Sleep disorders in later life

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Conflict of Interest Disclosures (5 years)

☐ The authors do not have any potential conflicts of interest to disclose,

OR

☒ The authors wish to disclose the following potential conflicts of interest:

<table>
<thead>
<tr>
<th>Type of Potential Conflict</th>
<th>Details of Potential Conflict</th>
</tr>
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<tbody>
<tr>
<td>Grant/Research Support</td>
<td>Eisai, General Sleep Corp, GSK, Jazz, Merck, Neurocrine, Pfizer, Philips-Respironics, Purdue Pharma, sanofi-aventis, Servier, Sepracor-Sunovion, Somnus</td>
</tr>
<tr>
<td>Consultant</td>
<td></td>
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<tr>
<td>Speakers’ Bureaus</td>
<td></td>
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<tr>
<td>Financial support</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Paid speaker at educational conferences: Astellas, Servier</td>
</tr>
</tbody>
</table>

☐ The material presented in this lecture has no relationship with any of these potential conflicts

☒ This talk presents material that is related to one or more of these potential conflicts, and references are provided throughout this lecture as support.
Who cares about sleep in older adults?

Survival as a function of sleep latency (time to fall asleep)

Sleep disorders in the elderly

- Normative characteristics of sleep in the elderly
  - Self-reports
  - Polysomnographic recordings of sleep
- Sources of age-related sleep changes
- Recognition and treatment of sleep disorders
  - Insomnia
  - Sleep apnea
  - Restless legs syndrome/ Periodic limb movements
  - REM Behavior Disorder
  - Advanced Sleep Phase Disorder
Age-related changes in self-reports of sleep

- Earlier
- Lighter
- Shorter
- More fragmented
- More insomnia
- More daytime sleepiness
Earlier timing of sleep in older adults

Buysse, JAGS, 1992

Young adults n=33

Older adults n=45
Age effects on sleep

Meta-Analysis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Direction</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>TST</td>
<td>↓</td>
<td>-0.60</td>
</tr>
<tr>
<td>Latency</td>
<td>↔</td>
<td>+0.27</td>
</tr>
<tr>
<td>Efficiency</td>
<td>↓</td>
<td>-0.71</td>
</tr>
<tr>
<td>Stage 1</td>
<td>↑</td>
<td>+0.38</td>
</tr>
<tr>
<td>Stage 2</td>
<td>↑</td>
<td>+0.28</td>
</tr>
<tr>
<td>Stage 3-4</td>
<td>↓</td>
<td>-0.85</td>
</tr>
<tr>
<td>REM</td>
<td>↓</td>
<td>-0.46</td>
</tr>
<tr>
<td>WASO</td>
<td>↑</td>
<td>+0.89</td>
</tr>
</tbody>
</table>

All effect size p values < .001

TST = Total Sleep Time. WASO = Wakefulness After Sleep Onset

Williams, EEG of Human Sleep, 1974

Ohayon et al., SLEEP 2004; 27: 1255-73
Sleep disorders in the elderly

- Normative characteristics of sleep in the elderly
  - Self-reports
  - Polysomnographic recordings of sleep
- Sources of age-related sleep changes
  - Medical/neuropsychiatric disorders
  - Homeostatic and circadian sleep regulation
- Recognition and treatment of sleep disorders
Buysse, Diagnosis and classification of insomnia disorders. From *Insomnia: Principles and Management*. Dingess, Kloss, Szuba (eds), 2003
Insomnia and health-related characteristics: Is age really the key factor?

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 75-84</td>
<td>1.06 (0.95 - 1.18)</td>
</tr>
<tr>
<td>Depression score &gt; 80%ile</td>
<td>2.53 (2.25 - 2.85)</td>
</tr>
<tr>
<td>Anxiolytic/barbiturate use</td>
<td>1.80 (1.51 - 2.15)</td>
</tr>
<tr>
<td>Respiratory symptoms</td>
<td>1.39 (1.25 - 1.54)</td>
</tr>
<tr>
<td>Female</td>
<td>1.36 (1.23 - 1.50)</td>
</tr>
<tr>
<td>≥ 2 Over the counter medications</td>
<td>1.22 (1.09 - 1.36)</td>
</tr>
<tr>
<td>Fair/poor health</td>
<td>1.20 (1.08 - 1.34)</td>
</tr>
<tr>
<td>Activities of Daily Living limitation</td>
<td>1.17 (1.00 - 1.38)</td>
</tr>
<tr>
<td>≥ 2 diseases</td>
<td>1.16 (1.05 - 1.29)</td>
</tr>
</tbody>
</table>

Prevalence of insomnia comorbid with medical disorders

<table>
<thead>
<tr>
<th>Condition</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer</td>
<td>2.1 (1.6-2.7)</td>
</tr>
<tr>
<td>Neurological problem</td>
<td>2.0 (1.5-2.7)</td>
</tr>
<tr>
<td>COPD</td>
<td>1.9 (1.5-2.5)</td>
</tr>
<tr>
<td>Migraine</td>
<td>1.8 (1.5-2.1)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>1.8 (1.5-2.2)</td>
</tr>
<tr>
<td>Menstrual</td>
<td>1.7 (1.3-2.1)</td>
</tr>
<tr>
<td>Asthma</td>
<td>1.6 (1.3-2.0)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>1.6 (1.2-2.3)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.5 (1.2-1.8)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.4 (1.05-2.0)</td>
</tr>
<tr>
<td>Colitis</td>
<td>1.4 (0.9-2.3)</td>
</tr>
<tr>
<td>Cancer</td>
<td>1.2 (0.8-1.8)</td>
</tr>
<tr>
<td>Thyroid disorders</td>
<td>1.1 (0.8-1.6)</td>
</tr>
</tbody>
</table>

Budhiraja, SLEEP, 2011; 34: 859-867.
Physiological control of sleep: Two-process model

**Reduced**
Homeostatic Sleep Drive
(How long you’ve been awake)

**Blunted**
Circadian Sleep Propensity
(Biological Clock)

Sleep rhythms in older and younger adults

Buysse, *SLEEP*, 2005; 28: 1365-1376
Sleep disorders in the elderly

- Normative characteristics of sleep in the elderly
  - Self-reports
  - Polysomnographic recordings of sleep
- Sources of age-related sleep changes
- Recognition and treatment of sleep disorders
  - Insomnia
  - Sleep apnea
  - Restless legs syndrome/ Periodic limb movements
  - REM sleep behavior disorder
  - Advanced Sleep Phase Disorder
  - Sleep in nursing homes
Assessment of sleep disorders in the elderly

- **Sleep timing**: What time do you normally go to bed/wake up?
- **Sleep quantity**: How much sleep do you need to feel alert and function well?
- **Sleep continuity**: Do you often have trouble falling asleep? How many times do you wake up? Do you have trouble falling back to sleep?
- **Key sleep symptoms**: 
  - Are you or your partner aware of snoring, gasping for air, or not breathing? (Obstructive sleep apnea)
  - Do you walk, eat, kick, punch, or scream during sleep? (Parasomnias)
  - Do you have an urge to move your legs/ uncomfortable feelings in your legs during rest or at night? (Restless Legs Syndrome)
- **Daytime sleepiness**: Are you sleepy or tired during much of the day? Do you usually take one or more naps? Do you usually doze off without planning to during the day?
- **Sleep medications**: Are you currently taking medication or other preparations to help you sleep?

Bloom et al., *JAGS* 2009; 57:761-89.
# Sleep diary

<table>
<thead>
<tr>
<th>DATE</th>
<th>Noon</th>
<th>P.M.</th>
<th>Evening</th>
<th>Midnight</th>
<th>A.M.</th>
<th>Morning</th>
<th>Sleep Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>12</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>T</td>
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<td>F</td>
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<td>Sa</td>
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<tr>
<td>Su</td>
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<tr>
<td>Su</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

**Instructions:** Use the symbols below to indicate your sleep times in the grid. Rate your sleep quality each night from 0 (poor) to 10 (excellent).

<table>
<thead>
<tr>
<th>Symbol</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓</td>
<td>Go to bed</td>
</tr>
<tr>
<td>↑</td>
<td>Get out of bed</td>
</tr>
<tr>
<td>↔</td>
<td>Actual sleep</td>
</tr>
</tbody>
</table>

**Comments**

---

[Handwritten notes indicating sleep times and ratings]
Graphic sleep diary in insomnia patient

- **Daytime rest periods**
- **Irregular wake times**
- **Irregular bedtimes**
# Types of sleep disorders

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insomnia</td>
<td>Difficulty with falling or staying asleep</td>
</tr>
<tr>
<td>Sleep-related breathing disorders</td>
<td>Sleep apnea</td>
</tr>
<tr>
<td>Hypersomnias</td>
<td>Conditions that cause severe daytime sleepiness (e.g., narcolepsy)</td>
</tr>
<tr>
<td>Circadian rhythm sleep disorders</td>
<td>Sleep disturbances resulting from problems with the biological clock (e.g., shift work problems)</td>
</tr>
<tr>
<td>Parasomnias</td>
<td>Unusual behaviors or experiences during sleep (e.g., sleep terrors, sleepwalking, nightmares)</td>
</tr>
<tr>
<td>Sleep-related movement disorders</td>
<td>Periodic leg movements, body rocking</td>
</tr>
</tbody>
</table>

American Academy of Sleep Medicine, International Classification of Sleep Disorders, 2nd Edition, 2005
Insomnia disorder: International Classification of Sleep Disorders, 2nd Edition

A. The individual reports one or more of the following sleep related complaints:
   1. difficulty initiating sleep
   2. difficulty maintaining sleep
   3. waking up too early, or
   4. sleep that is chronically nonrestorative or poor in quality

B. The sleep difficulty occurs despite adequate opportunity and circumstances for sleep.

C. At least one daytime impairment related to the nighttime sleep difficulty is reported (e.g., fatigue, irritability, poor concentration)

American Academy of Sleep Medicine, 2005
Prevalence, incidence, and remission of insomnia

Brief Behavioral Treatment of Insomnia: Four steps

- Reduce your time in bed
- Get up at the same time every day of the week, no matter how much you slept the night before
- Don’t go to bed unless you’re sleepy
- Don’t stay in bed unless you’re asleep

Adapted from Borbély, *Hum Neurobiol*, 1982

Acute response to BBTI vs. control condition in older adults with chronic insomnia

Categorical Outcome Responses

Response: Decrease in Pittsburgh Sleep Quality Index (PSQI) ≥ 3 points or increase in sleep efficiency ≥ 10%
Remission: Response + Sleep efficiency ≥ 85% and PSQI ≤ 5

\[ \chi^2 = 13.8, p < .001 \]

\% of Participants

<table>
<thead>
<tr>
<th>Condition</th>
<th>Remission</th>
<th>Response</th>
<th>Partial Response</th>
<th>Non-Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>BBTI n=39</td>
<td>20</td>
<td>30</td>
<td>15</td>
<td>15</td>
</tr>
<tr>
<td>IC n=40</td>
<td>5</td>
<td>35</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

\% Without Insomnia Dx Post-treatment

\[ \chi^2 = 15.5, p < .001 \]

Buysse, Arch Int Med, 2011; 171:887-895
# Medications for insomnia in older adults

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Examples</th>
<th>Potential Advantages</th>
<th>Potential Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzodiazepine receptor agonists (BzRA)</td>
<td>Zolpidem, zaleplon, eszopiclone, temazepam</td>
<td>• Efficacious</td>
<td>• Cognitive effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Variety of half-lives</td>
<td>• Falls</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Dependence</td>
</tr>
<tr>
<td>Sedating antidepressants</td>
<td>Doxepin, amitriptyline, nortriptyline</td>
<td>• No abuse</td>
<td>• Anticholinergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Effective for WASO</td>
<td>• Cardiac effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Falls</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>Diphenhydramine, doxylamine</td>
<td>• Widely available</td>
<td>• Cognitive effects</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Limited efficacy data</td>
</tr>
<tr>
<td>Melatonin, melatonin receptor agonist</td>
<td>Melatonin, ramelteon</td>
<td>• “Natural” mechanism</td>
<td>• Limited efficacy on WASO</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Some efficacy data</td>
<td></td>
</tr>
<tr>
<td>Sedating antipsychotics</td>
<td>Quetiapine, olanzapine</td>
<td>• Not BzRA</td>
<td>• Metabolic, neurological, cardiovascular</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Efficacy for psychosis, depression</td>
<td>effects</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>Gabapentin, pregabalin</td>
<td>• Not BzRA</td>
<td>• Limited sleep efficacy data</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Efficacy for pain</td>
<td></td>
</tr>
</tbody>
</table>

WASO = Wakefulness After Sleep Onset. 
Italics = Not FDA-approved for insomnia
Special considerations for pharmacologic treatment in older adults

- Medications may have very different effects in older vs. younger adults
- Hypnotics have higher risk-benefit ratio in older adults
- Important sources of differential effects
  - End organ (brain) changes: volume loss, white matter hyperintensities, neurodegenerative conditions
  - Pharmacokinetics
  - Pharmacodynamics
- *All* sedating drugs associated with falls

Glass et al., *BMJ*, 2005;331:1169-1175
Obstructive sleep apnea syndrome (OSA)

- Sleep disruption related to repeated airway closures during sleep
- Key symptoms and signs
  - Excessive daytime sleepiness
  - Loud snoring, rescucitative snort/gasp
  - Witnessed breathing pauses
  - Obesity
  - Hypertension
  - Upper airway “crowding”
- PSG findings
  - Repeated episodes of airflow cessation (apnea) or limitation (hypopnea) lasting >10 seconds
  - Oxygen desaturation
  - Repeated arousals

American Academy of Sleep Medicine, 2005
Polysomnography of obstructive sleep apnea

Kuna and Remmers, *Principles and Practice of Sleep Medicine*, 2000
Obstructive sleep apnea in younger and older adults

<table>
<thead>
<tr>
<th>Feature</th>
<th>Older Adults &gt;60 yo</th>
<th>Younger Adults &lt;60 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M = F (1:1)</td>
<td>M &gt; F (2:1)</td>
</tr>
<tr>
<td>Obesity</td>
<td>Not important</td>
<td>Very important</td>
</tr>
<tr>
<td>Witnesses apneas</td>
<td>Rarely reported</td>
<td>Strongly predictive</td>
</tr>
<tr>
<td>Snoring</td>
<td>Infrequently reported</td>
<td>Frequently reported</td>
</tr>
<tr>
<td>Prevalence AHI &gt; 5</td>
<td>30 – 40%</td>
<td>9% Men, 4% Women</td>
</tr>
<tr>
<td>Prevalence RDI &gt; 10</td>
<td>62%</td>
<td>10%</td>
</tr>
<tr>
<td>Morbidity, mortality</td>
<td>Nocturia, impaired cognition, atrial fibrillation, mortality</td>
<td>Death, coronary heart disease, depression, metabolic disorders</td>
</tr>
<tr>
<td>CPAP pressure</td>
<td>Lower</td>
<td>Higher</td>
</tr>
</tbody>
</table>

Obstructive sleep apnea syndrome (OSA)

- **Morbidity**
  - Neurocognitive
    - Sleepiness
    - Impaired memory, concentration
    - Traffic accidents
    - Depression
  - Medical
    - Hypertension, stroke, heart attack
    - Obesity

- **Treatment**
  - Positive airway pressure (CPAP, BiPAP, AVAPS)
  - Oral appliances
  - Upper airway surgery
  - Newer treatments: WinX (negative oral pressure)

- **New treatment models**
  - Home testing and titration
  - Advanced practice nurses, other staff to help with education, adherence
Continuous Positive Airway Pressure

Sullivan et al., 1981
Restless Legs Syndrome: Key symptoms

- Desire to move the limbs, usually associated with uncomfortable ("creepy-crawly") or painful sensations
- Muscle restlessness
- Symptoms worse at rest, partially relieved by movement
- Symptoms worse in the evening or at night
Periodic Limb Movement Disorder: Key symptoms

- Insomnia or excessive sleepiness
- Repetitive, leg jerks: extension of the big toe with partial flexion of ankle, knee, hip
- Present in 85-90% of individuals with Restless Legs Syndrome (RLS)
- May also occur without RLS
Restless Legs Syndrome: Actigraphy

Three-week actigraphic studies in normal and patient with RLS
Restless Legs Syndrome

- Etiology
  - Genetic component; increased in families
  - Associated with iron-deficiency anemia, kidney failure, pregnancy (up to 27%), medications

- Prevalence
  - 5-10% of adults

- Treatment
  - Dopamine agonist or precursor drugs: L-Dopa, pramipexole, ropinirole, rotigotine patch
  - Benzodiazepine hypnotics
  - Opioids
  - Others ( gabapentin, pregabalin, ?Vitamin D, magnesium)
Parasomnias

- Non-REM Sleep Related
  - Confusional arousals
  - Sleepwalking
  - Sleep Terrors
- REM Sleep Related
  - Nightmare disorder
  - REM sleep behavior disorder
- Others
  - Enuresis (bedwetting)
  - Sleep related eating disorder
REM sleep behavior disorder (RBD)

- **Key symptoms**
  - Violent dreams with good recall
  - Violent, injurious behavior consistent with dream
  - Onset in mid-late life, M > F

- **Polysomnographic findings**
  - Increased muscle tone during REM sleep

![Polysomnographic findings](image)
REM sleep behavior disorder (RBD)

- Pathophysiology
  - Release from brainstem-initiated atonia during REM
  - Association with alpha-synucleinopathies (Lewy Body dementia, Parkinson’s, Progressive Supranuclear Palsy, related disorders)

- Treatment
  - Benzodiazepine (e.g., clonazepam)
  - Melatonin in high dose (12 mg)
  - Avoid SSRI, SSNRI antidepressants
Circadian Rhythm Sleep Disorders

- Difficulty sleeping at night
- Difficulty staying awake during day
- Individual’s sleep and wake times are out of sync with the outside world or with the individual’s desired sleep times
- Can result in short overall sleep, symptoms of sleep deprivation

American Academy of Sleep Medicine, 2005
Circadian rhythm sleep disorders

Time of Day

4:00 pm                Midnight                  8:00 am                4:00 pm

Normal

Advanced Sleep Phase Syndrome

Delayed Sleep Phase Syndrome

Night Shift Work

Night Shift Work
Advanced Sleep Phase Disorder: Treatment

- **Behavioral**
  - Scheduling sleep to maximize quality and quantity
    - Focus on delaying bed time
  - Gradually shift times later
  - Good sleep habits to stabilize sleep-wake hours

- **Bright light treatment: Evening**

- **Pharmacological**
  - Melatonin
  - Hypnotics
  - Stimulants
Bright light treatment of circadian rhythm sleep disorders

Evening light delays sleep

Morning light advances sleep
Sleep in nursing homes

<table>
<thead>
<tr>
<th>Sleep Problems</th>
<th>Sources of Sleep Problems</th>
</tr>
</thead>
<tbody>
<tr>
<td>Night awakenings, agitation</td>
<td>Brain changes (dementia, circadian rhythms)</td>
</tr>
<tr>
<td>Daytime sleep, napping</td>
<td>Medical and psychiatric illness</td>
</tr>
<tr>
<td>Reduced circadian rhythm of sleep-wakefulness</td>
<td>Medication</td>
</tr>
<tr>
<td></td>
<td>Environmental</td>
</tr>
<tr>
<td></td>
<td>- Reduced light</td>
</tr>
<tr>
<td></td>
<td>- Reduced activity</td>
</tr>
<tr>
<td></td>
<td>Care routines</td>
</tr>
<tr>
<td></td>
<td>- Continence and medical care</td>
</tr>
<tr>
<td></td>
<td>- Long time in bed</td>
</tr>
</tbody>
</table>

Sleep in nursing homes: Interventions

- **Behavioral sleep measures**
  - Regular sleep-wake schedule
  - Minimize daytime napping
  - Increase daytime physical activity
  - Reduce time in bed

- **Nighttime environment**
  - Dark
  - Quiet
  - Comfortable temperature
  - Match roommates on nighttime care routine

- **Daytime environment**
  - Increase light; encourage outdoor activities
  - Encourage physical activity, especially in afternoon
  - Consistent meal and activity schedule

- **Medications**
  - Avoid sedatives, hypnotics when possible

Sleep disorders in the elderly: Take-home points

- Sleep in older adults is subjectively lighter, more fragmented, and earlier
- Objective methods confirm subjective reports
- Sleep changes in the elderly are related to changes in physiological regulation as well as the effects of neuropsychiatric and medical illness
- Age-related increases are observed in specific sleep disorders: insomnia, sleep apnea, restless legs syndrome, circadian rhythm disorders, insomnia/ hypersomnia related to medical illness
- Treatment involves behavioral, pharmacologic, and other treatments, combined with optimal medical care