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# *VA/Department of Defense 2010 Clinical Practice Guideline for Posttraumatic Stress Disorder*

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## VA/DOD CLINICAL PRACTICE GUIDELINES FOR PTSD (2010)

Presented by  
National Center for PTSD  
U.S. Department of Veterans Affairs

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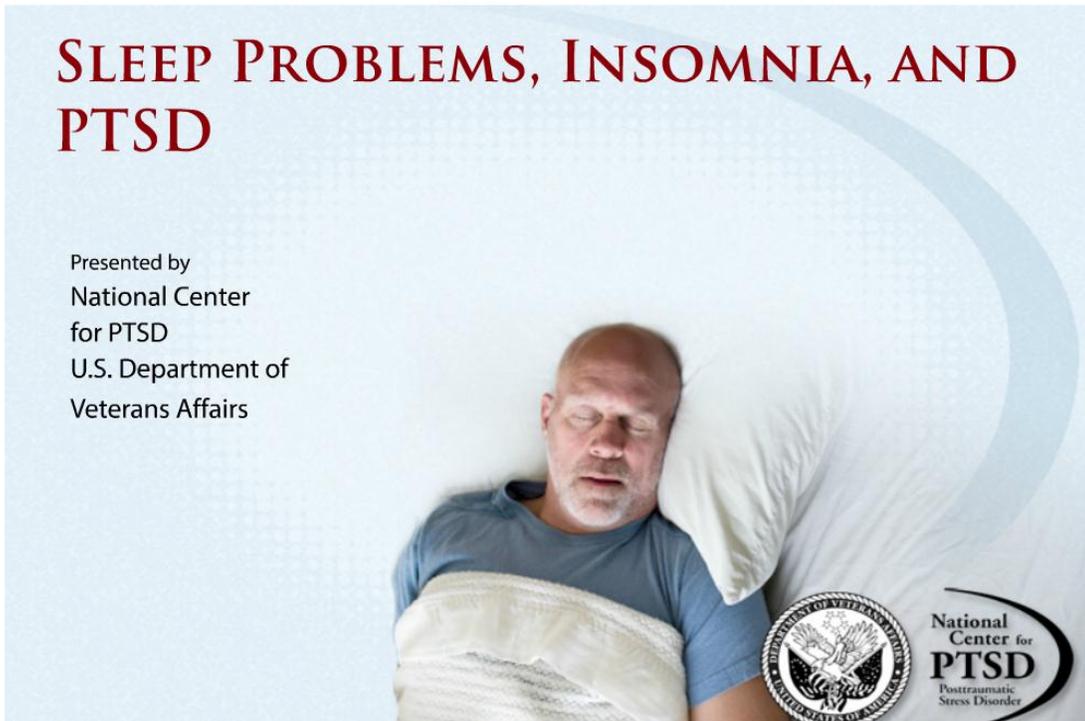
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# SLEEP PROBLEMS, INSOMNIA, AND PTSD

Presented by  
National Center  
for PTSD  
U.S. Department of  
Veterans Affairs



Thank you for tuning in to the VA/Department of Defense 2010 Clinical Practice Guideline for posttraumatic stress disorder education series. Today, we will be talking about sleep problems, insomnia and posttraumatic stress disorder.

## Meet the Presenters: Bruce Capehart, MD, MBA and Jason DeViva, Ph.D.

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I am your co-host, Dr. Bruce Capehart. I am a psychiatrist at the Durham VA Medical Center and the Medical Director for the OEF/OIF program. I also hold a faculty appointment at Duke University School of Medicine.

And, my name is Jason DeViva. I am a psychologist with the VA Connecticut Healthcare System. I work in the PTSD/Anxiety Treatment Program, and I also have faculty positions at the University of Connecticut School of Medicine and the Yale University School of Medicine.

# DISCLOSURE

- ▶ No financial relationships with any corporate entities in the pharmaceutical, biologic, diagnostic test, or medical device fields
- ▶ Dr. Capeheart: United States Patent Application 2010-0298305: Tizanidine for the Treatment of Posttraumatic Stress Disorder and Nightmares, November 25, 2010
  - Owned by the VA, Capehart listed as sole inventor
  - I have no commercial relationships associated with this patent
- ▶ Off-label use of medication will be discussed today

The disclosures I have to make before today's presentation are:

I have no financial relationships with any corporate entities with products or services that might be relevant to this presentation. I am named as an inventor on a patent application filed by the Department of Veterans Affairs, however, there are no known commercial relationships associated with this patent. And this presentation today will discuss off-label use of medication. And, as a reminder, off label use of medication is the use of prescription medication for which there is no approved indication by the US Food and Drug Administration.

### OBJECTIVES

1. Review the 2010 VA/DoD PTSD Clinical Practice Guideline recommendations on medical management of insomnia
2. Identify three comorbid conditions and three primary sleep disorders likely to affect sleep in PTSD populations
3. Describe the evidence base for three pharmacotherapies and three psychotherapies in the treatment of sleep problems related to PTSD
4. Describe a general approach to assessing and treating sleep problems associated with PTSD

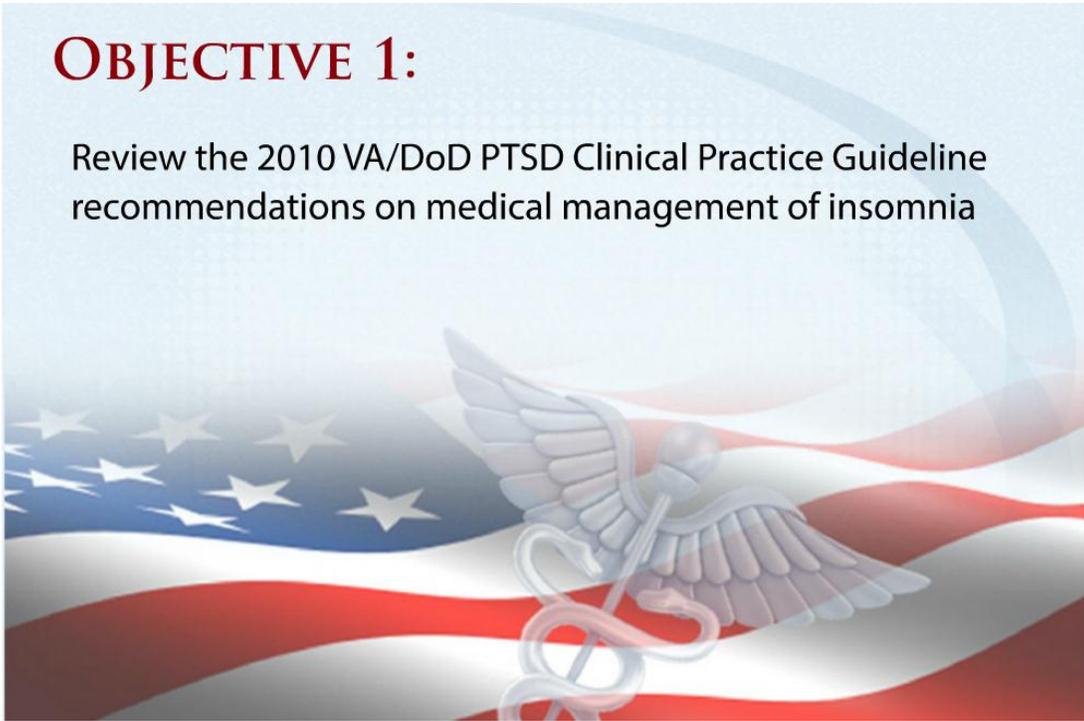
The education objectives for this talk are to review the 2010 VA/DoD PTSD Clinical Practice Guideline recommendations for medical management of insomnia, identify three comorbid conditions and three primary sleep disorders likely to affect sleep in Veterans with PTSD, describe the evidence base for three pharmacotherapies and three psychotherapies in the treatment of sleep problems related to PTSD and describe a general approach to assessing and treating sleep problems associated with PTSD.

**Objective 1: Review the 2010 VA/DoD PTSD Clinical Practice Guideline Recommendations for Managing Insomnia**

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**OBJECTIVE 1:**

Review the 2010 VA/DoD PTSD Clinical Practice Guideline recommendations on medical management of insomnia



Objective one: we will now review the 2010 VA/DoD PTSD Clinical Practice Guideline recommendations for managing insomnia.

## WHAT DOES THE VA/DoD CPG-PTSD RECOMMEND FOR INSOMNIA?

### ► Behavior / Lifestyle Changes

- Sleep hygiene
- Less caffeine
- Stop smoking
- Aerobic exercise

### ► Psychotherapy

### ► Medication: Initial & Middle Insomnia



So, what does the clinical practice guideline document recommend for insomnia? The first recommendation is to look for the simplest, easiest changes we can help our patients to make. This includes simple behavioral changes like reminders of sleep hygiene guidelines. These include guidelines such as: don't lay in bed for very long. Get out of bed and go somewhere else for a little while if you can't fall asleep. Don't nap during the day.

It is also very helpful to recommend to our patients that they cut back, if not eliminate, caffeine and absolutely eliminate caffeine in the afternoons and stop smoking. Smoking can lead to mild arousal, especially for that after dinner cigarette or that before going to bed cigarette, and stopping smoking can definitely make a difference in helping Veterans get to sleep.

And, finally, aerobic exercise can help. Aerobic exercise leaves people feeling a little bit more tired and less energetic and can help promote sleep at bedtime. The clinical practice guidelines also recommend psychotherapy for insomnia and PTSD. There are some recommendations for medication, which we will talk about in today's talk as well. And, finally today, we will also talk about medication recommendations for both initial and middle insomnia.

## BEFORE STARTING TREATMENT, MAKE A DIAGNOSIS

- ▶ PTSD and Insomnia discussions frequently move into treatment recommendations
- ▶ However, treatment must be matched with diagnosis
- ▶ We do not recommend treating all headaches with brain biopsy to find the presumed tumor, and we should not automatically treat insomnia with hypnotic medication.
- ▶ Consider what disorders might be present in a Veteran with PTSD and how they might interfere with sleep

When we talk about treating insomnia, I think the most important initial intervention is to make the correct diagnosis, because a different diagnosis will lead to a different treatment recommendation. And, just as we would never recommend treating all headaches with a brain biopsy to find a presumed brain tumor, we should never automatically treat insomnia with a hypnotic medication.

Instead, we should think about what conditions might be present in a Veteran with posttraumatic stress disorder or, for that matter, a civilian patient with posttraumatic stress disorder and how might these conditions interfere with sleep in a way that might confuse us to think that the sleep problem is only due to posttraumatic stress disorder, when really, a different intervention would be indicated.

## SLEEP & PTSD: SURVEYING THE LANDSCAPE

- ▶ Insomnia caused by PTSD
  - Initial (“I can’t fall asleep”)
  - Middle (“I wake up at night and can’t get back to sleep”)
  
- ▶ Insomnia caused by comorbid conditions
  - Substance Use Disorders (SUD)
  - Depression
  - Medical disorders
  - Primary sleep disorders



So, let’s begin by looking a little bit at sleep and posttraumatic stress disorder and quickly survey this landscape. I find it quite helpful to split insomnia into the initial insomnia, “I can’t fall asleep,” versus the middle insomnia, which is trouble staying asleep or trouble waking up at night.

I also think it is very helpful to look at insomnia that could be caused by comorbid conditions. And, several important conditions to think about are substance use disorders, major depression, comorbid medical disorders and primary sleep disorders.

## INSOMNIA IN PTSD

### ► Initial Insomnia

- Relationship to anxiety (hypervigilance, intrusive thoughts)
- Other aggravating factors (caffeine, nicotine, habits)
- Managed with behavior interventions, psychotherapy, and medications

### ► Middle Insomnia

- Relationship to anxiety (wake from nightmare)
- Managed with medications and psychotherapy

The insomnia in PTSD, as we look at initial insomnia, anxiety such as hypervigilance, or intrusive thoughts, reminiscing about the day, that can lead to initial insomnia with trouble falling asleep; when the patient will lay awake in bed and ruminate about what happened during the day. Or, be more alert, perhaps even get out of bed and need to repeatedly check the locks on the doors and windows in the house.

Initial insomnia can also be caused, or aggravated, by substances, such as caffeine or nicotine, and is usually best managed with behavioral interventions as well as treatments focused on the underlying PTSD.

Middle insomnia can be distinguished from initial insomnia typically by the presence of nightmares or bad dreams. And, sometimes, patients will awaken at night and report feeling as if they had a nightmare but they don't recall the nightmare. It is typically helpful that, I found, to treat those situations as the same. Even if the patient does not report a nightmare, just go ahead and make the assumption that a nightmare is probably occurring because the interventions tend to work fairly well.

**BEYOND THE ANXIETY, IS INSOMNIA BAD?**

- ▶ Medical and physical consequences
- ▶ The Heart and Soul Study showed PTSD associated with worse cardiovascular health
- ▶ Insomnia associated with:
  - Reduced slow wave sleep (Stage 3-4 NREM sleep)
  - Endocrine changes that stimulate daytime appetite
  - Insulin resistance
  - Weight gain
  - Greater risk for the metabolic syndrome, an important precursor to cardiovascular disease

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  - Endocrine changes that stimulate daytime appetite
  - Insulin resistance
  - Weight gain
  - Greater risk for the metabolic syndrome, an important precursor to cardiovascular disease
- ▶ PTSD reduces slow wave sleep

Likely implication: treating insomnia in PTSD may reduce the long-term risk of obesity, metabolic syndrome, and cardiovascular disease. The significance is very important given the high rates of smoking among combat veterans with PTSD. Cohen, 2009; Kobayashi, 2007; VanCauter, 2009

So, beyond patients feeling anxious, is insomnia like a bad thing, and is it just part of PTSD? Does it have any medical consequences beyond its effect on the posttraumatic stress disorder?

I think the answer is it absolutely does and, I think there is an obligation that we treat insomnia because of the physical impact of that. There is the Heart and Soul Study which looked at anxiety and cardiovascular health, and it showed a worsening effect of cardiovascular health related to anxiety.

One possible explanation for this could be that PTSD is known to reduce slow wave sleep. These are the deepest phases of the sleep cycle where some of the most physiologically restful sleep occurs. And, we know, from other published reports, that impaired slow wave sleep is associated with numerous changes in the endocrine system that can lead to insulin resistance and weight gain and a greater risk for the metabolic syndrome. And, when the metabolic syndrome occurs, patients tend to have poorly regulated blood sugar levels, higher than normal cholesterol levels, high blood pressure and a much greater risk for cardiovascular disease.

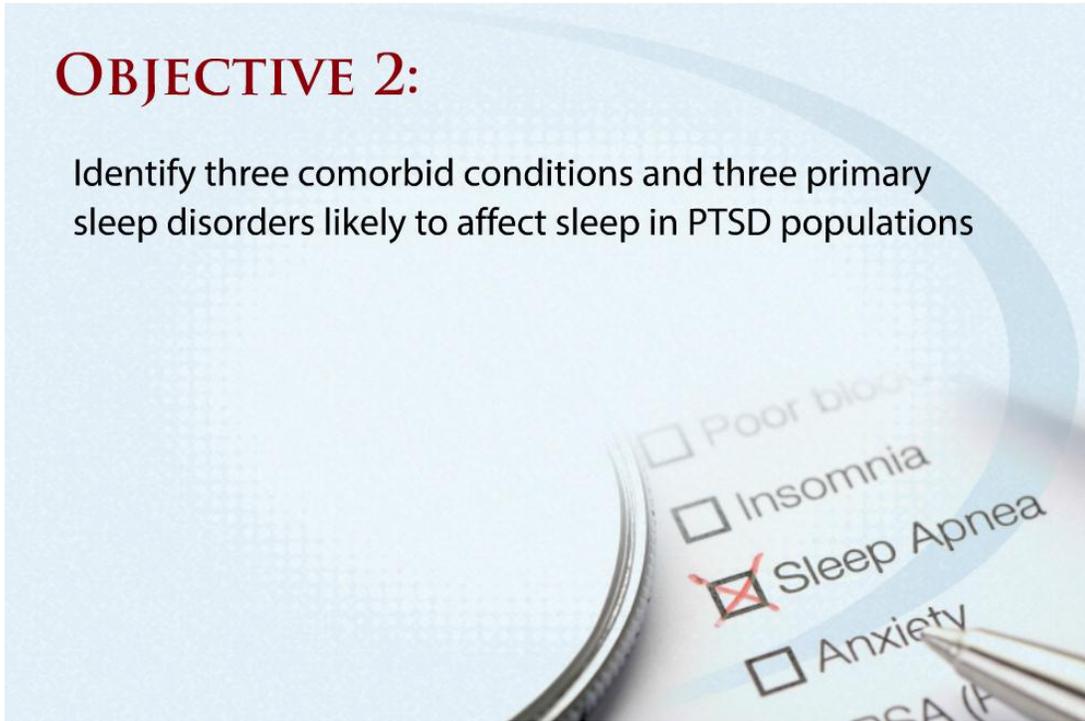
So, if we look at all that information together, I think there is a pretty good argument for stating that impaired sleep and posttraumatic stress disorder sets up risk factors for the metabolic syndrome which we know is a serious risk factor for cardiovascular disease.

## Objective 2: Identify Three Comorbid Conditions and Three Primary Sleep Disorders Likely to Affect Sleep in PTSD Populations

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### OBJECTIVE 2:

Identify three comorbid conditions and three primary sleep disorders likely to affect sleep in PTSD populations



So, now let's turn to objective two and identify three comorbid conditions and three primary sleep disorders likely to affect sleep in persons with PTSD.

## FIRST, CONDUCT A THOROUGH ASSESSMENT

- ▶ Consider non-PTSD causes of insomnia
- ▶ First, screen for substance use disorders and depression
  - Alcohol
  - Nicotine
  - Stimulants (Caffeine)
  - Major Depression
- ▶ Refer to the VA/DoD CPG on SUD at: [www.healthquality.va.gov](http://www.healthquality.va.gov) for the SUD and MDD guidelines and any of the other available CPG documents

So, the first step in this part of the evaluation of the patient is, conduct a thorough assessment and, as already mentioned on a previous slide, it is very important to consider disorders like substance use conditions and major depression as contributing to the patient's insomnia, and specific substances to look at here include alcohol, nicotine, stimulants – and remember caffeine is considered a stimulant – as well as major depression as a comorbid psychiatric issue.

If any of these conditions are present, either substance use disorder or major depression, refer to the VA/DoD Clinical Practice Guideline for that condition. Those are available at [www.healthquality.va.gov](http://www.healthquality.va.gov).

## SECOND, PRIMARY SLEEP DISORDERS

### ► Restless legs (RL)

- Prevalence: 2-5% of the population
- Irresistible urge to move the legs due to uncomfortable sensations
- Diagnosis: order a Polysomnogram (PSG; "sleep study")
- Treatment: iron supplements, dopaminergic agonists, benzodiazepines



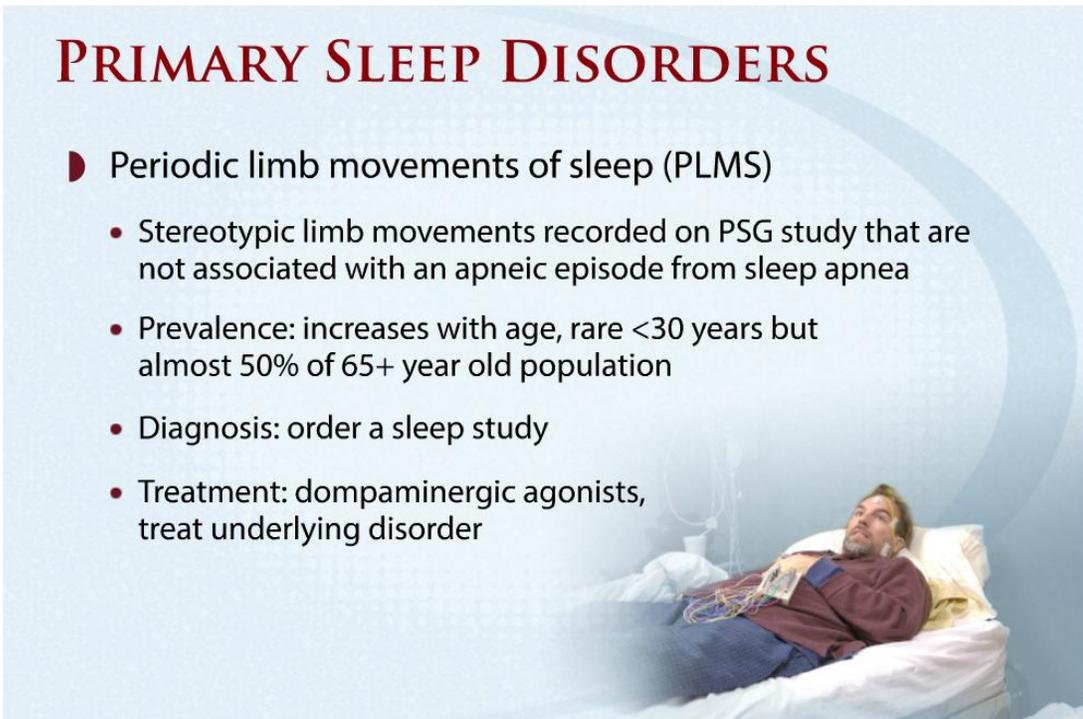
The second step in this assessment is to consider primary sleep disorders, and we'll talk about a few of the more common ones here. The first primary sleep disorder to look at is a condition called restless legs. Restless legs affects between 2-5% of the population in the United States, and it is typically characterized as an irresistible urge to move the legs due to an uncomfortable sensation in the leg, and this uncomfortable sensation is typically described by the patient as an uncomfortable pulling, or fullness sensation, in the leg that is only temporarily relieved by moving the leg. And, when it gets very bothersome, patients really cannot even sit still, and when they go to bed, they are unable to stop moving their legs in bed at night.

The best way to diagnose this is with a polysomnogram, also called a sleep study. Now, in many cases, it is possible to make a provisional diagnosis of restless legs just on the clinical history, and, if the history is fairly straightforward and consistent with restless legs, and there is not comorbid stimulant use that might better account for that, a trial of medication to treat restless legs may be indicated. Otherwise, the best option is to go ahead and order a polysomnogram – a sleep study – and or a consultation with a sleep medicine specialist.

The different treatments for restless legs can include iron supplements because low iron levels are very common in restless legs, dopaminergic agonist medication and, sometimes, long acting benzodiazepines.

## PRIMARY SLEEP DISORDERS

- ▶ Periodic limb movements of sleep (PLMS)
  - Stereotypic limb movements recorded on PSG study that are not associated with an apneic episode from sleep apnea
  - Prevalence: increases with age, rare <30 years but almost 50% of 65+ year old population
  - Diagnosis: order a sleep study
  - Treatment: dopaminergic agonists, treat underlying disorder



The next primary sleep disorder to consider is periodic limb movements of sleep. This disorder is usually characterized by stereotypic movements of limbs, and these are usually recorded on a polysomnogram study, and these movements are not associated with an episode where the patient stops breathing from sleep apnea, and these short episodes of stopping breathing is called apneic episodes.

The prevalence of periodic limb movements of sleep gradually increases with age. It's rather uncommon for persons under 30 years of age, but around half of the population has it by age 65. The diagnosis of periodic limb movements of sleep requires a polysomnogram and the treatment is similar to that for restless legs, with using dopaminergic agonist medication or treating the underlying disorder associated with the periodic limb movements of sleep.

## PRIMARY SLEEP DISORDERS

- ▶ **Obstructive sleep apnea (OSA)**
  - Intermittent obstruction of the upper airway that causes partial awakening to reposition the airway
  - Prevalence: up to 5-7% of adults
  - Usual complaints: loud snoring, intermittent failure to breathe
  - OSA may be attributable to snoring and not taken seriously by the patient
  - Diagnosis: order a sleep study
- ▶ **Treatment: continuous positive airway pressure (CPAP) delivered by machine via face mask**



The next primary sleep disorder to consider is obstructive sleep apnea, and, when we talk about primary sleep disorders, this is probably the only one with which most people are familiar. Sleep apnea is caused when there is an intermittent obstruction of the upper airway, and this causes a partial awakening in order to reposition the head and neck to open airway to breathe again.

It's thought that either low levels of oxygen, or rising levels of carbon dioxide, causes partial awaking from sleep that triggers the patient to move to reopen the airway. Obstructive sleep apnea is present in around 5-7% of the adult population, and it is often associated with being overweight and/or having a large neck or a short jaw.

Usual complaints from the patient or, more likely, the patient's bed partner, include loud snoring and sometimes an intermittent failure to take a breath. And, when those symptoms are reported, it is generally a good idea to order a sleep study because the diagnosis of sleep apnea without a sleep study is more or less impossible.

The sleep study is also very important to sleep apnea because of the treatment. The treatment for sleep apnea involves delivering continuous positive airway pressure, which is also called CPAP. CPAP is delivered by a mask that fits tightly over the face and requires a machine at the bedtime to deliver that positive pressure. The amount of pressure needs to be titrated to the individual patient, and for that, the sleep study is often required so we can then determine the exact amount of CPAP pressure required for that particular patient's sleep apnea.

So, now that we have talked about several different substance use, psychiatric and medical co-morbidities that can contribute to insomnia in posttraumatic stress disorder, let's turn our attention, now, to looking at a model of insomnia. And, for that I would like to turn this over to my colleague, Jason, so he can take us through that model and talk about some psychological interventions based on the model. Jason...

### MODEL OF INSOMNIA

- ▶ Sleep is more than just a symptom of PTSD
- ▶ Sleep can become its own problem
- ▶ Predisposing factors
  - Pre-existing tendencies that make disruption of sleep more likely
- ▶ Precipitating factors
  - Initial causes of acute sleep problems; may be of finite duration
- ▶ Perpetuating factors
  - Maladaptive responses to poor sleep that develop into patterns and continue to interfere with sleep (e.g., lying in bed “trying” to sleep)

Spielman et al., 1987

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  - Initial causes of acute sleep problems; may be of finite duration
- ▶ Perpetuating factors
  - Maladaptive responses to poor sleep that develop into patterns and continue to interfere with sleep (e.g., lying in bed “trying” to sleep)
- ▶ Conditioned arousal
  - Develops over time, interferes with sleep

Spielman et al., 1987

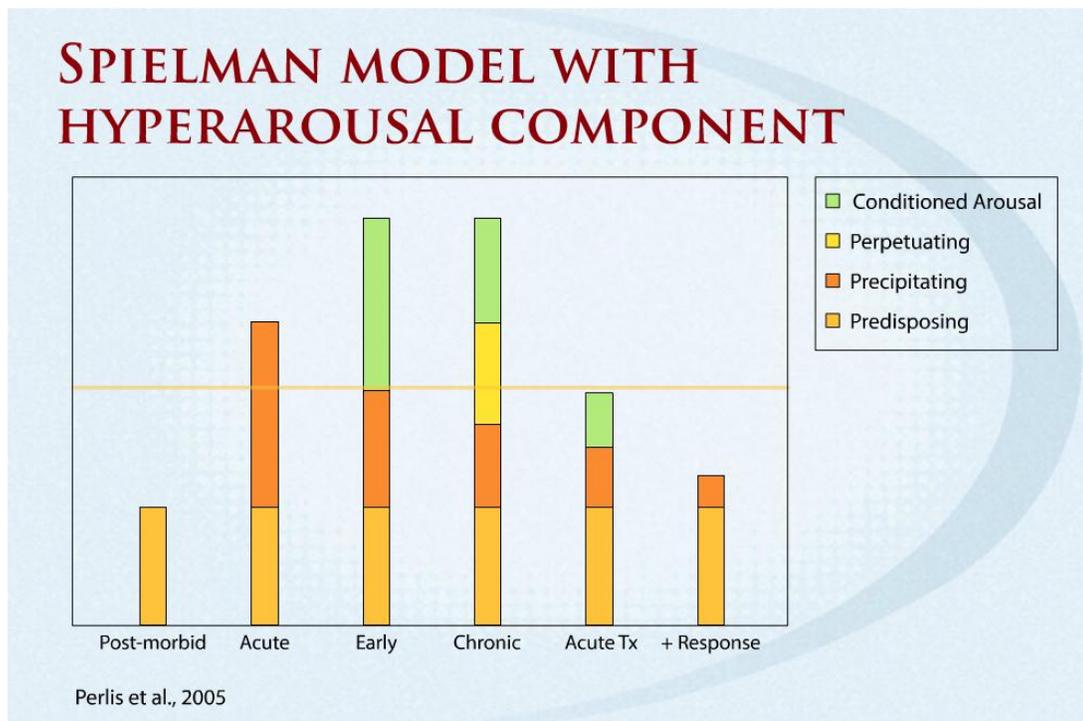
All right, thanks Bruce. Now one of the reasons Bruce has really been emphasizing the importance of thorough assessment, and assessment of comorbid conditions that can affect sleep, is that we have come to realize over time that sleep is more than just a symptom of posttraumatic stress disorder. It's more than just part of the posttraumatic spectrum of things that people experience. What we found is that sleep, in and of itself, can become its own condition; its own problem. And, that we really want to emphasize viewing sleep in this context, because that really allows you to come to a better conceptualization about how to treat the sleep of the patients you are seeing.

Now, the model of insomnia I am going to talk briefly about was advanced by Spielman in 1987, and Spielman looked at the different factors that can effect sleep. He broke them into three categories. The first are what we call predisposing factors, and these are the pre-existing tendencies each of us may have that make a disruption of sleep more or less likely. If you think of the stress diathesis model, the pre-disposing factors are sort of like the diathesis, or the predisposition we may have to developing sleep problems.

Now, the second category of factors Spielman talked about what he called precipitating factors, and these are the conditions that may interact with our predisposing factors to initiate an insomnia. So, examples of precipitants may include medical conditions that affect sleep. For example, I have a tendency to sprain my ankle which, is very unfortunate, and whenever I do that, it makes it really hard to be comfortable at night. So, that ankle sprain precipitates a short-term difficulty, for me, in both falling asleep and staying asleep.

Other precipitating factors might be significant worries/major life stressors. It is important to note that precipitating factors are often a finite duration. In other words, my ankle pain from a basic sprain lasts a week or two. However, what we know is that sleep problems often last for a pretty long period of time and tend not to remit on their own.

Spielman's model explains this through the development of what he call perpetuating factors. These are maladaptive responses to poor sleep that can develop into patterns that actually keep the poor sleep going. So, examples of perpetuating factors of insomnia can include trying to spend long periods of time in bed – and you can't see me making my air quotes – but “trying” to sleep. Often, when people lie in bed trying to sleep, it just tends to lead to more awake time in the bed, which makes bed more uncomfortable and actually lowers their chances of sleeping. Over time, what we have realized, is that people develop a conditioned arousal to the sleep setting. You have difficulty sleeping for a long time, sleep starts to become an anxiety provoking thing, and the bed becomes a place of struggle and strife.



Now, this graphic depiction does a pretty nice job of explaining the Spielman model visually, and I'll explain it. You'll notice at the bottom of each section there, there's a set level of predisposing factors, and those don't vary.

Now, up above in the sky, that floating line on this chart represents the threshold above which a person will develop a sleep problem. Now, in the second condition, right there, you can see that the combination of the predisposing factors, plus an additional precipitating set of factors, goes past that line, and once we pass that threshold, we will see an acute sleep disturbance.

We move to the third and fourth lines on there, and what we notice is that, even though the precipitants may have decreased to where they are below the threshold for sleep problems, a person can develop either sufficient perpetuating factors for a sleep problem or sufficient conditioned arousal to the sleep setting that the sleep problem will actually continue despite the fact that the precipitating factors have decreased.

Now, what we tend to see in treatment, or in a response to treatment, is what we see in the fifth and sixth sections of this little graph; that's that the precipitating factors that originally caused the sleep problem have decreased, and also, we have, through treatment, decreased those perpetuating factors, and we have also managed to decrease arousal. So, that the total amount of the factors that could cause a sleep problem have dropped below that threshold.

And, what we see, in a long term response for sleep treatment, is that we've removed the conditioned arousal, and we've taken care of the perpetuating factors, and the person is sleeping again. So, this is a visual way of explaining that model of insomnia.

## PTSD-RELATED PRECIPITATING FACTORS

- ▶ Safety-related beliefs and behaviors
- ▶ Nightmares
- ▶ Arousals from nightmares
- ▶ Fear/avoidance of sleep due to nightmares
- ▶ Conditioned arousal
- ▶ Conditioned anxiety from trauma in sleep context (i.e., traumas that occurred at night or in bed)

Now, if we adapt this model to talk a little bit about PTSD, and you think about the patients you tend to work with, there are a number of features of posttraumatic stress disorder that could precipitate sleep problems. For example, a lot of our patients engage in safety related kinds of behaviors at night that can interfere with sleep: keeping a lot of lights on, having a large dog in the room for safety – and large dogs don't tend to move around quietly.

Nightmares can also cause a significant amount of disturbance to sleep. On the one hand, patients will often wake up after a nightmare, and they will wake up at an arousal level that makes it very hard to go back to sleep. On the other hand, over time, a lot of PTSD patients will report that they are not always as inclined to sleep as the general population because they don't want to have nightmares. So patients may actually start avoiding sleep due to nightmares and, again, that can condition arousal to the sleep cycle.

Now, there is one other factor that some other researchers show is a little more common among patients with PTSD who sleep poorly and that's trauma in a sleep context. One thing we often overlook is that a lot of traumatic events, for example, child sexual abuse, a number of different kinds of combat situations, can occur in the sleep context, or at night.

A lot of combat Veterans will say that, "Bad things usually happened at night", and night was a time when they had to be on extra alert. If a person was sexually abused, or assaulted, in the bed, they may come to associate the bed with a place where harm can occur.

So, in very subtle ways, the actual traumatic events themselves can cause conditioned increase in anxiety in the sleep context that can interfere with sleep.

## Objective 3: Describe the Evidence Base for Three Psychotherapies and Three Pharmacotherapies in the Treatment of Sleep Problems Related to PTSD

### OBJECTIVE 3:

Describe the evidence base for three psychotherapies and three pharmacotherapies in the treatment of sleep problems related to PTSD

### TRAUMA-FOCUSED COGNITIVE BEHAVIORAL THERAPY (CBT)

- ▶ Exposure therapy, cognitive therapy, Eye Movement Desensitization and Reprocessing
- ▶ First-line PTSD treatment
- ▶ Effects on sleep usually not reported
- ▶ Studies indicate from 30-60% of participants show improvements in sleep
- ▶ For a sizable proportion of patients, sleep problems tend to persist despite remission of other PTSD symptoms

Belleville et al., 2011; Cooper & Clum, 1989; Galovski et al., 2009; Zayfert & DeViva, 2004

### Trauma-Focused Cognitive Behavioral Therapy (CBT)

So, now that we have set the stage for thinking about the sleep problems associated with PTSD from a larger context, I'm going to talk, now, about psychotherapy that can improve sleep associated with PTSD. The first category of treatment I am going to talk about is trauma-focused cognitive behavioral therapy, and by that I mean exposure therapy, cognitive therapy and also EMDR.

Now, trauma-focused CBT is generally recommended by most clinical practice guidelines as a first-line PTSD treatment. When we look at clinical trials that have examined CBT for PTSD, we find that the effects on sleep usually aren't reported. However, in the few studies that do report the effects of trauma focused CBT on sleep, they generally indicate that anywhere from 30-60% of participants do show improvements in sleep solely as a result of having received, for example, exposure therapy, Cognitive Processing Therapy. So, what we know is that even though they don't contain any interventions specifically targeting sleep, trauma-focused cognitive behavioral therapies do have a tendency to improve sleep in patients that complete and respond to them.

Now, this is probably because these treatments are addressing some of the issues that we described, on an earlier slide, as being precipitating factors that can impact sleep in the context of PTSD. So, for some patients, for example, decreasing nightmares and decreasing overall arousal is going to get rid of some of the overall barriers of sleep – some of those precipitants – and they are going to sleep better.

However, it is important to note, that for a sizable proportion of patients, sleep problems do persist despite remission of other PTSD symptoms. Some studies have shown that disturbed sleep is actually one of the more common symptoms to persist after response to cognitive behavioral therapy for PTSD.

## PRACTICE GUIDELINE RECOMMENDATIONS

- ▶ 2008 American Academy of Sleep Medicine guidelines recommend use of CBTI alone and recommend that CBTI supplement pharmacotherapy
- ▶ VA/DoD guidelines recommend use of CBTI with PTSD patients
- ▶ 2008 Expert Panel on Sleep Disturbance and Combat Trauma described it as a “promising” intervention for PTSD-related sleep difficulties

Now, related to cognitive behavioral therapy for PTSD is cognitive behavioral therapy for insomnia, and CBT for insomnia is an evidence-based, mostly behavioral therapy, that is associated with significant improvements in sleep.

Now, CBT for insomnia is generally delivered in the larger context of assessment for many other factors that affect sleep, such as, some of the primary sleep disorders that Bruce spoke about earlier as well as disorders of the circadian rhythm and other conditions that can affect sleep.

CBT for insomnia is a fairly large umbrella that tends to comprise a number of components. Some of the ingredients of CBT for insomnia are stimulus control, which is an intervention that looks at really strengthening the association between bed and other sleep triggers and sleep; sleep restriction, which involves shrinking a window during which a patient can sleep to try and encourage their sleep to occur in a more continuous kind of a chunk; sleep hygiene interventions, which are very common.

A lot of folks are familiar with sleep hygiene: they involve improving both the internal and external sleep environments to take away some of the obstacles to sleep. There is also cognitive restructuring, which is really classic Aaron Beck style cognitive restructuring but focused on beliefs that may interfere with sleep. And, also, progressive muscle relaxation is often included in CBT for insomnia interventions. Again, the idea there is to decrease arousal in order to facilitate sleep.

## EFFICACY

- ▶ Strong support for stimulus control, sleep restriction, and combined approaches in treating both primary and secondary insomnias; changes are durable
- ▶ Equal or superior to pharmacotherapy after 8 weeks of treatment, more effective in long-term
- ▶ No one has ever gotten addicted to cognitive-behavioral therapy
  - Persons with anxiety disorders, including PTSD, are at higher risk for substance use conditions
- ▶ Consider medical interventions if psychotherapy does not work, is not available, or sleep problem is very significant

And, as I mentioned, there is very strong evidence for the efficacy for CBT for insomnia in treating poor sleep. What we know is that the strong support for stimulus control and sleep restriction as mono-therapies, there is also significant support for combining those approaches in treating both primary and secondary insomnias.

What we know is that, in the short term, to about eight weeks of treatment, CBT for insomnia is equal, or superior, to pharmacotherapy in terms of its effects, and I think the real key to the usefulness of this treatment is that the changes are durable. CBT for insomnia tends to be effective in the long term, and its effects tend to persist.

The third point on this slide is something that I think is very important. I know it is to me as a medical provider. To my knowledge, no one has ever gotten addicted to cognitive behavioral therapy for insomnia. So, unlike medications, which can sometimes difficult to taper down and get a patient off of, usually, therapy's a pretty easy thing to end.

Jason, if I can make a point on this slide as well, I'd like to highlight your comment about addictions and cognitive behavior therapy. We know persons with anxiety disorders are at much greater risk to develop substance use conditions, which is yet another reason to recommend psychotherapy over potentially habit forming medications.

Psychotherapy alone can be extremely helpful for mild to moderate sleep problems and often curative by itself. However, for those occasions when psychotherapy either doesn't work, may not be available, or if the sleep problem is especially significant, it's useful to consider what kind of medical interventions can be done to help patients with their sleep difficulties.

## PRACTICE GUIDELINE RECOMMENDATIONS

- ▶ 2008 American Academy of Sleep Medicine guidelines recommend use of CBTI alone and recommend that CBTI supplement pharmacotherapy
- ▶ VA/DoD guidelines recommend use of CBTI with PTSD patients
- ▶ 2008 Expert Panel on Sleep Disturbance and Combat Trauma described it as a “promising” intervention for PTSD-related sleep difficulties

Now, because of the strong evidence of the efficacy of CBTI for insomnia, a number of organizations have recommended its use. For example, the 2008 American Academy of Sleep Medicine Guidelines recommend the use of CBT for insomnia – which I have there on the slide CBTI – alone in the treatment of insomnia as a first line treatment.

They also recommend that CBTI be used to supplement pharmacotherapy in the treatment of insomnia. Our most recent Veterans Affairs and Department of Defense Guidelines recommend the use of CBTI with PTSD patients. And, in 2008, an expert panel on sleep disturbances associated with combat trauma described CBTI as a promising intervention for PTSD related sleep difficulties.

So, given the evidence with insomnia in general, a number of organizations have recommended the use of CBTI with PTSD populations.

## EFFICACY WITH PTSD SAMPLES

- ▶ DeViva et al. (2004) found that a brief 5-session protocol improved sleep in a small sample after CBT for PTSD
- ▶ Several studies of combined CBTI and psychotherapy for nightmares found improvements in sleep
- ▶ CBTI is generally recommended in the treatment of insomnias related to other conditions



There is some evidence of efficacy for CBTI with PTSD samples. I, and some colleagues, found that a brief five-session CBT for insomnia protocol improves sleep in a small sample of patients who had already completed CBT for PTSD. These were patients who had already completed, and responded to, trauma-focused cognitive behavioral therapy, but they were still reporting sleep problems. And, we found that a brief CBTI intervention was associated with improvements in sleep.

There have also been several studies combining CBT for insomnia with psychotherapy for nightmares, and we're actually going to talk about psychotherapy for nightmares on the next slide, and these studies found that the combined interventions were associated with improvements in sleep. And, one thing we know from the general insomnia treatment literature, is that CBTI is generally effective in the treatment of insomnias that are related to other conditions, so even if an insomnia or sleep problem is caused by another condition, that sleep problem will still respond to CBT for insomnia.

## VA CBTI ROLLOUT

- ▶ Began in early 2011
- ▶ Goal is to train VA staff across the country in CBTI
- ▶ Modifications were put in place to address sleep factors specific to PTSD
  - 2008 Expert Panel on Sleep Disturbance and Combat Trauma also suggested modifications



Now, because of the strong evidence supporting the use of CBT for insomnia, the VA began a large scale dissemination project, or what we call a rollout of CBT for insomnia, in early 2011. The goal of this rollout is to train VA staff across the country in CBT for insomnia.

However, given that the training is taking place within a VA, the training curriculum included modifications to CBT for insomnia that were put in place to address some of the sleep factors specific to PTSD. And, this is actually consistent with recommendations from that 2008 expert panel on sleep disturbance in combat trauma. They had also suggested certain modifications to the CBTI protocol for PTSD specific factors.

## MODIFICATIONS TO CBTI

- ▶ Some trauma-related “precipitants” may have to be resolved to facilitate improvements in sleep
- ▶ To a degree, CBTI can be modified to do this
  - Assessing/decreasing arousal
  - Assessing/decreasing nighttime vigilance
  - Assessing for trauma in sleep context
- ▶ When do “modifications” become trauma-focused CBT?



Now, some other modifications that were recommended included assessing, and decreasing, patients overall arousal, as well as looking at the level of vigilance they have at night, and working with the patient to try and decrease any vigilance behaviors that may interfere with sleep. It's also recommended that providers assess for the history of trauma in a sleep context.

Now, it's important to note that first bullet point on there, that some trauma related precipitating factors may have to be resolved in order to facilitate improvements in sleep. And, that's why the VA's CBT for insomnia protocol includes modifications that will address those factors in order to make sleep more likely.

Now, one thing to consider, as you look at the patient in front of you in your office, is the question of when these modifications to the CBT for insomnia protocol actually become trauma-focused cognitive behavioral therapy. In other words, if you are trying to, say, decrease a person's nightmares, or decrease their level of vigilance or safety behaviors at night, is there a point where you are doing so much work to address those precipitating factors that you're actually doing a cognitive therapy or an exposure therapy? It's an important question to consider when you're planning what treatment am I going to start with the patient sitting in my office.

### IMAGERY REHEARSAL FOR NIGHTMARES

- ▶ Goal is to decrease frequency of nightmares
- ▶ Not specifically designed for treatment of trauma-related nightmares
- ▶ Described as “exposure-based”
- ▶ Patient chooses a repetitive, distressing nightmare
- ▶ Patient changes some detail of the nightmare and rewrites the nightmare with the change in it
- ▶ Patient rehearses the new version regularly

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- ▶ Patient rehearses the new version regularly
- ▶ Instructions vary widely

Now, the third treatment I’m going to talk about is imagery rehearsal for nightmares. Now, the goal of imagery rehearsal is to decrease the frequency of nightmares. Interestingly, imagery rehearsal was not originally designed for the treatment of trauma related nightmares. It was actually originally developed to treat nightmare disorder. Imagery rehearsal has been described as exposure-based. It’s not explicitly called an exposure therapy by a lot of people, but some folks do think there are exposure components to it. We’ll talk a little bit more about this in a few minutes.

Though instructions for imagery rehearsal vary pretty widely, there are some basic components. First, the patient chooses a repetitive distressing nightmare and writes it down, in all the detail they can. Second step is the patient changes some detail of that nightmare and then rewrites the nightmare with the change in it; and then the third step is the patient rehearses the new version of that nightmare regularly.

Now, the instructions for imagery rehearsal protocols vary widely. For example, some protocols suggest that the patient change anything in the dream and give no more instruction than that. Other protocols actually try and determine whether there is a theme to the dream, and then suggest that the patient change something related to that theme, a change that may resolve that theme.

So, if I’m having dreams where I am helpless, I have a recurring dream where I can’t do something, I may be instructed to make a change in that dream where I am able to do something; a change that resolves that helplessness. But, again, if you read a number of papers documenting some of the trials, some of the research on imagery rehearsal, you’ll notice pretty quickly that the instructions in the specific protocols vary pretty widely.

## POSSIBLE MECHANISMS OF CHANGE

- ▶ Most common explanation is that the procedure increases mastery and control
- ▶ Exposure?
  - Hard for there not to be exposure
  - One study found desensitization as effective as imagery rehearsal
- ▶ Cognitive restructuring?
  - Some protocols encourage positive changes and work on themes
  - Similar to imagery re-scripting and reprocessing treatments for trauma-related intrusive memories

Kellner et al., 1992

Now, there's some disagreement, as I mentioned earlier, when I was talking about the idea of exposure, about the exact mechanisms of change in imagery rehearsal. The most common explanation is that imagery rehearsal increases mastery over the nightmare, as well as a sense of control over the nightmare.

So, in rehearsing it over and over, patients feel a little bit more control over the dream experience and that increases their mastery. Though some people say that imagery rehearsal is not an exposure therapy, a lot of other folks find it really hard to believe that there is not exposure happening in there. In other words, in just writing it down and reading it, there has to be some exposure to the original dream content.

And historically, one study did find that simple desensitization to a nightmare, in other words, just reading over the account of the nightmare, was as effective as imagery rehearsal. So, that tells us that exposure, at least is potentially useful in the treatment of nightmares, regardless of how large or small a part it plays in the imagery rehearsal process. There's also the possibility that the imagery rehearsal is a different way of achieving cognitive restructuring of themes related to the nightmare.

As I noted earlier, some protocols look at themes occurring in nightmares and encourage making positive changes to the nightmares that resolve those themes. This is similar to cognitive restructuring. It's also similar to the imagery re-scripting, which is a treatment that uses imagery, and the changing of images, to work with trauma-related intrusive memories. So, it's also possible there is a cognitive restructuring, or information processing, component to imagery rehearsal that helps facilitate change.

### EFFICACY OF IMAGERY REHEARSAL

- ▶ Efficacious with participants with nightmare disorder
- ▶ Several studies have found that imagery rehearsal is associated with decreased frequency and intensity of dreams, decreased levels of PTSD symptoms, and improved sleep
- ▶ However:
  - Protocols vary in length and instructions.
  - Studies are generally minimally controlled
  - Most symptom measures are still above criteria for problematic at treatment completion.

Cook et al., 2010

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- ▶ However:
  - Protocols vary in length and instructions.
  - Studies are generally minimally controlled
  - Most symptom measures are still above criteria for problematic at treatment completion.
- ▶ No effects for imagery rehearsal on nightmares, sleep, or PTSD symptoms

Cook et al., 2010

Now, there are number of studies that support the efficacy of imagery rehearsal therapies with participants with nightmare disorder. Several studies have also found that imagery rehearsal is associated with decreased frequency, and intensity, of dreams in patients with PTSD or a history of trauma, as well as decreased levels of PTSD symptoms and improved sleep.

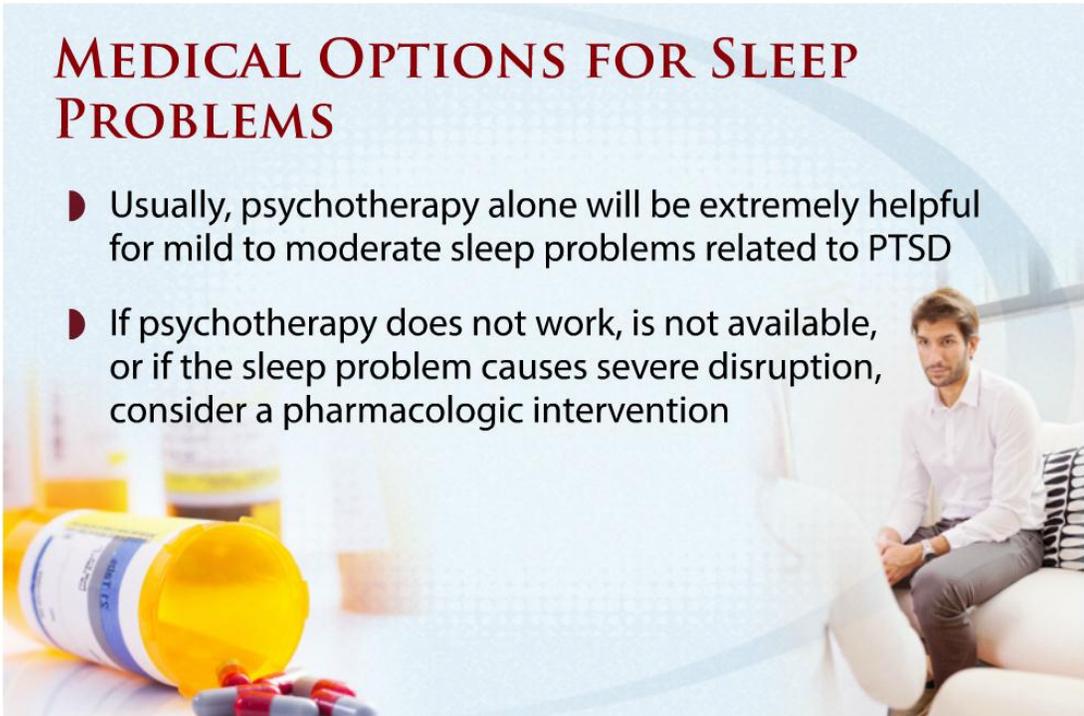
So, these seem like very promising interventions in that, not only do they decrease nightmares, they also appear to have a beneficial effect on PTSD symptoms in general, and also on sleep. However, as I noted earlier, there's a lot of variability in imagery rehearsal protocols; they vary in their length, they vary in the instructions given, and a lot of the studies we have are pretty minimally controlled.

When you also look at the outcomes for most of the studies, though there are significant decreases in a lot of symptoms, many symptom measures still remain above the criteria for classification as that symptom being problematic. So, in other words, certain symptom scores are still above significant levels even though they've decreased quite a bit.

And, in probably the best controlled study to date of imagery rehearsal, Joan Cook, and colleagues, found it imagery rehearsal had no effect at all on nightmares, sleep, or PTSD symptoms in a large sample of combat Veterans. So, imagery rehearsal, at this point, is a promising intervention, but there's still some questions about the mechanisms of treatment and also about its overall efficacy with PTSD patients.

## MEDICAL OPTIONS FOR SLEEP PROBLEMS

- Usually, psychotherapy alone will be extremely helpful for mild to moderate sleep problems related to PTSD
- If psychotherapy does not work, is not available, or if the sleep problem causes severe disruption, consider a pharmacologic intervention



Given the literature we have now, the evidence based on CBT for insomnia, as well as imagery rehearsal for nightmares, trauma-focused cognitive behavioral therapy, generally, we think psychotherapy alone is going to be extremely helpful for mild to moderate sleep problems associated with PTSD. However, what we know is that not everyone has access to these psychotherapies. Though, organizations like the VA and the Department of Defense are doing a great job in really disseminating, on a very large basis, trauma-focused cognitive behavioral therapies, CBT for insomnia, they are not always available.

Also, there may be instances where sleep problems are causing very severe disruption to a person's day time functioning, and, in these contexts, we think it may be wise for a provider to consider pharmacological interventions for treating insomnia. And, right now I'm going to turn it over to Bruce to go over some of the common pharmacological interventions that can be helpful for treating sleep problems in patients with PTSD. Go ahead Bruce.

## PHARMACOLOGIC CHOICES FOR INITIAL INSOMNIA

### ► Antidepressants

- Trazodone (alpha-1 blockade and possible orthostasis, especially when given with prazosin)
- Mirtazapine (usually associated with weight gain)
- Tricyclic antidepressants (anticholinergic effects upon bowel and bladder function)



Thanks, Jason. I would be glad to talk about some medication choices to help out with initial insomnia. I think some of the best medication choices we have for initial insomnia are the antidepressants; particularly Trazodone and Mirtazapine. Trazodone has a very long history of being used for treating sleep problems associated with PTSD and, I can remember in my training as a resident in the early 1990's, where we would frequently use Trazodone, and it is still commonly prescribed for this purpose today.

Mirtazapine is another antidepressant that has some very highly sedating properties as a side effect. And, while for many patients this can be an unfortunate side effect, for the patient with posttraumatic stress disorder and significant initial insomnia, it can actually be a helpful side effect.

And, a third consideration for antidepressants are the tricyclic antidepressants, particularly Amitriptyline. This medication can be most useful if the patient with PTSD also has a comorbid condition that would respond to a low dose of a tricyclic antidepressant. And two common conditions that might respond to tricyclic antidepressant include preventing migraine headaches and treating neuropathic pain, such as, the pain caused by longstanding diabetes.

Each of these three medications: Trazodone, Mirtazapine, and the tricyclic antidepressants also have side effects, so, as with any medication, it is important to consider the risk/benefit profile for that particular medication. Trazodone, in some persons, particularly the elderly, can cause some mild lowering of blood pressure, and it's important to remind patients of that ahead of time.

Mirtazapine may not be a good choice for a patient who already has diabetes or is overweight, because most patients gain around 10lbs with Mirtazapine. And, the tricyclic antidepressants can have prominent anticholinergic effects that can lead to mild constipation, or urinary retention, with the latter problem being more prominent among elderly men.

## PHARMACOLOGIC CHOICES FOR INITIAL INSOMNIA

- ▶ Antihistamines
  - Diphenhydramine, Hydroxyzine
- ▶ Every one of the medications for sleep (including benzodiazepines and the related “z-drugs”) have adverse effects on cognition

As a general rule, the best initial medication will be trazodone. It has the most favorable risk-benefit profile of these choices.

After the antidepressants, the antihistamine medications can also be helpful for helping patients control initial insomnia. Two of the antihistamines that are commonly used include Diphenhydramine and Hydroxyzine. Diphenhydramine is available as an over the counter medication, and Hydroxyzine is a prescription strength antihistamine that is even more sedating.

It's important to also think about comorbid conditions that might affect cognition because all of the antihistamines and antidepressants used for sleep, and, for that matter, all of the benzodiazepines and related drugs, like Zolpidem, have adverse effects on cognition, particularly with short term memory. And, again, those considerations need to enter into the discussion with your patient about what medication has the best risk/benefit profile.

As a general rule, however, the best initial choice for treating initial insomnia is Trazodone. Trazodone, typically, works out to have the most favorable risk/benefit profile of all of the medication choices for treating initial insomnia.

## WHAT NOT TO USE

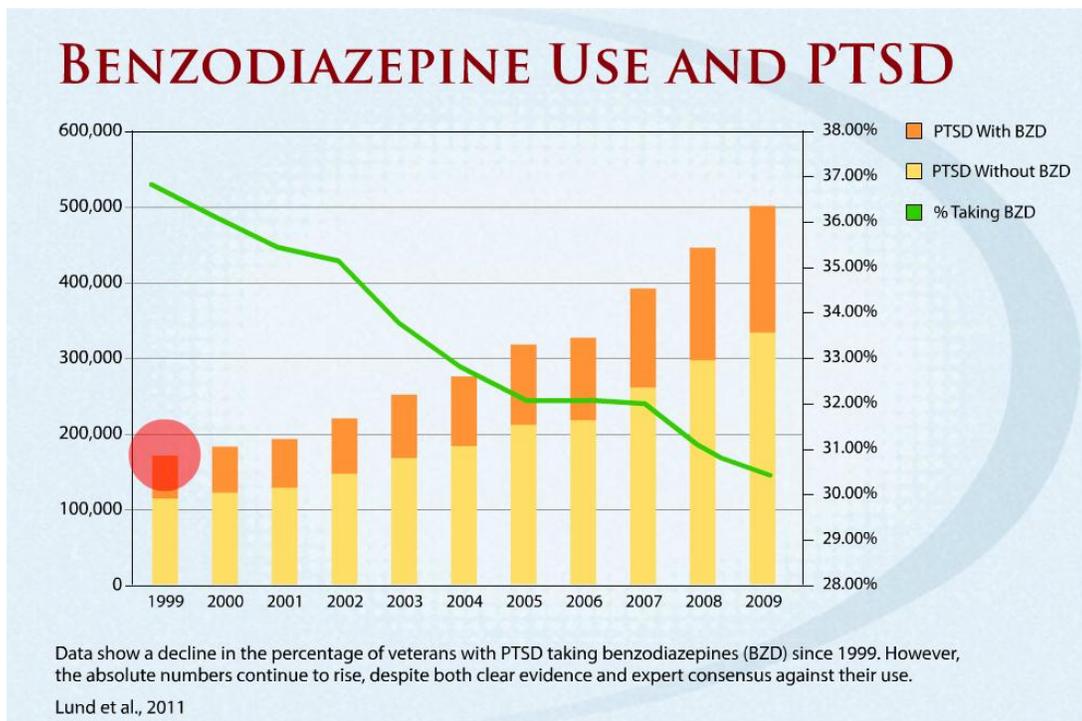
- ▶ Benzodiazepines are not helpful for PTSD
- ▶ Atypical antipsychotic medications carry an unfavorable risk to benefit ratio
- ▶ Benzodiazepines and similar medications (e.g. “z-drugs”) may be prescribed for short-term use
  - Short-term is defined as days to weeks
  - All sleep medications should be taken only 3-5 nights per week
- ▶ Some primary sleep disorders may require benzodiazepines
  - Periodic Leg Movement Syndrome or REM-Behavior Disorder
  - Consult with the sleep medicine clinic to discuss further

So, just as we talk about what medications are recommended for use, it's also helpful to talk about what medications are really not recommended for use. And, leading the pack in terms of medications that are not recommended for use in posttraumatic stress disorder, are the benzodiazepines. Benzodiazepines are not helpful for treating posttraumatic stress disorder, and when patients with PTSD are started on one of these medications, it can be very difficult to get them off of this medication.

Similarly, the atypical antipsychotic medications have an unfavorable risk to benefit ratio. While some of these medications are highly sedating, and can help patients fall asleep, they typically don't cause sedation any more or any less than Trazodone or one of the antihistamines, and the atypical antipsychotics carry a risk of metabolic syndrome.

In some cases, the benzodiazepines may be prescribed for short-term use, with short-term being defined here as being days to weeks. And, the sleep medication should be taken only on three to five nights per week. As a general rule, it is not recommended to give sleep medications seven nights per week.

Sometimes, a patient with a primary sleep disorder may require a Benzodiazepine. This may occur with one of the leg movement disorders, or another sleep disorder called REM behavior disorder. And, if a benzodiazepine is recommended for a sleep disorder, it is a good idea to consult with the sleep medicine specialist to see if there any non-benzodiazepine alternatives that could be tried first.



This slide shows a graph of benzodiazepine use in the VA health care system in posttraumatic stress disorder. This slide is taken from Lund, and coauthors, from a paper and journal of clinical psychiatry. What the data on this slide show are how many Veterans within the VA were diagnosed with posttraumatic stress disorder, and how many of them were taking benzodiazepines at the same time, and the data run from 1999 to 2009.

Now the good news from this slide, it shows that the percent of all Veterans diagnosed with PTSD receiving a benzodiazepine declined from little bit over 36% to just a little bit under 31%. That's a six percentage point drop over ten years, which is outstanding, and I think reflects the influence of clinical practice guidelines on the VA health care system.

On the other hand, because we're treating so many more Veterans now than we have past, the number of Veterans of PTSD was a little bit under 200,000 in 1999, and it's around 500,000 by 2009, the absolute number of Veterans receiving benzodiazepine has, unfortunately, increased.

So, while we are doing things well in the VA, and things are moving in the right direction, it's important to be continuously aware of benzodiazepine use and to make sure that we're treating PTSD properly, and we're not treating insomnia with the wrong medication.

## TREATING NIGHTMARES

- ▶ First, try selective serotonin reuptake inhibitor (SSRI)/ serotonin norepinephrine reuptake inhibitor (SNRI) for PTSD
- ▶ Persisting nightmares may respond to Prazosin, an antihypertensive medication that reduces adrenergic activity by blocking the alpha-1 receptor
- ▶ Two good RCTs demonstrated efficacy in reducing combat-related PTSD nightmares
- ▶ Coordinate care with the primary care physician to avoid excessive lowering of blood pressure

Raskind 2007, 2003

Nightmares are one of the most common sleep complaints from patients with posttraumatic stress disorder, and when I think about treating nightmares in PTSD, my first line intervention with medication is to make sure the patient is taking an SSRI or SNRI antidepressant. These antidepressants, such as Sertraline, Paroxetine, and Venlafaxine, are first line recommendations for PTSD from the clinical practice guidelines, and they work well. As these antidepressants reduce the core symptoms of PTSD, and lower anxiety, the patient will not only feel better during the day, the frequency, and the extent, of nightmares at night should go down, as should initial insomnia.

Now, for the patients who are taking an antidepressant and continue to have problems with nightmares, adding a medication called Prazosin is an outstanding next step. Prazosin is anti-hypertensive medication that reduces adrenergic activity in the brain, and it does so by blocking the alpha-1 adrenergic receptor.

There are several excellent placebo controlled randomized controlled trials showing efficacy for Prazosin in reducing nightmares related to posttraumatic stress disorder, and these studies have been performed in both Veterans and civilians with PTSD. And, I think the summary for Prazosin is it just flat out works and works well for controlling nightmares, and it is a highly recommended intervention.

One coordination that must be remembered with Prazosin, however, is that it will lower most patients' blood pressure because, after all, it is medication for treating high blood pressure, and it is important to coordinate the patient's care with the primary care physician to avoid excessively lowering the patient's blood pressure.

## IMPACT OF PRAZOSIN

- ▶ Observational report of Iraq/Afghanistan Veterans (N = 74) with PTSD, mild Traumatic Brain Injury (mTBI), insomnia, and headaches
- ▶ Intervention: sleep hygiene (all) and prazosin (some)
- ▶ Results at 9 weeks:
  - Improved sleep
  - Fewer headaches per month
  - Lower headache pain ratings
- ▶ Both interventions improved sleep and adding prazosin reduced headaches

Ruff, 2009



Let's look at a little bit of data that's underlying the Prazosin's efficacy. And, what I'd like to do is, not so much look at results from the placebo controlled randomized trials that were done with Prazosin, all of which show it works well, but to look at data that you may not be as familiar with.

There is one report, which was an observational report of Veterans from Iraq and Afghanistan, who had both posttraumatic stress disorder and mild traumatic brain injury. The intervention for this group was sleep hygiene training for all Veterans, and some Veterans received Prazosin on top of the sleep hygiene training. What the results of this study showed were that sleep was better in both groups with not much difference. But, there were fewer headaches per month in the group that received Prazosin and, the intensity of the headaches was lower in the group that received Prazosin.

What I take away from this study is, it appears to suggest that Prazosin may be improving the quality of sleep, whereas, this sleep hygiene intervention is improving the Veterans ability to go to sleep at night. And, perhaps, it's the fewer awakenings from deep sleep that are related to having fewer nightmares, which then lead to fewer headaches and lower headache pain.

### PRazosin VS. QUETIAPINE

- ▶ Atypical antipsychotic quetiapine used often for sleep in VA, but no more sedating than antihistamines
- ▶ Prazosin for nightmares not often used, despite promise
- ▶ Historical cohort study of 237 Veterans with PTSD initially prescribed either prazosin or quetiapine; followed for 3-6 years
- ▶ In the prazosin group, 8% were switched to quetiapine and none continued to the study end date
- ▶ In the quetiapine group, 20% were given prazosin in addition to quetiapine and nearly half continued the prazosin

Byers 2010

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- ▶ In the prazosin group, 8% were switched to quetiapine and none continued to the study end date
- ▶ In the quetiapine group, 20% were given prazosin in addition to quetiapine and nearly half continued the prazosin
- ▶ Quetiapine was less likely to improve sleep and more likely to cause side-effects (excess sedation in 21%, metabolic effects in 9%)

Byers 2010

One of the more commonly prescribed medications for sleep problems in Veterans with posttraumatic stress disorder is Quetiapine. Quetiapine is an atypical antipsychotic and, while it does have some sedating effects, it does not seem to be any more or less sedating than some of the older sedating antihistamines, such as Hydroxyzine.

Prazosin use, however, does not appear to be as widespread as it should be – or perhaps even could be – at least within the VA system for treating nightmares related PTSD. Quetiapine use, however, is fairly widespread. There was one team of VA investigators that looked at the use of Prazosin and Quetiapine in a naturalistic study where a group of Veterans in one VA health care system was followed for a period of three to six years, and there were some interesting results that came from that.

Among the Veterans who were initially given Prazosin, only 8% were switched to Quetiapine at a later date, and none of the Veterans switched to Quetiapine stayed on that medication by the time the study ended. On the other hand, Veterans who were initially treated with Quetiapine required Prazosin. Around 20% of the Quetiapine group was taking Prazosin, in addition to Quetiapine, and of those where Prazosin was added, about half of those Veterans continue taking Prazosin until the end of the study.

The authors concluded from their analysis that Quetiapine was less likely to improve sleep and much more likely to cause side effects, excess sedation, which is not terribly surprising, and metabolic effects. It's notable that the metabolic effects occurred in around 9% of the group taking Quetiapine, which is a rather high percentage.

### SUMMARY OF PHARMACOLOGICAL TREATMENT

- ▶ PTSD adversely affects sleep
- ▶ Disorders known to occur with PTSD also adversely affect insomnia. Consider ordering a sleep study.
- ▶ Insomnia in PTSD can be addressed by behavioral, psychotherapeutic, and pharmacologic means. Try them in that order.
- ▶ Benzodiazepines and the “z-drugs” should be avoided whenever possible.

### SUMMARY OF PHARMACOLOGICAL TREATMENT

Evaluation Goal: Consider PTSD as the cause of insomnia after addressing other potential etiologies.

Treatment Goal: Improve sleep with as little use as possible of benzodiazepines or similar medications.

So, to summarize some of the pharmacologic recommendations for sleep, it's important to remember that the PTSD can adversely affect sleep, and disorders that are known to co-occur with PTSD, also adversely affect sleep. When one of these disorders is present, it can be helpful to order a sleep study or a polysomnogram.

Insomnia occurring at posttraumatic stress disorder can be addressed by behavioral interventions, psychotherapy, and medications. I recommend trying those interventions in that order, behavior change first, followed by psychotherapy, and then followed by medication. Medications, such as the benzodiazepines, and the z-drugs, like Zolpidem, Zaleplon, and Zopiclone should be avoided whenever possible.

### WHY, WHY, WHY???

- ▶ In 2007, VA clinicians prescribed quetiapine for 72,312 Veterans, more than twice the number of the next most common antipsychotic medication
- ▶ 10.6% of all Veterans with PTSD took quetiapine in 2007
- ▶ These data are problematic because quetiapine:
  - Doesn't work well for insomnia (see next slide)
  - Can cause the metabolic syndrome
  - Can cause tardive dyskinesia
  - Can cause QTc prolongation – avoid citalopram

Leslie, 2009

### WHY, WHY, WHY???

- ▶ 10.6% of all Veterans with PTSD took quetiapine in 2007
- ▶ These data are problematic because quetiapine:
  - Doesn't work well for insomnia (see next slide)
  - Can cause the metabolic syndrome
  - Can cause tardive dyskinesia
  - Can cause QTc prolongation – avoid citalopram
  - Is expensive

Quetiapine, despite its popularity, should be used only after other treatments fail. This point is especially true for Veterans who should not gain weight (e.g. diabetes; obstructive sleep apnea; osteoarthritis)

Leslie, 2009

So, now that we've had a look at the recommended interventions for medications for insomnia, let's take a quick look again at Quetiapine prescriptions. In 2007, there were around 72,000 Veterans in the VA system who took Quetiapine. This is more than twice the number of the next most commonly prescribed antipsychotic medication.

A number of those Veterans had posttraumatic stress disorder, and that same study found around ten and a half percent of all Veterans of PTSD took Quetiapine in 2007. These data represent a problem for care of the Veteran with PTSD, because Quetiapine is not our best intervention for insomnia. As an atypical antipsychotic, it is linked to both the metabolic syndrome, and a risk of causing tardive dyskinesia, and, most recently, the FDA came out with a caution about QTc prolongation in Quetiapine.

Finally, Quetiapine is far more expensive than the alternatives, such as Trazodone or one of the antihistamines. In Quetiapine, despite its popularity as a medication, it should be used only after other interventions for insomnia have failed. And, I think this point is especially true for Veterans who should not gain weight and should not be at risk for the metabolic syndrome.

Some particular medical comorbidities to consider here are preexisting diabetes, osteoarthritis, where weight gain will increase the wear and tear on the patients' joints, and, finally, obstructive sleep apnea. We know sleep apnea is associated with a higher weight, and it does not seem reasonable to try to treat insomnia with a medication that might actually worsen another sleep problem.

## WHAT DOES “IATROGENIC” MEAN?

- ▶ One recent study examined polysomnogram (PSG) records for a relationship between atypical antipsychotic use and obstructive sleep apnea
- ▶ Results: diagnosis of depression with concomitant atypical antipsychotic use showed odds ratio of 4.5 compared to other groups
- ▶ Separately, benzodiazepines were associated with worse sleep apnea symptoms

So, when we look at Quetiapine, and sleep studies, there is one report that looked at records from a sleep medicine clinic, and examined polysomnogram reports and atypical antipsychotic prescriptions. The results in this study found that having a diagnosis of major depression and simultaneous atypical antipsychotic use, showed a markedly increased rate of obstructive sleep apnea.

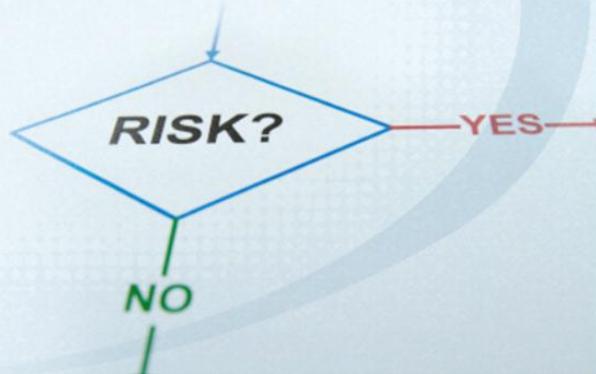
There are different ways to interpret the outcome of this, but one interpretation is the known association of weight gain with atypical antipsychotic use, and the known association of weight gain with obstructive sleep apnea. When I look at the Veterans that come into my clinic, particularly the Veterans who served in the Vietnam era, obesity is a fairly significant problem. And, it does not seem right to prescribe medications that can increase weight to a group that is already at risk for illnesses that we know are associated with obesity, which includes obstructive sleep apnea.

**Objective 4: Describe a General Approach to Assessing and Treating Sleep Problems Associated with PTSD.**

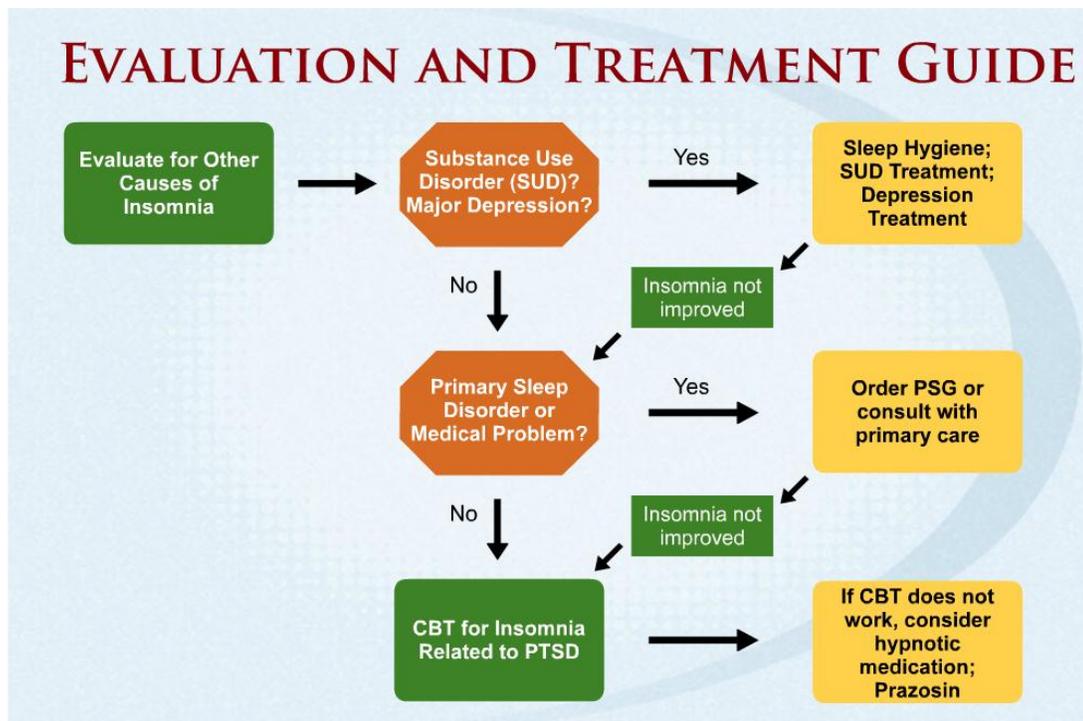
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## OBJECTIVE 4:

Describe a general approach to assessing and treating sleep problems associated with PTSD



This now brings us to objective number four: describe a general approach to assessing and treating sleep problems associated with PTSD.



The diagram you can see, in front of you on the screen, represents the approach that Jason and I advocate for evaluating and treating sleep problems associated with posttraumatic stress disorder. Our first recommended step is to evaluate for other causes of insomnia. These causes might include substance use disorders, or major depression.

If those disorders are present they should be treated in accordance with the VA/DoD clinical practice guidelines for that condition. If the insomnia is not better, or if those conditions aren't present, it's important to assess for a primary sleep disorder or a medical problem that may be contributing to the patient's sleep difficulty.

If one of those problems is present, or even might be present, it is worthwhile to seek consultation with primary care, or order a polysomnogram and a referral to a sleep medicine clinic. If the insomnia is still not improved, or if one of those other comorbid conditions is not present, we recommend cognitive behavior therapy for insomnia, as Jason discussed earlier in today's talk. And, finally, if cognitive behavior therapy does not work, or if, for some reason, is not available at your facility, we recommend considering hypnotic medications, such as Trazodone, and also consider Prazosin if the patients report regular nightmares.

So now, I'd like to turn over this microphone back over to Jason for a few minutes to have him offer us a summary of the treatment recommendations for treating insomnia and posttraumatic stress disorder. Jason, back over to you.

## TREATMENT RECOMMENDATIONS

- ▶ Screened for the presence of primary sleep disorders and comorbid psychiatric diagnoses that could affect sleep
- ▶ When possible, patients should receive evidence-based trauma-focused CBT
  - Best chance to improve PTSD symptoms
  - More likely than not that sleep will improve
  - If sleep does not improve, brief CBTI can be added and/or imagery rehearsal for nightmares

Thanks, Bruce. I'm just going to summarize what we've talked about so far. Again, we recommend that any treatment starts with a very strong assessment, and we recommend that you screen for primary sleep disorders, as well as any other comorbid psychiatric diagnoses that could affect sleep.

Now, when possible, we recommend that treatment start with evidence-based trauma-focused CBT. Overall, this treatment gives patients the best chance to improve PTSD symptoms. And also, it is more likely than not, that sleep is going to improve after receiving an exposure therapy, a Cognitive Processing Therapy, and, at that point, when treatment is complete, if patients have responded, but their sleep is still poor, a brief trial of CBT for insomnia can be added on the tail end of the treatment to address those sleep problems.

If trauma focus cognitive behavioral therapy is not an option, for some reason, or as I just said, if it does not improve sleep, patients may benefit from a combination of CBT for insomnia and imagery rehearsal therapy for nightmares. Obviously, that depends on the presence of nightmares. If there are no nightmares, there is no reason to add imagery rehearsal.

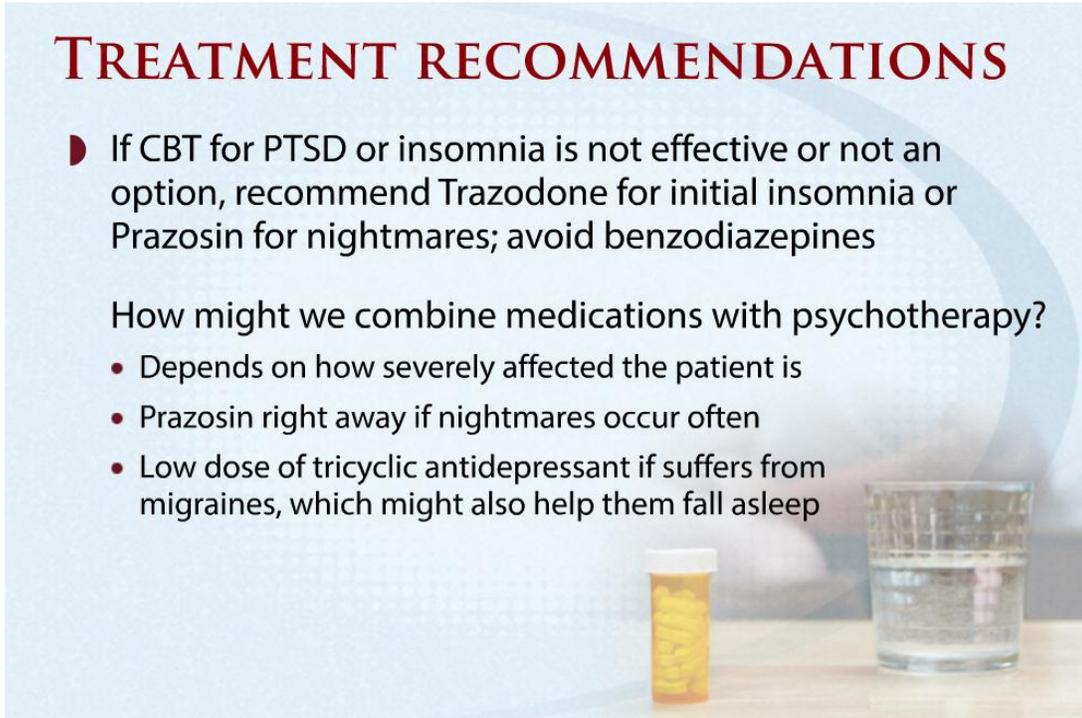
We recommended these treatments because they have the potential to improve sleep and nightmares, as well as PTSD symptoms. And, one other nice feature of CBT for insomnia, specifically, is it is not trauma-focused and does not get too intensely into emotions, thoughts. It's a treatment that can be very effective, so, for a lot of patients, CBT for insomnia can provide a very positive experience with psychotherapy in general. So, if the opportunity to engage in a more intensive trauma-focused therapy does come up, patients may be a little more likely to engage in that therapy given that they've already had a nice positive experience with psychotherapy.

## TREATMENT RECOMMENDATIONS

- ▶ If CBT for PTSD or insomnia is not effective or not an option, recommend Trazodone for initial insomnia or Prazosin for nightmares; avoid benzodiazepines

How might we combine medications with psychotherapy?

- Depends on how severely affected the patient is
- Prazosin right away if nightmares occur often
- Low dose of tricyclic antidepressant if suffers from migraines, which might also help them fall asleep



Now, as Bruce alluded to earlier, if CBT for either PTSD or insomnia is not effective, or is not an option, the first line medications we recommend considering are Trazodone, for initial insomnia, or Prazosin for nightmares, and we recommend avoiding benzodiazepines. Bruce, one thing I'd like you to speak to, if you can, can you talk a little bit about how we might combine medications with psychotherapy?

That is another excellent question Jason, and I sometimes do combine medications along with psychotherapy, and even occasionally before psychotherapy. I think the answer all depends on how severely affected the patient is. For example, with Prazosin, I will go ahead and start that medication if a patient reports nightmares that occur more than three to four times per week.

Similarly, if a patient suffers from migraine headaches, and is having them more to three or four times per week, then I may go ahead and start a low dose of a tricyclic antidepressant to help prevent migraines, but may also help the patient fall asleep.

Alright, thanks so much Bruce. Well, that concludes our talk for today. Thank you so much for listening and we wish you good luck in applying what we've talked about today in your clinical practice.