SLEEP TIGHT, HEART RIGHT

MANAGING SLEEP DISORDERS FOR CARDIOVASCULAR HEALTH

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Preventative Cardiovascular Nurses Association
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Learning Objectives

1. Explain the pathophysiology and clinical presentation of common sleep disorders, including obstructive sleep apnea (OSA), narcolepsy, restless legs syndrome (RLS) and insomnia.
2. Describe the relationship between sleep disorders and cardiovascular health, including their role in the development or exacerbation of CVD co-morbidities
3. Review current treatment strategies for managing sleep disorders with cardiovascular implications
4. Apply team-based care approaches to assess, educate, and manage patients with coexisting cardiovascular and sleep disorders

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Disclosures

- I have no relevant financial disclosures
- I will reference one medication that is not yet FDA approved for treatment of OSA (phase II data has been published, phase III trials complete / not published)
- I will briefly reference medications used off-label for insomnia

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Case Study

- 58 year old male w/ difficult to manage HTN presenting for follow up with persistently elevated BP readings
- Taking 3 medications currently with numerous tried and discontinued due to intolerance
- Denies awareness of snoring, however partner who is present strongly disagrees noting very loud snoring
- Works shift work, alternating days/nights
- Admits sleepiness during wakeful hours, takes naps when able, drinks “a lot” of caffeinated beverages
- Screening oximetry is ordered…

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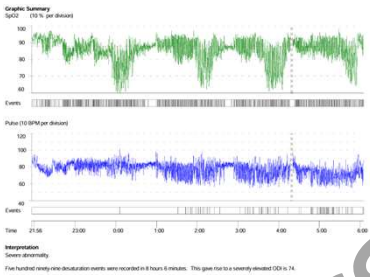
Screening Overnight Oximetry



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Watch-PAT Home Sleep Apnea Test

Breathing Events

	Supine	Prone	Left	Right	REM	NREM	Total
pAHI (events/vTST)	94.6	93.3	83.6	85.7	80.7	88.7	88.2
pRDI (events/vTST)	94.6	93.3	83.6	85.7	82.8	88.6	88.2
pAHIc					2.1	6.2	5.9
% CSR							0.0

Breathing events are defined using PAT signal and oximetry with desaturation ≥ 4%. AHI is calculated with apnea and hypopnea using vTST as the denominator. RDI includes apneas, hypopneas, and RERAs. Indices are calculated using vTST of 7 hrs. 30 min.

Heart Rate

Mean	71
Maximum	104
Minimum	42

Oxygen Saturation

Mean (%SpO2)	88 %
Minimum (%SpO2)	60 %

	<88%	<80%	<70%
Duration (minutes)	158.9	41.8	9.3

Snoring

% TST (>40 dB)	80.4 %

Technical Comments

Mail out diagnostic study

	Supine	Prone	Left	Right	REM	NREM	Total
ODI (≥4% desat.) (events/vTST)	87.7	81.6	69.7	77.4	80.7	79.9	80.0

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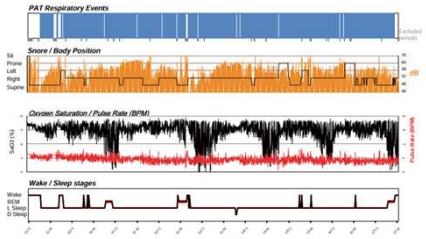
Watch-PAT Home Sleep Apnea Test



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Case Study Follow Up

- Referred to sleep lab for PAP titration due to severity of sleep disordered breathing; bi-level recommended as CPAP was insufficient
- Tolerated initial adaptation to bi-level with encouragement from you and his partner
- Noted BP readings improved slightly
- Reported improvement in daytime alertness, slow improvement in perceived sleep quality
- Sleep related symptoms continue to improve with time, increased sleep duration and discontinuation of shift work
- Difficult to control HTN persists with multiple medication intolerances, other likely contributing factors

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Obstructive Sleep Apnea

- Clinical Presentation:
  - Daytime sleepiness
  - Loud snoring, choking, gasping, otherwise abnormal breathing observed during sleep
  - Morning headaches
  - Insomnia
  - Nocturia
  - Nocturnal reflux
- Risk factors:
  - Crowded oropharyngeal airway
  - Obesity, large neck circumference
  - Craniofacial abnormalities, connective tissue disorders
  - Signs of associated conditions (hypertension, heart failure, pulmonary hypertension)
- Prevalence: estimated 15-30% males, 10-15% females (north America)

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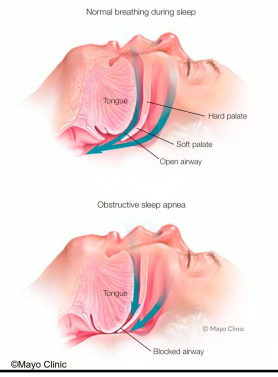
Obstructive Sleep Apnea

- Recurrent upper airway obstruction during sleep resulting in episodes of hypoxia and sleep fragmentation
- Interaction between unfavorable anatomic factors in the upper airway and sleep-related changes in upper airway function



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OSA – Evaluation

- Screening tests:
  - Overnight oximetry
  - *Smart watch data?*
- Formal diagnostic testing:
  - Home sleep apnea testing (HSAT)
  - Polysomnography (PSG)
- Treatment indications:
  - MILD obstructive sleep apnea
    - Apnea Hypopnea Index (AHI) of 5-14 events per hour with symptoms or pertinent comorbidity
  - MODERATE to SEVERE obstructive sleep apnea
    - AHI of 15 or greater regardless of symptoms or comorbidity

https://www.itamar-medical.com/watchpat-one/

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OSA & Cardiovascular Risk

- OSA associated with numerous CVD complications:
  - Hypertension
  - AF, other arrhythmias
  - CAD
  - Stroke
  - Pulmonary hypertension
  - CVD mortality
  - Diabetes and metabolic syndrome
- Mechanisms:
  - Intermittent hypoxemia / hypoxemic burden
  - Hypercapnia
  - Autonomic dysfunction
  - Repeated arousal/sleep disruption
  - Intrathoracic pressure change
  - Oxidative stress
  - Metabolic dysregulation

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OSA & Cardiovascular Disease

- Hypertension and OSA closely correlated – 30-50% of hypertensive patients have OSA, up to 80% in patients with resistant hypertension (Yeghiazarians 2021)
- Prevalence of OSA post stroke and TIA may exceed 70% of patients (systematic review/meta-analysis, 89 studies including 7,096 patients) (Seiler 2019)
- Prevalence of OSA in patients dx with pulmonary hypertension via right-sided heart catheterization as high as 70-80% (Jilwan 2013)

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AUDIENCE RESPONSE

What treatment option(s) are indicated for patients with mild obstructive sleep apnea (AHI 5-14 events per hour) and at least one cardiovascular comorbidity and/or symptoms including daytime sleepiness?

A. Weight loss w/ use of tirzepatide (Zepbound)
B. Oral appliance therapy
C. CPAP / auto CPAP therapy
D. Hypoglossal nerve stimulation (Inspire)
E. B and C
F. C and D

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AUDIENCE RESPONSE

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E. B and C
F. C and D

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OSA Treatment

- PAP therapy (CPAP, APAP, bi-level, ASV / bi-level ST)
- Oral appliance therapy / mandibular advancement device
- Surgical intervention – ENT surgery, various approaches including newer implantable hypoglossal nerve stimulators **(HG STIM only AHI 15+)**
- Weight loss (tirzepatide approved for obesity w/ OSA AHI 15+)
- Myofunctional therapy
- ExciteOSA (www.exciteosa.com)
- Medication options anticipated in coming years (AD109 – aroxybutinin/atomoxetine)

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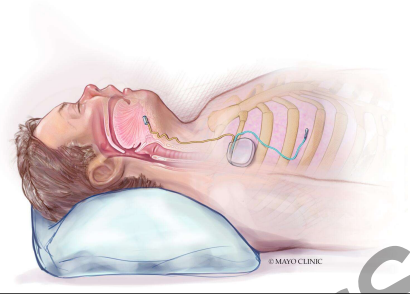
OSA Treatment – Hypoglossal Nerve Stimulation



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OSA & Cardiovascular Disease

- AHA *recommends* screening patients with:
  - resistant or poorly controlled HTN
  - pulmonary HTN
  - recurrent atrial fibrillation (after cardioversion or ablation)
- AHA *considers* screening patients if symptoms of OSA are present for patients with:
  - NYHA class II-IV HF symptoms
  - tach-brady syndrome
  - sick sinus syndrome
  - ventricular tachycardia
  - CVA
  - survivors of sudden cardiac death

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OSA Team-Based Care

- Collect history and conduct screenings
- Offer encouragement to patients through the process of diagnosis and treatment initiation and long-term adherence
- Assist in coordinating follow up care, including for patients who D/C therapy on their own
- Confirm therapy adherence, changes in response or changes in cardiovascular status that may impact sleep apnea management
  - Return of symptoms/change of symptoms in patient with recent cardiovascular event
  - Report of suboptimal PAP response based on download data
  - Note significant EF drop (<45%) in patients using ASV therapy and refer back to sleep medicine

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Narcolepsy

- Clinical presentation:
  - Excessive daytime sleepiness
  - Sleep disruption
  - RBD/dream enactment
  - Sleep paralysis
  - Hypnagogic hallucinations / hypnopompic hallucinations
  - Cataplexy (NT 1)
  - Mood disorders / depression
- Risk factors:
  - Genetic predisposition
    - HLA DB-Q1*06:02
  - Autoimmune origin suspected
  - Infection history (strep, influenza)
- Prevalence: NT1 estimated 25-50 per 100,000 people, NT2 thought slightly less common

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Narcolepsy

- Type 1 known now to be autoimmune mediated loss (permanent) of hypocretin (orexin) producing neurons in the lateral hypothalamus
- Type 2 not fully understood (lacks cataplexy)
  - Cataplexy can develop later, changing diagnosis to Type 1
- For NT1:
  - Loss of orexin -> loss of ability for prolonged periods of wakefulness, loss of ability to stabilize REM
  - Profound **instability of sleep-wake homeostasis** due to loss of orexin producing neurons results in symptoms

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Narcolepsy – Diagnostic Criteria

- ICSD 3 criteria for **NT1**:
  - Periods of irrepressible need to sleep or daytime lapses into sleep/drowsiness
  - Presence of one or both:
    - **Cataplexy** and either:
      - MSL </= minutes and 2 or more SOREMPs on MSLT
      - SOREMP on PSG (within 15 minutes of sleep onset)
    - **CSF hypocretin-1 concentration </= 110 pg/mL**
- ICSD 3 criteria for **NT2**:
  - Periods of irrepressible need to sleep or daytime lapses into sleep/drowsiness
  - MSL </= minutes and 2 or more SOREMPs on MSLT
  - SOREMP on PSG (within 15 minutes of sleep onset) can replace one nap SOREMP
  - **Cataplexy is absent**
  - CSF hypocretin-1 not measured or is > 110 pg/mL

**ICSD 3 – International Classification of Sleep Disorders 3 published 2014*

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Narcolepsy – Treatment

- Treatment is symptomatic – no disease modifying treatments yet available
- Lifestyle modification – timed napping, avoidance of sleep deprivation, sleep hygiene, regular sleep schedule etc
- Medications to increase wakefulness (stimulants, wakefulness promoters, oxybates)
- Medications to reduce cataplexy when present (oxybates, SNRI, pitolisant – selective H3 receptor antagonist/inverse agonist)
- Management of comorbidities

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Narcolepsy & Cardiovascular Risk

- Cardiovascular Burden of Narcolepsy Disease (CV-BOND): a real-world evidence study
  - PWN have higher risk of new-onset CV events, any stroke, HF, ischemic stroke, major adverse cardiac event, CV disease (Ben-Joseph 2023)
- PWN have increased risk for HTN, hyperlipidemia, diabetes, NAFLD, CVD composite risk and major adverse CV events (Kaufmann, 2025)
  - Results remained significant following adjustment for medication use (stimulants, wake-promoting agents and oxybates)

**PWN – person/people with narcolepsy*

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Narcolepsy & Cardiovascular Risk

- Mechanisms:
  - Fragmented sleep
  - Autonomic dysfunction
  - Nocturnal non-dipping
  - Weight gain (common in pediatric onset (Poli, 2013))
  - Indirect via lifestyle changes driven by excessive sleepiness and fatigue
- Treatment associated risks: elevated heart rate, increased blood pressure, arrhythmias and QT prolongation

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AUDIENCE RESPONSE

Which of the following has the highest sodium content, per serving/dose/packet?

A. Better Than Bouillon vegetable base (1 serving = 1 tsp/8 oz water)

B. Kikkoman Soy Sauce (1 serving = 15 mL/1 Tbsp)

C. LMNT electrolyte drink mix (1 serving = 1 packet)

D. Xyrem (full dose 9 g/night)

E. Xywav (full dose 9 g/night)

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AUDIENCE RESPONSE

Which of the following has the highest sodium content, per serving/dose/packet?

A. Better Than Bouillon vegetable base (1 serving = 1 tsp/8 oz water)
700 MG

B. Kikkoman Soy Sauce (1 serving = 15 mL/1 Tbsp)
960 MG

C. LMNT electrolyte drink mix (1 serving = 1 packet)
1000 MG

D. Xyrem/sodium oxybate (gamma hydroxybutyrate) (full dose 9 g/night)
1640 MG

E. Xywav/mixed-salt oxybate (gamma hydroxybutyrate) (full dose 9 g/night)
131 MG

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Narcolepsy & Treatment Associated CV Risks

- Modafinil – increased BP, tachycardia, palpitations; cardiac arrhythmias reported – thought related to sympathetic stimulation
- Armodafinil – not recommended w/ history of LVH or MVP developed with prior stimulant use, increased BP reported
- Traditional stimulants (methylphenidate, dextroamphetamine/amphetamine) – increased HR, increased BP, acute MI, stroke and sudden cardiac death reported; arrhythmia risk with long term use
- Pitolisant – may prolong QT interval
- Oxybates – some formulations high sodium, use in caution in patients with HF or HTN; edema reported as side effect (maximum Xyrem & Lumryz dose of 9 g nightly contains 1640 mg sodium; maximum Xywav dose of 9 g nightly contains 131 mg)

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Narcolepsy Team Based-Care

- **JAHA published expert panel consensus recommendations**:
  - Recognize risk of HTN and cardiovascular/cardiometabolic disease in PWN
    - Increased risk due to narcolepsy itself
    - Presence of other sleep disorders
    - Implement earlier/more frequent screening/monitoring
  - Reduce risk of hypertension and cardiovascular/cardiometabolic disease in PWN
    - Patient education
    - Consider treatment related risk
    - Treat comorbid OSA
  - Reduce sodium intake to lower risk of hypertension and cardiovascular disease in PWN
    - Modify pharmacotherapy
    - Educate / advise re: dietary intake, consider salt substitute/low Na diet

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Restless Leg Syndrome

- Clinical presentation:
  - Uncomfortable urge to move legs (or arms) when at rest
  - Relief with movement or getting up and walking
  - Can be isolated and related to episodes of inactivity, daily or nearly round-the-clock
  - Clinically significant definition occurs at least 2x per week, associated with moderate distress
- Risk factors:
  - Iron deficiency
  - Genetic predisposition
  - Sleep deprivation / disturbance (OSA)
  - Pregnancy
  - Use of antihistaminergic medications
  - CKD/ESRD
  - Peripheral neuropathy
  - Parkinson's disease

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Restless Leg Syndrome – Pathophysiology

- Pathophysiology unclear but likely involves CNS dopaminergic dysfunction along with other undefined mechanisms
- Brain iron deficiency likely involved
- Genetics likely involved

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Restless Leg Syndrome

Diagnostic criteria per IRLSSG all must be met:

- An urge to move the legs, maybe accompanied by or felt to be caused by uncomforted and unpleasant sensations in the legs
- The urge to move the legs and any accompanying unpleasant sensations begin or worsen during periods of rest/inactivity such as lying down or sitting
- The urge to move the legs and any accompanying unpleasant sensations are partially or totally relieved by movement such as walking or stretching, at least as long as activity continues
- The urge to move the legs and any accompanying unpleasant sensations during rest or inactivity occur only or are worse in the evening or night compared to during the day
- The occurrence of the above features is not solely accounted for as symptoms primary to another medical or behavioral concern (myalgia, venous stasis or leg edema, arthritis, leg cramps, positional discomfort, habitual foot tapping)

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AUDIENCE RESPONSE

What mechanisms are suspected to contribute to increased cardiovascular risk in patients with restless leg syndrome?

A. Iron deficiency
B. Sleep fragmentation
C. Sleep deprivation
D. Periodic limb movements of sleep
E. All of the above

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AUDIENCE RESPONSE

What mechanisms are suspected to contribute to increased cardiovascular risk in patients with restless leg syndrome?

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E. All of the above

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Restless Leg Syndrome & CVD Risk

- **Mechanisms** proposed (Gottlieb 2016)
  - Periodic limb movements of sleep (PLMS) associated with increases in HR and BP
  - Sleep fragmentation and sleep deprivation
  - Iron deficiency
- Cross-sectional association evaluated between RLS and CVD in Sleep Heart Health Study – association was stronger in those with symptoms at least 16 times per month, and stronger in those with severe bother from symptoms (Winkelman 2008)
- A follow up on cohort study revealed treatment lowers CVD risk:
  - Future CVD cases (MI, angina, stroke, a fib and HF) - HR 1.26 for treatment group and 1.53 for non-treatment group
  - Treatments included dopaminergics, anticonvulsants, benzodiazepines and opiates (Gao 2021)

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RLS & Cardiovascular Disease Pathophysiology


Circulation Research

REVIEW

Restless Legs Syndrome, Periodic Leg Movements, Hypertension and Cardiovascular Diseases

Yves Dauvilliers, Sofiene Chenini, Lucie Barateau, Virend K. Somers

ABSTRACT: Restless legs syndrome (RLS) is a frequent sleep-related sensorimotor disorder defined by an urge to move the legs in the evening while resting. Severe RLS symptoms can negatively impact sleep, mood, and quality of life. Periodic leg movements during sleep and wakefulness are found in 60% to 80% of patients with RLS. The pathophysiology of RLS and periodic leg movement is still poorly understood and involves brain iron deficiency, dopamine dysregulation, and genetic predisposition. Over the past decades, several cross-sectional and longitudinal studies have reported an association between RLS, cardiovascular disease, and hypertension although the magnitude, direction, and underlying mechanisms of these associations remain inconclusive. Periodic leg movements during sleep are concomitant with an increase in blood pressure and heart rate, which may affect the physiological nocturnal blood pressure dip and, therefore, lead to an increased incidence

https://www.ahajournals.org/doi/10.1161/CIRCRESAHA.125.325677

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Restless Leg Syndrome – Treatment

- **Test serum iron studies** including ferritin, transferrin saturation (fasting AM with 24 hours avoidance of iron-containing supplements/food)
  - Oral or IV iron replacement suggested if serum ferritin 75 ng/mL or less or transferrin saturation < 20%; RLS+ ESRD ferritin < 200 ng/mL
- Address exacerbating factors (alcohol, caffeine, antihistaminergic/serotonergic/antidopaminergic medications, untreated OSA)
- Consider medication recommendations: gabapentin, gabapentin enacarbil, pregabalin; opioids
- Consider bilateral high-frequency peroneal nerve stimulation (NIDRA device) (contraindicated for active medical device implants like pacemaker, DBS, SCS)
- AASM clinical practice guidelines now advise **against** standard use of dopamine agonists (pramipexole, ropinirole, transdermal rotigotine) (Winkelman 2025 – AASM Clinical Practice Guideline)

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RLS Team-Based Care

- Awareness of symptoms and presentation is key – many patients do not recognize this is what they are experiencing (may describe insomnia or anxiety type restlessness keeping them up at night)
- Check for completion of iron studies, consider updating iron studies with new or worsening symptoms
- Refer back to sleep medicine or neurology for uncontrolled symptoms

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Insomnia

- Difficulty initiating, maintaining sleep, or final awakening earlier than desired
- Fatigue, impaired concentration/attention/memory, impaired social/occupational/academic performance, mood disturbance, daytime sleepiness, behavioral problems, reduced energy/motivation, concerns/dissatisfaction with sleep
- Not explained by inadequate opportunity or circumstances (time, environment)
- Disturbance and symptoms occur 3+ times per week
- Disturbance and symptoms present for at least 3 months
- Not due to another medical, mental disorder or substance or medication use

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Insomnia

- **Psychophysiological insomnia** (heightened arousal/learned sleep preventing associations)
- **Idiopathic insomnia** (longstanding complaints, insidious onset in childhood)
- **Paradoxical insomnia** (previously sleep state misperception – complaint of severe sleep disturbance despite objective evidence of normal sleep)
- **Inadequate sleep hygiene** (daily activities inconsistent with maintenance of good quality sleep – napping, variable schedule, caffeine/tobacco/alcohol use, engaging in activating or upsetting activities too close to bedtime, failure to maintain environment conducive to sleep)
- Insomnia due to another mental disorder or due to a medical condition
- Insomnia due to drug or substance (cardiac meds play here!)

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Insomnia – Risk Factors

- Older age
- Female sex
- Prior episodes of insomnia
- Family history of insomnia
- "Light sleeper"
- Reaction to stressful life events
- Other sleep disorders
- Chronic pain
- Medication contributions
- Substance use (caffeine, alcohol, illicit drugs)
- Neurologic disease
- Cardiovascular disease
- Psychiatric/psychological factors (depression, anxiety, PTSD, substance abuse disorders)

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Insomnia & Cardiac Medications

- Beta blockers (lipophilic) – increase wake after sleep onset, decrease total sleep time, may decrease REM, nightmares/unpleasant dreams
- Ticagrelor – may induce central sleep apnea / periodic breathing (Javaheri 2024)

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Insomnia & Cardiovascular Health

- Mechanisms:
  - Elevated / dysregulated BP and hypertension
  - Insulin resistance, glucose dysregulation, type II diabetes
  - Stress and immune mechanisms and health behaviors (Fernandez-Mendoza 2025)
- Insomnia with short sleep duration (ISSD) is particularly problematic, associated with increased risk of HTN comparable to that of sleep apnea (Vgontzas 2009)

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Insomnia & Cardiovascular Risk

- Insomnia associated with increased risk for HTN, CAD, recurrent ACS and HF, potential bi-directional relationship (especially when associated with short sleep duration) (Javaheri 2017)
- Insomnia or poor sleep with total sleep < 6 hours duration on PSG associated with higher risk of incident CVD, but not all-cause mortality (Bertisch 2018)
- Insomnia symptoms in midlife when persistent or occurring with short sleep are associated with higher CVD risk among women (Thurston 2024)
- Insomnia with short sleep duration associated with increased risk for CV mortality and MI, and CV disease (Ali, 2023)

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Insomnia – Treatment

- Identify predisposing factors, precipitating events, perpetuating factors
  - Acknowledge and address modifiable factors
- Cognitive behavioral therapy for insomnia (CBT-i) – first line therapy
  - Behavioral sleep medicine psychologist
  - Self guided courses online, via app
  - Self guided via book
- Medication
  - Selection should be based on primary complaint (sleep initiation, maintenance, both), potential risks, and concern for morning sedation

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Cognitive Behavioral Therapy for Insomnia

- Sleep hygiene (SH)
  - Educate about behaviors that influence sleep, promotes better sleep practices (minimal effectiveness as stand-alone intervention)
  - Examples: limiting caffeine, alcohol consumption, limiting naps, regular exercise, creating comfortable sleep environment
- Sleep restriction therapy (SRT)
  - Understand sleep extension as a perpetuating factor for chronic insomnia (compensating for lost sleep by increasing time in bed)
- Stimulus control therapy (SCT)
  - Stimulus response based on conditioning - development of maladaptive response
  - Go to bed only when sleepy, use bed only for sleep or sex, get out of bed if unable to sleep withing 15-20 min* and return only when sleepy, repeat as necessary, get up same time each day and avoid napping throughout the day
- Cognitive therapy (CT)
  - Goal: develop realistic sleep expectations – identify dysfunctional thoughts about sleep, examine thoughts for accuracy and modifying them when necessary

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Insomnia – Pharmacotherapy

- Melatonin receptor agonist
  - ramelteon, tasmelteon (used in NON-24)
- Dual orexin receptor antagonists / DORAs
  - suvorexant, daridorexant, lemborexant
- Benzodiazepine receptor agonists
  - zolpidem, zaleplon, eszopiclone
- Off-label include amitriptyline, gabapentin, trazodone
- OTC options include melatonin, diphenhydramine, doxylamine, various herbs and spices

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Insomnia, CVD Risk & Treatment Benefit?

- Study currently enrolling to look at whether treatment of insomnia with CBT-i reduces CVD risk (SHADES study, https://clinicaltrials.gov/study/NCT06041581)
- Hypnotics?

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Insomnia Team-Based Care

- Monitor for changes in sleep related to CV event onset, medication initiation or dose adjustments
- Education and counseling on behaviors to better support healthy sleep
- Education and counseling for general lifestyle / cardiovascular health highly applicable to sleep as well, emphasize the dual benefit
- Identify local resources for CBT-I and psychological support for living with chronic illness
- Monitor safety with use of medications for sleep

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Future research / areas lacking

- Remote monitoring
- Smart watches / sleep trackers
- Use of AI for data processing, remote monitoring and identifying actionable data
- Better cardiovascular risk stratification for OSA patients, especially those who are truly asymptomatic
- Assessing risk / benefit of medication for management of insomnia

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Patient Education

- Patient education resources from AHA
  - PDF handout link in notes
  - http://www.heart.org/sleepdisorders

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Other Educational Resources

- Narcolepsy / idiopathic hypersomnia
  - Project Sleep – www.project-sleep.com
  - Narcolepsy Network – www.narcolepsynetwork.org
  - Hypersomnia Foundation - https://www.hypersomniafoundation.org
- RLS
  - https://www.irlssg.org
  - https://rlscurbside.org/resources
- American Academy of Sleep Medicine – www.aasm.org
- American Association of Sleep Technologists – www.aastweb.org

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QUESTIONS

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