

**Report of the Meeting of the
Expert Panel on Sleep Disturbance and Combat Trauma**

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I. EXECUTIVE SUMMARY

I. A. Introduction

Sleep disturbances are increasingly recognized as highly prevalent among Veterans, including those returning from recent deployments for Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF). In regard to the latter group, sleep disturbance is the second most common referral following post-deployment screening. It is also the case that insomnia is a transdiagnostic phenomenon; insomnia is associated with comorbid conditions common among VA patients such as depression, post-traumatic stress disorder (PTSD), traumatic brain injury (TBI) and heterogeneous types of chronic pain conditions. Even with effective treatments of these disorders, residual sleep disturbances often remain. For instance, up to half of patients responding positively to treatment for PTSD endorse having residual insomnia. Trauma-related sleep disturbance, therefore, represent a major problem among Veterans.

Although several efficacious treatments for sleep disturbances exist, limited knowledge and training of health care providers regarding these strategies hinder their dissemination within VA. This is true for sleep disturbances as a whole and perhaps even more so for trauma-related sleep disturbances. This current state of affairs is not limited to VA health care system, but due to the high prevalence of trauma-related sleep problems among Veterans, VA is well-positioned to take a lead in resolving the problem.

In order to address these issues and provide suggestions that may be useful to VA as well to VA health care providers and research investigators, several individual academicians (with and without VA affiliations) sought support to convene an expert panel and conference to address the topic of Sleep Disturbances and Combat Trauma. Financial and administrative support for the conference was provided by the VISN2 Center for Integrated Healthcare in Syracuse with joint sponsorship by the VISN2 Center of Excellence at Canandaigua. Additional financial support was provided by the University of Rochester Medical Center's Department of Psychiatry and its Sleep & Neurophysiology Research Laboratory.

The conference took place on September 8-9, 2008 in Rochester, New York. Participants included twelve experts (nine with current VA affiliations and 3 without) in the field of sleep and trauma and an additional 10 invited participants to provide input from VA primary care and psychology services. The group was also addressed by Dr. Bradley Karlin (Director, Psychotherapy Programs, VACO). A list of panel members and attendees and their affiliations, is provided on pages 34-36 including disclosures of potential conflicts of interest of the panel members (all of whom served as authors of this report).

The panel was charged with fulfilling a set of related goals:

- Develop a consensus statement on available empirically supported treatments for insomnia and other sleep disturbances associated with combat trauma;
- Recommend future steps that VA may take to augment its existing training initiatives in evidence-based psychotherapies, including sleep interventions, and to disseminate such training;
- Identify gaps in the research literature, both in terms of evidence-based treatments and broader research questions that are important to VA and propose a research agenda to bridge any such gaps;

- Agree on a core set of instruments, measures and/or methodologies for use in future research in the above areas; and
- Develop a dissemination plan for the recommendations of this conference and panel.

This executive summary provides an overview of the panel recommendations for each of the goals set forth above. Following the executive summary, a detailed report summarizes the discussion that took place during the conference including the contributions of invited attendees who are mental health and primary care providers from VISN 2 and members of the VA Center for Integrated Healthcare in Syracuse and the VA Center of Excellence at Canandaigua. The detailed report also lists specific panel recommendations for each of the goals set forth above.

I.B. Panel Recommendations (Executive Summary)

1. The panel recommends adoption of its Consensus Statement on Empirically Supported Treatments for Insomnia & Nightmares. Treatments were categorized into one of four categories based on the level of empirical evidence supporting them. The panel consensus organized by category is as follows:

- **Category 1: Evidenced-Based Treatment with considerable empirical support.** No treatments currently meet the standards of a Category 1 designation as the treatment literature with respect to sleep and trauma is in a relatively nascent stage.
- **Category 2: Promising Treatment with modest empirical support.** For insomnia, Cognitive-Behavioral Therapy for Insomnia (CBT) meets a Category 2 designation. For nightmares, the alpha-1 adrenoreceptor antagonist prazosin for nightmares (with ancillary benefit for insomnia) meets a Category 2 designation. For insomnia and nightmares combined, the combination of CBT and Imagery Rehearsal Therapy (IRT) delivered in tandem, meets a Category 2 designation. For PTSD-related sleep disturbances, novel antipsychotic drugs as a class, including risperidone, olanzapine, and quetiapine, meet the Category 2 designation based on the evidence base, but are more appropriate for second line use due to possible sedation and metabolic complications.
- **Category 3: Potentially Promising Treatment with limited/no empirical support, but modest-considerable empirical support in non-trauma populations.** For insomnia, the novel benzodiazepine receptor agonists (BZRAs), zolpidem, zaleplon and eszopiclone; the melatonin receptor agonist, ramelteon; and for nightmares, Imagery Rehearsal Therapy (IRT) meets the Category 3 designation. For PTSD-related sleep disturbances, Prolonged Exposure (PE) and Cognitive Processing Therapy (CPT) meet the category 3 designation of some limited empirical support.
- **Category 4: Insufficient Evidence (or negative evidence) to support this intervention for trauma-related sleep disturbance.** The following treatments have insufficient evidence (or negative evidence) for the treatment of trauma-related sleep disturbances: benzodiazepines; selective serotonin reuptake inhibitors (SSRIs); sedating antidepressants such as amitriptyline, trimipramine, doxepin and trazodone; the antihistamine and serotonin

receptor antagonist cyproheptadine; the alpha-2 adrenergic agonist guanfacine; and Acceptance and Commitment Therapy (ACT).

2. The panel recommends that VA utilize its existing training format(s) to widely disseminate:

- continuing education activities for primary care providers that focus on the identification and management of sleep disturbances, interventions that can be accomplished in the primary care setting, and when and how to refer patients to sleep specialists;
- continuing education activities for mental health providers related to managing sleep problems in Veterans with trauma exposure;
- competency training for mental health providers in CBT for insomnia; and
- advanced training in CBT for insomnia and IRT for mental health providers already trained in some other form of CBT.

3. As a practical way to widely disseminate basic training, while developing a growing number of expert providers, the panel recommends that the following be considered:

- draw from existing experts within VA to serve as initial trainers, but move towards a “train-the-trainer” model at an appropriate pace;
- set as a goal, on a VA determined timeline, having a clinician with expertise in behavioral sleep medicine on staff first at the VISN level and then at the VAMC level;
- set as a goal for all existing VA sleep disorders clinics having a clinician with expertise in behavioral sleep medicine on staff; and
- encourage VA experts in Collaborative and Integrated Health Care to meet with VA experts in behavioral sleep medicine to outline how to both provide both training and treatment within such models of care.

4. The panel also strongly recommends that the Iraq War Clinician’s Guide Appendix for Sleep Problems be revised and expanded (specific recommendations in the detailed summary).

5. The panel recommends a research agenda for trauma-related sleep disturbances for VA-sponsored Research and Development (R&D) programmatic areas most aligned with the topic. For VA Clinical Sciences Research and Development, the panel recommends the establishment of a systematic clinical science research agenda for trauma-related sleep disturbances that focuses on:

- definitive randomized controlled trials (with some large multi-site and/or cooperative studies) of CBT for insomnia, IRT and prazosin in various trauma populations including those with and without PTSD, with and without TBI, and with and without other common comorbidities such as chronic pain and depression; sequencing and combining sleep treatments with established treatments for PTSD, TBI and other common comorbidities; and

novel or under-studied treatments for sleep disturbances such as sedating antidepressant and novel antipsychotic medications;

- longitudinal observational studies be undertaken to assess the role of good sleep, natural short sleep tendency, and natural “owl” sleep tendency in resilience; the role of sleep disturbances as a risk factor for suicide; and the role of disturbed sleep in family/marital/domestic problems;
- strengthening assessment and diagnostic instruments pertaining to nightmares, disturbing dreams, parasomnias, and sleep-related movement disorders in veteran trauma populations; and
- including a variety of outcome measures regarding general health and functioning as well as the impact of treatment on comorbid conditions; assessing what patient specific factors are associated with enhanced adherence and improved outcomes; and assessing related sleep disturbances that may not receive targeted funding such as sleep related movement disorders.

6. For VA Biomedical Laboratory Research and Development, the panel recommends a targeted research agenda for trauma-related sleep disturbances that focuses on:

- developing animal and human models of stress-related sleep disturbances utilizing a variety of experimental approaches and measurement techniques; and
- identifying mechanisms and/or markers for the development and persistence of trauma-related sleep disturbances.

7. For VA Health Services Research and Development, the panel recommends a research agenda for trauma-related sleep disturbances that focuses on:

- the use and acceptance of current and emerging treatment strategies for trauma-related sleep disturbances across VA settings;
- the feasibility, comparative effectiveness, cost effectiveness and health care utilization impact of various treatment delivery models for current and to-be developed treatments for trauma-related sleep disturbances.
- examining the health related morbidity (e.g. cardiovascular disease risk) of long-term sleep disturbances associated with PTSD.
- development of patient, provider and system-level outcomes of training initiatives targeting treatment of sleep disturbances.

8. The panel recommends the use of a specific set of assessment tools (listed in the detailed summary) to be used for: 1) defining sleep disturbance for enrollment in research studies with trauma survivors; 2) assessment of sleep symptoms in research studies with trauma survivors; and 3) clinical assessment and monitoring.

9. The panel recommends that the results of this meeting and the content of this report be widely and actively disseminated by:

- presentations (in person) to appropriate VA centers such as the National Center for PTSD, VA MIRECCs and Centers of Excellence; and collaborations with these centers;
- targeting primary care, psychiatry, and psychology peer-reviewed journals read by VA providers for publication of these recommendations;
- developing general and specific internal marketing efforts to highlight the importance of sleep (general) and the resources currently available and planned for training (specific);
- developing a manual that can be disseminated to clinicians and that would facilitate training (if the Iraq Clinician Guide is revised and expanded it may serve this dual purpose)

II. DETAILED SUMMARY

II.A. Empirically Supported Treatments for Insomnia & Nightmares

While there is a good deal of efficacy data with respect to treating insomnia and related sleep disturbances with a range of cognitive-behavioral interventions and hypnotic medications, there are only limited efficacy data with respect to trauma-related sleep disturbances. For instance, as evidenced by revisions under consideration for American Psychiatric Association practice guidelines, it is increasingly clear that what has been demonstrated to be effective for PTSD in civilian cohorts may not generalize to combat-related PTSD (e.g., SSRIs shown to be effective in civilian PTSD, have shown no efficacy with combat-related PTSD). It also cannot be assumed that findings focused on older Veterans (e.g., Vietnam era Veterans) will necessarily be the same with the current cohort of Veterans.

Accordingly, the panel notes a need to adapt treatments to specific target populations (e.g., military sexual trauma victims and those who experienced trauma under sustained hyperarousal conditions). It remains unclear as to whether or not existing treatments are both broad enough and specific enough to be useful across diagnostic categories presenting with a sleep disturbance. To the extent that a selective treatment approach with different patient subgroups is most beneficial, it remains to be shown which treatment strategies need to be adapted and how they need to be modified.

Despite these barriers, sleep disturbances represent an excellent therapeutic target for several reasons. First, sleep disturbances tend to respond quite well to treatment, and the effect sizes tend to be rather large. Second, because sleep disturbances are transdiagnostic symptoms (i.e., symptoms indicative of several disorders), addressing these disturbances systematically may reach a large number of Veterans and have a large public health impact. Third, patients are generally pleased to have their sleep improved and believe that this helps them to function better in their occupational and social roles. Fourth, recent work has begun to show that improvements in sleep also generalize to improvements in comorbid conditions, thus sleep disturbances represent a modifiable risk factor for a number of conditions and health outcomes. Fifth, sleep is considered an acceptable symptom for which to seek treatment and it does not come with the stigma that can be attached to a “mental health” problem. Finally, treating sleep (particularly when a good outcome is achieved) becomes a positive introduction to treatment in general and may make accessing additional care for mental health/trauma problems more appealing to Veterans.

The panel also discussed in depth the unique sleep issues that may affect the sleep of OEF/OIF soldiers and/or Veterans. These include the nature of their sleep while in theatre, such as circadian rhythm disturbances from shift work; cultural influences that promote alertness and downplay the need for sleep; social sleeping (sleeping in groups), high consumption of caffeine and other stimulants, and use of hypnotics in the field. Following deployment and upon returning to a home environment learned sleep behaviors may create or exacerbate sleep disruption. Psychosocial factors associated with reintegration can also influence sleep. For example, anger may affect sleep by elevating baseline arousal, and, when arguments occur in bed, they may disrupt normal sleep routines. Medical and substance-related issues include the inappropriate use of alcohol as a sleep aid and the high rates of TBI and chronic pain, each of which are strongly associated with sleep disturbances. Mild TBI in particular has been associated with circadian rhythm disturbances that affect sleep. Parasomnia-like behaviors, including punching, yelling, walking and falling during sleep, have been anecdotally noted in OEF/OIF cohorts including punching, yelling, walking, and falling during sleep; the true prevalence of such nocturnal behaviors is not known in this population, nor is the mechanism or precise sleep disorder from which they derive. Finally, it bears

repeating that stigma associated with seeking any form of mental health services may reduce the probability of a veteran seeking help for sleep problems and that the concern about stigma is believed to be especially prevalent in current returning Veterans, contributing to their high no-show rates for mental health appointments.

When Veterans do present for treatment, it is important to ask about treatment and treatment delivery preferences. For instance, some Veterans, hoping for rapid improvement in the short term, may prefer medication over behavioral treatment, but others may voice concerns about the effects of chronic drug administration on their health. Also, many Veterans may request instruction in relaxation methods (many bases now have a relaxation room). Many clinicians believe that treatments that can be delivered quickly and efficiently tend to result in lower dropout rates and that, accordingly, initial success with brief interventions can create increased willingness to engage in more emotionally demanding treatment (e.g. PTSD treatments in which drop outs rates can be high). Younger Veterans may prefer to incorporate the use of technology in their treatment.

Some unique sleep issues pertain to Vietnam Era Veterans. They are an aging cohort, with the same high prevalence of a range of sleep disorders that occurs in other older groups. As is the case in the general population, other medical conditions may take precedence over sleep problems in the provision of health care to Vietnam Era Veterans; therefore, recent onset (or even long-existing) sleep disorders are often under-treated. Even clinicians who treat geriatric patients may be unaware that most of the treatments available for sleep disturbances retain their efficacy when delivered to older adults. Vietnam Veterans with long-standing trauma/PTSD for which they have been followed for many years may be less inclined to address sleep problems, believing that they have already tried all available treatments. Whether or not they have had treatment for PTSD, patients with sleep disturbances related to chronic PTSD may be more refractory to sleep-focused interventions; however, this is largely untested. At the very least, such patients present the clinician a more complex challenge than do younger Veterans. Given the efficacy of sleep interventions for older adults in the general population, reports of well-functioning older Veterans developing delayed-onset PTSD (or rekindling of remitted PTSD) as a result of either retirement and/or media coverage of the current conflicts suggest that there is a group of older Veterans for whom a sleep intervention may produce a good outcome.

The panel recognizes a number of issues related to the needs of VA providers that should be considered when developing treatments in a health care system that is seeing a large influx of Veterans seeking care. Group screenings have been used in both civilian and VA settings with some success and may be germane to sleep disturbances. Sleep disturbance could be part of the screening assessment in such settings. For example, patients identifying a sleep problem on the post-deployment screening (which includes some sleep items) may then participate in a sleep-specific group screening and sleep education session that sets the stage for treatment. The latter would result in a significant time-saving to providers, particularly if there were a report and list of recommendations to the primary care and/or mental health provider. In addition, VA culture has certainly established the group modality as an acceptable method of treatment delivery. Of course, to the extent that attendance is high enough, this can also save resources. Group therapy is a cost-effective alternative to individual treatment for insomnia management in the general population. The use of brief effective treatments, whether in group or individual format, can alleviate some of the burden on VA healthcare. Psychotherapeutic interventions for sleep disturbances are already brief, with even the longest structured interventions spanning 8 sessions at most, and with several briefer versions having been tested.

Taking these issues into consideration, the panel reviewed treatments for sleep disturbances in general and whether these have demonstrated effectiveness in any trauma populations and for combat trauma in particular. Recommendations were formulated based on the availability and nature of efficacy data for each treatment. Treatments were categorized into one of the following four categories; (1) Evidenced-Based Treatment with considerable empirical support; (2) Promising Treatment with modest empirical support; (3) Potentially Promising Treatment with limited/no empirical support, but modest-considerable empirical support in non-trauma populations; (4) Insufficient Evidence to support this intervention for trauma-related sleep disturbance. None of the treatments received a Category 1 designation, as the treatment literature with respect to sleep and trauma is in a relatively nascent stage.

Novel Benzodiazepine receptor agonists (BZRAs) are considered an evidenced based treatment with considerable empirical support for primary insomnia. The first BZRA medications developed and marketed as hypnotics were zolpidem and zopiclone with the more recent additions of zaleplon and eszopiclone. Each is chemically distinct, but they all act as agonists at the benzodiazepine receptor component of the GABA receptor chloride channel complex and preferentially bind to the alpha 1 receptor subunit; this is thought to explain their minimal anticonvulsant and muscle relaxant action. The selective hypnotic effect is an important advantage over the benzodiazepines, particularly for elderly individuals. BZRAs are less likely to produce residual “hangover” the next day, are safer than benzodiazepines in overdose, possess a low risk of withdrawal effects, and have minimal tolerance issues. There are emerging data that support the use of this class of hypnotic agents in some comorbid conditions (e.g., major depression), but limited evidence for their efficacy for trauma/PTSD-related insomnia.

In terms of cautions to consider with the BZRAs, there are well-publicized reports of complex and potentially dangerous nocturnal behaviors; there may be little or no recall for such events. The risk for such events appears to increase among individuals who use BZRAs in higher than prescribed dosages, combine them with other sedating substances, or are markedly sleep-deprived. As with any hypnotic medication, the combination of a BZRA with other sedatives, including alcohol, can be problematic and potentially lethal.

Panel Recommendation: Based solely on their efficacy in primary insomnia and insomnia comorbid with certain mental disorders, novel BZRAs are a potentially promising treatment for trauma-related insomnia. At this time, there is no basis to recommend novel BZRAs as first line treatments for trauma-related sleep disturbances.

Melatonin Receptor Agonist, namely ramelteon, acts as an agonist at the M1 and M2 melatonin receptors. There are good safety and modest efficacy data in both primary and comorbid insomnias. Ramelteon has an even more benign side-effect profile than the BZRAs with no evidence of tolerance, rebound insomnia or morning sedation. It is often used in older adults when there are concerns about such side effects.

Panel Recommendation: Ramelteon is a potentially promising treatment for trauma-related insomnia based solely on its efficacy in primary insomnia and some comorbid insomnias. At this time, there is no basis to recommend this agent as a first line treatment for trauma-related sleep disturbances.

The **Benzodiazepine (BZDs)** class of hypnotics binds to the benzodiazepine receptor component of the GABA receptor chloride channel complex. The alpha subunit of the GABA receptor is the main component of this complex, and at least five alpha subtypes have been recognized. Most of the older benzodiazepines bind to multiple alpha subtypes. This nonselective binding is thought to cause their hypnotic, anticonvulsant, muscle relaxant, and other CNS actions. Whereas there is demonstrated efficacy of BZDs for insomnia, there was historically concern about their side effect profile, including tolerance, abuse potential, rebound insomnia, daytime sedation, and negative effects on sleep architecture. As a class, the side effects were far less severe than those seen with the use of barbiturates as sedative-hypnotic agents. Nonetheless, with the advent of newer hypnotics (see BZRAs, above), BZDs are not considered optimal first line treatments for primary or comorbid insomnia.

BZDs are, however, often promoted for sleep-related movement disorders (e.g., clonazepam) with limited evidence of their efficacy. BZDs have also been evaluated for a treatment of PTSD with mixed results. For instance, both temazepam and alprazolam have shown no, to limited effect on either preventing or improving PTSD. There is also a case series report of adverse experience associated with benzodiazepine use (e.g., disinhibition, more severe withdrawal symptoms). An additional consideration is that recovery from PTSD may involve active learning (some of which may go on during sleep) and that BZDs may interfere with that process. Nonetheless, BZDs continue to be widely prescribed in VA as part of the management strategy for PTSD, partially based on the assumption that they may simultaneously address both anxiety and sleep symptoms, but with no evidence for this assumption.

Panel Recommendation: There is no evidence to support the use of benzodiazepines as a first line treatment of trauma-related sleep disturbances and some evidence that they may be contraindicated. BZDs may be considered in the absence of treatment response to other treatment approaches.

Sedating antidepressants are widely used to treat sleep disturbances despite an extremely limited empirical base. Given what some physicians believe to be minimal long-term efficacy data on BZRAs, a pervasive belief that chronic insomnia is a symptom of depression (acute or subclinical), and abundant data on the long-term efficacy and safety of sedating antidepressants for the treatment of depression, their status as non-scheduled drugs, and their low cost, many have opted to use sedating antidepressants for the long-term management of insomnia. The medications typically prescribed for this purpose are amitriptyline, trimipramine, doxepin and trazodone. This management strategy has burgeoned so dramatically that trazodone is prescribed in the USA as a hypnotic 30% more frequently than any other medication. This is so despite very limited evidence for its effectiveness in treating insomnia in the absence of depression¹⁶ and no safety data on its use for primary insomnia. Given the small handful of preliminary studies and the much larger anecdotal support for agents that target the 5HT_{2a} receptor improving sleep, including in PTSD patients, some new agents targeting this receptor have been developed and are currently in various phases of the FDA approval process. Unfortunately, generic drugs such as trazodone are unlikely to be evaluated empirically. Given its low cost and purported efficacy, a study of trazodone would provide useful information for the VA (see research recommendations).

Panel Recommendation: There is currently no evidence to support the use of sedating antidepressants as a first line treatment of trauma-related sleep disturbances.

Novel antipsychotics include resperidone, olanzapine, and quetiapine. These agents have had an enormous uptake in the treatment of PTSD (in both civilian and veteran populations), and appear to be prescribed for sleep disturbances (primarily insomnia). There are three blinded-control studies and four uncontrolled studies of the use of these agents in the treatment of PTSD, which provide some evidence that they are effective for the treatment of sleep disturbance. One significant downside of these agents is their harms profile. Adverse events for the novel antipsychotic class of agents include metabolic complications and sedation, such that even high functioning individuals may experience significant “hang-over” effect and/or impairment of daytime functioning.

Panel Recommendation: Novel antipsychotics represent a promising class of medications for trauma-related sleep disturbances based on the evidence base, though not as a first line treatment due to their harms profile.

Prazosin, which was originally introduced to treat hypertension, is a short-acting non-sedating generic alpha-1 adrenoreceptor antagonist that easily crosses the blood-brain barrier. It has been found to markedly reduce nightmares and sleep disturbance in two placebo-controlled trials with Vietnam Veterans and in one civilian PTSD cohort without producing sedation or fatigue. Prazosin does not eliminate dreaming, but patients report that dreams become more normal in that they may still have disturbing content, but that such content is less trauma-specific. Prazosin has not been found to decrease sleep latency (i.e. the ability to fall asleep), but has been shown to improve sleep maintenance and decrease disturbing dreams/nightmares. It has also been shown to reduce suicidal ideation and alcohol abuse as “self-medication” for sleep difficulty.

Patients with PTSD have been found to have a number of REM-related abnormalities including the following findings: (1) REM sleep is both more fragmented and has increased levels of phasic activity; (2) there is a failure of the normal inhibition of sympathetic noradrenergic activity during sleep (particularly REM sleep); (3) heart rate variability indices consistent with sympathetic activation are higher in the initial REM sleep period of those who are developing PTSD; and (4) dreams of PTSD patients are not only disturbing, but are more realistic than the dreams described by normal sleepers.. It has also been shown in various ways that noradrenergic input is important for consolidating/enhancing fear-enhanced memory. It is believed that if REM sleep is disturbed, then the normal processing of emotional memories is disrupted. Therefore, Prazosin, which is the one adrenergic blocker that maintains REM sleep, is putatively allowing REM sleep to occur in a more normal fashion.

Prazosin does have some limited potential adverse effects including orthostatic dizziness. This side effect can be avoided by starting patients with a low dose and titrating upward gradually. Slow titration is particularly important if prazosin is taken with other antihypertensives, or if one has a low baseline blood pressure. Assuming an upright posture gradually can reduce the risk of dizziness when prazosin is being titrated upwards. Some psychiatrists and other physicians have been reluctant to increase the dosage of prazosin for nightmares when patients do not respond to initial doses. Doses of up to 15 mg have been well-tolerated with limited side effects. The most common side effects, however, are headache and nasal congestion. Some older persons can also develop some pretibial edema. In general, prazosin is very well tolerated.

A potential limitation of this drug is that its discontinuation may be associated with a return of nightmares. However, there are anecdotal reports from current combat personnel that discontinuation following short-term prescription in OEF soldiers was not associated with a return of nightmares. An additional note of caution based on the anxiety literature is that when cognitive behavioral

interventions are combined with benzodiazepines, the medication can sometimes diminish the durability of treatment effects. Fear can return when medication is withdrawn because fear extinction can be context dependent (including medicated versus non-medicated states). It is not known whether prazosin might similarly affect learning during CBT for insomnia. On the other hand, prazosin may help patients tolerate the stress of exposure-based therapies so that such therapies can succeed. Clinicians need to consider the advantages and disadvantages of either initiating or discontinuing the use of prazosin when conducting CBT interventions for PTSD. The optimal strategy remains an empirical question to be answered. There are some suggestions that combining prazosin with some supportive group cognitive therapy that includes cognitive restructuring may be helpful, though this has not been tested. An additional consideration is that prazosin is off-patent and inexpensive. It is made generically by two different companies, but there have been occasional shortages worldwide.

Panel Recommendation: Prazosin is a promising treatment for trauma-related nightmares and distressed awakenings and this agent also improves overall sleep complaints; it has a modest level of empirical support, though a large, multi-site trial is now underway (a 13-site VA cooperative study of prazosin for combat trauma nightmares and sleep disruption in PTSD). In light of available evidence, prazosin should be considered a first line therapy for nightmares associated with combat trauma.

Other Medications have been used to treat sleep disturbances with mixed results. These include **Selective Serotonin Reuptake Inhibitors (SSRIs)**, which are the only FDA-approved treatment for PTSD, but this is based primarily on studies of predominately female civilian populations; they do not appear to be effective in chronic populations treated in VA settings. Whether this is due to gender differences, the nature of the trauma, or some other factor related to the populations selected for those trials is an open question. However, even when effective for treating PTSD, the SSRIs as a class typically do not address insomnia or nightmares. In several studies of major depressive disorder in civilian populations approximately 50% of participants responding to a variety of antidepressant medications had residual insomnia. In addition, SSRIs and some serotonin-norepinephrine reuptake inhibitors (SNRIs) are known to precipitate nocturnal motor activity and REM behavior disorder-like symptoms.

Cyproheptadine is an antihistamine and serotonin receptor antagonist that was highly promoted based on some open label reports. However, one study (Freidman) showed worsening nightmares with cyproheptadine treatment.

Clonidine/guanfacine (long-acting Clonidine) is an alpha2-adrenergic agonist that reduces central noradrenergic activity and is actually REM-suppressive. There is an anecdotal literature that clonidine reduces nightmares with PTSD, especially in children. No benefit has been found using this agent with combat Veterans, however, suggesting that the manner in which the adrenergic system is targeted is important (i.e. the possibility that alpha-1 antagonism and not alpha-2 agonism is effective in adults).

Novel “Pipeline” drugs have been developed and are in various stages of FDA approval. These include reformulations of existing approved agents that have higher binding affinities or modified release delivery mechanisms, agents that bind to non-synaptic benzodiazepine receptor sites, and agents that modulate gamma-aminobutyric acid (GABA), 5HT2a receptors, the orexin/hypocretin system and the histaminergic system. None of these agents has been studied in trauma populations although there are early trials underway to evaluate corticotropin releasing factor (CRF) antagonists in PTSD patients.

Panel Recommendation: There are no data to support the use of SSRIs, cyprohepatadine, or guanfacine in the treatment of trauma-related sleep disturbance and some evidence that they may be contra-indicated. The field awaits additional data with respect to pipeline drugs.

Cognitive-Behavioral Therapy for Insomnia (CBT) refers to a set of psychotherapeutic interventions that draw on cognitive therapy and behavioral therapy as they are applied to insomnia. Some individual psychological and behavioral interventions may be delivered effectively as mono-therapies, but multi-component CBT tends to have larger effect sizes than mono-therapies (although no dismantling studies have been undertaken to empirically test the components of CBT). Based on the available data and on clinical intuition, it remains widely accepted that multi-component CBT is the best approach to treatment. Multi-component CBT includes sleep education, three behavioral strategies (stimulus control, sleep restriction, and sleep hygiene; the latter considered by some to be more psychoeducation, than a behavioral strategy), cognitive therapy, relaxation therapy and, in some cases bright light therapy when indicated. Such a combined strategy addresses the multiple putative causes and perpetuators of insomnia and reflects clinical practice.

Sleep Education consists of providing patients with a basic knowledge about sleep processes and functions, sleep architecture, developmental changes in sleep, circadian rhythms, individual sleep needs, and sleep deprivation. Sleep education also often comprises providing a treatment rationale, setting treatment expectations and establishing motivation for treatment. This component is not always “broken out” as it tends to be delivered with the other treatment components.

Stimulus Control Therapy is considered a first line behavioral treatment for chronic primary insomnia and therefore should be prioritized accordingly. Stimulus control instructions are based on an operant conditioning model that explains the development and maintenance of insomnia. The goals of treatment are to strengthen the bed and bedroom as cues for sleep, weaken them as cues for arousal, and develop a consistent sleep-wake schedule. Typical instructions include: (1) keep a fixed wake time 7 days per week, irrespective of how much sleep you get during the night; (2) avoid any behavior in the bed or bedroom other than sleep or sexual activity; (3) leave the bedroom when awake for approximately 10-15 minutes.; (4) go to bed only when sleepy. The combination of these instructions re-establishes the bed and bedroom as strong cues for sleep and entrains the circadian sleep-wake cycle to the desired phase.

Sleep Restriction Therapy (SRT) requires patients to limit the amount of time they spend in bed to match their average total sleep time by strictly monitoring these variables with daily sleep diaries. The patient establishes a fixed wake time and then establishes a sleep window by setting a bedtime that will match the total sleep opportunity to their total sleep time from sleep diaries. Adjustments to the sleep window are based on weekly sleep efficiency derived from the prior weeks’ sleep diaries. If sleep efficiency (TST/sleep window) is $\geq 90\%$, the sleep window is increased by 15 minutes. If sleep efficiency is $< 90\%$ and $\geq 85\%$, the sleep window remains unchanged and if sleep efficiency is $< 85\%$ it is decreased by 15 minutes. This process continues on a weekly basis. One reason that sleep restriction is not considered a first-line monotherapy is that few studies have been done assessing sleep restriction as a monotherapy. Intervention research in insomnia has largely evaluated multi-component CBT. Sleep restriction is contraindicated in patients with histories of bipolar disorder, seizures, or untreated hypersomnolence (e.g. due to sleep apnea) as it may aggravate these conditions. Patients with chronic conditions, as commonly seen in the VA, may need a less restrictive approach to avoid fatigue and exacerbation of disease-related symptoms.

Sleep Hygiene requires that the clinician and patient review a set of instructions which are geared toward helping the patient maintain good sleep habits such as keeping an environment and routine conducive to sleep, maintaining a regular bed and wake time, and avoiding tobacco, alcohol, large meals and vigorous exercise for several hours prior to bed. It should be noted that sleep hygiene instructions are not helpful when provided as a monotherapy. Simply providing patients with a “handout” is likely to lead to noncompliance, a loss of confidence in the provider, and a sense that there may be nothing other than these ‘sleep tips’ to help with insomnia.

Cognitive Therapy for insomnia has been developed in a few forms that often overlap. Some have a more didactic focus, while others use paradoxical intention, cognitive restructuring, modification of safety behaviors, and/or attentional biases. While the approaches differ in procedure, all are based on the observation that patients with insomnia have negative thoughts and beliefs about their condition and its consequences. Helping patients to challenge the veracity and usefulness of these beliefs is the basis of cognitive therapy and is thought to decrease the anxiety and arousal associated with insomnia.

Relaxation Training is often, but not always, a component of CBT for insomnia, that has been found efficacious as part of a package. A variety of relaxation techniques are available and any of them may be used as part of CBT. These include progressive muscle relaxation, diaphragmatic breathing, biofeedback, and more formal meditative techniques. The optimal relaxation method for insomnia is the technique that is most acceptable to and/or easiest to learn for the patient. Some techniques may be contraindicated by medical conditions (e.g., progressive muscle relaxation might not be ideal for patients with chronic pain conditions, which can be quite prevalent in the Veteran population) or psychiatric disorders (e.g. some techniques are difficult for patients with untreated PTSD to tolerate as they can precipitate re-experiencing symptoms).

Bright Light Therapy has antidepressant and sleep-promoting effects and may be useful for patients who have pronounced shifts in their circadian rhythms (this may be quite relevant for some patients with mTBI who have been observed to have circadian rhythm disorders). It is not a standard part of CBT for insomnia, but may be considered an adjunctive intervention. If the patient’s insomnia has a phase delay component (i.e., the patient prefers to go to bed late and wake up late) waking early by alarm and exposure to morning bright light is indicated. If the patient’s insomnia has a phase advance component (i.e., the patient prefers to go to bed early and wakes up early) exposure to evening bright light is indicated. There are some side effects of bright light therapy for some patients, including hypomania, agitation, visual blurring, eye strain and headaches. Bright light therapy is contraindicated in patients who have or are at risk for eye-related problems (e.g. patients with diabetes) and those with bipolar disorder (as bright light can trigger mania), although careful timing and dosage of bright light exposure may mitigate this risk.

Standard Delivery of CBT for Insomnia is typically structured to allow for weekly sessions over 6-8 weeks in group or individual therapy, although group therapy is labor intensive given the need to calculate weekly mean sleep variable values from daily sleep diaries for therapy to proceed. Detailed treatment manuals exist for this duration of treatment and much of the efficacy data is based on studies of this length. A 6-8 session structure allows the patient and clinician to monitor progress, maintain compliance, and arrive at treatment end with reduced nighttime wakefulness and what is usually an acceptable level of total sleep time. In the clinical setting, the number of sessions can be altered based on treatment progress and the patient’s ability to self-administer (and monitor) the interventions. There is preliminary evidence that brief behavioral therapy for insomnia delivered in 2-4 sessions has good efficacy and even briefer forms of CBT have been developed and tested.

CBT is indicated for chronic insomnia and in acute insomnia where pharmacotherapy is contraindicated. Several meta-analyses summarize the extant literature for CBT. Based on these and other findings, a 2005 NIH State of the Science Conference, concluded that CBT is effective to treat insomnia in the short-term with relatively benign side effect profiles and that CBT has more durable effects than pharmacotherapy when active treatment is discontinued. It can be employed with both primary insomnia and insomnia comorbid with some medical or psychiatric condition.

Some evidence does exist for the use of CBT for insomnia in trauma populations. In a recent trial conducted in Veterans with primary insomnia and insomnia comorbid with PTSD, an intervention consisting of 4 individual sessions (based on earlier dose response studies for primary insomnia) over a period of 8 weeks, results were promising. There were improvements in sleep outcome variables, though some of the improvements were not to a level consistent with remission of insomnia. One reason for this may relate to Zayfert and colleagues proposal that nighttime vigilance and sleep avoidance is pronounced in trauma-related PTSD, that this is very much related to trauma occurring in a sleep context (e.g. sexual trauma or coming under attack in a war zone while asleep or trying to sleep), and that standard CBT may need to be modified to address these issues to achieve optimal improvements. One published case series supports this contention and at least one other trial is currently under way to further answer this question. From a clinical perspective, it is nonetheless reasonable to tailor CBT when these issues present.

Short adaptations of CBT for insomnia have been shown effective in civilian samples, and some preliminary data support benefits from brief behavioral treatments of insomnia. These typically combine sleep hygiene education, stimulus control, and sleep restriction, and are delivered over a two- to four-week period. These approaches have the advantages of reducing the time and costs of limited resources available in most military hospitals, VA clinics, or in primary and community care settings where military returnees are likely to seek and receive care. These brief treatment protocols appear to be effective, safe, and associated with clinically significant improvements in sleep and daytime symptoms in civilian samples; they may be effective for insomnia comorbid with PTSD and other post-deployment adjustment difficulties.

The mode of treatment delivery (e.g. in-person, telephone, Internet-based, and their combination) is a topic of ongoing inquiry. Both Internet and telephone-based sleep interventions have been evaluated, but the extant literature is too small to make any recommendation other than for these modalities to be subjected to further empirical work.

Panel Recommendation: CBT for insomnia is a promising treatment for trauma-related insomnia based both on its widely demonstrated efficacy for primary insomnia and some comorbid insomnias as well as on preliminary data of its efficacy in civilian and combat trauma populations.

Panel Recommendation: In order to fully treat the specific nature of combat-related insomnia, the unique issues surrounding sleep in a combat setting and trauma-related insomnia need to be both assessed and addressed in the context of CBT.

Panel Recommendation: Sleep hygiene alone (especially when it does not include stimulus control instructions as some sleep hygiene handouts do include) is to be avoided as a monotherapy when the treatment context allows. Sleep hygiene delivered only as a patient handout with limited discussion and follow-up should be avoided altogether.

Although outside of the scope of the panel's goals, the panel believes it important to note again that sleep and fatigue problems are common symptoms with TBI and that there is limited to no data on effective medications for TBI-related sleep disturbances. There is, however, pilot work demonstrating the efficacy of CBT for insomnia and fatigue in a civilian TBI cohort.

Imagery Rehearsal Therapy (IRT) refers to treatments that use one or both of two cognitive-behavioral techniques to treat nightmares. The first technique is based on exposure therapy in which the patient is asked to describe a distressing dream and to rehearse it (in some versions of this approach the dream is written down and rehearsed); the second technique is based loosely on cognitive-restructuring in which the patient is asked to change something about the dream content and to rehearse this changed dream. All versions of IRT use the latter technique and direct the patient to change his or her nightmare and to mentally rehearse the "new" dream and make it as vivid as possible. The rationale behind this is that nightmares are a learned behavior, and that what is learned may be unlearned and replaced. This rationale tends to resonate with patients and makes sense to them, so they are likely to accept IRT. Practitioners of IRT vary on what they tell their patients to change (i.e. the dream ending, the most disturbing feature of the dream, or anything in the dream). Thus, applications of IRT also vary in the extent to which the treatment involves exposure to traumatic images/memories. Other features also have not been standardized including the length of treatment (although typically it ranges from 1-6 face-to-face sessions), whether delivered individually or in groups, the extent of between-session practice, the dream that is the focus of treatment (e.g. a nightmare that reflects the actual traumatic event, the worst nightmare, a nightmare that is less threatening, etc.). Clinical experience to date suggests that changing anything in the dream is as effective as any other approach, that avoiding focusing on a nightmare that is exactly trauma-replicating is preferred and that the dream need not be at all related to the actual trauma.

With respect to these last two points it has been observed that Veterans tend to have the most difficulty working with dreams that they consider to be historically accurate because to change anything in the dream seems false to them (i.e. "that's not the way it happened"). In these cases, working with nightmares that are not replays of the actual traumatic event may provide an effective, alternative approach. On the other hand, trauma patients in general tend to want to avoid exposure to direct trauma memories. This raises the question of whether dream rehearsal alone without modification of the dream imagery or content, which has shown success in reducing nightmares in sub-clinical populations, might show utility for veterans or other populations of trauma survivors with PTSD.

While there clearly needs to be some consensus about a standard form of IRT, this is beyond the scope of this panel. Nonetheless, IRT in various forms has been tested in twelve randomized trials with very good results, though little of this work has been done with Veterans. In civilian patients, not only do nightmare frequency and severity decrease over the course of treatment, but gains have been maintained for up to six months. The improvements in nightmares have also been found to generalize to sleep quality and daytime symptoms of depression, irritability, anxiety, and PTSD symptoms. Overall results have been replicated by different studies and with different investigator groups, though again not in Veterans. One possible route of the indirect improvements in sleep may very likely be that as nightmare frequency and/or intensity diminish (in a large minority of patients nightmares persist, but in a way that they no longer bother patients), patients may be less anxious about sleep (for fear of nightmares) and/or have fewer awakenings following disturbing dreams that lead to long periods of sustained wakefulness. There is no rebound in nightmares following discontinuation of therapy in the short term, with limited follow-up data available.

There has been one case series in 12 Australian Vietnam Veterans showing clinically meaningful improvements post treatment and at the one-year follow-up. One recent and larger trial (n=124) was completed in American Vietnam Veterans showed some improvements in nightmare intensity, but not nightmare frequency compared to a control condition focusing on healthy sleep practices. In both of studies, IRT was delivered in a group format, and veterans were instructed to select combat-related nightmares, and possible changes to rescript combat-related nightmares were discussed in groups.

Among the trials conducted in civilian populations, a large randomized trial showed that IRT was associated with significant reductions in nightmare frequency and intensity compared to a wait-list control in sexual assault survivors. In this study, IRT was also delivered in a group format, but participants were specifically instructed not to select a nightmare that depicted a replay of the trauma. Rather, they were instructed to select a bad dream of lesser intensity to rescript and mentally rehearse. There were no group discussions of the original nightmare to be modified.

An expanded variant of IRT, called Exposure, Relaxation, and Rescripting Therapy, has been evaluated in a small heterogeneous sample of adult trauma survivors with PTSD. ERRT consists of the combination of education about trauma, PTSD, and sleep; exposure to the nightmare content and distress themes during the session; diaphragmatic breathing; daily progressive muscle relaxation over the course of the three week treatment; promotion of healthy sleep practices (including avoiding staying in bed when awake and reducing caffeine consumption); and rescripting of the nightmare scenario guided by therapists and group members. Compared to a wait-list control group, ERRT is associated with clinically meaningful improvements post-treatment on measures of nightmare frequency, depression symptom severity, PTSD symptom severity and sleep quality, and improvements were maintained at the six-month follow-up.

On the other hand, it is noted that prolonged exposure to trauma memories themselves is beneficial for PTSD and nightmares. There have also been reports of robust effects of self-exposure to nightmares in several studies. Finally, one study comparing nightmare exposure alone and nightmare exposure with modification of the dream found that the two approaches were equally effective.

In general, the available literature suggests that IRT and its variants may be associated with clinically meaningful improvements in nightmares. However, the relative heterogeneity of samples, delivery formats, the nature and intensity of the target nightmare, and the level of group participation in the rescripting of the original nightmares vary considerable across studies. The import of these factors remains to be fully tested. Until further work is done, the evidence available does support the benefits of IRT and its high tolerability and safety for adults with trauma histories and PTSD.

Panel Recommendation: IRT is a potentially promising treatment for trauma-related nightmares, with strong evidence in civilian populations and limited and mixed evidence in Veterans.

CBT & IRT have been combined in a few trials with good outcomes and additional trials are currently underway to further test this approach. There is no evidence yet to determine whether these treatments are more effective if sequenced in one way or another.

Panel Recommendation: The combination of CBT for insomnia and IRT is a promising treatment for trauma-related nightmares based primarily on their individual efficacies, some shared

theoretical underpinnings, and to a lesser extent on the small literature demonstrating efficacy when they are combined.

Acceptance and Commitment Therapy (ACT) has not been evaluated in terms of its effect on sleep disturbances.

Cognitive Processing Therapy (CPT) has been evaluated in one very recent RCT (N=108) comparing CPT to PE in a sample of female, adult rape survivors in which sleep was a measured outcome. After controlling for medication use, there was no between-group difference on sleep improvement over time as assessed by the Pittsburgh Sleep Quality Index (PSQI). When the groups were collapsed, there was a large pre-post treatment effect on the PSQI that was sustained at a 9 month follow-up, albeit the mean sleep score remained above clinical cutoffs for sleep disturbance. It is unclear whether these improvements were related primarily to improvement in nightmare or whether other aspects of sleep also were affected by PTSD treatment. Effects on sleep might be enhanced if CPT were combined with IRT and/or CBT for insomnia.

Prolonged Exposure (PE) therapy for PTSD also appears to have some positive effect on sleep disturbances, although data remains limited to the recent RCT noted above and an uncontrolled study from a clinical sample. Nightmares (as assessed by trauma instruments) do tend to diminish as a generalized outcome. It remains possible that if there were enough treatment sessions and PE were broadened to include exposure to focus on sleep cues (both nightmares and contextual sleep issues contributing to insomnia), that effects on sleep could be enhanced. One potential strategy is to combine PE with IRT and/or CBT for insomnia.

Panel Recommendation: There is no empirical support to consider ACT as a stand-alone first-line treatment for trauma-related sleep disturbances. Although there is evidence that CBT for PTSD can improve sleep for some patients, more data is needed to specifically document the effects of these treatments on sleep. Given some positive evidence, the panel does recommend, however, that particularly PE and CPT, be considered as potentially promising treatments for individuals suffering PTSD and sleep disturbances when efficacious treatments for sleep disturbances are not available. When these PTSD interventions show insufficient effects on sleep, clinicians should consider supplementing them with IRT and/or CBT for insomnia. CPT and PE should be evaluated when combined with IRT and/or CBT.

II.B. Recommended Plan to Train VA Providers in the Treatment of Trauma-Related Sleep Disturbances

Sleep disorders, in general, are under-recognized and under-treated within and outside the VA. This is especially pronounced with respect to insomnia, where a large barrier to delivering treatment resides in a vast under-supply of providers trained in the delivery of behavioral sleep medicine including cognitive-behavioral therapy for insomnia. The vast majority of mental health providers do not receive any training in treating sleep disorders. In addition, physicians and other health care providers, especially those in primary care where most patients are assessed (and sometimes treated) for sleep disturbances, have little or no specific training in managing sleep disorders. While excellent gains have been made in primary care's identification of sleep apnea and referral to sleep disorders specialists by primary care clinicians, this trend has not extended to the identification and management of insomnia. When treated, insomnia is typically managed with hypnotic medication, which can be appropriate, and with extensive off-label prescription of sedating antidepressants and anti-psychotics, which have little or no empirical

basis. Many providers would like to be able to refer to behavioral specialists who treat insomnia with the recommended first line treatment for chronic insomnia (CBT), but often complain of not being able to find such specialists. These problems are even more pronounced with respect to the identification and treatment of trauma-related sleep disturbances, wherein the primary treatment focus is appropriately on presenting complaints such as PTSD, depression and chronic pain. Although not dismissed, sleep disturbances tend to take a secondary role. Again this is exacerbated by the shortage of providers who can treat both the primary presenting complaints and the associated sleep disturbances.

Panel Recommendation: The panel strongly recommends that the VA focus on training VA providers at various levels of the health care system in the identification and management of the major sleep disturbances (not confined to trauma-related sleep disturbances) where the largest unmet patient needs exist.

Bradley Karlin (Director, Psychotherapy Services, VACO) spoke to the panel about the current VA initiatives to train mental health providers in evidence-based practices. Following the New Freedom Commission's report on Mental Health report, the VA's mental health strategic plan includes a strong commitment to realizing the potential of evidence-based therapies and bringing them from the lab to the therapy practice setting including disseminating evidence-based psychotherapies.

The first such dissemination effort commenced in 2007 and consisted of training over 1000 VA and 600 DoD providers in the delivery of cognitive processing therapy. The structure and roll-out of this initiative may serve as a model for training in sleep disturbance interventions. The psychotherapy Program Office at VACO is already considering CBT for insomnia training as the possible first specialty CBT training to conduct once a "general" CBT training has been rolled out.

Panel Recommendation: The panel recommends that VA utilize its existing training format to widely disseminate training in the treatment of insomnia and nightmares.

Panel Recommendation: The panel recommends that training begin with a focus on CBT for insomnia and move to training in imagery rehearsal techniques (IRT) in a subsequent initiative.

Panel Recommendation: There are a limited, but core number of individuals across the country (several with VA affiliations) that have Behavioral Sleep Medicine expertise and experience who may serve as initial trainers, but the panel recommends moving to a "train-the-trainer" model where expertise may be developed over time.

Panel Recommendation: The panel recommends VA consider setting a goal to have a behavioral sleep medicine expert on staff first at the VISN level and then at the VAMC level on a VA determined timeline.

Mental health providers, especially clinical psychologists, often have been trained in and are delivering forms of CBT other than that used for sleep disturbances. Training providers with CBT expertise can quickly enhance the number of providers able to use empirically-based approaches for sleep disturbances.

Panel Recommendation: The panel recommends that mental health providers already trained in CBT be targeted to receive training that is sleep-specific as a first step.

Panel Recommendation: The panel recommends the development of continuing education activities for all mental health providers be undertaken.

Other mental health providers including masters level practitioners, nurses, and social workers, can be trained to deliver effective treatment of sleep disturbances in uncomplicated cases. A stepped-care approach allows the expansion of delivering treatments for sleep disturbances beyond psychologists, to include who can be trained to deliver the intervention effectively. Referrals for more complicated cases can then be made to psychologists trained in these areas.

Panel Recommendation: The panel recommends that all mental health providers be targeted to receive competency training in basic CBT for insomnia.

Many VAMCs have sleep disorders clinics, but as is the case with civilian sleep disorders centers, most are dedicated to diagnosing and treating sleep-disordered breathing. Few are staffed with individuals trained in behavioral sleep medicine.

Panel Recommendation: The panel recommends that existing VA sleep disorders clinics consider identifying (or adding) staff members to be trained in the treatment of insomnia and nightmares.

Primary care providers in the VA health care system recognize the prevalence and importance of sleep disorders, but may have their own limited training in this area. Many physicians identify sleep disturbances and when warranted dispense sleep hygiene advice or prescribe hypnotic medications. There exists the possibility that primary care providers can deliver other effective behavioral treatments. A subset of patients will respond to such an intervention when it includes good tracking and follow-up. It is unclear what makes the most sense in the VA health care system in terms of how much treatment can and should be provided within primary care. Various collaborative care models wherein a psychologist is immediately available to primary care providers and/or a nurse provides treatment and refers complicated or unresponsive cases have good demonstrated effects and represent a model in which the VA has demonstrated expertise.

Panel Recommendation: The panel recommends VA develop continuing education activities for primary care providers that focus on the identification and management of sleep disturbances and have as a focus those interventions that can be accomplished in the primary care setting and when and how to refer and communicate with sleep specialists to manage their patients.

Panel Recommendation: The panel recommends VA experts in Collaborative and Integrated Health Care meet with VA experts in behavioral sleep medicine to outline how to address sleep disturbances in patients with TBI/PTSD within integrated care models.

The Iraq War Clinician Guide – Appendix on Sleep Problems

The Iraq War Clinician Guide's coverage of sleep problems (a two page appendix) should be updated in light of recent knowledge. The entire appendix is written for the patient, which encourages clinicians to use it as such, instead of as a tool for clinicians. Its primary emphasis is on sleep hygiene for insomnia, which has very poor empirical support as a monotherapy. The information also contains some suggestions that do not follow the accepted standard suggestions. For example, the suggestion that patients get up from bed after 30 minutes if they are not sleeping does not follow the originally published and typically standard time frame (i.e., 10-15 minutes). Providers untrained in behavioral

sleep medicine often give these kinds of suggestions to patients as a handout with little or no instruction and little or no follow-up. In the few studies wherein sleep hygiene has demonstrated its modest effects, it was delivered as a therapy over several sessions with active therapist involvement and patient-specific recommendations. The guide also has two paragraphs on nightmares, which could be expanded. This appendix mentions CBT in passing as a “talk therapy,” which may misrepresent the core aspects of CBT that require active engagement in the treatment plan with self-monitoring, homework, and integration of feedback.

Panel Recommendation: The panel strongly recommends that the Iraq War Clinician’s Guide Appendix for Sleep Problems be revised and expanded. Specific recommendations are as follows:

- Write with clinicians in mind and provide a greatly expanded offering.
- Describe all major sleep disorders and their empirically-based treatments.
- Note the ways in which sleep disturbances related to combat trauma may differ from their non-trauma versions and whether and how interventions might be adapted for combat-related sleep disturbances.
- In particular, define and articulate each component of CBT (and include examples of standard patient-therapist interactions). Many fine publications exist on the assessment and treatment of insomnia, on which this may be modeled.
- Address repeatedly how insomnia may present in combat Veterans and how the delivery of CBT may need to be modified.
- Outline the evidence base for pharmacotherapy options for sleep disturbances and how a psychotherapist can work effectively with primary care physicians and psychiatrists to manage one or more sleep disturbances.
- Include information on when and how to refer for a full outpatient sleep evaluation with a sleep disorders specialist and/or for overnight polysomnography.
- Utilize the guide as an opportunity to educate providers in a detailed but still introductory manner about sleep disturbances that they are likely to encounter and the evidence-based treatments they should consider learning to deliver proficiently.
- List existing training resources (and any VA plans to add to existing training resources)

II.C. Recommended Research Agenda for Trauma-Related Sleep Disturbances

The panel identified three main targets for investigation to correspond to three (of the four) programmatic areas of VA-sponsored Research and Development (R&D) most relevant to trauma-related sleep disturbances: Clinical Science Research, Biomedical Laboratory Research, and Health Services Research. Some of the recommended research topics identified by the panel may have overlap across two or more of these R&D domains. In such cases, the panel made its best effort to include the topic in the appropriate domain. In addition, some of the suggested research topics may also be appropriate for Rehabilitative Research and Development (RR&D) efforts, but these are not listed separately.

II.C.1. Clinical Science Research - Practical Treatments for Insomnia, Nightmares and Related Sleep Disturbances

For treatments that have a current evidence base (e.g., Cognitive Behavioral Therapy, Prazosin, Imagery Rehearsal Therapy), it is important to establish whether these treatments are effective in a variety of Veteran subpopulations including, but not limited to, female Veterans, Veterans of different age cohorts and Veterans with comorbidities. For instance, sleep-related problems among Veterans returning from combat are a key concern of clinicians. It is unclear whether existing treatments for sleep disorders can be used for patients with trauma exposure either with or without PTSD and/or TBI. Current, empirically-supported treatments may need to be tailored for use with patients suffering from PTSD and/or TBI with and without MDD.

With respect to PTSD-related insomnia, it also is not known whether treatments for PTSD and insomnia should be carried out in sequence or simultaneously to achieve optimal effects. Likewise, it also is unclear whether addressing core symptoms of PTSD is necessary prior to implementing CBT for insomnia. In a related vein, it also is not clear whether nightmares, which do tend to ameliorate following treatment of PTSD, should be treated as part of a sleep intervention in PTSD-related insomnia and nightmares. In addition, research should determine which nightmares should be targeted in treatment and whether including nightmare alteration produce optimal outcomes for Veterans. The same considerations apply to Veterans with TBI and Veterans with an active substance abuse disorder. Methods to adapt treatment protocols for people with cognitive limitations are needed.

Similarly, although CBT has demonstrated effectiveness for those who meet diagnostic criteria for insomnia disorders, it remains unclear what approach should be used for patients with sub-threshold insomnia. Adapting treatments for use among patients who do not meet full diagnostic criteria for insomnia, but still have disrupted sleep with daytime consequences is another area for research inquiry. This may take the form of brief interventions to prevent development of "full blown" insomnia.

With respect to nightmares in particular, it is unknown whether the aspects of the nightmare experience are associated with clinical course or treatment response (i.e., nightmares associated with a trauma vs. other distressing dreams; number and length of awakenings after nightmares, middle-of-the night vs. morning nightmares; nightmares that are especially horrific or that reinforce guilt). With respect to IRT (and its variants), many questions remain about optimal delivery formats, level of group participation in the rescripting of the original nightmare, the nature and intensity of the target nightmare, level of exposure to nightmares, and extent of desensitization associated with nightmare rehearsal encouraged in session or during homework sessions. Dismantling research studies are necessary to establish the relative impact of each of these factors on treatment response in military veterans.

Pharmacological management of sleep disturbances in Veterans requires more comprehensive study. Early findings support the use of prazosin for nightmares. Exploring the utility of reducing nightmares pharmacologically in conjunction with exposure therapy for PTSD may increase treatment adherence. Also, the use of prazosin soon after trauma-related nightmares develop might interrupt the process of developing PTSD, though this is untested. Such prevention models should be explored. The use of novel antipsychotics is an area for which additional empirical evidence is very much needed. Those evaluations should include looking at body mass index, lipids, and any negative effects of longtime use (which can lead to metabolic syndrome).

The utility of combining treatments deserves further study to determine whether, for instance, combining CBT with medications in Veterans affects the efficacy of the CBT. Such work also is needed to examine different combinations of pharmacological and non-pharmacological treatments in populations that are medicated for a comorbid condition (e.g., depression, chronic pain).

Studies are needed to determine whether patient specific factors are associated with superior outcomes in standard treatments including, but not limited to: comorbidities, age, gender and other demographics, and combat exposure. Similarly, understanding which aspects of interventions patients learn effectively, use consistently and/or find helpful may help guide the tailoring of treatments to specific groups. It will also be important to determine whether certain patients respond better to particular modalities (i.e., group vs. individual; brief vs. standard length; and interventions that employ technologies to deliver interventions vs. clinician-delivered methods).

The research agenda should be undertaken in a systematic way. Evaluating the effectiveness of established treatments in veteran populations is perhaps the most important initial step. This may be followed by dismantling studies, sequencing treatment studies, and/or studies that tailor existing interventions to specific populations based on theory-based rationale and hypothesis-driven research from the accumulated evidence. A worthwhile approach that may lead to improvements in direct patient care more expeditiously would be to have multi-site trials that examine multiple issues simultaneously. Cooperative studies wherein each site focuses/specializes on different subpopulations would also be useful. Alternatively, individual studies could use similar methodologies at different sites each focused on a specific population of patients.

One novel approach to arriving at initial treatment guidelines in the absence of clinical trial data is to utilize the RAND Health model of Assessing Care of Vulnerable Elders (ACOVE), wherein a content expert proposes a menu of treatment interventions and then clinician experts develop treatment guidelines from a menu of options.

As a general consideration, all studies should include a variety of outcome measures to determine not only whether sleep improves, but also to what extent mood, daytime function and other disorder-specific outcomes respond to interventions (e.g., PTSD severity, pain severity). In a complimentary fashion, studies undertaken in other areas in which sleep is not the focus of the intervention should be encouraged to measure and report on sleep outcomes.

Understudied areas in Veterans, which warrant attention, include: the role of sleep disturbances in suicidal ideation and suicide; the role of good sleep in resilience; the relationship of disturbed sleep or short sleep and adverse health outcomes (and their mediators); the impact of sleep problems on family (including children) and role functioning; whether natural “night owls” self-select for the military and whether they are more resilient with respect to sleep deprivation or shift-work.

The panel noted several areas in sleep assessment wherein current research is lacking. Additional validity and reliability work is necessary with the Disturbing Dream and Nightmare Severity Index (DDNSI). Research is mixed on whether the nightmare and sleep items on PTSD instruments correlate with prospective measures of sleep and nightmares. Further research is necessary to examine the concurrent validity of these scales and their validity per se with different populations of trauma survivors. Finally, more work is needed to better understand and define nightmares; questions include:

- How to distinguish a nightmare from a bad dream?

- Is an awakening necessary for the definition of a nightmare?
- Is fear upon awakening necessary? For instance, can a nightmare be defined by guilt, remorse, shame, or other negative emotions?
- How important is similarity of nightmare to original trauma?

Future research is necessary to examine whether parasomnic events warrant diagnosis and treatment as disorders comorbid to mental or medical conditions. Research is also needed to develop and validate measures examining symptomatic levels of parasomnic behaviors specifically (e.g., night terrors, bruxism, confusional arousals, acting out dreams, sleep paralysis) in the context of PTSD.

Panel Recommendation: The panel recommends the establishment of a systematic clinical science research agenda for trauma-related sleep disturbances that focuses on definitive randomized controlled trials of 1) CBT, IRT (and its variants) and prazosin in various trauma populations including those with and without PTSD, with and without TBI, and with and without other common comorbidities such as chronic pain and depression; 2) sequencing and combination sleep treatments with established treatments for PTSD, TBI and other common comorbidities; and 3) novel or under-studied treatments for sleep disturbances such as sedating antidepressant and novel antipsychotic medications.

Panel Recommendation: The panel recommends that consideration be given to large multi-site and/or cooperative studies to hasten the establishment of an empirical approach for treating trauma-related sleep disturbances.

Panel Recommendation: The panel recommends that all VA funded studies in the area of trauma-related sleep disturbances include: 1) a variety of outcome measures with respect to general health and function as well as specific assessment of any impact of treatment on comorbid conditions; 2) the ability to assess what patient specific factors are associated with enhanced adherence and outcomes and; 3) the assessment of related sleep disturbances that may not receive targeted funding such as sleep related movement disorders.

Panel Recommendation: The panel recommends that longitudinal observational studies be undertaken to assess: 1) the role of good sleep, natural short sleepers, and natural “night owl” sleep tendencies in resilience; 2) the role of sleep disturbances as a risk factor for suicide; and 3) the role of disturbed sleep in family/marital/domestic problems.

Panel Recommendation: The panel recommends research be undertaken to establish or strengthen assessment and diagnosis with respect to nightmares, disturbing dreams, parasomnias, and sleep-related movement disorders in veteran trauma populations.

II.C.2. Biomedical Laboratory Research – Elucidating Mechanisms of Sleep Disturbance in Veteran Populations

A number of basic, mechanistic, or translational areas of sleep research have relevance to Veterans. These include: novel and improved animal models for sleep disturbance associated with trauma and stress; identifying genetic, neuroanatomical, neurobiological, and/or psychological/behavioral markers for vulnerability; the developmental trajectory of sleep problems (including early manifestations, the role of early adversity, and the role and risk associated with multiple and extended deployments); the role of partial sleep restriction in expression of circadian regulating genes and initiation or exacerbation

of inflammatory processes; sleep architecture in comorbid populations and sleep architecture following both pharmacologic and behavioral interventions; the neurobiology of sleep-waking regulation (REM and non-REM sleep) and its relation to conditioning and fear circuitry; identifying novel neurochemical targets for pharmacological interventions in veteran populations; and studies that further basic understanding of sleep disturbances such as neurobiologic factors that maintain residual insomnia, underlying mechanisms of excessive movement in sleep, and the role of circadian dysregulation in deployment and in persisting TBI.

Panel Recommendation: The panel recommends the establishment of a targeted biomedical laboratory research agenda for trauma-related sleep disturbances that focuses on: 1) developing animal and human models of sleep disturbance under stress conditions utilizing a variety of experimental approaches and measurement techniques; 2) identifying mechanisms and/or markers for the development and persistence of trauma-related sleep disturbances.

II.C.3. Health Services Research – Identifying Best Practices for the Treatment of Trauma-Related Sleep Disturbances and the Systemic Impact of Delivering Such Treatments.

Studies are needed to identify current practices. This includes the degree to which evidence-based psychotherapies are utilized, the frequency of prescriptions of both novel and more evidence-based medications, in what settings such treatments are implemented and by what types of treatment providers. Along these lines, it would be helpful to understand the current capacity of the system to provide such services, whether there are any barriers to any of these treatment modalities, whether this varies by practice setting, and what contributes to any identified practice variability. On the patient side, it will be important to determine patient preferences as well as adherence and tolerability to treatments.

Studies are needed to address how to best to implement existing treatments and those that may be developed as part of the overall research agenda. This includes addressing a number of issues such as: how to integrate various treatment approaches in primary care or specialty settings for Veterans with and without one or more comorbidities; the evaluation of brief interventions or stepped care models; what types of providers (psychologists, nurses, case managers, etc.) can provide treatment effectively and whether level of training of the provider affects the effectiveness of the treatment.

Studies are also needed to evaluate the cost-effectiveness of the interventions, whether this varies by provider type, by intervention model, and/or by treatment setting. This should include careful analysis of resource involvement, cost offsets, and the impact on overall utilization of the system. To the extent that one or more of the treatments is included in a system-wide training roll-out, it will be important to take the opportunity to embed both health services research questions in such roll-outs as well as to include strong sleep measures to track outcomes over time at a systems level.

Once the evidence base matures, studies of effectiveness of the dissemination process and what are optimal dissemination procedures will be valuable. Once more is known about integrating and sequencing treatments, treatment modules can be developed and made available to practitioners; studies could then examine how these modules are used, by whom, in what settings, and to what extent they are effective on a broad range of outcomes.

Panel Recommendation: The panel recommends the establishment of a health services research agenda for trauma-related sleep disturbances that focuses on: 1) the use and acceptance of current treatment strategies across VA settings; 2) feasibility, comparative effectiveness, cost effectiveness and health care utilization impact of various treatment delivery models for current and to-be developed treatments for trauma-related sleep disturbances; and 3) examining the health related morbidity (e.g., cardiovascular disease risk) of long-term sleep disturbances associated with trauma.

Panel Recommendation: The panel recommends that any training initiatives targeting sleep disturbances include health services-related outcomes and assessments.

II.D. Recommended Core Battery for Trauma-Related Sleep Disturbances

Two key issues for research with sleep disturbance in trauma survivors are: (1) how to define and measure sleep disturbances and (2) how to characterize the sample (these are considerations for enrolling participants in studies). The recommendations that emerged from the Pittsburgh consensus conference on “Recommendations for a Standard Research Assessment of Insomnia” (Buysse, Ancoli-Israel, Edinger, Lichstein, and Morin, 2006) provide a good model for the kinds of assessments that should be made.

Given the early state of sleep research in patients with comorbid psychiatric and medical diagnoses, the measures presented here are recommendations, rather than guidelines. It is understood that studies are variable in their goals and require different assessments with varying levels of detail.

In addition, how to assess sleep disturbances and monitor progress and outcomes during and after treatment are pertinent questions in the clinical domain. Here some specific recommendations are warranted.

Defining Sleep Disturbance for Enrollment in Research Studies with Trauma Survivors

Specific Area	Recommended Measure	Reporting Standards
Sleep Disorders	Clinical history and/or questionnaire using International Classification of Sleep Disorders, 2 nd ed (ICSD-2) Criteria	<ul style="list-style-type: none"> • Specific methods used • Qualifications of interviewer • Exclusionary diagnoses • Number of participants judged to have an ICSD-2 sleep disorder • Examination of sleep disorder onset using timeline follow-back method in relation to (a) traumatic event, (b) psychiatric disturbance, (c) medical conditions (that might have resulted due to trauma). • Frequency of specific, current sleep complaints
	Polysomnography (PSG) (recommended but not required for every study)	<ul style="list-style-type: none"> • PSG is the gold standard for sleep disorder assessment. • Description of PSG protocol, Number of

Specific Area	Recommended Measure	Reporting Standards
		<p>channels, and equipment (including use of nasal pressure transducer)</p> <ul style="list-style-type: none"> • Apnea-Hypopnea Index (AHI), Periodic Leg Movement Arousal Index (PLMAI) levels to establish eligibility or diagnoses
Psychiatric Disorders	Structured Clinical Interview for the DSM-IV	<ul style="list-style-type: none"> • Specific modules to include PTSD*, Depression, Alcohol and Substance Use • Qualifications of interviewer • Exclusionary diagnoses • No. participants with specific psychiatric diagnoses
	*Clinician-Administered PTSD Scale (CAPS) PTSD Symptom Scale (PSS)	<ul style="list-style-type: none"> • The CAPS may be an alternative to SCID PTSD diagnosis, see Weathers et al., 1999 for scoring rule options. The PSS may also substituted
Trauma History	SCID, CAPS, or Trauma History/Questionnaire	<ul style="list-style-type: none"> • Specific methods used • Qualifications of interviewer • Trauma history in the case of multiple traumatic events • Description of traumatic event under study, including whether the event occurred within a sleep-related context
Medical Disorders	Medical history/questionnaire, including the assessment of traumatic brain injury and pain	<ul style="list-style-type: none"> • Specific methods used • Qualifications of evaluators • Specific exclusionary diagnoses • Number of subjects with comorbid medical conditions
Current medications and substances	List of medications (history, participant-generated list)	<ul style="list-style-type: none"> • Specific methods used • Qualifications of evaluators • Exclusionary medications/substances or exclusionary timeframe of changes • Number of participants using specific medication classes • Number of participants using and amount of caffeine, alcohol, and tobacco (mean/SD or median/range)

Diagnosis of Sleep Disorders within the Context of Trauma

Trauma survivors report experiencing a spectrum of problems with their sleep including, insomnia, nightmares, parasomnic events, and sleep-disordered breathing. Oftentimes the trauma itself results in chronic pain, traumatic brain injury, or other medical conditions that interfere with sleep or sleep/wake routine. Trauma survivors frequently suffer from posttraumatic stress disorder, depression, generalized anxiety, panic disorder, and alcohol and substance use problems. Because of the complex clinical picture with this population, researchers should attempt to use currently available sleep nosologies to provide better definitions of the range of these sleep problems. Moreover, it is recommended to use polysomnography (PSG) when possible to rule-out the sleep-disordered breathing and other primary

sleep disorders that may be contributing to insomnia. Nightmares do not occur frequently in the sleep laboratory; ambulatory recording may hold more promise for capturing their occurrence.

Both the ICSD-2 and the DSM-IV categorize insomnia occurring within the context of psychiatric and medical conditions as “Insomnia Due to a Mental Condition.” For this diagnosis, insomnia must be temporally associated with the mental disorder and also be of sufficient severity to warrant separate independent treatment. The timeframe of the development of the mental condition might be complex to determine, for instance, in the case of Delayed Onset PTSD. Although still subject to poor reliability, using timeline follow-back methods, such as that often employed through the SCID to document insomnia diagnoses may be helpful. Alternatively, if the DSM-V adopts classification language being considered by its work group, the appropriate diagnosis may simply be “Insomnia comorbid to a mental condition.”

Currently, no separate parasomnia diagnoses are available by either the ICSD or DSM nosologies for patients who have PTSD or other psychiatric or neurological conditions. In other words, nightmares, night terrors, bruxism, sleep paralysis, confusional arousals, and movement disorders occurring within the context of PTSD are considered part of the PTSD disorder. These disorders are reserved for patients who do not meet the DSM-IV criteria for PTSD or other mental disorders. Nonetheless, since these elements are important complaints related to sleep disturbance, it is recommended that they are included in initial and outcome assessments of the sleep in trauma survivors.

There are significant amounts of correlational data suggesting high rates of sleep disordered breathing in PTSD populations. However, no definitive data are available to suggest that sleep disordered breathing is temporally associated with PTSD. Therefore, PTSD should not be considered a rule out for sleep disordered breathing diagnoses. In other words sleep-related breathing disorders should be diagnosed with ICSD-2 criteria and considered comorbid disorders to PTSD.

Assessment of Sleep Symptoms in Research Studies with Trauma Survivors

The following measures were recommended for the assessment of sleep symptoms in research studies with trauma survivors.

Measure/Area	Recommended Measure	Reporting Standards
Global sleep	Pittsburgh Sleep Quality Index (PSQI) with PTSD Addendum	<ul style="list-style-type: none"> • Global M, SD • Subscale M, SD • Addendum M, SD
Global insomnia symptoms	Insomnia Severity Index	<ul style="list-style-type: none"> • Global M, SD • Number of participants in each severity range
Global nightmare symptoms	Disturbing Dream and Nightmare Severity Index	<ul style="list-style-type: none"> • Frequency of nightmares (Number of nightmares per week, number of nights of nightmares) • Intensity rating • Distress or severity rating
Daily self-report of sleep	Sleep Diary	<ul style="list-style-type: none"> • Duration, format, and information assessed • Thresholds or quantitative criteria

Measure/Area	Recommended Measure	Reporting Standards
		for insomnia or other sleep disorder diagnoses <ul style="list-style-type: none"> • M/SD of each outcome sleep measure: bedtime, final wake time, arising time, SOL, NWAK, WASO, TST, SE, SQ, nightmare frequency and intensity, timing and duration of naps
Rest-activity pattern	Actigraphy (recommended but not required for every study)	<ul style="list-style-type: none"> • Description of device, scoring software, and administration protocol • Thresholds or quantitative criteria for insomnia or other sleep disorder diagnoses • M/SD of each outcome sleep measure: sleep onset/offset times, SOL, NWAK, WASO, TST, SE, Nightmare frequency (via event marker)
Objective sleep	Polysomnography (recommended but not required for every study)	<ul style="list-style-type: none"> • Description of PSG protocol, No. channels dedicated to various indices, and equipment • Total recording time (and how it is determined) • M/SD for: AHI, PLMAI, SOL, NWAK, WASO, TST, SE, Sleep stage distribution, REM density

Additional Comments Regarding Specific Measures

Sleep Diaries

Sleep diaries are considered the gold standard assessment for insomnia and nightmare symptoms. Data has shown that retrospective recall may overinflate sleep symptom estimates; therefore, prospective data is highly recommended. It is recommended that at least one week of sleep diary data are gathered to include weekdays and weekends. Investigators should consider employing specific strategies to increase adherence to daily monitoring, such as having the participant call into voice mail service every morning or using a PDA or other form of electronic technology for collecting diary data. The OEF/OIF veteran cohort is especially comfortable using technology, and effort should be put into automation development that capitalizes on this technology.

Sleep diary data can vary widely with regard to how indices are computed or operationalized. A standardized daily sleep diary is currently under construction. In working with trauma survivors, it is recommended that nightmare frequency and nightmare intensity are included as two supplemental diary items. Further research is necessary to examine the inclusion of items related to: level of distress caused by nightmares, content similarity to the original traumatic event, disruptive behaviors (e.g., sleep

terrors, punching, kicking, and yelling), and other parasomnic events (e.g., bruxism, confusional arousals). In treatment studies, investigators are encouraged to carefully consider the use of dream content as an outcome, given the potential of contaminating treatment via exposure to traumatic memory.

PTSD Addendum to the Pittsburgh Sleep Quality Index

The PSQI is a 19-item self-report questionnaire that assesses sleep quality and sleep disturbances over a one-month period of time. It has been shown to have acceptable internal homogeneity, test-retest reliability, and validity. Substantial normative data has also been collected on the PSQI, which allow comparisons to sleepers with and without various sleep or psychiatric disorders.

The 7-item PSQI addendum assesses the frequency of disruptive nocturnal behaviors commonly reported by PTSD patients. Each item is scored from zero to 3, assessing how many times the behavior occurred in the past month. A score of 4 or more indicates that the respondent may have PTSD and should receive further evaluation. The measure was developed using a convenience sample from different groups, so further research is necessary to validate the measure in a military sample.

Disturbing Dream and Nightmare Severity Index (DDNSI)

The DDNSI is a 5 item self-report measure that assesses nightmare symptoms over the last week (nights per week with nightmares, nightmare count per week, awakenings due to bad dreams, severity of nightmare problem, and intensity of actual nightmares). It is an expanded version of the Nightmare Frequency Questionnaire, a measure that has been validated in sexual assault survivors with PTSD and appears to adequately correlate with prospectively gathered sleep diary data. The DDNSI has been used as a screening measure to identify sleep patients suffering from clinically salient nightmare conditions. More validation work is necessary to examine: (a) how well the DDNSI severity items correlate with prospective diary data, (b) test-retest reliability data (necessary for outcome studies), (c) whether the DDNSI is valid in a military population.

Additional Measures

The following measures were discussed and may be appropriate to administer within a subset of studies. The expert panel acknowledged that other measures may be available and more appropriate to use dependent upon population area studied.

Specific Area	Measure	Notes
Sleep Disorders	Duke Structured Interview Schedule for DSM-IV-TR and ICSD- 2 (DSI)	Semi-structured interview for the assessment of DSM-IV and ICSD sleep disorders
Fatigue	Multidimensional Fatigue Inventory OR Fatigue Severity Scale	Self-report questionnaires designed to measure daytime fatigue/energy level
Circadian rhythm disorders	Horne-Ostberg Questionnaire	Self-report symptom assessment of morningness/eveningness
Sleep apnea	Berlin Questionnaire STOP Questionnaire	Self-report questionnaires screening for sleep apnea
Pain	McGill Pain Questionnaire	Self-report measure of pain description and intensity

Specific Area	Measure	Notes
Quality of Life	SF-36	Abbreviated measure of quality of life perceptions across a number of functional dimensions (social, emotional, health, etc.)
Trauma History	Combat Experiences Scale	37-item self report scale describing exposure to various deployment-related experiences
Traumatic Brain Injury	VA TBI Screen	Currently use in VA settings to screen for TBI
Anxiety Symptoms	Clinician Assessment for PTSD Scale (CAPS)	Gold-standard clinician-administered instrument for PTSD
	Posttraumatic Stress Disorder Checklist (PCL); Modified PTSD Symptom Scale(MPSS)	Well-validated self-report measures of PTSD symptoms.
	State-Trait Anxiety Inventory (STAI)	Well-validated self-report instrument that assesses current state and general trait anxiety.
	Beck Anxiety Inventory	Well-validated self-report measure of general anxiety levels.
Depression Symptoms	Hamilton Rating Scale for Depression	Well-validated clinician administered measure of depressive symptoms with established cut-offs for detecting clinically significant depression
	Beck Depression Inventory II; Center for Epidemiologic Studies Scale for Depression Revised (CES-D-R)	Well-validated self-report measure of depressive symptoms with established cut-offs for detecting clinically significant depression
	Patient Health Questionnaire-9	A well-validated 9 item instrument for detecting depression.
Alcohol or Substance Use	AUDIT; AUDIT C	The Audit is a 10 item and the AUDIT-C a 3 item screen for alcohol abuse.
	NIDAMED	A screening tool for drugs of abuse developed by the National Institute of Drug Abuse
Nightmare Distress	Nightmare Distress Questionnaire	15-item self report measure assessing waking distress associated with nightmares
Dream Content	PTSD Dream Rating Scale	Morning dream diaries are assessed by consensus raters on the following indices: setting, character, objects, threat, contemporaneity, and distortion

Research is currently being conducted developing and testing the following scales with promising results:

Fear of Sleep Inventory. This measure assessing nocturnal hypervigilance and sleep avoidance is currently under construction.

Patient-Reported Outcomes and Measurement Information System (PROMIS) Sleep and Wake Disturbance Measures. These self-report scales include long version (27 items sleep, 16 items wake), and short versions (8 items sleep, 8 items wake) for both the sleep function and the wake function measures. They have developed a process to calibrate the instrument so individuals can be placed accurately on a normative continuum for both sleep and wake functioning. An advantage of the scale is

that it is broad-based and does not measure only one dimension of daytime function. The scales have been validated in a large general sample. They have not yet been validated in a PTSD sample.

Assessment Tools for Clinical Use

For the assessment of sleep disturbances, treatment monitoring, and measuring treatment outcome in the clinical arena, the following instruments are recommended as either required, suggested or optional.

Measure/Area	Measure	Clinical Use	Recommendation
Sleep Disorders	Clinical history and/or questionnaire using International Classification of Sleep Disorders, 2 nd ed (ICSD-2) Criteria	Assessment	Required
Global sleep	Pittsburgh Sleep Quality Index (PSQI) <u>with PTSD Addendum</u>	Assessment	Required
		Tx Monitoring	Optional
		Outcome	Suggested
Global insomnia symptoms	Insomnia Severity Index	Assessment	Required
		Tx Monitoring	Optional
		Outcome	Suggested
Global nightmare symptoms	Disturbing Dream and Nightmare Severity Index	Assessment	Required
		Tx Monitoring	Optional
		Outcome	Suggested
Daily self-report of sleep	Sleep Diary	Assessment	Suggested
		Tx Monitoring	Required
		Outcome	Required
Fear of Sleep	Fear of Sleep Inventory	Assessment & Outcomes	Optional
Sleepiness	Epworth Sleepiness Scale	All	Optional
Circadian Rhythm Disorders	Horne-Ostberg Questionnaire	Assessment	Optional
Rest-activity pattern	Actigraphy	All	Optional
Objective sleep	Polysomnography	When Sleep Disorders other than insomnia are suspected	Required

Measure/Area	Measure	Clinical Use	Recommendation
Fatigue, pain, depression, anxiety PTSD severity, TBI, substance abuse	Various as appropriate to population	all	Suggested

Panel Recommendation: The panel recommends the use of a specific set of assessment tools (listed in the detailed summary above) to be used for: 1) Defining Sleep Disturbance for Enrollment in Research Studies with Trauma Survivors; 2) Assessment of Sleep Symptoms in Research Studies with Trauma Survivors; and 3) Clinical Assessment and Monitoring.

II.E. Recommended Dissemination Plan for the Panel Recommendations

The panel agreed that results of this meeting should be widely and actively disseminated. The goal is to create system-wide awareness of the issues raised by the report, the need for and benefits of training, the current training available and suggested training models. The findings should *not* simply be communicated as a mandatory online training, although a well-designed product may nonetheless be a useful component of both the dissemination plan and the training plan. There are a number of target groups for dissemination of the report findings (as opposed to the dissemination of the training itself) and these include primary care physicians, physician extenders, and nurses; psychologists and other mental health providers; patients and their families; and VA central office.

Panel Recommendation: The panel recommends the following potential dissemination strategies be considered:

- Involve the National Center for PTSD in dissemination efforts
- Utilize the VA Employee Education System
- Presentations at the annual national Mental Health Meeting
- Presentations at the annual national HSR&D Meeting
- Write-up summary recommendations to present at MIRECCs and centers of excellence (e.g., in newsletters, via the National MIRECC Education Group, present panel findings to these groups in person)
- Develop general and specific internal marketing efforts to highlight the importance of sleep (general) and the resources currently available and planned for training (specific)
- Develop a manual that can be disseminated to clinicians and that would facilitate training (if the Iraq Clinician Guide is expanded it may serve this dual purpose)
- Target primary care, psychiatry, and psychology peer-reviewed journals read by VA providers for publication of these recommendations.

III. PANEL MEMBERS AND CONFERENCE ATTENDEES

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Conflict of Interest Disclosures of the Panel Members

All panel members have received research support from the VA, the Department of Defense, and/or the National Institutes of Health for work related to the content of this report.

In addition, the following panel members have the following disclosure to make regarding potential conflicts of interest with respect to their role as an expert panel member and co-author of the “Final Report of the Expert Panel on Sleep Disturbance and Combat Trauma”:

Jack D. Edinger, PhD

Grant Support: Philips/Respironics, Inc.

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Thomas C. Neylan, MD

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Wilfred R. Pigeon, PhD

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Richard J. Ross, MD, PhD

Honorarium from Glaxo Smith Kline to speak on the sleep disturbance in PTSD in 2008.

All other panel members reported they had no potential conflicts of interest to disclose.

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