

Getting those ZZzzzzzs

Colleen Christmas, MD

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Disclosures

- No relevant financial relationships with commercial interests
- No references to unapproved/unlabeled uses of drugs or products.
- No planner has indicated having any financial interests or relationships with a commercial entity in conjunction with the webinar

Objectives

- Review changes in sleep with normal aging
- Discuss an approach to evaluating sleep concerns
- Review data about drug and non-drug treatments

Sleep



- Sleep deprived society
- 1/3 of our life is spent sleeping
- Removes toxins
 - Increase the space between neurons in the brain
 - Increase the fluid bath flow while we sleep
 - Fluid bath removes metabolic waste, such as beta amyloid
- Consolidates learning
 - Finger tapping activity
 - Neurons more microns closer

Control of Sleep, Changes With Aging

- Sleep drive
 - Neurochemical receptor insensitivity weakens drive
- Circadian rhythm
 - Levels of melatonin declines and it's production in relation to light/dark declines
- Environment and behavioral factors
 - More time indoors and less exposure to bright light, less exercise

Normal Sleep Pattern

After sleep onset:

- Sleep usually progresses through NREM stages 1 to 4 within 45 to 60 min.
- Slow-wave sleep (NREM stages 3 and 4) predominates in the first third of the night and comprises 25% of total sleep time
- The first REM sleep episode usually occurs in the second hour of sleep.

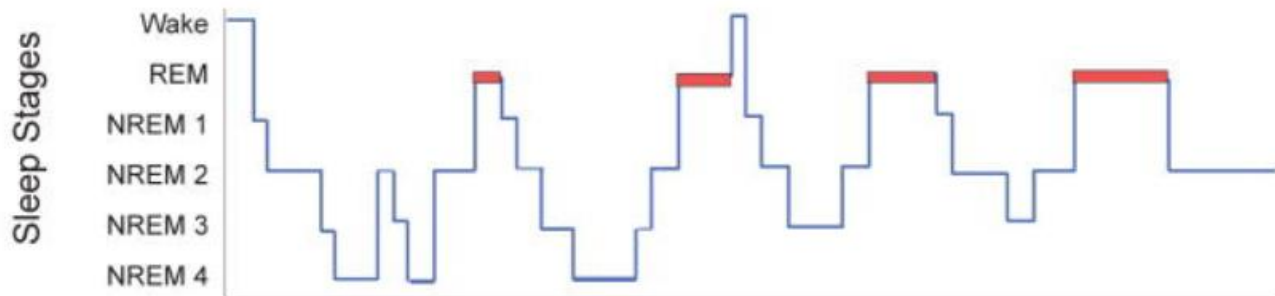
Changes in sleep with age

- Light sleep (Stages 1 and 2) increases with age
- Deep sleep (Stages 3 and 4) decreases to 0-3% of total sleep time
 - The depth of deep sleep also decreases
- Unchanged to slightly decreased REM sleep

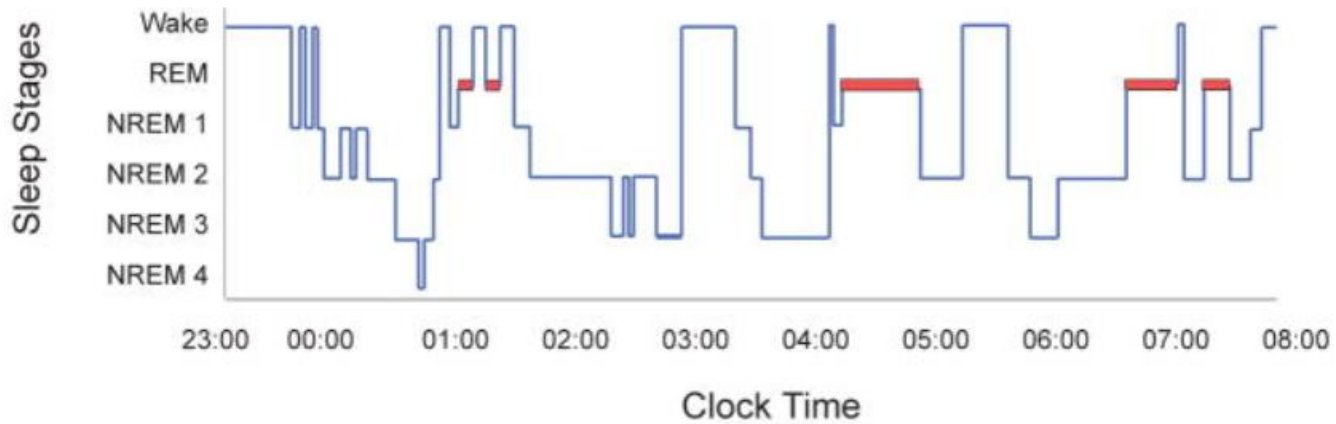
- Sleep quality and efficiency is reduced

A

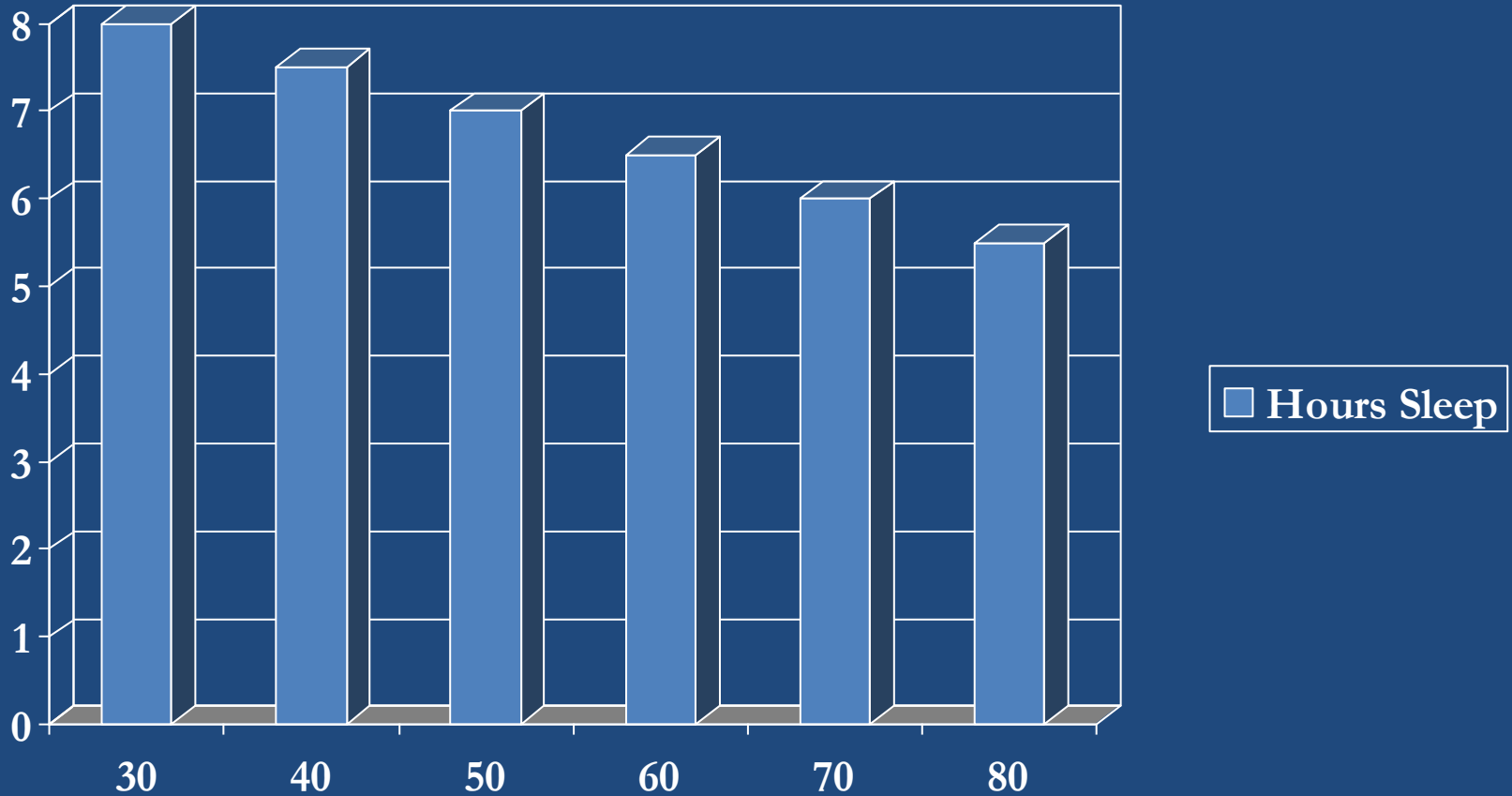
Young Adult



Older Adult



Decline in hours slept by age



The duration of sleep declines approximately 27 minutes for each decade of life

Mr. Pleasedrchristmashelpme

- 88 yo retired police officer with HOH, hypertension, “not too much” wine, gout, OA
- “Doc, I am begging you please to give me something so I can sleep. I am miserable.”
- 3 approaches:

1. Most common approach

- Can't sleep → Sleep med

2. Finucane's Nap Trap

- Can't sleep → Napping?
- If yes: that is the problem → Stop napping
- If no: then your body is trying to tell you are getting all the sleep you need → Stop worrying

3. “Textbook” approach

- Is this secondary to something other than primary insomnia
 - Pain, Nocturia, other physical sx
 - Alcohol or substance abuse
 - Depression, Anxiety, Depression, Depression
 - Another sleep disorder (PLN, OSA, RLS)
- Does this meet criteria for insomnia
- Treat primary insomnia

Epidemiology of Sleep Problems

- 1/3rd of adults will request sleeping meds
- 5-10% of those will meet criteria for insomnia

Definition of Insomnia

- Difficulty falling asleep, staying asleep, or nonrestorative sleep
- ****Results in impaired daytime function*****
(distinguishes from short duration sleep)
- Despite adequate opportunity to sleep
(distinguishes from sleep deprivation, which 1/3rd adults have)
- DSM 5 also says persists >1month, occurs >3x/week with preoccupation with sleeplessness

Evaluation

- **Sleep history**

- Timing of insomnia
- Sleep schedule
- Sleep environment
- Sleep habits
- Daytime effects
- Symptoms of other sleep disorders
- Log book or witness?

- **Medical history-**

- CoMorbid
 - Stressors
 - ETOH/Caffeine/nicotine use
 - Pain
 - BPH
 - GERD
- Medication review

- **Psychiatric history**

- Depression
- Mania
- Psychosis

Possible indications for sleep studies

I nsomnia

S noring

N octurnal awakenings/**N** ot breathing

O besity

R estorative sleep? Or do you feel **R** efreshed in AM?

E xcessive daytime somnolence

D riving difficulties due to sleepiness

Sleep Disordered Breathing



- Recurrent hypopnea and apnea episodes during sleep leading to repeated arousals from sleep, and hypoxemia
 - Prevalence Men > Women
 - Associated with HTN, cardiac and pulmonary dx.
- Main Sx is: snoring, pauses in respiration and excessive daytime sleepiness.
- Treatment- CPAP, weight loss, use of dental/mechanical devices, & surgery

Annals of IM: Metaanalysis CPAP vs sham CPAP

2013 Qaseem

- Twenty-four trials
- Mean baseline AHI scores between 22 and 68
- Follow-up ranged from 1 week to 3 months.
- CPAP was more effective than sham CPAP
 - reducing AHI scores,
 - improved ESS scores
- No differences for
 - oxygen saturation,
 - sleep efficiency,
 - sleep latency,
 - sleep quality
- Data on blood pressure were inconsistent
- No study investigated death or cardiovascular illness.

Periodic Limb Movements of Sleep

- Clusters of repeated leg jerking during sleep
- Dx made when PLMI is >5 .
- Prevalence 45% in elderly population
- No gender difference.

Treatment:

- Avoid alcohol, caffeine and TCA's
- Dopaminergic agents: Levodopa/carbidopa, pergolide, pramipexole, ropinirole, gabapentin

Restless Leg Syndrome

- Dysesthesia in the legs, usually creepy crawling sensation or pins and needles
- Only relieved with movement
- Sensations often occur when pt is in a restful relaxed state.
- High association with PLMS
- Treatment with iron or dopaminergic agents.



Primary Insomnia

- Inability to fall asleep, stay asleep or non-restorative sleep despite ample opportunity, with subjective daytime impairment in functioning
- Approaches:
 - Sleep hygiene
 - CBT-I
 - Sleeper medications

The Schedule

1. Follow a regular schedule
2. Sleep only what you need
3. Exercise at regular times each day
4. Develop bedtime routines that signal your body to sleep
5. Adjust your internal “sleep clock” by exposure to natural light in the afternoon each day
6. Empty your bladder before bedtime

Watch out for stimulants

1. Avoid stimulants late in the day
e.g. caffeine, MSG, nicotine, chocolate, tea
2. Don't use alcohol or cigarettes to make you sleep
(Avoid alcohol for > 4 hours before bedtime)
3. Review medications for possible stimulants (cold and allergy meds)
4. Avoid stimulants in the environment
TV, pet, cell phone notifications, blue light

The Environment

- Create a safe/comfortable sleep environment:
 - locks
 - smoke alarms
 - easy to use lamp and telephone at bedside
 - room should be dark, quiet, and well ventilated
 - room temperature adjusted to your preference
- The environment is part of the sleep ritual
 - Comfortable clothes
 - Lavender hand cream, chamomile tea maybe
 - Bed conditioning: 15 -20 minutes then out until sleepy again

Intervention	General Description	Specific Techniques
Sleep hygiene education	Promoting behaviors	Don't force sleep. Limit alcohol. Regular sleep schedule. Avoid naps. Exercise midday. Bedroom dark and quiet.
Stimulus control	Operant conditioning	Bed for sleep only. Get OOB after 15-25 min if unable to fall asleep, go in another room, and do something quiet. Wake up same time every day. Bright light in the morning
Sleep restriction therapy	Increase homeostatic sleep drive	Limit time awake in bed. Sleep schedule set to time actually asleep. Fixed wake up time. Restrict or advance time in bed targeting 85% efficiency.
Relaxation training	Decrease muscular tension that triggers arousals	Progressive muscle relaxation, guided imagery, paced breathing
Cognitive therapy	Replace dysfunctional beliefs and attitudes	Set realistic goals for sleep target. Journal to reduce rumination.
CBT	Multimodal	Combination of all of the above.
Brief behavior treatment	Multimodal	Combination of Stimulus control and Sleep restriction.

Great Resource for Patient Materials

<http://media.psychologytools.org>

- Large font patient sleep diaries
- Checklist for better sleep
- Guidelines for better sleep

Effectiveness of Non-pharmacological Treatment of Insomnia

- Improve symptoms of insomnia in 70-80% of patients with primary insomnia, largely studied in younger adults
- Effects last at least 6 months after treatment completed

Does CBT-I work in older adults?

YEP!

- Cognitive behavioral therapy for insomnia in older veterans using nonclinician sleep coaches: randomized controlled trial.
 - Alessi et al. JAGS Aug 2016
- PRCT 159 veterans randomized to 5 one hour weekly CBTI sessions vs control
- Improved sleep onset latency, total wake time, sleep efficiency, sleep quality, insomnia severity immediately after, and persisted 6 and 12 months later. QOL was not changed.

Maybe we can go digital?

- Randomized trial of digital CBTi associated with a small improvement in functional health, psychological well-being and large benefit in sleep-related quality of life, compared to hygiene education
- But mean age 48 years, 77% women, mostly white

– Espie CA et al. JAMA Psychiatry 2018

Do Drugs Work? SHOW ME THE DATA!

- Meta-analysis of 24 RCTs (2417 patients, nearly all SPIT)
 - drugs improved sleep quality, total sleep time (20 min), and awakenings to a small degree
 - 2-5 fold increase in adverse cognitive or psychomotor events
 - » Glass J, Lanctot KL, Herrmann N, et al. Sedative hypnotics in older people with insomnia: meta-analysis of risks and benefits. *BMJ* 2005;331:1169.

Hypnotics' association with mortality or cancer: a matched cohort study

Kripke DR, Langer RD, Kline LE
BMJ Open 2012;2:e000850

- Data from Geisinger Health System, longitudinal, integrated system and linked to death index
- Prospective matched cohort of 10K patients with at least once prescribed an Rx sleeping med
 - matched to 24K who hadn't
 - match age, gender, smoking
 - excluded dx of cancer within 18 mo of study
- Outcomes: death or new cancer in 2.5 yr
- 40% zolpidem (Ambien), 20% temazepam (Restoril)

Results

- Death: 6.1% Rx use, 1.2% no Rx
 - Hazard ratio of 4.56
 - Related to dose

Outcome	Dose (pill/yr)	Hazard ratio
Death	0.4-<18	3.6
	18-132	4.4
	>132	5.3

We are not doing so well here (From Up to Date)

- **High prevalence of potentially unsafe zolpidem dosing (September 2018)**
- In 2013, the FDA advised lowering of the recommended dose of zolpidem in women to 5 mg for immediate release products and 6.25 mg for extended release products.
- A large database study found that in 2015 among 3.8 million zolpidem users,
 - 64 percent of older adults and 68 percent of women reported taking higher than the recommended dose of zolpidem
 - 41 percent of patients reported concurrent use of one or more other central nervous system depressants (eg, opioids, benzodiazepines).
 - [Moore TJ, Mattison DR. Assessment of Patterns of Potentially Unsafe Use of Zolpidem. JAMA Intern Med 2018; 178:1275.](#)

Mr. Pleasdrchristmashelpme

- Ask about daytime impairment, depression, alcohol, INSNORED
- Provide basic components of CBT in office
- 5 years later, still unbothered by sleep

Take-home messages

- Sleep changes with healthy aging
- Concerns about insomnia are VERY prevalent
- Consider sleep study for very severe symptoms in an appropriate host
- CBT—best over the long term for those who are very impaired
- Sleeping drugs have higher risks than benefits
- CBT can even help with concomitant depression and dependence on sleepers

Mrs.

Pleasedrchristmasdontstopambien

- 92 y o woman with heart disease, depression
- “I’m telling you right now...”
- Ambien for 7 years

What do we do about folks dependent on sleepers?

- 1. Screen for drug side effects, but keep med until they have one
- 2. Try mightily to convince them to stop
- 3. Send for a sleep study

What do we do about folks dependent on sleepers?

- Lichstein KL et al. J Clin Psychol 2013 1056-65
 - 10 weekly 50 min Skype CBT sessions w/ grad students for 200 elderly with depression and insomnia
 - Improved sleep diaries, insomnia severity index, and depression scores
 - Even 2 months after intervention stopped

What do we do about folks dependent on sleepers?

- Psychiatry res 2012;210:515-21
 - 63 pt aged 20-77 yo on hypnotics chronically
 - randomized to usual care vs cbt biweekly or monthly for at least 2 sessions
 - 71% reduced insomnia to zero,
 - 79% decreased sleeper by half or more,
 - also improved depression scores

Nonbenzodiazepine benzodiazepine receptor agonists (BZRAs) in the management of insomnia in adults

Nonbenzodiazepine	Preparation(s)	Adult dose (usual)*	Dose in older adults (≥65 years)	Indication	Half-life (hours)	Potential for drug interactions [†]
Eszopiclone	Tablet	1 to 3 mg	1 to 2 mg	Sleep onset or sleep maintenance insomnia	Intermediate (6)	Moderate Eszopiclone is metabolized in part by CYP3A4
Zaleplon	Capsule	5 to 20 mg	5 mg	Sleep onset insomnia	Short (1)	Low
Zolpidem	Tablet, sublingual tablet, oral liquid (5 mg per spray)	Men 5 to 10 mg Women 5 mg	5 mg	Sleep onset insomnia	Short (1.4 to 4.5)	Low to moderate Zolpidem is metabolized in part by CYP3A4
Zolpidem extended release	Coated tablet	Men 6.25 to 12.5 mg Women 6.25 mg	6.25 mg	Sleep onset or sleep maintenance insomnia	Intermediate (1.6 to 4 ^Δ)	Metabolized more slowly by women, particularly with age
Zolpidem middle of the night	Dissolvable tablet (sublingual)	Men 3.5 mg Women 1.75 mg	1.75 mg	Sleep maintenance insomnia (middle of the night)	Short (1.4 to 4.5)	
Zopiclone (not available in the United States)	Tablet	3.75 to 7.5 mg		Sleep onset insomnia	Intermediate (5 to 7)	Moderate Zopiclone is metabolized by CYP2C8 and 3A4

* Initiate treatment using lowest dose shown for those with low body weight, debilitated patients, and those receiving treatment with opioid analgesics or other central nervous system or cardiorespiratory depressants.

[†] For specific drug interactions, including management recommendations and combinations that should be avoided, use Lexi-Interact drug interactions program included with UpToDate.

^Δ Duration of effect longer than predicted by half-life due to sustained release.