire body)	Not explained by known bodily injury or medical diagnosis	Pain triggers memories of trauma		
CO-OCCURING DISORDERS TO CONSIDER	**Concussion**		✓ *head/ neck				• Pain Scale • Consider PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Headache	✓	✓				• Pain Scale • Consider PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Posttraumatic Stress Disorder				✓	✓	• Pain Scale • PC-PTSD • Consider PHQ-2 • Consider assessment for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If patient admits pain, clarify characteristics of any pain • If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
	Acute Stress Disorder				✓	✓	• Pain Scale • PC-PTSD • Consider PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If PC-PTSD is positive on >2 items, administer Acute Stress Disorder Scale to further assess for possible ASD • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Depression			✓	✓		• Pain Scale • PHQ-2 • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI
	Chronic Pain	✓	✓				• Pain Scale • PHQ-2 • Consider assessment for quality of sleep and significant snoring • Consider AUDIT-C and investigation of substance use given frequent co-occurrence	• If patient admits pain, clarify characteristics of any pain • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • Consider sleep questionnaire such as the PSQI • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use
	Substance Use Disorder			✓			• Pain Scale • AUDIT-C and investigation of other substances • PHQ-2 • PC-PTSD • Consider assessment for quality of sleep and significant snoring	• If patient admits pain, clarify characteristics of any pain • If AUDIT-C ≥3 (F), ≥4 (M), then consider referral to Behavioral Health vs. education depending on symptom severity • Consider DAST-20 if suspicion of other substance use • If either question in PHQ-2 scores >2, administer PHQ-9 to further assess for possible depression • If PC-PTSD is positive on >2 items, administer PCL-M to further assess for possible PTSD • Consider sleep questionnaire such as the PSQI

MODIFYING FACTORS: Supportive family and social relationships are critical components of care for persons in chronic pain. Assess for exposure to pathogens, patient behaviors that would contribute to chronic pain.

SAFETY FACTORS: With chronic continuous pain the major concern is substance abuse for self-medication. Look for compulsive use of drugs or alcohol as a contraindication to opioid therapy prior to prescribing any narcotics. Use written opioid treatment agreements with patient and family and consult with substance abuse specialist if there is a concern. Potential of self- harm should be considered in cases of chronic pain.

✓ – Frequently associated with diagnosis BLANK – Less likely to be associated with diagnosis

Green text implies expert opinion as no guidance is given in CPGs

Chronic Pain

Table 2

Table 2: Treatment Tips for Chronic Pain Based on Potential Etiology

Primary Diagnosis Resulting in Symptom	Treatment Options: First Steps Evaluate for existing or emerging medical conditions that may be causing pain and could exacerbate below conditions. Initial treatment approach for all conditions includes evaluating for self-treatment of pain to include over-the-counter medications, alcohol, illicit substances and self-dosing of prescription drugs. Utilization of assessment tools may assist with identifying higher risk co-occurring conditions (Table 1). Tailor pain treatment to the characteristics of pain (i.e., type, frequency, duration, etc.).	Treatment Options: Second Steps Reassess for efficacy of initial intervention utilizing the same tools from First Steps.
Concussion	• Assess for red flags that may indicate need for immediate neuroimaging and/or specialty referral; Evaluate for potential co-occurring bodily injury • Educate patient and family about symptoms and recovery patterns of concussion • Treatment for physical complaints should be based upon a thorough evaluation, individual factors and symptom presentation • Treatment should include: – Non-pharmacological interventions (e.g., relaxation, PT/OT, acupuncture and modification of the environment) – Use of medications to relieve pain (e.g., non-narcotic pain meds, NSAIDS, Triptans for migrainous headaches) • Consultation or referral to specialist if there are atypical or other neurologic conditions • Be aware that pain interferes with sleep and cognition and treat aggressively prior to deciding the patient has an attention or other cognitive deficit secondary to a concussion	• Follow up in 2-3 weeks, sooner if clinically indicated • Re-examine for possible co-occurring psychological health diagnosis • Consider referral to specialty clinic if pain is resulting in significant functional deficits or requiring high dose narcotics
Headache	• Assess for red flags that may indicate need for immediate neuroimaging and/or specialty referral • Educate patient and family regarding diagnosis and management expectations • Treatment approaches should include consideration of: – Abortive medications: (e.g., NSAIDs, Triptans, antiemetics) – Prophylactic medications: consideration of medication to use should be based on potential side effects and potential for concurrent treatment of another condition • Prophylactic medications may not begin to take effect for 4-6 weeks • Recommend use of headache diary and a close assessment of potential triggers that may be addressed by other means (e.g., sleep disturbance, stress management, etc.)	• Follow up in 2-3 weeks, sooner if clinically indicated • Assess medication effects and consider dosage adjustments • Consider alternative therapies if indicated (e.g., biofeedback, acupuncture, etc.) • Consider Neurology referral if headaches are unresponsive to treatments or pain is resulting in significant functional deficits • Re-examine for possible co-occurring psychological health diagnosis
Posttraumatic Stress Disorder	• Assess for connection between PTSD and pain symptoms (pain triggering memories of trauma); Educate patient and family regarding the relationship between disorders • Consider non-pharmacological treatments (e.g., PT/OT, biofeedback, acupuncture, etc.) vs. a short course of medications for pain treatment if required, utilizing non-narcotics as possible • Consider referral to Behavioral Health early • Consider course of medications (e.g., SNRIs) that may be useful for both anxiety and neuropathic pain	• Follow up in 3-4 weeks, sooner if clinically indicated • If chronic narcotics are required, recommend utilization of a pain contract to ensure a single prescribing provider with consideration of concurrent referral to Pain Specialist • Re-examine for possible co-occurring psychological health diagnosis
Acute Stress Disorder	• Assess for connection between ASD and pain symptoms (pain triggering memories of trauma); Educate patient and family regarding the relationship between disorders • Consider non-pharmacological treatments (e.g., PT/OT, biofeedback, acupuncture, etc.) vs. a short course of medications for pain treatment if required, utilizing non-narcotics as possible • Consider referral to Behavioral Health early	• Consider follow up in 1-2 weeks minimum, sooner if clinically indicated; Patient needs to be seen 30 days post-event for assessment of progression to PTSD • If chronic narcotics are required, recommend utilization of a pain contract to ensure a single prescribing provider with consideration of concurrent referral to Pain Specialist • Consider referral to Behavioral Health if not completed • Re-examine for possible co-occurring psychological health diagnosis
Depression	• Educate patient and family about relationship between depression and pain; Depression lowers pain threshold and increases subjective 'suffering' induced by a given amount of pain • Consider non-pharmacological treatments (e.g., PT/OT, biofeedback, acupuncture, etc.) vs. a short course of medications for pain treatment if required, utilizing non-narcotics as possible • Consider course of medications (e.g., SNRIs) that may help both depression and neuropathic pain • Consider initiation of treatment for depression by medications vs referral to Behavioral Health	• Consider follow up in 3-4 weeks, sooner if clinically indicated • Adjust medications if started • If chronic narcotics are required, recommend utilization of a pain contract to ensure a single prescribing provider with specialty involvement, both Pain Clinic and Behavioral Health • Re-examine for possible co-occurring psychological health diagnosis • As depression treatment improves there is usually a decrease in associated pain symptoms unless there are underlying comorbidities; Thus, both conditions should be aggressively treated
Chronic Pain	• Educate patient and family regarding etiology of pain as well as increased risk for occurrence of co-occurring conditions, especially depression • Consider early involvement of Behavioral Health in those patients with chronic refractory pain • If chronic narcotics are required, recommend utilization of a pain contract to ensure a single prescribing provider with consideration of concurrent referral to Pain Specialist • Tailor treatment plan to patient's circumstances and pain characteristics • Consider use of non-pharmacological therapies when able (e.g., biofeedback, therapeutic exercise, acupuncture, etc.) • Refer to COT CPG for treatment of short, intermittent and continuous pain	• Consider follow up in 1-2 weeks initially, sooner if clinically indicated • Consider interdisciplinary approach
Substance Use Disorder	• Consider and assess whether substance use is a form of self-medication, or developed secondary to polypharmacy; In these cases, coordinate and refer for the treatment of chronic pain and for the treatment of substance use disorder • Educate patient and family on adverse effects of substance use • Consider baseline labs • Address co-occurring medical and psychological conditions • Refer for substance abuse therapy (and detoxification if needed) • Refer to community and peer support	• Follow up interval and frequency dependent on other treatments initiated during First Steps • Coordinate care with specialty clinics to include Pain Specialist • Interdisciplinary approach is strongly recommended • Recommend and offer nicotine cessation treatments to patients with nicotine dependence, monitoring for potential drug-drug interactions

Appendix I:
Medications

Table of Contents: Medication

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Potential Pharmacological Agents in Co-occurring Disorders Guide for Using the Medication Tables

How to use this guide

Purpose

The purpose of this guide is to assist the primary care provider in using the medication tables. This guide does not replace clinical judgment or specialty consultation.

How to use the tables

1. Identify the medication to be use based on the target symptoms (depression, substance use disorder, chronic pain, PTSD, sleep disorders, stimulation, smoking cessation and nightmares).
2. Refer to the specific table for the information on the medication desired. See below for specific guidance on each field.
3. Table 1 includes information on the specific medications. Reference this table for information on dosing, advantages, disadvantages, pregnancy risk, safety, efficacy, monitoring, referrals and warning.
4. Table 2 includes information on specific adverse effects with relative comparisons of the medications in a specific class.
5. Table 3 contains information on the pros and cons as it relates to using these medications for the co-occurring disorders.

Table 1: Medications

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin	Efficacy
This field includes the generic name first and then the brand name in parenthesis. There may be more than one brand name listed.	The doses are listed in this field. The initial starting dose is listed, titration information if available and the maximum dose per day. Adult and geriatric doses are listed.	Advantages pertaining to the specific medication are listed in this field. Information in this section may include FDA approved indications, co-occurring disorder indications and specific dosage instructions.	Disadvantages pertaining to the specific medication are listed in this field. Information in this section includes contraindications related to diseases, adverse side effects and common side effects.	The specific pregnancy categories are listed here and are either A, B, C or D.	Information in this section includes instructions on toxicity, overdose, contraindications with other medications, concomitant use with other medications and tapering information.	Included in this section is the medication efficacy as it relates to the co-occurring disorders.
Information in this section includes caution statements and general information pertaining to all the medications in each section.						

! **Monitoring, Referrals and Warnings:** Monitoring, referral and warning instructions are listed in this section.

Black Box Warning: Black box warnings or box warnings are listed in this section. These warnings appear on a prescription drug's label and are designed to call attention to serious or life-threatening risks.

Pregnancy category descriptions are:
A = Controlled studies show no risk
B = No evidence of risk in humans
C = Risk cannot be ruled out, but potential benefits may justify potential risk
D = Positive evidence of risk; However potential benefits may outweigh potential risks

Table 2: Adverse Drug Effects: Relative Comparisons									
Medication Name	Anticholinergic Activity (muscarinic)	Sedation	Orthostatic Hypotension	Cardiac Effects	GI Effects	Seizures	Weight Gain	Sexual Dysfunction	Mood Changes During Titration or Abrupt Discontinuation

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

TABLE 3	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros							
Cons							

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POTENTIAL PHARMACOLOGICAL AGENTS IN CO-OCCURRING DISORDERS

MEDICATION TABLE: Refer to the pharmaceutical manufacturer's literature for full prescribing information. The below tables are commonly prescribed medications for a number of conditions discussed in this toolkit. The decision to utilize one medication over another should be based on the individual patient, the symptom complaints, and the basic features and potential side effects of the medication in question. Some of the medications listed should be prescribed only with the specialty consultation depending on patient complexity and the condition being treated. If in doubt, consult with the appropriate specialty clinic. Unless specifically noted as IM dosing, the doses listed are for oral dosing.

Selective Serotonin Reuptake Inhibitors (SSRIs)						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for SSRIs**	**Efficacy for SSRIs**
Citalopram (Celexa)	• Initial adult dose = 20mg QD • Max dose/day = 60mg QD • Max geriatric dose/day = 40mg QD	• May be taken without regard to meals • AM daily dosing • May use in mTBI patients for irritability • Possibly fewer Cytochrome P450 (CYP450) interactions. • Generic	• **Contraindications include hypersensitivity to escitalopram** • Activation or jitteriness: start with low dose especially when the patient is experiencing comorbid anxiety disorder • High incidence of reported GI side effects (diarrhea, nausea) and sexual dysfunction	C	• Wide margin of safety, rare deaths reported on over dose • Contraindicated with pimozide or with MAOIs within two weeks of discontinuing MAOIs • Fluoxetine or paroxetine contraindicated with thioridazine within five weeks of discontinuing therapy • Contraindicated sertraline oral concentrate with disulfiram • Do not take citalopram and escitalopram concomitantly	• Depression: Response rate: mild depression = 4-8 weeks; Moderate depression = 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • Recommended as monotherapy as first-line therapy in PTSD • PTSD: Paroxetine IR and sertraline approved for use in PTSD; Efficacy for long-term use in PTSD has not been systematically evaluated
Escitalopram (Lexapro)	• Initial adult dose = 10mg QD • Max adult dose/day = 20mg QD • Initial geriatric dose = 10mg QD	• 10mg dose often effective • Once daily dosing without regard to meals • AM daily dosing	• **Contraindications include hypersensitivity to citalopram** • Activation or jitteriness: start with low dose especially when the patient is experiencing comorbid anxiety disorder • High incidence of reported GI side effects (diarrhea, nausea) and sexual dysfunction	C		

Selective Serotonin Reuptake Inhibitors (SSRIs) (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for SSRIs	Efficacy for SSRIs
Fluoxetine (Prozac)	• Initial adult dose = 20mg QD • Max adult dose/day = 80mg QD • Initial geriatric dose = 10mg QD • Use lower doses in the elderly	• Long half-life good for poor adherence, missed doses • May be taken with or without food • AM daily dosing • Lowest rate of discontinuation syndrome among the SSRIs • Generic	• Slower to reach steady state • May be stimulating and may have more CYP450 interactions • Associated with pharyngitis, rash and allergic events	C	• Do not initiate concomitant therapy with a benzodiazepine • Drug interactions may include Tricyclic Antidepressants, NSAIDs, SNRIs, Triptans, aspirin, carbamazepine, warfarin, nilotinib, sibutramine, tamoxifen, tetrabenazine and ziprasidone • Avoid concomitant use with alcohol, l-tryptophan and st. john's wort • Taper dose slowly to prevent clinically significant discontinuation symptoms	• Escitalopram and fluoxetine have good documentation for off-label use in PTSD
Fluoxetine (Prozac) Weekly	• 90mg Q week	• Once weekly dosing for maintenance therapy for patients who have responded to daily administration	• If a satisfactory response is not maintained with once weekly dosing, consider reestablishing a daily dosing regimen • Possibly more CYP450 interactions	C		
Paroxetine (Paxil)	• Initial adult dose = 20mg QD • Max adult dose/day = 50mg QD • Initial geriatric dose = 10mg QD • Max geriatric dose = 40mg QD	• May be taken with or without food. • AM daily dosing • Generic	• Of the SSRIs, highest reported rate of discontinuation syndrome, highest rate of sexual dysfunction and weight gain • Sometimes sedating and more anti-cholinergic symptoms • Possibly more CYP450 interactions	D		

Selective Serotonin Reuptake Inhibitors (SSRIs) (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for SSRIs	Efficacy for SSRIs
Paroxetine CR (Paxil CR)	• Initial adult dose = 25mg QD • Max adult dose/day = 62.5mg QD • Initial geriatric dose = 12.5mg QD • Max geriatric dose = 50mg daily QD	• May be taken with or without food • AM daily dosing • Do not crush or chew CR tab • Generic	• Of the SSRIs, highest reported rate of discontinuation syndrome, highest rate of sexual dysfunction and weight gain • Sometimes sedating and more anti-cholinergic symptoms • Possibly more CYP450 interactions	D		
Sertraline (Zoloft)	• Initial adult dose = 50mg QD • Max dose/day = 200mg QD • Initial geriatric dose = 25mg QD	• Useful in patients experiencing insomnia • Safety shown post MI • AM daily dosing • Also available as oral concentrate • May use in mTBI patients for irritability • Generic	• Higher rate of diarrhea than other SSRIs	C		

Drugs of this class differ substantially in safety, tolerability and simplicity when used in patients on other medications. Can work in Tricyclic Antidepressant (TCA) non-responders. Other possible uses are in Anxiety disorders, Posttraumatic Stress Disorder (PTSD), Obsessive Compulsive Disorder (OCD), Panic Disorder, Bulimia and Premenstrual Dysphoric Disorder (PMDD). SSRIs, Serotonin Norepinephrine Reuptake Inhibitors (SNRIs), bupropion, mirtazapine are first line therapy for adults with Major Depressive Disorder (MDD). Start with the lowest dose but this may be effective for some while others will require gradual titration. Reduce the dose in the elderly. See specific literature for hepatic, renal dosing. Photosensitivity may occur; Therefore, caution patients to take preventative measures. May cause insomnia or diaphoresis.

Clinical Pearl: Can add TCA to SSRI. However, if you add SSRI to TCA then there is a potential for increased TCA levels.

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Monitoring, Referrals and Warnings: Monitor for hyponatremia and weight change.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Appropriately monitor and closely observe for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Selective Serotonin Reuptake Inhibitors (SSRIs) (cont.)

SSRIs Adverse Drug Effects: Relative Comparisons									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Citalopram	0	0/+	0	0	+++	0	0	+++	+++
Escitalopram	0	0/+	0	0	+++	0	0	+++	+++
Fluoxetine	0	0/+	0	0/+	+++	0/+	0/+	+++	++
Paroxetine	0/+	0/+	0	0	+++	0	0/+	+++	+++
Sertraline	0	0/+	0	0	+++	0	0	+++	++

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

SSRIs	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	May be useful for some of the behavioral symptoms	Not in CPG but maybe useful as a prophylaxis	Not in CPG but can be used	Very effective first-line treatment	Very effective first-line treatment	No additional	Help with sobriety in instances where comorbid depressive symptoms are effectively targeted
Cons	During titration phase of treatment, may increase anxiety and fatigue	No additional	During titration phase of treatment, may increase anxiety, nightmares and fatigue	During titration phase of treatment, may increase anxiety, night-mares and fatigue	During titration phase of treatment, may increase anxiety, nightmares and fatigue	When used in conjunction with Opioids, sexual side effects may be even more pronounced	No additional

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs)						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for SNRIs**	**Efficacy for SNRIs**
Duloxetine (Cymbalta)	• Initial adult dose = 20 to 30mg BID • Max adult dose/day = 60mg • Initial geriatric dose = 10-20mg BID	• May take without regards to meals • Duloxetine approved for use in generalized anxiety disorder • Do not chew, crush or open capsules	• **Contraindications include uncontrolled narrow angle glaucoma** • May increase BP • Avoid in patients with substantial alcohol use or evidence of chronic liver disease • Avoid if CRCL < 30ml/min and in hepatic impairment	C; D in the 3rd trimester	• More lethal in overdose (with other drugs & alcohol) than SSRIs but not as lethal as TCAs • Contra-indicated concomitant use with MAOIs within two weeks of therapy • Duloxetine contraindicated with thioridazine • Avoid concomitant use with sibutramine, cimetidine, alcohol, Triptans, tramadol, Serotonergic agents, valerian, st.john's wort, SAMe and kava kava • Avoid concomitant use of venlafaxine with trifluoperazine or weight loss agents • Avoid concomitant use of duloxetine with fluvoxamine or Quinolones • Use with caution with either warfarin or NSAID with duloxetine	• Response rate: mild depression = 4-8 weeks; Moderate depression = 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • Efficacy of duloxetine for diabetic peripheral neuropathy has been established by two controlled studies where patients reported a 30% sustained reduction in pain • Duloxetine approved for use in diabetic peripheral neuropathy and fibromyalgia • May consider in the management of PTSD
Venlafaxine IR (Effexor IR)	• Initial adult dose is 25mg TID or 37.5mg BID • Max adult dose/day = 375mg • Initial geriatric dose = 25mg QD	• Take with food • Possibly fewer CYP450 interactions • BID or TID dosing • Generic	• May increase BP at higher doses • Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 ml/min • Venlafaxine has a higher rate of nausea, vomiting and discontinuation due to adverse effects than the SSRIs	C		

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for SNRIs	Efficacy for SNRIs
Venlafaxine XR (Effexor XR)	• Initial adult dose = 75mg QD • Max adult dose/day = 225mg • Initial geriatric dose = 37.5mg QD	• XR version administered QD • Possibly fewer CYP450 interactions • XR capsule dose may be swallowed whole or opened and sprinkled on apple sauce followed by a glass of water • Approved for use in generalized anxiety disorder, social anxiety and panic disorder • Take with food	• May increase BP at higher doses • Expensive • Reduce dose by 50% if hepatic impairment or if CRCL = 10-70 ml/min • Venlafaxine has a higher rate of nausea, vomiting and discontinuation due to adverse effects than the SSRIs	C	• Taper dose slowly to prevent clinically significant discontinuation symptoms	
Dual action drugs which are Serotonin and Norepinephrine Reuptake inhibitors. SSRIs, SNRIs, bupropion, mirtazapine are first-line therapy for adults with MDD. Possible efficacy in cases not responsive to TCAs or SSRIs. Reduce dose for the elderly. Start with lowest dose which may be effective but others may require gradual titration. Comparable to SSRIs at low dose.						

Monitoring, Referrals and Warnings: Monitor blood pressure regularly especially when initiating and titrating the dose. Monitor for hyponatremia. Monitor BUN, CR, transaminases and glucose in duloxetine. Monitor cholesterol in venlafaxine.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Closely monitor for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) (cont.)

SNRIs Adverse Drug Effects: Relative Comparisons									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Duloxetine	0	0/+	0/+	0/+	+++	0	0/+	+++	0/+
Venlafaxine	0	0	0	0/+	+++	0	0	+++	+++

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

SNRIs	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	May be useful for some of the behavioral symptoms	Not in CPG but may be useful as a prophylaxis	Not in CPG but can be used	Very effective first line treatment	Very effective first-line treatment	May be beneficial for neuropathic pain	Help with sobriety in instances where comorbid depressive symptoms are effectively targeted
Cons	During titration phase of treatment, may increase anxiety, nightmares and fatigue	No Additional	During titration phase of treatment, may increase anxiety, nightmares and fatigue	During titration phase of treatment, may increase anxiety, nightmares and fatigue	During titration phase of treatment, may increase anxiety, nightmares and fatigue	When used in conjunction with Opioids, sexual side effects may be even more pronounced	No Additional

Serotonin 2A Antagonist Reuptake Inhibitors (SARIs)						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for SARIs**	**Efficacy for SARIs**
Nefazodone (Formerly known as Serzone)	• Initial adult dose = 100mg BID • Max adult dose/day = 600mg • Initial geriatric dose = 50mg BID • Max geriatric dose/day = 400mg	• Minimal to no anticholinergic effects • Minimal to no orthostatic hypotension	• Avoid using in hepatic disease • Rare reports of priapism have occurred	C	• No serious systemic toxicity from OD • Nefazodone contraindicated with MAOIs, pimozide, carbamazepine, alcohol, eplerenone and Benzodiazepines including alprazolam and triazolam • Monitor digoxin levels with digoxin used concomitantly with nefazodone • Trazodone patients avoid concomitant use with MAOIs, sibutramine, alcohol, gingko biloba, valerian, st. john's wort, SAMe and kava kava • Use caution combining trazodone with SSRIs or other Serotonergic agents due to the possibility of serotonin sickness	• Response rate = mild depression 4-8 weeks; Moderate depression = 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • May consider in the management of PTSD • Trazodone: may dose prn in insomnia

Serotonin 2A Antagonist Reuptake Inhibitors (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for SARIs	Efficacy for SARIs
Trazodone (Formerly known as Desyrel)	• Initial adult dose for sleep: 25-50mg QHS • Initial adult dose = 50mg TID • Max adult dose/day = 600mg • Initial geriatric dose = 25-50mg QHS	• Causes fewer anticholinergic effects than TCAs • Trazodone has an unlabeled use in insomnia • Multiple trials confirm trazodone's effectiveness for the treatment of insomnia • Administer after meals to prevent light-headedness and postural hypotension • Generic	• May cause priapism including cases which have resulted in permanent dysfunction • Trazodone is not recommended for use during the initial recovery phase of an MI • If used for sleep, start with a low dose and closely monitor the patient	C	• Can interact with agents that decrease arousal, impair cognitive performance and interact with adrenergic agents that regulate blood pressure • Taper dose slowly to prevent clinically significant discontinuation symptoms	
Reduce the dose for the elderly. Start with the lowest dose with gradual titration. Use Trazodone with caution in cardiovascular patients, seizure disorder and the elderly.						

Monitoring, Referrals and Warnings: Perform WBC and differential counts if the patient develops a fever, sore throat or other signs of infection on trazodone therapy. Warn patients of the impaired abilities to perform activities that require mental alertness.

Nefazodone: monitor for signs and symptoms of liver dysfunction and consider routine LFT monitoring.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Closely monitor for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Cases of life-threatening hepatic failure have been reported in patients treated with nefazodone. Treatment should not be started in individuals with active liver disease or with elevated baseline abnormalities. Advise patients to be alert for signs and symptoms of liver disease (jaundice, anorexia, GI complaints and malaise) and report these symptoms immediately if they occur.

Serotonin 2A Antagonist Reuptake Inhibitors (cont.)

SARIs Adverse Drug Effects: Relative Comparisons									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Nefazodone	0	+++	0	0/+	++		0/+	0/+	+++
Trazodone	0	+++	0	0/+	++	0	+	+	++

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

SARI	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Helps with sleeping and non habit forming	Helps with sleep and not habit forming	Helps with sleep	Helps with sleep	Useful adjunct agent to SSRI in targeting neuro-vegitative symptoms of depression	No Additional	Not habit forming
Cons	No Additional	May increase headaches	No Additional	No Additional	No Additional	With Opioid, may further reduce sex drive	No Additional

Noradrenergic & Specific Serotonin Antidepressants (NaSSAs)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for NaSSAs	Efficacy for NaSSAs
Mirtazapine (Remeron)	• Initial adult dose = 15mg QHS • Max adult dose/day = 45mg QHS • Initial geriatric dose = 7.5mg QHS	• QHS dosing due to sedation • May be taken without regard to meals • Used as a treatment option for patients who have experienced intolerable sexual side effects from other antidepressants since it is unlikely to cause sexual dysfunction • SolTab is formulated to dissolve on the tongue without water. Immediately remove SolTab from blister pack and administer	• Significant sedation and weight gain makes this a difficult class for primary treatment of depression	C	• No serious systemic toxicity from OD • Contraindicated with MAOIs within 14 days of therapy • Avoid concomitant use with MAOIs, alcohol, sibutramine, valerian, st. john's wort, SAMe and kava kava	• Response rate = mild depression 4-8 weeks; Moderate = depression 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • May consider in the management of PTSD

SSRIs, SNRIs, bupropion, mirtazapine are first line therapy for adults with Major Depressive Disorder (MDD). Use with caution in seizure disorder, elderly patients, hepatic or renal impairment. Adjust dose in CRCL < 40ml/min. Use with caution in hepatic impairment. Start with lowest dose with gradual titration.

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Monitoring, Referrals and Warnings: Monitor for signs of agranulocytosis, neutropenia, sore throat, infection and lipid profile. Warn patients of the impaired abilities to perform activities that require mental alertness.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Closely monitor for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Noradrenergic & Specific Serotonin Antidepressants (cont.)

NaSSAs Adverse Drug Effects									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Mirtazapine	0	+++	0/+	0	0/+	0	+++	0	0/+

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

NaSSAs	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Useful with sleep and not habit forming	Useful with sleep and not habit forming	Useful with sleep and not habit forming	Useful with sleep and not habit forming	Useful adjunct agent to SSRI in targeting neuro-vegitative symptoms of depression	No Additional	No Additional
Cons	No Additional	No Additional	No Additional	No Additional	No Additional	When used in conjunction with Opioids, sexual side effects may be even more pronounced	No Additional

Dopamine and Norepinephrine Reuptake Inhibitors (DNRIs)						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for DNRIs**	**Efficacy for DNRIs**
Bupropion IR (Wellbutrin IR)	• Initial MDD adult dose = 100mg BID • Max MDD adult dose/ day =450mg • Initial MDD geriatric dose = 37.5mg BID	• Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other Antidepressants • May be taken without regard to meals • Generic	• **Contraindications include seizure disorder, anorexia, bulimia, patients undergoing abrupt discontinuation of ethanol or sedatives (including Benzodiazepines) and patients receiving other forms of bupropion** • Avoid bedtime dosing • May be more stimulating than other antidepressants so the last dose should be taken by 5 pm	C	• In higher doses may induce seizures in persons with seizure disorders or eating disorders; Seizure risk is dose dependent and increased when used in combination with other drugs that lower the seizure threshold • Contraindicated with MAOIs and ritonavir • Avoid concomitant use with alcohol, linezolid, valerian, st. john's wort, SAMe and kava kava • Also avoid use with meds that lower the seizure threshold such as other Antidepressants, Antipsychotics, Steroids and theophylline	• Response rate: mild depression = 4-8 weeks. Moderate depression = 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • May consider in the management of PTSD
Bupropion SR (Wellbutrin SR)	• Initial MDD adult dose = 150mg QD • Max MDD adult dose/ day = 400mg • Initial MDD geriatric dose = 100mg QD • Initial smoking cessation dose = 150mg QD X 3 days then 150mg BID for 7-12 weeks	• Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other Antidepressants • May be taken without regard to meals • Do not crush, chew or divide the tablet • Generic	• **Contraindications include seizure disorder, anorexia, bulimia, patients undergoing abrupt discontinuation of ethanol or sedatives (including Benzodiazepines) and patients receiving other forms of bupropion** • Avoid bedtime dosing • May be more stimulating than other antidepressants so the last dose should be taken by 5 pm	C		

Dopamine and Norepinephrine Reuptake Inhibitors (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for DNRIs	Efficacy for DNRIs
Bupropion XL (Wellbutrin XL)	• Initial MDD adult dose = 150mg QD • Max MDD adult dose/ day = 450mg QD	• Used as an alternative for patients who have experienced intolerable sexual side effects or weight gain from other Antidepressants • May be taken without regard to meals • Do not crush, chew or divide the tablet • Generic	• **Contraindications include seizure disorder, anorexia, bulimia, patients undergoing abrupt discontinuation of ethanol or sedatives (including Benzodiazepines) and patients receiving other forms of bupropion** • Avoid bedtime dosing • May be more stimulating than other antidepressants so the last dose should be taken by 5 pm • XL dose is in a non-absorbable shell that slowly releases and it may appear in the stool as a tablet	C	• Avoid concurrent use of Wellbutrin with Zyban (same active ingredient)	• Buproprion has been effective in treating neuropathic pain and tobacco cessation

SSRIs, SNRIs, bupropion, mirtazapine are first line therapy for adults with MDD. Bupropion is approved for use as an adjunct in smoking cessation and Seasonal Affective Disorder. Do not use if there is a history of renal or hepatic failure or severe head trauma. Increase dose gradually to decrease risk of seizures. Requires dose titration. Can work in TCA non-responders. Reduce dose for the elderly and hepatic impairment. Use with caution in patients with cardiovascular disease, hepatic or renal insufficiency and in the elderly. When converting from the IR tablet to the SR or XL tablet, administer the same total daily dosage when possible. Wellbutrin contains the same active ingredient as Zyban. Insomnia may be minimized by avoiding bedtime doses.

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Monitoring, Referrals and Warnings: Monitor weight. Monitor BP and HR when administering concomitantly with transdermal nicotine.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Closely monitor for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Dopamine and Norepinephrine Reuptake Inhibitors (cont.)

DNRIs Adverse Drug Effects									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Bupropion	0	0	0	0	++	+++	0	0	0/+

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

DNRIs	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Helpful in targeting symptoms of attention and concentration	No Additional	No Additional	Effective in targeting co-occurring depressive symptoms	Effective in targeting depressive symptoms	No Additional	Not habit forming and used for tobacco cessation
Cons	Slight increased risk of seizures	No Additional	May worsen insomnia	May worsen insomnia	May worsen insomnia	No Additional	No Additional

Tricyclic Antidepressants (TCAs)						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for TCAs**	**Efficacy for TCAs**
Amitriptyline (Formerly known as Elavil or Endep)	• Initial adult dose = 50mg QHS up to TID • Max adult dose/day = 300mg • Initial geriatric dose = 10-25mg Qhs	• May use in mTBI patients for headache or for sleep • Generic	• **Contraindications include acute recovery phase following MI** • Adverse Side Effects: cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), anticholinergic (constipation, dry mouth, blurred vision, urinary retention, increased intraocular pressure), sedation, weight gain, sexual dysfunction, and decreased seizure threshold • Amitriptyline and doxepin have a higher probability of weight gain than other TCAs • Higher doses may be required for smokers taking Amitriptyline due to increased metabolism	C	• Lethal in OD • Contraindicated with MAOIs within past 14 days of therapy • Bupropion, Haloperidol and SSRIs may increase the TCA's level which may increase pharmacologic and adverse effects. Wait 5 weeks after discontinuing fluoxetine before starting a TCA • Quinolones (Gatifloxacin, Moxifloxacin) if used with TCA's may cause QT prolongation and may increase the risk of life-threatening cardiac arrhythmias • Quinolones (Grepafloxacin, Sparfloxacin) if used with TCAs have an increased risk of life-threatening arrhythmias including torsades de pointes	• Response rate = mild depression 4-8 weeks; Moderate depression = 8-12 week; Severe depression = augmentative strategies, concurrent administration of adjuncts (referral to specialist) • Recommended as monotherapy as second-line therapy in PTSD • Amitriptyline has fair documentation for efficacy in use for fibromyalgia • Good evidence exists from multiple well-designed clinical trials that amitriptyline has medium to high efficacy in the prevention of migraines

Tricyclic Antidepressants (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for TCAs	Efficacy for TCAs
Imipramine (Tofranil)	• Initial adult dose = 25mg QD to QID • Max adult dose/day = 300mg • Initial geriatric dose = 10mg-25mg Qhs	• Consider using to ameliorate the symptoms of Acute Stress Disorder (ASD) • Consider using for hyperarousal, excessive arousal and panic attacks for up to 7 days • Therapeutic plasma concentrations can be used to guide treatment • Therapeutic levels for depression (in conjunction with psychiatry consultation): 200-350 ng/ml • Generic	• **Contraindications include acute recovery phase following MI** • Adverse Side Effects: cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), anticholinergic (constipation, dry mouth, blurred vision, urinary retention, increased intraocular pressure), sedation, weight gain, sexual dysfunction, and decreased seizure threshold	D	• Contraindicated use with desipramine and thioridazine • Slow system clearance	• Doses typically are lower for migraine treatment than for depression treatment • Nortriptyline has been used in clinical studies for smoking cessation
Nortriptyline (Pamelor) (Formerly known as Aventyl)	• Initial adult dose = 25mg TID – QID • Max adult dose/day = 150mg • Initial geriatric dose = 10-25mg Qhs	• Secondary amine – lower orthostatic hypotension and sedation than other TCAs • Equal efficacy and fewer side effects than the parent tertiary amines (Amitriptyline and Imipramine)	• **Contraindications include acute recovery phase following MI** • Adverse Side Effects: cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), anticholinergic (constipation, dry mouth, blurred vision, urinary retention, increased intraocular pressure), sedation, weight gain, sexual dysfunction, and decreased seizure threshold	D		

Tricyclic Antidepressants (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for TCAs	Efficacy for TCAs
Desipramine (Norpramin)	• Initial adult dose = 25mg TID or 75mg QD • Max adult dose/day = 300mg • Initial geriatric dose = 10mg-25mg Qhs	• Therapeutic plasma concentrations can be used to guide treatment • Therapeutic levels (in conjunction with psychiatry consultation): 125-300 ng/ml • Generic • Secondary amine – lower orthostatic hypotension and sedation than other TCAs • Equal efficacy and fewer side effects than the parent tertiary amines (Amitriptyline and Imipramine)	• **Contraindications include acute recovery phase following MI** • Adverse Side Effects: cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), anticholinergic (constipation, dry mouth, blurred vision, urinary retention, increased intraocular pressure), sedation, weight gain, sexual dysfunction, and decreased seizure threshold	C	• Avoid concomitant use with clonidine, levodopa, Quinolones, guanethidine, alcohol, valerian, st. john's wort, kava kava, nilotinib, sibutramine, tetrabenazine, thioridazine and ziprasidone	

Tricyclic Antidepressants (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for TCAs	Efficacy for TCAs
Doxepin (Sinequan)	• Initial adult dose = 25 – 75mg QHS or BID • Max adult dose/day = 300mg • Use lower dose in the elderly and increase gradually	• Approved for use in anxiety. • Generic	• **Contraindications include urinary retention, narrow angle glaucoma and acute recovery phase following MI** • Adverse Side Effects: cardiovascular (orthostatic hypotension, syncope, tachycardia, arrhythmias), anticholinergic (constipation, dry mouth, blurred vision, urinary retention, increased intraocular pressure), sedation, weight gain, sexual dysfunction, and decreased seizure threshold • Amitriptyline and doxepin have a higher probability of weight gain than other TCAs	C		• TCAs are considered to be the drug of choice by some clinicians for symptomatic relief of neuropathic pain (postherpetic neuralgia) • Doxepin is approved for use in anxiety associated with alcoholism

Administer at bedtime to reduce daytime sedation. Therapy should not be abruptly discontinued in patients receiving high doses for prolonged periods of time. Start with lowest dose with gradual titration. Use a lower dose and slower titration for hepatic disease. May alter glucose control, use caution in diabetics. Nortriptyline and desipramine have equal efficacy and fewer side effects than amitriptyline, imipramine and doxepin. Highest response rates with amitriptyline, imipramine and doxepin. Photosensitivity may occur. May be used in insomnia.

Use with caution in the elderly and use nortriptyline or desipramine first. Avoid using amitriptyline, imipramine and doxepin in the elderly but reduce the dose if necessary. Avoid use in glaucoma, urinary retention, cardiovascular disease, patients at risk for suicide and patients with cognitive impairment.

Clinical Pearl: if combining SSRI's and TCA's then add TCA's to SSRI's and not vice-versa.

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Monitoring, Referrals and Warnings: Consider baseline ECG and monitoring of QT intervals. Monitor weight, BP, pulse, prior to and during initial therapy. Monitor ECG in older adults and those with cardiac disease. If using the TCAs for depression then consider a specialty consultation. Obtain blood levels for compliance. Monitor blood levels after one week of treatment for depression. Draw blood sample 10-12 hours after last dose. Monitor for signs of infection and obtain a CBC if fever or sore throat occurs.

Black Box Warning: Antidepressants increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Appropriately monitor and closely observe for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with Antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with Antidepressants compared to placebo in adults aged 65 and older.

Tricyclic Antidepressants (cont.)

TCAs Adverse Drug Effects: Relative Comparisons									
Medication Name	**Anticholinergic Activity (muscarinic)**	**Sedation**	**Orthostatic Hypotension**	**Cardiac Effects**	**GI Effects**	**Seizures**	**Weight Gain**	**Sexual Dysfunction**	**Mood Changes During Titration or Abrupt Discontinuation**
Amitriptyline	+++	+++	+++	+++	0/+	++	++	++	0
Imipramine	++	++	++	+++	0/+	++	++	++	0/+
Nortriptyline	+	+	+	++	0/+	+	+	++	0
Desipramine	+	0/+	+	++	0/+	+	+	++	0
Doxepin	++	+++	++	+++	0/+	++	++	++	0

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

TCAs	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Effective in treating anxiety and sleep problems Not habit forming	Useful as prophylactic. Desipramine and nortriptyline have less systemic side effects than amitriptyline, imipramine and doxepin	Effective in treating anxiety and sleep problems Not habit forming	Effective in targeting co-occurring depressive symptoms	No Additional	Useful in chronic neuropathic pain Not habit forming	Not habit forming
Cons	May increase cognitive symptoms	No Additional	No Additional	No Additional	Serious toxicity with overdose	May worsen constipation, especially when used with Opioids	Serious toxicity with overdose

Opioid Agonist Therapy (OAT) for Opioid Dependence						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for OAT**	**Efficacy for OAT**
Methadone (Dolophine, Methadose)	• Specialty consultation advised • Titrate carefully, consider methadone's delayed cumulative effects • Individualize dosing regimens (AVOID the same fixed dose for all patients)	• Give orally in a single daily dose • FDA approved for detoxification treatment and maintenance treatment of Opioid dependence in conjunction with appropriate social and medical services	• **Contraindications include any situation where Opioids are contraindicated, such as patients with respiratory depression (in the absence of resuscitative equipment or in unmonitored situations) and patients with acute bronchial asthma or hypercarbia and known or suspected paralytic ileus** • May prolong QTc intervals on ECG; Risk of cardiac arrhythmias • Discontinue or taper the methadone dose and consider an alternative therapy if the QTc > 500ms • Plasma half-life may be longer than the analgesic duration • Delayed analgesia or toxicity may occur because of drug accumulation after repeated doses, e.g., on days 2 to 5; If patient has excessive sedation during this timeframe, consider temporarily holding dose(s), lowering the dose, and/or slowing the titration rate	C/D	• Serious overdose and death may occur if benzodiazepines, sedatives, tranquilizers, antidepressants, alcohol or other CNS depressants are taken in addition • Avoid concurrent use of methadone with nilotinib, tetrabenazine, ziprasidone, alcohol, st. johns wort, valerian, kava kava and grapefruit juice • Methadone contraindicated with selegiline	• Methadone is FDA approved for the management of moderate to severe pain

Opioid Agonist Therapy (OAT) for Opioid Dependence (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for OAT	Efficacy for OAT
Buprenorphine (Subutex)	• Specialty consultation advised • Individualize dosing regimens	• FDA approved for management of Opioid dependence	• Major Adverse Effects: hepatitis, hepatic failure and respiratory depression (usually when misused intravenously with other CNS depressants) • Common Adverse Effects: headache, pain, abdominal pain, insomnia, nausea, vomiting, sweating and constipation • Tablets should be placed under tongue until dissolved.;Tablets should not be swallowed • Dose should not be started until effects of withdrawal are evident	C	• Avoid concurrent use of buprenorphine with alcohol, st. johns wort, valerian and kava kava	
Buprenorphine/ Naloxone (Suboxone)	• Specialty consultation advised • Individualize dosing regimens	• FDA approved for management of Opioid dependence • Combination product recommended for maintenance therapy not initial treatment • Tablets contain either 2mg buprenorphine /0.5mg naloxone or 8mg buprenorphine /2mg naloxone • Addition of naloxone is intended to decrease the potential for parenteral abuse	• Major Adverse Effects: hepatitis, hepatic failure and respiratory depression (usually when misused intravenously with other CNS depressants) • Common Adverse Effects: headache, pain, abdominal pain, insomnia, nausea, vomiting, sweating and constipation • Tablets should be placed under tongue until dissolved; Tablets should not be swallowed. Drinking warm fluids prior to administration may aid in dissolution	C		

Opioid Agonist Therapy (OAT) for Opioid Dependence (cont.)

Specialty consultation advised. Methadone or sublingual buprenorphine/naloxone maintenance are first line therapy due to documented efficacy in improving retention and reducing illicit Opioid use and cravings.

Consider appropriate adjustment of Opioid agonist doses to maintain a therapeutic range between signs/symptoms of overmedication (e.g., somnolence, miosis, itching, hypotension, and flushing) and Opioid withdrawal (e.g., drug craving, anxiety, dysphoria, and irritability). Opioid antagonists may precipitate withdrawal. Store in a secure place out of the reach of children. Abrupt cessation may precipitate withdrawal.

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Monitoring, Referrals and Warnings: Consider baseline ECG and physical examination for methadone patients at risk for QT prolongation or arrhythmias. Perform baseline liver transaminases for buprenorphine or buprenorphine/naloxone therapy. Drug testing for both methadone and buprenorphine should also be considered to ensure compliance with the prescription and for detection of possible diversion. Relapse monitoring to promote effective outcomes. Monitor respiratory status, mental status and blood pressure.

Methadone Black Box Warning: Deaths and life-threatening adverse events, including respiratory depression and cardiac arrhythmias have occurred upon initiation of treatment for Opioid dependence. Dosage should be selected carefully, titrated slowly and the patient monitored carefully. Use may prolong the QTc interval and increase the risk for torsade de pointes. May cause respiratory depression. For oral administration only. When used for treatment of narcotic addiction, it may only be dispensed by Opioid treatment programs certified by the Substance Abuse Mental Health Services (SAMHSA).

OAT	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No additional	No additional	No additional	No additional	No additional	May be used for moderate to severe pain	First line therapy for illicit Opioid use
Cons	No additional	No additional	No additional	No additional	High risk of lethal overdose	High risk of lethal overdose	High risk of lethal overdose

Opioid Antagonist Therapy for Opioid Dependence						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin**	**Efficacy**
Naltrexone (Depade, ReVia)	• Specialty consultation advised • Extended dosing intervals, using equivalent weekly doses, may be used with supervised administration	• Only the oral formulation of naltrexone is currently FDA-approved for maintenance therapy of Opioid dependence • Side effects, if any, tend to occur early in treatment and can typically resolve within 1-2 weeks after dosage adjustment • Take with food to minimize nausea especially during the first week	• **Contraindications include acute hepatitis or liver failure, current physiological dependence on Opioids with use within past 7 days, ongoing acute Opioid withdrawal or failed naloxone challenge test, receiving Opioid agonists or positive urine Opioid screen** • Common Adverse Effects: nausea • No Opioid agonist effects • Patients continue to have cravings and may thereby not be motivated to maintain adherence to the medication regimen • Patients must be fully withdrawn for up to 7-10 days before beginning naltrexone treatment • Precautions include active liver disease, severe hepatic dysfunction and severe renal failure • Naltrexone is unpopular with many Opioid dependent patients since maintenance therapy requires complete abstinence from Opioids; Treatment dropouts are common	C	• Limited clinical experience with over dosage in humans • Drug Interactions include: Opioid-containing medications, including over-the-counter (OTC) preparations, thioridazine, oral hypoglycemic and Antiretrovirals • Very large doses of Opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death • Small doses of Opioids, such as in Analgesic, Antidiarrheal, or Antitussive drugs, may be blocked by Naltrexone and fail to produce a therapeutic effect	• FDA approved for use in alcohol dependency

Opioid Antagonist Therapy for Opioid Dependence (cont.)

Consider Opioid Agonist Treatment (OAT) or long-term therapeutic community before naltrexone treatment as a first line approach for chronic Opioid dependent patients. Also, consider engagement in a comprehensive management program that includes measures to ensure medication adherence.

Monitoring, Referrals and Warnings: Specialty consultation advised. Baseline evaluation include: naloxone challenge test, transaminase levels and urine toxicology. Therapy is most effective when the patient is engaged in addiction-focused counseling with monitored administration. Repeat transaminase levels monthly for the first 3 months and every 3 months thereafter. Discontinue or reduce naltrexone if transaminase levels rise significantly. Warn patient that if signs and symptoms of acute hepatitis occur, discontinue naltrexone and contact their provider immediately.

Warn patients that attempts to overcome Opioid blockade could lead to fatal overdose. Monitor closely for suicidal thoughts and depression.

Black Box Warning: Naltrexone has the capacity to cause hepatocellular injury when given in excessive doses. Patients should be warned of the risk of hepatic injury and advised to stop the use of naltrexone and seek medical attention if they experience symptoms of acute hepatitis.

Medication Therapy for Alcohol Dependence

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin	Efficacy
Naltrexone Oral (Depade, ReVia)	• Specialty consultation advised	• Side effects, if any, tend to occur early in treatment and can typically resolve within 1-2 weeks after dosage adjustment • Take with food to minimize nausea especially during the first week	• **Contraindications include receiving Opioid agonists, physiologic Opioid dependence with use within past 7 days, acute Opioid withdrawal, failed naloxone challenge test, positive urine Opioid screen and acute hepatitis or liver failure** • Common Adverse Effects: nausea • Need at least 3-5 days of pretreatment abstinence before starting therapy • Precautions for use in active liver disease or severe renal failure	C	• Limited clinical experience with over dosage for naltrexone in humans • Drug Interactions for naltrexone include: Opioid-containing medications, including over-the-counter (OTC) preparations, thioridazine, oral Hypoglycemic and Antiretrovirals • Very large doses of Opioids may overcome the effects of naltrexone and lead to serious injury, coma, or death	• Naltrexone is also FDA approved for use in Opioid dependency

Medication Therapy for Alcohol Dependence (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin	Efficacy
Naltrexone Inj (Vivitrol)	• Specialty consultation advised	• Pretreatment abstinence is not required but improves response • Once monthly IM injections	• **Contraindications include receiving Opioid agonists, physiologic Opioid dependence with use within the past 7 days, acute Opioid withdrawal, failed naloxone challenge, positive urine Opioid screen, acute hepatitis or liver failure and inadequate muscle mass** • Major Adverse Effects: Eosinophilic pneumonia, depression and suicidality • Common Adverse Effects: Injection-site reactions, nausea, headache and asthenic conditions • Precautions for use in active liver disease or moderate to severe renal Insufficiency • Potential injection site reactions • Discontinue IM naltrexone if there is NO detectable benefit within 3 months	C	• Small doses of Opioids, such as in Analgesic, Antidiarrheal, or Antitussive drugs, may be blocked by naltrexone and fail to produce a therapeutic effect	

Medication Therapy for Alcohol Dependence (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin	Efficacy
Acamprosate (Campral)	• Specialty consultation advised	• May be taken without regard to meals however administration with meals may improve compliance • Tablets should be swallowed whole, do not chew or crush	• **Contraindications include severe renal impairment (CrCl ≤ 30 mL/min)** • Major Adverse Effects: suicidality • Common Adverse Effects: diarrhea • Abstinence at treatment initiation and during treatment • Do not administer to patients with severe renal impairment	C	• Avoid disulfiram if alcohol intoxicated • Avoid concurrent use of disulfiram with alcohol in food such as sauces, vinegars or beverages, and medications such as cough syrup	
Disulfiram (Antabuse)	• Specialty consultation advised	• Can be used in alcohol dependence combined with cocaine • Can be used with failure of or contraindication to naltrexone therapy • Used in one who has the capacity to appreciate risks and benefits and to consent to treatment • More effective with monitored administration (e.g., in clinic or with spouse or probation officer)	• **Contraindications include severe cardiovascular, respiratory, or renal disease, severe hepatic dysfunction (i.e., transaminase levels > 3 times upper limit of normal or abnormal bilirubin), severe psychiatric disorders, especially psychotic and cognitive disorders and suicidal ideation, poor impulse control and metronidazole or ketoconazole therapy which already induce a similar reaction to alcohol or hypersensitivity**	C		

Medication Therapy for Alcohol Dependence (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin	Efficacy
(cont.) Disulfiram (Antabuse)			• Major Adverse Effects: hepatotoxicity, peripheral neuropathy, psychosis, delirium and severe disulfiram ethanol reaction • Common Adverse Effects: somnolence, metallic taste and headache • Abstinence > 24 hours and BAL equal to 0			
Success is enhanced by engagement in a comprehensive management program that includes psychosocial therapy. Naltrexone po or IM or acamprosate should be routinely considered when treating alcohol dependence with addiction counseling. Disulfiram should only be used when abstinence is the goal. Compliance improves when disulfiram administration is directly observed. Inform the patient to use caution when operating vehicles and hazardous machinery since disulfiram may cause sedation.						

Monitoring, Referrals and Warnings: Naltrexone: Oral and IM baseline evaluation include liver transaminase, bilirubin and urine beta-HCG for females. Naltrexone IM also should have baseline CR levels drawn. Repeat naltrexone liver transaminase levels at 6 and 12 months and then every 12 months thereafter. Naltrexone IM may cause allergic pneumonia, monitor appropriately. Monitor for signs and symptoms of acute hepatitis occur, discontinue naltrexone if signs appear and contact provider immediately. Patients who have previously used Opioids may be more sensitive to toxic effects of Opioids after discontinuation of naltrexone.

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Disulfiram: If the patient consumes alcohol with disulfiram then a disulfiram-alcohol reaction will occur and may persist for 30 minutes to several hours afterwards. Reaction can include flushing, throbbing in the head or neck, nausea, vomiting, sweating, chest pain, palpitation, tachycardia, hypotension, syncope, weakness, vertigo, blurred vision and confusion. Severe reactions include respiratory depression, cardiovascular collapse, arrhythmias, MI, convulsions and death. Warn patients accordingly. Family members should not administer disulfiram without informing the patient. Provide patients with wallet cards that indicate the use of disulfiram.

Monitor closely for suicidal thoughts and depression.

Black Box Warning: Black box warnings exist for naltrexone and disulfiram. See prescribing information for specific warnings.

Opioid Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Opioid**	**Efficacy for Opioid**
Morphine IR (Morphine IR, Roxanol)	• Initial dose = 10 to 30mg q 4 hour • Titration: individually titrate as needed and tolerated	• Available as oral solution • Available as rectal suppository	• **Contraindications include respiratory depression in the absence of resuscitative equipment, acute or severe bronchial asthma or hypercarbia and known or suspected paralytic ileus**	C	• Serious potential for overdose in the Opioid novice, use with caution and with gradual dose increase. Start with the lowest dose possible • All Opioids are contraindicated in patients who have received MAOIs within 14 days • Morphine has active metabolites (M3G and M6G) which may accumulate in renal impairment and contribute to toxic effects	• Long acting Opioids are effective for continuous, chronic pain • Opioids are highly effective in pain management • Methadone is FDA approved for the detoxification treatment of Opioid addiction; If used in detoxification, then it must be used as part of an FDA approved program
Morphine Controlled Release (CR), Sustained Release (SR), (MS Contin, Oramorph SR); Extended Release (ER) (Avinza, Kadian)	• Initial dose = 15mg q8-12 hours (CR/SR) • Initial dose = 30mg Q24h (ER) • Titration: total daily increments of < 30-40mg/day may be made Q 2 days • Avinza = maximum of 1600mg per day	• Preferred first-line long-acting agent because of similar efficacy to other long-acting Opioids, comparable safety profile, provider familiarity with its use and lower cost • Controlled-release tablets should be swallowed whole, not broken, chewed, or crushed	• **Contraindications include respiratory depression in the absence of resuscitative equipment, acute or severe bronchial asthma or hypercarbia and known and suspected paralytic ileus**	C		

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
(cont.) Morphine Controlled Release (CR), Sustained Release (SR), (MS Contin, Oramorph SR); Extended Release (ER) (Avinza, Kadian)		• For patients who have difficulty swallowing, SR and ER capsules may be opened and the pellets may be sprinkled onto a small amount of soft food (such as apple sauce); The mixture should be taken within 30 minutes of sprinkling. The pellets must not be chewed or crushed, and the mouth should be rinsed to ensure that all pellets have been swallowed • Avinza: 24-hour extended release capsules			• Use extreme caution using Opioids in patients with conditions accompanied by hypoxia, hypercapnia, or decreased respiratory reserve • Avinza: due to fumaric acid content, doses above 1600 mg may result in serious renal toxicity	

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
Codiene: used alone or in combination with Aspirin (ASA) or Acetaminophen (APAP); (Tylenol with Codeine)	• Initial dose = 30mg q 4 to 6 hours. • Titration: Increase dose as needed and tolerated to a maximum of 360mg/day of codeine (4000mg/day maximum of APAP; 2000mg/day maximum of APAP in chronic alcoholics) • Ceiling effect occurs at doses > 60mg/dose	• Codeine in combination with APAP or ASA is a more effective Analgesic than codeine alone since codeine alone is a weak analgesic	• **Contraindications include respiratory depression, acute or severe bronchial asthma, hypercarbia and paralytic ileus** • May cause elevated plasma amylase and lipase due to spasm of sphincter of Oddi	C	• Ultra-rapid CYP2D6 metabolizers may convert codeine into morphine more rapidly and completely than others, resulting in higher than expected serum morphine levels and possible overdose symptoms • Use extreme caution and frequent monitoring in patients receiving transdermal fentanyl and any CYP3A4 inhibitor	
Fentanyl transdermal patch (Duragesic)	• Initial dose = 25mcg/h transdermally q 72h • Titration: Increments should be based on supplemental Opioid doses, using a ratio of 12mcg/h transdermal fentanyl for every 45mg/24 h of supplemental oral morphine equivalent • Make dose increases at least 3 days after initial dose then not more often than q 6 days thereafter as necessary	• Treatment for chronic persistent pain. Do not use post-op or for acute pain • Consider in patients with persistent, moderate to severe pain who cannot take oral long acting morphine or methadone • The use entails special safety considerations. All prescribers should be thoroughly familiar with the product's prescribing information	• **Contraindications include patients who are not Opioid tolerant, management of acute pain or for short-term treatment, management of post-op pain, mild pain, or intermittent pain, significant respiratory depression (especially in unmonitored settings), acute or severe bronchial asthma and known or suspected paralytic ileus**	C		

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
(cont.) Fentanyl transdermal patch (Duragesic)		• Patients must receive a copy of the Medication Guide • In order to avoid any confusion, always write fentanyl in mcg/hr	• Should not be used in patients particularly susceptible to intracranial effects of CO2 retention (increased intracranial pressure, impaired consciousness, coma) • Fentanyl patches should **only** be used in patients who are already receiving Opioid therapy, are Opioid-tolerant, and require a daily dose at least equivalent to fentanyl 25mcg/hour • Avoid application of external heat sources (e.g., heating pads, electric blankets, heat lamps, saunas, hot tubs, hot baths, sunbathing, or heated water beds) to the application site while the patch is worn as heat may increase the release of fentanyl; Monitor for Opioid adverse effects and adjust dosage as necessary		• Do not administer Opioid agonist/antagonist Analgesics (pentazocine, nalbuphine, butorphanol) or partial agonists (buprenorphine) to a patient who is receiving a course of therapy with a pure agonist Opioid Analgesic since it may precipitate withdrawal symptoms • Avoid concomitant use with valerian, st. john's wort and kava kava	

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
(cont.) Fentanyl transdermal patch (Duragesic)			• Do not cut or alter the patch which could result in over dosage • If leakage of the fentanyl gel occurs then wash any skin that has come in contact with the gel with copious amounts of water only. Do not use soap or alcohol			
Oxycodone (Oxycodone IR) alone or in combination with APAP (Percocet) or ASA (Percodan)	• Initial dose = 5mg q 6 hours • Titration: Increase dose as needed and tolerated • For combination products, maximum daily dose is limited by APAP or ASA content (4000mg/ day for both; 2000mg/ day APAP in chronic alcoholics)	• Also available as oral solution	• **Contraindications include any situation where Opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations), acute bronchial asthma, hypercarbia and known or suspected paralytic ileus**	B		

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
Oxycodone CR (Oxycontin)	• Initial dose = 10 mg orally q 12 hour • Titration: May increase to 20 mg q 12 hours after 1 or 2 days • Thereafter, the total daily dose may be increased by 25% to 50% of the current dose every 1 or 2 days	• Recommended for patients who experience intolerable, unmanageable adverse effects to long acting morphine and to methadone • Controlled-release tablets should be swallowed whole and not broken, chewed or crushed	• **Contraindications include any situation where Opioids are contraindicated, such as patients with significant respiratory depression (in absence of resuscitative equipment or unmonitored situations), acute bronchial asthma, hypercarbia and known or suspected paralytic ileus**	B		
Hydrocodone (in combination with APAP or ASA or Ibuprofen); (Vicodin, Lorcet, Lortab, Ibudone, Reprexain, Vicoprofen)	• Initial dose = 5 to 10 mg q 4 to 6 hours • Titration: Increase dose as needed and tolerated • Maximum dose = 60mg/day (4000 mg/day of APAP; 2000 mg/day of APAP in chronic alcoholics) for hydrocodone + APAP combination • Max dose of 37.5mg/day (1000mg/day of ibuprofen) for hydrocodone and ibuprofen combination	• Combination product of a C3 narcotic with either APAP or ASA or Ibuprofen	• Dosing limit due to acetaminophen content	C		

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
Oxymorphone (Opana)	• Initial dose = 10 to 20mg q 4 to 6 hours (may start at 5mg to improve tolerability) • Titration: Individually titrate as needed and tolerated	• Must be taken on an empty stomach at least 1 hour before or 2 hours after a meal; Food has been shown to increase peak levels by 38%	• **Contraindications include hypersensitivity to morphine analogs such as codeine, respiratory depression (except in monitored settings and in the presence of resuscitative equipment), acute or severe bronchial asthma, hypercarbia, known or suspected paralytic ileus and patients with moderate to severe hepatic impairment**	B	• Oxymorphone is contraindicated with alcohol	
Oxymorphone ER(Opana ER)	• Initial dose = 5mg orally every 12 h • Titration: May increase by 5 to 10mg every 12 hours every 3–7 day	• Must be taken on an empty stomach at least 1 hour before or 2 hours after a meal; Food has been shown to increase peak levels of oxymorphone ER by 50%	• **Contraindications include hypersensitivity to morphine analogs such as codeine, respiratory depression (except in monitored settings and in the presence of resuscitative equipment), acute or severe bronchial asthma, hypercarbia, known or suspected paralytic ileus and patients with moderate to severe hepatic impairment**	B		

Opioid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Opioid	Efficacy for Opioid
Methadone (Dolophine, Methadose)	• Initial dose = 2.5 to 10mg orally q 8 to 12 hours. • More frequent administration (q 6 hours) may be necessary during initiation to maintain analgesia. Use extreme caution to avoid over dosage due to long plasma half-life • Titration: Increments of 2.5mg q 8 hours may be made every 5 to 7 days • **Start low and go slow**	• Recommended first- or second-line long-acting agent, but prescribers of methadone should be thoroughly familiar with its complex pharmacokinetic and pharmacodynamic properties or consult a clinician with experience in dosing methadone • The only long-acting Opioid available as an oral solution • Once a stable analgesic dose is reached, the dosing interval may be extended to q 8 to 12 hours or longer	• **Contraindications include any situation where Opioids are contraindicated, such as patients with respiratory depression (in the absence of resuscitative equipment or in unmonitored situations), acute bronchial asthma, hypercarbia and known or suspected paralytic ileus** • May prolong QTc intervals on ECG; Risk of cardiac arrhythmias • Discontinue or taper the methadone dose and consider an alternative therapy if the QTc > 500ms • Methadone should not be used as prn supplemental Opioid therapy • Plasma half-life may be longer than the analgesic duration • Delayed analgesia or toxicity may occur because of drug accumulation after repeated doses, e.g., on days 2 to 5; If patient has excessive sedation during this timeframe, consider temporarily holding dose(s), lowering the dose, and/or slowing the titration rate	B	• Methadone has little cross-tolerance with other Opioids; Therefore, even patients with a high degree of Opioid tolerance may be at risk for overdose when switched to methadone • Avoid concomitant use of methadone with Benzodiazepines or TCAs with morphine due to respiratory depression	

Opioid Medications (cont.)

May develop tolerance within days or need a dose increase. Taper Opioids when discontinuing. Taper by 20-50% per week for patients who are not addicted. The longer the patient has been on the Opioids, the slower the taper should be. Consider using adjuvant agents such as Antidepressants to manage irritability, sleep disturbances or Anticonvulsants for neuropathic pain. Do not treat withdrawal symptoms with Opioids or Benzodiazepines after discontinuing Opioids. Consider using clonidine 0.1mg two to three times daily to control any withdrawal symptoms if there are no contraindications. Supplemental medications will often be required as clonidine will not address all withdrawal symptoms. Monitor patient safety and comfort during the initial phase of Opioid abstinence.

Opioid therapy should be tapered off and discontinued if the medication fails to show partial analgesia with incremental dose titration, trials with different agents provide inadequate analgesia, there is other evidence that the pain may not be Opioid responsive, real or potential harms outweigh real or potential benefits, or upon patient request. Consider decreasing the Opioid dose when pain level decreases in stable patients.

Adverse effects can be minimized through the use of low starting doses, slower titration rates, prophylactic and symptomatic treatments and specific patient education provided at initiation of therapy. If side effects do occur, then recommend modifying the dose or rotating the Opioid agent to minimize adverse effects.

Initiate a bowel regimen at the start of Opioid therapy. Initial bowl regimens should contain a stimulant laxative and a stool softener. Do not use a bulk forming agent as they may cause intestinal obstruction. For nausea and vomiting, consider prophylactic Antiemetic therapy; Add or increase non-Opioid adjuvants; If analgesia is satisfactory, decrease Opioid dose by 25%. For sedation: determine whether sedation is due to the Opioid; Eliminate nonessential CNS depressants; If analgesia is satisfactory, reduce Opioid dose by 10-15%; Add or increase non-Opioid or non-sedating adjuvant for additional pain relief so that the Opioid can be reduced; Add stimulant drug during the day such as Caffeine, or change the Opioid.

Use caution in patients with head injury, hypothyroidism, CNS depression, elderly, renal, hepatic and debilitated patients. Use caution since the Opioids may induce or aggravate seizures.

Opioid Medications (cont.)

Monitoring, Referrals and Warnings: Methadone: Careful monitoring in patients with a history of cardiac conduction abnormalities, on medications affecting cardiac conduction, and other situations suggesting an increased risk of dysrhythmia. Obtain an ECG before initiation of methadone, after 30 days and yearly. Perform an ECG if the dose exceeds 100mg/day or if the patient has unexplained syncope or seizures. Monitor methadone patients extra carefully during initiation, conversions to and from other Opioids and dose titration.

Fentanyl: Monitor patients for adverse effects and modify dosage as necessary if the patient has a fever.

Opioids: Monitor patient for constipation at every office visit. Consider monitoring bone density in patients at risk for osteoporosis. Refer to a more structured program for patients with substance abuse history, psychiatric comorbidity and persistent or troublesome aberrant behavior. Refer to a Substance Use Disorder (SUD) specialty for redirecting addiction behaviors and continued Opioid therapy. Refer patients with comorbid psychiatric disorders to appropriate mental health providers. Perform urine drug testing in patients with a history of SUD as an adjunctive tool at regular intervals.

Black Box Warning: Black box warnings exist for morphine, fentanyl patches, oxycodone, oxymorphone and methadone. See prescribing information for full list of warnings.

Morphine 8-12 hour Extended Release tablets: Swallow tablets whole; Taking broken, chewed, dissolved, or crushed tablets leads to rapid release and absorption of a potentially fatal dose.

Morphine 24-hour Extended Release capsules: Do not chew, crush, or dissolve due to risk of rapid release and absorption of a potentially fatal dose. Avinza (brand name) – Patients must not consume alcoholic beverages or medications containing alcohol; May result in rapid release and absorption of a potentially fatal dose of morphine.

Fentanyl Patches: Use only in patients who are already receiving Opioid therapy, have demonstrated Opioid tolerance, and require a total daily dose at least equivalent to fentanyl transdermal system 25 mcg/hour. Use in non-Opioid tolerant patients may lead to fatal respiratory depression. Serious or life-threatening hypoventilation may occur, even in Opioid-tolerant patients, during the initial application period. Concomitant use with CYP 3A4 inhibitors may increase plasma concentrations, increase or prolong adverse drug effects, and cause potentially fatal respiratory depression. Using damaged or cut fentanyl transdermal patches can lead to rapid release of fentanyl and absorption of a potentially fatal dose. Potential for temperature-dependent increases in fentanyl release, resulting in possible overdose and death.

Oxycodone 12-hour Controlled Release tablets: Swallow whole; Rapid release if broken, chewed, or crushed may lead to absorption of a potentially fatal dose.

Oxymorphone 12-hour Extended Release tablets: Swallow whole; Taking broken, chewed, dissolved, or crushed tablets may lead to rapid release and absorption of a potentially fatal dose of oxymorphone. Patients must not consume alcoholic beverages or medications containing alcohol; May result in increased plasma levels and a potentially fatal overdose of oxymorphone.

Methadone: Deaths reported during initiation of methadone for Opioid dependence; Some cases appear related to too-rapid titration without appreciation for accumulation of methadone over time. Strongly caution patients against self-medicating with CNS depressants during initiation of methadone. Peak respiratory effects typically occur later and persist longer than peak analgesic effects, particularly in the early dosing period; Can contribute to iatrogenic overdose. QTc interval prolongation and serious arrhythmia (torsades de pointes) observed; More common in patients being treated for pain with large, multiple daily doses.

Opioid Medications (cont.)

Opiod Medications	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No additional	No additional	No additional	Manage pain effectively, unmanaged pain may trigger PTSD symptoms	No additional	Effective in pain management	No additional
Cons	May cause confusion and fatigue	Chronic therapy not recommended; Caution when used as abortive therapy due to risk of medication overuse headaches	No additional	No additional	Risk of overdose	Habit forming Risk of overdose	Habit forming Risk of overdose

Anticonvulsant Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Anticonvulsants**	**Efficacy for Anticonvulsants**
Lamotrigine (Lamictal)	• Initial PTSD dose = 25mg QOD X 2 weeks then 25mg QD X 2 weeks then may increase by 25-50mg QD Q1-2 weeks • Max PTSD dose = 400mg/day • Use lower doses in the elderly	• Take without regard to meals. May take with food if it causes GI upset	• **Contraindications include increased chance of a rash if taken with alproic acid** • Adverse Events: Stevens-Johnson syndrome, fatigue, dizziness and nausea • Max dose of 200mg if taking with Valproic Acid • Discontinue at the first sign of a rash • Decrease dose in renal and hepatic impairment	C	• Can experience serious toxicity, narrow window of safety • Carbamazepine use contraindicated with nefazodone or within 14 days of MAOI use • Avoid concurrent use with alcohol and CNS depressants • Avoid concomitant use of Carbamazepine with darunavir, etravirine, nilotinib, ranolazine and voriconazole; Avoid concurrent use with grapefruit juice	• PTSD: some evidence supports the use of lamotrigine • Nightmares: topiramate has been shown to have significant suppression • Migraines: topiramate and Valproic Acid are FDA approved for prophylaxis use • Hyperarousal: Valproic Acid has been shown to reduce it

Anticonvulsant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Anticonvulsants	Efficacy for Anticonvulsants
Valproic Acid (Depakene, Stavzor); Divalproex (Depakote	• Target PTSD dose = 10-15mg/kg/day • Max PTSD dose = 60mg/kg/day • Use lower doses in the elderly and increases should be done slowly • Divalproex initial headache dose = 250mg BID • May increase by 250mg/day every week • Maximum dose = 1000mg/day	• Take with food to avoid GI upset • Swallow whole and do not crush or chew Depakote, Depakote ER, Depakene and Stavzor • May sprinkle Depakote sprinkles on apple sauce or pudding and swallow whole • Since divalproex is a prodrug of valproate, it shares the same indications along with the same cautions of Valproic Acid • May use in mTBI patients for headache	• **Contraindications include impaired liver function, thrombocytopenia and urea cycle disorders** • Adverse Events: nausea/vomiting, sedation, ataxia, thrombocytopenia, asthenia, dizziness, somnolence, tremor and diplopia • Tends to be hepatotoxic, monitor appropriately • Valproic Acid may produce false positive test for urine ketones and may affect the accuracy of thyroid function tests	D	• Avoid concurent use of oxcarbazepine with nilotinib, nisoldipine, ranolazine • Avoid concurrent use with evening primrose, valerian, st. john's wort and kava kava	• Bipolar disorder: lamotrigine is FDA approved for use; Valproic Acid (Stavzor) is FDA approved for use in mania in bipolar disorder; Carbamazepine (Equetro) is FDA approved for use in acute manic and mixed episodes associated with bipolar disorder • Trigeminal neuralgia: Carbamazepine (except Equetro) is FDA approved for use • Alcohol withdrawal: Carbamazepine has fair documentation for use and oxCarbamazepine has good documentation for use • Posthepetic neuralgia: gabapentin is FDA approved for use • Neuralgia, chronic pain and neuropathy: gabapentin has fair documentation for use

Anticonvulsant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Anticonvulsants	Efficacy for Anticonvulsants
Carbamazepine (Tegretol, Carbatrol, Equetro)	• Initial PTSD dose = 200mg BID • Administer in two divided doses • Max PTSD dose = 1600mg/day	• Take with food to prevent GI upset • Do not chew or crush the XR capsule • ER capsules may be opened and sprinkled over food	• **Contraindications include bone marrow suppression particularly leukopenia and hypersensitivity to the Tricyclic Antidepressants** • Adverse Events: Leukopenia, SIADH, drowsiness, dizziness and ataxia • Stevens Johnsons syndrome has been reported	D		
OxCarbazepine (Trileptal)	• Initial dose = 300mg BID • Max dose = 2400mg/day	• May be taken with or without food	• Adverse Events: somnolence, dizziness, headache, ataxia, fatigue, vertigo, nausea, vomiting and abnormal vision • Stevens Johnsons syndrome has been reported • Most patients cannot tolerate the higher dose of 2400mg/day due to CNS effects • Adjust the dose in renal impairment	C		
Topiramate (Topamax)	• Initial PTSD dose = 25-50mg/day given in 2 divided doses and increase by 15-50mg/week to the maximum dose or as tolerated	• May cause weight loss in some patients • May use in mTBI patients for headache	• **Contraindications include hepatic impairment** • Adverse Events: Angle closure glaucoma, anorexia, sedation, dizziness and ataxia			

Anticonvulsant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Anticonvulsants	Efficacy for Anticonvulsants
(cont.) Topiramate (Topamax)	• Target PTSD dose = 200-400mg/day • Max PTSD dose = 400mg/day • Headache dose = 25-100mg twice daily		• Adjust the dose in renal impairment • Do not use in patients with h/o kidney stones or glaucoma • Common issues in mTBI: may worsen cognitive dysfunction, may cause renal stones • Instruct patient to maintain adequate hydration to prevent kidney stone formation			
Gabapentin (Neurontin)	• Initial PTSD dose = 300mg QHS • Max PTSD dose = 3600mg/day	• May be taken without regard to meals • May use in mTBI patients for headache	• **Contraindications include renal impairment** • Adverse Events: sedation, ataxia, dizziness, somnolence and peripheral edema • Administer the first dose at bedtime to avoid somnolence and dizziness	C		
Slow titration is required for all medications either beginning or discontinuing the medication. Development of a skin rash requires discontinuation. Anticonvulsants are preferred for mood stabilization over Antipsychotics as they can augment Antidepressants and help with mood stabilization. Fewer serious long-term side effects are seen than in Antipsychotics. Therapeutic blood levels are not established for PTSD, but blood level monitoring may be useful in cases of suspected toxicity. Use with caution in renal and hepatic disorder.						

Anticonvulsant Medications (cont.)

Monitoring, Referrals and Warnings: Monitor for increased depression or suicidality after initiation.

Topiramate: Monitor for nephrolithiasis, glaucoma-like symptom or visual disturbances, sodium bicarbonate levels and ammonia level.

Valproic Acid: Monitor for hepatotoxicty, pancreatitis, thrombocytopenia, hyperammonemia, and valproic acid levels. Routinely monitor LFTs, CBCs, PT/PTT and serum ammonia levels.

Carbamazepine: Monitor for blood cell abnormalities, carbamazepine levels, LFTs, Na, Urinalysis, Iron, BUN and Lipids. Perform baseline and periodic eye exams.

OxCarbazepine: Monitor for hyponatremia.

Black Box Warning: Black box warnings exist for lamotrigine, valproic acid and carbamazepine. See prescribing information for full list of specific warnings.

Valproic Acid: Hepatotoxicity has occurred resulting in fatalities. Perform liver function tests prior to therapy and at regular intervals especially during the first 6 months.

Carbamazepine: Aplastic Anemia and agranulocytosis have been reported with the use of carbamazepine. Obtain complete pretreatment hematological testing as a baseline. Consider discontinuation if any evidence of significant bone marrow depression develops.

Anticonvulsants	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Useful in increasing seizure threshold	Useful prophylactic therapies, typically at lower doses than for seizures	Useful adjunct sleep aid	Reduces irritability and impulsivity	Augments effectiveness of SSRI and SNRI, reduces irritability	Useful for neuropathic pain May improve mood	Not habit forming Help with irritability and mood stabilization
Cons	May increase fatigue, mood changes, cognitive symptoms and dizziness	No additional	No additional	No additional	No additional	Mindful of drug/drug interactions	No additional

Benzodiazepine Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Benzodiazepine**	**Efficacy for Benzodiazepine**
Diazepam (Valium)	Vestibular Suppression in mTBI dosing: • Initial dose = 2mg daily • Max daily dose = 2.5mg QID PTSD Dosing: • Initial dose = 5mg BID • Max daily dose = 10mg QID	• Available as oral solution and rectal gel • Available as oral concentrate solution (must be diluted in liquid or semisolid foods just prior to use) • May be taken with water or food if stomach upset occurs	• **Contraindications: include myasthenia gravis, severe respiratory insufficiency, sleep apnea syndrome and acute narrow-angle glaucoma** • Adverse Effects: sedation, memory impairment, ataxia, respiratory depression, tolerance, abuse and/or dependence	D	• Avoid co-administration of Benzodiazepines with methadone which may substantially increase the potential of a fatal outcome due to potentiation of respiratory depressant effects • Alprazolam and clonazepam are contraindicated with ketoconazole and itraconazole • Avoid concomitant use of citalopram, sertraline, clozapine, valerian, kava kava and gotu kola • Grapefruit juice may increase the serum levels • Avoid concomitant use of cigarettes and alprazolam • Avoid medications that contribute to cognitive slowing, fatigue or daytime drowsiness	• Highly effective anti-anxiety medication for short term use. Response within 15-20 minutes to an hour • Fair overall quality of evidence for using Benzodiazepines for sleep disturbance, insomnia, hyperarousal, excessive arousal, and panic attacks • May be used for up to 5 days in ASD for sleep disturbance or insomnia • Recommend against long-term use of Benzodiazepines to manage core symptoms in PTSD • Alprazolam did not show efficacy in PTSD • Alprazolam showed no effect on response to loud tones • Clonazepam has no beneficial effect in PTSD • Clonazepam has no effect on auditory startle in PTSD
Lorazepam (Ativan)	Vestibular Suppression in mTBI dosing: • Initial dose = 0.5mg BID. PTSD Dosing: • Initial dose = 0.5mg TID to QID • Max daily dose = 1mg QID or 2mg BID	• Available as oral concentrate solution (must be diluted in liquid or semisolid foods just prior to use) • May be taken with water or food if stomach upset occurs	• **Contraindications: include severe respiratory insufficiency and acute narrow-angle glaucoma** • Adverse Effects: sedation, memory impairment, ataxia, respiratory depression, tolerance, abuse, and/or dependence	D		

Benzodiazepine Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Benzodiazepine	Efficacy for Benzodiazepine
Alprazolam (Xanax, Niravam)	PTSD Dosing: • Initial dose = 0.5mg TID • Increase dose at intervals of 3 to 4 days • Max daily dose = 1mg QID	• Available in orally disintegrating tablet • Available as oral concentrate solution (must be diluted in liquid or semisolid foods just prior to use) • May be taken with water or food if stomach upset occurs	• **Contraindications: include severe respiratory insufficiency and narrow-angle glaucoma** • Adverse Effects: sedation, memory impairment, ataxia, respiratory depression, rebound anxiety, withdrawal symptoms after stopping drug, tolerance, abuse, and/or dependence	D	• Benzodiazepines may increase the levels of alcohol and other CNS depressants • Reduce the dose of Alprazolam by 50% if used with nefazodone • Avoid concurrent diazepam use with mirtazapine • Therapeutic doses sustained for greater than 2 months require tapering off over 4 weeks; Abrupt discontinuation may cause withdrawal symptoms, rebound or seizure	
Clonazepam (Klonopin)	Vestibular Suppression in mTBI dosing: • Initial dose = 0.25mg BID • Max daily dose = 0.5mg BID PTSD Dosing: • Initial dose = 0.25mg BID • Increase by 0.25mg every 1 – 2 days • Max daily dose = 5mg QID	• Available as orally disintegrating tablets • Extemporaneous suspension can be compounded • Off label alternative route of administration- may be administered rectally • May be taken with water or food if stomach upset occurs	• **Contraindications: include narrow angle glaucoma and significant liver disease** • Adverse Effects: sedation, memory impairment, ataxia, sexual dysfunction, respiratory depression, tolerance, abuse, and/or dependence	D		

Benzodiazepine Medications (cont.)

Use with caution in the elderly and patients with impaired liver function, impaired renal function, respiratory disease and depression. Reduce the dosage in the elderly. Risk of abuse in patients with history of substance abuse. Pharmacotherapy for PTSD with clonazepam, diazepam or lorazepam should be carefully considered due to their sedating and addictive qualities. Avoid use of Benzodiazepine pharmacotherapy in mTBI if at all possible as it contributes to confusion. If used in mTBI, therapy should be carefully considered due to their sedating and addictive qualities. The dose of narcotics should be decreased by 1/3 when diazepam is added.

Benzodiazepines are the treatment of choice for alcohol withdrawal. For inpatient treatment of alcohol withdrawal, use Benzodiazepines over non-Benzodiazepine sedative-hypnotics because of documented efficacy, and a greater margin of safety. Benzodiazepines are the drug of choice in this setting, given adequate monitoring, because they reduce withdrawal severity, incidence of delirium, and seizures. All Benzodiazepines appear to be effective, but agents without active metabolites such as lorazepam may be preferred in patients with liver impairment. Dose and withdrawal scales should be individualized for each patient. Geriatric patients should start with lower doses of Benzodiazepines than younger adults.

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Monitoring, Referrals and Warnings: Monitor heart rate, blood pressure, respiration, excess sedation and mental status, especially suicidality. Perform periodic monitoring of liver and kidney function, hematocrit and CBC. Patients should be advised that Benzodiazepine use may impair the ability to perform hazardous activities requiring mental alertness or physical coordination (e.g, operating machinery and driving a motor vehicle).

Black Box Warnings: No black box warnings.

Benzodiazepines	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	No Additional	Decrease arousal allowing sleep May help sleep	Decrease arousal allowing sleep May help sleep	May help sleep	No Additional	First line medication to treat substance use withdrawal symptoms in a monitored setting
Cons	Worsening cognitive symptoms Possible delay of recovery Increased seizure risk with withdrawal	No Additional	Addiction, dependence potential	Addiction, depedence potential Withdrawal can mimic hyper-arousal	Addiction, dependence potential Overdose potential Potential decrease treatment efficacy for depression Alprazolam may cause depression in >10% of patients	Negative interaction with narcotics with increased risk of respiratory depression	Jeopardize sobriety

Sleep Aid Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Sleep Aids**	**Efficacy for Sleep Aids**
Zolpidem (Ambien, Zolpimist, Edluar	Dosing for mTBI patients for sleep: • Initial Dose = 5mg at night • If poor results after 3 nights, increase to 10mg nightly • Max daily dose = 10mg at bedtime • Max duration of 10 days • PTSD dose = 5 -10mg at bedtime • Initial elderly, debilitated and hepatic impairment dose = 5mg QHS	• First-line agent for mTBI patients with sleep disorder • Used for short-term treatment of insomnia with difficulty in sleep onset • Available as oral metered dose spray (Zolpimist) and sublingual tablets (Edluar) • Good response and fewer side effects than other agents • Fewer disturbances to sleep stages compared to Benzodiazepines • Do not take with or after a meal	• Adverse Effects: sedation, ataxia, rebound insomnia, headache, dizziness, somnolence • Zolpidem may worsen depression • Use only when the patient is able to stay in bed for at least 7-8 hours before being active again	C	• Zolpidem contraindicated with Ritonavir • Triazolam contraindicated with nefazodone, ketoconazole, itraconazole • Avoid concurrent use with alcohol • Concomitant use of zolpidem with SSRIs increases the effect of zolpidem • Avoid concomitant use with valerian, st. john's wort, kava kava, gotu kola except for chloral hydrate • Avoid grapefruit juice with Triazolam • Abuse with zolpidem and zaleplon has occurred resulting in withdrawal reactions • Abrupt discontinuation may lead to withdrawal symptoms or rebound insomnia; Taper dose	• Zolpidem has poor quality of evidence for efficacy in PTSD • Zaleplon and eszopiclone have no evidence in PTSD as no studies have been done • Chloral hydrate has a fair overall quality of evidence for usage in sleep disturbances or insomnia in ASD; Recommend usage for up to 5 days • Benzodazepines (triazolam) recommended for use in sleep disturbances or insomnia in ASD for up to 5 days • Benzodiazepines have a fair overall quality of evidence for use in sleep disturbance, insomnia, hyperarousal, excessive arousal or panic attacks

Sleep Aid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Sleep Aids	Efficacy for Sleep Aids
Zolpidem CR (Ambien CR)	• Initial dose = 12.5mg QHS • Initial elderly, hepatic impairment and debilitated dose = 6.25mg QHS	• Good response and fewer side effects than other agents • Fewer disturbances to sleep stages compared to Benzodiazepines • Used for short-term treatment of insomnia with difficulty in sleep onset and/or sleep maintenance • Do not take with or after a meal • Do not crush, chew or divide • Controlled release tablet for longer duration of action	• Adverse Effects: sedation, ataxia, rebound insomnia, headache, dizziness, somnolence • Zolpidem may worsen depression • Use only when the patient is able to stay in bed for at least 7-8 hours before being active again	C		
Zaleplon (Sonata)	• PTSD dose = 5 -10mg QHS • Initial elderly and mild to moderate hepatic impairment dose = 5mg QHS	• Avoid taking with or after a heavy, high-fat meal since it will reduce absorption • Used for short-term treatment of insomnia (7-10 days) but has been demonstrated to be effective in up to 5 weeks	• Adverse Effects: sedation, ataxia, rebound insomnia, headache • Do not use in severe hepatic impairment. • Tablets contain tartrazine, avoid in patients with sensitivity and use caution in asthmatics	C		

Sleep Aid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Sleep Aids	Efficacy for Sleep Aids
Eszopiclone (Lunesta)	• Initial dose = 2mg at bedtime • Max daily dose = 3mg at bedtime • Initial geriatric dose for difficulty falling asleep = 1mg QHS • Max geriatric dose = 2mg QHS • Initial geriatric dose for difficulty staying asleep = 2mg QHS • Initial dose in severe hepatic impairment = 1mg QHS	• Longer acting, elimination half life of 6 hours • Avoid taking with meals • Do not chew, crush or divide	• Adverse Effects: headache, unpleasant taste, somnolence, dizziness • No studies have been done in its use for PTSD • Only use if the patient can dedicate 8 hours to sleep	C		
Chloral Hydrate (Somnote, formerly known as Noctec or Aquachloral)	• Initial dose = 500-1000mg 30 minutes before bedtime • Max daily dose = 2000mg 30 minutes before bedtime	• Available as capsule, syrup and rectal suppository • Capsules must be swallowed whole, do not chew. Take with a full glass of water • Dilute syrup in a half glass of water or fruit juice • Short term use for insomnia for less than 2 weeks	• **Contraindications: include severe cardiac disease, gastritis, marked hepatic or renal impairment** • Adverse Effects: nausea, vomiting, diarrhea, residual hangover • May contain tartrazine, avoid in patients with sensitivity and use caution in asthmatics • Avoid in gastritis, esophagitis, gastric or duodenal ulcers	C		

Sleep Aid Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Sleep Aids	Efficacy for Sleep Aids
Triazolam (Halcion)	• Usual adult dose = 0.25mg QHS • Max adult dose = 0.5mg QHS • Initial geriatric dose = 0.125mg QHS • Max geriatric dose = 0.25mg QHS	• Short term use for insomnia (generally 7-10 days; Use for more than 2-3 weeks requires a complete reevaluation	• Adverse Effects: somnolence, asthenia, day-time tiredness, confusion • Reduce dose or avoid using in cirrhosis • Do not use when a full night's sleep is not possible	X		

Use with caution in elderly patients, patients with impaired liver function and patients with alcohol or drug abuse history. Use with caution in patients with depression.

Hypnotics/sedatives have been associated with abnormal thinking and behavioral changes, evaluate appropriately. Take immediately before bedtime. Use for no more than 5-14 days. Hypnotics/sedatives have been associated with hypersensitivity reactions such as anaphylaxis and angioedema. The failure to resolve insomnia in 7-10 days may indicate psychiatric and/or mental illness and should be evaluated. Usage may result in night time amnesic periods, somnambulism or sleep driving. Prescription quantities should not be written for more than a month.

May also consider Trazodone (see Serotonin Antagonist Reuptake Inhibitors (SARIs), Mirtazapine (see Noradrenergic and Specific Serotonin Antidepressants (NaSSAs) and Amitriptyline (see TCA section).

Monitoring, Referrals and Warnings: Warn patients about performing tasks which require mental alertness (operating machinery or driving a motor vehicle).

Black Box Warnings: No black box warnings.

Sleep Aids	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	May help to re-regulate sleep cycle	May help to re-regulate sleep cycle	Probably help with decrease arousal allowing sleep	Probably help with decrease arousal allowing sleep	Useful in targeting symptoms of sleep, during initial phase of titration with SSRI	No Additional	No Additional
Cons	May worsen dizziness, concentration, memory	No Additional	No Additional	No Additional	May mask one of the target symptoms of SSRI, which may make it difficult to assess the effectiveness of SSRI	May increase the sedative effect of Opioids Potential additive effect on respiratory depression	Jeopardize sobriety Can be habit forming

Typical Antipsychotic Medications

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Typical Antipsychotics	Efficacy for Typical Antipsychotics
Haloperidol (Haldol)	• Initial PTSD dose = 0.5mg TID or 1mg BID • Max PTSD = 5mg QID	• Used in PTSD but therapeutic doses not established • The Opioid side effect of delirium may be treated with Haloperidol if pharmacologic treatment is deemed necessary • Haloperidol may be considered for patients who have agitated delirium, because of its efficacy and low incidence of cardiovascular and anticholinergic side effects	• **Contraindications: include parkinson's disease, QTc prolongation, coma or depressed states due to CNS depression or other causes, bone marrow suppression and severe cardiac or hepatic disease** • Adverse Events: sedation, akathisia, dystonia, drug-induced parkinsonism, tardive dyskinesia (may occur with long term use), neuroleptic malignant syndrome (NMS) and QTc changes • Use should be well justified in the medical record because of the risk of tardive dyskinesia • Bronchopneumonia has occurred; It has been postulated that lethargy and decreased sensation of thirst may lead to dehydration and reduced pulmonary ventilation; Discontinue therapy if these symptoms occur • When used to control mania in bipolar disease, there may be too rapid of a swing to depression	C	• Thioridazine contraindicated with medications that prolong the QT interval and with CPY2D6 inhibitors (fluoxetine, fluvoxamine, paroxetine, duloxetine, pindolol and propranolol) • Avoid concurrent use of haloperidol and chlorpromazine with nilotinib, thioridazine, ziprasidone, alcohol, kava kava, valerian, gotu kola and st. john's wort • Avoid concurrent use of thioridazine with nilotinib, ziprasidone, alcohol, kava kava, valerian, gotu kola and st. john's wort • Avoid use of chlorpromazine with tamoxifen • Taper upon discontinuation to avoid adverse effects	• Poor quality of evidence for the use of typical antipsychotics in PTSD • Chlorpromazine is FDA approved for use in mania in manic-depressive illness

Typical Antipsychotic Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Typical Antipsychotics	Efficacy for Typical Antipsychotics
Chlorpromazine (formerly known as Thorazine)	• Initial PTSD dose = 25mg QID • Max PTSD dose = 200mg QID	• Used in PTSD but therapeutic doses not established	• **Contraindications: include parkinson's disease, QTc prolongation, severe CNS depression and coma** • Adverse Events: sedation, orthostatic hypotension, akathisia, dystonia, drug-induced parkinsonism, tardive dyskinesia (may occur with long term use), NMS and QTc changes • Use should be well justified in the medical record because of the risk of tardive dyskinesia	C		
Thioridazine (formerly known as Mellaril)	• Initial PTSD dose = 50mg BID • Max PTSD dose = 200mg QID or 400mg BID due to pigmentary retinopathy	• Used in PTSD but therapeutic doses not established • Avoid antacid use within 2 hours of dosing	• **Contraindications: include parkinson's disease, QTc prolongation, hypertensive or hypotensive heart disease of extreme degree, history of cardiac arrhythmia or congenital long QT syndrome, severe CNS depression, coma, bone marrow suppression and blood dyscrasias**	C		

Typical Antipsychotic Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Typical Antipsychotics	Efficacy for Typical Antipsychotics
(cont.) Thioridazine (formerly known as Mellaril)			• Adverse Events: sedation, orthostatic hypotension, akathisia, dystonia, drug-induced parkinsonism, tardive dyskinesia (may occur with long term use), NMS and QTc changes • Use should be well justified in the medical record because of the risk of tardive dyskinesia			
May be used in delirium but generally not used in these conditions. False positive pregnancy tests have occurred. Reduce the dose for the elderly and those with renal or hepatic failure. Use with caution in cardiac disease and predisposition to seizures. Photosensitivity may occur. Use caution in hot weather since these drugs may increase susceptibility to heat stroke. Use caution to avoid overheating and dehydration. Use caution in patients at risk for aspiration pneumonia. Esophageal dysmotility and aspiration has been associated with antipsychotic use. Avoid use in mTBI.						

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Monitoring, Referrals and Warnings: Monitor vital signs, BMI, Fasting Glucose at baseline, ECG, lipid profile, abnormal involuntary movements, extrapyramidal symptoms. Monitor periodic eye exams and serum potassium with Thioridazine.

Immediately discontinue antipsychotics if signs and symptoms of NMS occur. Symptoms include hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or bp, tachycardia, diaphoresis and cardiac arrhythmias).

May impair the mental or physical abilities required for the performance of hazardous tasks such as driving a car. Warn the patient accordingly. May elevate prolactin levels, monitor appropriately. Advise patient of the possibility of orthostatic hypotension especially during the initial dose titration.

Black Box Warning: Thioridazine has been associated with prolonging the QT interval and torsade-de-pointes type of arrhythmias and sudden death. Because of the potential for significant life-threatening effect, reserve the use of thioridazine to those who fail to show an acceptable response to treatment with other medications. Do not initiate therapy if QTc >450ms.

Elderly patients with dementia-related psychosis treated with antipsychotics are at an increased risk of death as compared to placebo. An increased incidence of cerebrovascular adverse events has been reported in elderly patients with dementia related psychosis.

Typical Antipsychotic Medications (cont.)

Typical Antipsychotic Adverse Drug Effects: Relative Comparisons					
Medication Name	**Extrapyramidal Symptoms**	**Anticholinergic**	**Sedation**	**Orthostatic Hypotension**	**Weight Gain/ Diabetes Mellitus**
Haloperidol	+++	0	+	++	+
Chlorpromazine	++	++	+++	+++	+++
Thioridazine	++	+++	+++	+++	+++

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

Typical Antipsy-chotics	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	May sometimes be used by headache specialists as part of an abortive therapy mix	No Additional	No Additional	Useful in aug-mentation of SSRI and SNRI in the treat-ment of severe depression with psychotic features	No Additional	No Additional
Cons	Drowsiness, sedation	No Additional	No Additional	No Additional	No Additional	No Additional	No Additional

Second Generation Antipsychotic Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Second Generation Antipsychotics**	**Efficacy for Second Generation Antipsychotics**
Risperidone (Risperdal)	• Initial PTSD dose = 1mg QD or 0.5mg BID • Max PTSD dose = 6mg QD	• Used in PTSD but therapeutic doses not established • May be taken with or without food	• **Contraindications: include parkinson's disease** • Adverse Events: sedation, weight gain and NMS • Higher doses may cause akathisia, drug-induced parkinsonism especially with doses > 6mg/day • The risk of tardive dyskinesia as compared to the typical antipsychotics has not been established	C	• Avoid concomitant use of risperidone and quetiapine with nilotinib, thioridazine, ziprasidone • Avoid concomitant use with alcohol, kava kava, gotu kava, valerian and st. john's wort • Taper upon discontinuation to avoid adverse effects	• Good overall quality of evidence for the use of second generation antipsychotics in the treatment of PTSD • Olanzapine, risperidone and quetiapine IR indicated for use in bipolar depression
Quetiapine IR (Seroquel)	• Initial dose for nightmares in mTBI = 25mg qHS • Max daily dose for nightmares = 100mg QHS	• Use QHS in PTSD due to benefit in treating nightmares • Used in PTSD but therapeutic doses not established • May be taken with or without food	• **Contraindications: include parkinson's disease** • Adverse Events: sedation, weight gain and NMS • Higher doses may cause akathisia or drug-induced parkinsonism • The risk of tardive dyskinesia as compared to the typical antipsychotics has not been established	C		

Second Generation Antipsychotic Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Second Generation Antipsychotics	Efficacy for Second Generation Antipsychotics
Quetiapine XR (Seroquel XR)	• Used in PTSD but therapeutic doses not established • May be taken with or without food	• Used in PTSD but therapeutic doses not established • May be taken with or without food	• **Contraindications: include parkinson's disease** • Adverse Events: sedation, weight gain and NMS • Higher doses may cause akathisia, drug-induced parkinsonism especially with doses > 6mg/day • The risk of tardive dyskinesia as compared to the typical antipsychotics has not been established	C		
Olanzapine (Zyprexa, Zydis)	• Initial PTSD dose = 5mg QD • Max PTSD dose = 20mg QD	• Used in PTSD but therapeutic doses not established • May be taken without regard to meals	• **Contraindications: include parkinson's disease** • Adverse Events: sedation, weight gain and NMS • Significantly greater incidence of weight gain as compared to the other second generation antipsychotics • Higher doses may cause akathisia, drug-induced parkinsonism • The risk of tardive dyskinesia as compared to the typical antipsychotics has not been established			
Use caution in patients at risk for aspiration pneumonia. Esophageal dysmotility and aspiration has been associated with antipsychotic use. Use caution in hot weather since these drugs may increase susceptibility to heat stroke. Use caution to avoid overheating and dehydration. Use lower doses and more gradual increases in the elderly, debilitated, renal and hepatic patients.						

Second Generation Antipsychotic Medications (cont.)

Monitoring, Referrals and Warnings: Monitor for the development of diabetes, hyperglycemia. Monitor vital signs, lipid profile, BMI, fasting glucose at baseline, weight gain, bp, mental status, orthostatic bp, abnormal involuntary movements, extrapyramidal symptoms.

May impair the mental or physical abilities required for the performance of hazardous tasks such as driving a car. Warn the patient accordingly. May elevate prolactin levels, monitor appropriately. Advise patient of the possibility of orthostatic hypotension especially during the initial dose titration.

Monitor for NMS and immediately discontinue antipsychotics if signs and symptoms of NMS occur. Symptoms include hyperpyrexia, muscle rigidity, altered mental status (including catatonic signs) and evidence of autonomic instability (irregular pulse or bp, tachycardia, diaphoresis and cardiac arrhythmias). The chances of NMS occurring in second generation antipsychotics is less than in the first generation antipsychotics.

May be used as augmentation to antidepressants by specialty clinics in patients with treatment resistant depression.

Black Box Warning: Second generation antipsychotics are not approved for use in dementia related psychosis. Elderly patients with dementia-related psychosis treated with second generation antipsychotics are at an increased risk of death. The causes of death has been varied but has appeared to be either cardiovascular or infectious.

Quetiapine IR may increase the risk of suicidal thinking and behavior in young adults (18-24) with MDD and other psychiatric disorders. Appropriately monitor and closely observe for clinical worsening, suicidality or unusual changes in behavior particularly during the initial 1-2 months and during periods of dosage adjustments. Short-term studies did not show an increase in the risk of suicidality with antidepressants compared to placebo in adults beyond age 24; There was a reduction in risk with antidepressants compared to placebo in adults aged 65 and older.

Second Generation Antipsychotic Adverse Drug Effects: Relative Comparisons

Medication Name	Extrapyramidal Symptoms	Anticholinergic	Sedation	Orthostatic Hypotension	Weight Gain/ Diabetes Mellitus
Risperidone	+	0	+	++	+
Quetiapine	+/0	0	++	++	+
Olanzapine	+	+	++	++	+++

The side effect description is: 0 = minimal to none; + = low; ++ = moderate; +++ = high

Second Generation Antipsy-chotics	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	No Additional	May help reduce anxiety and help with sleep	May help reduce anxiety and help with sleep	Also indicated for mood stabilizers. May help reduce anxiety and help with sleep	No Additional	No Additional
Cons	May worsen fatigue, cognitive symptoms and dizziness	No Additional	No Additional	No Additional	No Additional	No Additional	Not typically habit forming but abused by some patients

Stimulant Medications						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Stimulants**	**Efficacy for Stimulants**
Methylphenidate IR (Ritalin IR)	• Initial stimulant dose in the mTBI patient = 5mg Q 8 am and 1 pm • May increase total daily dose by 5mg Q 2 weeks • Max stimulant dose in the mTBI patient = 20mg BID	• Take 30-45 minutes before a mea	• **Contraindications: include a history of ongoing substance abuse, idiosyncratic reactions to sympathomimetic amines, marked anxiety, tension and agitation, glaucoma and family history or diagnosis of Tourette's syndrome or tics** • Adverse Events: insomnia, decreased appetite, GI upset, headaches, dizziness, motor tics, irritability, anxiousness and tearfulness • Possible addiction potential • Requires additional prescription regulation under federal and state law • Cannot be refilled, only one month of therapy at a time may be prescribed • Use may include drug holidays to assess usefulness	C	• Methylphenidate and Modafinil contraindicated within 14 days following MAOI therapy • Contraindications with Methylphenidate are halogenated anesthetics; Do not administer on the day of surgery • Avoid concurrent use with alcohol • Avoid concurrent use of Methylphenidate with ephedra and yohimbe	

Stimulant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Stimulants	Efficacy for Stimulants
Methylphenidate Long Acting (Ritalin SR, LA, Concerta, Metadate CD and ER)	• Initial stimulant dose for Metadate ER and Ritalin SR = may be given in place of immediate release products once the daily dose is titrated and the titrated 8 hour dose corresponds to the SR or ER tablet • Max dose = 60mg/day • Initial stimulant dose for Metadate CD and Ritalin LA = 20mg QD • Titrate in 10-20mg increments weekly • Max dose = 60mg/day • Initial stimulant dose for Concerta = 18mg QAM • May increase in 18mg increments weekly • Max dose = 72mg per day	• Take 30-45 minutes before a meal • Take Concerta with water, milk or juice • Metadate CD should be taken before breakfast • Metadate ER should be taken before breakfast and lunch • Metadate CD and Ritalin LA capsules may be opened and contents sprinkled on applesauce; Swallow applesauce without chewing; Do not mix with warm applesauce since the release properties may be affected	• **Contraindications: includes a history of substance abuse, idiosyncratic reactions to sympathomimetic amines, marked anxiety, tension and agitation, glaucoma and family history or diagnosis of Tourette's syndrome or tics; Additional contraindications for Metadate are severe hypertension, heart failure, arrhythmia, hyperthyroidism, thyrotoxicosis and recent MI or angina** • Adverse Events: insomnia, decreased appetite, GI upset, headaches, dizziness, motor tics, irritability, anxiousness and tearfulness • Possible addiction potential • Requires additional prescription regulation under federal or state law • Cannot be refilled, only one month of therapy at a time may be prescribed	C		

Stimulant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Stimulants	Efficacy for Stimulants
(cont.) Methylphenidate Long Acting (Ritalin SR, LA, Concerta, Metadate CD and ER)			• Do not chew, crush or divide • Use may include drug holidays to assess usefulness			
Modafinil (Provigil)	• Initial stimulant dose in the mTBI patient = 100mg QAM • Increase in increments of 100mg using split daily doses • Max stimulant dose in the mTBI patient = 400mg per day	• Use as a stimulant for treating fatigue in mTBI patients	• Adverse Events: headache and asthesia • Reduce the dose to one-half that recommended in one with hepatic impairment	C		
Amantadine (Symmetrel)	• Initial stimulant dose in the mTBI patient = 100mg QD • Max stimulant dose in the mTBI patient = 200mg BID	• Use as a stimulant for treating fatigue in mTBI patients	• Adverse Events: nausea, dizziness and dry mouth	C		

Stimulant Medications (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Stimulants	Efficacy for Stimulants

Potential for suicide risk. May initiate neurostimulant therapy after symptoms of fatigue persist for more than 4 weeks post mTBI injury. Medication trials should persist for at least 3 months. Review of illicit drugs, alcohol, tobacco, caffeine and other stimulants should be performed. Use with caution in the elderly, hepatic and renal impairment.

Modafinil: rare multiorgan hypersensitivity reactions and Stevens Johnsons Syndrome has occurred. Use is not recommended in patients with a history of angina or cardiac disease. Do not use in one with a history of recent MI, unstable angina, depression, mania or psychosis.

Methylphenidate: use caution with Methylphenidate in patients with hyperthyroidism or seizure disorder. Use is not recommended in patients with a history of angina or cardiac disease. Do not use in one with a history of recent MI, unstable angina, depression, mania or psychosis. Conduct a thorough medical history review and physical exam to detect the presence of cardiac disease before therapy and conduct further cardiac evaluation. Do not use Concerta in patients with esophageal motility disorders.

Amantadine: may cause CNS depression. Caution patients about driving or operating machinery. Avoid in untreated angle closure glaucoma. Use with caution in seizure disorder, CHF, peripheral edema and orthostatic hypotension. Use caution in getting up suddenly from a sitting position. If dizziness or lightheadedness occurs, inform patient to notify the MD.

The psychostimulants may have a role as augmentation agents in the treatment of Major Depressive Disorder (MDD) under specialty consultation, although the evidence is stronger in support of other augmentation agents. Psychostimulants should not be prescribed for patients with uncontrolled hypertension or cardiovascular disease. Psychostimulants are best avoided in patients with a co-morbid anxiety or for those in whom anxiety is a significant symptom of their depression. All psychostimulants are Schedule II drugs with the exception of modafanil which is Schedule IV.

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Monitoring, Referrals and Warnings: Specialty consultation advised. Monitor blood pressure, heart rate, and signs of depression or psychiatric disorder. Reassess sleepiness frequently and rule out sleep disorder. Refer to a sleep specialist. Monitor CBC and platelet counts, LFT with Methylphenidate. Monitor for signs of rash with Modafinil. Monitor renal function with Amantadine.

Methylphenidate Black Box Warning: Give Methylphenidate cautiously to emotionally unstable patients such as those with a history of drug dependence or alcoholism since they may increase their dosage on their own initiative. Potential for dependency exists, avoid abrupt discontinuance in patients who have received these for long periods of time. Carefully supervise the patient during withdrawal because severe depression along with chronic over activity can be unmasked.

Stimulants	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	Help with day time alertness and reduce confusion	No Additional	No Additional	No Additional	Help patient feel more energetic and less fatigued	No Additional	No Additional
Cons	May interfere with sleep	No Additional	May interfere with sleep May increase anxiety	May interfere with sleep May increase anxiety	No Additional	No Additional	Caution with prior history of stimulant abuse

Beta-Adrenergic Blockers						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Beta-Adrenergic Blockers**	**Efficacy for Beta-Adrenergic Blockers**
Propranolol IR (Formerly known as Inderal)	• PTSD dose = 40mg QD • Chronic preventative headache dose (for headaches greater than 4 weeks), Initial dose = 10mg QD • Max dose = 80mg TID (BP & PTSD effects)	• Propranolol has only been used in a single dose for prevention of PTSD • Take on an empty stomach	• **Contraindications: include sinus bradycardia, congestive heart failure, cardiogenic shock, heart block (2nd or 3rd degree), asthma, COPD, Raynaud's syndrome and myasthenia gravis** • Adverse Effect: orthostatic hypotension, bronchospasm, bradycardia and nightmares • Non-selective agent which may have benefit on autonomic effects of PTSD • Has side effects labeled as depression • Can reduce physiologic response to stress reaction e.g. tachycardia, sweating; It does not target panic or fear response	C	• Generally well tolerated • Contraindicated use with thioridazine • Avoid concomitant use with methacholine and topotecan • Life-threatening increases in bp have occurred after discontinuation of clonidine in patients receiving a Beta-Blocker or after simultaneous withdrawal; Beta-Blockers should be discontinued several days before gradual reduction of clonidine in patients receiving both clonidine and Beta-Blockers concurrently	• Propranolol has a good overall quality of evidence for treating ASR and for hyperarousal, excessive arousal and panic attacks • FDA approved for migraine prophylaxis

Beta-Adrenergic Blockers (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Beta-Adrenergic Blockers	Efficacy for Beta-Adrenergic Blockers
Propranolol LA (Inderal LA)	• Chronic preventative headache (for headaches greater than 4 weeks): Initial dose = 80mg QD • Max dose = 240mg QD (BP & PTSD effects)	• Take with or without food but always take consistently • Administer once daily at bedtime	• **Contrain-dications: include sinus bradycardia, congestive heart failure, cardiogenic shock, heart block (2nd or 3rd degree), asthma, COPD, Raynaud's syndrome and myasthenia gravis** • Adverse Effect: orthostatic hypotension, bronchospasm, bradycardia and nightmares • Non-selective agent which may have benefit on autonomic ef-fects of PTSD • Has side effects labeled as depression • Can reduce physiologic response to stress reaction e.g. tachycardia, sweating; It does not target panic or fear response • Do not crush or chew	C		

Consider using in PTSD for hyperarousal, excessive arousal or panic attacks for up to 10 days. May be considered for treatment of immediate post-event stress. Acute, post-trauma propranolol may have a preventive effect on subsequent PTSD.

Advise patients to use caution if consuming alcohol. May cause drowsiness, dizziness, lightheadedness or blurred vision. Caution patient while driving or performing tasks requiring alertness. Use low initial doses in hepatic impairment and geriatric patients. Use caution in renal and hepatic impairment.

Use caution in diabetes since it can mask signs of hypoglycemia; In hyperthyroidism since it may mask signs of thyrotoxicosis; In psychiatric disease since it may cause CNS depression; In patients with a history of severe anaphylaxis to allergens since patients taking Beta-Blockers may become more sensitive to repeat challenges and in peripheral vascular disease. May alter thyroid function tests.

Adequate alpha blockade is required prior to the use of any Beta-Blocker for patients with untreated pheochromocytoma.

Beta-Adrenergic Blockers (cont.)

Monitoring, Referrals and Warnings: Monitor heart rate, blood pressure. Monitor for worsening mood/depression and cognitive symptoms.

Black Box Warning: There have been reports of exacerbation of angina and myocardial infarction following abrupt discontinuation of therapy. The dose should be gradually tapered over at least a few weeks when discontinuing. The patient should be warned against interruption or cessation of therapy.

Propranolol	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	Useful prophylactic option	Reduce anxiety by targeting physiologic symptoms	Reduce anxiety by targeting physiologic symptoms	No Additional	No Additional	No Additional
Cons	Worsen cognitive/ behavioral symptoms, increase fatigue	No Additional	No Additional	No Additional	Worsen depression, worsen fatigue	No Additional	No Additional

Smoking Cessation Aids

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Smoking Cessation Aids	Efficacy for Smoking Cessation Aids
Varenicline (Chantix)	• Begin initial dose one week before the quit date at 0.5mg QD for 3 days • Increase to 0.5mg BID for 4 days. • Followed by 1mg BID for 3 months • Instruct patient to quit smoking on day 8, when dosage is increased to 1mg BID	• In order to reduce nausea, take on a full stomach • In order to reduce insomnia, take the second pill at supper rather than at bedtime	• Adverse Effect: nausea, trouble sleeping and abnormal/ vivid/strange dreams	C	• Avoid combining varenicline with other Nicotine Replacement Agents since there has been a higher incidence of side effects (nausea, headache)	• FDA approved to aid in smoking cessation for up to 6 months of therapy • Shown to consistently increase abstinence rates • Studies have shown that 1mg total daily dose doubles and 2mg total daily dose triples a smoker's likelihood of long-term abstinence

Smoking Cessation Aids (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Smoking Cessation Aids	Efficacy for Smoking Cessation Aids
(cont.) Varenicline (Chantix)		• Evidence is available showing that doses of 1mg QD are effective; Therefore, the 1mg daily dose is a viable alternative should the patient experience dose-related side effects from the 2mg total daily dose				
Consider other treatment modalities first. See the DNRI section as Bupropion is also used for smoking cessation. Use with caution in patients with significant kidney disease (CrCL < 30ml/min), patients on dialysis or those with serious psychiatric illness. Caution patients that Varenicline may affect the ability to drive or operate heavy machinery due to sedation. Therapy is most effective when the patient is engaged in addiction-focused counseling.						
!	**Monitoring, Referrals and Warnings:** Monitor changes in mood and behavior when prescribing this medication. Request patients to tell their health care provider about any history of psychiatric illness prior to starting this medication. Clinicians should consider eliciting information on their patients' psychiatric history. **Black Box Warning:** Advise patients and caregivers that the patient should stop taking Chantix and contact a healthcare provider immediately if agitation, hostility, depressed mood, or changes in behavior or thinking that are not typical for the patient are observed, or if the patient develops suicidal ideation or suicidal behavior while taking Chantix or shortly after discontinuing Chantix. Weigh the risks of Chantix against benefits of its use since it has been demonstrated to increase the likelihood of abstinence from smoking for as long as one year compared to treatment with placebo.					

Varenicline	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	No Additional	No Additional	No Additional	No Additional	No Additional	Useful adjunct in nicotine addiction
Cons	May worsen behavioral symptoms	No Additional	May increase anxiety	May increase anxiety	May worsen depression May increase risk of suicide	May increase behavioral symptoms	No Additional

Central Hypotensives

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Central Hypotensives	Efficacy for Central Hypotensives
Prazosin (Minipres)	• Initial dose for nightmares in mTBI = 1mg QHS for 3 days • May increase to 2mg QHS through day 7 • If patient continues to have night-mares, the dosage may be increased to 4mg QHS through day 14 • The dosage could be increased to 6mg QHS through day 21 and to 10mg QHS through day 28 • The maxi-mum daily nightmare dose = 10mg QHS. • Initial Sympa-tholytic dose in PTSD = 1mg QHS • May increase dose as blood pres-sure allows	• Consider prazosin to augment the management of nightmares and other symptoms of PTSD • Primar-ily used for management of recurrent distressing dreams and/ or violent outbursts or agitation dur-ing sleep	• Adverse Effect: orthostatic hypotension, dizziness, head-ache, nausea and palpitations • May cause day time sedation • Associated with first-dose effect orthostatic hypotension or syncope; This can occur with the first few doses, upon rapid increases in dose or if an-other antihyper-tensive is added; Effect may be minimized by beginning initial dose with 1mg Qhs and slowly increasing the dose • Not recom-mended in hypotension or dizziness. • Rare reports of priapism have ccurred	C	• Serious toxicity with overdose • Avoid concurrent use with alcohol	• Open trials and clinical experience suggest it may be useful for ASR; However, this has not been systematically studied • In four relatively small studies prazosin has demonstrated a value in reducing night-mares and in improving Clinician-Administered PTSD Scale (CAPS), CGI, and CGIC scores • Prazosin has a fair overall quality of evidence for use in PTSD

Use with caution in the elderly and renal impairment. Titrate dose. Use caution when driving or operating machinery due to possible drowsiness.

Monitoring, Referrals and Warnings: Monitor blood pressure. Use caution with rising from a sitting or lying position.

Black Box Warning: No black box warnings.

Central Hypotensives (cont.)

Prazosin	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	No Additional	May help nightmares	May help nightmares	No Additional	No Additional	No Additional
Cons	May increase confusion and fatigue Avoid significant hypotension in acute mTBI	No Additional	No Additional	No Additional	No Additional	No Additional	No Additional

Lithium						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for Lithium**	**Efficacy for Lithium**
Lithium (formerly known as Eskalith)	• Specialty consultation advised	• Available as capsules, tablets and syrup • Take with meals to avoid GI upset • Drink 2.5-3 liters of fluids daily	• **Contrain-dications: include severe cardiovascu-lar or renal disease, severe debilitation, dehydration and depletion** • Adverse Effect: lethargy, fatigue, muscle weakness, tremor, headache, hand tremor, nausea, diarrhea, vomit-ing, abdominal pain, polyuria and polydipsia • Normal fluid and salt intake must be maintained during therapy • Half life 24 hrs (average) increases with age and/or decreased renal function	D	• Narrow window of safety within therapeutic range only • Lithium contra-indicated with ACE Inhibitors and Diuretics • Antipsychotics may increase lithium neuro-toxicity • Avoid concomi-tant use with sibutramine and potassium Iodide • Monitor lithium levels when used with SSRIs, SNRIs, nefazodone, trazodone or mirtazapine since there is an increased potential for serotonin syndrome	• FDA approved for use in bipo-lar disease • Lithium has been used in PTSD and augmentation therapy in MDD

Lithium (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for Lithium	Efficacy for Lithium
(cont.) Lithium (formerly known as Eskalith)			• Write doses in mg (milligrams) to avoid any confusion with meq • May lead to osteoporosis • Limit caffeine		• Increased lithium serum concentrations with Prozac, NSAIDSs, Calcium Channel Blockers and metronidazole • Reduced lithium level with acetazolamide and theophylline	
Lithium ER (Lithobid, formerly known as Eskalith CR)	• Specialty consultation advised	• Take with meals to avoid GI upset • Drink 2.5-3 liters of fluids daily • Do not crush or chew SR tabs	• **Contraindications: include severe cardiovascular or renal disease, severe debilitation, dehydration and depletion** • Adverse Effect: lethargy, fatigue, muscle weakness, tremor, headache, hand tremor, nausea, diarrhea, vomiting, abdominal pain, polyuria and polydipsia • Normal fluid and salt intake must be maintained during therapy • Half life 24 hrs (average) increases with age and/or decreased renal function • Write doses in mg (milligrams) to avoid any confusion with meq • May lead to osteoporosis • Limit caffeine	D		

Lithium (cont.)

Use with caution in thyroid disease, mild-moderate cardiovascular disease, mild-moderate renal disease, patients with significant fluid loss, patients at risk of suicide and the elderly.

Avoid use in the mTBI patient. Patients currently taking lithium may develop a neurotoxic syndrome marked by increased mental confusion, disorientation, and unresponsiveness when used with electroconvulsive therapy.

Lithium has been studied as augmentation in MDD for first-line medications and Tricyclic Antidepressants. Bupropion SR and buspirone are recommended as initial choices for augmentation since their efficacy has been demonstrated in at least one randomized clinical trial and their safety and tolerability profiles are more favorable than lithium.

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Monitoring, Referrals and Warnings: Referral to specialist. Monitor Lithium levels, renal function, thyroid function, CBC with differential, electrolytes, urinalysis, fluid status and cardiac function.

Lithium levels should be checked twice weekly until both patients status and levels are stable then levels must be monitored at least every 2 months. Draw trough levels just before the next dose (8-12 hours after the previous dose). Target lithium plasma concentration is >0.5 and <1 meq/L for MDD augmentation. Warn patients to discontinue therapy immediately and contact their provider if signs of lithium toxicity occur. Signs are diarrhea, vomiting, tremor, ataxia, drowsiness and muscular weakness.

Lithium may impair the patient's alertness, warn the patient regarding driving a car or operating machinery.

Black Box Warning: Lithium toxicity is closely related to serum levels and can occur at therapeutic doses; Serum lithium determinations are required to monitor therapy.

Lithium	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	Not in the CPG but may be used as a headache prophylaxis (specialty referral)	No Additional	No Additional	Useful augmenting agent (specialty referral)	No Additional	No Additional
Cons	May worsen cognitive symptoms, fatigue	No Additional	No Additional	No Additional	No Additional	No Additional	No Additional

Nonsteriodal Anti-Infammatory Drugs (NSAIDs), Acetaminophen and Tramadol						
Generic (Brand Name)	**Adult Starting Dose (Max Per Day)**	**Advantages**	**Disadvantages**	**Pregnancy Category**	**Safety Margin for NSAIDs, Acetaminophen and Tramadol**	**Efficacy for NSAIDs, Acetaminophen and Tramadol**
Naproxen (Aleve, Anaprox, Naprosyn)	• Initial adult Headache (HA) dose in mTBI = 500mg BID • Initial geriatric dose = 220mg BID	• Take with food or milk to minimize GI upset	• **Contraindications: include hypersensitivity to aspirin or other NSAIDs, perioperative pain in the setting of coronary artery bypass graft (CABG) surgery. Do not give to one who has had symptoms from other NSAIDs of asthma, rhinitis, urticaria, nasal polyps, bronchospasm or other symptoms of allergic or anaphylactic reactions** • Adverse Events: GI upset, GI bleed, dizziness, vertigo • Potential renal impairment with long term use • Do not use if CrCL < 30ml/min • Stevens-Johnson syndrome may occur. Discontinue use at first sign of rash • May cause hyperkalemia	B/D (D in the 3rd trimester)	• Avoid concomitant use with alcohol • Avoid concomitant use of NSAID with salicylates • If using warfarin with NSAIDs, monitor PT closely	• NSAIDs are effective medications for pain relief for patients with mTBI • Ibuprofen liquid filled gel caps are FDA approved to treat migraines

NSAIDs, Acetaminophen and Tramadol (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for NSAIDs, Acetaminophen and Tramadol	Efficacy for NSAIDs, Acetaminophen and Tramadol
Ibuprofen (Advil, Motrin)	• 400mg to 600mg 3 to 4 times daily for HA in the mTBI patient • For episodic HA, use prn at HA onset up to 3 days per week	• Take with food or milk to minimize GI upset • When using combination products, do not exceed maximum recom-mended daily doses of ibuprofen • Maximum of 3200mg/day	• **Contraindica-tions: include hypersensitiv-ity to aspirin or other NSAIDs. Do not give to one who has had symptoms from other NSAIDs of asthma, rhini-tis, urticaria, nasal polyps, bronchospasm or other symptoms of allergic or anaphylactic reactions** • Adverse Events: GI upset, GI bleed, dizziness, vertigo • Potential renal impairment with long term use • May cause hyperkalemia • Stevens-Johnson syndrome may occur. Discon-tinue use at first sign of rash • Avoid use in severe hepatic impairment	B/D (D in the 3rd trimeste	• If patients exhibit gastrointestinal side effects with NSAIDs, therapy with proton-pump inhibitors and histamine blockers may be considered	

NSAIDs, Acetaminophen and Tramadol (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for NSAIDs, Acetaminophen and Tramadol	Efficacy for NSAIDs, Acetaminophen and Tramadol
Acetaminophen (Tylenol)	• 325mg to 650mg Q 4-6 hours or 1000mg 3-4 times daily • Do not exceed 4000mg/day • Do not exceed 2000mg per day in chronic alcoholics	• Acetaminophen (APAP) is often the best tolerated in terms of lower likelihood to produce gastrointestinal distress. When used appropriately, side effects with acetaminophen are rare • Acetaminophen is used in combination with other medications; Combination drugs may be more effective than acetaminophen alone	• **Contraindications: include hepatitis** • The most serious side effect is liver damage due to large doses, chronic use or concomitant use with alcohol or other drugs that also damage the liver • APAP alone or in combination with caffeine can have rebound headaches with continuous use • Use with caution in patients with any type of liver disease • Use longer dosing intervals in renal impairment • When using combination products, do not exceed the maximum recommended daily doses of APAP	B	• Acetaminophen may cause severe hepatic toxicity on acute overdose • Acetaminophen should not be used concurrently with any other product containing acetaminophen	

NSAIDs, Acetaminophen and Tramadol (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for NSAIDs, Acetaminophen and Tramadol	Efficacy for NSAIDs, Acetaminophen and Tramadol
Tramadol (Ultram)	Pain Management dosing: • Initial dose = 25mg every morning • Increase by 25mg as separate doses every 3 day to 100mg/day (25mg q 6 hours) • Subsequent increments of 50mg/day may be made every 3 day to 200mg/day (50mg q 6 hour) • After titration, may give 50 to 100mg q 4 to 6 hours • Maximum daily dose = 400mg/day • In patients >75 years: give < 300mg/day in divided doses • Decrease dosage to 50mg q 12 hour in patients with cirrhosis • Increase dosing interval to 12 hour and decrease maximum daily dose to 200mg in patients with a CrCl < 30 ml/min	• Tramadol appears to be effective for neuropathic pain • May be used alone or in combination with APAP • Slower initiation and titration improves tolerability • When using for migraine attacks then the side effect of sedation can be useful as migraine attacks can abate with sleep • Take acetaminophen content of combination product into account	• **Contraindications: include hypersensitivity to acetaminophen alone or in combination products, any component, or Opioids. Any situation where Opioids are contraindicated, including acute intoxication with alcohol, hypnotics, narcotics, centrally acting analgesics, Opioids or psychotropic drugs; May worsen central nervous system and respiratory depression in these patients** • Should not be used in liver disease nor in renal dysfunction if CrCl less than 30ml/min	C	• Avoid concomitant use of tramadol with MAOIs or SSRIs, SNRIs, nefazodone, trazodone, mirtazapine since there may be an increased risk of seizures, serotonin syndrome • Avoid concomitant use of tramadol with carbamazepine	

NSAIDs, Acetaminophen and Tramadol (cont.)

Generic (Brand Name)	Adult Starting Dose (Max Per Day)	Advantages	Disadvantages	Pregnancy Category	Safety Margin for NSAIDs, Acetaminophen and Tramadol	Efficacy for NSAIDs, Acetaminophen and Tramadol
(cont.) Tramadol (Ultram)			• Serious anaphylactic reactions reported, often following the first dose. Other allergic reactions reported. Patients with a history of anaphylactic reaction to codeine and other Opioids may be at increased risk • Dose carefully or use another agent in patients on serotonergic agents due to serotonergic properties • Use naloxone with caution in overdose; May precipitate seizures • Stevens Johnson syndrome has occurred			

NSAIDs, Acetaminophen and Tramadol (cont.)

NSAID and non-narcotic pain medications are recommended for use in the mTBI treatment of headaches. NSAID and acetaminophen are considered first-line treatment for treating tension headaches as an abortive agent. The choice of an NSAID or acetaminophen depends upon individual response and severity of side effects. Pain treatment is more likely to be successful if the medication is taken at the onset of a headache rather than waiting for the headache pain to escalate.

Headaches associated with chronic NSAID/acetaminophen usage should be addressed to a headache specialist. Episodic tension-type headaches usually respond to NSAID that can be obtained over-the-counter.

NSAIDs: Use with caution and lower doses in hepatic impairment, renal impairment and in the elderly. May cause fluid retention and peripheral edema. Use caution in compromised cardiac function, hypertension or patients on chronic diuretic therapy. May inhibit platelet aggregation. Photosensitivity may occur. Advise patients to use caution and take protective measures. May cause drowsiness, dizziness, blurred vision. Advise patients to use caution when driving or operating machinery. Risk of GI irritation or GI bleed.

Tramadol: Use with caution in debilitated patients on tramadol IR. When using tramadol ER, use caution in the elderly > 65 years, starting at low end of the dosing range; Use even greater caution in patients > 75 years. Seizures reported within the recommended dosage range; Increased risk above recommended dosage range and in patient with seizure disorder, history of seizures, in conditions with increased risk of seizures, or with other drugs that increase seizure risk. Observe maximum dose limits. Use caution in patients with increased intracranial pressure or head injury.

Acetaminophen: Use with caution in patients with alcoholic liver disease and in patients with G6PD deficiency. Patients who consume 3 or more alcohol containing drinks per day should ask their clinician whether to use acetaminophen or an alternative analgesic.

!

Monitoring, Referrals and Warnings: *NSAIDs:* Monitor for occult blood loss, periodic LFT, CBC, BUN, serum CR, urine output and anemia. Monitor renal function. Monitor periodic ophthalmic exams if visual changes or disturbances occur or if on long-term use.

Black Box Warning: Black box warnings exist for NSAIDs and Tramadol. See prescribing information for a full list of specific warnings.
Tramadol: Deaths have occurred in patients with previous histories of emotional disturbances or suicidal ideation or attempts, as well as histories of misuse of tranquilizers, alcohol, and other CNS-active drugs. Serious potential consequences of over dosage with tramadol are central nervous system depression, respiratory depression and death.

NSAIDs, Acetaminophen and Tramadol (cont.)

Tramadol	mTBI	Headache	Acute Stress	PTSD	Depression	Chronic Pain	Substance Use Disorder
Pros	No Additional	No Additional	No Additional	Manage pain effectively, unmanaged pain may trigger PTSD symptoms	No Additional	Effective in pain management which in turn is helpful in sleep maintenance Tramadol may be more effective for neuropathic pain	No Additional
Cons	May cause confusion and fatigue	Chronic therapy not recommend-ed; Caution when used as abortive therapy due to risk of medication overuse headaches	No Additional	No Additional	Risk of overdose	Habit forming Risk of overdose	Habit forming Risk of overdose

Appendix II:
Patient Education

Appendix II: Patient Education Web Sites

General

http://afterdeployment.org

http://www.dcoe.health.mil/ForWarriors.aspx

http://www.centerforthestudyoftraumaticstress.org/

Depression

http://www.nimh.nih.gov/health/publications/depression/complete-index.shtml

http://www.suicidepreventionlifeline.org/Veterans

Concussion

http://www.dvbic.org

http://www.traumaticbraininjuryatoz.org

PTSD and ASD

http://www.ptsd.va.gov/

Substance Use Disorder

http://www.drugabuse.gov/

Appendix III:
Provider Resources

Appendix III: Provider Resources

Provider Resources Websites

http://www.dcoe.health.mil/
General information regarding TBI/concussion and psychological health conditions commonly affecting the nation's military communities, sevicemembers and families.

http://afterdeployment.org
General information regarding concussion and psychological health conditions commonly seen post-deployment.

http://www.pdhealth.mil/respect-mil/index1.asp
Information regarding depression and PTSD in the primary care setting.

http://dvbic.org
Information regarding TBI.

http://www.suicidepreventionlifeline.org/Veterans
Information for providers regarding suicide prevention. This includes patient handouts.

http://www.centerforthestudyoftraumaticstress.org/
Information for providers regarding traumatic exposures. This includes patient handouts.

http://www.cdc.gov/ncipc/pub-res/tbi_toolkit/physicians/mtbi/mtbi.pdf
Center for Disease Control and Prevention provider toolkit for concussion.

http://www.drugabuse.gov/
Provider resources regarding drugs of abuse from the National Institute of Drug Abuse.

Additional Provider Tools

PHQ-2 (pg. 108), PHQ-9 (pg. 109)
For Major Depressive Disorder (MDD).

AUDIT-C (brief Alcohol Screening Questionnaire for Unhealthy Alcohol Use) (pg. 111)
For SUD.

PTSD Checklist-Military (PCL-M) (pg. 113)
For PTSD.

Pain Assessment Tool (pg. 114)
For COT.

www.ensuringsolutions.org/usr_doc/DAST.pdf
For DAST-20.

http://www.sleep.pitt.edu/content.asp?id=1484&subid=2316
For PSQI.

http://www.psych.on.ca/files/nonmembers/AcuteStressDisorderScale_DRN_March_5_2010.pdf
For ASD Scales.

Tools for MDD

- The PHQ tools are reliable, valid, and efficacious clinical tools for primary care settings.
- The PHQ-2 is effective for identifying patients with depression and can also be used to measure treatment outcomes.
- The PHQ-9 is effective for assessing the presence and severity of depression.

Patient Health Questionnaire 2 (PHQ - 2)

Over the past two weeks, how often have you been bothered by either of the following problems?

A) Little interest or pleasure in doing things. (0-3)

B) Feeling down, depressed, or hopeless. (0-3)

Not at all	Several days	More than half the days	Nearly every day
0	1	2	3

Patients with a score of 3 or greater should be followed up with PHQ-9.

Score	% Prob. of MDD	% Prob. of Any Depressive Disorder
1	15.4%	36.9%
2	21.1%	48.3%
3	38.4%	75.0%
4	45.5%	81.2%
5	56.4%	84.6%
6	78.6%	92.9%

For more information on the PHQ-2 and PHQ-9, as well as the Clinical Practice Guidelines for Major Depressive Disorder, please visit: http://www.healthquality.va.gov/index.asp

Tools for MDD (cont.)

Patient Health Questionnaire 9 (PHQ - 9)

Name:_____ Date:_____

Over the last two weeks, how often have you been bothered by any of the following problems? (use "✓" to indicate your answer)

	Not at All	Several Days	More Than Half the Days	Nearly Every Day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself—or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed. Or the opposite—being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead, or of hurting yourself in some way	0	1	2	3

Add Columns: _____ + _____ + _____

Total: _____

10. If you checked off any problems, how *difficult* have these problems made it for you to do your work, take care of things at home, or get along with other people?

☐ Not Difficult at All ☐ Somewhat Difficult ☐ Very Difficult ☐ Extremely Difficult

Tools for MDD (cont.)

Patient Health Questionnaire 9 (PHQ - 9) (cont.)

PHQ-9 Score	DSM-IV-TR Criterion Symptoms	Depression Severity	Proposed Treatment Action
1-4	Few	None	None
5-9	< 5	Mild Depressive Symptoms	Watchful waiting; Repeat PHQ-9 at follow-up
10–14	5-6	Mild Major Depression	Treatment plan; Consider counseling, follow-up, and/or pharmacotherapy
15–19	6-7	Moderate Major Depression	Immediate initiation of pharmacotherapy and/or psychotherapy
20-27	> 7	Severe Major Depression	Immediate initiation of pharmacotherapy and, if severe impairment or poor response to therapy, expedited referral to a mental health specialist for psychotherapy and/or collaborative management

Reference: Public domain available at http://www.phqscreeners.com

Tool for SUD

AUDIT-C (brief Alcohol Screening Questionnaire for Unhealthy Alcohol Use)

Overview

The AUDIT-C is a 3-item alcohol screen that can help identify persons who are hazardous drinkers or have active alcohol use disorders (including alcohol abuse or dependence). The AUDIT-C is a modified version of the 10 question AUDIT instrument.

Clinical Utility

The AUDIT-C is a brief alcohol screen that reliably identifies patients who are hazardous drinkers or have active alcohol use disorders.

Scoring

The AUDIT-C is scored on a scale of 0-12. Each AUDIT-C question has 5 answer choices. Points allotted are: a = 0 points, b = 1 point, c = 2 points, d = 3 points, e = 4 points

- **In men**, a score of 4 or more is considered positive, optimal for identifying hazardous drinking or active alcohol use disorders.
- **In women**, a score of 3 or more is considered positive (same as above).
- However, when the points are all from Question #1 alone (#2 & #3 are zero), it can be assumed that the patient is drinking below recommended limits and it is suggested that the provider review the patient's alcohol intake over the past few months to confirm accuracy.[3]
- Generally, the higher the score, the more likely it is that the patient's drinking is affecting his or her safety.

Psychometric Properties

For identifying patients with heavy/hazardous drinking and/or Active-DSM alcohol abuse or dependence:

	Men[1]	Women[2]
≥3	Sens: 0.95 / Spec. 0.60	Sens: 0.66 / Spec. 0.94
≥4	Sens: 0.86 / Spec. 0.72	Sens: 0.48 / Spec. 0.99

For identifying patients with active alcohol abuse or dependence:

≥ 3	Sens: 0.90 / Spec. 0.45	Sens: 0.80 / Spec. 0.87
≥ 4	Sens: 0.79 / Spec. 0.56	Sens: 0.67 / Spec. 0.94

1. Bush K, Kivlahan DR, McDonell MB, et al. The AUDIT Alcohol Consumption Questions (AUDIT-C): An effective brief screening test for problem drinking. Arch Internal Med. 1998 (3): 1789-1795.
2. Bradley KA, Bush KR, Epler AJ, et al. Two brief alcohol-screening tests from the Alcohol Use Disorders Identification Test (AUDIT): Validation in a female veterans affairs patient population. Arch Internal Med Vol 163, April 2003: 821-829.
3. Frequently Asked Questions guide to using the AUDIT-C can be found via the website: www.oqp.med.va.gov/general/uploads/FAQ%20AUDIT-C

Tool for SUD (cont.)

AUDIT-C Questionnaire

Patient Name _____ Date of Visit _____

1. How often do you have a drink containing alcohol?

- ☐ A. Never
- ☐ B. Monthly or less
- ☐ C. 2-4 times a month
- ☐ D. 2-3 times a week
- ☐ E. 4 or more times a week

2. How many standard drinks containing alcohol do you have on a typical day?

- ☐ A. 1 or 2
- ☐ B. 3 or 4
- ☐ C. 5 or 6
- ☐ D. 7 to 9
- ☐ E. 10 or more

3. How often do you have six or more drinks on one occasion?

- ☐ A. Never
- ☐ B. Less than monthly
- ☐ C. Monthly
- ☐ D. Weekly
- ☐ E. Daily or almost daily

AUDIT-C is available for use in the public domain.

Tool for PTSD

PTSD Checklist – Military Version (PCL-M)

Patient Name _____

Instruction to patient: Below is a list of problems and complaints that veterans sometimes have in response to stressful military experiences. Please read each one carefully, put an "X" in the box to indicate how much you have been bothered by that problem in the last month.

No.	Response:	Not at all (1)	A little bit (2)	Moderately (3)	Quite a bit (4)	Extremely (5)
1.	Repeated, *disturbing memories*, *thoughts*, or *images* of a stressful military experience?					
2.	Repeated, disturbing *dreams* of a stressful military experience?					
3.	Suddenly *acting* or *feeling* as if a stressful military experience *were happening again* (as if you were reliving it)?					
4.	Feeling *very upset* when *something reminded* you of a stressful military experience?					
5.	Having *physical reactions* (e.g., heart pounding, trouble breathing, or sweating) when *something reminded* you of a stressful military experience?					
6.	Avoid *thinking about* or *talking about* a stressful military experience or avoid *having feelings* related to it?					
7.	Avoid *activities* or *situations* because *they remind you* of a stressful military experience?					
8.	Trouble *remembering important parts* of a stressful military experience?					
9.	Loss of *interest in things that you used to enjoy*?					
10.	Feeling *distant* or *cut off* from other people?					
11.	Feeling *emotionally numb* or being unable to have loving feelings for those close to you?					
12.	Feeling as if your *future* will somehow be *cut short*?					
13.	Trouble *falling* or *staying asleep*?					
14.	Feeling *irritable* or having *angry outbursts*?					
15.	Having *difficulty concentrating*?					
16.	Being "*super alert*" or watchful on guard?					
17.	Feeling *jumpy* or easily startled?					

Weathers, F.W., Huska, J.A., Keane, T.M. PCL-M for DSM-IV. Boston: National Center for PTSD – Behavioral Science Division, 1991. This is a Government document in the public domain.

Tool for PTSD (cont.)

Suggested Cutoff Scores for Screening and Diagnosis: Goal of Assessment

Setting	Screening	Diagnosis
VA PTSD specialty mental health clinic1	48	56
VA Primary Care clinic1	25	33
Active duty Iraq/Afghanistan (OEF/OIF)2	25	28
Civilian substance abuse residential3	36	44
4-5 Civilian primary care	25	30-38
6 Civilian motor vehicle accidents	44	50*

* Note that Blanchard et al. (6) chose a cutoff score of 44 for diagnosis based on diagnostic efficiency. However, the psychometrics they presented for a cutoff score of 50 yielded optimal sensitivity and specificity.

Tool for COT

Numeric Rating Pain Scale

0 – 10 Numeric Rating Scale

None	Mild	Moderate	Severe

0 1 2 3 4 5 6 7 8 9 10

Indications:

Adults and children (> 9 years old) in all patient care settings who are able to use numbers to rate the intensity of their pain.

There are advantages to using a numeric rating scale (NRS) for assessing pain and function. The NRS has been found to be valid and reliable, and to be sensitive to changes in acute, cancer, and chronic pain.

Instructions:

1. Intensity of pain should be measured using a numeric rating scale (0-10 scale) for each of the following:
   - Current pain (pain level patient is having right now)
   - When pain is the worst
   - When pain is the best
   - "Usual" or "average" pain in last week
   - Acceptable (or tolerable) amount of pain
2. When the explanation suggested in #1 above is not sufficient for the patient, it is sometimes helpful to further explain or conceptualize the NRS in the following manner:
   - 0 = No Pain
   - 1-3 = Mild Pain (nagging, annoying, interfering little with ADLs = Activities of Daily Living)
   - 4-6 = Moderate Pain (interferes significantly with ADLs)
   - 7-10 = Severe Pain (disabling; unable to perform ADLs)
3. The interdisciplinary team in collaboration with the patient/family (if appropriate), can determine appropriate interventions in response to Numeric Pain Ratings
4. The patient's response to current pain treatments should be assessed using questions such as:
   - "What is your intensity of pain after taking (use of) your current medication?"
   - "How long does your pain relief last after taking your medication?"
   - "How does taking your treatment/medication affect your functioning?"
   - Ask specifically whether the patient suffers from headache

1. Breivik & Skoglund, 1998; De Conno et al., 1994; Farrar et al., 2000; Paice & Cohen, 1997
2. McCaffery, M., & Beebe, A. (1993). Pain: Clinical Manual for Nursing Practice. Baltimore: V.V. Mosby Company.

Refer to the DSM-IV TR for full diagnostic criteria

Appendix III: DSM-IV Definitions

When an individual who has been exposed to a traumatic event develops anxiety symptoms, reexperiencing of the event, and avoidance of stimuli related to the event lasting less than four weeks they may be suffering from this Anxiety Disorder.

Diagnostic criteria for 308.3 Acute Stress Disorder (DSM-IV)

A. The person has been exposed to a traumatic event in which both of the following were present:
1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
2. The person's response involved intense fear, helplessness, or horror

B. Either while experiencing or after experiencing the distressing event, the individual has three (or more) of the following dissociative symptoms:
1. A subjective sense of numbness, detachment, or absence of emotional responsiveness
2. A reduction in awareness of his or her surroundings (e.g., "being in a daze")
3. Derealization
4. Depersonalization
5. Dissociative amnesia (i.e., inability to recall an important aspect of the trauma)

C. The traumatic event is persistently reexperienced in at least one of the following ways:
1. Recurrent images
2. Thoughts
3. Dreams
4. Illusions
5. Flashback episodes
6. A sense of reliving the experience
7. Distress on exposure to reminders of the traumatic event

D. Marked avoidance of stimuli that arouse recollections of the trauma (e.g., thoughts, feelings, conversations, activities, places, people)

E. Marked symptoms of anxiety or increased arousal (e.g., difficulty sleeping, irritability, poor concentration, hypervigilance, exaggerated startle response, motor restlessness)

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or impairs the individual's ability to pursue some necessary task, such as obtaining necessary assistance or mobilizing personal resources by telling family members about the traumatic experience

G. The disturbance lasts for a minimum of 2 days and a maximum of 4 weeks and occurs within 4 weeks of the traumatic event

H. The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition, is not better accounted for by Brief Psychotic Disorder, and is not merely an exacerbation of a pre-existing Axis I or Axis II disorder

When an individual who has been exposed to a traumatic event develops anxiety symptoms, reexperiencing of the event, and avoidance of stimuli related to the event lasting more than four weeks they may be suffering from this Anxiety Disorder.

Diagnostic criteria for 309.81 Posttraumatic Stress Disorder (DSM-IV)

A. The person has been exposed to a traumatic event in which both of the following were present:
1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
2. The person's response involved intense fear, helplessness, or horror;
   Note: In children, this may be expressed instead by disorganized or agitated behavior

B. The traumatic event is persistently reexperienced in one (or more) of the following ways:
1. Recurrent and intrusive distressing recollections of the event, including images, thoughts or perceptions;
   Note: In young children, repetitive play may occur in which themes or aspects of the trauma are expressed
2. Recurrent distressing dreams of the even;
   Note: In children, there may be frightening dreams without recognizable content
3. Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated);
   Note: In young children, trauma-specific reenactment may occur
4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
5. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:
1. Efforts to avoid thoughts, feelings, or conversations associated with the trauma
2. Efforts to avoid activities, places, or people that arouse recollections of the trauma
3. Inability to recall an important aspect of the trauma
4. Markedly diminished interest or participation in significant activities
5. Feeling of detachment or estrangement from others
6. Restricted range of affect (e.g., unable to have loving feelings)
7. Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:
1. Difficulty falling or staying asleep
2. Irritability or outbursts of anger
3. Difficulty concentrating
4. Hypervigilance
5. Exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C, and D) is more than 1 month

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

Specify if:
Acute: duration of symptoms is less than 3 months
Chronic: duration of symptoms is 3 months or more
With Delayed Onset: onset of symptoms is at least 6 months after the stressor

MDD diagnosis is based on the following list of symptoms, and requires the presence of symptom A, B, or both; and at least 5 of 9 symptoms overall; These symptoms must persist for at least 2 weeks

A. Depressed mood nearly every day for most of the day, based on self report or observation of others
B. Marked reduction or loss of interest or pleasure in all, or nearly all, activities for most of the day, nearly every day
C. Significant non-dieting weight loss or weight gain (> 5% change in body weight)
D. Insomnia or hypersomnia nearly every day
E. Psychomotor agitation or retardation (should be observable by others)
F. Fatigue/loss of energy nearly every day
G. Feelings of worthlessness or excessive/inappropriate guilt (possibly delusional) nearly every day
H. Diminished cognitive function (reduced ability to think or concentrate, or indecisiveness) nearly every day
I. Recurrent thoughts of death and/or suicide, suicide planning, or a suicide attempt

DSM-IV-TR Criteria for Substance Abuse

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by one (or more) of the following, occurring at any time in the same 12-month period:

A. Recurrent substance use resulting in a failure to fulfill major role obligations at work, school, or home
B. Recurrent substance use in situations in which it is physically hazardous
C. Recurrent substance-related legal problems
D. Continued substance use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of the substance

DSM-IV-TR Criteria for Substance Dependence:

A maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three (or more) of the following seven criteria, occurring at any time in the same 12-month period:

A. Tolerance, as defined by either of the following:
1. A need for markedly increased amounts of the substance to achieve intoxication or desired effect
2. Markedly diminished effect with continued use of the same amount of the substance

B. Withdrawal, as defined by either of the following:
1. The characteristic withdrawal syndrome for the substance (refer to DSM-IV-TR for further details)
2. The same (or a closely related) substance is taken to relieve or avoid withdrawal symptoms

C. The substance is often taken in larger amounts or over a longer period than was intended

D. There is a persistent desire or there are unsuccessful efforts to cut down or control substance use

E. A great deal of time is spent in activities necessary to obtain the substance (e.g., visiting multiple doctors or driving long distances to see one), use the substance (e.g., chain smoking), or recover from its effects

F. Important social, occupational, or recreational activities are given up or reduced because of substance use

G. The substance use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by the substance (e.g.,current cocaine use despite recognition of cocaine-induced depression or continued drinking despite recognition that an ulcer was made worse by alcohol consumption); Dependence exists on a continuum of severity: remission requires a period of at least 30 days without meeting full diagnostic criteria and is specified as Early (first 12 months) or Sustained (beyond 12 months) and Partial (some continued criteria met) versus Full (no criteria met)

American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders (DSM), 4th ed, Text Revision. Washington, DC: American Psychiatric Association; 2000.

DSM-IV & DSM-IV-TR Cautionary Statement

- The specified diagnostic criteria for each psychological disorder are offered as guidelines for making diagnoses, because it has been demonstrated that the use of such criteria enhances agreement among clinicians and investigators; The proper use of these criteria requires specialized clinical training that provides both a body of knowledge and clinical skills
- These diagnostic criteria and the DSM-IV Classification of psychological disorders reflect a consensus of current formulations of evolving knowledge in our field; They do not encompass, however, all the conditions for which people may be treated or that may be appropriate topics for research efforts
- The purpose of DSM-IV is to provide clear descriptions of diagnostic categories in order to enable clinicians and investigators to diagnose, communicate about, study, and treat people with various psychological disorders; It is to be understood that inclusion here, for clinical and research purposes, of a diagnostic category such as Pathological Gambling or Pedophilia does not imply that the condition meets legal or other nonmedical criteria for what constitutes psychological disease, psychological disorder, or psychological disability The clinical and scientific considerations involved in categorization of these conditions as psychological disorders may not be wholly relevant to legal judgments, for example, that take into account such issues as individual responsibility, disability determination and competency

Appendix III: TBI Criteria

Traumatic Brain Injury (DoD 2007)

A traumatically induced structural injury and/or physiological disruption of brain function as a result of an external force that is indicated by new onset or worsening of at least one of the following clinical signs immediately following the event:

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

Mild Traumatic Brain Injury Criteria (DoD 2007)

- Structural imaging: normal
- Loss of consciousness: 0-30 minutes
- Alteration of consciousness/mental state (AOC): ≤ 24 hours
- Posttraumatic amnesia (PTA): ≤ 24 hours

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