



PRESENTING TO

## Behavioral and Pharmacologic therapies for sleep disturbances

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#### Objectives

- Correctly identify and diagnose insomnia as well as other sleep disturbances
- Become familiar with risk factors, comorbidities, and contributing factors that increase the incidence of insomnia
- Understand options for behavior and pharmacologic therapies

#### Insomnia

- Insomnia is one of the most common complaints generating over 5 million office visits per year in the United States alone.
- Frequently coexists with other medical, psychiatric, and or neurological disorders.
- Can also be due to acute stress, medications, substance use, poor sleep habits, or change in sleep environment.
- Insomnia is especially common in older adults, women, unemployed, divorced, widowed, separated, and of lower socioeconomic status.
- Types of insomnia include: Short term and Chronic





#### Clinical Features

- Difficulty initiating or maintaining sleep.
  - Most well-rested adults take about 10-20 minutes to fall asleep and spend less than 30 minutes awake during the night.
  - Patients with insomnia usually take 30 or more minutes to fall asleep and spend over 30 minutes awake during the night.
- Compromised daytime function
  - fatigue, poor attention and concentration, social, job, educational difficulties, mood disturbance, daytime sleepiness, low energy and motivation, increased accidents, behavioral problems, ongoing worry about sleep.



- Older age
- Female gender (especially peri and postmenopausal)
- Previous episode of insomnia
- Family history of insomnia
- Predisposition toward easy arousal from sleep
- An exaggerated sleep disruption response to stressful events
- Psychiatric disorders



#### Comorbidities/Contributing Factors

- Insomnia commonly coexists with psychiatric and medical disorders.
- Medications that can contribute to insomnia.
- It is difficult to assess whether the insomnia is primary (without comorbidities) or secondary (i.e., associated with a conditions such as anxiety).
- Successful treatment requires attention to both insomnia and comorbidities.



#### Psychiatric Disorders and Insomnia

- Approximately half of patients with chronic insomnia have a psychiatric disorder.
- The majority of patients with a psychiatric disorder have insomnia.
- Studies have shown that there is a significant increased risk of developing a psychiatric disorder (particularly MDD) within one year when compared to those without insomnia.
- Depression Insomnia is one of the diagnostic symptoms.
   Up to 80% of depressed patients have insomnia. Early morning awakening is a hallmark symptom.



#### Psychiatric/Medical Conditions

- Anxiety The majority of patients with anxiety have insomnia
- Substance use
- Post traumatic stress disorder one review reported 70-90% of patients with PTSD have insomnia. Associated with nightmares, fear of falling asleep.
- Medical conditions Pulmonary disease, hypertension, diabetes, cancer, chronic pain, heart failure, rheumatologic disease, benign prostatic hyperplasia, menopause.

## Medications Contributing to Insomnia

- CNS stimulants caffeine, methylphenidate, amphetamine, and modafinil.
- Respiratory stimulants-theophylline
- Appetite suppressants
- MAOI antidepressants, SSRIs (fluoxetine) in 5-35% of patients
- Norepinephrine and dopamine reuptake inhibitors such as bupropion are associated insomnia in 5-20% of patients.
- Beta blockers can produce sleep-onset insomnia, increased awakening, and dreams.
- Glucocorticoids such as prednisone contribute to insomnia in 50-70% of patients.
- Alcohol, tobacco
- OTC medications such as nasal decongestants





## Sleep Disorders that Contribute to Insomnia

- Sleep apnea- approximately 50-55% of patients with sleep apnea report insomnia.
- Restless legs syndrome characterized by an urge to move the legs, sensations that are described as creeping, crawling, itching, or jitteriness in the legs. It is estimated that 85% of patients with RLS have difficulty falling asleep.
- Circadian rhythm sleep-wake disorder Jet lag causes insomnia with an acute course. Night shift work is also commonly associated with insomnia.



#### Diagnosis of Insomnia

- Types of Insomnia
  - Short term few days to a few weeks (Less than 3 months) and usually occurs with an identifiable stressor.
  - Chronic Occurs three times per week and persists for at least 3 months. (Has taken the place of primary, secondary, and comorbid insomnia according to the third edition of the International Classification of Sleep Disorders (ICSD-3).)

#### Diagnosis of Insomnia

- Difficulty initiating or maintaining sleep.
- Occurs despite adequate time and environment for sleep.
  - Early morning awakening
  - 30+ minutes to fall asleep and over 30 min awake during the night.
- Compromised daytime function Required for the diagnosis of insomnia.
- Insomnia is often persistent and/or recurrent.





#### Common Comorbidities

- Insomnia commonly coexists with medical and psychiatric disorders
- Hard to distinguish or draw firm conclusions about the causality between insomnia and comorbidities. Insomnia is no longer considered a secondary condition.
- Successful treatment requires attention to both insomnia and comorbidities.



#### Differential Diagnosis

- Short sleep duration Some people require less than 7 hours of sleep on average.
- Chronic sleep insufficiency insufficient opportunity to sleep.
- Delayed sleep-wake phase disorder circadian sleep-wake rhythm disorder
  - "night owl" More common in adolescence.
  - Sleep logs show a persistent delayed sleep (often midnight or later) wake cycle on weekdays and weekends with curtailment of sleep time due to forced awakenings.

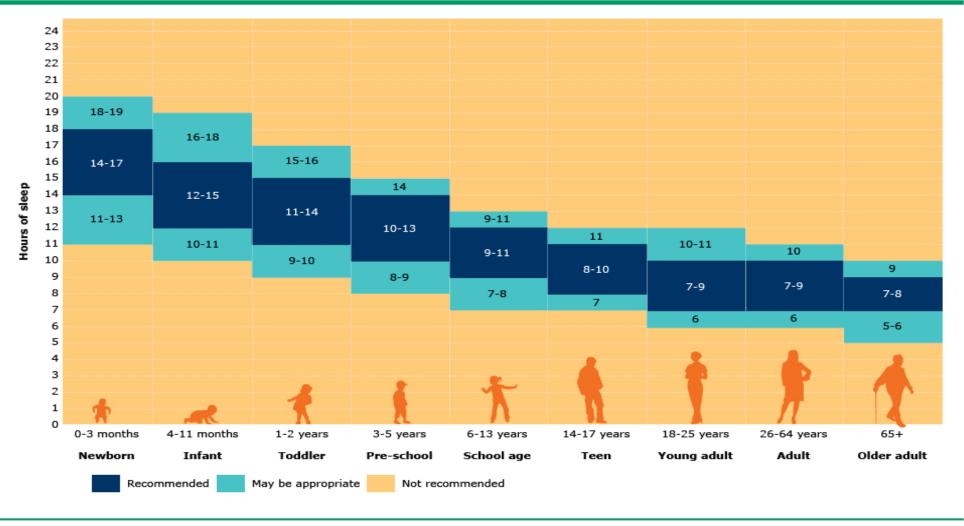


#### Differential Diagnosis cont.

- What happens when they are on vacations or weekends when they can go to sleep and wake up when they want to?
- By contrast, patients with insomnia have difficulty falling asleep any time of night.
- Advanced Sleep-wake phase disorder advanced circadian phase
  - Tend to fall asleep early and wake up early morning even if they forced themselves to stay awake until late evening. Most common in older adults.
  - \*\*Can be distinguished from insomnia by asking patients what happens if they allow themselves to go to bed early.

#### Sleep duration recommendations by age from the National Sleep Foundation\*





<sup>\*</sup> These recommendations are very similar, but not identical to those from the American Academy of Sleep Medicine (AASM).[1,2]

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Paruthi S, Brooks LJ, D'Ambrosio C, et al. Recommended amount of sleep for pediatric populations: A statement of the American Academy of Sleep Medicine. J Clin Sleep Med 2016; 12:785.

Consensus Conference Panel, Watson NF, Badr MS, et al. Recommended amount of sleep for a healthy adult: A Joint Consensus Statement of the American Academy of Sleep Medicine and Sleep Research Society. J Clin Sleep Med 2015; 11:591.



#### Sleep History and Sleep Diary

- Sleep history details about awakenings, duration of awakenings, duration of the insomnia, sleep times, nap times, nap lengths, sleep environment, daytime sleepiness, fatigue.
- Sleep diary one to two weeks. Records sleep times, sleep problems, and subjective sleep quality. Helps prevent recall errors.
- Screening tools tracks changes in chronic insomnia.
- Sleep questionnaires Pittsburgh Sleep Quality Index and Sleep problems questionnaire.

#### Consensus Sleep Diary



	Sample					ID/Name:		
Today's date	4/5/11							
1. What time did you get into bed?	10:15 PM							
2. What time did you try to go to sleep?	11:30 PM							
3. How long did it take you to fall asleep?	55 min							
<ol> <li>How many times did you wake up, not counting your final awakening?</li> </ol>	6 times							
5. In total, how long did these awakenings last?	2 hours 5 min							
6a. What time was your final awakening?	6:35 AM							
6b. After your final awakening, how long did you spend in bed trying to sleep?	45 min							
6c. Did you wake up earlier than you planned?	X Yes  □ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No	☐ Yes ☐ No
6d. If yes, how much earlier?	1 hour							
7. What time did you get out of bed for the day?	7:20 AM							
8. In total, how long did you sleep?	4 hours 10 min							
9. How would you rate the quality of your sleep?	☐ Very poor  ☑ Poor ☐ Fair ☐ Good ☐ Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good	Uery poor Poor Fair Good Very good
10. How rested or refreshed did you feel when you woke up for the day?	☐ Not at all rested ☑ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	☐ Not at all rested ☐ Slightly rested ☐ Somewhat rested ☐ Well-rested ☐ Very well-rested	□ Not at all rested □ Slightly rested □ Somewhat rested □ Well-rested □ Very well- rested
11a. How many times did you nap or doze?	2 times							
11b. In total, how long did you nap or doze?	1 hour 10 min							
12a. How many drinks containing alcohol did you have?	3 drinks							
12b. What time was your last drink?	9:20 PM							
13a. How many caffeinated drinks (coffee, tea, soda, energy drinks) did you have?	2 drinks							
13b. What time was your last drink?	9:20 PM							
14. Did you take any over-the- counter or prescription medication(s) to help you sleep?  If so, list medication(s)	☐ Yes ☐ No Medication(s): Relaxo-Herb Dose: 50 mg	☐ Yes ☐ No Medication(s): Dose:						
dose, and time taken	Time(s) taken: 11 PM	Time(s) taken:						
15. Comments (if applicable)	I have a cold							



#### Pitts

sb	urgh Sleep Quality Index	c (PSQI) questionnaire							
am	e:								
<b>)#</b> :			Date:		Age:				
ie p	FRUCTIONS: The following questi past month. se answer all questions.	ons relate to your usual sleep habits d	uring the past month <i>only</i> . Your answer	s should indicate the most accurate repl	y for the <i>majority</i> of days and nights i				
1.	During the past month, when ha	ve you usually gone to bed at night?							
2.	During the past month, how long NUMBER OF MINUTES	g (in minutes) has it usually take you to fall asleep each night?							
3.	During the past month, when ha	ve you usually gotten up in the morning	9?						
4.	During the past month, how man	ny hours of <i>actual sleep</i> did you get at n	ght? (This may be different than the nu	mber of hours you spend in bed.)					
VS lea	<b>FRUCTIONS:</b> For each of the remains answer all questions.	aining questions, check the one best re	sponse.						
5.	During the past month, how often have you had trouble sleeping because you	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week				
	(a)cannot get to sleep within 30 minutes								
	(b)wake up in the middle of the night or early morning				0				
	(c)have to get up to use the bathroom								
	(d)cannot breathe comfortably								
	(e)cough or snore loudly								
	(f)feel too cold								
	(g)feel too hot			-					
	(h)had bad dreams (i)have pain								
	(j) Other reason(s), please describe:								
	How often during the past month have you had trouble sleeping because of this?								
		Very good	Fairly good	Fairly bad	Very bad				
6.	During the past month, how would you rate your sleep quality overall?								
		Not during the past month	Less than once a week	Once or twice a week	Three or more times a week				
7.	During the past month, how often have you taken medicine (prescribed or "over the counter") to help you sleep?								
8.	During the past month, how often have you had trouble staying awake while driving, eating meals, or engaging in social activity?								
		No problem at all	Only a very slight problem	Somewhat of a problem	A very big problem				
9.	During the past month, how much of a problem has it been for you to keep up enough enthusiasm to get things done?								
		No bed partner or roommate	Partner/roommate in other room	Partner in same room, but not same bed	Partner in same bed				
о.	Do you have a bed partner or roommate?								
	If you have a roommate or bed partner, ask him/her how often in the past month have you had	Not during the past month	Less than once a week	Once or twice a week	Three or more times a week				
	(a)loud snoring								
	(b)long pauses between breaths while asleep			0	0				
	(c)legs twitching or jerking while you sleep								
	<ul><li>(d)episodes of disorientation or confusion during sleep</li></ul>								
	(e)other restlessness while you sleep; please describe								



#### Diagnostic criteria for chronic insomnia disorder

Diagno	ostic criteria A-F must be met:
A	The patient reports, or the patient's parent or caregiver observes, one or more of the following:  ■ Difficulty initiating sleep*  ■ Difficulty maintaining sleep¶  ■ Waking up earlier than desired△  ■ Resistance to going to bed on appropriate schedule  ■ Difficulty sleeping without parent or caregiver intervention
В	The patient reports, or the patient's parent or caregiver observes, one or more of the following related to the nighttime sleep difficulty:  Fatigue/malaise  Attention, concentration, or memory impairment  Impaired social, family, occupational, or academic performance  Mood disturbance/irritability  Daytime sleepiness  Behavioral problems (eg, hyperactivity, impulsivity, aggression)  Reduced motivation/energy/initiative  Proneness to errors/accidents  Concerns about or dissatisfaction with sleep
С	The reported sleep-wake complaints cannot be explained purely by inadequate opportunity (ie, enough time is allotted for sleep) or inadequate circumstances (ie, the environment is safe, dark, quiet, and comfortable) for sleep
D	The sleep disturbance and associated daytime symptoms occur at least three times per week
E	The sleep disturbance and associated daytime symptoms have been present for at least three months
F	The sleep/wake difficulty is not better explained by another sleep disorder

<sup>\*</sup> In general, delays of >20 minutes for children and young adults and >30 minutes for middle-aged and older adults are considered clinically significant.

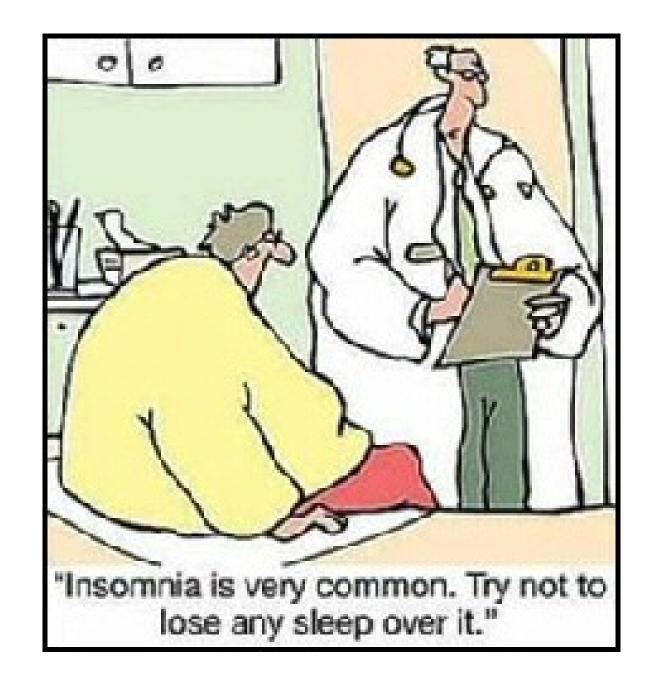
 $\Delta$  In general, waking up >30 minutes before normal awakening time is considered clinically significant.

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<sup>¶</sup> In general, periods of awakening in the middle of the night of >20 minutes for children and young adults and >30 minutes for middle-aged and older adults are considered clinically significant.







#### **Testing**

- Polysomnography indicated for a sleep disorder such as obstructive sleep apnea is suspected. Some symptoms of sleep apnea include treatment resistant insomnia, daytime sleepiness. The prevalence of sleep apnea may be as high as 90 percent.
- Actigraphy is important adjunct to sleep diaries when a circadian sleepwake rhythm disorder is suspected or when an objective estimation of total sleep time is needed. Actigraphy is a noninvasive way to measure sleep parameters over a period of days to weeks. It is worn like a wristwatch.
- Consider a referral when insomnia does not respond to therapy and in patients that report profound daytime sleepiness or symptoms of sleep apnea, narcolepsy, parasomnias, circadian rhythm sleep-wake disorder, or periodic limb movements.



#### Adverse Outcomes

- Quality of life fatigue, sleepiness, confusion, tension, anxiety, and depression.
  - More medical complications
  - Less promotions, more sick time, poor work performance.
- Cognitive function and performance
- Self-medication over the counter remedies, higher risk for substance abuse (especially alcohol).
- Increased suicidal thoughts and behaviors.
- Cardiovascular risk and mortality
- Increased risk for diabetes. Treatment of insomnia has been shown to improve glycemic control.



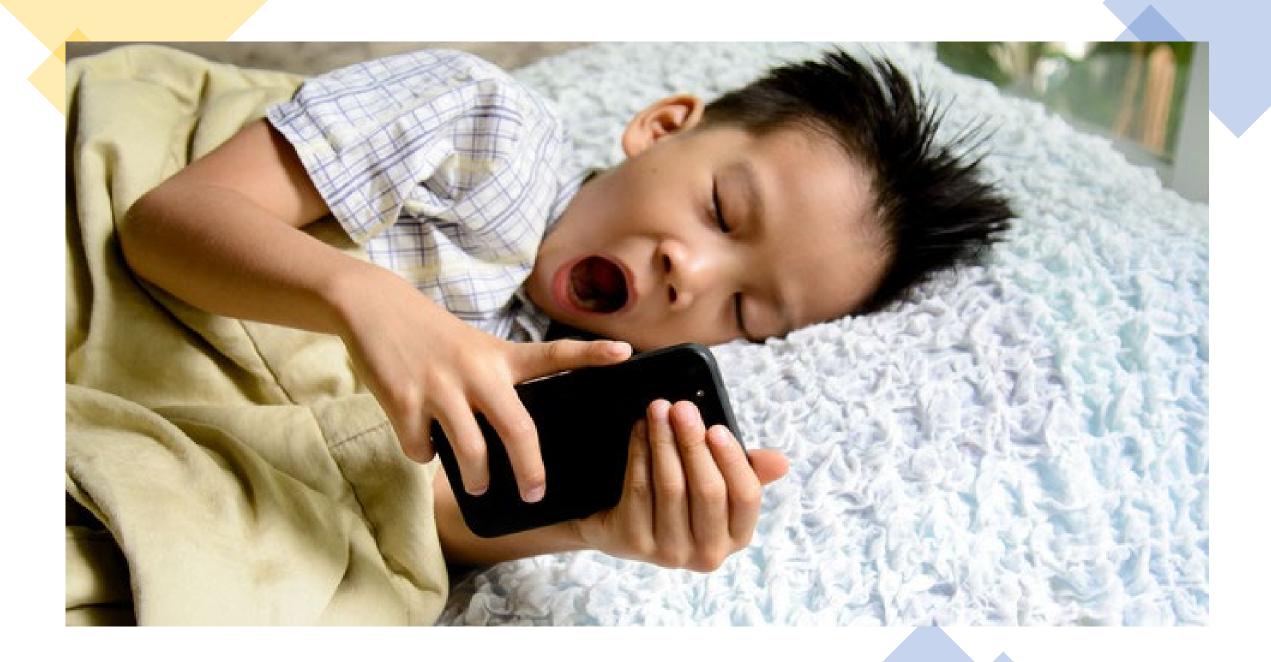
#### Therapeutic Approaches for Insomnia

- Treat any medical, psychiatric illness, substance abuse, or sleep disorder.
- Basic behavioral counseling about sleep hygiene.
- Stimulus control



# Cognitive Behavioral Therapy for Insomnia (CBT-I)

- A strategy that combines several of the previously described approaches over several weeks.
- Example of an eight session CBT-I program:
  - Introductory sleep education class
  - Stimulus control
  - Sleep restriction
  - Cognitive therapy
  - Sleep hygiene
  - Review and integrate the previously learned behaviors
  - Future problems
  - Stress and relapse





## Sleep hygiene: Basic rules for a good night's sleep

Sleep only as much as you need to feel rested and then get out of bed

Keep a regular sleep schedule

Do not try to sleep unless you feel sleepy

Exercise regularly, preferably at least 4 to 5 hours before bedtime

Avoid caffeinated beverages after lunch

Avoid alcohol near bedtime: no "night cap"

Avoid smoking, especially in the evening
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Do not go to bed hungry

Make the bedroom environment conducive to sleep

Avoid prolonged use of light-emitting screens before bedtime

Deal with your worries before bedtime





#### Stimulus control therapy rules

- 1. Go to bed only when sleepy.
- Do not watch television, read, eat, or worry while in bed. Use bed only for sleep and sex.
- Get out of bed if unable to fall asleep within 20 minutes and go to another room. Return to bed only when sleepy. Repeat this step as many times as necessary throughout the night.
- Set an alarm clock to wake up at a fixed time each morning, including weekends.
- 5. Do not take a nap during the day.

Data from: Bootzin RR, Perlis ML. Nonpharmacologic treatments of insomnia. J Clin Psychiatry 1992; 53:37.





#### Other Therapies

- Progressive relaxation some research that shows this can be helpful
- Sleep restriction therapy Limits the total time allowed in bed including naps and other sleep periods outside of bed in order to increase the drive to sleep.
  - Start by decreasing the time in bed to the same amount of time the patient reports sleeping. The clinician computes the sleep efficiency (reported sleep time divided by the reported time in bed). The time in bed is increased by 15-30 minutes once the sleep efficiency exceeds 85 percent. The process is repeated until the patient reports improved sleep.
  - Naps are not permitted.



#### Medications

- Medications that are approved to treat insomnia
  - Benzodiazepines
  - nonbenzodiazepine hypnotics
  - melatonin agonists
  - Doxepin
  - Dual orexin receptor antagonists



#### Benzodiazepines

- Benzodiazepines that have been used for the treatment of insomnia include
  - triazolam (short-acting),
  - estazolam, lorazepam, temazepam (intermediate acting),
  - flurazepam and quazepam(long acting).
- Potential for habit forming, and rebound insomnia may occur when discontinued
- Meta-analyses of randomized, placebo-controlled trials indicate that benzodiazepines decrease sleep latency and the number of awakenings, while improving sleep duration and sleep quality



#### Nonbenzodiazepines (Hypnotics)

- Nonbenzodiazepines commonly used to treat insomnia include <u>zaleplon</u>, <u>zolpidem</u> (<u>Ambien</u>), <u>eszopiclone</u> (<u>Lunesta</u>), <u>and</u> zolpidem extended release
- Improve both subjective and objective sleep outcomes
- Complex sleep-related behaviors may occur- sleepwalking, eating, sleep driving.
  - Can occur after just one dose, D/C and further contraindicated
- meta-analyses of randomized, placebo-controlled trials indicate that nonbenzodiazepines decrease sleep latency and the number of awakenings, while improving sleep duration and sleep quality



#### Melatonin agonists

- Ramelteon is a melatonin agonist.
  - In randomized trials, short-term use of ramelteon is associated with improvement in sleep onset and total sleep time.
  - Binds to melatonin receptors with a much higher affinity than melatonin itself
- Less side effects than benzo and non-benzos
- Little abuse potential, not scheduled



#### Orexin receptor antagonists

- Orexin A and orexin B are hypothalamic neuropeptides that play a key role in promoting wakefulness and regulating the sleep-wake cycle
- Suvorexant- studies showed improvement in subjective total sleep time as well as subjective time to sleep onset
- Lemborexant- improved objective sleep latency and efficiency compared to placebo
- Not recommended for use in combo with moderate to strong CYP3A inhibitors or inducers\*\*



#### Antidepressants

- Doxepin- FDA approved for tx of insomnia
- Amitriptyline, trazodone: sedating, and may be useful in management of patients with depression associated insomnia (however not approved by FDA for tx of insomnia)
  - Although modest sleep-promoting effects, not routinely used for insomnia not recommended because of the short-lived sedation effect and likelihood of side effects.



### Diphenhydramine

- Found in many OTC sleep aids
- Little evidence to support that it improves insomnia and d/t long half-life may cause sedation next day.
- Routine use to treat insomnia is not recommended



#### Melatonin

 Recommended when sleep disturbances are due to delayed sleep-wake phase syndrome or in patients with low endogenous melatonin, such as in elderly



# American Academy of Sleep Medicine practice guideline suggestions for initial trial of pharmacologic therapy

- To treat sleep onset insomnia, a relatively short-acting medication may improve the insomnia with less residual somnolence the following morning.
  - <u>zaleplon</u>, <u>zolpidem</u>, <u>triazolam</u>, and <u>ramelteon</u>. (<8 hour duration effect)
- For patients with sleep maintenance insomnia, use longer-acting
  - <u>zolpidem</u> ER, <u>eszopiclone</u>, <u>temazepam</u>, <u>lorazepam</u>, <u>estazolam</u>, low dose <u>doxepin</u>, and <u>suvorexant</u>.
    - · However, increased risk for hangover sedation.
- For patients with awakening in the middle of the night
  - <u>zaleplon</u> and a specific sublingual tablet form of <u>zolpidem</u> have been developed for use during the night
    - \*\*Constraint that there will be at least four hours of time in bed remaining after administration.



#### Considerations

- Pregnancy Sedative-hypnotics may increase the risk of fetal malformations if used during the first trimester.
- Alcohol consumption Sedative-hypnotics should not be combined with alcohol due to risk of CNS suppression
- Renal or hepatic disease Most sedative-hypnotic medications undergo hepatic and renal clearance.
   Metabolic clearance may be delayed in patients who have renal or hepatic disease, leading to accumulation and excessive sedation.
- **Pulmonary disease or sleep apnea** Many sedative-hypnotics are respiratory suppressants that can worsen obstructive sleep apnea or hypoventilation.
- Nighttime decision makers Sedative-hypnotics should not be taken by individuals who may be called upon to make important decisions during the night (nighttime clinicians, parents)
- **Older adults** The risk of adverse effects is increased in older adults due to CNS changes with aging, especially those who are older than 75 years.



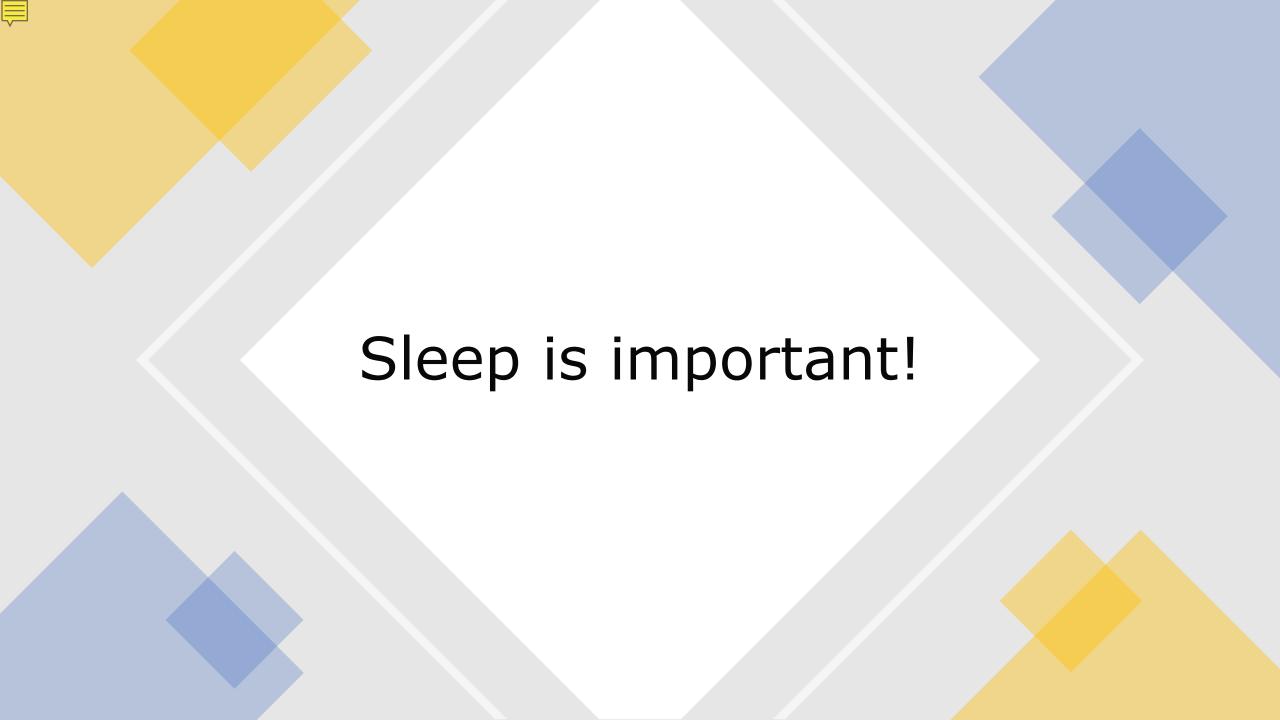
#### Goals of therapy and treatment

- If the treatment is successful, patients will report both improved sleep at night and improvement of daytime deficits.
- Patients who have little improvement during the initial trial of cognitive behavioral therapy, pharmacologic therapy, or combination therapy may have other causes of poor sleep.
  - Adherence with the prescribed therapy should be confirmed and then additional diagnostic evaluation performed.



#### Pearls and summary

- Treat not only the insomnia, but coexisting medical conditions that may be precipitating or exacerbating the insomnia
- For short term insomnia that is caused by an identifiable trigger, reassurance and education may be all that is needed, however can do a short-term benzo.
- Chronic insomnia first line therapy is CBT, then followed by combination therapy with medication.
- Continue behavioral and pharmacologic therapy for 6-8 weeks, and if good response, can taper medication while continuing therapy.









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