

I'M TIRED OF BEING TIRED

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DISCLOSURES

•None

Objectives

- Identify the 6 different categories of sleep disorders
- Identify the most common sleep disorders
- Identify the treatment options for the most common sleep disorders

Sleep Disorders

- 1.Sleep Related Breathing Disorders
 - OSA
 - CSA
 - Mixed or Complex Apnea
- 2.Insomnias
 - Chronic Insomnia
 - Acute Insomnia
 - Other insomnia disorder
- 3.Circadian Rhythm Sleep Disorders
 - Delayed sleep-wake phase disorder
 - Advanced sleep wake phase disorder

- Irregular sleep wake phase disorder
 - Non 24 hour sleep wake rhythm disorder
 - Shift work disorder
 - Jet lag
 - Other
- 4.Parasomnias
- Non Rem related parasomnias
 - Confusional arousals
 - Sleep walking
 - Sleep talking
 - Night terrors
 - Sleep related eating disorders

- Rem related parasomnias
 - REM behavior sleep disorder
 - Recurrent isolated sleep paralysis
 - Nightmare disorder
- Other parasomnias
 - Exploding head syndrome
 - Sleep enuresis

5. Sleep Related Movement Disorders

- Restless leg syndrome
- Periodic limb movement disorder
- Bruxism
- Leg cramps

6. Hypersomnia's

- Narcolepsy Type 1
- Narcolepsy Type 2
- Idiopathic hypersomnia
- Insufficient sleep syndrome
- Hypersomnia due to medical disorder, medication or psychiatric disorder

Most common sleep disorders

- Sleep Related Breathing Disorders
- Hypersomnia's
- Insomnias

Definitions

Sleep: reversible behavioral state of perceptual disengagement from and unresponsiveness to the environment

Apnea: absence of ventilation, cessation of breathing for more than 10 seconds and usually associated with oxygen desaturations and arousals

Cataplexy: abrupt loss of muscle tone triggered by strong emotional stimuli or physical exercise. Patients are usually aware of their surroundings and have clear memory for the complete event

Sleep Paralysis: inability to move during the transition into or out of sleep

Hypnagogic hallucinations: hallucinations that occur with sleep onset, may be visual, auditory or tactile

Hypnopomic hallucinations: hallucinations that occur at the end of sleep, may be visual, auditory or tactile

Hypopnea: reduction in but not cessation of ventilation

AHI: apnea hypopnea index which is the number of apneas plus hypopneas divided by the number of hours of sleep

Alpha intrusion: brief occurrence of alpha activity during a stage of sleep. Most consistent during relaxed wakefulness

Sleep Related Breathing Disorders

- Obstructive Sleep Apnea
- Mixed Sleep Apnea or Complex
- Central Sleep Apnea



OBSTRUCTIVE SLEEP APNEA

- Obstruction of the airway resulting in continued breathing effort but inadequate ventilation
- Characterized by the repetitive collapse of the upper airway during sleep, usually at the oropharyngeal level, with consequent cessation of breathing
- Leads to brief and frequent arousals during which leads to chronic and excessive daytime sleepiness (EDS)
- Patients frequently experience loud and disruptive snoring and report awakening with episodes of gasping, choking, snorting or apnea
- Generally associated with a decrease in oxygen saturation of the oxyhemoglobin

RISK FACTORS

- Age
- Gender
 - Men 3 times more at risk
 - Gender difference decreases in women after menopause
- Obesity
 - BMI > 30 kg/m²
 - neck circumference
 - Men 17 inches
 - Women 16 inches
- Upper airway soft tissue abnormalities
 - Soft tissue trauma

- Craniofacial abnormalities
 - Small, hypoplastic and or retroposed mandible and maxilla
 - Narrow posterior airway space
 - Inferior positioned hyoid bone
- Nasal obstruction
 - Increases pharyngeal negative pressure resulting in a more collapsible airway
- Heredity
 - Due to craniofacial abnormality
- Smoking, Alcohol, Medications
 - Smoking increases upper airway edema and congestion
 - ETOH is a respiratory depressant and suppresses the dilator muscles of the upper airway, increases collapsibility, increases upper airway resistance and predisposes to apnea

- Benzodiazepines, barbiturates, sedative hypnotics can relax the upper airway and decrease arousal response to hypoxia or hypercapnia
- Narcotics may result in central apnea and desaturations
- Androgens worsen OSA in hypogonadal men
- Anesthesia

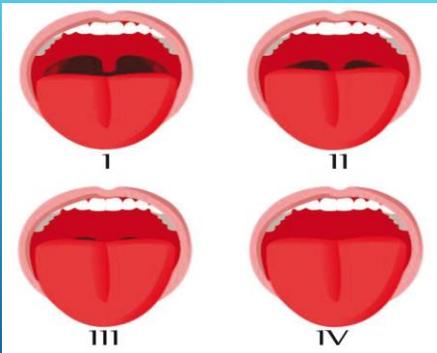
- Side Effects of Untreated Sleep Apnea**
- Increased mortality
 - Systemic hypertension
 - Pulmonary hypertension
 - Myocardial infarction
 - Congestive heart failure

- Cardiac Arrhythmias
 - Bradycardias
 - Ventricular
 - Atrial Fibrillation
- Cerebrovascular disease and stroke
- Diabetes
- Depression
- Erectile dysfunction

Mallampati score

In anesthesia, the Mallampati score, also Mallampati classification, is used to predict the ease of intubation.

A high Mallampati score (class 3 or 4) is associated with more difficult intubation as well as a higher incidence of sleep apnea.



Symptoms of Sleep Apnea

Primary symptoms

- Snoring
- Witnessed apnea
- Excessive daytime sleepiness
- Awakening with gasping, choking, coughing

Secondary symptoms

- Insomnia
- Nocturia
- Dry mouth
- Night Sweats
- Morning headache

- Poor memory/cognition
- Mood changes
- Fatigue or lack of energy
- Cold hands/feet

Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to feeling just tired? This refers to your usual way of life in recent times. Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the **most appropriate number for each situation:**

- 0 = would **never doze**
- 1 = **slight chance of dozing**
- 2 = **moderate chance of dozing**
- 3 = **high chance of dozing**

It is important that you answer each question as best you can.
Situation Chance of Dozing (0-3)

- Sitting and reading _____
- Watching TV _____
- Sitting, inactive in a public place (e.g. a theatre or a meeting) _____
- As a passenger in a car for an hour without a break _____
- Lying down to rest in the afternoon when circumstances permit _____
- Sitting and talking to someone _____
- Sitting quietly after a lunch without alcohol _____
- In a car, while stopped for a few minutes in the traffic _____

Interpretation

0-7: It is unlikely that you are abnormally sleepy.

8-9: You have an average amount of daytime sleepiness.

10-15: You may be excessively sleepy depending on the situation. You may want to consider seeking medical attention.

16-24: You are excessively sleepy and should consider seeking medical attention.

Reference: Johns MW. A new method for measuring daytime sleepiness: The Epworth Sleepiness Scale. Sleep 1994; 17(6):540-5

Central sleep apnea

- Cessation of respiration which can be associated with hypoxemia
- No inspiratory effort during respiratory pause
- Less frequent than OSA

Causes

- Autonomic dysfunction
- Brain stem disorders
- CVA
- Encephalitis
- Tumors
- Neuromuscular disorders
- Poor health

Treatment

- Good sleep hygiene
- Weight loss
- Eliminate certain medications and substances
- CPAP
- Upper airway surgery

- Oral appliances
- Positional therapy
- Pharmacological treatment
- Oxygen

Treatments continued

- CPAP
- Auto PAP
- BiPap
- ASV



CPAP

- Gold standard
- Goal
 - Eliminate apneas, hypopneas, oxygen desaturations, arousals, snoring
- Objective
 - Acts as a pneumatic splint to prevent the upper airway soft tissue from collapsing

- Complications
 - Annoying to patient
 - Poor fitting mask
 - Skin abrasions over nose bridge
 - Mask leak
 - Nasal and upper airway dryness
 - Rhinorrhea
 - Epistaxis – rare

AutoPAP

- Noninvasively detects variations in the upper airway obstruction and airflow limitations including snoring, hypopneas and apnea.
- Automatically increases the pressure until the flow limitation has been resolved.
- Used when set pressure of CPAP cannot be determined

BiPAP

- Allows the independent adjustment of the expiratory positive airway pressure and the inspiratory positive airway pressure
- Used for people intolerant of cpap
- OSA with concurrent respiratory disease or
- Obesity hypoventilation syndrome.

Adaptive Servo Ventilation

- Noninvasive ventilatory treatment option created specifically for the treatment of adults who have OSA and CSA and or complex sleep apnea
- Air pressure target is adjusted according to the input from the patient and it adapts to the patients breathing pattern and continually adjusts itself to meet the patients
- Every time the machine detects a pause in breathing during the night, it will adjust the pressure inside the mouth and throat so that the patient can resume breathing at 90 percent of what the breathing had been before the pause occurred. The machine will also "turn off" whenever normal breathing returns.

CPAP Qualifications

- In order to qualify for CPAP the patient must meet one of the following criteria:
 - AHI \geq 15 events per hour or
 - AHI \geq 5 events per hour and \leq 14 events per hour with documented symptoms of EDS, Impaired cognition, mood disorder, insomnia, or documented hypertension, ischemic heart disease or history of stroke

- In order for insurance to pay for the machine :
- Patient must have a face to face follow up within the first 31-90 days of starting treatment with a minimum of 70% compliance
- For ASV: A face to face follow up within 61-90 days with a minimum of 70% compliance

Hypoglossal Nerve Stimulation (HGNS)

- Approved by the FDA in 2014
- Targets adults with moderate to severe OSA
- Indicated in patients who have a BMI of less than 32, and in whom drug induced sleep endoscopy excludes concentric obstruction of the airway during sleep
- A nerve stimulator is implanted in the patient's chest; leads are connected to the hypoglossal nerve (cranial nerve XII), which controls tongue movement, and to a breathing sensor.

- The system monitors the patient's breathing patterns and stimulates the hypoglossal nerve during inhalation in order to maintain an open airway and minimize OSA.
- The patient operates the system using a remote control that is activated before going to sleep and that deactivates upon waking.
- In the largest study published to date the median Apnea-Hypopnea Index (AHI) score decreased 68 percent.

•The overall rate of serious adverse events was less than 2 percent, and 98 percent of participants were still using the system at the end of the 12 months.

The diagram shows a human torso with three components of the Inspire system:

- Stimulation Lead:** A lead that goes from the neck down to the chest, labeled "Delivers mild stimulation to maintain multilevel airway patency during sleep".
- Generator:** A small device implanted in the chest, labeled "Monitors breathing patterns".
- Breathing Sensor Lead:** A lead that goes from the neck down to the chest, labeled "Senses breathing patterns".

NARCOLEPSY

Disorder of sleep dominated by the persistent, unrelenting daytime sleepiness that can be alleviated transiently by short naps. In addition, patients with narcolepsy can have other peculiar manifestations that include cataplexy or sudden bouts of generalized muscle weakness, hallucinations on falling asleep or waking up and sleep paralysis



- Prevalence estimated at 1 in 3000 individuals in North America
- Men and women are equally affected
- Alleged precipitants include head trauma, pregnancy or infection
- Onset typically occurs in adolescence but can be as early as age 5 and as late as 35
- In 10% of patients, cataplexy can occur later in the course of the disease

- When left untreated, it is socially disabling and isolating
- Patients have a tendency to fail in school and are often dismissed from their jobs
- Driving may be avoided due to fear of a motor vehicle accident
- Inability to sleep at night may contribute to a loss of control over their schedule
- Depression and weight gain are common

- Symptoms**
- EDS with repeated daily inappropriate excessive episodes of irrepressible need to sleep
 - Cataplexy episodes of generally brief (<2 minutes) usually bilateral symmetrical sudden loss of muscle tone with retained consciousness
 - Episodic precipitated by strong emotion
 - Transient, reversible loss of deep tendon reflexes during an attack
 - Disruption of nocturnal sleep or inability to maintain continuous sleep

- Hypnagogic hallucinations
- Hypnopompic hallucinations
- Sleep paralysis

Narcolepsy Type 1

Diagnostic Criteria

- Patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months
- The presence of one or both of the following
 - Cataplexy and a mean sleep latency ≤ 8 minutes and 2 or more SOREM's on a MSLT or a SOREM within 15 minutes of sleep onset on PSG
 - CSF hypocretin – 1 concentration is either ≤ 110 or $< 1/3$ of mean values obtained in normal subjects

- Characterized by excessive daytime sleepiness and signs of REM sleep dissociation, the most specific of which is cataplexy
- Caused by a deficiency of hypothalamic hypocretin(orexin) signaling in CSF

Narcolepsy Type 2

Diagnostic Criteria

- The patient has daily periods of irrepressible need to sleep or daytime lapses into sleep occurring for at least 3 months
- A mean sleep latency of ≤ 8 minutes and two or more sleep onset REM periods are found on a MSLT performed according to standard techniques.
- A SOREMP within 15 minutes of sleep onset on the preceding nocturnal polysomnogram may replace one of the SOMREMPs on the MSLT

- Cataplexy is absent
- The hypersomnolence and or MSLT findings are not better explained by other causes such as insufficient sleep, OSA, delayed sleep phase disorder or the effect of medications or substances or their withdrawal

Treatment

- Includes social aspects, behavior modification and pharmacologic treatment
- Patient education
- Pharmacologic treatment is the cornerstone of management
- Responds best to CNS stimulants

Pharmacological Treatment

Antinarcotics which are Class IV drugs

- Modafinil
 - Dosage: 200-400mg a day
 - Consider lower doses in elderly patients
 - Generally well tolerated
 - Most common side effect is headache
 - Does not reduce cataplexy
- Armodafinil
 - Dosage 50mg, 150mg, 250mg
 - Generally well tolerated
 - Most common side effect is headache
 - Does not reduce cataplexy

Stimulants

Most common Class II drugs used

- Methylphenadate (Ritalin)
 - Doseage forms: 5mg, 10 mg, 20mg
 - Long acting form ranges from 10-60mg
 - Both can be given bid or tid
 - Side effects include behavior changes, irritability, insomnia, arrhythmias, cardiac structural abnormalities
 - Does have a black box warning
 - Warn of possible psychotic episodes
 - Tolerance tends to develop with prolonged use

Dextroamphetamine/amphetamine sulfate (Adderall)

- Dosage forms: 5,7.5,10,12.5,15,20,30mgs
- Extended release forms: 5,10,15,20,25,30mg
- Does have a Black Box Warning
- Side effects include cardiac structural abnormalities, arrhythmias, agitation
- Warn of possible psychotic episodes
- Tolerance tends to develop with prolonged use

Other Class II Drugs

Lisdexamfetamine (Vyvanse)

- Schedule II drug
- Dosage forms: 10,20,30,40,50,60,70mg
- Can cause psychosis

Atomoxetine (Statterra)

- Not a controlled substance
- Dosage forms: 10,18,25,40,60,80,100mg
- Can cause psychosis, QT prolongation

Sodium Oxybate

INDICATIONS AND USAGE: a Central Nervous System depressant indicated for the treatment of: Cataplexy in narcolepsy, Excessive daytime sleepiness (EDS) in narcolepsy

DOSAGE AND ADMINISTRATION

- Initiate dose at 4.5 grams (g) per night administered orally in two equal, divided doses: 2.25 g at bedtime and 2.25 g taken 2.5 to 4 hours later
- Titrate to effect in increments of 1.5 g per night at weekly intervals (0.75 g at bedtime and 0.75 g taken 2.5 to 4 hours later)

- Recommended dose range: 6 g to 9 g per night orally
- Take each dose while in bed and lie down after dosing
- Allow 2 hours after eating before dosing
- Prepare both doses prior to bedtime; dilute each dose with approximately ¼ cup of water in pharmacy-provided vials
- Hepatic Impairment: starting dose is 2.25 g per night administered orally in two equal, divided doses of approximately 1.13 g at bedtime and approximately 1.13 g taken 2.5 to 4 hours later
- Concomitant use with divalproex sodium (Depakote): an initial reduction in dose of at least 20% is recommended

WARNINGS AND PRECAUTIONS

- CNS depression: Use caution when considering the concurrent use of with other CNS depressants
- Caution patients against hazardous activities requiring complete mental alertness or motor coordination within the first 6 hours of dosing or after first initiating treatment until certain that Xyrem does not affect them adversely
- Depression and suicidality: Monitor patients for emergent or increased depression and suicidality
- Confusion/Anxiety: Monitor for impaired motor/cognitive function
- Parasomnias: Evaluate episodes of sleepwalking
- High sodium content: Monitor patients with heart failure, hypertension, or impaired renal function

ADVERSE REACTIONS

Most common adverse reactions:

- Nausea,
- Dizziness,
- Vomiting,
- Somnolence,
- Enuresis,
- Tremor

INSOMNIA

Definition: Persistent difficulty with sleep initiation, duration, consolidation or quality that occurs despite adequate opportunity and circumstances for sleep and results in some form of daytime impairment

Prevalence: 10-40% of the population

Prevalence in primary care: 50% with occasional insomnia, 10% with chronic insomnia

Annual direct cost of insomnia in US is \$1.97 billion for medications and \$11.97 billion for health care services.

Diagnostic criteria

Criteria A-F must be met

- A. The patient or patient caregiver or parent reports/observes one or more of the following:
 1. difficulty initiating sleep
 2. difficulty maintaining sleep
 3. waking up earlier than desired
 4. resistance to going to bed on appropriate schedule
 5. difficulty sleeping without caregiver or parent intervention

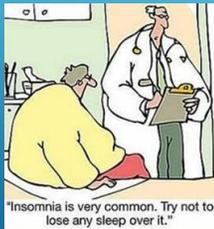
- B. The patient reports or the parent/caregiver observes one or more of the following related to nighttime sleep difficulty
 1. Fatigue/malaise
 2. Attention, concentration, or memory impairment
 3. Impaired social, family, occupational, or academic performance

- 4. Mood disturbance or irritability
- 5. Daytime sleepiness
- 6. Behavioral problems(Hyperactivity, impulsivity, aggression)
- 7. Reduced motivation/energy/initiative
- 8. Proneness for errors/accidents
- 9. Concerns about or dissatisfaction with sleep

Diagnostic criteria continued

- C. The reported sleep/wake complaints cannot be explained purely by inadequate opportunity (i.e., enough time is allotted for sleep) or inadequate circumstances (i.e., The environment is safe, dark, quiet and comfortable) for sleep
- D. The sleep disturbance and associated daytime symptoms occur at least three times a 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



CLINICAL FEATURES

- Patients with insomnia typically present with complaints of difficulty initiating sleep, difficulty maintaining sleep, or waking up too early. In addition, they also complain of compromised daytime function (e.g., daytime sleepiness).
- Insomnia commonly coexists with psychiatric or medical disorders, other sleep disorders, or use of certain medications or substances
- Insomnia is a clinical diagnosis. Therefore, a sleep history is the only diagnostic evaluation that is required to confirm or exclude insomnia.

- Insomnia is often confused with a short sleep requirement, circadian rhythm disorders or chronic sleep restriction.
- A short sleep requirement can be distinguished from insomnia because patients with short duration sleep do not have daytime impairment, whereas patients with insomnia do.
- Patients with advanced or delayed sleep-wake phases fall asleep and sleep normally if they go to bed and get up at times consistent with their circadian rhythm, while patients with chronic insomnia may have sleep difficulty whenever they attempt to sleep.

- Chronic sleep restriction can be distinguished from insomnia because patients with sleep restriction rapidly fall asleep if given the opportunity, whereas patients with insomnia do not.

Insomnia Severity Index

The Insomnia Severity Index has seven questions. The seven answers are added up to get a total score. When you have your total score, look at the 'Guidelines for Scoring/Interpretation' below to see where your sleep difficulty fits.

For each question, please CIRCLE the number that best describes your answer.
 Please rate the *CURRENT* (i.e. LAST 2 WEEKS) SEVERITY of your insomnia problem(s).

Insomnia Problem	None	Mild	Moderate	Severe	Very Severe
1. Difficulty falling asleep	0	1	2	3	4
2. Difficulty staying asleep	0	1	2	3	4
3. Problems waking to early	0	1	2	3	4

4. How SATISFIED/DISSATISFIED are you with your CURRENT sleep pattern?
 Very Satisfied Satisfied Moderately Satisfied Dissatisfied Very Dissatisfied
 0 1 2 3 4

5. How NOTICEABLE to others do you think your sleep problem is in terms of impairing the quality of your life?
 Not at all Noticeable A Little Somewhat Much Very Much Noticeable
 0 1 2 3 4

6. How WORRIED/DISTRESSED are you about your current sleep problem?
 Not at all Worried A Little Somewhat Much Very Much Worried
 0 1 2 3 4

7. To what extent do you consider your sleep problem to INTERFERE with your daily functioning (e.g. daytime fatigue, mood, ability to function at work/daily chores, concentration, memory, mood, etc.) CURRENTLY?
 Not at all Interfering A Little Somewhat Much Very Much Interfering
 0 1 2 3 4

Guidelines for Scoring/Interpretation:
 Add the scores for all seven items (questions 1 + 2 + 3 + 4 + 5 + 6 + 7) = _____ your total score

Total score categories:
 0–7 = No clinically significant insomnia
 8–14 = Subthreshold insomnia
 15–21 = Clinical insomnia (moderate severity)
 22–28 = Clinical insomnia (severe)

Risks associated with insomnia

- Metabolic: obesity, Type 2 Diabetes
- Cardiovascular: CAD and MI, HTN, CHF
- Psychological: Depression, Anxiety, unhealthy behaviors such as heavy drinking, binge drinking, physical inactivity
- Most at risk:
 - Women due to menopause, menstrual periods, pregnancy
 - Older adults due to medical conditions, sleep disorders, pain, environmental stimuli

Medications associated with Insomnia

- Anticonvulsants : Lamotrigine
- Antidepressants: Bupropion,, Fluoxetine, Venlafaxine
- Beta Blockers: Propanolol, metoprolol
- Bronchodialtors: Theophylline
- Decongestants: Phenylpropanolamine, Pseudoephedrine

- Steroids: Prednisone
- Stimulants: Dextroamphetamine, Methamphetamine, Methylphenidate, Modofinil, Armodofinil,

Sleep Hygiene

- 1. Stick to a schedule and don't sleep late on weekends
- 2. Don't eat or drink a lot before bedtime. Avoid heavy meals before bedtime. Or eat something that triggers serotonin which makes you sleepy such as carbohydrates or foods containing L-tryptophan such as milk, tuna, or turkey
- 3. Avoid caffeine and nicotine. Addictive stimulants can keep you awake and can cause withdrawal at night
- 4. Exercise



- 5. A slightly cool room is ideal for sleeping
- 6. Sleep primarily at night. Limit daytime sleep to one hour and no later than 3pm
- 7. Keep it quiet
- 8. Make your bed
- 9. Soak and sack out
- 10. Don't rely on sleeping pills

Treatments for Insomnia

- Good sleep hygiene
- Cognitive Behavioral Therapy
 - Improves patient's understanding of his/her sleep
 - Establish realistic expectations regarding sleep
 - Review simple relaxation techniques

- Stimulus control
 - If unable to get to sleep, get up and go to another room
 - Return to bed only when drowsy
 - Set an alarm and get up same time each day
 - Eliminate daytime naps
 - Lie down in bed only when sleepy

Medications

Over The Counter

- Valerian, kava kava, chamomile tea
- Melatonin: dosage 0.2-20mg
- Antihistamines
 - mild to moderate sedation
 - tolerance may develop

Antidepressants: minimal efficacy

- Tricyclic antidepressants and other sedation agents
 - Amitriptyline: 10,50,75,100,125,150mg
 - can cause ventricular arrhythmias, QT prolongation
 - Doxepin: 10,25,50,75,100,150mg
 - For insomnia 10-50mg
 - Reduce dose in elderly

Miscellaneous Sedating Antidepressants

- Trazodone: 50,100,150,300mg
 - For insomnia 25-50mg, max 200mg
- Mirtazapine: 15,30,45,mg
 - May cause RLS and PLMD
 - Multiple drug-drug interactions

Benzodiazepines: Schedule IV

- Many potential adverse effects
- Daytime sedation common
- Short acting agents may cause rebound insomnia and early morning awakening
- May worsen sleep apnea
- Rapid withdrawal can lead to nightmares, and arousals and increased sleep latency

- Flurazepam: 15, 30mg
- Temazepam: 7.5,15,22.5,30mg
- Triazolam: 0.125, 0.25mg: max dose 0.5mg

Nonbenzodiazepine receptor agonists

- Rapid onset of action
- Few side effects but respiratory depression may occur
 - Zaleplon: 5,10mg: max dose 20mg
 - Zolpidem: 5, 10mg
 - Zolpidem ER: 6.25, 12.5mg
 - Eszopiclone:1,2,3mg,

Melatonin receptor agonist

- Ramelteon: 8mg
- Rapid onset of action with a short half life
- good safety profile

Questions?

Thank You
