SPECIAL ARTICLES

JCSM
Journal of Clinical Sleep Medicine

Best Practice Guide for the Treatment of Nightmare Disorder in Adults

Standards of Practice Committee:

R. Nisha Aurora, M.D.[1]; Rochelle S. Zak, M.D.[2]; Sanford H. Auerbach, M.D.[3]; Kenneth R. Casey, M.D.[4]; Susmita Chowdhuri, M.D.[5]; Anoop Karippot, M.D.[6]; Rama K. Maganti, M.D.[7]; Kannan Ramar, M.D.[8]; David A. Kristo, M.D.[9]; Sabin R. Bista, M.D.[10]; Carin I. Lamm, M.D.[11]; Timothy I. Morgenthaler, M.D.[8]

[1]Mount Sinai Medical Center, New York, NY; [2]Sleep Disorders Center, University of California, San Fancisco, San Fancisco, CA; [3]Boston University School of Medicine, Boston, MA; [4]Cincinnati Veterans Affairs Medical Center, Cincinnati, OH; [5]Sleep Medicine Section, John D. Dingell VA Medical Center, Detroit, MI; [6]Penn State University Hershey Medical Center, Hershey, PA and University of Louisville School of Medicine, Louisville, KY; [7]Barrow Neurological Institute at Saint Joseph's, Phoenix, AZ; [8]Mayo Clinic, Rochester, MN; [9]University of Pittsburgh, Pittsburgh, PA; [10]University of Nebraska Medical Center, Omaha, NE; [11]Children's Hospital of NY – Presbyterian, Columbia University Medical Center, New York, NY

Summary of Recommendations: Prazosin is recommended for treatment of Posttraumatic Stress Disorder (PTSD)-associated nightmares. Level A

Image Rehearsal Therapy (IRT) is recommended for treatment of nightmare disorder. Level A

Systematic Desensitization and Progressive Deep Muscle Relaxation training are suggested for treatment of idiopathic nightmares. Level B

Venlafaxine is *not* suggested for treatment of PTSD-associated nightmares. Level B

Clonidine may be considered for treatment of PTSD-associated nightmares. Level C

The following medications may be considered for treatment of PTSD-associated nightmares, but the data are low grade and sparse: trazodone, atypical antipsychotic medications, topiramate, low dose cortisol, fluvoxamine, triazolam and nitrazepam, phenelzine, gabapentin, cyproheptadine, and tricyclic antidepressants. Nefazodone is not recommended as first line therapy for nightmare disorder because of the increased risk of hepatotoxicity. Level C

The following behavioral therapies may be considered for treatment of PTSD-associated nightmares based on low-grade evidence: Exposure, Relaxation, and Rescripting Therapy (ERRT); Sleep Dynamic Therapy; Hypnosis; Eye-Movement Desensitization and Reprocessing (EMDR); and the Testimony Method. Level C

The following behavioral therapies may be considered for treatment of nightmare disorder based on low-grade evidence: Lucid Dreaming Therapy and Self-Exposure Therapy. Level C

No recommendation is made regarding clonazepam and individual psychotherapy because of sparse data.

Keywords: Nightmare disorder, nightmares, prazosin, clonidine, cyproheptadine, nefazodone, trazodone, olanzapine, topiramate, risperidone, cortisol, tricyclics, fluvoxamine, triazolam, nitrazepam, phenelzine, aripiprazole, gabapentin, venlafaxine, clonazepam, cognitive behavioral therapy, imagery rehearsal therapy, lucid dreaming therapy, sleep dynamic therapy, exposure relaxation and rescripting therapy, hypnosis, self-exposure therapy, systematic desensitization, progressive deep muscle training, psychotherapy, testimony method

Citation: Aurora RN; Zak RS; Auerbach SH; Casey KR; Chowduri S; Krippot A; Maganti RK; Ramar K; Kristo DA; Bista SR; Lamm CI; Morgenthaler TI. Best practice guide for the treatment of nightmare disorder in adults. *J Clin Sleep Med* 2010;6(4):389-401.

1.0 INTRODUCTION

There has been a burgeoning literature about pharmacotherapy and behavioral treatment of nightmare disorder in adults, but no systematic review has been available. The Standards of Practice Committee (SPC) of the American Academy of Sleep Medicine (AASM) commissioned a task force to assess the literature on the treatment of nightmare disorder. The Board of Directors authorized the task force to draft a Best Practice Guide based on review and grading of the literature and clinical consensus.

2.0 METHODS

The SPC of the AASM commissioned among its members 7 individuals to conduct this review and develop best practice principles. Work began in December 2007 to review and grade evidence in the peer-reviewed scientific literature regarding the treatment of nightmare disorder in adults. A search for articles on the medical treatment of nightmare disorder was conducted using the PubMed database, so that clinically relevant articles on the treatment of nightmare disorder could be collected and evaluated. Other databases such as PsychLit and Ovid were not searched, since it was felt that these databases would not include clinically relevant material. The PubMed search was conducted with no start date limit until February 2008, and subsequently updated in March 2009 to include the most current literature. The key words were: [(Nightmares OR nightmare OR nightmare disorder OR nightmare disorders OR recurrent nightmares) AND (treatment OR drug therapy OR therapy)] as well as [Post-traumatic stress disorder AND (nightmare disor-

der OR recurrent nightmares OR nightmares) AND treatment]. A second search using the keyword combination "anxiety dreams" with no limits was also conducted in February 2010. "Post-traumatic stress disorder," alone, was not a search term. Although the majority of studies of both pharmacologic and nonpharmacologic treatments of posttraumatic stress disorder (PTSD) assess improvement of global manifestations, very few of these studies have isolated nightmares for evaluation of response to intervention and may not have included "nightmares" as a keyword. The evidence basis for this Best Practice Guide includes only those PTSD studies in which improvement in nightmares could be specifically identified as an evaluable outcome measure.

Each search was run separately and findings were merged. When the search was limited to articles published in English and regarding human adults (age 19 years and older), a total of 1428 articles were identified. Abstracts from these articles were reviewed to determine if they met inclusion criteria. The articles had to have a minimum of 3 subjects to be included in the analysis. The articles had to address at least one of the "PICO" questions (acronym standing for Patient, Population or Problem, provided a specific Intervention or exposure, after which a defined Comparison is performed on specified Outcomes) that were decided upon ahead of the review process (see **Table 1**). Articles meeting these criteria in addition to those identified by pearling (i.e., checking the reference sections of search results for articles otherwise missed) provided 57 articles for review and grading.

Evidence was graded according to the Oxford Centre for Evidence-based Medicine Levels of Evidence (**Table 2**).[1] All evidence grading was performed by independent review of the article by 2 members of the task force. Areas of disagreement were addressed by the task force until resolved. Recommendations were formulated based on the strength of clinical data and consensus attained via a modified RAND/UCLA Appropriateness Method.[2] The nomenclature for the recommendations and levels of recommendation are listed in **Table 3**. Recommendations were downgraded if there were significant risks involved in the treatment or upgraded if expert consensus determined it was warranted. This Best Practice Guide with recommendations was then reviewed by external content experts in the area of nightmare disorder.

The Board of Directors of the AASM approved these recommendations. All members of the AASM SPC and Board of Directors completed detailed conflict-of-interest statements and were found to have no conflicts of interest with regard to this subject.

The Best Practice Guide endorses treatments based on review of the literature and with agreement by a consensus of the task force. These guidelines should not, however, be considered inclusive of all proper methods of care or exclusive of other methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding propriety of any specific care must be made by the physician, in light of the individual circumstances presented by the patient, available diagnostic tools, accessible treatment options, and resources.

The AASM expects these recommendations to have an impact on professional behavior, patient outcomes, and, possibly, health care costs. These assessments reflect the state of knowledge at the time of publication and will be reviewed, updated, and revised as new information becomes available.

Table 1—Summary of PICO questions

1. Do patients with nightmares demonstrate clinical response to noradrenergic blocking medications compared with natural history or other medications?
2. Are there other medications to which patients with nightmare disorder demonstrate clinical response compared with natural history or other medications?
3. Do patients with nightmare disorder demonstrate clinical response to cognitive behavioral therapies and, if so, which are the most effective?

Table 2—AASM classification of evidence (Adapted from Oxford Centre for Evidence-based Medicine)

Evidence Levels	Study Design
1	High quality randomized clinical trials with narrow confidence intervals
2	Low quality randomized clinical trials or high quality cohort studies
3	Case-control studies
4	Case series or poor case-control studies or poor cohort studies or case reports

Table 3—Levels of recommendation

Term	Level	Evidence Levels	Explanation
Recommended / Not recommended	A	1 or 2	Assessment supported by a substantial amount of high quality (Level I or II) evidence and/or based on a consensus of clinical judgment
Suggested / Not Suggested	B	1 or 2—few studies 3 or 4—many studies and expert consensus	Assessment supported by sparse high grade (Level I or II) data or a substantial amount of low-grade (Level III or IV) data and/or clinical consensus by the task force
May be considered / Probably should not be considered	C	3 or 4	Assessment supported by low grade data without the volume to recommend more highly and likely subject to revision with further studies

3.0 BACKGROUND

3.1 Definition

The International Classification of Sleep Disorders, second edition (ICSD-2)[3] has classified nightmare disorder as a parasomnia usually associated with R sleep. The minimal diagnostic criteria proposed by the *ICSD-2* are as follows:

A. Recurrent episodes of awakenings from sleep with recall of intensely disturbing dream mentations, usually involving fear or anxiety, but also anger, sadness, disgust, and other dysphoric emotions.
B. Full alertness on awakening, with little confusion or disorientation; recall of sleep mentation is immediate and clear.
C. At least one of the following associated features is present:
   i. Delayed return to sleep after the episodes
   ii. Occurrence of episodes in the latter half of the habitual sleep period.

3.2 Types of nightmares

Nightmares may be idiopathic (without clinical signs of psychopathology) or associated with other disorders including PTSD, substance abuse, stress and anxiety, and borderline personality, and other psychiatric illnesses such as schizophrenia-spectrum disorders. Eighty percent of PTSD patients report nightmares ("PTSD-associated nightmares").[4] PTSD is a condition manifesting symptoms classified in three clusters: (1) intrusive/re-experiencing, (2) avoidant/numbing, and (3) hyperarousal. Nightmares are generally considered to be a component of the intrusive/re-experiencing symptom cluster. It is not clear that nightmares unrelated to PTSD coexist with features of the other PTSD symptom clusters, specifically hyperarousal.[5] Nevertheless, among nightmares, the PTSD-associated nightmare is the most studied. Presence of nightmares following a traumatic experience predicts delayed onset of PTSD. Even when PTSD resolves, PTSD-associated nightmares can persist throughout life.[3] Nightmares can also be induced following exposure to drugs that affect the neurotransmitters norepinephrine, serotonin, and dopamine.[6] Withdrawal of R-suppressing agents, and drugs affecting GABA and acetylcholine, can also be associated with nightmares.[3] Whether nightmares induced by drugs have long term sequelae (even after removing the offending agent) is not known. It is not clear if these different types of nightmares have a common underlying pathophysiology.

3.3 Assessment

Self-reported retrospective questionnaires and prospective logs are the most commonly used methods to assess nightmare characteristics. Though retrospective questionnaires could lead to underestimation of nightmare frequency due to recall bias,[7] prospective logs may overestimate the frequency of nightmares by increasing dream recall by an increased focus on dreams.[8] The advantage of using self-reported questionnaires and logs are that they can distinguish nightmare frequency from distress. The gold standard diagnostic interview for PTSD is Clinician-Administered PTSD Scale (CAPS).[9] This scale, which was developed by the National Center for PTSD, is a structured interview that assesses the frequency and intensity of 17 symptoms using standard questions and behaviorally anchored rating scales, including for nightmares associated with PTSD. Several versions of CAPS have been used over the years[10]: CAPS-DX (formerly CAPS-1), a diagnostic version to assess PTSD symptom severity over the past month or for the worst month since the trauma; CAPS-SX (formerly CAPS-2), a symptom status version to measure PTSD symptom severity over the past week intended for repeated assessments over relatively brief intervals; and a combined version called CAPS. Other psychometric scales have been used including the Symptom Checklist-90 (SCL-90),[11] a 90-question instrument that evaluates a broad range of psychological problems and can be used for measuring patient progress or treatment outcomes, and the Symptom Questionnaire (SQ),[12] a yes/no questionnaire with brief and simple items on state scales of depression, anxiety, anger-hostility, and somatic symptoms.

Overnight polysomnography (PSG) is not routinely used to assess nightmare disorder but may be appropriately performed to exclude other parasomnias or sleep-disordered breathing. PSGs may underestimate the incidence and frequency of PTSD-associated nightmares and may also influence the contents of the dreams.[13] Patients with both idiopathic and PTSD-associated nightmares have increased phasic R sleep activity, decreased total sleep time, increased number and duration of nocturnal awakenings, decreased slow wave sleep, and increased periodic leg movements during both R and NREM (N) sleep.[14] PTSD-associated nightmares, though commonly reported in R sleep, can occur earlier in the night, during sleep onset, and in N sleep.[15] Patients with PTSD-associated nightmares compared to those with idiopathic nightmares have decreased sleep efficiency due to higher nocturnal awakenings,[16] and a higher incidence of other parasomnias and sleep-related breathing disorders.

3.4 Consequences of nightmare disorder

Nightmare disorder is common, affecting about 4% of the adult population[3] with a higher proportion affecting children and adolescents. The presence of nightmare disorder can impair quality of life, resulting in sleep avoidance and sleep deprivation, with a consequent increase in the intensity of the nightmares. Nightmare disorder can also predispose to insomnia, daytime sleepiness, and fatigue.[17-19] It may also cause or exacerbate underlying psychiatric distress and illness. Nightmare disorder can be associated with waking psychological dysfunction, with the frequency of nightmares being inversely correlated with measures of well-being and measures of nightmare distress being associated with psychopathology such as depression and anxiety.[20] Patients who have their nightmares successfully treated appear to have better sleep quality, feel more rested on awakening, and report less daytime fatigue and sleepiness, and improvement in their symptoms of insomnia.[17-19]

4.0 TREATMENT FOR NIGHTMARE DISORDER

The purpose of this Best Practice Guide is to present recommendations on therapy of nightmare disorder. Treatment modalities for nightmare disorder include medications, most prominently prazosin, and several behavioral therapies, of which the nightmare-focused cognitive behavioral therapy variants, especially image rehearsal therapy, are effective. Interest-

ingly, there are no large-scale, well-controlled trials comparing pharmacologic with non-pharmacologic therapies.[21]

4.1 The following are medication treatment options for nightmare disorder

A variety of medications have been studied for possible benefit in patients with nightmares. The studies of most medications assess efficacy only in the treatment of PTSD-associated nightmares. It is unknown if treatments that demonstrate efficacy for PTSD-associated nightmares are also effective for idiopathic or drug-related nightmares, or if these therapies would work for patients who have bad dreams that do not fulfill *ICSD-2* criteria for nightmare disorder, such as those that occur in the first half of the night or that are not associated with an awakening. Even if the focus is limited to PTSD-associated nightmares, there is an insufficient number of controlled trials to formulate rigorous evidence-based guidelines on nightmare disorder,[22] although an evidence-based systematic review of pharmacotherapy for PTSD, not specifically related to improvement in nightmares, has been published.[23] Many patients with PTSD are on multiple psychotropic medications, making the assessment of efficacy of monotherapy of any particular medication difficult. A summary of the volume and grade of literature is in **Appendix Table 1** and discussed in detail below.

4.1.1 Prazosin is recommended for treatment of PTSD-associated nightmares. Level A

The rationale for the use of pharmacologic reduction of CNS adrenergic activity in the treatment of PTSD has recently been reviewed by Boehnlein and Kinzie.[24] Norepinephrine appears to play an important role in the pathophysiology of PTSD-related nightmares, arousal, selective attention, and vigilance. Norepinephrine levels in the cerebrospinal fluid and urine are elevated in patients with PTSD. CSF norepinephrine concentration appears to correlate with the severity of PTSD symptoms. It has been proposed that the consistently elevated CNS noradrenergic activity may contribute to disruption of normal R sleep and that agents that reduce this activity could be effective for treatment of some manifestations of PTSD, particularly arousal symptoms such as nightmares and startle reactions.[24]

Propranolol, a non-selective β-adrenergic blocker, has been investigated for treatment and perhaps prevention of PTSD.[25] Paradoxically, β-blockers are often associated with sleep disorders including nightmares and insomnia.[26] The literature review found no studies related to the use of propranolol or other beta-blockers for treatment of nightmares, even in patients with PTSD.

Prazosin is an α_1-adrenergic receptor antagonist introduced as an antihypertensive agent. It reduces CNS sympathetic outflow throughout the brain. Several CNS phenomena implicated in the pathogenesis of PTSD are regulated by α_1-adrenergic receptors including a number of sleep/nightmare phenomena, and cognitive disruption.[24] In a placebo-controlled study, the effects of prazosin on sleep included increased total sleep time, increased REM sleep time, and increased mean R period duration without alteration of sleep-onset latency.[27]

The data supporting efficacy of prazosin in the treatment of PTSD-associated nightmares consist of 3 Level 1 placebo-controlled studies,[27-29] all of which are from the same group of investigators, and 4 Level 4 studies.[30-33] Prazosin was found to be moderately to strongly beneficial in all the studies. Ninety-eight patients were studied. The 3 Level 1 studies evaluated 10 Vietnam combat veterans (mean age 53 years),[29] 34 military veterans (mean age 56 years),[28] and 13 civilian trauma victims (mean age 49 ± 10 years, 11/13 women)[27] in placebo-controlled trials; all found a statistically significant reduction in trauma-related nightmares versus placebo as measured by Item No. 2 "recurrent distressing dreams" on CAPS (initial rating 4.8 to 6.9 in the Level 1 studies; final rating after prazosin treatment was 3.2 to 3.6). The treatment length ranged from 3 to 9 weeks. All patients maintained their ongoing concurrent psychotherapy and psychotropic medications during the trials. Treatment was generally started at 1 mg at bedtime and increased by 1 to 2 mg every few days until an effective dose was reached. The average dose was approximately 3 mg, although 1 mg to over 10 mg were used and found to be effective, with higher doses used in 2 of the Level 1 studies treating PTSD-associated nightmares in military veterans (mean of 9.5 mg/day[29] and 13.3 mg/day[28]). In all of the studies, prazosin appeared to be generally well tolerated; nevertheless, the clinician should monitor the patient for orthostatic hypotension.

4.1.2 Clonidine may be considered for treatment of PTSD-associated nightmares. Level C

Clonidine is an α_2-adrenergic receptor agonist that suppresses sympathetic nervous system outflow throughout the brain. It is widely used to treat opioid withdrawal, in which context it blocks an elevated startle reaction. Clonidine shares the therapeutic rationale as well as the potential for postural hypotension of prazosin but has not been investigated with the same rigor. It has been reported that low-dose clonidine increases R sleep and decreases N sleep, whereas medium-dose clonidine decreases R sleep and increases N2 sleep.[34] There were 2 Level 4 case series demonstrating efficacy of 0.2 to 0.6 mg clonidine (in divided doses) to reduce the number of nightmares in 11/13 Cambodian refugees (no statistical analysis done).[35,36] Follow-up ranged from 2 weeks to 3 months with one report of a fall in blood pressure with increasing dose. These were from a single site, and 9 were also treated with imipramine. Boehnlein and Kinzie[24] report that "clonidine has been a mainstay of PTSD treatment for severely traumatized refugees for over 20 years," yet no randomized placebo-controlled trials of clonidine for the treatment of nightmares or other aspects of PTSD have been reported. Despite the long history of use and the pharmacologic similarity to prazosin, the paucity of hard data relegates this medication to a lower level recommendation.

4.1.3 The following medications may be considered for treatment of PTSD-associated nightmares, but the data are low grade and sparse: trazodone, atypical antipsychotic medications, topiramate, low dose cortisol, fluvoxamine, triazolam and nitrazepam, phenelzine, gabapentin, cyproheptadine, and tricyclic antidepressants. Nefazodone is not recommended as first line therapy for nightmare disorder because of the increased risk of hepatotoxicity. Level C

4.1.3.1 Trazodone

A Level 4 survey[37] of 74 patients who were given trazodone found that it was effective in decreasing the frequency of night-

mares but also had significant side effects. Of 60 veterans prescribed trazodone during an 8-week hospitalization, 72% found it decreased nightmares, with a fall from an average occurrence of 3.3 nights per week to 1.3 nights per week ($p < 0.005$). The dose ranged from 25 to 600 mg, with a mean of 212 mg. Sixty percent (36/60) of those who tolerated trazodone therapy complained of the following side effects (decreasing order of frequency): daytime sedation, dizziness, headache, priapism, and orthostatic hypotension Nineteen percent of the original sample (14/74) discontinued the drug because of side effects (priapism, daytime sedation, more vivid nightmares, severe dry mouth and sinuses). Only 1 subject was not on additional psychotropic medications (mostly antidepressants, but also antipsychotics and pain medication).

4.1.3.2 Atypical antipsychotic medications: olanzapine, risperidone, and aripiprazole

Olanzapine is an atypical neuroleptic which has been shown to be useful in the treatment of schizophrenia and bipolar mania. It was used in a small uncontrolled case series[38] (Level 4 evidence) of 5 patients with combat-related PTSD resistant to treatment with SSRIs and benzodiazepines because of reports that it improved sleep. The authors reported rapid improvement after 10-20 mg olanzapine was added to the current psychotropic treatment regimen. There was no quantification of medication effect and no long-term follow-up. No adverse events were seen.[38]

Risperidone is an atypical antipsychotic medication that demonstrates significant α_1-noradrenergic antagonism.[39] Two Level 4 case series[40,41] showed moderate to high efficacy of risperidone in treating patients with PTSD-related nightmares. The 6-week results of an open-label, flexible dosage (1 to 3 mg/day) trial[40] of 17 Vietnam combat veterans showed a statistically significant fall in the CAPS score of recurrent distressing dreams ($p = 0.04$) with a reduction in the proportion of diaries documenting trauma dreams (38% to 19%, $p = 0.04$). Many of these patients were taking others medications as well (antidepressants, mood stabilizers, and anxiolytics). A retrospective study[41] of 10 adult burn patients on pain medications reported that all subjects experienced improvement in nightmares (no quantitative analysis done), as well as other distressing acute stress symptoms, 1-2 days after starting risperidone (0.5 to 2 mg; average 1 mg). Neither study reported side effects, and there was no long-term follow-up.

There is a Level 4 case series[42] on the effect of aripiprazole with CBT or with sertraline in 5 patients suffering from combat-related PTSD. Aripiprazole, 15 to 30 mg at bedtime, resulted in significant improvement but not total resolution of sleep disturbances such as nightmares in 4/5 cases. The patient who did not respond stopped the medication because of agitation and inability to sleep. Duration of follow-up was not specified.

4.1.3.3 Topiramate

A Level 4 case series[43] studied the efficacy of topiramate in 35 civilians who suffered from PTSD primarily due to physical assault or unwanted sexual experience. Dosage titration began at 12.5 to 25 mg daily and was increased in 25 to 50 mg increments every 3 to 4 days until a therapeutic response was achieved or the drug was no longer tolerated. Topiramate reportedly reduced nightmares in 79% of patients, with full suppression in 50%. The final dosage for 91% of full responders was 100 mg/day or less, but the range was 12.5 to 500 mg/day. Follow-up ranged from 1 to 119 weeks. Nine patients discontinued treatment due to side effects, which included urticaria, eating cessation, acute narrow-angle glaucoma, severe headaches, overstimulation/panic, emergent suicidal ideation, and memory concerns.

4.1.3.4 Low-dose cortisol

Low-dose cortisol (10 mg/day, either in the morning or half at noon and half in the evening) was found to have medium-to-high benefit with low side effects in 3 civilians with PTSD in a Level 4 study for 1 month.[44] There was a significant reduction in the frequency of nightmares but not intensity in 2 subjects; there were no data on nightmare effect for the third subject. One of the patients was also on mianserin and chlorprothixene. There were no reported side effects and no long-term follow-up.

4.1.3.5 Fluvoxamine

Two Level 4 case series[45,46] showed moderate-to-high efficacy in 42 patients with up to 300 mg fluvoxamine. One study[46] of 21 Vietnam veterans reported a statistically significant fall in the Impact of Event Scale-Revised (IES-R) level of "dreams about combat trauma" but a non-significant fall in the rating of "bad dreams" from the Stress Response Rating Scale at 10 weeks. No side effects were noted in the study. The patients were on no other psychoactive medications. The second study[45] of 24 Dutch WWII Resistance veterans reported a qualitative decrease in nightmares in 12 subjects. No further details were given. Of note, 12 subjects dropped out of the trial, 9 due to gastrointestinal problems and worsening of sleep, and 3 for physical complaints not related to fluvoxamine. Follow-up ranged from 4 to 12 weeks. Some of the patients were on benzodiazepines.

4.1.3.6 Triazolam and nitrazepam

In a 3-day Level 2 cross-over study[47] comparing the hypnotic efficacy of triazolam versus nitrazepam in 40 patients with "disturbed sleep," 0.5 mg triazolam was found to be superior to 5 mg nitrazepam in terms of objective measures of sleep duration and quality. However, both drugs were equally effective at reducing the number of subjects who noted unpleasant dreams, from 23 prior to medication administration to 1 subject for nitrazepam and 2 subjects for triazolam. Each drug was given for just one night and the measure of nightmare frequency was limited. There was no difference in side effects, which were considered minor and consisted of difficulty concentrating in the morning and morning sedation.

4.1.3.7 Phenelzine

Two Level 4 studies[48,49] studied phenelzine as a single medication in a total of 26 military veterans. The dosage in these studies ranged from 30 to 90 mg. One study[48] with 5 subjects found that phenelzine eliminated nightmares entirely within 1 month with long-term follow-up up to 18 months later. Three of the 5 subjects were nightmare-free without medication. The other study[49] demonstrated a fall in an average "traumatic

dream" severity scale in 21 veterans from just above moderate (2.2/4) to just below moderate (1.8/4), a change that reflected an improvement of 18%, but just missed the level of statistical significance ($p = 0.05$). Six patients stopped treatment within 8 weeks because of a lack of improvement. Treatment was ultimately discontinued in the remaining subjects because the initial improvement was minor or short-lived or reached a plateau felt to be sufficiently unsatisfactory to justify a change to an alternate medication. Reported side effects included dizziness, drowsiness, and malaise. Although not specifically stated, the ability of phenelzine to reduce R sleep was cited. As an MAOI, phenelzine can cause a hypertensive crisis if taken with sympathomimetic medications or with high tyramine-containing foods.[50]

4.1.3.8 Gabapentin

There is a Level 4 study[51] of 30 veterans with PTSD that used adjunctive gabapentin at 300-3600 mg/day, most of whom were on antidepressants with some on antipsychotics and anxiolytics. The results showed a medium to high effect, with 77% of patients showing a moderate or greater improvement in insomnia, and most of those subjects noting a decrease in the frequency and/or intensity of nightmares over a follow-up period of 1 to 36 months (this response was not quantified in the paper). The mean dosage for patients with moderate or marked clinical improvement was 1344 ± 701 mg, and for those with mild or no improvement it was 685 ± 227 mg. Sedation and mild dizziness were the most commonly reported side effects.

4.1.3.9 Cyproheptadine

The evidence for cyproheptadine, which has serotonin antagonism properties, consists of 3 Level 4 papers with conflicting data.[52-54] A small case series[52] of 4 veterans with combat-related PTSD, who were said to be representative of "about 80" patients treated with effective doses ranging from 16-24 mg, reported that cyproheptadine eliminated nightmares in 3 patients on doses ranging from 2-6 mg nightly. When effective, it generally took effect within a few days. The proposed mechanism of effect was through increasing serotonin levels by blocking feedback inhibition. Long-term follow-up was not reported. A retrospective review[54] of psychiatric records of patients who received cyproheptadine as treatment for nightmares provided incomplete information. Only 9 patients whose responses varied from "complete remission" to decreased intensity and frequency were described in detail, and the total number of records reviewed was not reported. Four of 16 patients studied at a VA PTSD treatment center reported cyproheptadine to be effective but there was no change in report of nightmare presence and intensity over a one-month period at a dose of 4-8 mg in any of the 16 subjects. All but 2 of the 16 patients were taking a wide variety of other psychotropic medications. Side effects included drowsiness, irritability, hallucinations, nausea, headache, and worsening of nightmares.[53]

4.1.3.10 Tricyclic Antidepressants

There was 1 Level 4 study[55] of 10 Cambodian concentration camp survivors treated with tricyclic antidepressants for PTSD. Nightmares ceased in 4/10 and improved in another 4/10 with no worsening of nightmares and no reported side effects. Unfortunately, they were all on different regimens, including imipramine as monotherapy (75 mg-125 mg; 3 subjects), imipramine (150 mg) with phenelzine alone or phenelzine and doxepin and amitriptyline (2 subjects), amitriptyline (100 mg) with doxepin (1 subject), and doxepin alone (50-100 mg, 4 subjects). The 2 subjects who did not have any improvement in nightmares were either on doxepin 100 mg or imipramine (150 mg) with doxepin (150 mg), phenelzine (30 mg bid), and amitriptyline (100 mg). Although follow-up occurred at 1 year, the paper did not detail the length of treatment with each medication. In addition to medication, the patients also had monthly clinic visits to discuss ways to handle stress.

4.1.3.11 Nefazodone

There are 3 Level 4 studies that evaluated nefazodone as monotherapy in a total of 39 patients. An open-label 12-week clinical and sleep EEG study of 12 male veterans treated with nefazodone (mean dosage 441 mg) demonstrated significantly fewer nightmares (30% fewer at 12 weeks) and sleep problems. There were no changes in polysomnographic variables compared to baseline.[56] An additional study of 10 Vietnam-era veterans (dosage 500-600 mg/day) reported improvement in nightmares (as measured by a decrease in the IES-R nightmare assessment from 3.5 to 2.1, $p = 0.003$) in response to nefazodone.[57] A third uncontrolled study of 17 civilians with PTSD with a mean nefazodone dose of 386 ± 192 mg/day reported a 58.3% response rate for nightmares on the Structured Interview for PTSD (SIP) after 2 weeks of treatment and a 50% response rate at week 12.[58] This drug, now only available in generic form, must be used with caution and careful monitoring, as cases of hepatic failure have been associated with nefazodone.[59] The following side effects were noted in the studies: bitter taste, increased appetite, drowsiness, headache, dry mouth, dizziness, and hypersomnia.

4.1.4 Venlafaxine is <u>not</u> suggested for treatment of PTSD-associated nightmares. Level B

This assessment is based on 1 Level 1 study[60] of venlafaxine ER (37.5 to 300 mg/d) with 340 subjects treated for PTSD (combination of combat-related and non-combat related). This study was a pooled analysis of 2 randomized, double-blind, placebo-controlled trials assessing response (via CAPS-SX_{17}) at 12 weeks of therapy. The study showed no significant difference between the effects of placebo and venlafaxine ER in the CAPS-SX_{17} item Distressing Dreams. No side effects were noted in the study, and there was no long-term follow-up. Although venlafaxine did not result in a greater improvement in nightmares than did placebo, it resulted in statistically significant improvement in 13 other PTSD symptoms when compared with placebo.

4.1.5 No recommendation is made regarding clonazepam because of sparse data.

This assessment is based on only 1 Level 2 study[61] of 6 veterans with PTSD and may be revised if more data become available. The study was a randomized, single-blind, placebo-controlled, crossover clinical trial which found that clonazepam was largely ineffective for treatment of sleep dis-

turbances associated with combat-related posttraumatic stress disorder. Although 1 to 2 mg of clonazepam at bedtime improved problems with sleep initiation and maintenance, the differences were not statistically significant and there was no improvement in nightmare intensity or frequency. Side effects were indiscernible from placebo, and there was no long-term follow-up.

4.2 The following are non-pharmacological treatment options for nightmare disorder

The etiology of nightmares is suggested to be multifactorial and may be influenced by psychological factors to a great extent. There is an immense literature demonstrating efficacy of psychotherapeutic interventions for PTSD, including trauma-focused Cognitive Behavioral Therapy (CBT). Trauma-focused CBT, particularly IRT, has been shown to be effective treatment for sleep-related issues in PTSD as summarized in a systematic review[62] and 2 meta-analyses[63,64] that included 36 RCTs related to disturbed sleep in PTSD patients. These studies focused on general sleep characteristics in PTSD and not specifically on nightmares. The discussion that follows addresses the efficacy of those treatments for nightmares. Although some treatments were only studied on patients with PTSD, it is possible that these treatment modalities would also be effective in patients with idiopathic nightmares or disturbing dreams that do not fulfill *ICSD-2* criteria, as illustrated by the efficacy of IRT in a diverse patient population. **Appendix Box 1** summarizes the non-pharmacological therapies available to the practitioner for patients suffering from nightmare disorder.

4.2.1 Cognitive Behavioral Therapy (CBT)

CBT is psychotherapeutic approach that focuses on distorted/dysfunctional thoughts, emotions, and behavior through a goal-oriented, structured and time limited procedure. CBT is often used as a broad term for a number of psychotherapeutic and behavioral techniques tailored to uncover, alter, and correct distortions of cognition and behavior in an individual. Some of the early interventions used basic CBT principles[65,66] effectively to manage nightmares until more effective and specialized CBT techniques targeting the symptoms of nightmares evolved. The documented variants of CBT that are specifically focused on treatment of nightmares include Image Rehearsal Therapy and its modifications, Lucid Dreaming Therapy, Sleep Dynamic Therapy, Self-exposure Therapy, and Systematic Desensitization. CBT also includes an IRT variant, Exposure, Relaxation and Rescripting Therapy.

4.2.1.1 Image Rehearsal Therapy (IRT) is recommended for treatment of nightmare disorder. Level A

Image Rehearsal Therapy (IRT) is a modified CBT technique that utilizes recalling the nightmare, writing it down, changing the theme, story line, ending, or any part of the dream to a more positive one, and rehearsing the rewritten dream scenario so that the patient can displace the unwanted content when the dream recurs. IRT acts to inhibit the original nightmare, providing a cognitive shift that empirically refutes the original premise of the nightmare.[67] This technique is practiced for 10-20 minutes per day while awake.

This recommendation is based on 1 Level 1,[67] 1 Level 2,[68] 1 Level 3,[69] and 7 Level 4 studies.[65,70-75] Although the Level 1, Level 2, and Level 3 studies are from a single site, the data are sufficiently compelling to merit a Level A recommendation. The Level 1 study[67] demonstrated that IRT is a brief, effective, well-tolerated treatment for chronic nightmares associated with PTSD. This RCT of 168 women with moderate-to-severe PTSD symptoms demonstrated that IRT significantly improved disturbing dreams, sleep quality, and posttraumatic stress symptoms (60% reduction) and the effect was maintained at 3- and 6-month follow-up evaluations compared to control group. However, there was a high drop-out rate (32%) and the control group was a wait-list control [see footnote on page 398] and blinding for treatment was not possible.

A Level 2 study[68] demonstrated sustained reduction of nightmare frequency at 30 months in 2 groups of 10 patients each treated for chronic nightmares with CBT. The initial 3-month data were reported in an earlier Level 2 study[76] but were not considered separately as this longer-term report superseded the earlier reference. As part of CBT, 1 group learned IRT and the other group recorded the nightmares in a diary for 1 month. At 3-month follow-up the IRT group had a 72% reduction ($p < 0.006$) in nightmare frequency (7.2/month to 2.0/month) compared to a 42% reduction ($p < 0.02$) in frequency (9.4/month to 5.0/month) noted in the recording-only group. Interestingly the study showed that the IRT group also had substantial decrease in anxiety, somatization, hostility, and total distress scores on the SCL-90 and SQ when compared with the recording-only group (no p-value given). The subsequent addition of imagery rehearsal and rescripting to the first group that used only nightmare recording did not produce further decrease in symptoms at 30-month follow-up. The initial effects of these 2 individual techniques appeared to be the most potent in reducing nightmares.

In a Level 3 study[69] of 58 subjects with chronic nightmares, IRT demonstrated a clinically meaningful and significant decrease in nightmare frequency with long-term follow-up. At 18 months, 68% of the remaining 53 subjects no longer met criteria for nightmare disorder. This study is a follow-up from a prior Level 2 study[77] of 58 subjects with nightmare disorder who were not screened for psychiatric illness and likely represented both idiopathic and PTSD-associated nightmare disorder (personal communication from the author).

Additionally there were 7 other Level 4 studies,[65,70-75] comprising 187 subjects, that indicated strong benefits for IRT in the management of nightmares in patients with PTSD-associated and idiopathic nightmares. These were mainly case series or studies with few subjects and with either no control group or no blinding.

IRT appears to be effective in the management of nightmares exhibited in patients with PTSD as well as idiopathic nightmares. This was generally a well-tolerated treatment although there was 1 report[72] of a subject who developed paradoxical hyperarousal with an increase in nightmare frequency (although this could also represent the natural progression of the disorder). This may indicate the potential for this type of treatment to induce an exacerbation of PTSD symptoms during the therapeutic process. It is important to mention that several of the higher-level data are from a single-site or contributions associated with a particular expert in the field. Additional high level

studies from different sites demonstrating the effectiveness of treatment are limited.

4.2.1.2 Lucid Dreaming Therapy (LDT) may be considered for treatment for nightmare disorder. Level C

A variant of IRT, the cognitive-restructuring technique of LDT allows one to alter the nightmare story line during the nightmare itself by realizing that one is dreaming or being "lucid" during the nightmare.

This recommendation is based on 1 Level 3[78] (16 subjects in the treatment arms) and 1 Level 4 study[79] (5 subjects). The Level 3 study demonstrated that at 12-week follow-up, 2 hours of individual LDT counseling ($p = 0.0002$) was more effective than 2 hours of group LDT ($p = 0.02$) instruction although both showed a statistically significant fall in the frequency of nightmares when compared with baseline. The wait-list control group ($p = 0.30$) did not demonstrate a statistically significant reduction. A Level 4 case series of 5 patients, with either idiopathic or PTSD nightmares, showed alleviation of recurrent nightmares at 1 year when lucid dreaming was added to the subjects who were initially trained in progressive muscle relaxation and guided imagery.

Low grade evidence suggests LDT may be helpful. However, it may have only limited applicability in terms of availability and incorporation of treatment.

4.2.1.3 Exposure, Relaxation and Rescripting Therapy (ERRT) may be considered for treatment of PTSD-associated nightmares. Level C

Exposure, Relaxation and Rescripting Therapy (ERRT) is a specialized treatment modality targeting anxiety, which may manifest as physiological, behavioral, and cognitive dysfunction. The treatment involves psychoeducation, sleep hygiene, and progressive muscle relaxation training. Exposure procedures such as writing out and rescripting the nightmares, homework assignments, problem solving, and coping strategies are intended to help deal with the nightmares. This form of treatment is similar to IRT except for type of exposure utilized.

This assessment is based on 1 small Level 4 study.[80] ERRT was found to decrease the frequency and severity of trauma-related nightmares in 4 subjects at 3- and 6-month follow-up evaluations.

4.2.1.4 Sleep Dynamic Therapy may be considered for treatment of PTSD-associated nightmares. Level C

Sleep Dynamic Therapy is an integrated program combining standard clinical sleep medicine instructions including sleep quality and sleep hygiene with psychotherapeutic interventions using principles of CBT like stimulus control, IRT, etc. A sample protocol of this treatment includes conveying 6 educational/therapeutic principles (including sleep quality assessment with behavioral deconditioning, sleep hygiene, stimulus control, IRT, education on 3 defining posttraumatic stress symptoms, and physiologic assessment) in weekly 2-hour sessions.

This assessment is based on 1 Level 4 pilot study[75] of 66 PTSD subjects without a control group that demonstrated improvements in insomnia and nightmares at the 12-week follow-up with a significant reduction in the Nightmare Severity Index (Cohen $d = 1.09$, $p < 0.0001$).

4.2.1.5 Self-exposure Therapy may be considered for treatment of nightmare disorder. Level C

Self-exposure Therapy is a variant of CBT that utilizes a technique of "graded exposure." The patient is instructed to make a hierarchical list of anxiety-provoking events/dreams. The patient is then instructed to move through the situations on the list at his or her own rate, starting with lowest anxiety situation until the fear/anxiety has decreased. The exposure is done on a daily basis with documentation in a journal of his or her experiences.

This recommendation is based on 1 Level 2 and 1 Level 3 study of patients with idiopathic or PTSD related nightmares. The Level 2 RCT[81] involved 206 subjects randomized to 4 weeks of (a) self-exposure treatment at home ($n = 83$), (b) self-relaxation treatment at home ($n = 61$), and (c) a wait-list control group ($n = 62$), all instruction coming from a treatment manual received in the mail. Self-exposure therapy ($p < 0.0005$) was better than self-relaxation therapy or wait-list control for reducing nightmare frequency. The limitations of the study included a high drop-out rate (17%) and the fact that the nightmare intensity was not greatly reduced after 4 weeks of self-exposure, which may indicate the need for longer treatment duration. In a Level 3 open randomized study[82] involving 20 subjects with recurrent nightmares, 10 each were randomized to a correspondence-based self-exposure therapy trial and a control group. At the 4-week follow-up, the self-exposure group had significant improvements in nightmare frequency and intensity ($p < 0.001$), and the benefit was maintained at the 4-year follow-up. This small study had no drop-outs and the subjects served as their own controls.

4.2.1.6 Systematic Desensitization is suggested for treatment of idiopathic nightmares. Level B

Systematic Desensitization is a type of behavioral therapy that uses the principle of gradually exposing the patient to what he fears. This technique is also called "graduated exposure therapy." The patient is trained to cope and manage the stressors gradually before the patient is actually exposed to the feared object or situation.

This recommendation is based on 1 Level 1, 1 Level 2, and 1 Level 4 study. The Level 1 study[83] compared Progressive Deep Muscle Relaxation (PDMR) (11 subjects) with systemic desensitization (10 subjects) and wait-listed controls (11 subjects). Although both intervention groups showed similar decrease in frequency of nightmares, at 25-week follow-up the desensitization group ($p < 0.026$) showed significantly greater reduction in nightmare intensity compared to the relaxation group (see PDMR section for details). A Level 2 8-week randomized control study[84] randomly assigned 29 subjects to a Systemic Desensitization treatment group (10 subjects), a continuous self-recording group (9 subjects), and a nightmare-related discussion placebo treatment group (10 subjects). The short-term Systemic Desensitization treatment was found to produce favorable changes in frequency ($p < 0.01$) and rated intensity of the nightmares ($p < 0.01$). However, follow-up nightmare information was available for only 65% of the subjects.

The Level 4 study[73] involved 36 subjects with chronic nightmares, of whom 14 received 1 single treatment instruction of desensitization with progressive muscle relaxation and 14 with

rehearsal of changed nightmares. Eight were excluded after intake. All subjects were contacted via telephone at 4 months and 7 months. Both the treatment groups showed a decrease in frequency of nightmares ($p < 0.0001$).

Although the studies are multicenter and well-designed, demonstrating statistical significance, more data on larger groups of subjects with lower drop-out rates would be helpful to fully understand the usefulness of this technique.

4.2.2 Progressive Deep Muscle Relaxation Training is suggested for treatment of idiopathic nightmares. Level B

Progressive Deep Muscle Relaxation (PDMR) involves tensing and releasing the muscles, one body part at a time, to bring about a feeling of physical relaxation and reduction in anxiety and stress.

This recommendation is based on 1 Level 1 study[83] of 32 females self-referred with complaints of nightmares. They were randomly assigned to PDMR training, systemic desensitization, and wait-list controls. Both treatments reduced nightmare frequency by 80% in 20/21 subjects ($p = 0.001$ compared with wait-listed controls), and 12 of these subjects had total elimination of symptoms. The treatment groups showed greater decrease in nightmare frequency compared to wait-listed controls ($p < 0.001$) at week 15. After week 25, although the effect on frequency of nightmares was favorable and consistent, the desensitization group had a more favorable effect on intensity ($p < 0.026$) of the nightmares, especially favoring the earlier-treated group ($p < 0.046$) over the later-treated wait-listed controls indicating improved benefit with longer duration of treatment.

The data for PDMR based on this 1 small study is statistically compelling. However, further research is warranted to validate these findings.

4.2.3 Hypnosis may be considered for treatment of PTSD-associated nightmares. Level C

Hypnosis or Hypnotherapy is a trance-like state of mind. Hypnosis creates a state of deep relaxation which helps the mind to concentrate intensely on a specific thought, memory, feeling, or sensation without distractions and making the person open to suggestions that can be used to change certain thought or behavior.

This recommendation is based on 2 Level 4 studies. In a small case series[85] involving 10 patients with nightmares treated with hypnosis, 71% had improvement or were symptom-free at 18 months and 67% at 5-year follow-up. Another Level 4 case series[86] involving 3 subjects showed that brief hypnotic therapy of 1 to 5 sessions were found to be beneficial for repetitive nightmares.

4.2.4 Eye Movement Desensitization and Reprocessing (EMDR) may be considered for treatment of PTSD-associated nightmares. Level C

Eye Movement Desensitization and Reprocessing (EMDR) is a specialized psychotherapeutic intervention integrating elements from psychodynamic, cognitive behavioral, interpersonal, experiential, and body-centered therapies.[87,88] The principle is to induce the processing of disturbing memories and experiences by stimulating neural mechanisms that are similar to those activated during REM sleep. An 8-phase approach is employed using bilateral eye movements, tones, and taps to identify and process the disturbed memory and past experience, current triggers, and positive experiences to formulate insight and adaptive behavior in patients suffering from traumatic experience.

This recommendation is based on 2 Level 4 studies[89,90] addressing its efficacy in treating nightmares. A case series[90] of 83 veterans with PTSD (including nightmares) compared EMDR with Relaxation training and Biofeedback at initial evaluation, hospital admission at 2 months or later, and 90 days after admission. This was an in-house program evaluation study (conducted at a VA-hospital-based inpatient PTSD program) rather than an experiment and was based on patient self-report. The EMDR subjects did better than controls and the other 2 treatment groups in all variables including nightmares ($p < 0.01$). The second cohort study[89] reported on 7 subjects who had nightmares and PTSD symptoms for at least 3 months after being assaulted or kidnapped. They were treated with 5 EMDR sessions. EMDR improved PTSD symptoms and quality of sleep. This study did not specifically address the quality and frequency of nightmares in these patients, but addressed recurrent nightmares as part of sleep quality which showed improvement ($p = 0.003$).

4.2.5 The Testimony method may be considered for treatment of PTSD-associated nightmares. Level C

The Testimony method is a brief variant of a trauma exposure technique. Trauma survivors are invited to tell the story of their traumatic experiences and document them in a written format with the help of the therapist.

In a Level 3 case-control trial[91] in a community setting, 206 Mozambican civil war survivors were sorted into a case and a non-case group. The case group of 137 subjects was randomized to an intervention group and a control group. One 60-minute session of Testimony intervention was performed with each subject, although 7 cases required a second session. The nightmare impact (NITE) scores indicated significant reduction in anxiety dreams ($p < 0.01$) at post-intervention and 11-month follow-up. Although this study was designed as a case-control study, the local circumstances interfered with the design, especially with controlling the intervention in a small rural community.

4.2.6 No recommendation is made regarding Individual Psychotherapy because of sparse data.

Individual psychotherapy refers to a treatment intervention between a patient and a therapist, who is usually a psychiatrist, psychologist, or an individual with specialized training in psychotherapeutic techniques such as therapeutic alliance, psychoanalysis, etc. The therapy may focus on issues that are current or in the past along with associated thoughts, experiences, behaviors, and interactions and their role in the patient's life.

This assessment is based on a single Level 4 case series[92] of 3 veterans with PTSD and recurrent nightmares who responded well to individual psychotherapy. The therapeutic principle focused on understanding of the individual's war experiences and how they were represented in each individual's postwar life. The literature describes high-level effectiveness of this treatment modality in case reports and descriptive treatment protocols. RCTs and comparative studies are unavailable.

5.0 AREAS FOR FUTURE RESEARCH

There is a wealth of data about pharmacological and behavioral interventions for the treatment of nightmare disorder, yet a great majority of the research focuses on management of individual patients and case reports. Thus, there is paucity of research with randomized controlled trials and Level 1 studies. In addition, consistency in nightmare metrics would improve the ability to compare results among trials. There is also a need for investigations to determine if different approaches are necessary for idiopathic versus PTSD-associated nightmares. Emphasis should be placed on trials directly comparing various pharmacotherapy and behavioral techniques, combination treatments with medication and psychotherapy, and duplication and verification of results on a broader scale involving multicenter or registry approaches.

FOOTNOTE FROM PAGE 395

This refers to a group of people in the waiting list scheduled to get the intervention in the future, who serve as the control group while the active group receives the intervention. This method is usually used in psychotherapeutic outcome trials. Usually everyone receives the intervention by the end of the study.

REFERENCES

1. Phillips B, Ball C, Sackett D, et al. Oxford Centre for Evidence-Based Medicine - Levels of Evidence (March 2009). 2009; http://www.cebm.net/index.aspx?o = 1025.
2. Fitch K, Bernstein SJ, Aguilar MS, et al., eds. *The RAND/UCLA Appropriateness Method User's Manual* 2000.
3. American Academy of Sleep Medicine. *International classification of sleep disorders, 2nd ed.: Diagnostic and coding manual*. Westchester, IL: American Academy of Sleep Medicine; 2005.
4. Kilpatrick D, Resnick H, Freedy J, et al. Posttraumatic stress disorder field trial: Evaluation of PTSD construct criteria A through E. In: Widiger T, Frances A, Pincus H, et al., eds. *DSM-IV Sourcebook.* Vol 4. Washington, D.C.: American Psychiatric Press; 1994.
5. Berger W, Mendlowicz M, Marques-Portella C, et al. Pharmacologic alternatives to antidepressants in posttraumatic stress disorder: a systematic review. *Prog Neuropsychopharmacol Biol Psych* 2009;33:169-180.
6. Pagel JF, Helfter P. Drug induced nightmares - an etiology based review. *Hum Psychopharmacol* 2003;18:59-67.
7. Zadra A, Donderi DC. Nightmares and bad dreams: their prevalence and relationship to well-being. *J Abnorm Psychol* 2000;109:273-81.
8. Schredl M. Questionnaires and diaries as research instruments in dream research: methodological issues. *Dreaming* 2002;12:17-26.
9. Blake DD, Weathers FW, Nagy LM, et al. The development of a Clinician-Administered PTSD Scale. *J Trauma Stress* 1995;8:75-90.
10. Weathers FW, Keane TM, Davidson JRT. Clinician-Administered PTSD Scale: A review of the first ten years of research. *Depress Anxiety* 2001;13:132-56.
11. Derogatis LR, Lipman RS, Covi L. SCL-90: and outpatient psychiatric rating scale--preliminary report. *Psychopharmacol Bull* 1973;9:13-28.
12. Kellner R. A symptom questionnaire. *J Clin Psychiatry* 1987;48:268-74.
13. Woodward S, Arsenault N, Murray C, Bliwise DL. Laboratory sleep correlates of nightmare complaint in PTSD inpatients. *Biol Psychiatry* 2000;48:1081-7.
14. Fisher C, Byrne J, Edwards A, Kahn E. A psychophysiological study of nightmares. *J Am Psychoanal Assoc* 1970;18:747-82.
15. van der Kolk B, Blitz R, Burr W, Sherry S, Hartmann E. Nightmares and trauma: a comparison of nightmares after combat with lifelong nightmares in veterans. *Am J Psychiatry* 1984;141:187-90.
16. Germain A, Nielsen TA. Sleep pathophysiology in posttraumatic stress disorder and idiopathic nightmare sufferers. *Biol Psychiatry* 2003;54:1092-8.
17. DeViva JC, Zayfert C, Mellman TA. Factors associated with insomnia among civilians seeking treatment for PTSD: An exploratory study. *Behav Sleep Med* 2004;2:162-76.
18. Krakow B, Artar A, Warner TD, et al. Sleep disorder, depression, and suicidality in female sexual assault survivors. *Crisis* 2000;21:163-70.
19. Zayfert C, DeViva J. Residual insomnia following cognitive behavioral therapy for PTSD. *J Trauma Stress* 2004;17:69-73.
20. Levin R, Fireman G. Nightmare prevalence, nightmare distress, and self-reported psychological disturbance. *Sleep* 2002;25:205-12.
21. Stein MB. A 46-Year-Old man with anxiety and nightmares after a motor vehicle collision. *JAMA* 2002;288:1513-22.
22. Van Liempt S, Vermetten E, Geuze E, Westenberg H. Pharmacotherapeutic treatment of nightmares and insomnia in posttraumatic stress disorder. *Ann NY Acad Sci* 2006;1971:502-7.
23. Stein DJ, Ipser JC, Seedat S. Pharmacotherapy for post traumatic stress disorder (PTSD). *Cochrane Database Syst Rev* 2006(1):Art. No. CD002795.
24. Boehnlein JK, Kinzie JD. Pharmacologic reduction of CNS noradrenergic activity in PTSD: the case for clonidine and prazosin. *J Psychiatr Pract* 2007;13:72-8.
25. Cukor J, Spitalnick J, Difede J, Rizzo A, Rothbaum BO. Emerging treatment for PTSD. *Clin Psychol Rev* 2009;29:715-26.
26. Betts T, Alford C. Beta-blockers and sleep: a controlled trial. *Eur J Clin Pharmacol* 1985;28(suppl):65-8.
27. Taylor F, Martin P, Thompson C, et al. Prazosin effects on objective sleep measures and clinical symptoms in civilian trauma posttraumatic stress disorder; a placebo controlled study. *Biol Psychiatry* 2008;63:629-32.
28. Raskind M, Peskind E, Hoff D, et al. A parallel group placebo controlled study of prazosin for trauma nightmares and sleep disturbance in combat veterans with post-traumatic stress disorder. *Biol Psychiatry* 2007;61:928-34.
29. Raskind MA, Peskind ER, Kanter ED, et al. Reduction of nightmares and other PTSD symptoms in combat veterans by prazosin: a placebo-controlled study. *Am J Psychiatry* 2003;160:371-3.
30. Daly C, Doyle M, Radkind M, Raskind E, Daniels C. Clinical case series: the use of Prazosin for combat-related recurrent nightmares among Operation Iraqi Freedom combat veterans. *Mil Med* 2005;1706:513-5.
31. Peskind ER, Bonner LT, Hoff D, Raskind MA. Prazosin reduces trauma-related nightmares in older men with chronic posttraumatic stress disorder. *J Geriatr Psychiatry Neurol* 2003;16:165-71.
32. Raskind M, Dobie D, Kanter E, Petrie E, Thompson C, Peskind E. The alpha1- adrenergic antagonist prazosin ameliorates trauma nightmares in veterans with posttraumatic stress disorder: a report of 4 cases. *J Clin Psychiatry* 2000;61:129-33.
33. Taylor F, Raskind M. The alpha1-adrenergic atagonist prazosin improves sleep and nightmares in civilian trauma posttraumatic stress disorder. *J Clin Psychopharmacol* 2002;22:82-5.
34. Miyazaki S, Uchida S, Mukai J, et al. Clonidine effects on all night human sleep: opposite action of low- and medium-dose clonidine on human NREM-REM sleep proportion. *Psychiat Clin Neurosci* 2004;58:138-44.
35. Kinzie J, Leung P. Clonidine in Cambodian patients with posttraumatic stress disorder. *J Nerv Ment Dis* 1989;177:546-50.
36. Kinzie J, Sack R, Riley C. The polysomnographic effects of clonidine on sleep disorders in posttraumatic stress disorder: a pilot study with Cambodian patients. *J Nerv Ment Dis* 1994;182:585-7.
37. Warner M, Dorn M, Peasbody C. Survey on the usefulness of trazodone in patients with PTSD with insomnia or nightmares. *Pharmacopsychiatry* 2001;34:128-31.
38. Jakovljevic M, Sagud M, Mihaljevic-Peles A. Olanzapine in the treatment-resistant, combat-related PTSD - a series of case reports. *Acta Psychiatrica Scandinavica* 2003;107:394-6.
39. Richelson E. Receptor pharmacology of neuroleptics: relation to clinical effects. *J Clin Psychiatry* 1999;60(Suppl 10):5-14.
40. David D, De Faria L, Mellman TA. Adjunctive risperidone treatment and sleep symptoms in combat veterans with chronic PTSD. *Depress Anxiety* 2006;23:489-91.
41. Stanovic JK, James KA, Vandevere CA. The effectiveness of risperidone on acute stress symptoms in adult burn patients: a preliminary retrospective pilot study. *J Burn Care Rehabil* 2001;22:210-3.
42. Lambert MT. Aripiprazole in the management of post-traumatic stress disorder symptoms in returning Global War on Terrorism victims. *Int Clin Psychopharmacol* 2006;21:185-7.
43. Berlant J, van Kammen D. Open-label topiramate as primary or adjunctive therapy in chronic civilian posttraumatic stress disorder; a preliminary report. *J Clin Psychiatry* 2002;63:15-20.

44. Aerni A, Traber R, Hock C, et al. Low-dose cortisol for symptoms of posttraumatic stress disorder. *Am J Psychiatry* 2004;161:1488-90.
45. De Boer M, Op den Velde W, Falger PJR, Hovens JE, De Groen JHM, Van Duijn H. Fluvoxamine treatment for chronic PTSD: a pilot study. *Psychother Psychosom* 1992;57:158-63.
46. Neylan TC, Metzler TJ, Schoenfeld FB, et al. Fluvoxamine and sleep disturbances in posttraumatic stress disorder. *J Trauma Stress* 2001;14:461-67.
47. Ellingsen PA. Double-blind trial of triazolam 0.5 mg vs. nitrazepam 5 mg in outpatients. *Acta Psychiatr Scand* 1983;67:154-8.
48. Hogben GL, Cornfield RB. Treatment of traumatic war neurosis with phenelzine. *Arch Gen Psychiatry* 1981;38:440-5.
49. Lerer B, Bleich A, Kotler M, Garb R, Hertzberg M, Levin B. Posttraumatic stress disorder in Israeli combat veterans. Effect of phenelzine treatment. *Arch Gen Psychiatry* 1987;44:976-81.
50. http://www.pdr.net/druginformation/FDAMonographsInfo.aspx?MonographID = 1033
51. Hamner MB, Brodrick PS, Labbate LA. Gabapentin in PTSD: a retrospective, clinical series of adjunctive therapy. *Ann Clin Psychiatry* 2001;13:141-6.
52. Brophy M. Cyproheptadine for combat nightmares in post-traumatic stress disorder and dream anxiety disorder. *Mil Med* 1991;156:100-1.
53. Clark R, Canive J, Calais L, Qualls C, Brugger R, Vosburgh T. Cypoheptadine treatment of nightmares associated with posttraumatic stress disorder. *J Clin Psychopharmacol* 1999;19:486-7.
54. Gupta S, Popli A, Bathurst E, Hennig L, Droney T, Keller P. Efficacy of cyproheptadine for nightmares associated with posttraumatic stress disorder. *Compr Psychiatry* 1998;39:160-4.
55. Boehnlein JK, Kinzie JD, Ben R, Fleck J. One-year follow-up study of posttraumatic stress disorder among survivors of Cambodian concentration camps. *Am J Psychiatry* 1985;142:956-9.
56. Gillin JC, Smith-Vaniz A, Schnierow BJ, et al. An open-label, 12-week clinical and sleep EEG study of nefazodone in chronic combat-related posttraumatic stress disorder. *J Clin Psychiatry* 2001;62:789-96.
57. Neylan T, Lenoci M, Maglione M, et al. The effect of nefazodone on subjective and objective sleep quality in posttraumatic stress disorder. *J Clin Psychiatry* 2003;64:445-50.
58. Davidson J, Weisler RH, Malik ML, Connor KM. Treatment of posttraumatic stress disorder with nefazodone. *Int Clin Psychopharmacol* 1998;13:111-3.
59. www.drugs.com.
60. Stein DJ, Pedersen R, Rothbaum BO, et al. Onset of activity and time to response on individual CAPS-SX17 items in patients treated for post-traumatic stress disorder with venlafaxine ER: a pooled analysis. *Int J Neuropsychopharmacol* 2009;12:23-31.
61. Cates M, Bishop M, Davis L, Lowe J, Wooley T. Clonzaepam for treatment of sleep disturbances associated with combat-related posttraumatic stress disorder. *Ann Pharmacother* 2004;38:1395-9.
62. Spoormaker VI, Montgomery P. Disturbed sleep in post-traumatic stress disorder: secondary symptom or core feature? *Sleep Med Rev* 2008;12:169-84.
63. Bisson J, Andrew M. Psychological treatment of post-traumatic stress disorder (PTSD). *Cochrane Database Syst Rev* 2007;Jul 18:CD003388.
64. Bisson J, Ehlers A, Matthews R, Pilling S, Richards D, Turner S. Psychological treatments for chronic post-traumatic stress disorder. Systematic review and meta-analysis. *Br J Psychiatry* 2007;190:97-104.
65. Bishay N. Therapeutic manipulation of nightmares and the management of neuroses. *Br J Psychiatry* 1985;147:67-70.
66. Germain A, Shear MK, Hall M, Buysse DJ. Effects of a brief behavioral treatment for PTSD-related sleep disturbances: a pilot study. *Behav Res Ther* 2007;45:627-32.
67. Krakow V, Hollifield M, Johnston L, et al. Imagery rehearsal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder: a randomized controlled trial. *JAMA* 2001;286:584-8.
68. Krakow B, Kellner R, Neidhardt J, Pathak D, Lambert L. Imagery rehearsal treatment of chronic nightmares: with a thirty month follow-up. *J Behav Ther Exp Psychiatry* 1993;24:325-30.
69. Krakow B, Kellner R, Pathak D, Lambert L. Long term reduction of nightmares with imagery rehearsal treatment. *Behav Cogn Psychother* 1996;24:135-48.
70. Forbes D, Phelps A, Mc Hugh A, Debenham P, Hopwood M, Creamer M. Imagery rehearsal in the treatment of posttraumatic nightmares in Australian veterans with chronic combat-related PTSD: 12-month follow-up data. *J Trauma Stress* 2003;16:509-13.
71. Forbes D, Phelps A, Mc Hugh T. Treatment of combat-related nightmares using imagery rehearsal: a pilot study. *J Trauma Stress* 2001;14:433-43.
72. Germain A, Nielsen T. Impact of imagery rehearsal treatment on distressing dreams, psychological distress, and sleep parameters in nightmare patients. *Behav Sleep Med* 2003;1:140-54.
73. Kellner R, Neidhardt J, Krakow B, Pathak D. Changes in chronic nightmares after one session of desensitization or rehearsal instructions. *Am J Psychiatry* 1992;149:659-63.
74. Krakow B, Johnston L, Melendrez D, et al. An open-label trial of evidence-based cognitive behavior therapy for nightmares and insomnia in crime victims with PTSD. *Am J Psychiatry* 2001;158:2043-7.
75. Krakow B, Melendrez D, Johnston L, et al. Sleep Dynamic Therapy for Cerro Grande Fire evacuees with posstraumatic stress symptoms: a preliminary report. *J Clin Psychiatry* 2002;63:673-84.
76. Neidhardt EJ, Krakow B, Kellner R, Pathak D. The beneficial effects of one treatment session and recording of nightmares on chronic nightmare sufferers. *Sleep* 1992;15:470-3.
77. Krakow B, Kellner R, Pathak D, Lambert L. Imagery Reharsal Treatment for Chronic Nightmares. *Behav Res Ther* 1995;33:837-43.
78. Spoormaker VI, van den Bout J. Lucid dreaming treatment for nightmares: a pilot study. *Psychother Psychosom* 2006;75:389-94.
79. Zadra A, Pihl R. Lucid dreaming as a treatment for recurrent nightmares. *Psychother Psychosom* 1997;66:50-5.
80. Davis JL, Wright DC. Case series utilizing exposure, relaxation, and rescripting therapy: Impact on nightmares, sleep quality and psychological distress. *Behav Sleep Med* 2005;3:151-7.
81. Burgess M, Gill M, Marks I. Postal self-exposure treatment of recurrant nightmares. Randomised controlled trial. *Br J Psychiatry* 1998;172:257-62.
82. Grandi S, Fabbri S, Panattoni N, Gonnella E, Marks I. Self-exposure treatment of recurrent nightmares: waiting-list-controlled trial and 4-year follow-up. *Psychother Psychosom* 2006;75:384-88.
83. Miller WR, DiPilato M. Treatment of nightmares via relaxation and desensitization: a controlled evaluation. *J Consult Clin Psychol* 1983;51:870-7.
84. Celluci AJ, Lawrence PS. The efficacy of systematic desensitization in reducing nightmares. *J Behav Ther Exp Psychiatry* 1978;9:109-14.
85. Hauri PJ, Silber MH, Boeve BF. The treatment of parasomnias with hypnosis: a 5-year follow-up study. *J Clin Sleep Med* 2007;3:369-73.
86. Kingsbury SJ. Brief hypnotic treatment of repetitive nightmares. *Am J Clin Hypn* 1993;35:161-9.
87. Shapiro F. EMDR 12 years after its introduction: Past and future research. *J Clin Psychiatry* 2002;58:1-22.
88. Shapiro F, Maxfield L. Eye movement desensitization and reprocessing (EMDR): information processing in the treatment of trauma. *J Clin Psychiatry* 2002;58:933-46.
89. Raboni M, Tufik S, Suchecki D. Treatment of PTSD by eye movement desensitization reprocessing (EMDR) improves sleep quality, quality of life, and perception of stress. *Ann N Y Acad Sci* 2006;1071:508-13.
90. Silver S, Brooks A, Obenchain J. Treatment of Vietnam War veterans with PTSD: a comparison of eye movement desensitization and reprocessing, biofeedback, and relaxation training. *J Trauma Stress* 1995;8:337-42.
91. Igreja V, Kleijn WC, Schreuder BJN, Van Dijk JA, Verschuur M. Testimony method to ameliorate post-traumatic stress symptoms. *Br J Psychiatry* 2004;184:251-7.
92. Hendin H. Psychotherapy for Vietnam veterans with posttraumatic stress disorders. *Am J Psychother* 1983;37:86-99.

ACKNOWLEDGMENTS

The committee would like to thank Sharon Tracy, Ph.D., for her efforts in the development of this manuscript.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication May, 2010
Accepted for publication May, 2010
Address correspondence to: Sharon L. Tracy, Ph.D., American Academy of Sleep Medicine, 2510 North Frontage Road, Darien, IL 60561-1511; Tel: (630) 737-9700; Fax: (630) 737-9790; E-mail: stracy@aasmnet.org

DISCLOSURE STATEMENT

The Standards of Practice Committee members have indicated no financial conflicts of interest.

Appendix Table 1

Section	Intervention	Level (no. of studies)	References
4.1.1	Prazosin	1 (3)	27-29
		4 (4)	30-33
4.1.2	Clonidine	4 (2)	35, 36
4.1.3.1	Trazodone	4 (1)	37
4.1.3.2	Olanzapine	4 (1)	38
	Risperidone	4 (2)	40, 41
	Aripiprazole	4 (1)	42
4.1.3.3	Topiramate	4 (1)	43
4.1.3.4	Low-dose cortisol	4 (1)	44
4.1.3.5	Fluvoxamine	4 (2)	45, 46
4.1.3.6	Triazolam	2 (1)	47
	Nitrazepam		
4.1.3.7	Phenelzine	4 (2)	48, 49
4.1.3.8	Gabapentin	4 (1)	51
4.1.3.9	Cyproheptadine	4 (3)	52-54
4.1.3.10	Tricyclic antidepressants	4(1)	55
4.1.3.11	Nefazodone	4 (3)	56-58
4.1.4	Venlafaxine (negative results)	1 (1)	60
4.1.5	Clonazepam (sparse data)	2 (1)	61
4.2.1.1	IRT	1 (1)	67
		2 (1)	68
		3 (1)	69
		4 (7)	65, 70-75
4.2.1.2	Lucid Dreaming	3 (1)	78
		4 (1)	79
4.2.1.3	ERRT	4 (1)	80
4.2.1.4	Sleep Dynamic Therapy	4 (1)	75
4.2.1.5	Self Exposure Therapy	2 (1)	81
		3 (1)	82
4.2.1.6	Systematic Desensitization	1 (1)	83
		2 (1)	84
		4 (1)	73
4.2.2	Progressive Deep Muscle Relaxation Training	1 (1)	83
4.2.3	Hypnosis	4 (2)	85, 86
4.2.4	EMDR	4 (2)	89, 90
4.2.5	Testimony	4 (1)	91
4.2.6	Psychotherapy	4 (1)	92

Appendix Box 1

Cognitive Behavioral Therapy [CBT]: is a psychotherapeutic approach that focuses on distorted/dysfunctional thoughts, emotions, and behavior through a goal oriented, structured and time limited procedure. CBT is often used as an umbrella term for a number of psychological and behavioral techniques tailored to uncover, alter, and correct distortions of cognition and behavior in an individual. CBT includes Image Rehearsal Therapy; Systemic Desensitization; Lucid Dreaming Therapy; Sleep Dynamic Therapy; Exposure, Relaxation and Rescripting Therapy; and Self-exposure Therapy.

Imagery Rehearsal Therapy [IRT] (Recommended) Level A: is a modified CBT technique that utilizes recalling the nightmare, writing it down, changing the theme, story line, ending or any part of the dream to a more positive one, and rehearsing the rewritten dream scenario so that the patient can displace the unwanted ending when the dream recurs. IRT acts to inhibit the original nightmare, providing a cognitive shift that empirically refutes the original premise of the nightmare. This technique is practiced for 10-20 minutes per day while awake.

Lucid Dreaming Therapy (May be Considered) Level C: is a cognitive restructuring technique and a variant of IRT that allows one to alter the nightmare story line during the nightmare itself by realizing that one is dreaming or being "lucid" during the nightmare.

Exposure, Relaxation and Rescripting Therapy [ERRT] (May be Considered) Level C: is a specialized treatment modality targeting anxiety, which may manifest as physiological, behavioral and cognitive dysfunction. The treatment involves psychoeducation, sleep hygiene, and progressive muscle relaxation training. Exposure procedures such as writing out and rescripting the nightmares, homework assignments, problem solving, and coping strategies are intended to help deal with the nightmares. This form of treatment is similar to IRT except for type of exposure utilized.

Sleep Dynamic Therapy (May be Considered) Level C: is an integrated program combining standard clinical sleep medicine instructions including sleep quality and sleep hygiene with psychotherapeutic interventions using principles of cognitive behavioral therapy like stimulus control, IRT, etc.

Self-exposure Therapy (May be Considered) Level C: is a variant of CBT that utilizes a technique of "graded exposure." The patient is instructed to make a hierarchy list based of the severity of anxiety provoking events/ dreams. The patient is then instructed to move through the situations on the hierarchy at his or her own rate, starting with lowest anxiety situation on the list until the fear/anxiety has decreased. The exposure is done on a daily basis with documentation in a journal of his or her experiences.

Systematic Desensitization (Suggested) Level B: is a type of behavioral therapy that uses the principle of gradually exposing the patient to what he or she fears. This technique is also called "graduated exposure therapy." The patient is trained to cope and manage the stressors gradually before the patient is actually exposed to the feared object or situation.

Progressive Deep Muscle Relaxation [PDMR] (Suggested) Level B: involves tensing and releasing the muscles, one body part at a time, to bring about a feeling of physical relaxation and reduction in anxiety and stress.

Hypnosis or Hypnotherapy (May be Considered) Level C: is a trance-like state of mind. Hypnosis creates a state of deep relaxation which helps the mind to concentrate intensely on a specific thought, memory, feeling, or sensation without distractions and making the person open to suggestions that can be used to change certain thought or behavior.

Eye Movement Desensitization and Reprocessing [EMDR] (May be Considered) Level C: is a specialized treatment modality targeting anxiety, which may manifest as physiological, behavioral and cognitive dysfunction. The treatment involves psycho-education, sleep hygiene and progressive muscle relaxation training. Exposure procedures such as writing out and rescripting the nightmares, home work assignments, problem solving, and coping strategies are intended to help deal with the nightmares. This form of treatment is similar to IRT except for type of exposure utilized.

The Testimony Method (May be Considered) Level C: is a brief variant of a trauma exposure technique. Trauma survivors are invited to tell the story of their traumatic experiences and document them in a written format with the help of the therapist.

Individual Psychotherapy (No recommendation): refers to a treatment intervention between a patient and a therapist, who is usually a psychiatrist, psychologist or an individual with specialized training in psychotherapeutic techniques such as therapeutic alliance, psychoanalysis etc. The therapy may focus on issues that are current or in the past along with associated thoughts, experiences, behaviors, and interactions and their role in the patient's life.