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BRAIN HEALTH ACADEMY

UsAgainstAlzheimer's

Sleep and Dementia

Acknowledgements

This course is presented and developed in partnership with the American Academy of Sleep Medicine.

Presenters

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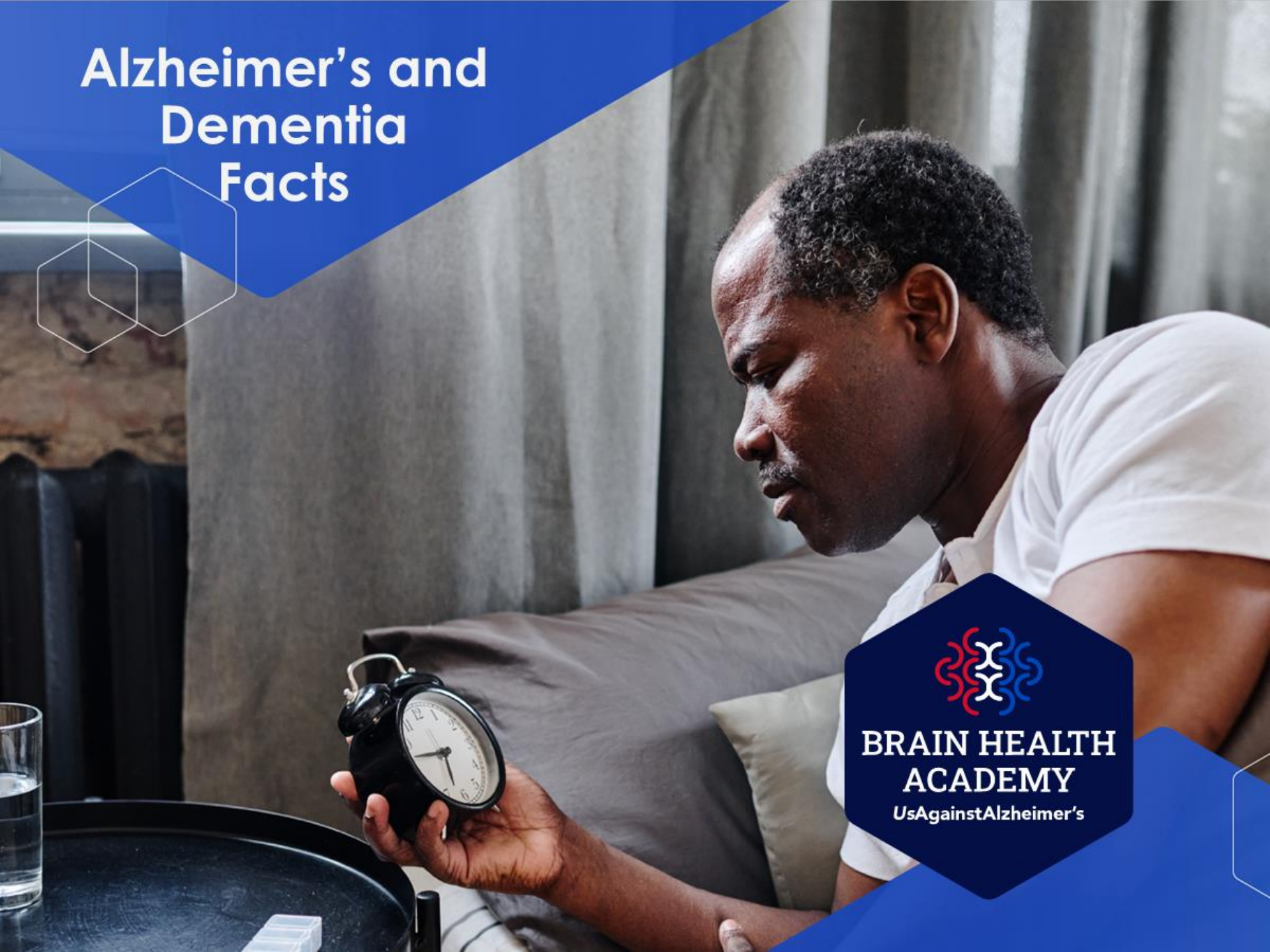
Course Description

It's no secret that sleep is important and most Americans don't get enough of it. So, how can healthcare and wellness professionals work with patients and clients to prioritize sleep and stick to a long-term plan? Learn about the association between sleep and dementia, effective screening tools, and strategies to optimize quality sleep.

Learning Objectives

- Participants will be able to list 6 or more modifiable risk factors for dementia.
- Participants will be able to summarize the link between **sleep** and dementia.
- Participants will be able to identify effective interventions and strategies to address **sleep** with a special focus on adults 45+.
- Participants will be able to identify special considerations for high-risk populations.

Alzheimer's and Dementia Facts



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Scope of the Epidemic (U.S.)[1]

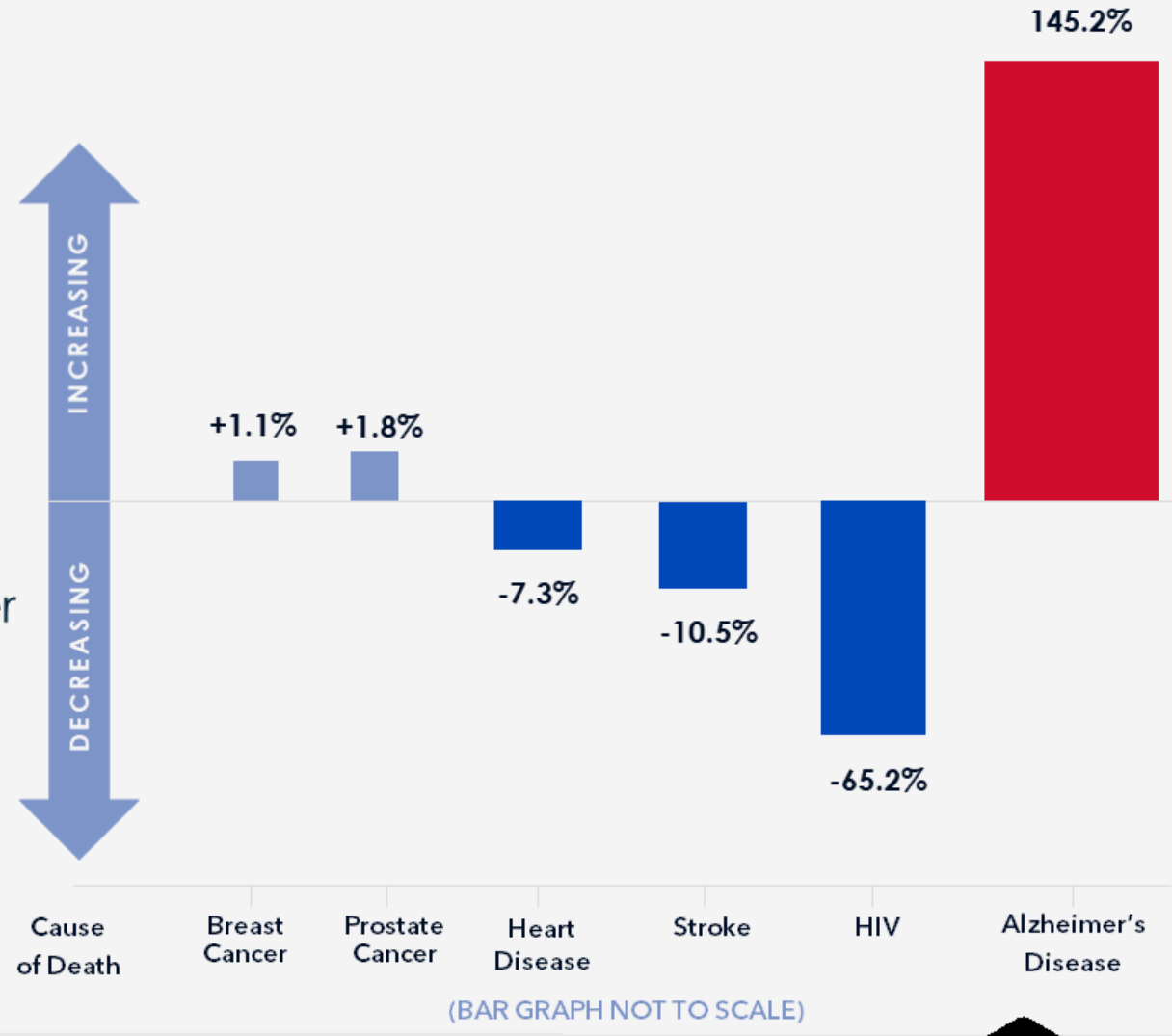
6.5 million adults

1 in 9 adults age ≥65

1 in 3 adults age ≥85

2/3 are women

Alzheimer's deaths increased 145% from 2000-2019, while other top causes of death have declined



Inequities in Brain Health[2, 3, 4]

African American people are
2X AS LIKELY
to have Alzheimer's

Latino people are
1.5X AS LIKELY
to have Alzheimer's

Less likely than White patients to receive a timely diagnosis;

More likely to report experiencing racial discrimination along their patient and caregiver journeys;

Less likely to be enrolled in cutting-edge Alzheimer's and brain health research.

Modifiable Risk Factors for Dementia

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Alzheimer's: Non-Modifiable Risk Factors[6, 1, 7, 8]

Age

Number one risk factor is advancing age.

Risk doubles every 5 years after age 65.

Family History

Genetics vs environmental factors.

Education

Fewer years of formal education and lower levels of cognitive engagement may be risk factors.

Sex

2/3 of those with Alzheimer's are women.

16% of women age ≥ 71 (11% of men).

After age 65, have more than 1 in 5 chance (1 in 11 for men).

Modifiable Risk Factors[9]

40%

of dementia cases could be prevented by addressing these lifestyle factors

INCREASE

- Education
- Physical Activity
- Social Contact

DECREASE

- Hearing Loss
- Hypertension
- Obesity
- Smoking
- Depression
- Diabetes
- Excessive Alcohol Intake
- Head Injury
- Air Pollution

Source: Lancet Commission on Dementia Prevention and Care

Link Between Sleep and Dementia

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Sleep and Dementia Associations

Sleep and sleep disturbances are strongly associated with dementia.

Both inadequate quantity and quality of sleep have been associated with dementia risk.

- Fewer than 5 hours of sleep per night is associated with an approximate doubling of dementia risk.
- Low oxygen levels associated with sleep apnea raise risk for dementia and cognitive impairment.
- Abnormal sleep behaviors, especially violent acting of dreams, is associated with a high risk of later dementia and parkinsonism.

Sleep and Dementia Associations - Sleep Quantity: Different Across the Ages

Category	Age Range	Recommended Sleep Duration	Optional Sleep Duration	Not Recommended
Young Adults	18-25 Yrs.	7-9 Hrs.	6, 10-11 Hrs.	<6, >11 Hrs.
Adults	26-64 Yrs.	7-9 Hrs.	6, 10 Hrs.	<6, >10 Hrs.
Older Adults	65+ Yrs.	7-8 Hrs.	5-6, 9 Hrs.	<5, >9 Hrs.

Sleep and Dementia Associations - Sleep Quality: An Elusive Concept and Construct [12]

Sleep quality can be considered subjectively and objectively (i.e., with polysomnography/sleep study measures)

Subjective sleep quality variably related to objective polysomnographic and other sleep measures

Objective measures of sleep architecture include:

- Sleep efficiency/times: Overall quantity/quality measure
- Sleep stages: Sleep depth
- Arousals: Sleep stability

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Ways Poor Sleep May Lead to Dementia

Sleep is essential for "brain washing" -- clearance of toxic proteins, especially amyloid and tau, depends on sleep

Sleep homeostasis ("Slow Wave", i.e., N3 sleep) linked to synaptic mechanisms underlying memory consolidation

Sleep apnea causes low oxygen to the brain and heart, and "non-dipping" of blood pressure, and has been linked to dementia risk

Ways Poor Sleep May Lead to Dementia: Sleep-Dependent Glymphatic Clearance [16, 17]

Sleep essential for "brain washing" -- clearance of proteins, especially amyloid and tau is sleep-dependent

Interstitial brain channels ("glymphatic system") greatly expand during sleep, clearing wake-cumulative metabolic byproducts:

https://en.wikipedia.org/wiki/File:Video_schematic_of_glymphatic_flow.ogv

Converging evidence that CSF amyloid, tau, and synuclein decrease during sleep and increase following sleep restriction

Even one night sleep deprivation increases amyloid in areas associated with dementia

Ways Poor Sleep May Lead to Dementia: Deep Sleep and Synaptic Homeostasis [18, 19]

Sleep homeostasis ("Slow Wave", i.e., N3 sleep) linked to synaptic mechanisms underlying memory consolidation

- Rebound (greatly increased) N3 follows sleep deprivation
- Localized enriched N3 brain waves in sleep following specific experimental tasks
  - Slow wave stimulation could possibly enhance cognition
- Disruption, and/or age-decreases in N3 sleep may be deleterious to memory and cognition

Ways Poor Sleep May Lead to Dementia: Sleep Apnea and Sleep Hypoxemia 20-25

Sleep apnea results from airway obstruction and reduced airflow during sleep

Main symptoms: Disruptive snoring, poor quality, daytime sleepiness in about half

Sleep apnea causes reduced oxygen to the brain and heart, and "non-dipping" of blood pressure

Sleep apnea is common: 10-30% of adult populations, 15-70% in elderly, up to 90% of AD patients

Sleep apnea independently associated with dementia risk

Sleep Interventions

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Assess Sleep Quality: Validated Tools 26-29

Pittsburgh Sleep Quality Index

- Assesses sleep quantity and quality over a 1-month interval; brief, only 5–10 minutes to complete; however, non-specific as to cause(s) of poor sleep, and tricky to score.

Epworth Sleepiness Scale (ESS)

- Brief (<2 min) tool; Scores > 10 indicate sleepiness (again, non-specific as to cause of sleepiness)

Mayo Sleep Questionnaire (MSQ)

- Brief, well validated core question concerning dream enactment given to bedpartner/spouse or patient; also asks re: other key sleep disturbing symptoms of sleep apnea, RLS, sleep walking, cramps, and alertness.

"Have you ever seen the patient appear to "act out his/her dreams" while sleeping? (punched or flailed arms in the air, shouted or screamed)"

https://www.mayoclinic.org/documents/msq-copyrightfinal-pdf/doc-20079462

Assess Sleep Quality: Validated Tools – Epworth Sleepiness Scale [28, 30]

How likely are you to doze or fall asleep in the following situations, in contrast to feeling just tired, in recent times?

For each situation, choose either:

0 = Never doze
1 = Slight chance of dozing
2 = Moderate chance
3 = High chance

Sitting and reading
Watching TV
Sitting inactive in a public place
As a passenger in a car for an hour
Lying down in the afternoon when able
Sitting and talking to someone
Sitting quietly after lunch
In a car, stopped in traffic for a few minutes

Interpretation:

Scores > 10 indicate sleepiness

0-5: Lower Normal DS
6-10: Higher Normal DS

11-12: Mild EDS

13-15: Moderate EDS
16-24: Severe EDS

Sleep disorders [31, 32]

An individual may have a sleep disorder if they experience one or more of the following:

- Trouble falling or staying asleep three times a week for at least 3 months > INSOMNIA
- Frequent snoring > SLEEP APNEA SUSPECT
- Persistent daytime sleepiness > SLEEP APNEA OR SLEEP QUALITY DISTURBANCE OR CIRCADIAN DISORDER
- Uncomfortable urge to move legs before sleep = RESTLESS LEGS SYNDROME
- Acting out of dreams during sleep = PARASOMNIA, REM SLEEP BEHAVIOR DISORDER

Sleep medicine consultation should be sought to consider polysomnography (sleep study) and further evaluation for sleep disturbances and suspected sleep disorders.

Sleep Disturbances and Disorders: INSOMNIA[33]

Patients having difficulty falling or staying asleep for more than 3 months have chronic insomnia.

May in part reflect prodromal/early neurodegeneration of sleep promoting brain structures

Current recommended first line management approach: cognitive behavioral therapy for insomnia (CBTI) – integrates and personalizes cognitive and behavioral interventions to correct maladaptive sleep behaviors.

- Best supervised by a psychologist or professional with CBTI expertise; growing application of validated telehealth models

- Prescription hypnotic medications can be offered in select cases

Sleep Disturbances and Disorders: SLEEP APNEA[34, 35]

Sleep apnea is a key treatable cause of mild cognitive impairments (esp. attention and memory).

Should be sought in middle age and older adults with symptoms of cognitive impairment; consider STOP-BANG and oximetry screening.

Current diagnostic approaches include home sleep apnea testing and polysomnography.

Treatment options can be personalized; positive airway pressure still best for most, but position restriction, weight loss, dental appliances, and surgical approaches useful for many.

Sleep Disturbances and Disorders: SLEEP APNEA[34, 35]

Oximetry

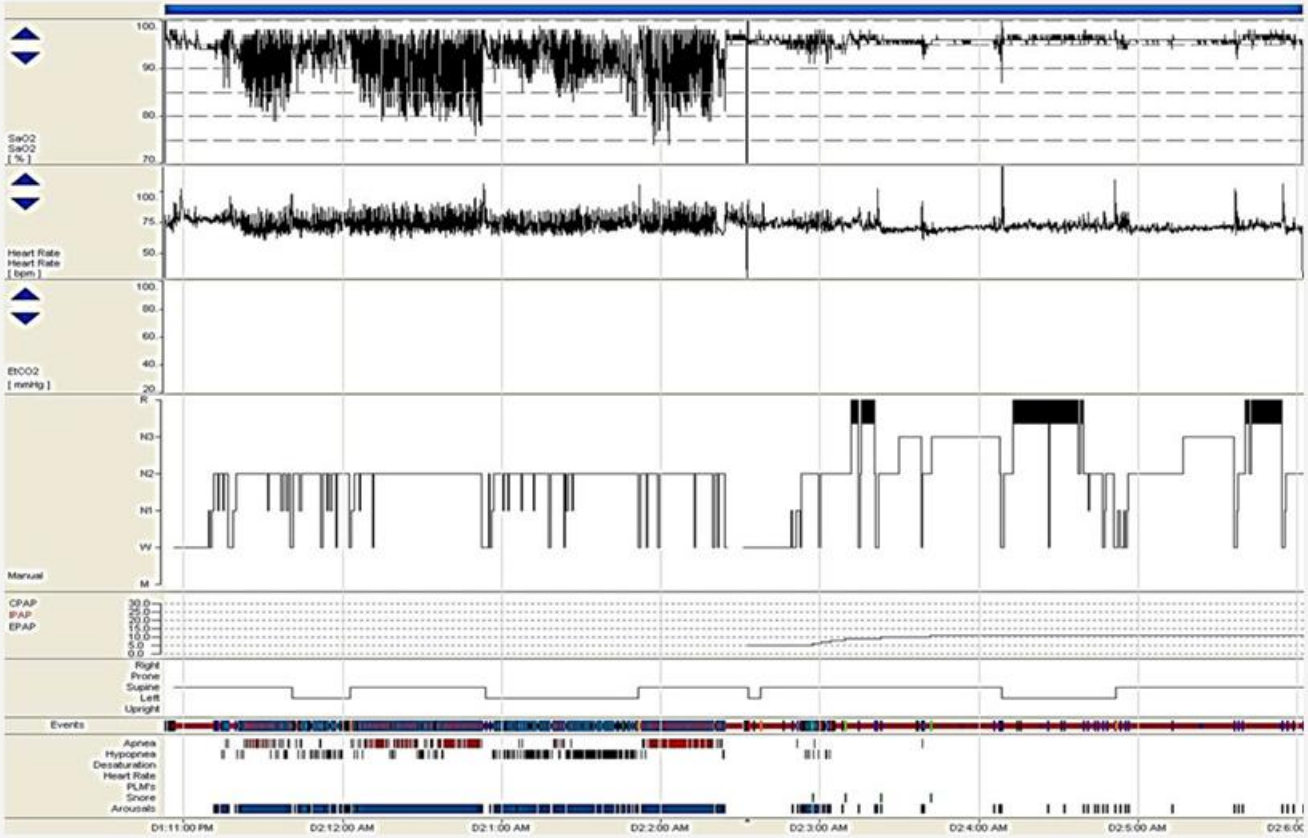
Heart Rate

Sleep Stage Hypnogram

CPAP Pressure

Body Position

Events



Assessing Sleep Apnea: Validated Tools[36]

Consider screening for sleep apnea with STOP-BANG and/or portable overnight oximetry (scores>3 suggestive):

S: disruptive Snoring

T: daytime Tiredness (sleepiness)

O: Observed breathing pauses (apneas)

P: Pressure too high (hypertension)

B: BMI over 35 kg/m2

A: Age > 50 yrs

N: Neck circumference > 40 cm (17 inches)

G: Gender=male sex

Sleep Disturbances and Disorder
RESTLESS LEGS SYNDROME[37]

Restless legs syndrome is a *clinical* diagnosis, based on key features of:

U: uncomfortable Urge to move legs

R: Rest occurrence

G: Getting up/movement improves symptoms

E: Evening predominance

Look for iron deficiency early and often!

Ferritin < 75 mcg/L and/or transferrin saturation < 20% suggest need for iron replacement therapy

Symptomatic therapies: gabapentin/pregabalin, dopamine agonists, opioids

Sleep Disturbances and Disorders: REM SLEEP BEHAVIOR DISORDER[38, 39]

Potentially injurious dream enactment behavior during sleep

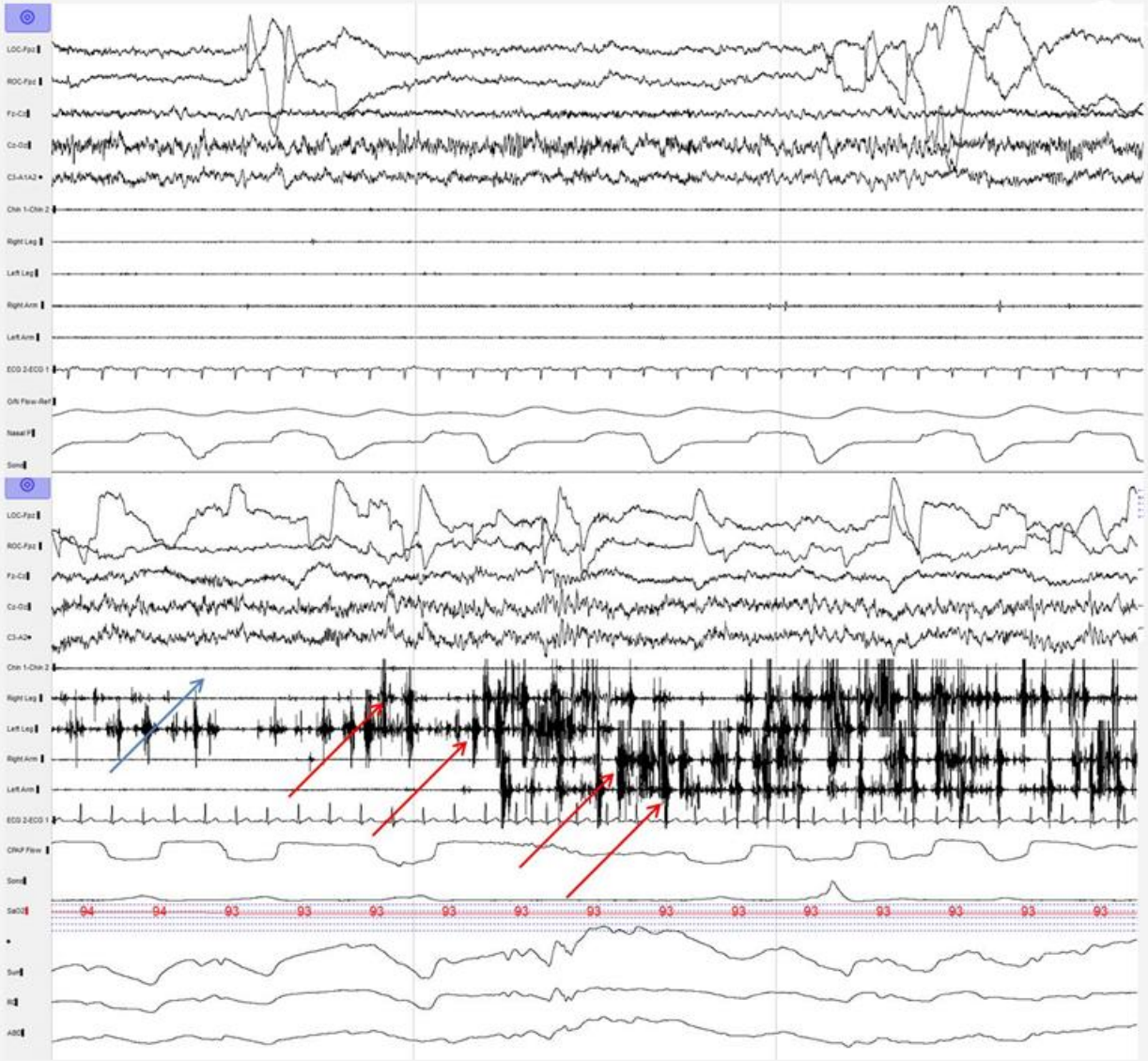
REM Sleep Atonia Loss (aka REM Sleep without Atonia, RSWA) – polysomnography required for diagnosis

Strong association with synucleinopathy and later development of a defined neurodegenerative disorder

2 fold greater risk of MCI/dementia/PD with RBD symptoms

Sleep Disturbances and Disorders: REM SLEEP BEHAVIOR DISORDER[38, 39]

Normal REM Atonia vs. REM Sleep without Atonia



Considerations for Implementation

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Considerations [26]

Ask patients about their medications and whether they may be affecting nighttime sleep or contributing to daytime sleepiness.

- Consider changing the timing of when medications are taken to minimize their impact on sleep quality (i.e., activating meds in AM, sedating meds in PM)
- Evaluation and treatment for mood/anxiety, chronic pain disorders, and asthma may improve sleep disturbances and sleep quality

Tips for aiding sleep (in general, and especially for insomnia sufferers):

- Get good activity level and engagement during the daytime, limiting napping
- Keep the bedroom environment dark/quiet, free of distractions (treat snoring/sleep apnea in partners!) and relatively cool temperature
- Avoid lying sleepless or doing activities in bed
  - When sleepless x 20-30 minutes, get up and leave the bedroom, pursuing quiet activity (reading/TV watching) in another room
- Avoid clock watching
- Keep electronic media out of the bedroom
- Limit screen time for at least one hour before bedtime
- Limit time in bed (consider sleep restriction therapy for insomnia sufferers; should be supervised by sleep practitioner competent in CBT (cognitive behavioral therapy)

Social Determinants and Equity

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Social Determinants of Sleep and Sleep Disorders

- Insufficient sleep and insomnia risk factor associations:
  - Female sex
  - White or Black/African-American race
  - Adverse neighborhood or social environment
  - Being unemployed or without health insurance
  - Being single
  - Decreased income, education, physical activity
  - Worse diet and overall health
  - Increased household size, alcohol, and smoking

- Black/African-American race associated with more severe sleep apnea, greater sleepiness, and younger age at diagnosis

Patient Resources

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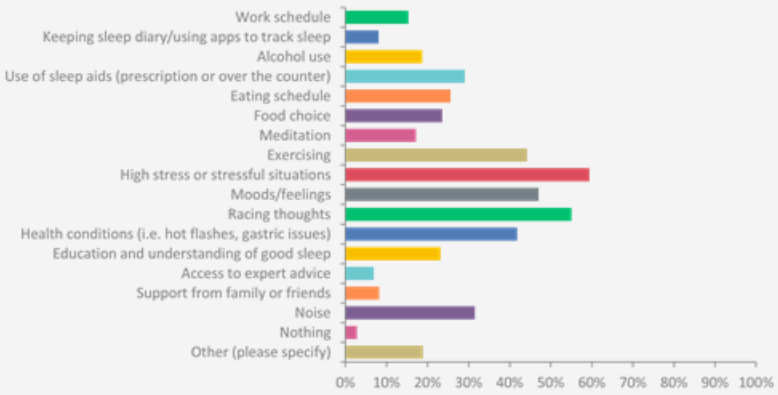
What Matters Most: Sleep Survey Results

- Overall, only **44%** believe they get enough sleep and feel well rested
- Statistically significantly more current caregivers say they do not get enough sleep or feel well rested as compared to those interested in brain health
- **52%** overall worry about getting enough sleep, with current caregivers more likely to worry
- **50%** of those with sleep concerns have not spoken with their health care provider about their sleep
- Top sources of information on sleep: **50%** news articles, **50%** internet, **45%** health care provider

USAGAINSTALZHEIMER'S A-LIST

Top factors impacting ability to get enough sleep

- 59% high stress/stressful situations
- 55% racing thoughts
- 47% moods/feelings
- 44% exercising
- 42% health conditions (i.e. hot flashes, gastric issues)



N=678 (of which 641 provided classification: ADRD/MCI diagnosis: 42; high risk for ADRD: 188; current caregivers: 94; former caregivers: 186; general interest in brain health: 131)

Provider-Patient Resources

Share tips and information regarding sleep:

https://www.sleepfoundation.org/aging-and-sleep

https://www.mayoclinic.org/diseases-conditions/sleep-disorders/symptoms-causes/syc-20354018

Information about dream enactment (NAPS study for REM sleep behavior disorder):

https://www.naps-rbd.org/

Thank you!

This presentation and related resources are available at:
https://www.usagainstalzheimers.org/nutrition-and-dementia

Please register for additional courses at:
https://www.usagainstalzheimers.org/brain-health-academy

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References

[1] Alzheimer's Association. (2022). *2022 Alzheimer's Disease Facts and Figures*. Alzheimer's Association. https://www.alz.org/media/Documents/alzheimers-facts-and-figures.pdf

[2] Aranda, Maria P., Vega, William A., Richardson, Jason R., Resendez, Jason. (2019). Priorities for Optimizing Brain Health Interventions Across the Life Course in Socially Disadvantaged Groups. Florida International University and UsAgainstAlzheimer's.

[3] Tsoy E, Kiekhofer R.E., Guterman E.L., et al. (2021). Assessment of Racial/Ethnic Disparities in Timeliness and Comprehensiveness of Dementia Diagnosis in California. JAMA Neurol. https://doi.org/10.1001/jamaneurol.2021.0399

[4] Development. of an NIA Practice-Based Research Network to Conduct Alzheimer's and Related Dementias Clinical Research. (2021). National Institute on Aging

[5] Mudrazija, S., Vega, W., Resendez, J., & Monroe, S. (2020, November 15). Place & Brain Health Equity: Understanding the County-Level Impacts of Alzheimer's. UsAgainstAlzheimer's. www.usagainstalzheimers.org/sites/default/files/2020-11/Urban_UsA2%20Brain%20Health%20Equity%20Report_11-15-20_FINAL.pdf

[6] Alzheimer's Association. (2022). *Causes and Risk Factors for Alzheimer's Disease*. Alzheimer's Association. https://www.alz.org/alzheimers-dementia/what-is-alzheimers/causes-and-risk-factors

[7] Alzheimer's Association. (2022). *Younger/Early-Onset Alzheimer's*. Alzheimer's Association. https://www.alz.org/alzheimers-dementia/what-is-alzheimers/younger-early-onset

[8] Podcasy, J. L., & Epperson, C. N. (2016). Considering sex and gender in Alzheimer disease and other dementias. *Dialogues in clinical neuroscience*, *18*(4), 437.

[9] Livingston, G., Huntley, J., Sommerlad, A., Ames, D., Ballard, C., Banerjee, S., ... & Mukadam, N. (2020). Dementia prevention, intervention, and care: 2020 report of the Lancet Commission. The Lancet, 396(10248), 413-446.

References (cont.)

[10] National Sleep Foundation.

[11] Hirshkowitz et al, Sleep Health 2015;1(4):233-243.

[12] McCarter et al, Sleep Med Rev 2022; Jun 9;64:101657.

[13] Ohayon et al, Sleep. 2004;27:1255–1273;

[14] Oh et al, Alzheimers Dement. 2019;15(10):1253-1263;

[15] Stratmann K et al, Brain Pathol. 2016;26(3):371-86.

[16] Xie et al, Science 2013; 342(6156):373-7.

[17] Shokri-Kojori et al, PNAS 2018;115(17):4483-4488.

[18] Tononi and Cirelli, Neuron 2014;81(1):12-34.

[19] Malkani et al, *Sleep Med Clin.* 2020;15(1):101-115

[20] Young et al, 2002, 2009.

[21] Peppard et al, 2013.

[22] Ancoli-Israel S et al, 1989, 1995.

[23] Emamian et al, Front Aging Neurosci. 2016;8:78.

[24] Gaeta AM et al, J Neurol. 2020;267(4):1012-1022.

[25] Yaffe et al, JAMA 2011;306(6):613-9.

[26] Sabbagh, M. N., Perez, A., Holland, T. M., Boustani, M., Peabody, S. R., Yaffe, K., ... & Tanzi, R. E. (2022). Primary prevention recommendations to reduce the risk of cognitive decline. Alzheimer's & Dementia.

References (cont.)

[27] Buysse et al, Psych Res 1989; 28: 192-213.

[28] Johns MW, Sleep 1991;14(6):540-5.

[29] Boeve BF et al, Sleep Med. 2011;12(5):445-53.

[30] https://epworthsleepinessscale.com/about-the-ess/

[31] Mansukhani et al, Conn's Current Therapy 2021; 755-770.

[32] St Louis, Neurol Clin Pract. 2014;4(1):16-25.

[33] Avidan and Neubauer. Continuum (Minneap Minn) 2017; 23 (4, Sleep Neurol):1064-1092.

[34] Foldvary-Schaefer and Waters, Continuum (Minneap Minn) 2017; 23 (4, Sleep Neurology):1093-1116.

[35] St Louis EK. Pract Neurol (Fort Wash Pa). 2010;9(5):26-31.

[36] Vasu et al, Arch Otolaryngol Head Neck Surg 2010; 136:1020-4.

[37] Gossard TR et al, Neurotherapeutics 2021;18(1):140-155

[38] St Louis and Boeve, Mayo Clin Proc. 2017;92(11):1723-1736.

[39] Högl et al, Nat Rev Neurol. 2018;14(1):40-55.

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