

# Preventing Adverse Consequences of Sleep Loss and Excessive Sleepiness

## Practical Assessment and Management Strategies

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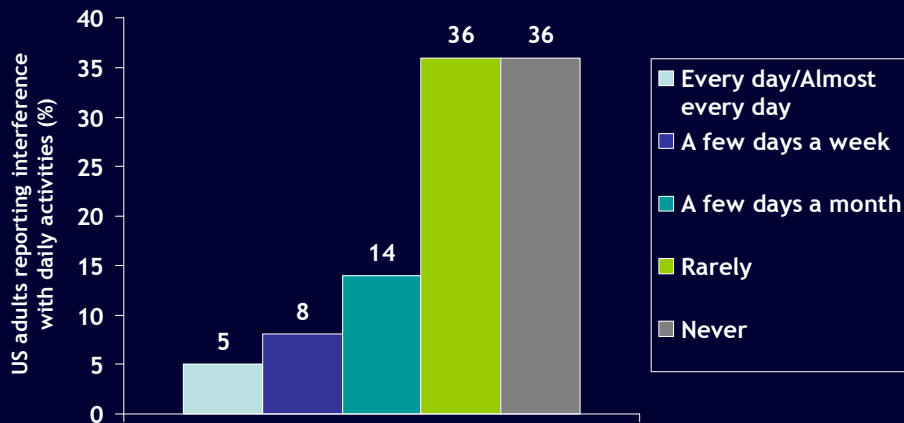


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Philadelphia, Pennsylvania



## How often does sleepiness interfere with daily activities?



N=1000.

National Sleep Foundation. 2008 Sleep in America Poll: Summary of Findings.  
<http://www.sleepfoundation.org/sites/default/files/2008%20POLL%20SOF.PDF>. Accessed August 12, 2009.

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## What are some causes of Excessive Daytime Sleepiness (EDS)?

- Behavioral
  - Sleep deprivation (most common)
  - Irregular timing of sleep
- Medical conditions
  - Cardiovascular disease, asthma, Parkinson's disease, movement disorders, chronic pain, medication side effects
- Psychiatric conditions
  - Depression, anxiety

Thorpy MJ et al. *Am J Manag Care.* 2007;13:S132-S139; Mahowald MW. *Postgrad Med.* 2000;107:108-123.

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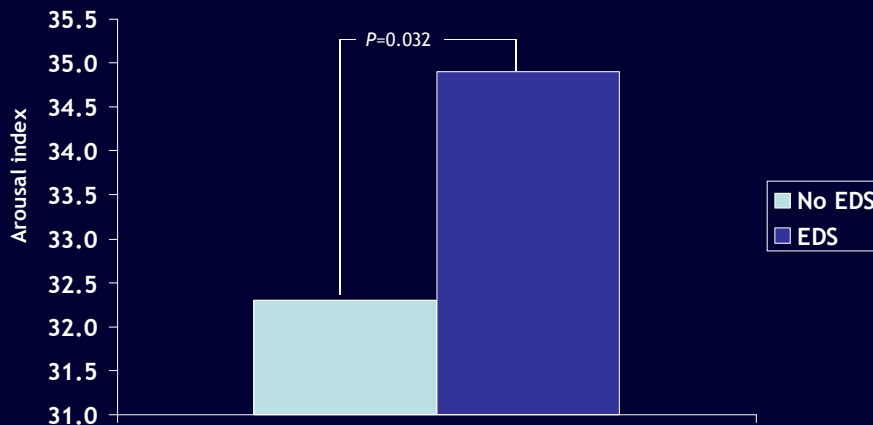
## What sleep disorders cause EDS?

- Sleep-related breathing disorders
  - Obstructive sleep apnea (OSA)
- Hypersomnia not due to a sleep-related disorder
  - Narcolepsy, idiopathic hypersomnia
- Circadian rhythm sleep disorders
  - Jet lag, shift work
- Sleep-related movement disorders
  - Restless legs syndrome, periodic limb movement

Thorpy MJ. *Sleep Med.* 2005;6(suppl 1):S13-S20.

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## How is fragmented sleep related to EDS?



Arousal index=total number of EEG arousals per hour of total sleep time; no EDS=mean sleep latency (MSL)>10; EDS=MSL<10.

Seneviratne U, Puvanendran K. *Sleep Med.* 2004;5:339-3443.

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## How do you categorize sleep disturbances?

- Inadequate **quantity** of sleep
  - Personal requirements
  - Age-dependent
- Poor **quality** of sleep
  - Fragmented
  - Multiple arousals

Kushida CA. *Curr Treat Options Neurol*. 2006;8:361-366.

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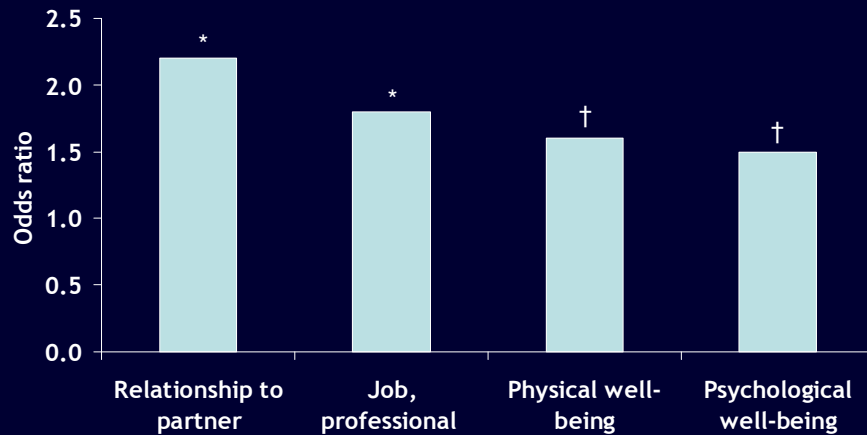
## How is sleep related to health?

- Biology of sleep
  - Performs an essential restorative function
  - Sleep propensity: a homeostatic process
    - Increases after sleep deprivation
    - Decreases during sleep
- Deviant sleep patterns
  - Increased risk of morbidity and mortality
  - Poor quality of life

Zisapel N. *Cell Mol Life Sci*. 2007;64:1174-1186.

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



\* $P < 0.01$ ; † $P < 0.05$ .

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

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## What is the difference between fatigue and sleepiness?

### Fatigue

- Sense of tiredness
- May be caused by medical illness; prolonged physical or mental activity; primary insomnia

### Sleepiness

- Urge to sleep
- May be caused by medical illness; behavioral factors; specific sleep disorders

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

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## How do you screen patients for EDS?

### Single-Question Sleepiness Screening Tool

“Please measure your sleepiness on a typical day”



## What questionnaires are available?

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

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## What are the added benefits of using questionnaires?

- Obtain various types of information
- Increase patient history data
- Involve patients in making diagnoses

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## How do you diagnose sleep problems?

- Accurate history from patient and sleep partner
- Physical examination
- Laboratory tests
- Sleep diary, sleep log
- Screening tools: Questionnaires
- Formal sleep studies
- Referral to sleep specialist

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

## What are treatment approaches for sleep loss and EDS?

- Nonpharmacologic
  - Behavioral (eg, sleep hygiene)
  - Mechanical devices (eg, CPAP)
  - Environmental modifications (eg, bright light therapy)
- Pharmacologic
  - Sleep-promoting agents
  - Wake-promoting agents

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CPAP=Continuous positive airway pressure.  
Thorpy MJ et al. *Am J Manag Care.* 2007;13:S140-S147.

## Case 1

- 29-year-old woman; corporate attorney
- Business dinners with drinks 2 to 3 times per week
- Consumes caffeinated coffee at dinner
- Goes to bed at 11:00 PM and watches TV until falling asleep (between 1:00 and 2:00 AM)

- Single-question screener score **8**



## Caffeine

- Short-acting stimulant
- No major disruptive effect on sleep  $\geq 8$  hours after administration
- Frequent use can lead to tolerance and negative withdrawal effects

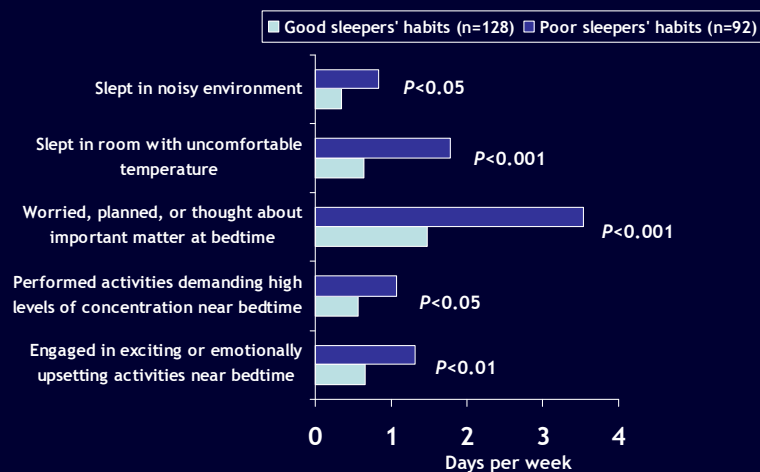
## What are nonpharmacologic recommendations for sleep loss?

- Good “sleep hygiene”
  - Regularity, timing, duration of nighttime sleep
  - Stimulus control: associate bed with either sleeping or sexual activity
- Diet
  - Avoid caffeine, alcohol before bedtime
  - Avoid heavy meal before bedtime
- Naps/Rest periods
- Exercise
  - >2 hours before bedtime

Kushida CA. *Curr Treat Options Neurol.* 2006;8:361-366; Thorpy MJ et al. *Am J Manag Care.* 2007;13:S140-S147; Ting L, Malhotra A. *Prim Care Clin Office Pract.* 2005;32 :305-318.

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## How do sleep hygiene practices affect sleep quality?



Good sleepers=Pittsburgh Sleep Quality Index (PSQI) score <5; Poor sleepers=PSQI score >7.  
Gellis LA, Lichstein KL. *Behav Ther.* 2009;40:1-9.

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## What are some recommendations for sleep hygiene?

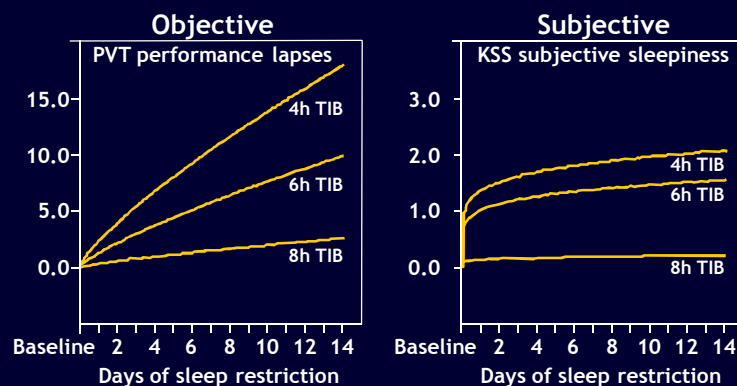
- Set routine bedtime and waking hours
- Do not force sleep
- Avoid naps during daytime
- Avoid exercise 2 hours before bed
- Avoid coffee, alcohol or excessive amounts of beverages before bedtime
- Avoid heavy meals before bedtime
- Make the sleep environment as comfortable as possible (lighting, temperature,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

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

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## Do patients underestimate the impact of sleepiness?

People frequently underestimate the cognitive impact of sleep restriction and overestimate their performance readiness when sleep is restricted.



PVT=Psychomotor Vigilance Task; TIB=time in bed; KSS=Karolinska Sleepiness Scale.  
Banks S, Dinges DF. *J Clin Sleep Med.* 2007;3:519-528.

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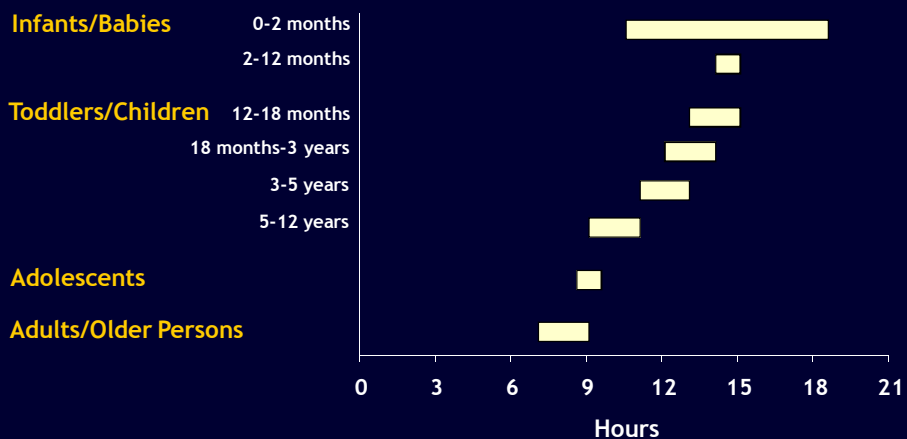
## What are consequences of excessive sleepiness?

- Cognitive impairment
  - Alertness, memory, psychomotor performance
- Behavioral changes
  - Too tired to play with one's children, difficulty engaging in social interactions, falling asleep at the movies

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

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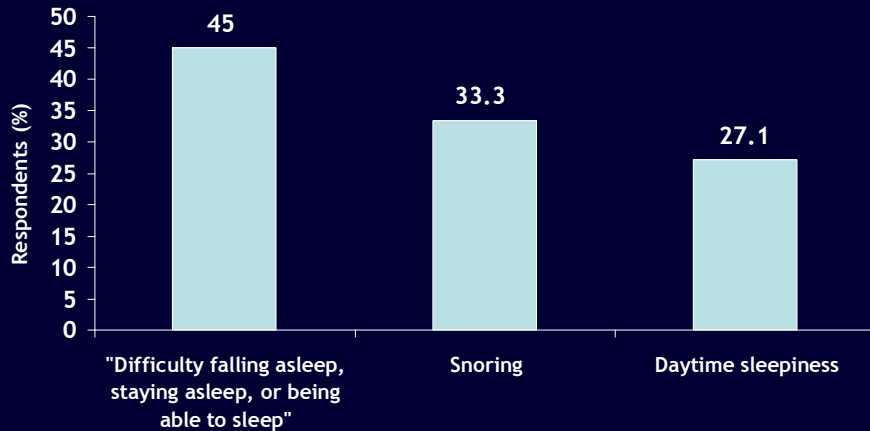
## How do sleep requirements vary with age?



National Sleep Foundation, Let Sleep Work for You. <http://www.sleepfoundation.org/let-sleep-work-you>. Accessed August 12, 2009.

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## How common are sleep problems in the elderly?



N=1503; mean age=75.5 years; M:F ratio=38:62.

Reid KJ et al. *Am J Geriatr Psychiatry*. 2006;14:860-866.

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## How does sleep change with aging?

- Decreased total nocturnal sleep
- Delayed onset of sleep
- Advanced circadian phase
  - Early to bed, early to rise
- Reduced threshold for arousal
- Fragmented sleep with multiple arousals
- Daytime napping

Wolkove N et al. *CMAJ*. 2007;176:1299-1304.

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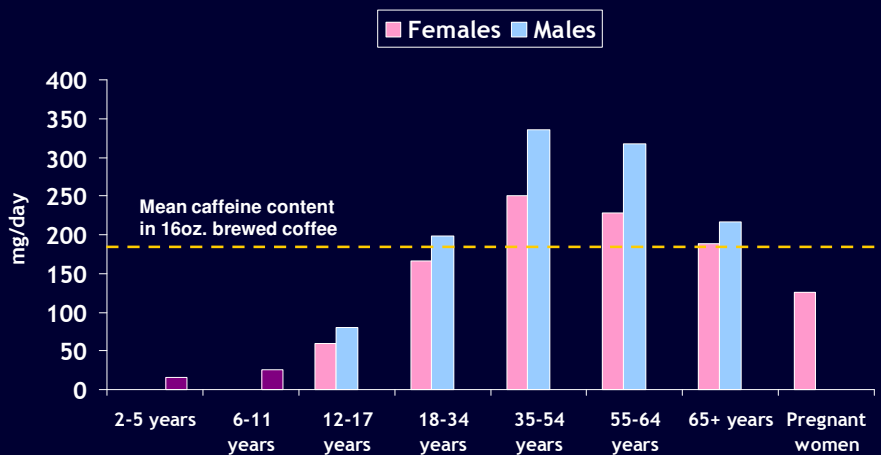
## What are sources of caffeine?

- Chocolate- and coffee-flavored dairy products: 0.4%
- Sweetened grains (chocolate flavored): 0.5%
- Sugars and sweets (chocolate): 0.4%
- Coffee: 70.7%
- Tea: 12.1%
- Soft drinks (cola-type, pepper-type, chocolate flavored, fruit flavored with caffeine): 15.9%

Frory CD et al. *J Am Diet Assoc.* 2005;105:110-113.

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## How much caffeine is consumed in the US?



Based on a 2-day average from Continuing Survey of Food Intakes by Individuals (CSRI) 1994 to 1996, 1998 data.

Frory CD et al. *J Am Diet Assoc.* 2005;105:110-113; Kaiser L et al. *J Am Diet Assoc.* 2008;108:553-61.

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## Case 2

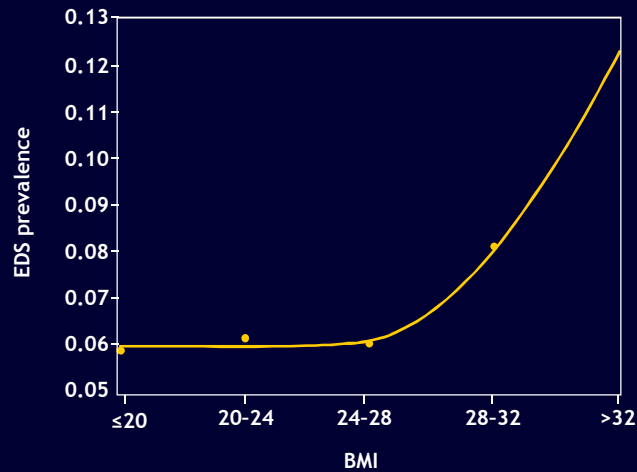
- 33-year-old man diagnosed with OSA
- Using CPAP: average 7 hours per night
- Lost 10 pounds over past 6 months
- Seen in the ER last night following a car accident; doesn't remember seeing the traffic light turning red
- Single-question screener score **9**



## What are the consequences of OSA?

- Most common symptom: EDS
- Associated with obesity, hypertension, type 2 diabetes, cardiovascular disease
- Diminished work performance
- Reduced concentration and memory
- Increased incidence of motor vehicle accidents

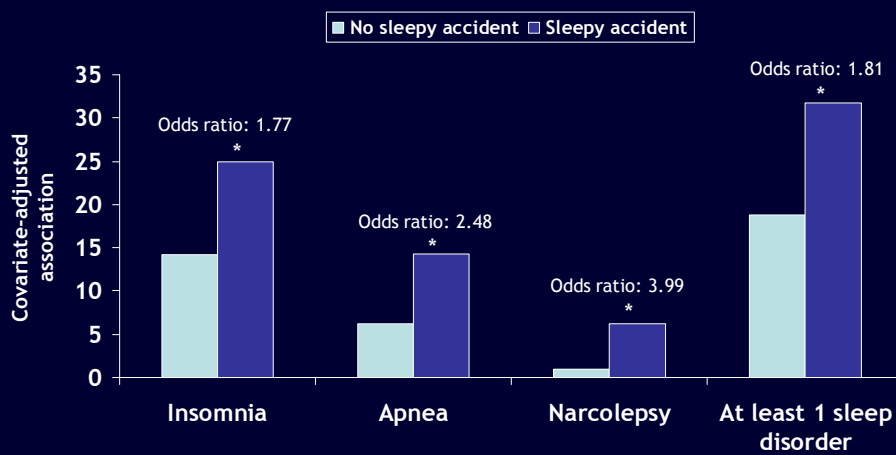
## What is the relationship between weight and EDS?



BMI=body mass index.  
Bixler EO et al. *J Clin Endocrinol Metab.* 2005;90:4510-4515.

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## Sleep-Wake Disorders and Motor Vehicle Accidents



\* $P < 0.001$ .  
Powell INB et al. *Sleep.* 2007;30:331-342.

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## What are the challenges associated with CPAP treatment for OSA?

- Nonadherence\* rates: 46%-83%
- Reasons for nonadherence
  - Difficult to use
  - Embarrassment
  - Physical discomfort
  - Psychological factors (eg, claustrophobia)
  - Patient lacks perception of symptoms and/or improvement in sleepiness and daily functioning

\* <4 hours/night.

Rosenberg R, Doghramji P. *Adv Ther.* 2009;26:295-312; Weaver TE, Grunstein RR. *Proc Am Thorac Soc.* 2008;5:173-178.

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## What interventions can improve CPAP adherence?

- Behavioral interventions
  - Education, support, positive reinforcement
  - Cognitive behavioral therapy
- Machine design
  - Bilevel CPAP (lower expiratory pressure)
  - Auto-CPAP (varies pressure levels through the night)
  - Flexible CPAP (alternates exhalation/inhalation pressures breath by breath)
- Humidification of the airway

Weaver TE, Grunstein RR. *Proc Am Thorac Soc.* 2008;5:173-178.

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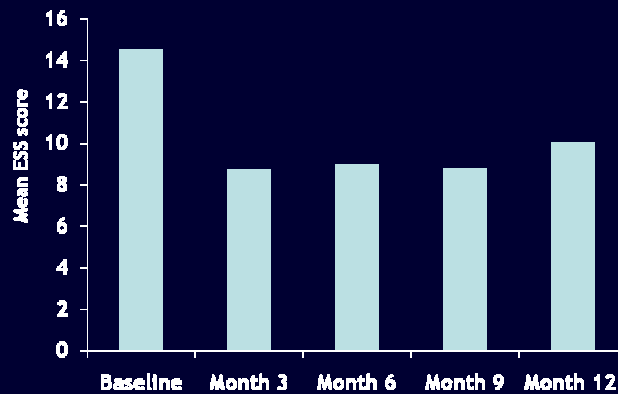
## How common is residual sleepiness in patients optimally treated with CPAP for OSA?

- Optimal treatment:  $\geq 6$  hours/night
- Incidence of residual sleepiness
  - 22% measured subjectively
  - 52% measured objectively
- Persistent arousals and respiratory events
- Possible explanations
  - Inadequate CPAP pressure
  - Altered sleep-promoting mechanism or wakefulness drive

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

## Effect of Adjunctive Modafinil on Wakefulness and Quality of Life in Patients With OSA



Patients received CPAP therapy and treated with modafinil 200-400 mg/day.  
12-month open-label study, N=266.

\* $P < 0.0001$ .

Hirshkowitz M, Black J. *CNS Drugs.* 2007;21:407-416.

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## What are the metabolic consequences of sleep deprivation?

- Altered glucose metabolism
- Upregulation of appetite
- Decreased energy expenditure
- Altered hormone levels (eg, leptin, ghrelin, insulin)
- Altered target organ response to hormones (insulin resistance)

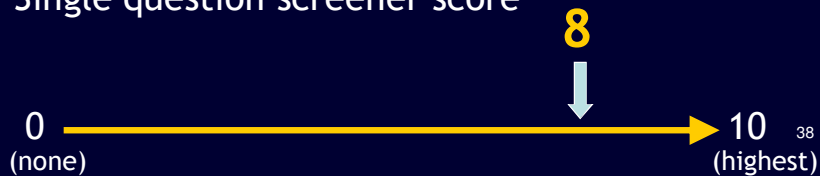
Knutson KL et al. *Sleep Med Rev.* 2007;11:163-178.

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## Case 3

- 50-year-old woman with metastatic breast cancer
- Receiving chemotherapy after surgery
- History of depression, currently taking SSRIs
- Reports fatigue, trouble sleeping, sadness, loss of interest in activities she once enjoyed, guilt over the burden her illness has on her family

- Single question screener score



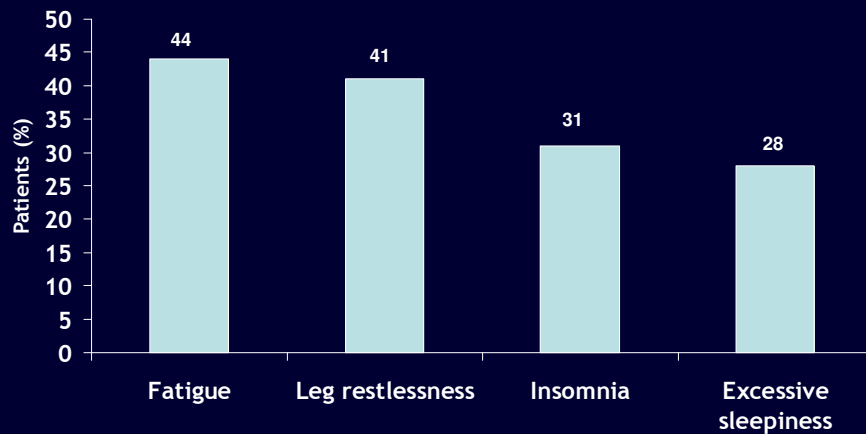
## What is the relationship between depression and sleep disorders?

- Hypersomnia: associated symptom in depressive disorders
  - Mental disorders present in 10% of sleepy individuals
  - 10%-75% of depressed patients complain of hypersomnia
- 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

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## How common are sleep disturbances in patients with cancer?

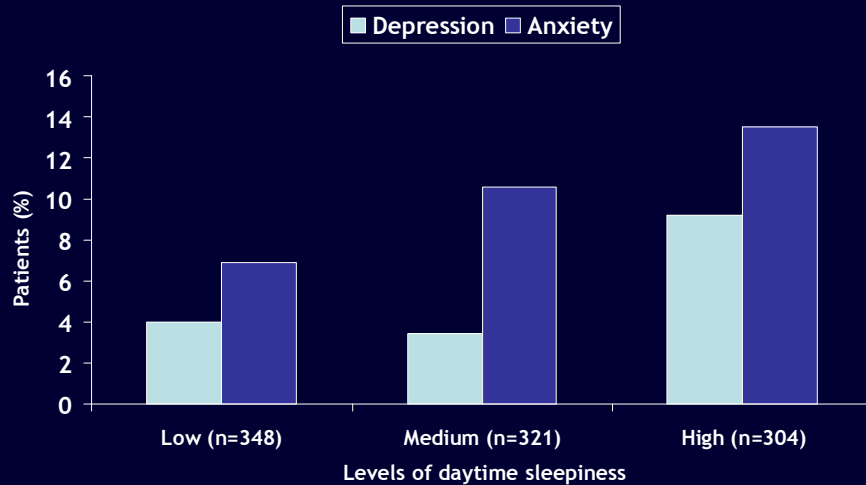


N=982; mean age=65 years.

Davidson JR et al. *Soc Sci Med.* 2002;54:1309-1321.

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## Are depression and anxiety potential determinants of EDS?



Major depression:  $P=0.002$ ; any anxiety:  $P=0.02$ .  
Breslau N et al. *Am J Public Health*. 1997;87:1649-1653.

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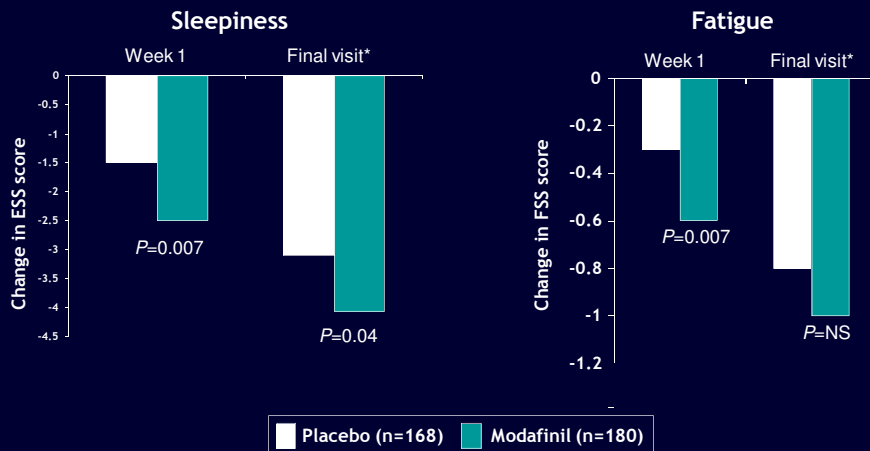
## Is there a role for additional pharmacotherapy in this patient?

- Stimulant drug to increase wakefulness
  - Dose, duration of action, and time of administration to relieve EDS without disturbing nighttime sleep
- Facilitate normal levels of attention and energy throughout the wake period
- Facilitate good sleep when desired
- Minimize side effects that impair functioning or normal sleep patterns

Black J et al. *CNS Spectr*. 2007;12:(2 suppl 2):1-16; Thorpy MJ et al. *Am J Manag Care*. 2007;13:S140-S147.

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## Modafinil Augmentation of SSRI Therapy: Effects on Fatigue and Sleepiness



\*Week 6 or 8; baseline ESS: placebo=14.4, modafinil=14.5; baseline FSS: placebo=5.7, modafinil=5.6. 43  
ESS=Epworth Sleepiness Scale; FSS=Fatigue Severity Scale; SSRI=selective serotonin reuptake inhibitor.  
Fava M. *Ann Clin Psychiatry*. 2007;19:153-159.

## What are pharmacological approaches for patients with fatigue/sleepiness and depression?

- Avoid antidepressants that worsen sleepiness and fatigue
- Choose antidepressant medications that promote wakefulness
- Use adjunctive pharmacotherapies to target fatigue and sleepiness

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Baldwin DS, Papakostas GI. *J Clin Psychiatry*. 2006;67(suppl 6):9-15; Doghramji K. *J Clin Psychiatry*. 2003;64(suppl 14):24-29.

## What negatively affects sleep quality in patients with cancer?

- Poor quality of life (physical and mental components)
- Post-traumatic stress disorder
- Depression
- Anxiety
- Pain, physical discomfort
- Medication side effects
- Feelings of helplessness and inability to cope

Mystakidou K et al. *Palliat Med.* 2009;23:46-53.

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## What are non-pharmacological approaches for patients with fatigue/sleepiness and depression?

- Behavioral strategies
  - Sleep hygiene education
  - Improve nighttime sleep by avoiding daytime naps
  - Avoid alcohol at bedtime
  - Avoid caffeine during the day
- Bright light therapy to restore proper sleep-wake cycling

Doghramji K. *J Clin Psychiatry.* 2003;64(suppl 14):24-29.

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## Clinical Pearls

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- Sleep disorders are common
- Important to assess patients' sleep/wake patterns, especially in primary care practice
- Diagnostic tests (eg, questionnaires) can be helpful
- Referral to sleep specialists for formal sleep studies and comanagement may be indicated

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## Panel Discussion

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## Panel Discussion Questions

- *Avoiding daytime naps is recommended as good sleep hygiene, but scheduling naps is considered a nonpharmacologic treatment for EDS? When does one outweigh the other?*

## Panel Discussion Questions

- *When would a 'power nap' be beneficial?*

## Panel Discussion Questions

- *Older agents for treating sleep problems have stigmas associated with their use. How does the safety of the newer agents compare with older ones?*

## Panel Discussion Questions

- *Should patients take agents to help them sleep on an as-needed (PRN) basis, or is it always recommended to keep to a schedule?*

## Panel Discussion Questions

- *Are there other safety concerns with use of these agents to treat sleep disorders?*

## Panel Discussion Questions

- *There are a number of over-the-counter medications that can be used to treat sleeping problems. Could you comment on the use of these?*

## Panel Discussion Questions

- *We hear that sleep debt is cumulative, and that it is incredibly difficult to regain lost sleep. How true is this and how should we be advising our patients?*

## Panel Discussion Questions

- *How does inadequate sleep during your growing years impact your adult life?*

## Panel Discussion Questions

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- *Can you speak on the use of sodium oxybate in clinical practice?*

**Thank You!**

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