
Neurosciences and Spine Symposium
May 9, 2026 | Meydenbauer Center | Bellevue, Washington
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# Disclosures

- Farrokh Farrokhi, MD
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CME Planners have no disclosures

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# Foundations of Sleep Medicine for Clinicians

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# Sleep Apnea 101

David Corley MD, Medical Director, Sleep and Neurodiagnositcs, VMFH

May 9, 2026

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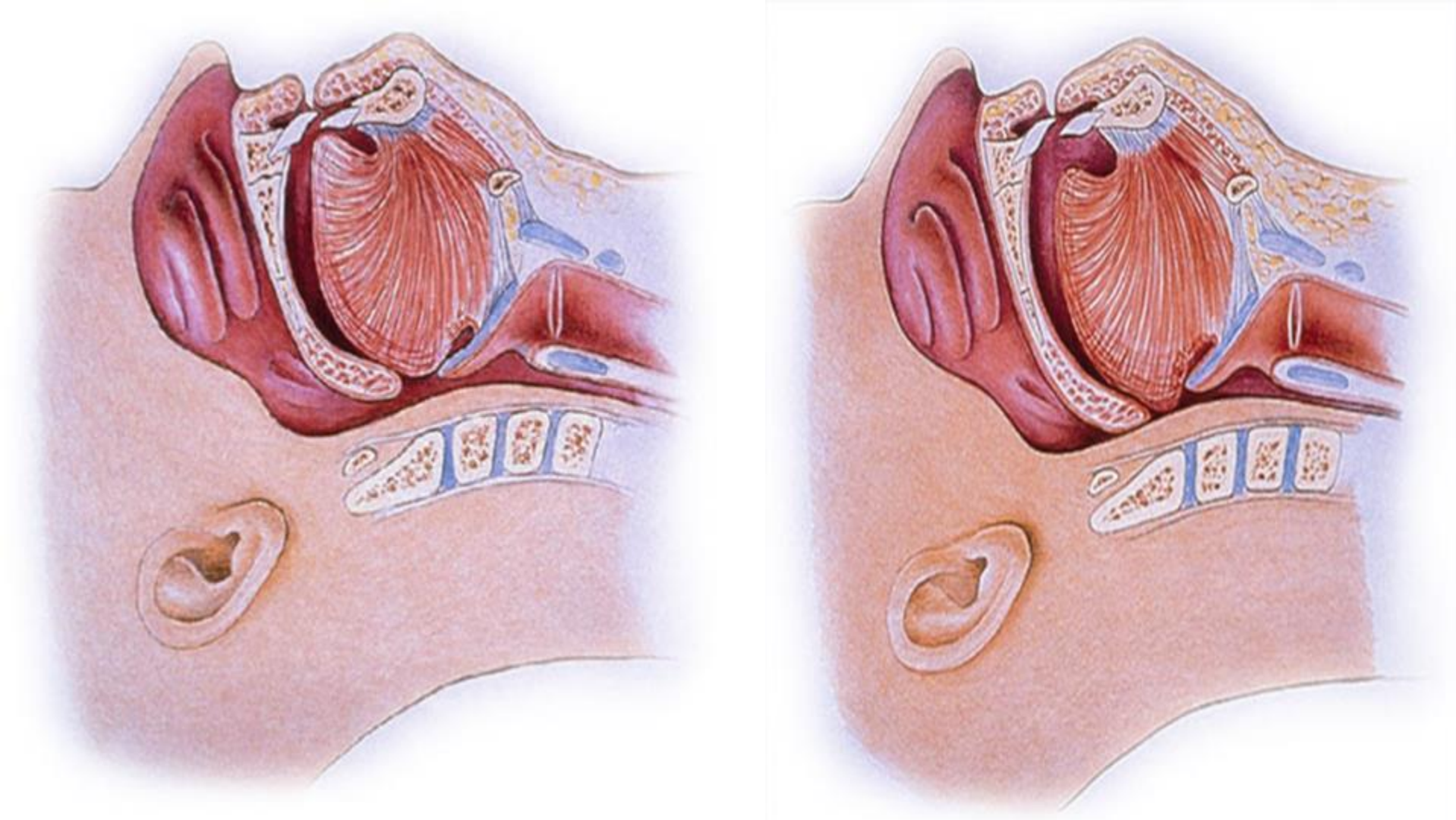

# Prevalence

| | |
|---|---|
| BMI 25-28 | 20% |
| BMI 30-40 | 40% |
| HTN | 50% |
| CVA | 50% |
| “Lone” Atrial Fibrillation | 30% |
| Atrial Fibrillation requiring cardioversion | 50% |
| CHF | 30% |

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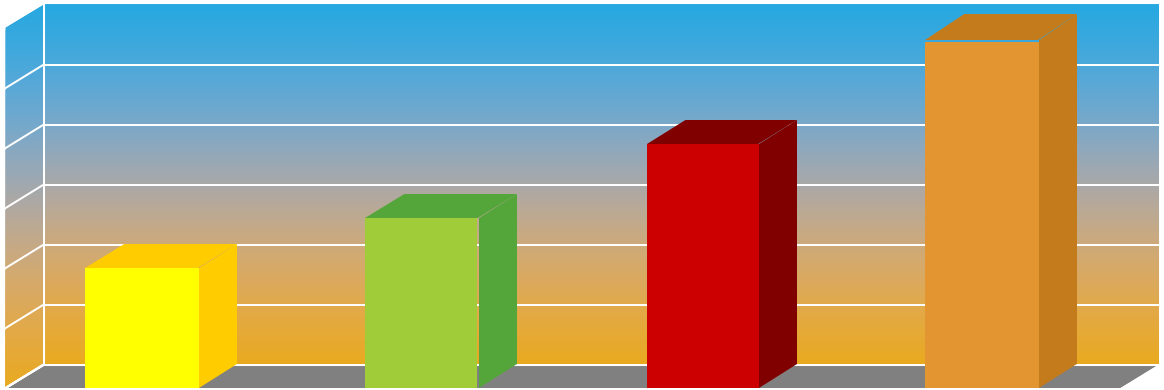
# Cardiovascular Consequences: Hypertension

## Prospective Study of Association Between OSA and Hypertension

Odds Ratio



Adjusted for age, sex, BMI, neck circ., cigs., E

Apnea / Hypopnea Index (AHI)

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Adapted from Peppard PE et al. N Engl J Med 2000;342.

# Who to Test? STOP-BANG Questionnaire

- Snoring ?
- Tiredness ?
- Observed Apneas ?
- Pressure (hypertension) ?
- BMI (over 35 kg/m2) ?
- Age (over 50) ?
- Neck (over 40 cm) ?
- Gender (male) ?

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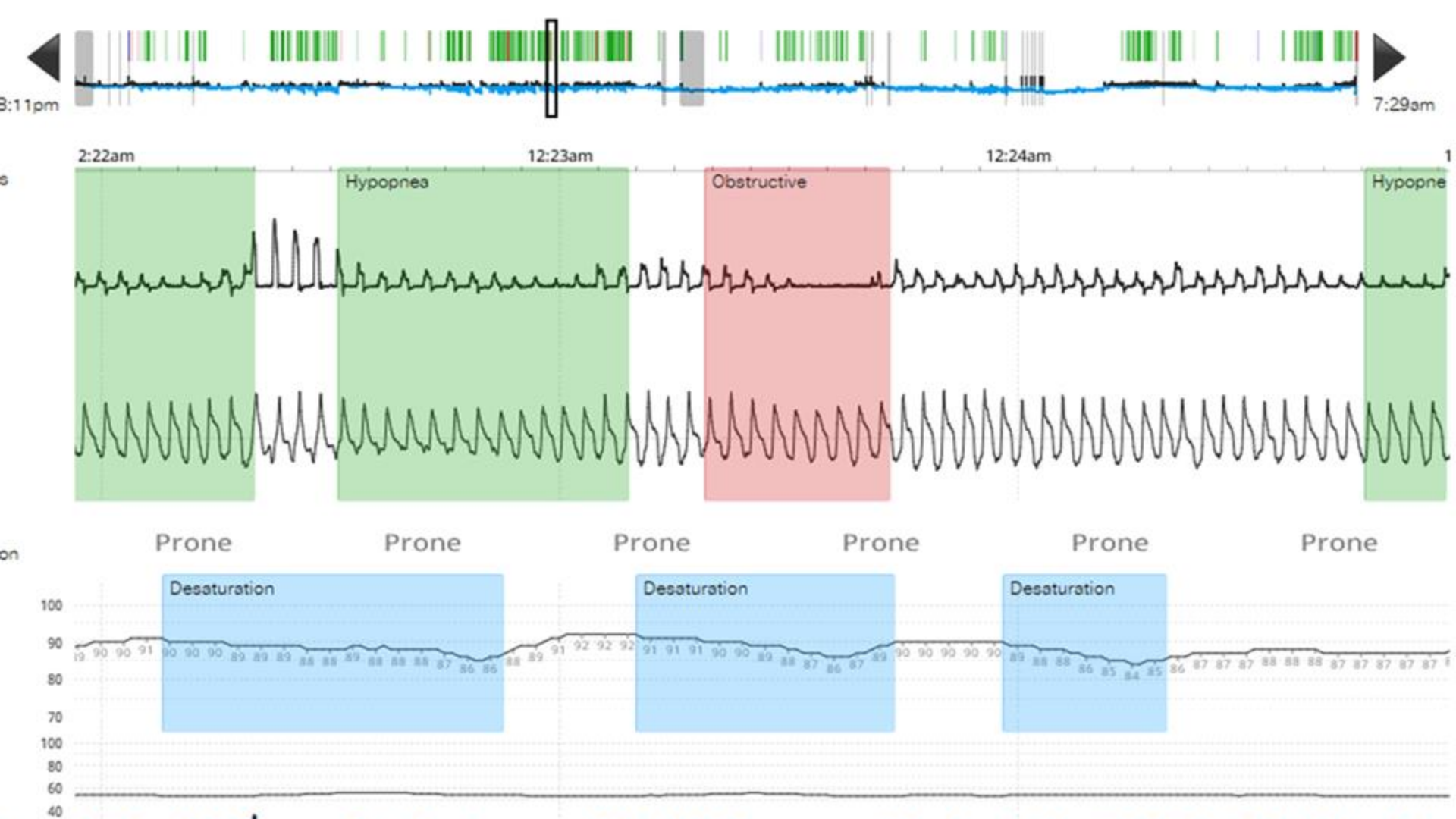
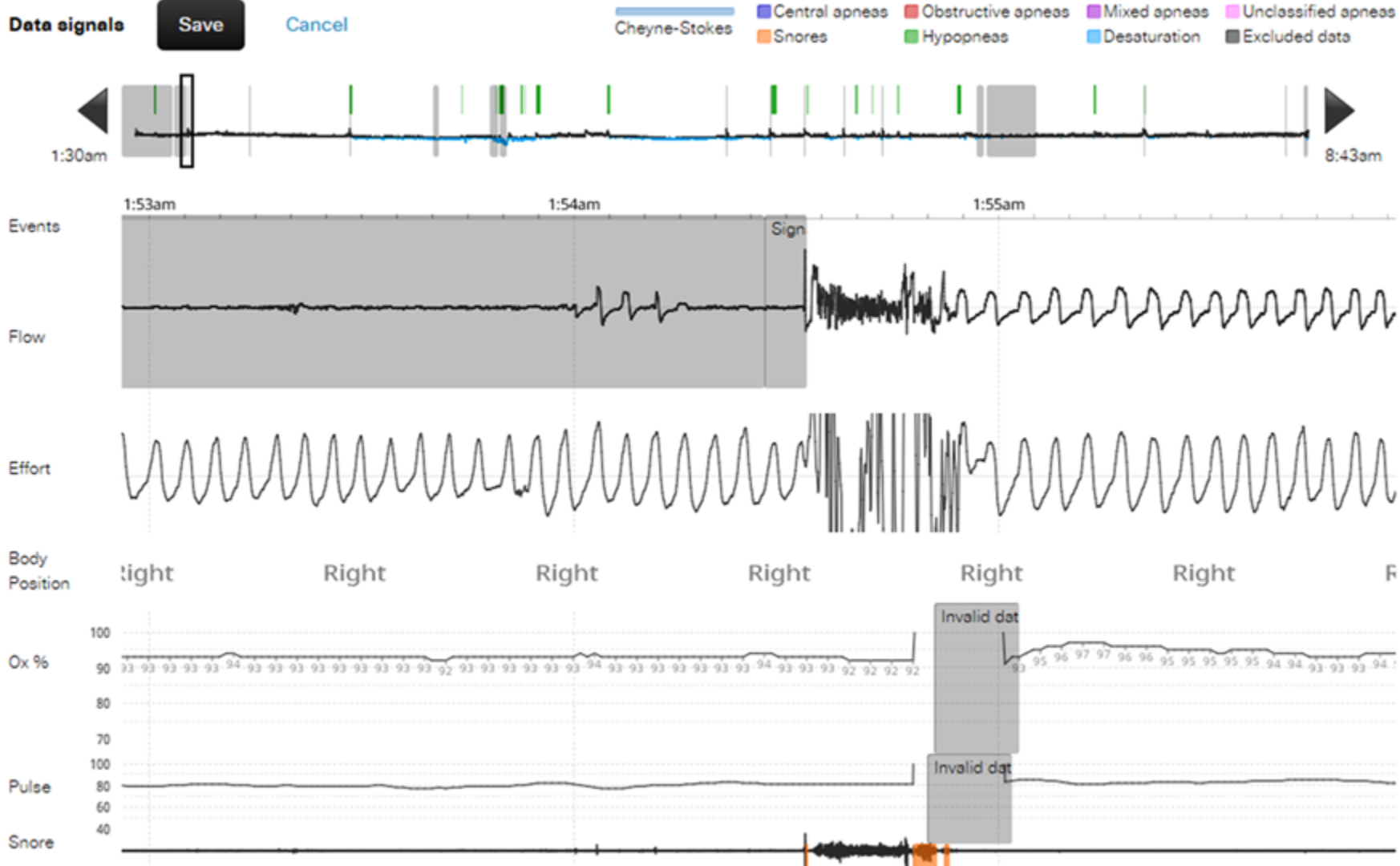

8:11pm
7:29am
2:22am
12:23am
12:24am
Hypopnea
Obstructive
Hypopne
Prone
Prone
Prone
Prone
Prone
Prone
Desaturation
Desaturation
Desaturation
100
90
80
70
100
80
60
40


Data signals
Save
Cancel
Cheyne-Stokes
Central apneas
Obstructive apneas
Mixed apneas
Unclassified apneas
Snores
Hypopneas
Desaturation
Excluded data
1:30am
8:43am
1:53am
1:54am
1:55am
Events
Sign
Flow
Effort
Body Position
Right
Right
Right
Right
Right
Right
Ox %
Invalid dat
Pulse
Invalid dat
Snore

# HST Report

| | |
|---|---|
| REI < 5/hour: | normal |
| REI 5-15/hour | mild |
| REI 15-30/hour | moderate |
| REI > 30/hour | severe |

Hypoxemia burden = time with oxygen saturations less than 89%

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AirView

Gender: Male

## Diagnostic Report

| Recording details | | | | | 07/25/2015 |
|---|---|---|---|---|---|
| Device | | | | Type: | III |
| Recording | Start: 7:53pm | | End: 6:00am | Duration - hr: | 10:07 |
| Flow Evaluation | Start: 8:03pm | | End: 5:58am | Duration - hr: | 9:23 |
| Oxygen saturation evaluation | Start: 8:03pm | | End: 6:00am | Duration - hr: | 9:57 |

### Statistics


| | | | | |
|---|---|---|---|---|
| Events index | AHI: 15.0 | AI: 4.3 | HI: 10.8 | |
| Supine | | Time - hr 5:52 | Percentage: 62.6 | |
| | AHI: 21.9 | AI: 6.7 | HI: 15.3 | |
| Non-supine | | Time - hr 3:28 | Percentage: 36.9 | |
| | AHI: 3.5 | AI: 0.2 | HI: 3.2 | |
| Upright | | Time - hr 0:02 | Percentage: 0.5 | |
| | AHI: 0.0 | AI: 0.0 | HI: 0.0 | |
| Events totals | | Apnea: 40 | Hypopnea: 101 | |
| Apnea Index | Obstructive: 1.9 | Central: 2.1 | Mixed: 0.2 | Unclassified: 0.0 |
| Cheyne-Stokes respiration | | | Time - hr: 0:00 | Percentage: 0 |
| Oxygen desaturation | | | ODI: 16.1 | Total: 160 |
| Oxygen saturation % | Baseline: 96 | | Avg: 95 | Lowest: 83 |
| Oxygen saturation - eval time % | <=90%sat: 2 | | <=85%sat: 0 | <=80%sat: 0 |
| | | | <=88%sat: 1 | <=88%Time - hr: 0:05 |
| Breaths | Total:9653 | | Avg/min: 17.1 | Snores: 744 |
| Pulse - bpm | Min: 43 | | Avg: 59 | Max: 93 |

Analysis guidelines: **AASM 2012, Automatic scoring**

# Positional Therapy

Lateral Body Positioning

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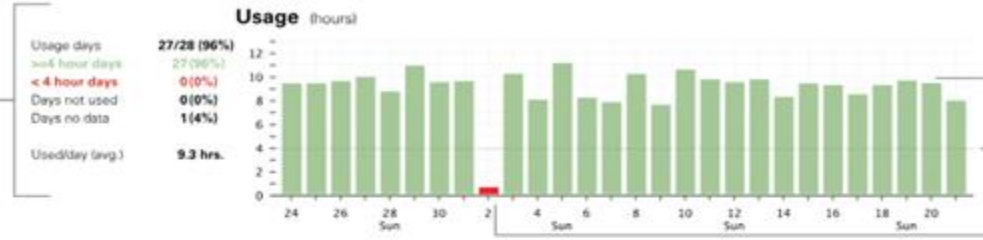
# Graph descriptions

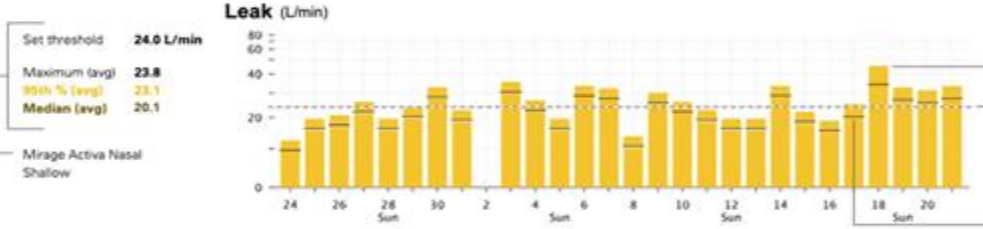
**Usage**
Breakdown of patient's usage in days and hours, indicating their usage patterns




**Leak**
Refers to unintentional leak

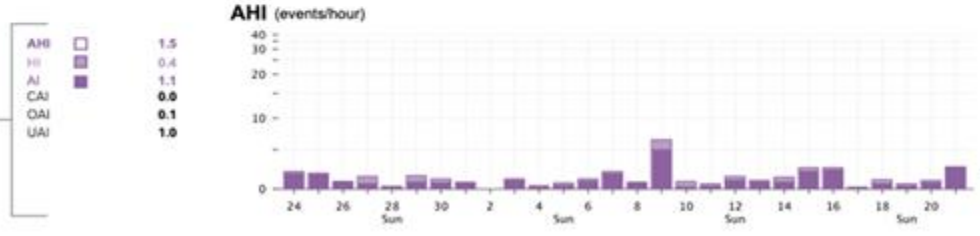
Tip: 95th percentile value should be ≤ 24 L/min. If > 24 L/min, check mouth leak or mask fit

**Mask information**
Per prescription entered into AirView




**Events**
Type and occurrence per hour

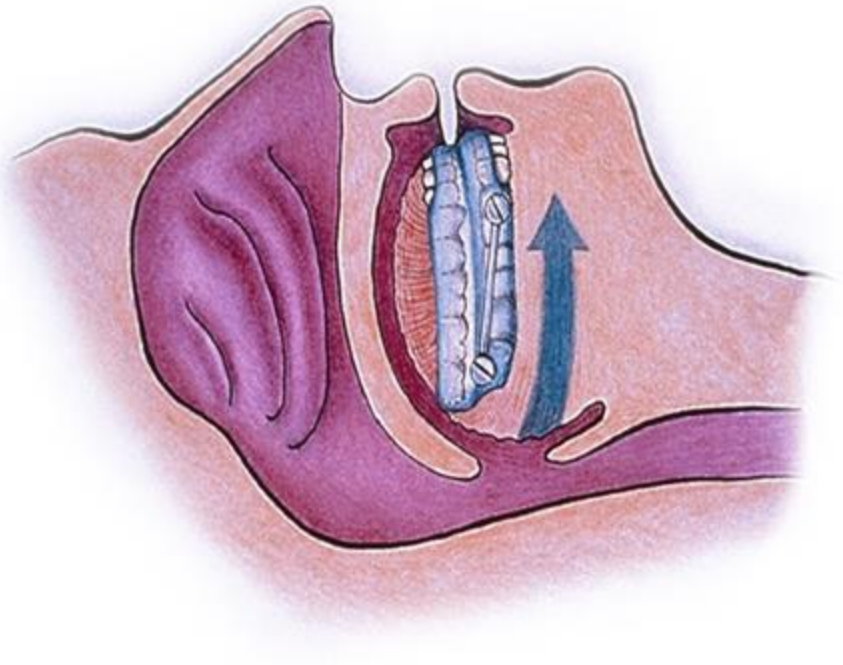
Tip: AHI should be below patient's recommended threshold. If it is above the threshold, check the AI, HI, CAI, OAI and UAI[1]



# Summary, Step by Step

- 1. Identify risk factors (STOP-BANG).
- 2. Order a Home Sleep Test.
- 3. If REI is over 15/hour (or over 5/hour with symptoms or co-morbitities), order auto-PAP 5-15 cm H2O or as recommended on the HST interpretation. If less than 15/hour consider in-lab sleep study or refer for consultation.
- 4. Patients on PAP therapy will need a visit within three months to review PAP data download and certify compliance for most insurances. Consider referral to sleep center for long term follow up.
- 5. Annual visits are needed to review PAP data and document compliance for most insurances. Again, consider sleep center referral for long term follow up.

# Mandibular Advancement Devices



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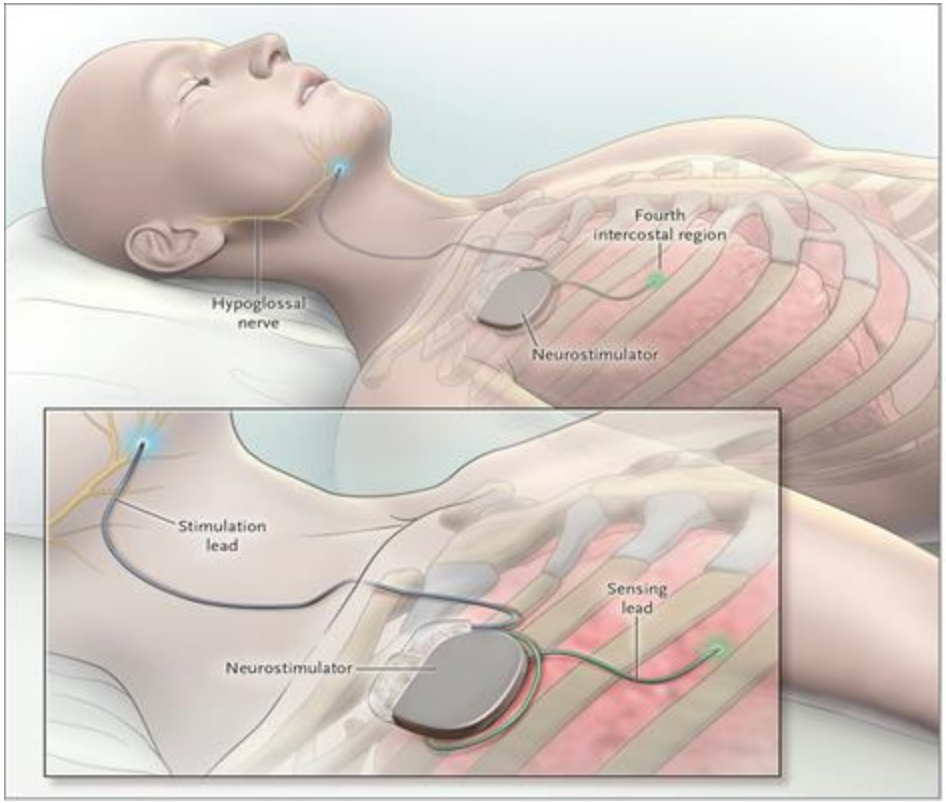
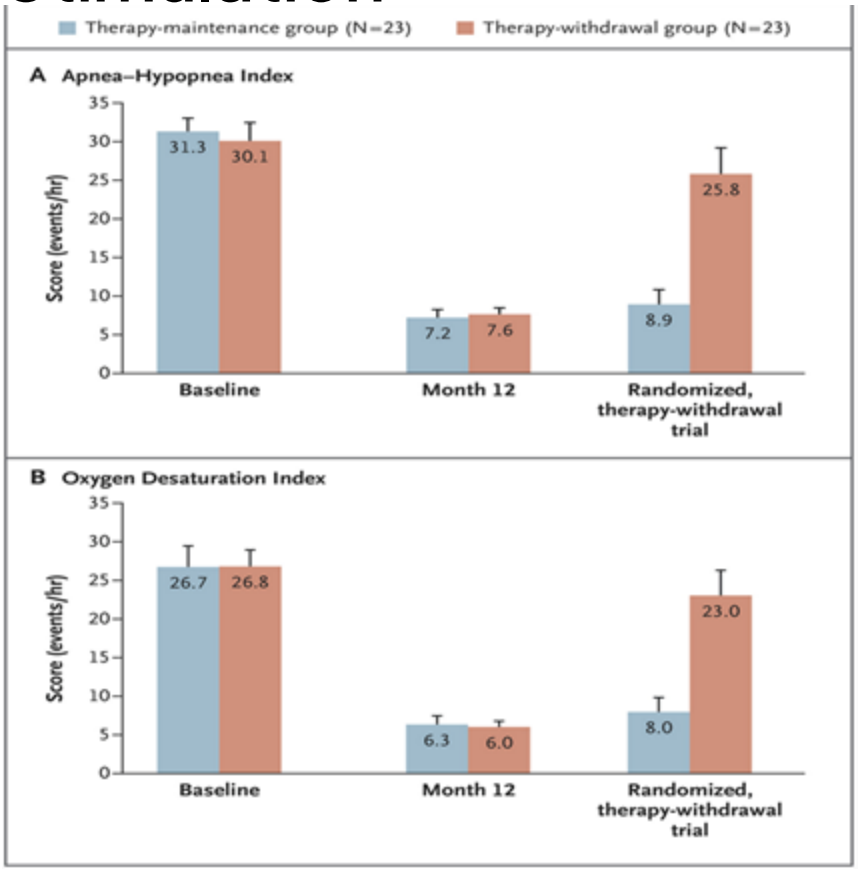
# Hypoglossal Nerve Stimulation

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# Hypoglossal Nerve Stimulation

- **FDA Criterion (Adult Patients > 22 years):**
  - **Severity 15-100 events/hour**
  - **Documented failure or intolerance of CPAP/BPAP**
  - **BMI < 40 kg/m2 (optimal < 32)**
  - **Airway anatomy: absence of concentric collapse on endoscopy**
  - **Apnea type (>75% obstructive)**
  - **Able to operate remote**
  - **Contraindications: >25% central/mixed apneas, severe psychiatric or neurologic issues, inability to undergo MRI, pregnancy**

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ORIGINAL ARTICLE

# Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

This article has been corrected. VIEW THE CORRECTION

**Authors**: Atul Malhotra, M.D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, M.D., M.P.H., Ali Azarbarzin, Ph.D., Scott A. Sands, Ph.D., +5 , for the SURMOUNT-OSA Investigators* Author Info & Affiliations

Published June 21, 2024 | N Engl J Med 2024;391:1193-1205 | DOI: 10.1056/NEJMoa2404881 | VOL. 391 NO. 13



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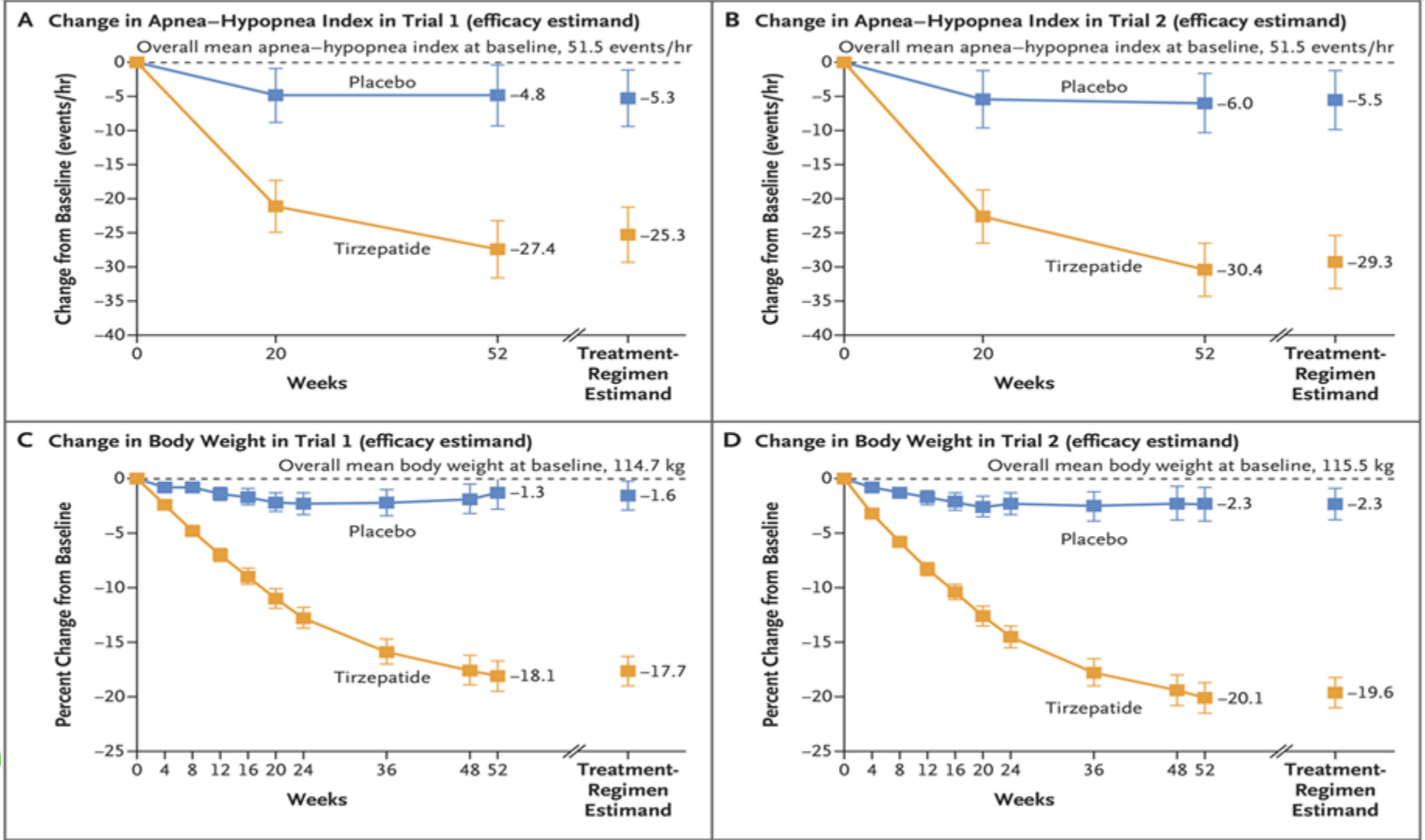
A Change in Apnea–Hypopnea Index in Trial 1 (efficacy estimand)
Overall mean apnea–hypopnea index at baseline, 51.5 events/hr
Change from Baseline (events/hr)
0
−5
−10
−15
−20
−25
−30
−35
−40
Placebo
−4.8
−5.3
Tirzepatide
−27.4
−25.3
0
20
52
Weeks
Treatment-Regimen Estimand
B Change in Apnea–Hypopnea Index in Trial 2 (efficacy estimand)
Overall mean apnea–hypopnea index at baseline, 51.5 events/hr
Change from Baseline (events/hr)
Placebo
−6.0
−5.5
Tirzepatide
−30.4
−29.3
Weeks
Treatment-Regimen Estimand
C Change in Body Weight in Trial 1 (efficacy estimand)
Overall mean body weight at baseline, 114.7 kg
Percent Change from Baseline
0
−5
−10
−15
−20
−25
Placebo
−1.3
−1.6
Tirzepatide
−18.1
−17.7
0 4 8 12 16 20 24 36 48 52
Weeks
Treatment-Regimen Estimand
D Change in Body Weight in Trial 2 (efficacy estimand)
Overall mean body weight at baseline, 115.5 kg
Percent Change from Baseline
Placebo
−2.3
−2.3
Tirzepatide
−20.1
−19.6
0 4 8 12 16 20 24 36 48 52
Weeks
Treatment-Regimen Estimand

# Why is My Patient So Tired?

*A Guide to Evaluating Sleepiness*

**Amir Sabzpoushan, MD**
Department of Sleep Medicine
Virginia Mason Franciscan Health
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# Introduction and definition

## General Definition

Excessive Daytime Sleepiness (EDS) is defined as excessive when it causes a subjective complaint or interferes with function.

## ICSD-3-TR Criteria

The inability to maintain wakefulness and alertness during major waking episodes, with sleep occurring unintentionally almost daily for at least 3 months.

# Importance and Statistics

## Clinical Prevalence

Complaints of EDS, fatigue, and lack of energy are among the most common issues presented to clinicians.

## Diagnostic Significance

EDS can signal an undiagnosed sleep disorder or other treatable condition. Recognition is critical.

## Safety & Quality of Life

Impacts a broad range of activities and raises safety risks while driving or operating machinery.

## Population Statistics

**10 – 25%**

of the general population reports EDS.


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# Differential diagnosis of excessive daytime sleepiness

## Insufficient sleep

- Sleep deprivation
- Environmental intrusions

## Sleep disorders

**Respiratory & Neurological**

- Obstructive & Central sleep apnea
- Sleep-related hypoventilation/hypoxemia
- Narcolepsy type 1 or 2, Kleine-Levin syndrome, Idiopathic hypersomnia
- Restless legs & Periodic limb movement disorder

**Circadian Rhythm Disorders**

- Delayed, Advanced, or Irregular sleep-wake phase disorders
- Non-24-hour sleep-wake rhythm disorder & Jet lag/Shift work

# Other neurologic disorders

## Neurodegenerative & Systemic

- Parkinson disease
- Dementia with Lewy bodies
- Alzheimer disease
- Multiple system atrophy
- Myotonic dystrophy
- Multiple sclerosis

## Injury & Infectious

- Amyotrophic lateral sclerosis (via sleep-related breathing disorders)
- Structural lesions affecting thalamus, hypothalamus, or brainstem
- Traumatic brain injury
- Stroke with and without sleep-related breathing disorders
- Encephalitis lethargica
- Cerebral trypanosomiasis

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# Differential diagnosis of excessive daytime sleepiness

## Medical and genetic disorders

- Hypothyroidism
- Anemia
- End-stage renal disease
- Hepatic insufficiency
- Hepatic encephalopathy
- Myotonic dystrophy
- Prader-Willi syndrome

## Psychiatric disorders

- Depression
- Anxiety
- Substance abuse: Alcohol, Opioid/Prescription opioid, Stimulant withdrawal
- Psychogenic sleepiness

## Medications

- **Benzodiazepines**
- **Nonbenzodiazepine sedatives**
- **Antipsychotics**
- **Antiepileptics**
- **Beta-blockers (lipophilic)**
- **Barbiturates**
- **Antihistamines**
- **Anti-spasm medications**
- **Sedative antidepressants**

# Evaluating Sleepiness, Tiredness, and Fatigue

## Key Questions in Clinical Evaluation

- How likely are you to fall asleep during the day?
- Is daytime sleepiness a problem for you?
- Is it difficult to keep your eyes open at times?
- Do you struggle to stay awake during the day?
- Do you ever feel "foggy"?
- How often and how long do you nap?
- Do you fall asleep at times you do not want to?
- Do you feel tired, fatigued, or have low energy?
- Do you lack energy for daily activities?
- Do you tire easier than others when active?

## Differentiating Stress from Related Complaints

- Does your problem bother you more if you sit to read for an hour or if you go out shopping?
- Which is the single most important problem: sleepiness, tiredness, fatigue, or lack of energy?
- Which most interferes with your ability to accomplish what you would like to do?
- Which is the one problem you would most like to address effectively?

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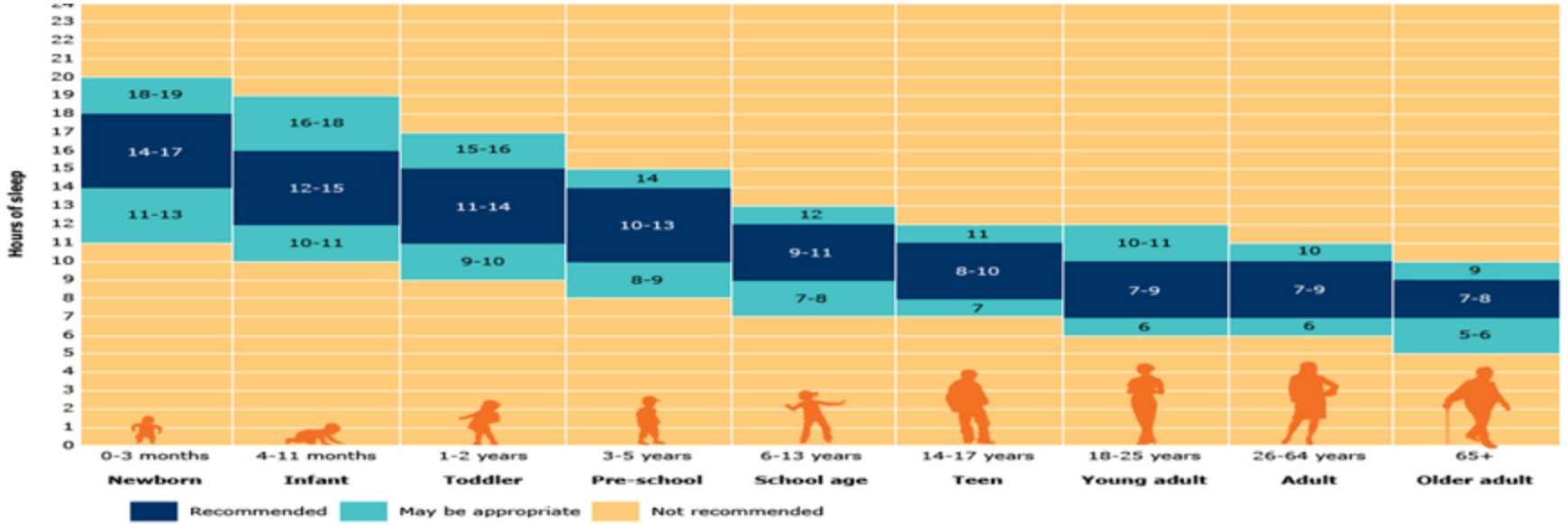
Adapted from: 1. Maschalleck G. Semin Neurol. 2011; 31:42. 2. Chervin RD. Chest. 2000; 118:372.




These recommendations are very similar but not identical to those from the American Academy of Sleep Medicine[1,2].


*ferences:*

1. *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.*
2. *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.*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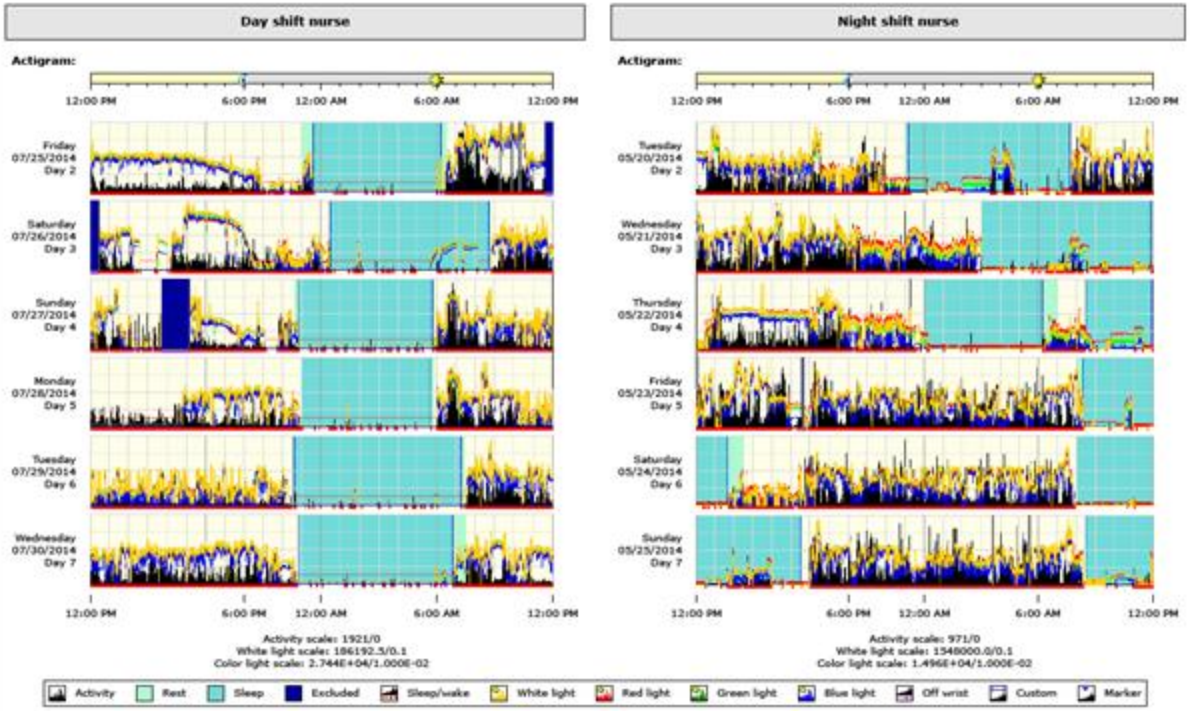
## Shift work actigram




These actigraphic recordings are from a nurse who works the day shift and a nurse who works the night shift. A 24-hour time interval (ranging from 12:00 PM to 12:00 PM) is depicted on the X-axis; sequential dates are depicted on the Y-axis. Note that typical sleep periods (eg, 10:00 PM to 6:00 AM) are in the center of the actigram. The actigram denotes physical activity in black, which correlates with wakefulness. An absence of physical activity correlates with pronounced inactivity and periods of sleep. Periods of sleep (aqua) are determined by the actigraphy software. This actigram also provides light exposure by wavelength, including white, red, green, and blue. In this figure, the day shift nurse appears to go to bed between 11:00 PM and 12:30 AM each night and gets out of bed between 6:00 AM and 7:00 AM each day with the exception of day 3 (Saturday), when they appear to stay in bed until 9:00 AM. In contrast, the night shift nurse has variable sleep-wake periods that correspond to their work schedule. For example, the night shift nurse appears to

# Stanford Sleepiness Scale (SSS)

The SSS is the best validated subjective measure of sleepiness.

| | |
|---|---|
| 1 | **Feeling active, vital, alert, wide awake** |
| 2 | Functioning at a high level, not at peak, able to concentrate |
| 3 | Relaxed, awake, not at full alertness, responsive |
| 4 | A little foggy, not at peak, let down |
| 5 | Fogginess, losing interest in remaining awake, slowed |
| 6 | Sleepiness, prefer to be lying down, fighting sleep, woozy |
| 7 | Almost in reverie, sleep onset soon, losing struggle to remain awake |

# Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD)

Use the following scale to choose one number that best describes what has been happening to you during each activity listed below. It is important that you answer each question as best you can.

Scale: **0 = Never fall asleep | 1 = Slight chance of falling asleep | 2 = Moderate chance of falling asleep | 3 = High chance of falling asleep**

| | |
|---|---|
| Sitting and reading | ( 0 - 3 ) |
| Sitting and watching TV or a video | ( 0 - 3 ) |
| Sitting in a classroom during the morning | ( 0 - 3 ) |
| Sitting and riding in a car or bus for about half an hour | ( 0 - 3 ) |
| Lying down to rest in the afternoon | ( 0 - 3 ) |
| Sitting and talking to someone | ( 0 - 3 ) |
| Sitting quietly by yourself after lunch | ( 0 - 3 ) |
| Sitting and eating a meal | ( 0 - 3 ) |

# Epworth Sleepiness Scale (ESS) & Exam

Clinical assessment of subjective sleepiness

**A score greater than 10 is consistent with excessive sleepiness**

The ESS is widely available, reliable, and can be performed easily and quickly

**Physical Indicators of OSA:**

- Excessive oropharyngeal tissue
- Retrognathia and obesity
- Large neck circumference

# Sleep study and sleep consult

**Polysomnogram (PSG)**
Ordered for suspected OSA, sleep-related breathing disorders, periodic limb movement disorder, narcolepsy, central hypersomnias, seizures during sleep, or unexplained insomnia.

**Home Sleep Apnea Test (HSAT)**
Appropriate alternative to lab PSG when history and physical suggest high pretest probability for moderate to severe OSA.

**Multiple Sleep Latency Test (MSLT)**
Used for narcolepsy, central hypersomnolence, or when objective assessment of daytime sleepiness is desired.

**MWT (Maintenance of Wakefulness Test)**

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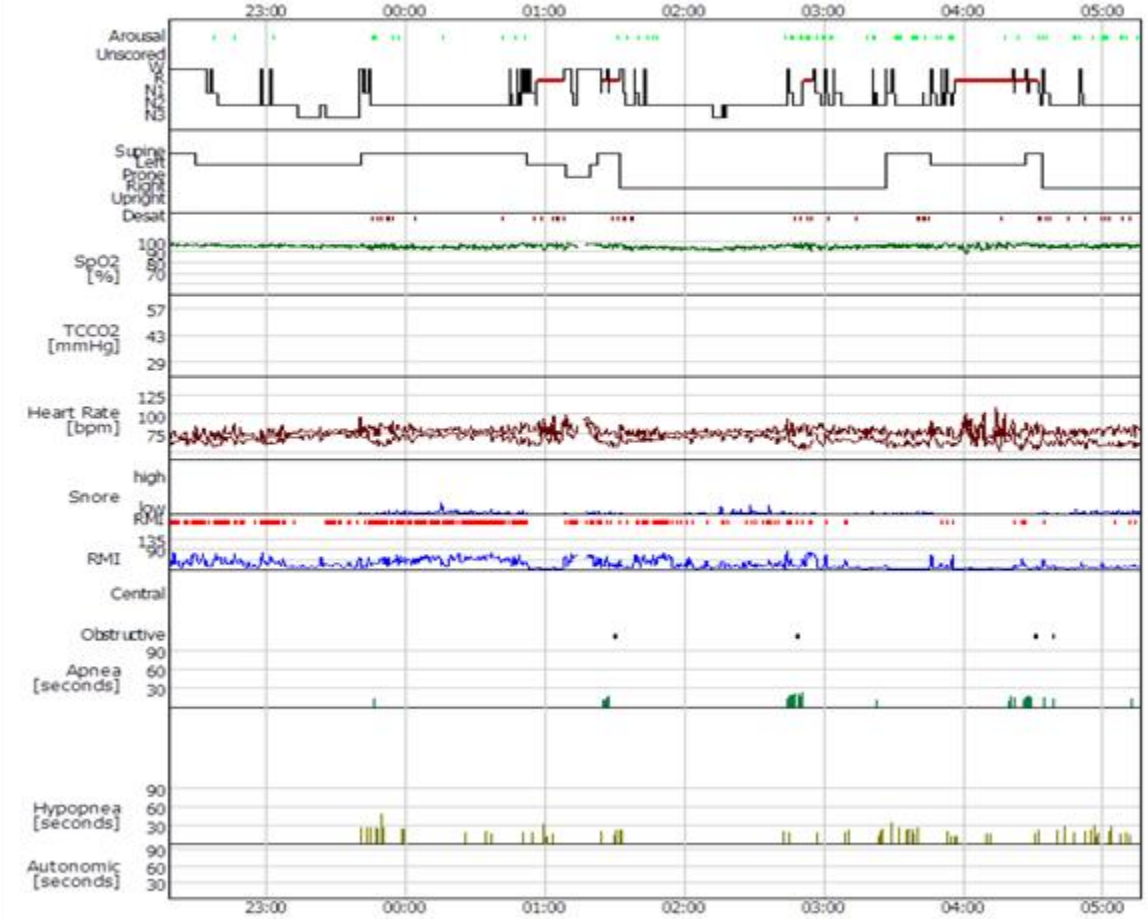
# Visual summary of polysomnographic data

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**Goal:** To expedite testing and treatment for patients with straightforward sleep apnea.

## Required Patient Information

- Loud Snoring & Witnessed Apneas
- Excessive Daytime Sleepiness
- Epworth Sleepiness Score **≥10**

**Co-morbid Conditions Check:**
Insomnia, Hypertension, Diabetes, A-Fib, Bariatric Surgery, Mood Disorders.
*Avoid for: Chronic pain (narcotics), CHF, pulmonary disease, severe insomnia, or parasomnias.*

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# Summary

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### Insufficient Sleep

Can be self-imposed or a result of work, external obligations, or environmental factors.

air

### Sleep-Related Breathing Disorders

Includes Obstructive Sleep Apnea (OSA), circadian rhythm disorders, narcolepsy, and RLS.

cho
log

### Associated Conditions

Chronic pain and neurological or psychiatric conditions linked to unexplained hypersomnia.

dic
ati

### Common Medications

EDS associated with benzodiazepines, sedatives, antihistamines, opioid analgesics, and antipsychotics.

**Clinical Recommendations:** Sleep consult, PSG, Direct home sleep study, and PSG/MSLT assessment.

# Thank You

## Questions?

.

**"Doctor, I keep falling asleep in meetings!"**

*"Is it during my presentation?"*

sentiment_very_satisfied

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# Restless Legs and Beyond:
## Evaluating Sleep-Related Movement Symptoms

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VMFH Neurology/Sleep Medicine
Medical Director St. Clare's Sleep Lab
May 9, 2026

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# Overview – Restless Legs Syndrome (RLS)

- RLS - How to diagnose
- RLS versus PLMs/PLMD and mimics
- Causes of RLS
- Exacerbating factors
- Workup recommendations
- Treatment approach for RLS
- Updated AASM 2024 Guidelines
- Augmentation
- Clinical approach and considerations

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# RLS – Overview

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# RLS – Diagnosis

AASM

- Sleep related movement disorder
- Based on clinical history/symptoms
- Sleep study is not required for RLS diagnosis
- Unpleasant, itchy, creepy, crawly, throbbing, 1 or both legs
- 4 cardinal symptoms RLS “URGE”
  - (U)rge to move legs due to discomfort symptoms
  - Occurs predominantly at (R)est or inactivity
  - (G)ets better with movement
  - Worse in the (E)vening/night (circadian)
- Dopamine dysfunction

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# RLS Mimics

- Akathisia
- Foot tapping/fidget
- Muscle cramps or jerking
- Peripheral neuropathy
- Peripheral vascular disease
- Arthritis
- Degnerative disc disease
- PLMs/PLMD

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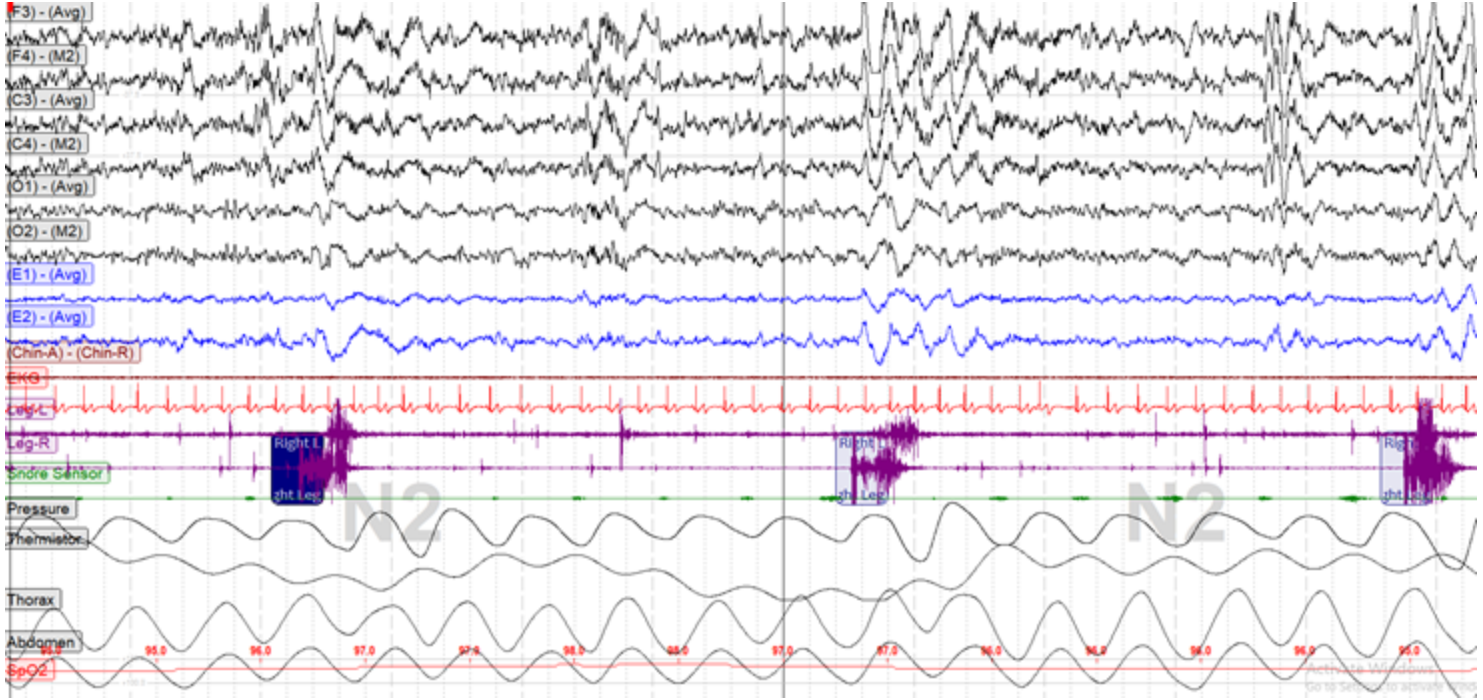
# RLS versus PLMs/PLMD

- Periodic limb movements of sleep (PLMs) are common
- PLMs on PSG do NOT mean RLS
- PLMS ≠ PLMD
- Periodic limb movement disorder (PLMD) is characterized by periodic episodes of repetitive, highly stereotyped limb movements that occur during sleep (PLMs), in conjunction with clinical sleep disturbance or fatigue that cannot be accounted for by another primary sleep disorder or other etiology.

# PLMs on PSG

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# RLS – Causes/Other Factors

- Pathophysiology is only partially understood, both brain iron deficiency and genetics play a role
- CNS iron is difficulty to measure
- Diabetes
- Chronic kidney dysfunction
- Pregnancy (RLS common)


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# RLS – Exacerbating Factors

- Caffeine
- Alcohol
- Tobacco
- Untreated OSA
- Medications
  - Antiemetics/anti-dopaminergic
  - Antihistamines
  - Serotonergic

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# RLS – Workup

- Iron studies: ferritin, iron, TIBC (ferritin > 75, ideally >100, transferrin > 20)
  - Ferritin ≤ 75 ng/mL, transferrin saturation < 20% – oral or IV iron
  - Ferritin 75 – 100 ng/mL – IV iron
  - Oral iron poorly absorbed if ferritin > 50
- Diabetes
- Chronic kidney dysfunction
- Pregnancy
- Medications (SSRI, antihistamine/central acting), dopamine antagonists (antiemetics)

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# RLS – Treatment Approach

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# RLS – Address any exacerbating/co-morbid issues

- CPAP for OSA
- Replace iron or address any deficiencies
- Address exacerbating medications
  - If possible

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# RLS – AASM Guidelines – 2012

- In **2012** AASM Clinical Practice Guidelines on RLS
  - Dopamine agonists (pramipexole and ropinirole) were STANDARD treatments
  - Levodopa, opioids, gabapentin enacarbil, and cabergoline (with caveats) were considered GUIDELINE level recommendations.
- AASM has modified Clinical Practice Guidelines to 2 levels
  - STRONG or CONDITIONAL recommendations, for or against use

# RLS – Updated AASM Guidelines – November 2024

- **STRONG FOR**:
  - Three alpha-2-delta ligand calcium channel blockers
    - Gabapentin
    - Gabapentin enacarbil
    - Pregabalin
  - IV iron
    - IV ferric carboxymaltose

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# RLS – Updated AASM Guidelines – November 2024

- **CONDITIONAL FOR:**
  - IV LMW iron dextran
  - IV ferumoxytol
  - Ferrous sulfate
  - Dipyridamole
  - Oxycodone ER and other opioids
  - Peroneal nerve stimulation

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# RLS – Updated AASM Guidelines – November 2024

- **CONDITIONAL AGAINST:**
  - Levodopa
  - Pramipexole ***
  - Transdermal rotigotine
  - Ropinirole ***
  - Bupropion
  - Carbamazepine
  - Clonazepam
  - Valerian
  - Valproic acid
- **STRONG AGAINST:**
  - Cabergoline

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# RLS – Address any exacerbating/co-morbid issues

- CPAP for OSA
- Replace iron or address deficiencies
- Address exacerbating medications, if possible

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# RLS – What is Augmentation?

- Iatrogenic worsening of RLS symptoms
- Gradual worsening of RLS symptom intensity and duration, which occurs over months to years of exposure to dopaminergic agents
- Dopamine agonists (DA) were initial RLS treatment in 86% and exceeded doses in 46% of cases (Martin-Garcia et al., 2025)
  - Earlier onset of symptoms
  - More severe symptoms (both legs, arms, etc).
  - Shorter duration of relief/decrease in relief
  - May not always be reversible
  - Difficult to get off DA/dependency

# RLS – Dopamine Agonists

- Side effects
  - AUGMENTATION **
  - Sleep attacks
  - Impulse control disorders
  - Lower extremity edema
  - Hallucinations
  - Nausea


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# What to do about dopamine agonists?

# RLS – Augmentation Discussion

- Educate the patient!
- Understand the risks
- Drug holiday
- Consider wean, bridge, switch - take your time
- Flare is almost always expected
- Have a long term plan


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# RLS – Treatment – Pharmacologic

- Iron
  - Side effect: constipation
- Gabapentin, pregabalin, gabapentin enacarbil
  - Dizziness, sedation, drowsiness, weight gain
  - Interaction with opioids - respiratory depression
- Opioids
  - Pros and cons, try to reserve for refractory case
- Timing!
  - Should be consistent with RLS timing/symptoms
  - Should evening focused


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# RLS – Treatment – Non-pharmacologic

- Warm or cool baths
- Massage
- Weighted blanket
- Stretching
- Hydration
- Devices

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# RLS – Treatment Devices

Tonic Motor Activation System (TOMAC)

Bilateral Peroneal Nerve Stimulator

Foot Orthosis

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# RLS – Summary

- Obtain a clear history, URGE
- Review possible causes/factors (PSG, labs, imaging, EMG/NCS)
- Check iron and other potential causes (ferritin, iron, TIBC), ferritin < 75 – treat
  - Other considerations: B12, folate, HbA1C, CPK
- Education about augmentation/side effects - pros and cons
- Update on AASM Guidelines (2024)
  - STRONG FOR - IV iron and alpha-2-delta ligand calcium channel blockers
  - CONDITIONAL AGAINST - dopamine agonists
- Treatment
  - Dosing and timing is key!


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# References


- American Academy of Sleep Medicine (AASM).
- Raquel Martín-García, Laura Lillo Triguero, Celia García-Malo. Augmentation in restless legs syndrome: a comprehensive observational study of a Spanish cohort. *Sleep Medicine*, Volume 136 (2025).
- Winkelman, J., Berkowski, J., DelRosso, L. *et al.* Treatment of restless legs syndrome and periodic limb movement disorder: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med* 21, 137–152 (2025).

# Thank you!

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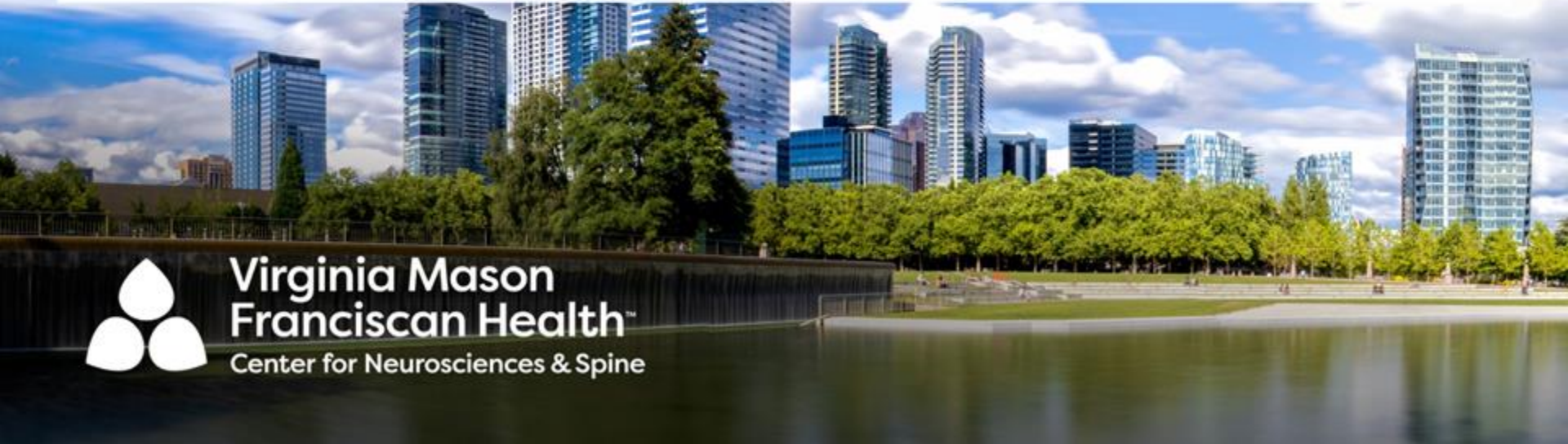
# Question & Answer

Audience - please raise hand for roaming mic

Virtual Attendees - please click on Q&A button



# Demystifying Common Neurologic Conditions

Virginia Mason Franciscan Health™

Center for Neurosciences & Spine

# Parkinson Disease

In 15 minutes or less…

Chris Tapia, MD

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# DISCLOSURES

***I have no relevant financial relationships to disclose and I do not intend to discuss off-label investigative use of a drug/device/product.***

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# EDUCATIONAL OBJECTIVES

- Diagnosis of PD
- Red flags
- Management Strategies

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# GOT A TREMOR? SEND THEM MY WAY

Assessment:

- Tremor

Plan:

- Refer to neurology 

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# MOTOR PARKINSONISM REQUIRED TO DIAGNOSE PARKINSON'S DISEASE

The diagnosis of Parkinson's disease requires the presence of:

**BRADYKINESIA + ( REST TREMOR OR RIGIDITY )**

## 1. BRADYKINESIA

*Slowness of movement (must be present)*

**Examples:**

- Slowness in initiating movements
- Slowness in repetitive movements
- Decrement in amplitude/speed

+

## 2A. REST TREMOR

*Involuntary tremor occurring at rest*

**Key features:**

- Tremor is present when muscles are relaxed
- Often in hands ("pill-rolling")
- May involve jaw, legs or other body parts

OR

## 2B. RIGIDITY

*Increased resistance to passive movement*

**Key features:**

- Muscle stiffness or resistance felt during passive movement

**Bradykinesia must be present, plus either rest tremor OR rigidity.**

**Other supportive features** (not required for diagnosis): postural instability, loss of smell, REM sleep behavior disorder, constipation, dopaminergic response, etc.

***Note:*** *Diagnosis is clinical and requires exclusion of alternative causes of parkinsonism.*

***Source:*** *MDS Clinical Diagnostic Criteria for Parkinson's Disease (2015)*

# PARKINSONIAN REST TREMOR

- Classically a “pill-rolling” tremor, but may be wrist or finger flexion/extension, forearm supination/pronation, whole arm.
- May only be present with mental distraction or when pt under stress.
- Typically abolished with limb movement and re-emerges after seconds once assuming a new posture.

# PD VS ET TREMOR

| Clinical features | Parkinson disease tremor | Essential tremor |
|---|---|---|
| Age at onset | >50 years | Bimodal 2nd and 6th decade |
| Sex | Male ≥ Female | Male = Female |
| Family history | ~10 to 15 percent | ~50 percent |
| Asymmetry | +++ | + |
| Frequency | 4 to 6 Hz | 6 to 12 Hz |
| Character | At rest | Postural, kinetic |
| | Supination-pronation | Flexion-extension |
| Distribution | Hands, legs, chin, tongue | Hands, head, voice |
| Associated features | Bradykinesia, rigidity, postural instability, micrographia | Mild gait disorder or cerebellar signs in a minority |

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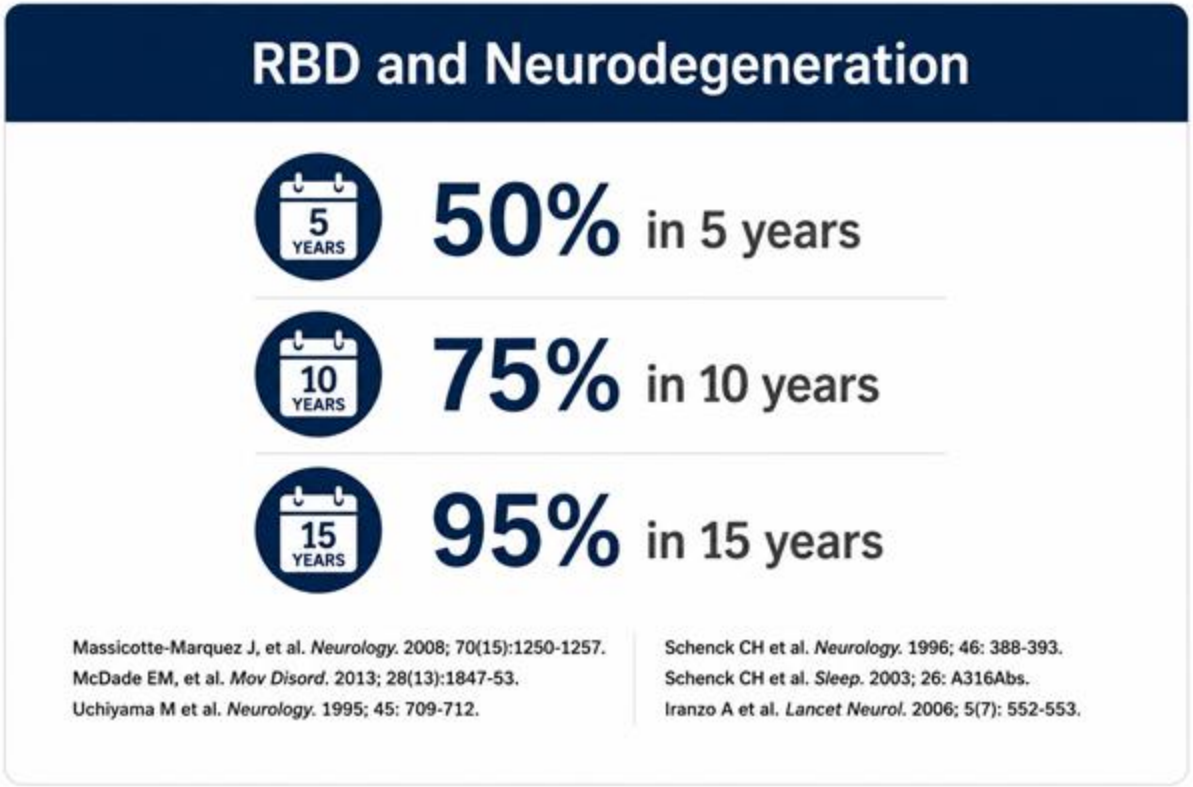
# DIAGNOSTIC CLUES

## PRODROMAL SYMPTOMS OF PARKINSON'S DISEASE

*Non-motor and subtle changes that can occur years before the onset of classic motor symptoms*

| SYMPTOM / SIGN | WHAT IT LOOKS LIKE | NOTES / IMPORTANCE |
|---|---|---|
| Loss of Smell (Hyposmia/Anosmia) | Reduced ability to smell foods, perfumes, smoke, etc. | Very common; can precede motor symptoms by years |
| Constipation | Infrequent bowel movements or difficulty passing stool | Common; may occur many years before diagnosis |
| REM Sleep Behavior Disorder (RBD) | Acting out dreams, talking, punching, kicking, or yelling during sleep | One of the strongest predictors of future Parkinson's disease |

# DIAGNOSTIC CLUES



# DDX OF PARKINSONISM

- Drug-induced
- Metabolic: Hypoparathyroidism
- Manganese toxicity
  - Hepatolenticular degeneration
  - Methcathinone abuse
- Post-encephalitic: EBV, HHV6, Japanese B, Eastern Equine encephalitis
- Paraneoplastic: Anti-CV2/CRMP5, anti-Ma2
- Vascular Parkinsonism

# DRUG-INDUCED PARKINSONISM

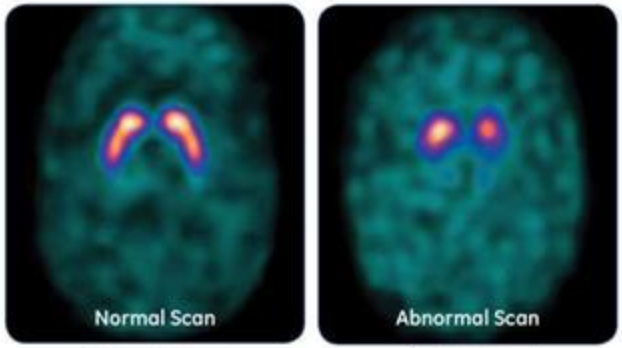
- Antipsychotics (50%)
  - Typical >> atypical
  - Occurs within 3m of starting drug
  - 2/3 resolve on stopping drug
  - Can co-exist with tardive dyskinesias
- Metoclopramide (30%) - F > M
- Dopamine depletory - Tetrabenzine
- Lithium (More likely postural tremor)
- Sodium Valproate (More likely to cause a postural tremor; rarely causes parkinsonism)
- Calcium channel blockers

Dx Clue: Drug-induced Parkinsonism is more likely to be symmetric, and less often have tremor.

# DX OF PD

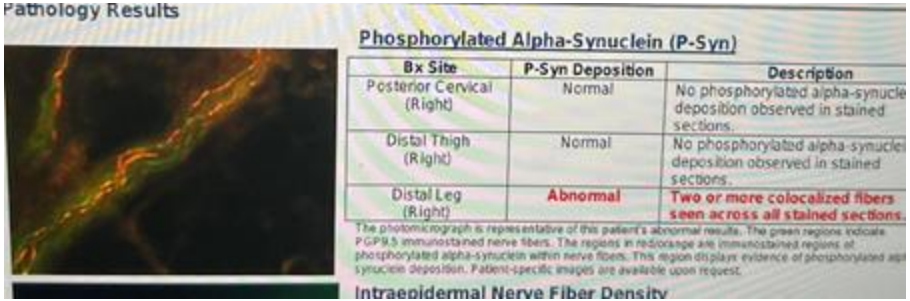
## Ancillary Testing

1) DaTscan
2) Syn-one alpha-synuclein skin biopsy




"Comma"-shaped
Possible essential tremor

"Period"-shaped
Possible parkinsonian syndrome

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# STARTING TX

- If you're going to start levodopa, go slow.
  - C/L IR 25/100 1 tab qd x1wk, then 1 tab BID x1wk, then 1 tab TID x1wk.
- Space out doses q4-6 hrs while awake. 7a – 11a – 4p. Don't need to take before bed when starting it.
- Take 1 hour before a meal or 2 hours after meal.
- If nausea encountered: take with light snack. Nothing high in protein.
- If still nauseous, can add extra carbidopa 25mg to each dose, or can try switching to C/L ER.

# STARTING TX

”Doc I didn’t notice any difference.”

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# THE END

# Alzheimer Disease: Improving Patient Care

Justin Stahl, MD
Virginia Mason Franciscan Health Neuroscience Institute

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# Outline

- ❑ Overview
- ❑ History
- ❑ Pathology
- ❑ Genetics and Other Risk Factors
- ❑ Clinical History and Making the Diagnosis
- ❑ Neuroimaging and Biomarkers
- ❑ Management & Treatment

# Objectives

- Develop a framework to understand cognitive impairment with focus on Alzheimer's Dementia
- Work up and evaluation for dementia
- Treatment for Alzheimer's Dementia

# Disclosures

None

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# Overview

The 2nd Law of Thermodynamics:

The state of entropy of the entire universe will always increase over time.

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# Overview

- ❑ Alzheimer's Disease(AD) is a progressive neurodegenerative disorder
- ❑ In 2024, 7 million people had AD in USA
- ❑ By 2050, 13 million projected to have AD in USA
- ❑ The incidence of AD is age related and doubles every 10 years after age 60
- ❑ The prevalence is 5-10% in 60-69 to at least 25% thereafter but likely higher. 90+ at 65%.
- ❑ Fifth leading cause of death in USA for >65 y/o

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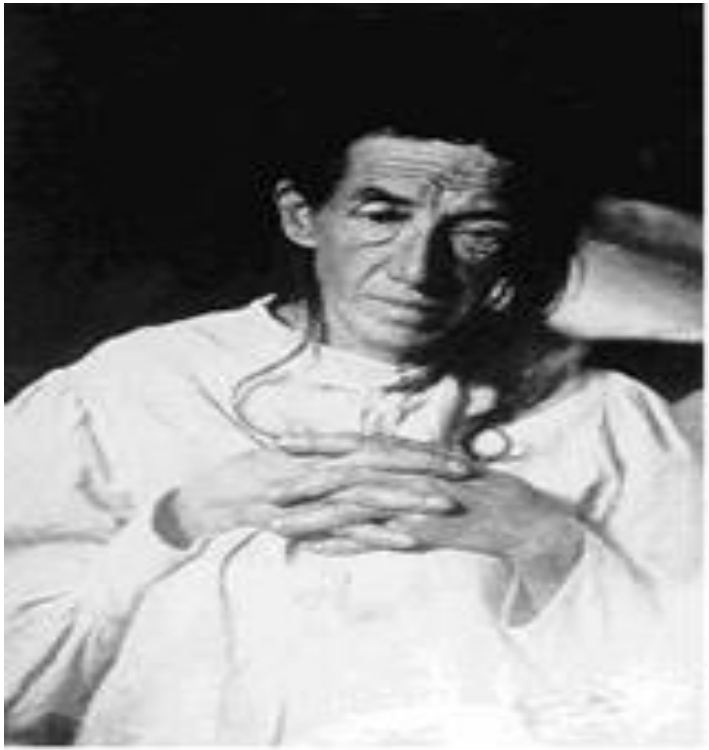
Alzheimers Dement. 2013 Jan;9(1):63-75.e2
World Alzheimer Report 2015: The Global Impact of Dementia http://www.alz.co.uk/research/world-report-2015 (Accessed on October 30, 2015).
J Am Geriatr Soc. 2012 Aug;60(8):1448-56. Epub 2012 Jun 26.

# History

- In 1901, Alois Alzhiemer presented case of Auguste D.
- 51 year old woman with cognitive difficulty, aphasia, delusions, disorientation and loss of behavioral control



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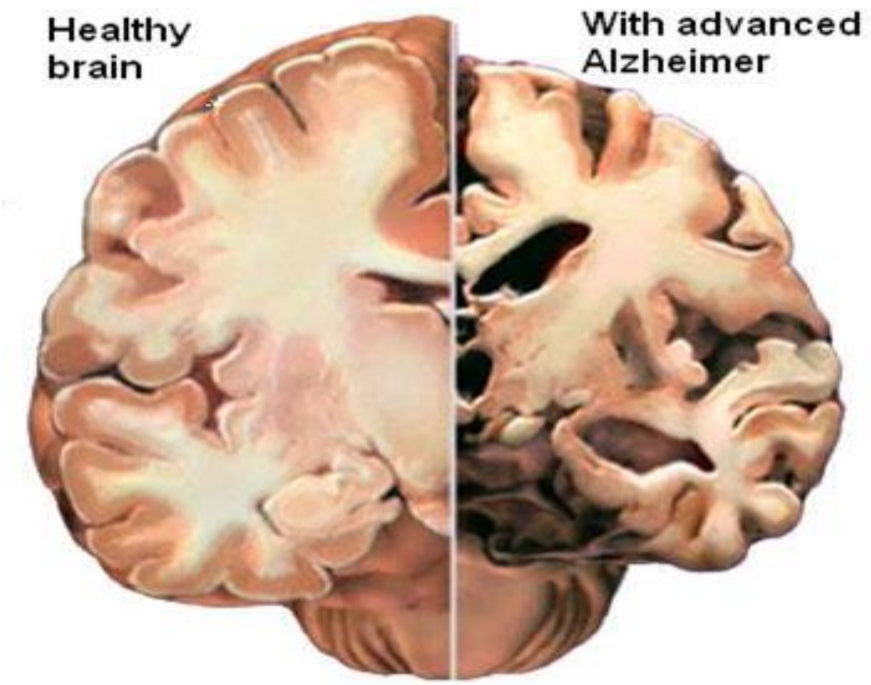
# Pathology

- Neuronal loss leads to cortical atrophy
- Note: sulcal widening, gyral atrophy, thinning of cortical ribbon and ventricular enlargement.
- Involvement is initially temporal and parietal lobes with relative sparing of occipital pole

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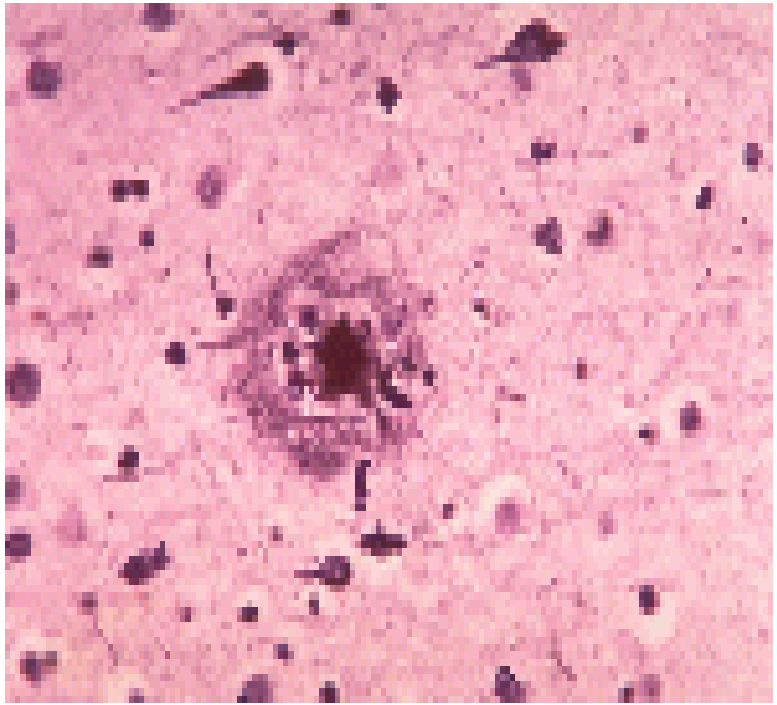
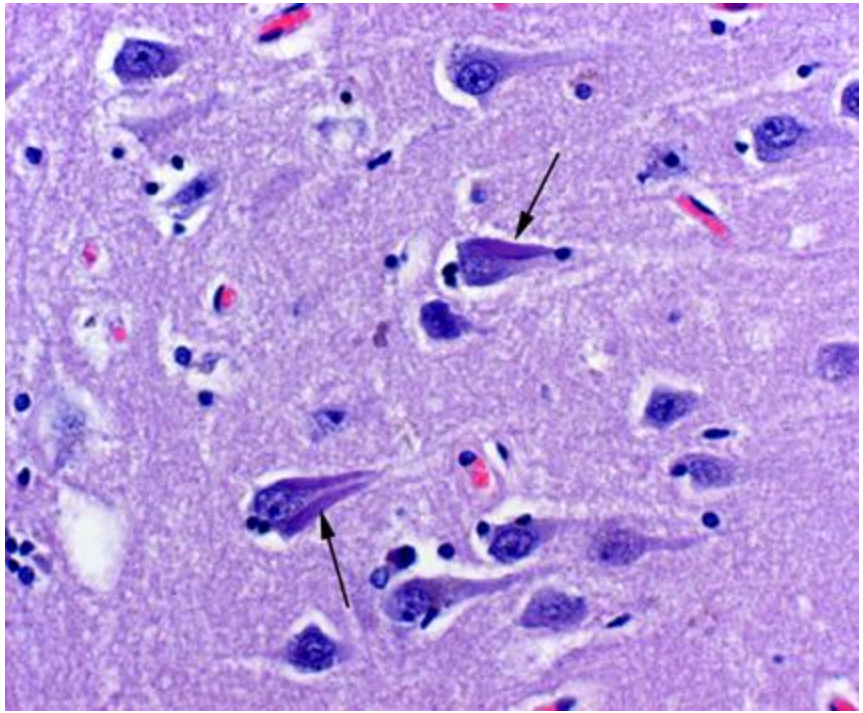
# Pathology

- Neuritic plaques are composed of a β-amyloid core surrounded by swollen neuritic process
- β-amyloid protein is a 40-42 amino acid peptide that is derived from cleavage of amyloid precursor protein (APP)



# Pathology

- Neurofibrillary tangles (NFTs) are intraneuronal cytoplasmic inclusions containing hyperphosphylated tau.
- Tau is a normal axonal protein involved with microtubule binding and stabilization



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Iqbal K, etal. Biochem Biophys Acta 2005; 1739(2-3):198-210

# Genetics

- In familial AD, 95% of cases are late onset (after 60-65 years), 5% are early onset (before 60) with cases as early as 30s reported
- For early onset AD, 60% of cases are familial and 40% sporadic
- 3 genes identified with early onset familial AD:
  - APP on chromo 21 (10-15% of cases)
  - Presenilin 1 (PSEN1) on chromo 14 (70% of cases)
  - Presenilin 2 (PSEN2) on chromo 1 (less than 5%)

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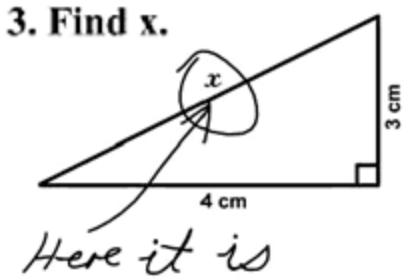
Jayadev S, Leverenz J, Steinbart E, Stahl J, Klunk W, Yu C, Bird T. Brain 2010; 133:1143-1154

# Risk Factors

- “The concept of cognitive reserve posits that individual differences in how tasks are processed provide differential reserve against brain pathology or age-related changes”
- Epidemiologic studies suggest that higher IQ, higher education, occupational attainment, and participation in leisure activities may have a protective effect

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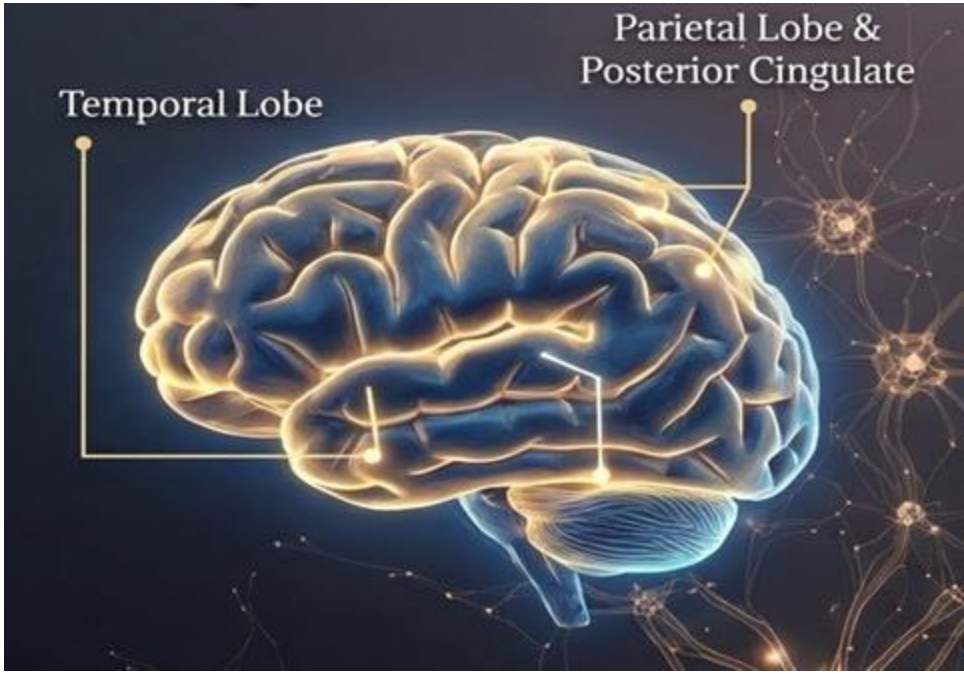
Stern, Y. Alz Dis Assoc Disorder 2006; 20:S69-S74

# Relative Risk for Developing Dementia Based on Several Risk Factors Over the Life Span[1]

| | Relative Risk for Dementia (95% CI) | Risk Factor Prevalence, % |
|---|---|---|
| **Early life (<45 y)** | | |
| Less education | 1.6 (1.3-2.0) | 23.2 |
| **Midlife (45-65 y)** | | |
| Hearing loss | 1.4 (1.0-1.9) | 59.0 |
| High LDL cholesterol | 1.3 (1.3-1.4) | 76.5 |
| Depression | 2.2 (1.7-3.0) | 7.2 |
| TBI | 1.7 (1.4-1.9) | 12.1 |
| Physical inactivity | 1.2 (1.2-1.3) | 27.5 |
| Smoking | 1.3 (1.2-1.3) | 22.3 |
| Diabetes | 1.7 (1.6-1.8) | 9.3 |
| Hypertension | 1.2 (1.1-1.4) | 31.1 |
| Obesity (BMI ≥30) | 1.3 (1.0-1.7) | 13.0 |
| Alcohol (>21 units/wk) | 1.2 (1.0-1.5) | 13.3 |
| **Later life (>65 y)** | | |
| Social isolation | 1.6 (1.3-1.8) | 24.0 |
| Air pollution | 1.1 (1.1-1.1) | 75.0 |
| Untreated vision loss | 1.5 (1.4-1.6) | 12.7 |

# Clinical History

- Insidious episodic memory impairment (e.g. names and objects) reflecting temporal lobe injury. ANOSOGNOSIA may be present
- Visual spatial dysfunction (e.g. lost of disorientation with navigating environment) reflecting parietal lobe and posterior cingulate injury.
- Reduced Spontaneous verbal output, word finding difficulties and less complex grammar.

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# Clinical History

With disease progression, executive function difficulty, agnosia, and apraxia may occur.

Neuropsychiatric symptoms (e.g. Depression, apathy, agitation, anxiety, delusions, paranoia) can be seen in up to 80% of AD, usually in later stages.

Neurologic examination besides mental status largely unremarkable in early AD but later may see pyramidal signs of extrapyramidal signs.

# Clinical History

Frontal lobe involvement manifest with unmasking of primitive reflexes (e.g. positive Gabellar tap, hand grasp reflex, palmomental reflex)

Late stage dysphagia contributing factor leading to death with pneumonia

Seizures occur in 10-20% of AD, usually later stages

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# PCP Barriers to Diagnosis

**Figure 1** PCP-Rated Reasons for Agreeing That MCI/Mild Dementia Due to AD Is Underdiagnosed


AD = Alzheimer disease; MCI = mild cognitive impairment; PCP = primary care physician.

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Neurol Clin Pract. 2026;16:e200568. doi:10.1212/CPJ.0000000000020056

# Making the Diagnosis

- AAN Practice Parameters recommend screening for potential "reversible causes" of dementia including mood disorder, B12, hypothyroidism, sleep disorders, polypharmacy with sedating medication
  - CBC, CMP, TSH, B12. HIV, Syphilis IgG depending on scenerio
- Neuroimaging with CT or MRI to r/o structural lesion
- Depending on clinical scenario, EEG, PET FDG scan, Amyloid scan or CSF analysis can be considered.
- Blood test for plasma Tau and Amyloid.

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Knopman, et al. Neurology 2001;56(9):1143-1153

# Making the Diagnosis

- ❑ Bedside mental status examination screen helpful in further evaluating domains of cognitive function that would be concern in Alzhiemer (e.g. Folstein MMSE, MOCA, Mini-cog, Kokmen Short Test of Mental Status)
- ❑ Depression or Anxiety Screen (e.g. PHQ9, GDS)
- ❑ Sleep Medicine Referral
- ❑ Audiogram
- ❑ Referral to neurology to help with diagnostic accuracy or treatment with Amyloid therapy.

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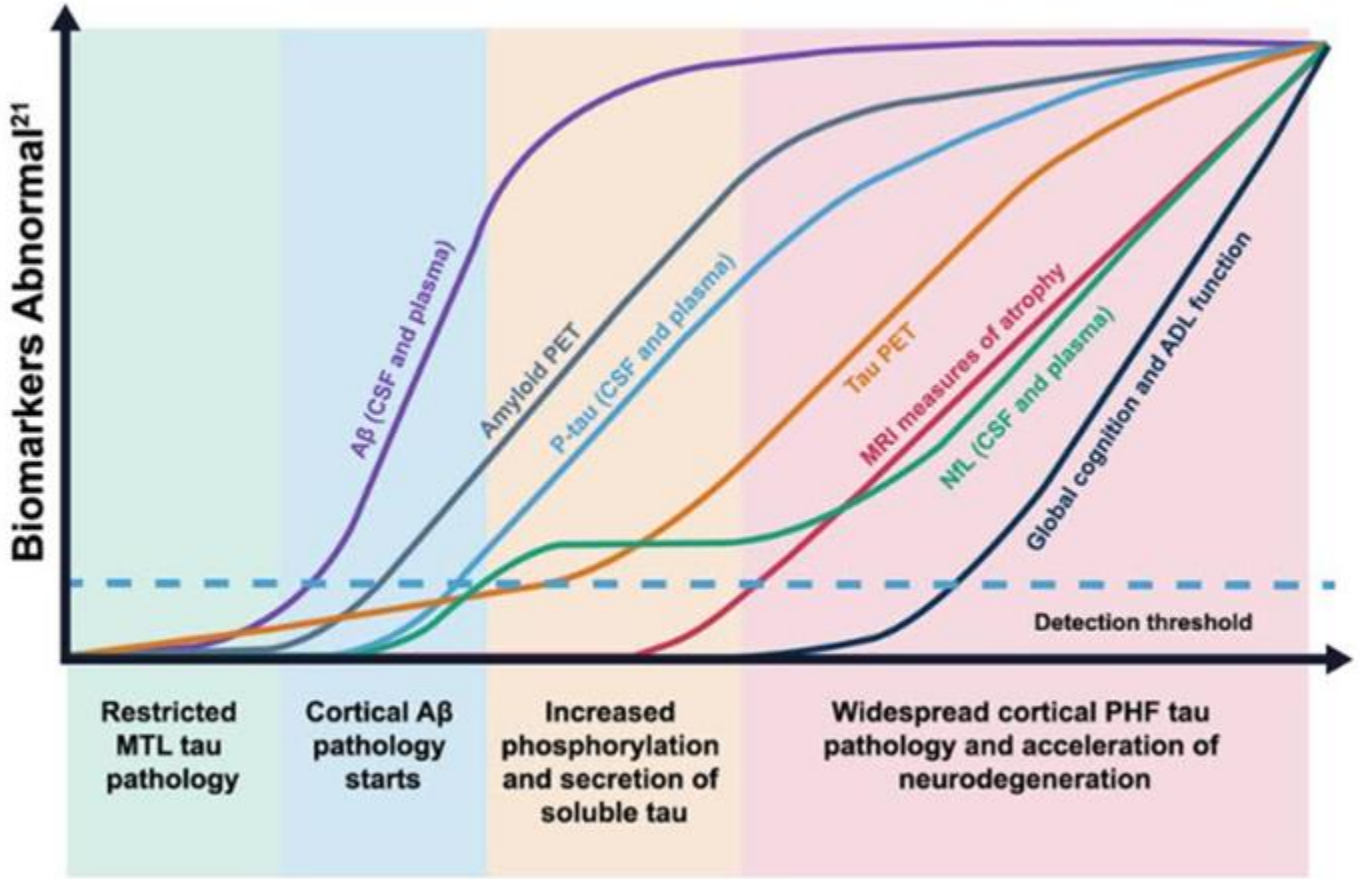
# United States Alzheimer Disease Centers Uniform Data Set (UDS)

| Domains Assessed | Assessment Tools |
|---|---|
| Multidomain general cognitive screen | MMSE |
| Verbal episodic memory | Wechsler Memory Scale-Revised<br>Logical Memory IA-immediate |
| Delayed verbal episodic memory | Wechsler Memory Scale-Revised<br>Logical Memory IIA-Delayed |
| Attention | Digit Span forward and backward |
| Executive function | Trailmaking test Part B |
| Psychomotor speed | Trailmaking Test Part A |
| Language | Category fluency |
| Functional status | Clinical Dementia Rating<br>Functional Assessment Questionnaire |
| Behavioral assessment | Geriatric Depression Scale<br>Neuropsychiatric Inventory Questionnaire |

Morris JC, et al. Alzheimer Dis Assoc Disord 2006;20(4):210-216

# Mild Cognitive Impairment

- Individuals who develop a degenerative dementia go through a transitional state of milder impairment
- Term “Mild Cognitive Impairment” (MCI) has become universally used to define this state
- Clinical Heterogeneity of MCI: Amnestic MCI; Multiple domains MCI; and Single non-memory domain MCI



# Neuroimaging

- Typically seen with AD is generalized nonspecific atrophy that may be more pronounced in medial temporal lobe (hippocampal volume and entorrhinal cortex) and parietal lobe
- [F18]flouro-deoxyglucose (FDG)–PET
- MRI Volumetric analysis
- Amyloid PET scan

# CSF and Serum Biomarkers

## CSF Biomarkers

- Low **CSF Aβ42** (ratio of Aβ42:Aβ40)
- Increased **phospho-tau** and **total tau**

## Serum Biomarkers

- **pTau217/Beta-Amyloid 1-42 plasma** ratio (FDA approved)
- **pTau217**
- **pTau181**(FDA approved)
- **GFAP** (marker of inflammation, not AD specific)
- **Neurofilament light (Nfl)** (serum marker for neuroaxonal damage & severity, not specific to AD)

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Preische O etal. Serum neurofilament dynamics predicts neurodegeneration and clinical progression in presymptomatic Alzheimer's disease. Nat Med 2019: 25(2):277-283.
Suzanne E. Schindler, MD, PhD, et al. Neurology. 2019 Oct 22; 93(17): e1647–e1659.
Barthelemy Et al, Blood plasma phosphylated tau isoform tracks CNS change in Alzheimer's disease. J Exp Med 2020;217(11): e20200861

| FDA-cleared *In Vitro* Diagnostic Tests (IVDs) Available in the U.S. Meeting Confirmatory Criteria | | | | | | |
|---|---|---|---|---|---|---|
| Laboratory | Biomarker(s) | Sensitivity / Specificity | Cohort Sample Size | Aβ Prevalence in Study Population | Intermediate / Uncertain Range | Test ID |
| Fujirebio | p-tau217/β-Amyloid 1-42 Plasma Ratio | 97.6% / 90.8% | 499 | 51.1% | 19.6% | Lumipulse® G pTau 217/ β-Amyloid 1-42 Plasma Ratio |

| Laboratory Developed Tests (LDTs) Available in the U.S. Meeting Confirmatory Criteria | | | | | | |
|---|---|---|---|---|---|---|
| Laboratory | Biomarker(s) | Sensitivity / Specificity | Cohort Sample Size | Aβ Prevalence in Study Population | Intermediate / Uncertain Range | Test ID |
| ARUP Laboratories | p-tau217 | 90% / 90% | 524 | 64.9% | 17% | Phospho-Tau 217, Plasma |
| Lucent Diagnostics | p-tau 217, Aβ42/40, NfL, GFAP | 90% / 90% | 1082 | 55% | 12% | LucentAD™ Complete |
| Mayo Clinic Laboratories | p-tau217 | 92% / 96% | 427 | 64% | 20% | PT217 |
| Neurocode | p-tau217 | 94% / 94% | 51 | 65% | 16% | Plasma p-tau217 |
| Quest Diagnostics | Aβ42/40, p-tau217 | 91% / 91% | 215 | 46% | 15% | AD-Detect™ (Aβ 42/40 and p-tau217) |

## Availability of IVD BBMs

Labcorp

Quest Diagnostics

www.alzdiagnostichub.org/blood-test-performance-database

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# Rx Med Treatment

FDA approved medications for symptomatic treatment of AD:

**Cholinesterase inhibitors: donepezil, galantamine, and rivastigmine**

- Approved for mild to moderate AD with indication for severe AD given to donepezil

**Noncompetitive NMDA receptor antagonist: memantine**

- Approved for moderate to severe AD

**Human anti-amyloid beta monoclonal antibody that binds both soluble and insoluble aggregated forms of amyloid beta, including oligomers, protofibrils, and fibrils: Lecanumab and Donanemab**

- Approved for MCI or Mild AD

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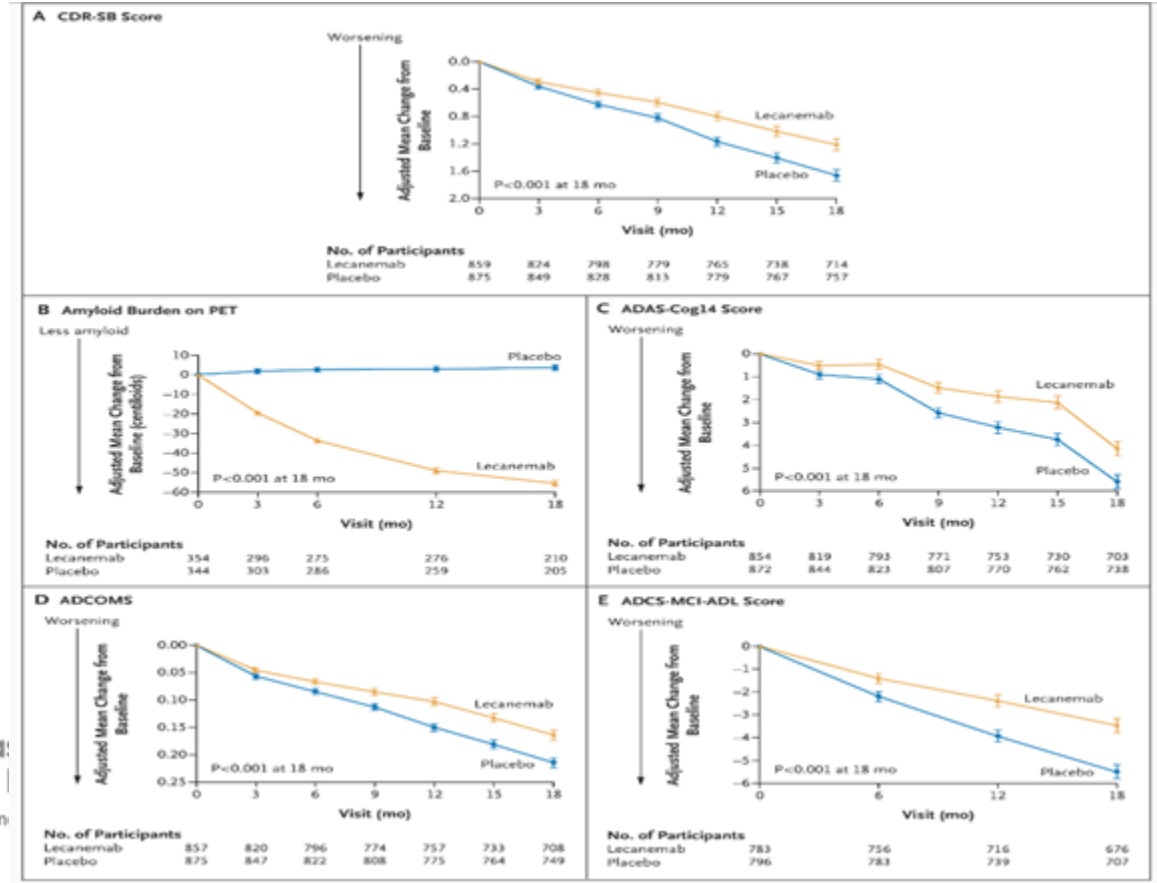
# Treatment

| | Donepezil | Galantamine | Rivastigimine (oral) | Rivastigmine (patch) | Memantine |
|---|---|---|---|---|---|
| Mechanism of action | Cholinesterase inhibitor | Cholinesterase inhibitor | Cholinesterase inhibitor | Cholinesterase inhibitor | NMDA receptor antagonist |
| Dose (beginning and max) | 5mg PO qday to 10mg PO qday<br>23mg PO Qday | 4mg PO BID to 12 mg PO BID | 1.5mg qday to 6.0 mg PO qday | Transdermal 4.6mg q24hours to 9.5mg q24hours | 5mg PO qday to 10mg PO BID |
| Absorption affected by food | No | Yes | Yes | No | No |
| Serum half life (hours) | 70-80 | 5-7 | 2-8 | 3-4 | 60-80 |
| Side effects | N/V, diarrhea, muscle cramps, weight loss, vivid dreams | N/V, diarrhea, weight loss, dizziness | N/V, diarrhea, weight loss, dizziness | Possibly less GI side effects | Dizziness |

# Lecanumab outcomes

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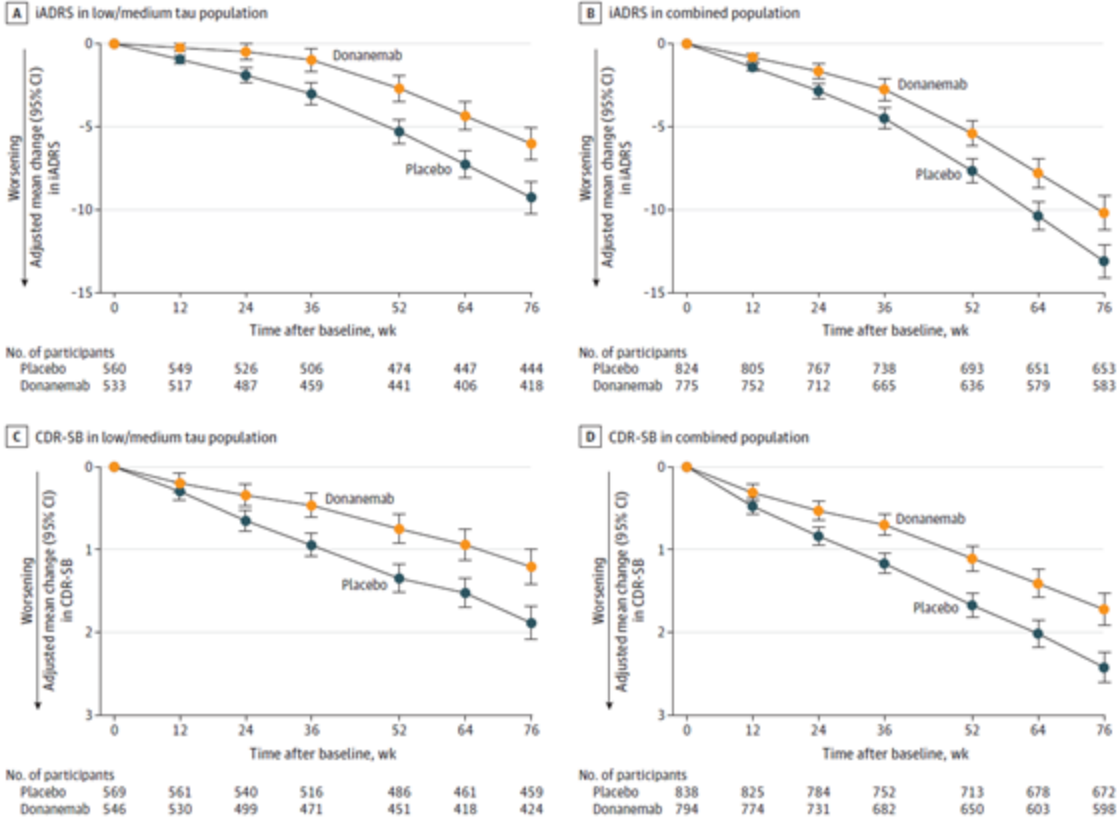
# Donanemab outcomes

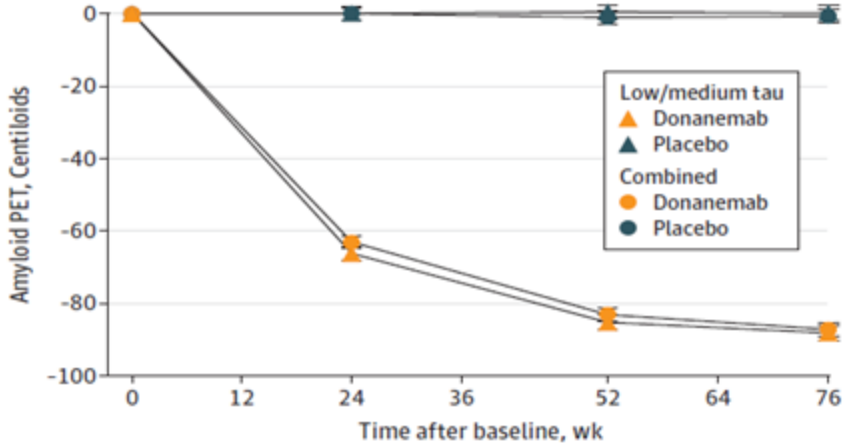
Figure 2. Integrated Alzheimer Disease Rating Scale (iADRS) and Sum of Boxes of the Clinical Dementia Rating Scale (CDR-SB) From Baseline to 76 Weeks



# Donamemab outcomes

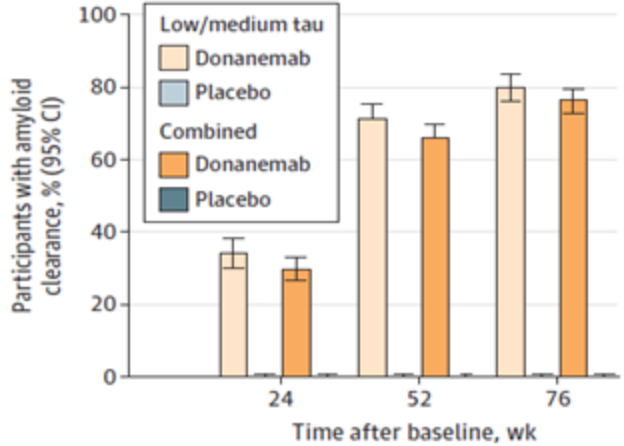
**Figure 3. Brain Amyloid, Plasma Phosphorylated Tau 217 (P-tau217), and Hazard Ratios for Risk of Disease Progression**

**A** Adjusted mean change (95% CI) in amyloid PET




| No. of participants | | | | | 76-wk value, Centiloids | Difference from baseline % |
|---|---|---|---|---|---|---|
| Low/medium tau | | | | | | |
| Donanemab | 525 | 521 | 463 | 433 | -88.0 | -85.5 |
| Placebo | 556 | 552 | 498 | 470 | 0.2 | 0.2 |
| Combined | | | | | | |
| Donanemab | 765 | 760 | 670 | 614 | -87.0 | -83.7 |
| Placebo | 812 | 805 | 729 | 690 | -0.7 | -0.7 |

**B** Participants with amyloid clearance (<24.1 Centiloids)




| No. of participants | | | |
|---|---|---|---|
| Low/medium tau | | | |
| Donanemab | 521 | 463 | 433 |
| Placebo | 553 | 498 | 470 |
| Combined | | | |
| Donanemab | 761 | 670 | 614 |
| Placebo | 805 | 730 | 690 |

# Adverse Effects

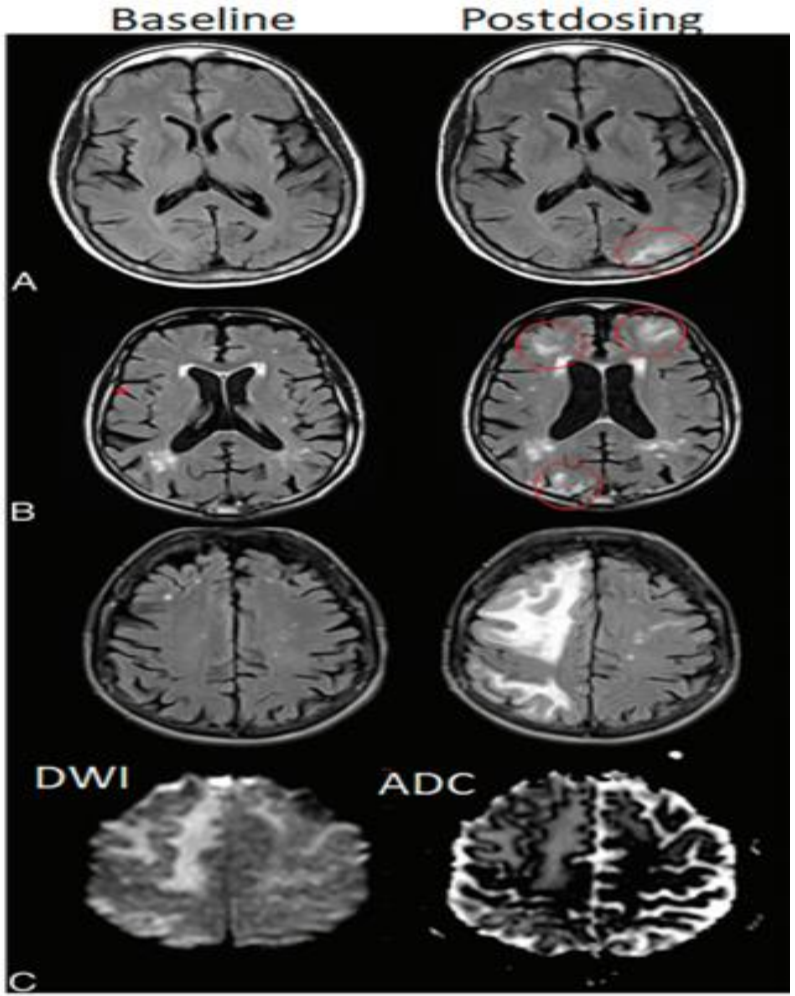
## Amyloid-related imaging abnormalities (ARIA)

**ARIA refers to radiographic abnormalities observed with anti-Aβ antibodies**

- ARIA-Edema (ARIA-E) refers to brain vasogenic edema or sulcal effusion
- ARIA-Hemorrhage (ARIA-H) refers to brain microhemorrhages or localized superficial siderosis

*ARIA may result from increased cerebrovascular permeability as a consequence of antibody binding to deposited Aβ*

# ARIA –E

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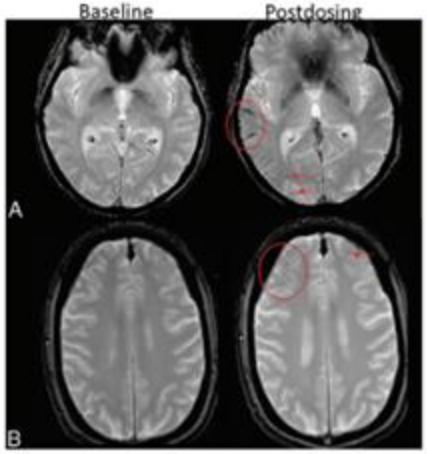
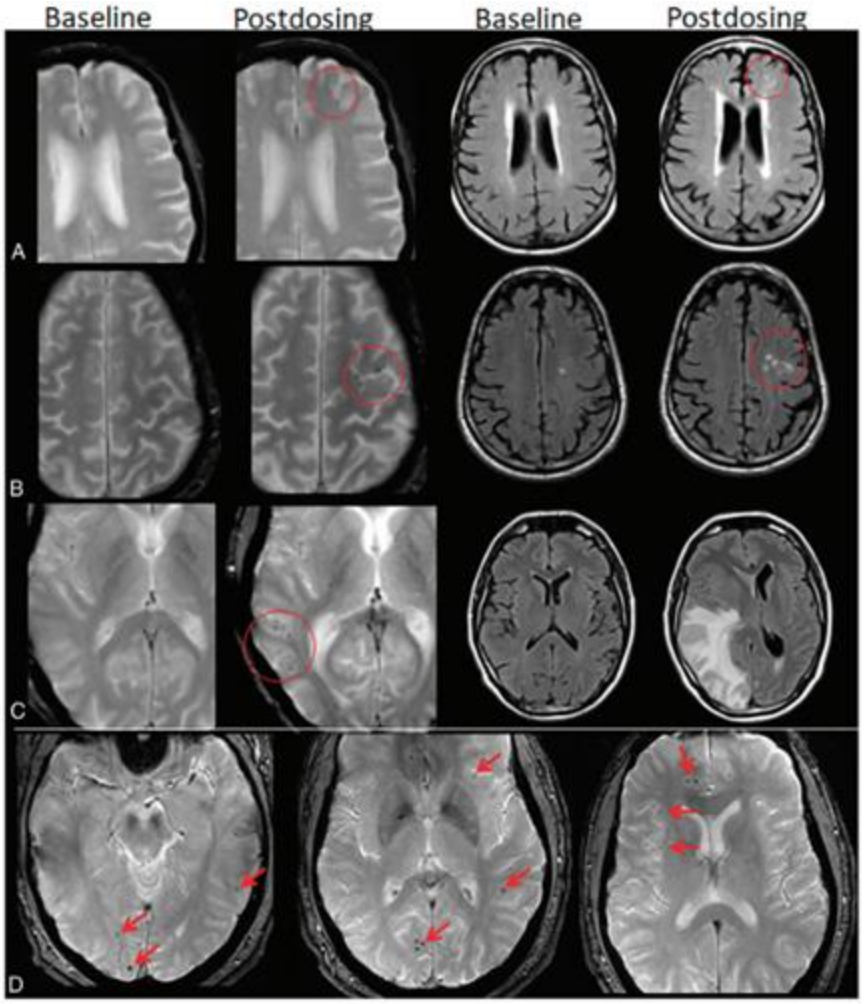
# ARIA-H

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# Lecanumab ARIA

| Event | Lecanemab (N=898) | Placebo (N=897) |
|---|---|---|
| ARIA‡ | | |
| ARIA-E — no. (%) | 113 (12.6) | 15 (1.7) |
| Symptomatic ARIA-E — no. (%)§ | 25 (2.8) | 0 |
| ApoE ε4 noncarrier — no./total no. (%) | 4/278 (1.4) | 0/286 |
| ApoE ε4 carrier — no./total no. (%) | 21/620 (3.4) | 0/611 |
| ApoE ε4 heterozygote | 8/479 (1.7) | 0/478 |
| ApoE ε4 homozygote | 13/141 (9.2) | 0/133 |
| ARIA-E according to ApoE ε4 genotype — no./total no. (%) | | |
| ApoE ε4 noncarrier | 15/278 (5.4) | 1/286 (0.3) |
| ApoE ε4 carrier | 98/620 (15.8) | 14/611 (2.3) |
| ApoE ε4 heterozygote | 52/479 (10.9) | 9/478 (1.9) |
| ApoE ε4 homozygote | 46/141 (32.6) | 5/133 (3.8) |
| ARIA-H — no. (%) | 155 (17.3) | 81 (9.0) |

# Donanemab ARIA

| Event | Donanemab (N=131) | Placebo (N=125) | P Value |
|---|---|---|---|
| ARIA-E or ARIA-H — no. (%) | 51 (38.9) | 10 (8.0) | 61 (23.8) |
| ARIA-E | | | |
| Any — no. (%) | 36 (27.5) | 1 (0.8) | 37 (14.5) |
| Symptom status — no. (%) | | | |
| Asymptomatic | 28 (21.4) | 0 | 28 (10.9) |
| Symptomatic | 8 (6.1) | 1 (0.8) | 9 (3.5) |
| *APOE* genotype — no./total no. (%) | | | |
| ε2/ε3 | 0/1 | 0/1 | 0/2 |
| ε2/ε4 | 0/2 | 0/2 | 0/4 |
| ε3/ε3 | 4/35 (11.4) | 0/31 | 4/66 (6.1) |
| ε3/ε4 | 21/68 (30.9) | 0/62 | 21/130 (16.2) |
| ε4/ε4 | 11/25 (44.0) | 1/28 (3.6) | 12/53 (22.6) |
| ARIA-H — no. (%) | | | |
| Any | 40 (30.5) | 9 (7.2) | 49 (19.1) |

# Treatment

- Cognitive Training with a Speech Language Therapist
  - Various strategies employed to help with issues of word retrieval, visual memory, auditory memory
- Mediterranean diet or MIND diet
- Physical exercise
- Personalized management of other modifiable risk factors (FINGER study, U.S. POINTER)
- Family referral to available resources such as Alzheimer Association and support groups in the area
- Discussion of advance directives
- Caregiver stress
- Attention towards medication, financial and driving oversight
- OT driver screen or roadside assessment
- Synapticure for Dementia Care GUIDE for Medicare PartA/B

# Treatment



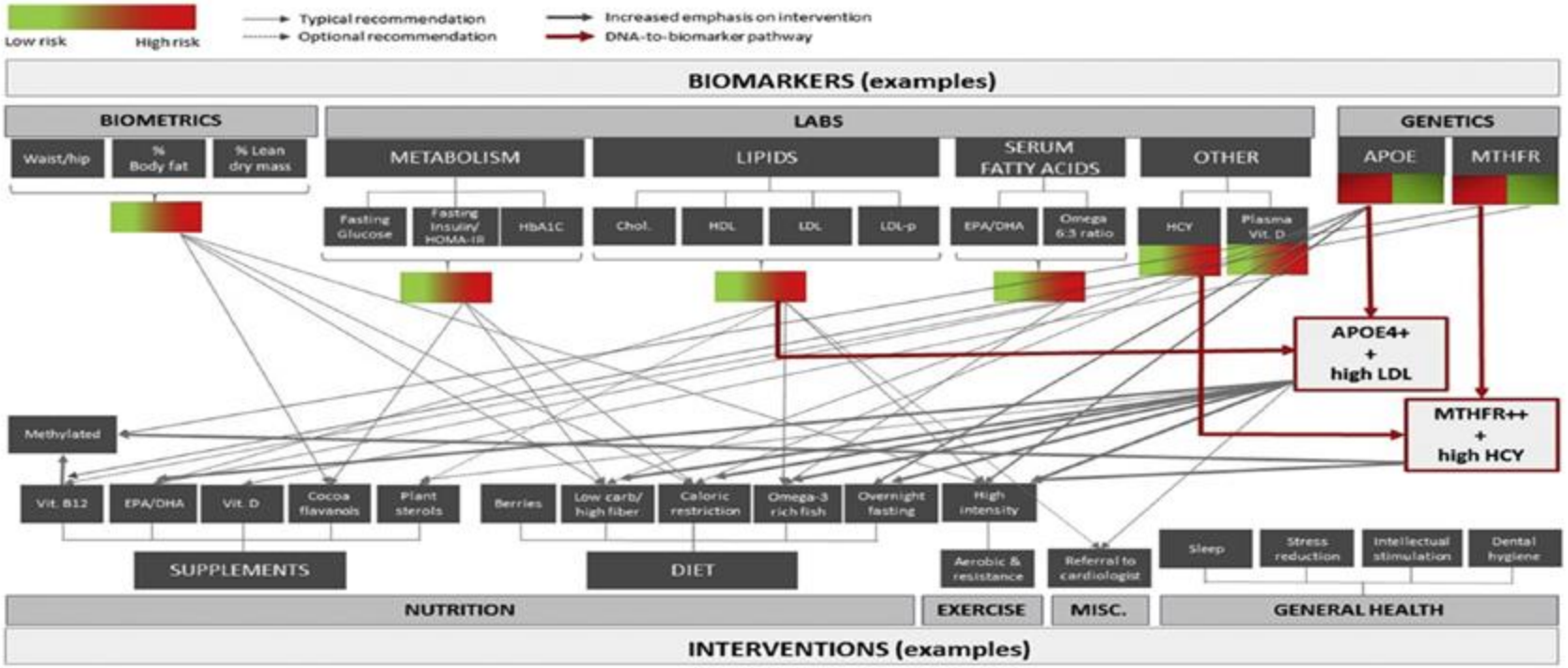


Fig. 1. Example biomarker to intervention paradigm; NOTE. Each data point collected during the initial clinical intake and evaluation, as well as at each follow-up visit, is used to inform which precision medicine interventions are recommended per participant.

# Social work in Neurology

A clinic based MSW acts as a crucial support navigator for addressing emotional, financial, and practical needs by providing:

- **Psychosocial support:** offering counseling for patients and facing the emotional impact of neurological conditions, addressing grief, anxiety, and adjustment to disability
- **Care Coordination & Navigation:** bridge gaps between medical treatments and daily life, linking patients with home care, equipment, and local agencies,
- **Financial & Legal Assistance:** help navigate disability claims, insurance, employment issues (life FMLA) and other financial stressors
- **Advance Care Planning (ACP):** facilitated discussions on values, goals, and decisions about future care, and help to identify healthcare proxies
- **Resource Connection:** identifies and connects families to essential community resource, support groups and respite care
- **Goal Setting:** works with the multidisciplinary team members to create realistic goals, ensuring the patient's wishes aguide care
- **Advocacy & Education**: Advocates for the patients needs, interprets complex medical information, and educates the family on treatment options and what to expect

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for prompt control of

# senile agitation

## THORAZINE*

(chlorpromazine, S.K.F.)

"Thorazine" can control the agitated, belligerent senile and help the patient to live a composed and useful life.

Smith Kline & French Laboratories

# Behavioral changes seen in Alzheimer Disease

| Behavioral Change | Frequency, % |
|---|---|
| Depression | 25-50 |
| Disinhibition | 20-35 |
| Delusions | 15-50 |
| Hallucinations | 10-25 |
| Agitation | 50-70 |
| Anxiety | 30-50 |
| Aggression | 25 |
| Sexual Disinhibition | 5-10 |

Cummings JL, et al. The Neuropsychiatric Inventory: comprehensive assessment of psychopathology in dementia. Neurology 1994;44:2308-2314

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# Nonpharmacologic behavioral interventions

- Creation of a “no fail” environment
  - Patients eventually develop anosognosia (don’t recognize own deficits)
  - Failure to perform these tasks lead to frustration
  - Create environment that is simple with tasks they are able to perform
  - Create routine
- Confronting patients on their deficits typical leads to more behavioral problems

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Stewart JT. Management of behavior problems in the demented patient. Am Fam Physician 1995;52: 2311-2322

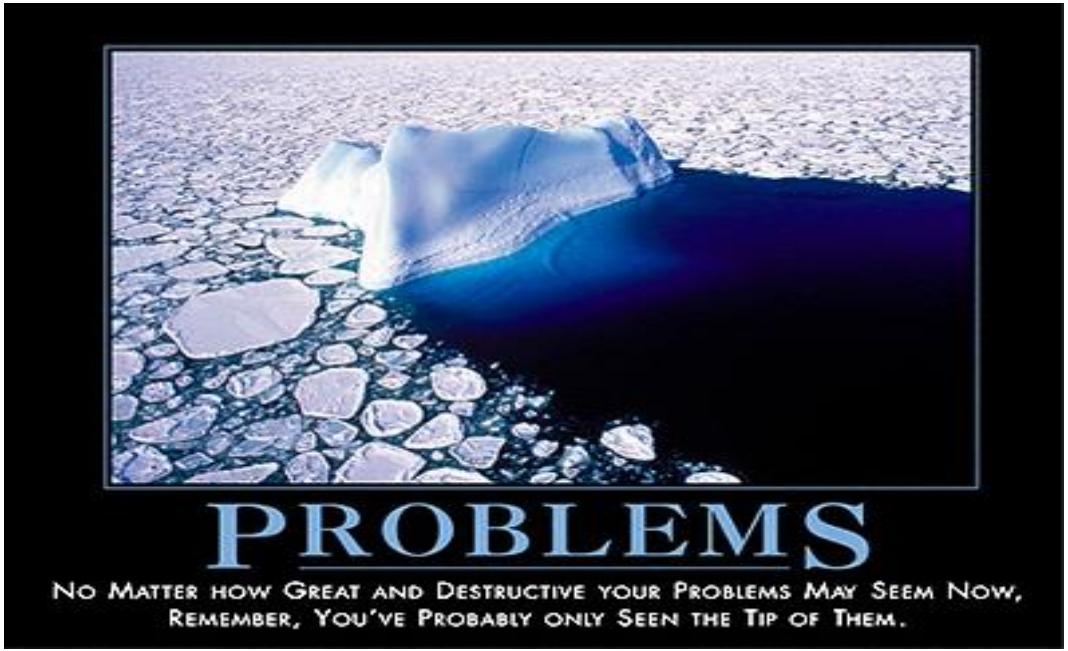
# Nonpharmacologic behavioral interventions

| Condition | Behavioral intervention |
|---|---|
| Resistiveness | Slow, gentle approach, minimize goals of care |
| Delusions | Reassurance, distraction, redirection |
| Hallucinations | Benign neglect, Reassurance, distraction, increase social contact |
| Screaming | Assess, manage discomfort, discontinue restraints, increase sensory stimuli |
| Sexual disinhibition | Redirection, limit access to vulnerable females, restrictive garments |
| Wandering | Provide purposeful activities, exercise, provide secure area, safety measures, visual barriers, manage sleep disturbance |
| Sleep disturbance | Maximize exposure to sunlight, phototherapy, avoid excessive naps, provide exercise, provide nightlight, keep room quiet and cool, restrict etoh and caffeine |
| Agitation, fearfulness | Quiet environment, avoid conversations that could lead to misinterpretation, protective measures |
| Catastrophic reactions | Non-confrontive, “no-fail” environment |

# Pharmacologic behavioral interventions

| Condition | Pharmacologic intervention |
|---|---|
| Resistiveness | Lorazepam prior to care |
| Delusions, hallucination | Neuroleptics |
| Screaming | Consider a trial of antidepressant |
| Sexual disinhibition | Medroxyprogesterone 100-500mg/wk, SSRIs |
| Wandering | Neuroleptic agent |
| Sleep disturbance | Temazepam, zolpidem, trazodone |
| Depression | SSRIs, mirtazepine, venlafaxine nefazodone, nortiptyline, ?donepezil |
| Agitation | Neuroleptics, trazodone, buspirone, propranolol, carbamazepine, valproic acid, lorazepam, prazosin, pimavanserin |
| Anxiety | Oxazepam, lorazepam, buspirone, propranolol |

# Future Considerations

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# Why Does My Head Hurt?
# Essentials of Primary Headache Disorders

Kara Ellingson, MD

5/9/2026

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# Overview

- Approach to Primary Headache Disorders
  - Rule Out Secondary Headache Disorders (SNOOP4)
  - Migraines
    - International Classification of Headache Disorders 3rd Edition (ICHD-3) Classification
    - Abortive Therapies
    - Prophylactic Therapies
  - Tension Headaches
  - Trigeminal Autonomic Cephalgias
    - Cluster Headaches
  - Other Primary Headache Disorders

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# Approach to Primary Headache Disorders

- Rule out secondary headache disorders through history and red flag screening
  - SNOOP4
    - Systemic symptoms
    - Neurological exam or behavioral changes
    - Onset, sudden
    - Older age at onset (age > 50 years)
    - Pattern change
    - Precipitated by Valsalva maneuver
    - Postural
    - Papilledema or visual field deficits

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# Approach to Primary Headache Disorders

- While migraine has a prevalence of 12% in the general population, several studies have suggested that migraines may account for up to ~75-94% of patients presenting with “headache” as their primary concern in a primary care setting.
  - Though this number goes down when headache is not the primary concern
- Next step: Rule out migraine
- Use of screening tools can be helpful in ruling out migraine
  - ID Migraine (mnemonic- PIN)
    - 1. Photophobia?
    - 2. Incapacity (either physical or intellectual)?
    - 3. Nausea?
    - Two positives would be considered a positive screen
      - Positive increases pretest probability to 84%
      - Negative decreases pretest probability to 23%

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# Migraine

- ICHD-3 Criteria for Migraine Without Aura
- A. At least 5 attacks that fulfill criteria B-D
- B. Headache lasting 4-72 hours untreated or unsuccessfully treated
- C. Two of the following four:
  - 1. Unilateral
  - 2. Throbbing/pulsatile
  - 3. Moderate to Severe In Intensity
  - 4. Made worse by or causing avoidance in activity
- D. During headache at least one of the following:
  - 1. Nausea and/or vomiting
  - 2. Photophobia and phonophobia
- E. Not better accounted for by a different ICHD-3 diagnosis

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# Migraine

- ICHD-3 Criteria for Migraine With Aura
- A. At least 2 attacks fulfilling criteria B and C
- B. One or more of the following fully reversible aura symptoms:
  - Visual, sensory, speech and/or language, motor, brainstem, retinal
- C. At least 3 of the following 6 characteristics:
  - 1. At least one aura symptom spreads gradually over >/= 5 minutes
  - 2. Two or more aura symptoms occur in succession
  - 3. Each individual aura symptom lasts 5-60 minutes (motor can be up to 72 hours)
  - 4. At least one aura symptom is unilateral
  - 5. At least one aura symptom is positive
  - 6. The aura is accompanied, or followed within 60 minutes, by a headache
- D. Not better accounted for by a different ICHD-3 diagnosis

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# Migraine

- Chronic Migraine
  - 15 or more migraine days per month for more than 3 months
- Probable Migraine
  - Meets all but one criteria for migraine
    - In practice, this means that any headache that causes limitation in activity and is moderate to severe in intensity lasting at least 4 hours could be considered probable migraine

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# Migraine

- Abortive therapies
  - Acetaminophen and NSAIDs (i.e. ibuprofen, naproxen)
  - Triptans
    - Rizatriptan and sumatriptan
    - Eletriptan, naratriptan, frovatriptan, zolmitriptan
  - Small-Molecule CGRP-Antagonists: ubrogepant and rimegepant
    - No contraindication in patients with prior stroke or MI
  - Lasmiditan
    - No contraindication in patients with prior stroke or MI
    - Though carries an 8 hour driving restriction secondary to CNS depressive effects
  - Ergotamines
    - Limited in use secondary to significant rebound headache risk and side effect profile
  - Butalbital-based treatments
    - Limited in use secondary to significant rebound headache risk

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# Migraine

- Prophylactic Therapies
  - First line therapies (can take 4-8 weeks to show full effect, therefore recommend 8 week trials)
    - TCAs/SNRIs: amitriptyline, nortriptyline, venlafaxine
    - Anti-seizure medications: topiramate, divalproex sodium
    - Beta-blockers: propranolol, metoprolol, timolol, atenolol
  - Second line therapies
    - Injectable CGRP-Antagonists (monoclonal antibodies): galcanezumab, fremanezumab, erenumab-aooe
      - Monthly administration (recommend 3 dose trial)
    - Botulinum Toxin Injections
      - Every 12 week administration (recommend 3 dose trial)
    - Small-Molecule CGRP-Antagonists: rimegepant (every other day dosing), atogepant
    - Intravenous CGRP-Antagonist (monoclonal antibody): eptinezumab-jjmr (every 3 month dosing)

# Tension-Type Headaches

- ICHD-3 Criteria for Tension-Type Headaches
  - A. Not going into detail here, though overall this is differences in frequency definitions and stating that criteria B-D need to be met
  - B. Lasting 30 minutes to 7 days
  - C. At least two of the following four characteristics:
    - 1. Bilateral location
    - 2. Pressing or tightening (not pulsating) quality
    - 3. Mild or moderate intensity
    - 4. Not aggravated by routine physical activity such as walking or climbing stairs
  - D. Both of the following:
    - 1. No nausea or vomiting
    - 2. No more than one of photophobia or phonophobia
  - E. Not better accounted or by another ICHD-3 diagnosis

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# Trigeminal Autonomic Cephalgias

- Unilateral in location, often with marked parasympathetic autonomic features on the side of the headache
- Cluster headaches
- Paroxysmal Hemicrania
- SUNCT/SUNA
- Hemicrania continua
- Probable autonomic cephalgia

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# Trigeminal Autonomic Cephalgias

- ICHD-3 Criteria for Cluster Headaches
  - A. At least 5 attacks fulfilling B-D
  - B. Severe or very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15-180 minutes (untreated)
  - C. Either or both of the following:
    - 1. At least one of the following symptoms or signs, ipsilateral to the headache:
      - Conjunctival injection and/or lacrimation
      - Nasal congestion and/or rhinorrhea
      - Eyelid edema
      - Forehead and facial swelling
      - Miosis and/or ptosis
    - 2. A sense of restlessness or agitation
  - D. Occurring with a frequency between one every other day and 8 per day
  - E. Not better accounted for by another ICHD-3 diagnosis

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# Other Primary Headache Syndromes

- ICHD-3 criteria exist for several other primary headache syndromes
  - Primary cough headache
  - Primary exercise headache
  - Primary headache associated with sexual activity
  - Primary thunderclap headache
  - Cold-stimulus headache
  - External pressure headache
  - Primary stabbing headache
  - Nummular headache
  - Hypnic headache
  - New daily persistent headache

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# Thank you

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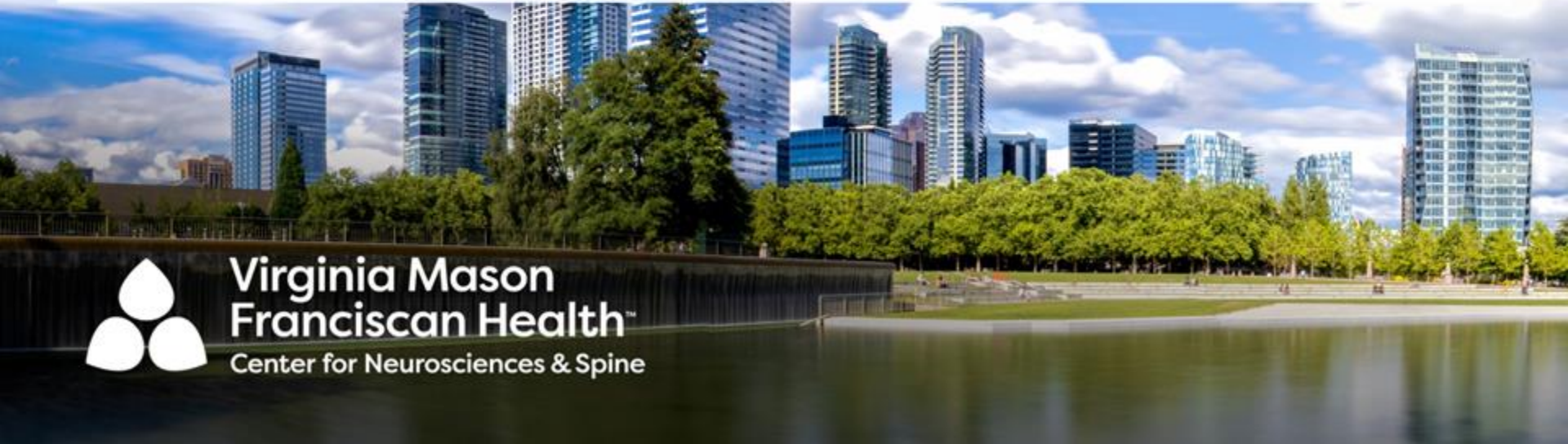
# Question & Answer

Audience - please raise hand for roaming mic

Virtual Attendees - please click on Q&A button



# Exhibits and Refreshments