Impact of Sleep Disorders & Screening and Treatment of Common Sleep Disorders

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Lifestyle - Lettieri

CHRISTOPHER J. LETTIERI, M.D. FACP, FCCP, FAASM: Hello everybody. My name is Christopher Lettieri. I'm a Professor of Medicine at the Uniformed Services University of the Health Sciences and today I'm going to be discussing the Impact of Sleep Disorders and the Screening and Treatment of Common Sleep Disorders that you see in clinical practice.

I have no relevant disclosures.

Specifically, today we're going to be talking about the effects of sleep on common medical disorders and we'll change focus and talk about the impact of insufficient sleep which is a very important topic for all of us. Then we're going to talk about insomnia and really getting down into understanding what insomnia and how it can be treated in primary care or in any clinical practice. Then we move into obstructive sleep apnea and we'll finish with the discussion on restless leg syndrome.

The first part of this talk is going to be discussing the effects on sleep on common medical disorders. Both the quality of our sleep and underlying sleep disorders share a bidirectional relationship with many common medical conditions. This is especially true of behavioral health disorders and cardiopulmonary diseases.

As I'll highlight in the following slides poor sleep is hallmark and often a diagnostic criterion for many behavioral health disorders. We know that having a sleep disorder particularly insomnia and sleep apnea can lead to the development of depression and anxiety. The same bidirectional relationship exists between sleep and cardiopulmonary diseases. Fragmented and poor sleep quality is common in these patients and the treatment of those conditions may actually further fragment sleep. Likewise, it's well established that's sleep disorders, especially obstructive sleep apnea can cause or contribute to the development of chronic respiratory disorders and cardiovascular diseases.

There are normal physiologic changes that occur during sleep that impact the respiratory system. As we heard in the past section with Dr. Surkin, normal sleep leads to diminished mucociliary clearance and cough, there's a nadir in our pulmonary function during the night and an increase in airway resistance as we sleep. Sleep often leads to a ventilatory perfusion mismatch and results in a relative hypo-ventilatory state. For most individuals this is clinically meaningless and just a normal effect of sleeping. However, among patients with asthma or COPD, those changes can lead to an increase in symptoms and can contribute to poor outcomes. Now specifically with regards to asthma, the normal circadian alterations of the respiratory mechanics do have an impact on most asthmatics and can lead to nocturnal symptoms. While common nocturnal symptoms of asthma are regarded as a sign of poor asthma control and an independent risk factor for exacerbations. In fact, most exacerbations and asthma related deaths occur during the night.

In addition to the potential impact that sleep itself has on the pulmonary system and on asthmatics, the association between asthma and obstructive sleep apnea is well established. Because of its deleterious effects it's worth highlighting. Not only is obstructive sleep apnea more common among asthmatics but asthma itself is an increased risk factor for the development of sleep apnea independent of corticosteroid use.

As we learned from the Wisconsin Sleep Cohort, they found that having a diagnosis of asthma increased the risk of developing sleep apnea with an adjusted relative risk of 1.4. The reverse relationship is also true; having sleep apnea impairs asthma control and individuals with sleep apnea are 3.6 times more likely to have uncontrolled asthma and 3.4 times more likely to experience an exacerbation compared to asthmatics who don't have sleep apnea.

Because of the strong relationship between asthma and LSA and because of the marked increased risk of poor outcomes the national asthma education and prevention program recommends that all patients with difficult to control asthma be screened for sleep apnea.

The association between asthma and sleep apnea is a good segue into discussion of CORE syndrome which is made up of chronic cough or cough variant asthma, obstructive sleep apnea, chronic rhinitis and esophageal reflux. All four conditions are commonly associated with each other. They can all have overlapping or mimicking symptoms and each can exacerbate the other. As we just heard, sleep apnea and asthma are commonly associated. We know that rhinitis is common among asthmatics especially those with more atopic symptoms. Similarly, at least 40% of apneics have chronic rhinitis.

Sleep apnea causes nocturnal reflux and GERD is common among those with poorly controlled asthma. Upper airway closure leads to transthoracic pressure changes so instead of sucking air in, we tend to such acid out and any acid in the distal esophagus can cause a compensatory constriction of the airways and because our heads are at the same height as our stomach when we sleep that ACD can move to the upper airways causing chronic cough and rhinitis. It's not hard to visualize how each can contribute to the other and likewise all four more commonly occur at night. We just discussed that the majority of asthmatics experience nocturnal symptoms. Sinuses can be drained more in a recumbent position; nocturnal esophageal reflux is underappreciated and most reflux does occur during sleep. Gastric acid secretion peaks during the first half of the night and occurs at the same time where our lower esophageal sphincter time [phonetic] and peristalsis are diminished and obviously sleep apnea occurs during sleep.

The symptoms, especially nocturnal symptoms clearly overlap and can be confusing to differentiate clinically. For example, waking up in the middle of the night with coughing, choking and shortness of breath can be due to any or potentially of these conditions. A simple historic questioning does not necessarily help us establish the diagnosis. Given that, I strongly recommend that you consider all four of these conditions in patients with compatible symptoms especially when they're not responding to therapy.

As mentioned, the normal physiologic changes that occur during sleep can clearly contribute to symptoms among those with COPD. Not surprisingly, sleep complaints are highly prevalent in these patients. Not only does COPD lead to poor sleep quality, but

LAMAs, LABAs, and methylxanthines all can fragment sleep.

The most important association between sleep and COPD is hypoventilation and has resultant hypoxia. As I mentioned, normal sleep creates a state of relative hypoventilation so if CO2 is a byproduct energy production and we breathe primarily to eliminate CO2 so the more energy we burn the more we have to breathe. During sleep our energy expenditure decreases and as a result we have to breathe less. However, that decrease in - - ventilation is actually greater than our decrease in energy expenditure and even in the normal state our CO2 levels increase during sleep. This is largely driven by a decrease in our CO2 sensitivity and a decrease in patterned [phonetic] during sleep.

Again, in most individuals this is clinically meaningless and a normal physiologic phenomenon. However, if you have an underlying ventilatory state such as COPD, that can lead to significant alveolar hyperventilation with result in hypoxia and CO2 retention. It should be strongly considered in those with an FEV1 under 50% predicted so a large majority of our patients who we see in clinic with moderate and severe COPD. It's absolutely important to consider as it is associated with poor outcomes and has a near linear association with decreased survival.

As previously discussed, chronic rhinitis may be associated with the CORE syndrome which is more common at night. But chronic rhinitis itself has an independent relationship with sleep and a sleep quality. Symptoms of rhinitis are more common at night and are primarily driven by postural changes that lead to more sinus drainage when we lay down. Rhinitis can fragment sleep and decrease sleep quality because we don't cough in our sleep and we don't swallow in our sleep so any sinus drainage that occurs in that recumbent position pools in our upper airway and at some point, leads to sleep fragmentation so you can clear your airway.

It's been shown that treating rhinitis can improve sleep, sleep related quality of life and daytime sleepiness.

We just discussed the association between GERD and sleep but to highlight the key takeaway points, nocturnal reflux is more common than daytime symptoms but it's often silent and doesn't necessarily result in frequent heartburn so it can often be missed clinically. Normal changes in the GI system at night promote more reflux and reflux events. As I mentioned, gastric acid secretion is greatest in the evening and the first half at the night and it peaks between about 9 p.m. and 2 a.m. At the same time that we have a high gastric acid secretion, we have a delayed gastric emptying with decreases and we have a limited or absent peristalsis of the intestines and the esophagus which can also contribute to more reflux events. In addition, lower esophageal sphincter tone diminishes during sleep so all of these ultimately lead to more reflux events and a prolonged acid contact time that occurred during sleep.

As I said, any acid in the lower esophagus not only fragments sleep but also leads to a compensatory constriction of the airways and causes or at least contributes to nocturnal asthma. This is a fairly common association and approximately one quarter of those with poorly controlled asthma have underlying GERD. In addition, acid suppression has been shown to include both lung function and symptoms among asthmatics. It's also been

shown to improve the outcomes in other chronic respiratory conditions such as idiopathic pulmonary fibrosis.

We'll go into more depth regarding sleep disorders and heart failure later in this program when Dr. Surkin comes back to speak.

For now, I'd like to highlight the effects of reduced cardiac function on normal sleep and the impact that physiologic changes that occur during sleep have on cardiac function especially among those with heart failure. There are several reasons why a person with heart failure, especially those with reduced ejection fraction, will have poor sleep quality. Orthopnea can make falling asleep difficult and often leads to nocturnal awakenings. Diuretics can cause sleep fragmentation and nocturnal awakenings. Statins, especially lipophilic preparations can lead to daytime somnolence and beta blockers can fragment sleep, increase nightmares and cause daytime sleepiness. Not surprisingly nearly two-thirds of those with heart failure report subjective sleep quality.

Objectively a reduced ejection fraction is associated with a decrease in sleep continuity more nocturnal arousals and a diminished amount of both slow wave sleep and REM sleep.

While pulmonary edema and medications clearly have an adverse effect on sleep, sleep can also have an adverse effect on cardiac function especially among those who are susceptible. Just simply lying in a supine position alters our - - zones and leads to a ventilation profusion mismatch. Sleep also leads to an increase in pulmonary vascular pressures of about 5 millimeters of mercury. Again, in most people that's clinically insignificant but those who have underlying pulmonary vascular disease this can put them over the top and lead to more symptoms.

Both are significantly more pronounced among those experiencing nocturnal hypoxia. Again, in most people it's normal and unimportant but for those with underlying pulmonary hypertension or right sided heart failure it can exacerbate symptoms.

In summary, there are normal physiologic changes that occur during sleep that can adversely impact underlying cardiopulmonary diseases and those same cardiopulmonary disease can have a negative impact on sleep and sleep quality.

This portion of today's program will focus on the detrimental effects of insufficient sleep and chronic sleep debt.

As we'll discuss, insufficient sleep is a common and growing problem and is associated with numerous adverse effects on health, mood, cognitive function, physical performance, health and survival.

Let's start by clarifying a few definitions. Somnolence or sleepiness is a normal and expected effect that's mediated by both a circadian influence and endogenous homeostatic processes. Like all animals, our homeostatic processes are largely regulated by a circadian pacemaker. With regards to sleep this internal clock tells us when it's time to be awake and when it's time to be asleep. When it's past our biologic bedtime we feel

sleepy.

Sleep is also mediated by how long we're awake and how much metabolic expenditure we have during the day. To simplify this process the longer we're awake and the more calories we burn, the more adenosine we accumulate and at some point, we exceed a threshold where adenosine produces sleepiness. Interestingly the antagonist of adenosine is caffeine which is why coffee and caffeinated products help us feel more awake or actually they work by making us feel less sleepy. Being physically active or staying awake longer often makes us feel sleepy. We'll discuss these in more detail on subsequent slides, but in short, being sleepy is normal.

However, hypersomnolence or being excessively sleepy to the point where it impairs normal wakefulness or causes sleep at unwanted or inappropriate times is pathologic. Unfortunately, this is not uncommon and occurs in approximately one-third of American adults.

How much sleep do we really need? There is clearly some individual variation. Some people are high performers with only six hours of sleep while others don't do well unless they're in bed for over nine hours. However, how people feel or what they think they may need does not necessarily reflect their physiologic requirements for sleep. Often, those who are able to function on less sleep do so because of habits or behavioral modifications that can compensate for insufficient sleep. In addition, we can become habituated or tolerant of the increased levels of adenosine.

As I've mentioned, the accumulation of adenosine helps us feel sleepy but for those who are chronically sleep deprived, the sedating effects of adenosine are less pronounced. Now in contrast, those who feel they need excessive amounts of sleep may be compensating for poor sleep quality or some other underlying condition that impairs wakefulness. That being said, a person's habitual sleep duration may not be a true reflection of their actual sleep needs. Again, how much sleep do we really need? If we look at large physiologic studies among normal adults, they consistently show an adult needs approximately seven and a half hours of sleep per night. That's how much sleep we need but how much sleep are we actually getting?

In the 1970s a large poll found that the average American slept 7.7 hours a night. Unfortunately, since them we've decreased our sleep time by nearly two hours in some studies. Other polls have not found as large of a decrease however all measures consistently report that the average American is sleep deprived with the latest sleep in America poll reporting the average of 6.8 hours a night. There are also several subpopulations that habitually achieve even less sleep. Not surprisingly members of the military, urban professionals and medical trainees obtain considerably less sleep than most average Americans. A recent study found that nearly two-thirds of all Americans sleep less than seven hours per night which would be considered sleep deprived. That same study found that over a quarter of adults were severely sleep deprived and have achieving less than six hours of sleep per night.

There are numerous consequences of chronic sleep debt. From a neurologic perspective insufficient sleep has been shown to slow cognitive response times and executive

functioning. It narrows attention span with a clear association between ADD and ADHD, it decreases problem solving, impairs situational awareness and even diminishes moral reasons and chronic sleep deprivation can lower the seizure threshold.

Behavioral health associations include an increase in irritability, more depression and anxiety, including both the symptoms and the diagnoses of both. There are higher divorce rates among those who are chronically sleep deprived and more substance and alcohol abuse. Sleep debt also impairs quality of life and has been associated with chronic pain and increased risk of PTSD and more suicidality.

Chronic sleep debt increases the risk for hypertension and has been shown to be an independent risk factor for heart attack, stroke and cardiovascular death with odds ratios greater than those seen with diabetes, smoking, or obesity. Insufficient sleep also increases the risk of gaining weight and developing diabetes which I'll discuss in a subsequent slide.

As I mentioned, insufficient sleep diminishes cognitive function and executive performance. More recently there's been a large focus on the association between chronic sleep debt and dementia. An insufficient amount of quality sleep, whether it's from sleep debt, sleep fragmentation or disorders of disruptive sleep such as sleep apnea, they've all been associated with a marked increased risk for developing dementia. In fact, there is a linear correlation between habitual sleep duration, and cognitive decline. Recently the role of the glymphatic system on cognitive health has been discovered. Like the body's lymphatic system, the CNS's glymphatic system helps clear waste products, particularly beta amyloid. The system is the most active during sleep, in fact, it's most active during slow wave [phonetic] sleep so impaired sleep, quality or quantity can lead to an accumulation of beta amyloid which has been shown to be a precursor for Alzheimer's. In addition, insufficient sleep leads to an increase in tau proteins which are associated with cellular damage and also in increased risk of dementia.

Sleep, chronic pain, and behavioral health disorders share a closely linked and interdependent relationships. Patients who experience chronic pain are more likely to develop behavioral health disorder, especially depression. Likewise, those with depression report more pain and are more likely to habitually use prescription and nonprescription opioids. A similar relationship exists between sleep and pain and between sleep and behavioral health disorders which I'll discuss next.

There is a clear reciprocal relationship between pain and sleep. Chronic sleep debt increases the pain response and decreases the pain threshold meaning that those with less sleep experience more pain. Those with chronic pain report diminished sleep quality, more insomnia, and more sleep fragmentation. In fact, the amount of pain that you experience during the day will predict the quality of sleep that night and the quality of sleep at night correlates with both reported pain and the use of pain medications the following day.

In fact, disturbed sleep has an interdependent and linear correlation—excuse me, independent and linear correlation with pain severity. The majority of those with chronic pain will have a decrease in both subjective and objective measures of sleep and sleep

quality so when present, this is associated with poorer quality of life indices and increase in healthcare utilization, an increase in the use of prescription pain medications and an increase in the risk for developing depression.

A similar bidirectional relationship exists between sleep and behavioral health disorders. Sleep complaints are common with most psychiatric conditions and frequently serve as a diagnostic criterion. Psychiatric conditions are also more likely to occur in those with preexisting sleep disorders and insomnia, sleep apnea, and insufficient sleep all which have been shown to be independent risk factors for the development of behavioral health disorders. Specifically, insomniacs are three times more likely to develop depression within three to five years compared with normal sleepers. Similarly, those with sleep apnea have a nearly twofold increase risk for developing a behavioral health disorder compared with non-apneics. Similar to pain, when this relationship is present, it portends a much worse outcome with a diminished response to treatment, more treatment failures and relapses, more hospitalizations, for behavioral health conditions, higher rates of PTSD and unfortunately greater suicidality.

Chronic sleep debt has a clear and well-established negative impact on metabolic health and is an independent cause of weight gain and development of diabetes. Chronic insufficient sleep leads to an altered glucose metabolism through an increase in insulin secretion, peripheral insulin resistance and a persistently elevated cortisol level and also leads to an imbalance of leptin and ghrelin to create an insensitivity that alter our hunger and satiety relationships meaning that people who are chronically sleep deprived eat more and don't get full as quickly.

In addition, while a short-term sleep loss increases our metabolic rate, over time chronic sleep debt increases our basal metabolic expenditures. These consequences occur in a near linear fashion with greater habitual sleep debt leading to increased weight and higher probability for the development of diabetes.

The final lecture in today's program will focus on sleep and cardiovascular disease. However, I wanted to specific to this topic, I wanted to highlight the effects of sleep debt on cardiovascular health over the next few slides.

There is a strong causal relationship between chronic sleep debt and the development of cardiovascular disease. Unstuffing sleep creates a systemic proinflammatory state and an increased autonomic tone that causes endothelial dysfunction and impaired fibrinolysis. As we just discussed, sleep debt can cause or contribute to weight gain and insulin resistance. These factors have been shown to have an independent impact on cardiovascular health.

Not only is cardiovascular disease more common in those who are habitually sleep deprived, sleep debt increases the risk for major cardiovascular events. This association has been observed in numerous clinical trials and observational studies. For example, a meta-analysis of 15 prospective longitudinal studies found that compared to those who obtained seven to eight hours of sleep a night, short sleepers were 48% more likely to develop or die from coronary artery disease and were 13% more likely to have or die from stroke. A similar relationship was found for those who had excessive sleep of greater than

nine hours per night.

The association between sleep duration and survival was explored in several large population-based studies. The Nurse Health Study, the Japanese Collaborative Cohort and the NHANES Registry all observed similar findings that - - sleep durations were closely correlated with length of life in a u-shaped curved pattern. Compared to those who achieved an appropriate amount of sleep each night both shorter and longer sleepers had greater mortality and shorter life expectancies.

The next section of this program will focus on understanding and treating insomnia.

The purpose of this session is to provide you with a primer on how to recognize and treat insomnia. We will discuss a practical approach as to what you can do in both a primary care and specialty practice when managing patients with insomnia. As importantly, we'll discuss some of the things that you probably shouldn't do when approaching insomnia. To those ends, we'll first discuss what insomnia is and how prevalent it is in clinical practice. We'll then discuss the different elements of therapy with a focus on what can be done in a primary care setting.

Why does this matter? Insomnia is a common disorder that's steadily increasing in prevalence and because it's a contributing factor to numerous chronic comorbid conditions it's even more prevalent among those seeking medical attention. Unfortunately, despite it being a common condition that's associated with several comorbid conditions it's often overlooked in clinical practice. In one large study insomnia was reported by 19% of patients evaluated by their primary care providers. Unfortunately, those complaints were addressed in only 7% of individuals. Another large multicenter trial explores the rates of different insomnia therapies provided during primary care visits. Of those who were treated, only 8% patients received education about sleep and healthy sleep habits and only 2% of the cohort were referred for cognitive behavioral therapy.

For treatment choices, 6% of patients were treated conservatively while 94% of patients were prescribed a sleep aid with over half prescribed two or more medications specifically intended for sleep. Nearly a quarter were given an antipsychotic agent. I'll discuss each of these options on subsequent slides. I do appreciate the constraints of managing a busy clinic and the pressures to appease patients but I'm hoping by the end of this presentation you'll see how this approach may be counterproductive.

To appreciate how to properly recognize and treat insomnia I think it's important to briefly discuss what insomnia really is. As I mentioned, insomnia is a highly prevalent condition. While it's not necessarily one of the most commonly coded diagnoses in primary care, several reports have claimed it to be one of the most common complaints among primary care patients. Nearly all of us will experience some intermittent episode of insomnia during our life. For most individuals these are the isolated events that are self-resolved and don't warrant any therapy. However, 15 to 30% of adults will have a course of chronic insomnia at some point in their life. Insomnia is definitely more

common among women and its incidence increases progressively with increased age.

Insomnia is largely a junk box term that describes any process that causes difficulty falling and/or staying asleep which also leads to an adverse consequence in daytime function, mood or quality of life. I want to specify that. It's not just I have a hard time falling asleep. Insomnia is I can't fall asleep or stay asleep or both and like any other condition, it has to have an adverse consequence. If a patient only had a hard time falling asleep but it doesn't have any adverse consequence in life, it's not insomnia disorder.

It can be called by numerous things. Medications, caffeine, smoking, comorbid conditions, noisy neighbors, your dog, really technically anything can cause insomnia. Because of that, we used to previously categorize insomnia as either primary or secondary depending on whether or not there was an identifiable cause or contributing factor. That concept is now pretty antiquated. We diagnose insomnia in a person who can't initiate sleep, can't maintain sleep or has terminal awakenings, that are not better explained and treated by another reason. Insomnia doesn't have to occur on all nights but it should be present on most nights for more than three months to be considered a chronic disorder.

To truly understand insomnia, we need to understand what regulates sleep and wake. These are mutually exclusive phenomenon mediated by their own unique transmitters that promote wake or promote sleep. To be awake we have to both turn on wake and turn off sleep. To be asleep we have to turn on sleep and block wake. Insomnia may be the result of some imbalance in our ability to turn off weight and/or turn on sleep. Again, if that occurs on most nights for more than three months that also causes an adverse consequence in our health or quality of life.

There are several factors that increase the risk for insomnia. As I mentioned, insomnia is more common among women and the incidence increases with age. The greatest risk factor for future insomnia is a prior history of insomnia. Unfortunately, some individuals are just prone to be insomniacs. This brings us to the Spielman model of insomnia or the three Ps. The classic insomniac is someone who has a predisposition to insomnia which is probably genetic. Then a course of insomnia is often triggered by some life event that may be their good or bad stressor but often disrupts a normal sleep/wake cycle. What typically leads to chronic insomnia is our behaviors that results from poor sleep that perpetuate the problem. What do we do when we have a bad night's sleep? We drink more coffee or we don't exercise and if we can't fall asleep at our normal bedtime, we may start staying up later and later. All of these lead to perpetuation of insomnia.

These maladaptive strategies just propagate the cycle of insomnia where insomnia begets more insomnia. Eventually individuals can ingrain both poor sleep habits and a defeatist mentality where they essentially convince themselves that they can't fall asleep. This conditioned response then leads to a conscious or unconscious sleep preventing associations and more anxiety about sleep. This contributes to heightened arousal which can further decrease the ability to block wake and in order to promote sleep.

As we're going to talk about in a subsequent slide, perhaps the healthiest sleep habit we can have is to maintain a regimented sleep/wake cycle where we go to bed and wake up at the same time every day. This not only helps us regulate our sleep/wake cycle, it also

helps to ensure a normal circadian rhythm of numerous homeostatic processes. Insomnia that prevents falling asleep at normal bedtimes makes people stay up later in an attempt to force sleep onset or leads to an increased use in weight promoting substances that counteract the fatigue of insufficient sleep. All of this is really just further desynchronizes the circadian rhythm and propagates more insomnia.

That's insomnia in a nutshell. Now let's talk about how to properly treat it. Before you consider treating insomnia make sure it's actually insomnia. Make sure their sleep environment is conducive to good sleep and not the cause of their sleep disruptions. Consider the effects of medications and adjusting if possible and optimize the treatment of any medical disorder that might be mimicking insomnia, especially sleep apnea. Once you make sure that its insomnia and not some other identifiable thing, or even just a circadian rhythm disorder like a person's a night owl and they're trying to go to bed at 9:00 when their normal traditional bedtime should be more like midnight or 1. Once you are sure that's it's actually insomnia both the prescriber and the patient have to remember that if insomnia is chronic then so is its treatment. I'm not saying that if you prescribe Ambien, they need to be on Ambien for the rest of their life. Absolutely not. Remember that chronicity of insomnia before reaching for that prescription pad. I usually talk to my patients. I make sure that they understand that this is usually lifetime condition or at least a long-term condition and they don't want to be on long-term medications.

The best way to treat insomnia in the long run is to help your patients relearn how to achieve healthy sleep. Treatment can be categorized as behavioral or pharmacologic and we'll explore both of those. However, remember that behavioral modification is the cornerstone to successful therapy. It can provide a successful resolution of their sleep disturbances by itself. No medication is going to be effective without proper sleep habits. Behavioral modification primary focus on health sleep behaviors and habits in an attempt to reestablish a normal circadian rhythm and lead to a positive conditioned response where a patient stops feeling victimized by their insomnia. It revolves around proper sleep hygiene, stimulant control, relaxation, and cognitive behavioral therapy. Before you shy away, I promise you that the basics can be easily implemented in your primary care clinics without significant allocation of time for many patients.

Pharmacologic therapy does have a role however it's best used as a short-term bridge for patients beginning their behavior modifications or for those who have persistent and consequential insomnia despite conservative therapy. If at all possible, prescription sleep aids should be used for a limited duration.

There are several different guidelines for the management of insomnia. The three I like the best were produced by the American College of Physicians, the American Academy of Sleep Medicine and the Joint venture between the Department of Veterans Affairs and the Department of Defense. All three are available open access online and they're worth reading. If you haven't read the ACPs clinical practice guidelines of the management of insomnia, I highly recommend that you do. It's fairly quick and easy to read and provides an excellent overview of the literature as well as the pros and cons of different management options. Like other insomnia guidelines it strongly recommends the use of

behavioral modification and cognitive behavioral therapy as the initial treatment option for chronic insomnia. It also recommends that patients be part of the management decision and that they fully understand the potential harms of using prescription medications.

Let's explore behavioral modifications a little closer. Life's responsibilities and stressors make it very easy to sacrifice sleep and sleep is definitely been deprioritized in our society. We all need to make a sleep a priority especially those with chronic sleep disorders. There are several healthy sleep habits that should be adopted by everyone and particularly those with chronic insomnia. There are numerous patient focused materials that you can download for your insomnia patients for free and I recommend that you discuss these concepts with our patients.

It really doesn't take very long and to improve sleep health what we really need to focus on is regimenting a sleep/wake cycle, optimizing their sleep environment, avoiding or at least limiting naps, reducing or eliminating alcohol, limiting the use of caffeine and absolutely avoiding it in the afternoon or later, obtaining regular exercise definitely helps with sleep onset and continuity, limiting light exposure in the evening because bright light suppresses melatonin onset. Bright lights in the morning, dim lights in the evening. That includes limiting screen time or at least using a night filter that most screens have built into them now. Then preparing our body, mind and the bedroom for sleep.

Sleep hygiene refers to healthy sleep behavior and activities that promote an optimal sleep/wake cycle. Again, these should be adopted by everyone and need to be stressed to your insomniacs. The bed should only be used for sleep so when we get into bed we are conditioned to sleep. Doing other activities in bed like watching TV or reading can confuse this association and create a dysfunctional sleep relationship. Again, the most important aspect of healthy sleep is to maintain a regimented sleep/wake cycle where we go to bed and wake up at the same time every day. We also need to avoid behavior that promote wake and embrace behaviors that help prepare our bodies and minds for sleep. Nicotine, caffeine, and light all promote wake so we need to avoid these as much as possible in the evening. In addition, to our circadian rhythms that regulate when we should be awake and when we should be asleep, sleep also is facilitated by external sleep drives. Basically, the longer we're awake and the more calories we burn, the sleepier we get so not surprisingly exercise improves sleep onset and sleep continuity. It's also stimulating so you can't do it within three to four hours of sleep.

We have to remember that the accumulative sleep drive helps us fall asleep so napping diminishes that sleep drive and makes it harder for us to fall asleep when we do go to bed. Naps by themselves are not a bad behavior but if you have insomnia, they can absolutely be detrimental, they should be avoided.

The concept of stimulus control is to create healthy associations between the bed and sleep and to promote a faster sleep onset and better sleep continuity. Like other behaviors sleep is susceptible to training and as we discussed in the sleep hygiene slide, the bed should only be used for sleep and intimacy and we need to break associating being in bed with doing anything else. This includes being awake because of insomnia. If you've ever had insomnia, you know how frustrating it can be. That frustration just makes

it that much harder to fall asleep. It creates a negative conditioning response when insomniacs will be going to associate being in bed with being awake and being frustrated.

If you haven't fallen asleep within 30 minutes, instead of laying there frustrated get out of bed, engage in some non-stimulating activity in dim light and then go back to bed only when you're sleepy. This will limit your total time in bed, it's better to have good sleep for a shorter duration than it is to lay in bed awake all night. We also need to prepare our minds for sleep so instead of ruminating on life stressors the idea is to perform simple realization, meditation or even light stretching prior to going to bed which has all been shown to improve sleep onset.

In my experience, sleep restriction and gradual expansion is the most effective treatment for insomnia, far better than any medication. What is it and why does it work so well? We have to go back to the concept of good sleep where a person falls asleep relatively quickly, stays asleep, has normal sleep architecture and then wakes up refreshed. How does all this happen? We have to go to bed at the time our circadian rhythm dictates that it's time to be asleep and we need enough sleep drive to help us fall asleep and we need to remain asleep for a sufficient amount of time to benefit from sleeps restorative properties.

Often patients will say that they lay in bed for hours unable to fall asleep. Like I mentioned, that just leads to frustration and propagates more insomnia. The idea of sleep restriction is to go to bed or to delay bedtime until you're tired enough to fall asleep quickly. I start by asking when a patient has to wake up for the purposes of this exercise, let's say that they have to wake up at 6 a.m. Set this as their fixed wake up period that they have to adhere to every day no matter what. Then determine what time they go to bed and how long it normally takes them to fall asleep. Try to determine what time they actually fall asleep each night, not necessarily the time they go to bed.

For example, if they go to bed at 11, and they typically lay in bed for 60 to 90 minutes then you can say that they're probably asleep by 12:30 every night. Instead of continuing to go to bed at 11 and getting frustrated that they can't fall asleep tell them to delay bedtime until 12:30 or even 1:00. Remember that they have to get out of the bed at 6 a.m. You might be asking why would I be recommending that a patient only attains five, five and half hours of sleep a night when we know that he needs seven to eight and I just had a whole lecture on the detrimental effects of sleep dep. Right now, all we're worried about is sleep onset, sleep continuity. We'll worry about sleep duration later.

The idea is to have them be able to fall asleep and stay asleep. Once we fix that we can try to achieve getting more sleep. Having patients keep a log or a diary of their progress, when they can go to bed, let's say you have your set bedtime at 12:30. When they can go to bed at 12:30, and reliably fall asleep in 20 minutes then they can start advancing the time they go to bed by 15 minutes. In this case, once they've mastered 12:30, they can start going to bed at 12:15 and then at 12 and so on and so forth. I typically advance patients one increment per week. The ultimate goal is to have their bedtime be about eight hours before they have to wake up for school or for work and to be able to fall asleep within 15 to 30 minutes after they try to go to bed and of course, sleep throughout the night. I promise you that this works in the majority of patients and does not require

medications and you can accomplish with only one to two office visits. It takes commitment.

In this example the patient has to wake up at 6 a.m. The optimal bedtime would have been 10 p.m. Remember, they were going to bed at 11 so they were already sleep deprived and we've taken them up to 90 minutes to fall asleep, so they weren't falling asleep till 12:30. They were getting five and a half hours of sleep which is two and a half hours of sleep less than we need and it's two and a half hours of sleep that we have to slowly advance in that patient. At 15-minute intervals it's going to take ten weeks to accomplish this. As I said, this is simple to do but it does take commitment of our patients. If you can fix a long-term disorder in ten weeks without the use of medications, then I say that's a huge win.

Let's discuss cognitive behavioral therapy for insomnia. CBT-I is without question the best way to treat chronic insomnia and it's recommended as first-line therapy by all published guidelines. In reality it's nothing more than we've just been talking about but it's delivered in a formal manner by an expert in sleep behavior disorders.

It combines cognitive therapy strategies with education about sleep regulation and hygiene, stimulus control, mindfulness, relaxation, and methods to counteract the arousal threshold. It also utilizes sleep restriction therapy that we just discussed. Most programs typically take four to eight sessions with a behavioral sleep medicine provider. While very effective, it's pretty resource intensive, it's not covered by many insurances and there's a limited availability of insomnia specialists. The guidelines can say that everyone with insomnia should undergo CBT-I but the reality is that this can't happen. However, I'm hoping that by the end of this lecture you realize that you can provide sufficient therapy for many of your patients and reserve CBT-I for those who can't be fixed with more conservative measures.

Because of the paucity of behavioral sleep medicine specialists several mobile platforms have been developed that can deliver the fundamental of CBT-I. Obviously, these platforms are not as effective as a face-to-face visit, but they're widely available, they're convenient and they're often preferred by patients. Most are free and overall, they appear to be very beneficial for our patient.

CBT-I is the preferred treatment for insomnia because it works. There have been countless studies showing its benefits and it has been consistently shown to be superior to prescription sedative products.

I thought it would be important to cover some over the counter sleep aids because they are commonly used and often abused by patients. While not necessarily an over-the-counter sleep aid, alcohol is the most common self-treatment for insomnia and it's frequently used in conjunction with other sleep aids or prescription sleep mediations. Why is it so commonly used? Because it helps people fall asleep. Alcohol decreases sleep latency meaning it helps people fall asleep faster and it causes the perception of better sleep continuity. However, alcohol is not an effective sleep aid. First, while it does improve sleep onset it only does so for the first three to four hours of sleep. In the latter half of the night alcohol causes more sleep fragmentation and more nocturnal

awakenings. Alcohol alters normal sleep architecture meaning that they may be asleep but they're not getting normal sleep. These factors can often contribute to nonrestorative sleep and a dose dependent relationship meaning the mor alcohol you drink, the faster you fall asleep but the more fragmented your sleep becomes. Alcohol can obviously precipitate other underlying comorbid conditions especially sleep apnea so given this, alcohol should not be encouraged as a treatment of insomnia.

Nearly a quarter of adults intermittently use over-the-counter sleep aids and approximately 14% of adults use them regularly. The prevalence increases with increasing age, which is unfortunate because the side effects often increase with increased age. One study found that almost half of those over the age of 60 use some form of over-the-counter agent to help them fall asleep. One large study found that nearly two-thirds of patients who sought medical care for their insomnia were using an over-the-counter sleep aid.

Most of these agents contain antihistamine and despite what all those commercials suggest, they are not an effective way to promote good sleep. Remember sleep requires different neural chemicals that both turn off wake and turn on sleep. Antihistamines don't do either of those. Histamine is not a major wake promoter transmitter and antihistamines don't stimulate sleep receptors. They do cause some degree of sleepiness but antihistamines primarily block alertness and vigilance. Taking them does shorten sleep latency for most individuals meaning you can fall asleep quicker but they do disrupt normal sleep architecture with the reduction in both REM sleep and slow wave sleep. This can lead to nonrestorative sleep and impairment in next day wakefulness and cognitive performance. In short, antihistamines may help you fall asleep quicker but it disrupts normal sleep and leads to more daytime impairment than insomnia does.

Melatonin is a naturally occurring hormone that helps regulate sleep cycling in humans. Melatonin supplements can actually be helpful. One of the problems is that the studies exploring its benefits have shown very mixed results. That's probably because that all other treatments for insomnia drugs alone won't be effective unless there is a concomitant focus on behavior modifications. Another reason is that melatonin is an unregulated supplement so you never know what you're getting from those pills. Plus, there is a great debate over what the optimal dose is. Higher doses do have more soporific properties but they also lead to significant phase shifting in the circadian rhythm. That means that I do use melatonin in my practice. I will primarily use it if I'm trying to phase shift someone's sleep/wake cycle. Imagine a teenager who has a hard time falling asleep at a reasonable hour during the school year. Usually when I'm trying to phase shift somebody, or as an alternative to prescription medications. When I do recommend melatonin, I primarily limit to the pharmaceutical quality extended-release formulations which are available over-the-counter.

The last section of this talk will cover prescription sleep aids. I purposely left this to the end because in my opinion, this should be used as the last resort and for most patients only used at a temporary measure and as a bridge to more conservative therapy. Prescription sedative-hypnotics do work. They help people fall asleep faster and some people can stay asleep longer with these pills. They work right away and they're effective

in most individuals and most people incorrectly think that they will work without any real effort or changes in their behavior. Unfortunately, that's what makes them so attractive an often sought out by patients. The problem with prescription sleep aids is that they don't work as well as most people think. They can definitely lead to psychological dependencies, where many patients convince themselves that they can't sleep without them and they often do not promote normal sleep and many lead to next day sleepiness and impairments. Most of all, they do into address the cause of insomnia and only treat the symptom.

They definitely have a place in clinical practice. I can say that in my time practicing sleep medicine I only have a handful of people that I treat with long-term pharmacotherapy. The overwhelming majority of my patients are successfully managed without the habitual use of these drugs including those who were chronically using sleeping pills when I first met them. When I do prescribe sleeping pills I do so for short periods of time and often as a bridge or jumping start to behavioral modifications or if they have relapse with insomnia down the road, I'll give them a short course of sleeping pills to help the reestablish a normal sleep cycle and break that pattern of insomnia. The pills I use are usually the ones specifically intended for sleep, which I'm going to cover in the next several slides.

There are four main classes of soporific medications that largely depend on the neurotransmitter or the receptor that they target that either promote sleep or block wake. These include GABA or melatonin receptor agonists, antihistamines and orexin antagonists. I'll discuss all of these in the next few slides.

Nonbenzodiazepine receptor agonists are the most commonly prescribed sleep aids. These are the Z drugs. GABA is our primary sleep neurotransmitter and these agents primarily target the GABA A alpha receptor complex which is primarily responsible for sleep. Eszopiclone is the longest acting of this group and has a wider range of GABA A alpha subunit affinity which naturally promote both sleep onset and sleep continuity. It also has more benzo-like activity than the shorter acting agents which gives it some weak antidepressant and anxiolytic proper sites. These agents are relatively safe and effective however misuse and abuse are very common. They can all-cause next day cognitive impairments, and they have been associated with the potential for precipitating complex sleep behaviors which is led to a black box warning for this entire class.

Like both naturally occurring and supplemental melatonin, melatonin receptor agonists help regulate sleep cycling and circadian rhythmicity and can shorten sleep latency in most patients. Unlike most over-the-counter melatonin supplements, these agents have better pharmacokinetics and potency. They're also unscheduled medications with low abuse potential and have a relatively short elimination half-life.

Orexin or hypocretin is a major wake promoting agent in the CNS. Suvorexant is a relatively new and unique class of sleep medications that promote sleep by suppressing the wake drive mediated by orexin. Orexin causes wakefulness. This class of drugs blocks the orexin so it blocks the wake promoting substance of orexin. It's been shown to improve sleep onset latency and sleep efficiency and decrease nocturnal awakenings. It does have a relatively long elimination half-life which can lead to residual daytime

sleepiness especially in the elderly. Lemborexant is another orexin receptor antagonist that was recently improved for insomnia. I personally haven't tried this one yet in my clinical practice but the initial Phase III trials found that it also improved sleep onset and sleep continuity. A third DORA, daridorexant, is expected to be approved in the next few months (now approved as of January 10, 2022). The initial clinical trials have shown that it's highly effective and similar to the other two but because it has a shorter elimination half-life compared to the older agents in this class, they should have less impact on next day function.

Doxepin has been around for a long time but was relatively recently repurposed as a sleep aid. It's somewhat unique in that it's a tricyclic antidepressant with antihistamine properties and its effect as an antihistaminergic sleep aid or as an antidepressant are somewhat dose dependent. For the purposes of sleep, lower doses are used to block the wake and alerting activity of histamine. Unlike most sleep aids, it's unscheduled and has a low risk for abuse but it does have a relatively long elimination half-life and it's not universally effective.

While those are the medications specifically intended for sleep, several agents are often prescribed in an off-label fashion as first and second-line therapy for insomnia. Because they're commonly used for insomnia, I felt it was important to discuss these. The four most common classes of agents are shown on this slide and the four most commonly used specific agents are trazodone, clozapine, Xanax and Seroquel.

These agents are commonly used and they have a side effect of causing sleepiness. Not only is there little to no evidence showing the benefit when used specifically for sleep, there are consistent data showing that these agents are often harmful for our insomniac patients. While I'm not describing their efficacy in other disease processes, the evidence is compelling enough for published guidelines to make a strong recommendation against their use solely for insomnia. These agents often have long elimination half-lifes, they disrupt normal sleep architecture and commonly cause next day impairment and I would urge you not use these as a treatment for insomnia.

I wanted to specifically call out trazadone because despite several recommendations against its use for insomnia, it's still commonly prescribed. In fact, a study I saw yesterday showed that following the initiation of the COVID pandemic, trazadone is now the most commonly used sleep aid in America with a 40% market share for a drug that has strong recommendations against its use. It has no measurable effect in a third of patients meaning that a third of people don't fall asleep better because of it. It leads to unacceptable side effects in another third so right off the bat, it's not efficacious in two-thirds of patients. There are better and more effective medications for insomnia. Plus, priapism is a real concern and I have literally never met anybody on trazadone who was counseled about their risk for priapism when given that first prestation. To put it simply, it doesn't work in the majority of patients, there are better drugs out there and you just shouldn't use it for insomnia.

Going back to why this matters, and why it should matter to internists of people in clinical practice insomnia is common. It's often overlooked, it can cause or contribute to numerous comorbid conditions and it's worth your time and effort to look for it and

address it in your clinical practices. The two most important things for you to take away from this talk should be one, that insomnia can't be effectively treated without behavioral change, patients have to re-brace healthy sleep habits which are the key to long-term success. Number two, medications, whether they're over-the-counter or prescription are not an effective long-term solution to insomnia. They can absolutely be helpful if used occasionally or for limited periods of time but for the majority of patients habitual use can actually be detrimental. If you do use an over-the-counter agent, use high-quality melatonin and if you prescribe a sleep aid, use ones that are specifically designed for insomnia and try to limit their duration of use.

In this portion of the program we'll discuss obstructive sleep apnea. Specifically, we will discuss the pathophysiology and the adverse physiological effects of sleep disorder breathing. We'll also talk about the epidemiology of sleep apnea and how to recognize it in clinical practice. Finally, we'll briefly discuss the different treatment options.

While sleep apnea is highly prevalent in clinical practice this section of the program was intentionally shortened to avoid overlap with topics that will be covered during the cardiovascular sleep medicine lecture that you'll hear that the end of this program.

What is obstructive sleep apnea and how does it occur? In an oversimplified explanation our airways are kept open by muscle tone. During sleep our muscles relax, including those that maintain airway patency. As a result, we all experience a narrowing of the upper airways during sleep. There is clearly a spectrum of narrowing. Most individuals will maintain sufficient patency to allow for normal breathing. Others will narrow enough to cause turbulent airflow which manifests as snoring and for some, this will lead to a partial or complete obstruction of the airways that limits airflow and results in apneas or hypoxias. There are numerous potential reasons why the airways narrow more or result in airflow obstruction in one person compared to another. It could be due to anatomic differences such as a smaller upper airway or enlarged tongue. It could be due to increase adipose tissue or more collapsibility of the airway structures. These differences are largely influenced by genetics, anatomy, weight, substances that impair airway muscle activity, the amount of physical activity performed during the day, and even how much you sit during the day.

That being said, obstructive sleep apnea is a condition manifested by subluxation of the oral pharynx that leads to recurrent and repetitive airway obstruction during sleep. Closure of the upper airway leads to apneas and/or hypoxias that result in an arousal or awakening. Basically, patients with OSA choke themselves awake repetitively during the night. That sounds bad but interestingly that's not the real problems with sleep apnea.

While sleep apnea results in apneas and hyposthenia's it's the complex of the upper airway closure, ineffective ventilation and arousal from sleep that leads to all the pathophysiologic derangements that result as a consequence of sleep disorder breathing.

Ineffective breathing can lead to a hyper-ventilatory state and intermittent hypoxia. Frequent arousals from sleep alter normal sleep continuity and architecture which lead to

nonrestorative sleep and diminishes the benefits that sleep have on physical and cognitive function and the intermittent arousals with resultant hypoxia lead to an increase in catecholamines and an elevated sympathetic tone that can cause or contribute to cardiovascular disease.

OSA is highly prevalent and it's found in nearly a quarter of the U.S. population. One in five adults has at least mild disease and 1 in 15 has moderate to severe sleep apnea. It's significantly more common among certain populations especially those admitted with atrial fibrillation, heart failure or strokes, and nearly three quarters of elderly people in long-term care facilities have sleep disorder breathing. Despite how prevalent it is and how much it reverses and impacts health and quality of life, it remains underdiagnosed and significantly undertreated. Several studies have concluded that less than 5% of those with sleep apnea are receiving therapy and significantly fewer are sufficiently treated. There are several factors contributing to this. One common reason is diagnostic profile. Many still believe that OSA is a disease limited to older overweight individuals. While the presence of sleep apnea does increase with increasing age and increasing BMI, it clearly occurs in younger persons of normal weight. This profiling unfortunately leads to many missed diagnoses.

Another common reason why OSA is underdiagnosed is that many patients and providers don't fully understand treatment options or their benefits and as such, may avoid exploring this diagnosis.

That being said, how do we recognize this clinically? There are several features that make underlying OSA more likely and should help you identify it in your patients. Perhaps the most commonly recognized symptom is snoring. The majority of patients with sleep apnea do snore. However, not everyone who snores has sleep apnea and not everyone with sleep apnea snores.

Sleep apnea leads to daytime sleepiness but there are numerous other reasons why a patient many be somnolent which may cause them to ignore the symptom or lead providers to dismiss sleep apnea as a potential cause. In addition, somnolence is a subjective complaint and as such, it's hard to quantify, qualify or explain. One person's fatigue could be another person's sleepiness and could be another person's impairedness [phonetic].

Witnessed apneas are another commonly associated features of sleep apnea however the diagnostic accuracy of witnessed apnea is only 52% meaning that the presence or absence of these events in isolation is of limited value. Sleep apnea also causes nocturnal awakenings and arousals and leads to restless and nonrestorative sleep. Other common sleep complaints include being sweaty at night, having a dry mouth upon awakening and experiencing nocturia. In my opinion there's are the most common and consistent complaints that should make you think of sleep apneas.

Being overweight increase the probability for sleep apnea and obesity is the single greatest identifiable risk factor. However, remember that sleep apnea does occur in those with normal BMIs. There are certainly craniofacial patterns that increase the likelihood of sleep apnea such as retro or micrognathias or macroglossia. Finally, you should consider

sleep apnea in those with common comorbid conditions or consequential medical disorders including GERD, hypertension, diabetes, depression, prior stroke or those with erectile dysfunction especially when it occurs at a younger age.

Any of those features in isolation should not by itself raise concerns for sleep apnea, rather you should look at the constellation of these symptoms when determining the likelihood that your patient has sleep disorder breathing. Likewise, a patient does not need to have all of these features to have sleep apnea. Finally, even if they did, you can't establish a diagnosis of OSA based on symptoms alone. When they have compatible symptoms, I strongly recommend sleep testing.

The STOP BANG is a validated clinical screening tool to help you recognize sleep apnea. The pneumonic is spelled out for you on the slide. The more positive features the more likely a patient has sleep apnea. If they have it, further testing is recommended, especially those who meet two STOP or three STOP BANG criteria. While it's a useful tool, remember that it primarily identifies disease in a very classic population. That is, it's better at identifying sleep apnea in middle aged overweight men with typical symptoms. What it's not good for is identifying OSA in younger, thinner patients with less typical presentation.

OSA is common and it leads to several physiologic or pathophysiologic consequences that adversely impact both health and quality of life. There are several common comorbid conditions that have a proven or strongly associated causal relationship with sleep apnea. In fact, prior studies have established that OSA occurs with or causes or contributes to seven of the ten most common outpatient diagnoses seen in clinical practice.

We can see on this slide that sleep apnea is associated with numerous conditions we commonly see every day. To help you understand a few of these associations, I'd like to briefly discuss their shared prevalence and overlapping pathophysiologies.

Headaches are commonly associated with sleep apnea. At least 4% of those with OAS report recurrent headaches and OSA is observed in at least one-fifth of those with chronic headache disorders. This may be due to CO2 retention from nocturnal hyperventilation that causes an increase in cerebral blood flow. It could be from stress and anxiety that result from unrefreshed sleep or a manifestation of craniofacial patient from bruxism and clenching that commonly occur with sleep apneas.

Chronic pain and chronic pain syndromes are also more common among those with OSA and share a bidirectional relationship that we previously discussed. OSA disrupts normal sleep architecture and decreases the amount of slow wave sleep that occurs. Slow wave sleep is when we have the greatest benefit with regards to muscle restoration and recovery from injuries. Less slow wave sleep leads to more pain and pain medications, especially opioids, commonly lead to obstructive and central sleep apneic events.

Obstructive sleep apnea is commonly associated with anxiety and depression where anxiety and depression are more common manifestations of core and nonrestorative sleep and sleep apnea has been found to be an independent risk factor for the future development of depression.

As mentioned nocturia is a common features of sleep apnea. This is the result of increase in efforts to breathe against a closed glottis that result in transient increases in pulmonary vascular pressures and arterial stretch. That strain on the atria lead to - - results nocturia. This is part of the reason why sleep apnea is commonly identified with heart failure and atrial fibrillation. In fact, sleep apnea is now the most common identifiable cause of AFib and has clear associations with outcomes and the response to therapy.

As I mentioned before, recurrent episodes of hypoxia and nocturnal arousals cause an increase in catecholamines and an elevated sympathetic tone. This leads to endothelial dysfunction and vasculopathies that independently increase the risk for pulmonary vascular disease, hypertension, myocardial infarction, and stroke. Finally, obstructive sleep apnea leads to an increase in cortisol and alterations of glucose metabolism that contribute to if not cause diabetes and metabolic syndrome.

Obstructive sleep apnea especially moderate to severe disease warrants treatment and there are several treatment options available. Like most disease processes, the cornerstone of any successful treatment plan is conservative management. With regards to sleep apnea, sleep expansion that results in an appropriate amount of time in bed, weight loss, an avoidance of alcohol or other CNS depressants have all been shown to reduce the frequency and severity of obstructive events. In addition, positional therapy that prevents sleeping on your back can also reduce OSA severity. For some people especially those with borderline or very mild disease these measures may provide reasonable treatment. However, for most individuals those measures will not result in sufficient improvement in the hypopnea index and they should be treated with some form of primary therapy.

Currently there are four options for the treatment of sleep apnea; surgery, oral appliances, hypoglossal nerve stimulation and positive airway pressure. Each has its own strengths and weaknesses and treatment selection should be individualized in order to choose the right therapy for the right patient.

Oral appliances are devices that advance the mandible which helps to prevent subluxation of the tongue, face and collapsibility of the oral pharynx. They're most effective in thinner patients with less severity disease but can provide sufficient therapy even in those with severe sleep apnea.

There are several different surgical options with variable likelihoods of success. Those that involve craniofacial reconstruction are typically more effective options. Hypoglossal nerve stimulation is the newest of the treatment options discussed and can provide a modest reduction in obstructive events among those with moderate to severe disease.

The most widely utilized treatment for sleep apnea is positive airway pressure devices. Whether it's CPAP, APAP, OR BIPAP, positive airway pressure provides a column of air that pneumatically stents open the airways to prevent obstructive events. It's noninvasive and highly efficacious. Unfortunately, it's effectiveness is frequently limited by poor adherence. About 40% of patients meet criteria for regular use or I should say only 40% of patients meet criteria for regular use. Although take that with a grain of salt because

what's defined as regular use is the use of PAP for more than four hours per night for at least 70% of nights. That definition is somewhat arbitrary and is largely insufficient. In fact, if you do the numbers, a person could be considered adherent with CPAP if they use the device for about one-third of the recommended sleep time each week.

If we use a more strict definition of adherence that requires CPAP use on all nights for at least six hours per night, less than a quarter of PAP users would be considered adherent. That doesn't mean that PAP is intolerable at all and several studies have shown that adherence rates of greater than 80% can be achieved with minimal interventions. Regardless, it does tell us that PAP is not the right treatment for all patients and our approach to the care obstructive sleep apnea needs to be individualized.

I would now like to change our focus and discuss restless leg syndrome or Willis Ekbom disease. RLS is a relatively common condition that often goes overlooked in clinical practice. There are several reasons why this condition is underrecognized. Like most sleep disorders, its symptoms are often not reported by patients or explored by providers. More importantly despite its characteristic clinical presentation the symptoms of RLS are often confused with other disorders including peripheral neuropathies, vasculopathies and chronic pain. Because of frequently impaired sleep onset it's often confused for generalized insomnia. Regardless the symptom complex occurs in approximately 10 to 15% of both adults and children with clinically important disease that warrants medical therapy occurring in at least 5% of the population.

The diagnosis of RLS is made clinically based on the presence of four cardinal symptoms. The pneumonic to help you remember these diagnostic symptoms is URGE. Or U for urge to move, R for rest worsens symptoms, G stands for symptoms get better with activity, and E is for symptoms are worse in the evening. Let's explore each of these cardinal symptoms a little further.

As the name implies restless leg syndrome is a condition that causes restlessness or an uncontrollable urge to move because inactivity precipitates symptoms and movement makes them better. These symptoms are often experienced in the legs. However, symptoms are not confined to the legs and can occur in the upper extremities or even the low back which can make identifying RLS more challenging in some patients. In addition, while discomfort is the most prevailing symptom, the description of that sensation if not uniform. Some experience pain or others report cramping, aching, throbbing or paresthesias or just some uneasy feeling. Regardless it's the unpleasant sensation that causes an urge to move. As mentioned, movement lessens symptoms. However, it may not resolve symptoms. This does help differentiate it from other conditions such as claudication.

Symptoms often occur during rest or immobility and long car rides and plane flights can be very challenging for many patients. Finally, RLS follows a circadian pattern where symptoms onset typically occurs in the evening or at night, however, for some patients, symptoms can occur throughout the day especially those with more severe disease or as a result of medical therapy.

RLS can occur at any age. It does affect both adults and children. The typical age onset is

during the fifth decade. It's seen twice as often among women and is significantly more common among those of northern European decent.

Thera are several theories as to the pathogenesis of RLS. The most widely accepted theories are that this is due to abnormal CNS dopaminergic activity, a dysregulation of iron processing in the central nervous system and microvascular disease. Likely it's probably due to some combination of all three or even more likely it's a common manifestation of several overlapping disease processes. Regardless these theories do help us understand some of the common associations with RLS. For example, RLS symptoms are more common to occur in those with an iron deficiency. This does not necessarily mean the person has to be anemic, and ferritin levels of less than 50 can precipitate symptoms in susceptible individual. It's also more common in those with diabetes, peripheral vascular disease, venous insufficiency, and chronic kidney disease supporting the theory that this may be associated with microvascular disease. It's highly prevalent among those with Parkinson's disease and has been associated with more insomnia and worse outcomes among these patients. Not surprisingly the most widely used medications for RLS are antiparkinsonian dopaminergics.

It's not uncommon among with untreated sleep apnea, and interestingly enough treatment for sleep apnea typically resolves RLS symptoms. It can also be precipitated by antidepressants and antihistamine medications and it occurs in over 20% of pregnancies and is associated with worse maternal fetal outcomes.

There are several treatment options for patients with RLS. As mentioned, iron should be measured in all patients and replaced in those with ferritins less than 50 as this may very well resolve symptoms without further management. The most common agents used to treat RLS are the dopaminergic ropinirole and pramipexol. These can be highly effective but need to be balanced against side effects. Gabapentin and pregabalin are also commonly used and can be quite effective. Opioids and benzos are listed in the RLS treatment guidelines and can be effective, however it would recommend that you reserve those for severe and refractory cases only.

Finally, nonpharmacologic therapies may also provide relief for your patients. Massage, stretching and yoga have all been shown to be somewhat helpful although they've had mixed results in clinical trials. We previously published a trial that found significant benefits with the use of sequential compressive devices typically used to prevent DVTs in inpatients although those are hard to get for some people.

My advice with regards to the treatment of RLS is this; first try to address any precipitating issue such as a triggering medication, iron deficiency or untreated sleep apnea. Then try to determine how distressing those symptoms really are to a patient. While 10 to 15% of people experience RLS symptoms most have mild disease. Even if they meet criteria and may not really matter, if they're symptoms are infrequent or don't cause significant distress, the side effects of medication may not be justified. I tend to limit therapy to those whose symptoms impair sleep onset, limit social interactions or cause significant emotional distress.

Thank you very much for this opportunity to speak with you.