

# Preventing Adverse Consequences of Sleep Loss and Excessive Sleepiness

## Practical Assessment and Management Strategies

### Joseph A. Lieberman III, MD, MPH

Associate Editor, Delaware Medical Journal  
Hockessin, Delaware  
Professor of Family Medicine  
Jefferson Medical College  
Thomas Jefferson University  
Philadelphia, Pennsylvania



### Brian H. Foresman, DO

Medical Director, Sleep Medicine Program  
Roudebush VA Medical Center  
Indianapolis, Indiana



### Fredric Jaffe, DO

Assistant Professor of Medicine  
Division of Pulmonary and Critical Care Medicine  
Sleep Disorders Center  
Temple Lung Center  
Temple University Hospital  
Philadelphia, Pennsylvania

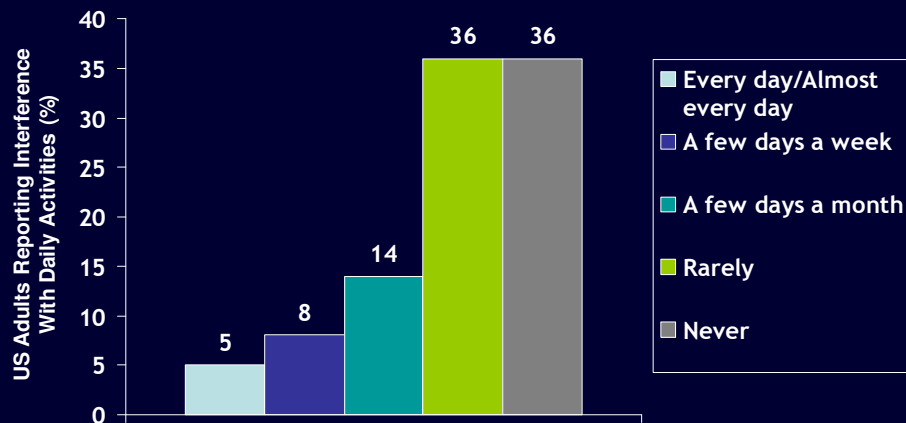


## What is Excessive Daytime Sleepiness (EDS)?

- Sleep propensity during wakefulness
- Interferes with activities of daily living (work, child care, driving)
- Physical, mental, social, public health, and safety consequences
- Distinguished from fatigue (state of tiredness)

Ohayon MM. *Sleep Med Rev.* 2008;12:129-141; Thorpy MJ et al. *Am J Manag Care.* 2007;13:S132-S139.

## How common is sleepiness in America?



n = 1000

<http://www.sleepfoundation.org/sites/default/files/2008%20POLL%20SOF.PDF>. Accessed August 12, 2009.

## What are some of the conditions that cause sleep loss or EDS?

- Obstructive sleep apnea (OSA)
- Insomnia
  - Chronic
  - Transient or occasional
- Shift work sleep disorder (SWSD)
- Narcolepsy
- Medical and psychiatric disorders

*Sleep deprivation is cumulative*

Mahowald MW. *Postgrad Med.* 2000;107:108-123; Benca RM. *Psychiatr Serv.* 2005;56:332-343.

## What medical conditions affect sleep?

- Respiratory - asthma, nasal congestion, COPD, orthopnea
- Cardiac - congestive heart failure
- Neurologic - Parkinson's disease, myotonic dystrophy, multiple sclerosis, pain
- Rheumatologic - arthritis
- Gastrointestinal - GERD, constipation
- Other symptoms - frequent nocturia, pruritis
- Medication side effects
- Aging

Thorpy MJ. *Sleep Med.* 2005;6 (suppl 1):S13-S20; Thorpy MJ et al. *Am J Manag Care.* 2007;13:S132-S139.

## How is EDS related to psychiatric illness?

- Hypersomnia: an associated symptom in 10% to 75% of depressed patients
- Symptoms mimic depression
  - Lack of energy or motivation, poor concentration, memory disturbances, reduced interest in life
- Sleep disorders and depression may coexist
  - Sleepiness may masquerade as or exacerbate depression

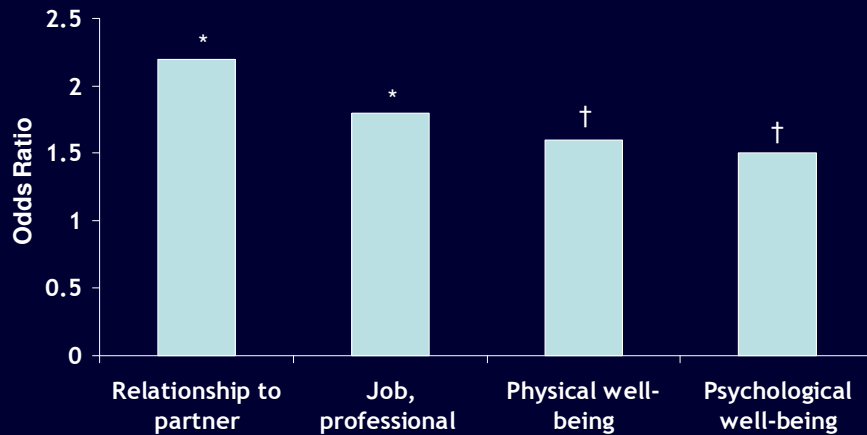
Ohayon MM. *Sleep Med Rev.* 2008;12:129-141; Thorpy MJ et al. *Am J Manag Care.* 2007;13:S132-S139; Black J et al. *CNS Spectr.* 2007;12:2(suppl 2):1-16; Mahowald MW. *Postgrad Med.* 2000;107:108-123.

## What are the consequences of sleep loss and EDS?

- Psychosocial problems
  - Impaired alertness
  - Decreased work performance
  - Self-consciousness
  - Low self-esteem
  - Social isolation
- Accidental injury
- Comorbid medical and psychiatric conditions
- Reduced quality of life

Black J et al. *CNS Spectr.* 2007;12:2(suppl 2):1-16.

## How significant is the negative impact of EDS on quality of life?



\* $P < 0.01$ ; † $P < 0.05$

Hasler G. *J Clin Psych*. 2005;66:521-529.

## How do we diagnose sleep problems?

- Accurate history from patient and sleep partner
  - Quantity and quality of sleep
- Physical examination
  - Crowded oropharynx, neck size, hypertension, weight
- Laboratory tests
  - Thyroid function tests (sleep apnea)
  - Ferritin levels (restless leg syndrome)
- Sleep diary, sleep log
- Screening tools: Questionnaires
- Formal sleep studies

Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147; Thorpy MJ et al. *Am J Manag Care*. 2007;13:S132-S139.

## Single-Question Sleepiness Screening Tool

“Please measure your sleepiness on a typical day”



Zallek SN. *J Clin Sleep Med.* 2008;4:143-148.

## What types of questionnaires can we use?

- Quality of life questionnaires
- Depression questionnaires
- Fatigue questionnaires
  - Fatigue Severity Scale
  - Chalder Fatigue Scale
- Sleepiness questionnaires
  - Epworth Sleepiness Scale
  - Stanford Sleepiness Scale

## Epworth Sleepiness Scale

Situation	Chance of Dozing
Sitting and reading	_____
Watching television	_____
Sitting, inactive in a public place (eg, a theater or meeting)	_____
As a passenger in a car for 1 hour without a break	_____
Lying down to rest in the afternoon when circumstances permit	_____
Sitting and talking to someone	_____
Sitting quietly after a lunch without alcohol	_____
In a car, while stopped for a few minutes in traffic	_____
<b>Total</b>	

Use the following scale to choose the most appropriate number for each situation: 0=Would never doze, 1=Slight chance of dozing, 2=Moderate chance of dozing, 3=High chance of dozing.

Scoring: 0-10, normal range; 10-12, borderline; 12-24, abnormal.

Johns MW. *Sleep*. 1991;146:540-545.

## When should a patient be referred to a sleep specialist?

- Suspected sleep apnea
- Reason for a patient's excessive sleepiness is not well understood by the primary care physician

Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147.

## When should a patient be referred to a sleep specialist?

- Suspected sleep apnea
- Reason for a patient's excessive sleepiness is not well understood by the primary care physician

*For evaluation ± comanagement*

## What formal sleep studies are available?

- Actigraphy
  - Measures gross motor activity
  - Possible diagnoses
    - Circadian rhythm sleep disorder
    - Excessive sleepiness (ES)
    - Insomnia

## What formal sleep studies are available?

- Polysomnography
  - Measures overnight sleep state
  - Possible diagnoses
    - Central sleep apnea
    - Nonobstructive hypoventilation
    - OSA
    - Periodic limb movements in sleep

Kushida CA et al. *Sleep*. 2005;28:499-521.

## What formal sleep studies are available?

- Multiple Sleep Latency Test
  - Measures sleep tendency
  - Possible diagnoses
    - Narcolepsy
    - ES
- Maintenance of Wakefulness Test
  - Measures ability to stay awake
  - Possible diagnosis
    - ES

Littner MR et al. *Sleep*. 2005;28:113-121.

## If there is clinical suspicion of a sleep disorder...

- Conduct an accurate history and physical examination
- Perform specific sleep/wake testing
- Refer to sleep specialist in complex cases

## Case 1

- 60-year-old woman presents to PCP for her annual physical examination
- Complains of feeling tired all the time
- ROS: Occasional hot flashes, nocturia
- Single-question screener score

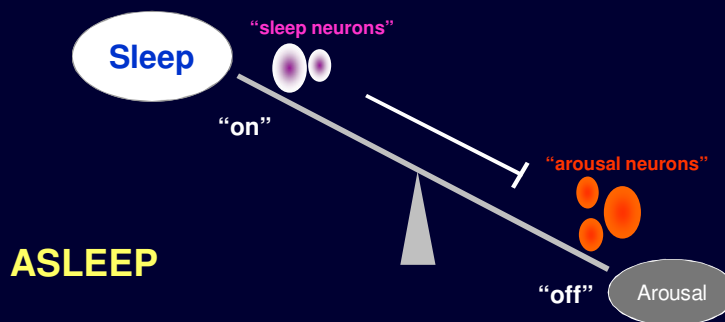


## How do we distinguish EDS from fatigue?

- Fatigue correlates with insomnia
- Sleepiness may be caused by medical illness, behavioral factors, specific sleep disorders (OSA), and factors affecting nocturnal sleep
- Patients with OSA may complain of fatigue, tiredness, and lack of energy as frequently as the more expected complaint of sleepiness

Bailes S et al. *J Psychosom Res.* 2006;60:605-613.

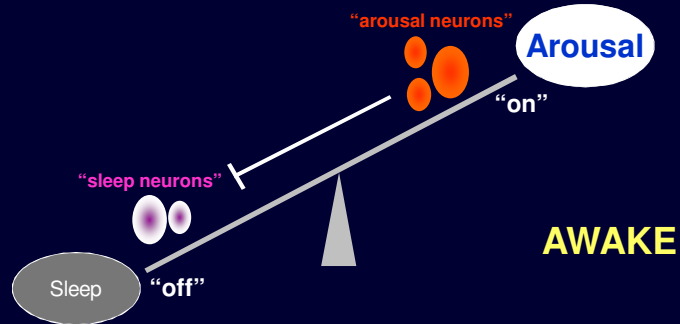
## What is the physiological basis of sleep and wakefulness?



*In patients with EDS, continued activation of sleep centers can lead to sleepiness*

Saper CB et al. *Nature.* 2005;437:1257-1263.

## What is the physiological basis of sleep and wakefulness? (cont'd)



*In patients with insomnia, continued activation of arousal centers can lead to fatigue; patients will be tired but unable to fall asleep*

Saper CB et al. *Nature*. 2005;437:1257-1263.

## Question to Ask Your Patients: "Would you be able to nap right now?"

Patient with insomnia

"Would love to,  
but can't!"

## Question to Ask Your Patients: “Would you be able to nap right now?”

Patient with insomnia

Would love to,  
but can't!

Patient with EDS

Absolutely!

## What else should be included in the sleep history of this patient?

- Snoring?
- Witnessed apneas?
- Disrupted sleep pattern?
- Other questions to ask
  - When do you sleep?
  - When do you wake up?
  - How well do you sleep?
  - How alert are you during the day?

## Insomnia

- Difficulty initiating or maintaining sleep
- More common in women, the unemployed, the elderly
- Chronic insomnia associated with daytime hyperarousal ( $\pm$  fatigue) rather than EDS
- Sleep fragmentation associated with EDS

Bonnet MH, Arand DL. *Sleep Med Rev.* 2009; Jul 27 [Epub ahead of print]; Thorpy MJ. *Sleep Med.* 2005;6 (suppl 1):S13-S20; Thorpy MJ et al. *Am J Manag Care.* 2007;13:S132-S139.

## What treatment modalities are available for insomnia?

- Nonpharmacologic
  - Cognitive behavioral therapy
  - Sleep hygiene
- Pharmacologic (hypnotics)
  - Helps patient sleep without residual daytime sleepiness
  - Sleep-promoting medications
    - Sedating antidepressants, benzodiazepines, nonbenzodiazepines (eg, zolpidem, eszopiclone, zaleplon), melatonin-receptor agonist (ramelteon)

Thorpy MJ et al. *Am J Manag Care.* 2007;13:S140-S147.

## What are some recommendations for sleep hygiene?

- Limit time spent in bed to sleeping
- Set routine bedtime and waking hours
- Do not force sleep
- Avoid naps during daytime
- Avoid exercise 2 hours before bed
- Avoid coffee, alcohol or excessive amounts of beverages before bedtime
- Avoid heavy meals before bedtime
- Make the sleep environment as comfortable as possible (lighting, temperature, noise, etc)

Ting L. *Prim Care Clin Office Pract.* 2005;32:305-318.

## Clinical Pearls

- Insomnia causes fatigue, not EDS
- Association between aging, menopause and sleep disorders
- When patients present for their annual physical, it is important to assess sleep history
- Use of behavioral modifications ± sleep-promoting therapy for patients with insomnia

## Case 2

- 35-year-old man approaches his internist while at work in a hospital
- Works as an RN on the night shifts Monday through Friday
- Complains his sleep is recurrently and chronically disrupted
  - Has difficulty staying awake at work; a medication error caught by a patient
  - Cannot enjoy his family activities during weekend; feels “tired all the time”
- Single-question screener score



## What is Shift Work Sleep Disorder?

- Circadian rhythm disorder
- Primary symptoms
  - Insomnia
  - Excessive sleepiness
- More absenteeism from work, absences from family and social events, sleepiness-related accidents, neuroticism

Pagel JF. *Am Fam Physician*. 2009;79:391-396; Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147; Drake CL et al. *Sleep*. 2004;27:1453-1462.

## How do you evaluate a patient for SWSD?

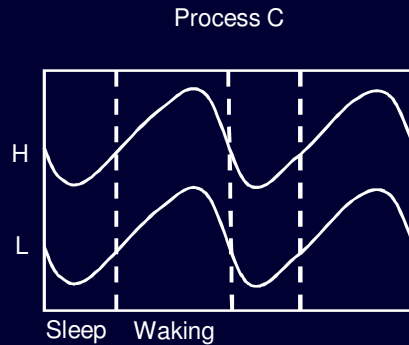
- Accurate history (sleep pattern)
- Physical examination
- Sleep logs
- Sleep diaries

## How common is SWSD?

- 20% of employees in industrialized countries are shift workers
  - ~10% prevalence among shift workers
  - 1% prevalence among general working population
- Individuals with unconventional working hours, such as prolonged, variable or split schedules
- Parents of young children

*Population changes resulting in a new paradigm for shift work*

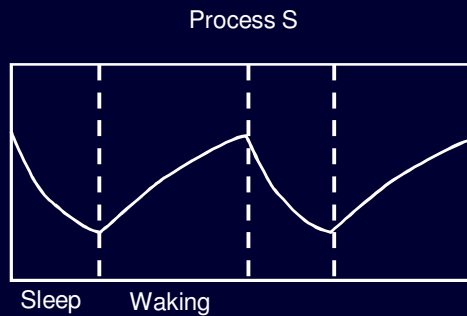
## What is the two-process model of sleep regulation?



The circadian Process C modulates high and low thresholds, which generates the timing of sleep and waking

Achermann P. *Aviat Space Environ Med.* 2004;75(3 suppl):A37-A43.

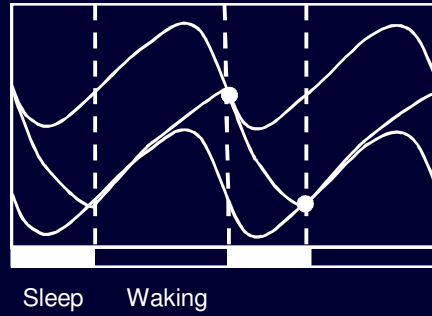
## What is the two-process model of sleep regulation? (cont'd)



The homeostatic Process S rises during waking and declines during sleep

Achermann P. *Aviat Space Environ Med.* 2004;75(3 suppl):A37-A43.

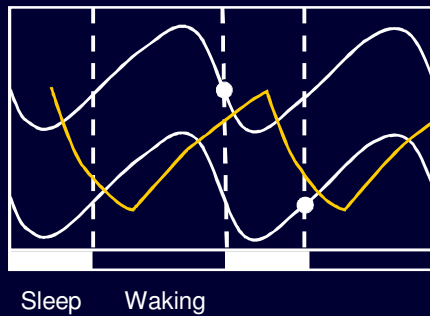
## What is the two-process model of sleep regulation? (cont'd)



Interaction of S with C determines the beginning and end of a sleep episode

Achermann P. *Aviat Space Environ Med.* 2004;75(3 suppl):A37-A43.

## What is the two-process model of sleep regulation? (cont'd)



**Shift work sleep disorder**

Achermann P. *Aviat Space Environ Med.* 2004;75(3 suppl):A37-A43.

## What are the consequences of SWSD?

- Cognitive impairment
  - Alertness, memory, psychomotor performance
- Behavioral changes
  - More absenteeism from work, absences from family and social events, sleepiness-related accidents, neuroticism
  - Too tired to engage in social interactions

Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147.

## What nonpharmacologic interventions are recommended for SWSD?

- Maintain constant sleep/wake schedule as often as possible
- Nap if possible
- Use bright light during work
- Avoid morning sunlight
- Improve sleep hygiene
- Protect the sleep environment

Schwartz JRL, Roth T. *Drugs*. 2006;66:2357-2370.

## What pharmacologic interventions are available for SWSD?

- Stimulant drugs to increase wakefulness
- Select dose, duration of action, and time of administration to relieve EDS without disturbing nighttime sleep
  - Caffeine
  - Modafinil
  - Armodafinil

Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147.

## Why use alerting medications?

- Enhance wakefulness during wake periods
- Improve alertness
- Facilitate normal levels of attention and energy throughout the wake period
- Facilitate good sleep when desired
- Ensure adequate sleep duration and improve sleep quality
- Minimize side effects that impair functioning or normal sleep patterns

Black J et al. *CNS Spectr*. 2007;12:(2 suppl 2):1-16.

## What pharmacologic interventions are FDA-approved for SWSD?

- FDA-approved medications
  - Modafinil (mixture of R- and S-enantiomers)
  - Armodafinil (R-enantiomer)
- Half-life
  - R-modafinil 10-14 hours
  - S-modafinil 3-4 hours
- Schedule IV drugs
  - Modafinil 200 mg/day
  - Armodafinil 150-250 mg/day
- Side effects: headache, infection, nausea, anxiety, insomnia

Bonnet MH et al. *Sleep*. 2005;28:1163-1187; Kushida CA. *Curr Treat Options Neurol*. 2006;8:361-366; Roth T et al. *Sleep Breath*. 2008;12:53-62.

## What about caffeine?

- Short-acting stimulant
- Improves alertness and performance in studies with sleep deprivation, restriction, or circadian sleep reversals
- No major disruptive effect on sleep  $\geq 8$  hours after administration
- Dependence can develop after short periods of regular daily use with relatively low daily doses
- Frequent use can lead to tolerance and negative withdrawal effects

Bonnet MH et al. *Sleep*. 2005;28:1163-1187; Roehrs T, Roth T. *Sleep Med Rev*. 2008;12:153-162.

## What are the adverse effects of caffeine?

- Tachycardia, palpitations, insomnia, restlessness, nervousness, tremor, headache, abdominal pain, nausea, vomiting, diarrhea, diuresis
  - Particularly in people with hypertension, children, adolescents, and the elderly
- Withdrawal symptoms
  - Headaches, fatigue, drowsiness, irritability, difficulty concentrating, depressed mood, nausea, myalgia

Higdon JV, Frei B. *Crit Rev Food Sci Nutr.* 2006;46:101-123.

## Clinical Pearls

- SWSD is becoming more prevalent with changes in work/home schedules
- Nonpharmacologic interventions should be tailored to the individual's circumstances
- Alerting agents are useful as adjunctive therapy

## Case 3

- 65-year-old overweight female
- History of type 2 diabetes
- Snores at night
- Friends and family noted increased “grumpiness”
- Memory/concentration problems
  
- Single-question screener score



## What is Obstructive Sleep Apnea Syndrome?

- Prevalence: 2% of women, 4% of men
- More common in adults, snorers, the elderly, people who are overweight
- Recurrent episodes of upper airway obstruction with intermittent apnea-hypopnea
- Clinical diagnosis requires sleep studies

Doghramji PP. *J Fam Pract.* 2008;57(8 suppl):S17-S23; Mahowald MW. *Postgrad Med.* 2000;107:108-123; Lieberman JA 3rd. *Postgrad Med.* 2009;121:33-41.

## Is snoring a problem?

- Upper airway narrowing
- Peak prevalence: 50 to 60-year-olds
- Risk factors for loud snoring and sleep apnea in middle-aged men
  - Obesity, hypertension, angina
- Medical consequences
  - Hypertension
  - Ischemic heart disease
  - Stroke
- Associated with obesity, diabetes, arthritis, sleep apnea, EDS

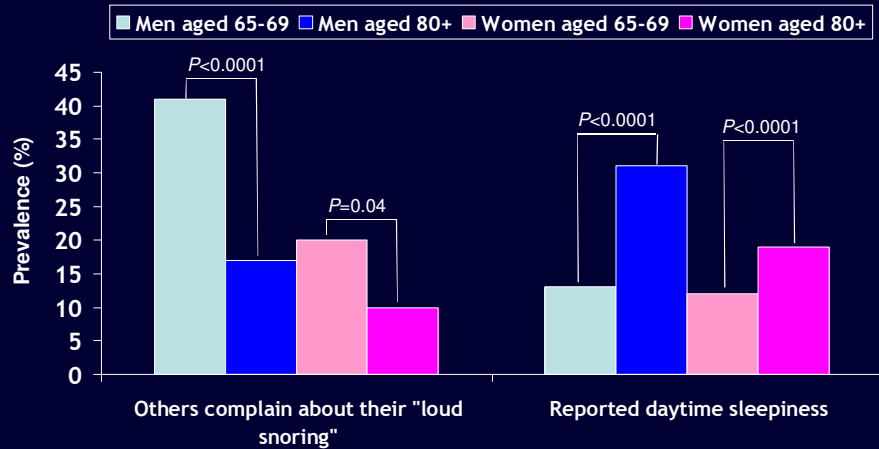
Wolkove N et al. *Can Med Assoc J.* 2007;176:1299-1304; Enright PL et al. *Sleep.* 1996;19:531-538.

## What about habitual snoring in children?

- 10% to 12% of young children snore; decreased frequency after age 9
- Symptom of increased airway resistance (OSA)
- Associated with
  - daytime sleepiness
  - restless sleep
  - behavioral hyperactivity
  - learning problems
  - attention deficits
  - anxious/depressive symptoms
  - social problems
  - neurocognitive impairments

O'Brien LM et al. *Pediatrics.* 2004;114:44-49.

## How common are snoring and daytime sleepiness in the elderly?



Enright PL et al. *Sleep*. 1996;19:531-538.

## What are the clinical manifestations of OSA?

- Snoring
- Frequent nocturnal awakenings
- Systemic hypertension
- Pulmonary hypertension
- Polycythemia
- Obesity-hypoventilation syndrome
- Daytime sleepiness
- Personality changes
- Intellectual deterioration

Millman RP. *Clin Chest Med*. 1987;8:253-264.

## Why is screening for OSA important in primary care practice?

- Majority of patients present in the primary care setting but not complaining of OSA symptoms
  - Obesity, hypertension, fatigue
- Up to 80% to 90% of cases are undiagnosed
- OSA severity is not proportional to excessive sleepiness
- Symptoms may progress over relatively short periods
  - Predictors of progression
    - Excess body weight, central obesity, CV disease, diabetes, increased age, habitual snoring

Lieberman JA 3rd. *Postgrad Med.* 2009;121:33-41.

## How would you evaluate this patient?

### Formal sleep studies

- Indicated for patients with snoring and other phenotypic characteristics suggestive of OSA
  - Overweight, diabetes, personality changes, cognitive decline

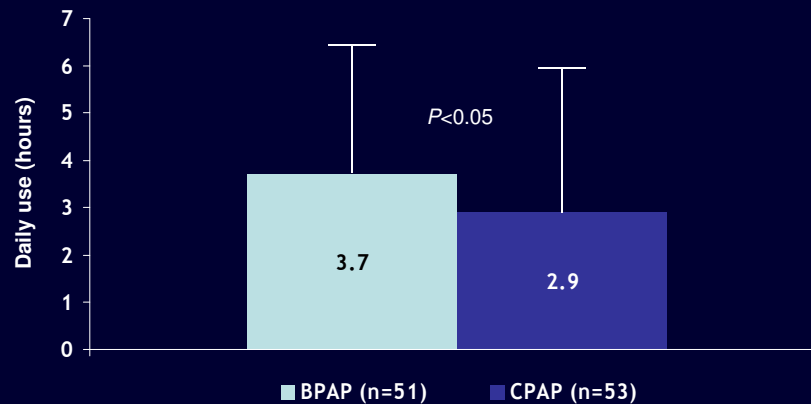
## What mechanical treatments are available for OSA?

- Continuous positive airway pressure
  - Provides pneumatic splint to prevent nocturnal airway collapse
  - More hours of use result in better outcomes
- Bilevel positive airway pressure (Bilevel PAP)
- Dental/oral devices
- Surgery (tonsillectomy/adenoidectomy)



Ozsancak A et al. *Chest*. 2008;133:1275-1286; Weaver TE et al. *Sleep*. 2007;30:711-719; Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147.

## Does bilevel PAP improve treatment compliance in patients with OSA?



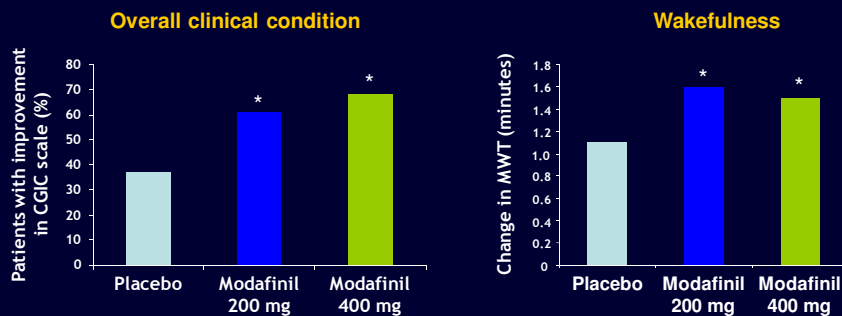
Length of study: 90 days  
Ballard RD. *J Clin Sleep Med*. 2007;3:706-712.

## What about residual sleepiness in patients adequately treated with CPAP for OSA?

- Residual sleepiness in optimally treated patients
  - $\geq 6$  hours/night: 22% measured subjectively or 52% measured objectively
- Alerting agents (eg, modafinil, armodafinil)

Rosenberg R, Doghramji P. *Adv Ther.* 2009;26:295-312; Weaver TE et al. *Sleep.* 2007;30:711-719.

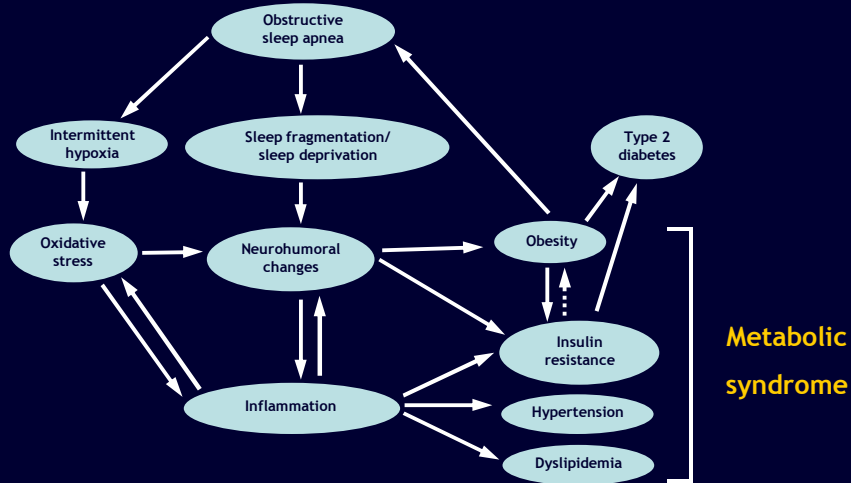
## Modafinil for Residual Excessive Sleepiness in CPAP-Treated Patients With OSA



\* $P < 0.001$  vs placebo; 12-week study.  
CGIC=Clinical Global Impression of Change; MWT=Maintenance of Wakefulness Test.

Black JE, Hirshkowitz M. *Sleep.* 2005;28:464-471.

## What is the relationship between OSA and metabolic syndrome?



Tasali E, Ip MSM. *Proc Am Thorac Soc.* 2008;5:207-217.

## Clinical Pearls

- Treating OSA may improve control of diabetes and reduce other cardiovascular risk factors
- Increasing incidence of OSA parallels obesity epidemic and aging population

## Panel Discussion

---

### Panel Discussion Questions

---

- *Are there any specific laboratory tests or other diagnostics that you would recommend to perform routinely in patients complaining of excessive sleepiness?*

## Panel Discussion Questions

- *As a primary care physician, when do I use the one-question screener, is it at every routine visit, or only at sick visits?*

## Panel Discussion Questions

- *Do patients with insomnia develop daytime sleepiness?*

## Panel Discussion Questions

---

- *Are there any serious adverse consequences to using CPAP?*

## Panel Discussion Questions

---

- *Have you found that BiPAP is accompanied by better adherence rates?*

## Panel Discussion Questions

- *How often do people have good results, at least initially, with Uvulopalatopharyngoplasty (UPPP), and what are the recurrence rates of OSA after the procedure?*

## Panel Discussion Questions

- *With CPAP machines, what are considered to be adequate adherence rates and percentage of time used for people holding commercial driver licenses (bus and train drivers)?*

## Panel Discussion Questions

- *With CPAP machines, what are considered to be adequate adherence rates and percentage of time used for people holding commercial driver licenses (bus and train drivers)? (cont'd)*

## Panel Discussion Questions

- *Combination treatments that are commonly used for nocturia include amitriptyline and trazodone. Is it acceptable to use these in patients with nocturia and OSA?*

## Panel Discussion Questions

- *Does trazodone have good supporting evidence as a hypnotic agent?*

## Panel Discussion Questions

- *When using behavioral treatments for sleep disorders, what would be an appropriate time for follow-up?*

**Thank You!**