Insomnia—In the Eye of the Beholder?

Barbara Phillips, MD, MSPH, FCCP
Objectives

• 1. Define insomnia

• 2. Describe one effective treatment for chronic insomnia

• 3. Identify the best-documented consequence (or symptom) of insomnia.
Insomnia Vs Sleep Deprivation

- A 24-year old internal medicine resident who is married and the mother of a 2 year-old
- Gets up at 06:30
- Works and mothers all day
- Goes to bed about midnight
- (Except when on call)
- She gets about 6 ½ hours of sleep a night
Insomnia Vs Sleep Deprivation

- A 58 year old women, who is married and whose husband has retired
- Gets up at 08:30
- Goes to church, reads, plays bridge
- Goes to bed about 10:00
  - Sleeps until 1:30
  - Is “up and down” the rest of the night
  - Finally gets out of bed about 08:30
- Sometimes naps
- She gets about 6 ½ hours of sleep a night
Who’s at Risk?
Short Sleep Duration Increases Risk, Especially for Younger People

- Impaired performance in house officers
- Increased risk of crash
- Maybe cardiovascular disease
Residents averaging ≤ 5 hours sleep/night were more likely to report:

serious accidents or injuries \( \text{OR} = 1.84 \ (1.23 - 2.74) \)

conflict with other professional staff \( \text{OR} = 1.41 \ (1.08 - 1.84) \)

use of medications to stay awake \( \text{OR} = 1.91 \ (1.39 - 2.62) \)

working in an “impaired condition” \( \text{OR} = 2.19 \ (1.79 - 2.68) \)

making significant medical errors \( \text{OR} = 1.74 \ (1.47 - 2.06) \)

being named in malpractice suit \( \text{OR} = 2.02 \ (1.17 - 3.47) \)

Correlates of Reduced Sleep Duration: Residents

Baldwin & Daugherty, SLEEP 2004
Sleep Deprivation (post call) in Residents: Performance

- **Surgery:**
  - 20% more errors and 14% more time required to perform simulated laparascopy post-call (two studies) (Taffinder et al, 1998; Grantcharov et al, 2001)

- **Internal Medicine:**
  - Efficiency and accuracy of ECG interpretation impaired in sleep-deprived interns (Lingenfelser et al, 1994)

- **Pediatrics:**
  - Time required to place an intra-arterial line increased significantly in sleep-deprived (Storer et al, 1989)

- **Emergency Medicine:**
  - Significant reductions in comprehensiveness of history & physical exam documentation in second year residents (Bertram 1988)
  - Longer intubation time required after call (Smith-Coggins, 1994)

- **Family Medicine:**
  - Scores achieved on the ABFM practice in-training exam negatively correlated with pre-test sleep amounts (Jacques et al, 1990)

- **Surgery:**
  - 20% more errors and 14% more time required to perform simulated laparascopy post-call (two studies) (Taffinder et al, 1998; Grantcharov et al, 2001)

- **Internal Medicine:**
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  - Scores achieved on the ABFM practice in-training exam negatively correlated with pre-test sleep amounts (Jacques et al, 1990)
The Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations, in contrast to just feeling tired? This refers to your usual way of life in recent times. Even if you have not done some of these things recently, try to work out how they would have affected you. 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

<table>
<thead>
<tr>
<th>Situation</th>
<th>Chance of Dozing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sitting and reading</td>
<td></td>
</tr>
<tr>
<td>Watching TV</td>
<td></td>
</tr>
<tr>
<td>Sitting, inactive, in a public place</td>
<td></td>
</tr>
<tr>
<td>As a passenger in a car for an hour</td>
<td></td>
</tr>
<tr>
<td>Lying down in the afternoon</td>
<td></td>
</tr>
<tr>
<td>Sitting and talking to someone</td>
<td></td>
</tr>
<tr>
<td>Sitting quietly after a lunch without alcohol</td>
<td></td>
</tr>
<tr>
<td>In a car, while stopped for a few minutes in traffic</td>
<td></td>
</tr>
</tbody>
</table>
Sleepiness in residents is equivalent to that found in patients with serious sleep disorders. Mustafa and Strohl, unpublished data. Papp, 2002.
Sleep Duration and Death
(Patel SR, Sleep 2004, n=82,969)
Sleep Duration and Coronary Heart Disease in Women

(Ayas et al, 2003, n=71,617)
Sleep Duration and Obesity
(Taheri S, PLoS 2004, WSCS, n=1024)

Graph showing the adjusted body mass index (BMI) at different average nightly sleep durations. The graph includes data points for 6, 7, 8, and 9 hours of sleep, with the respective sample sizes indicated in parentheses. The BMI values are shown on the y-axis, and the average nightly sleep durations are on the x-axis.
Kripke, Arch Gen Psych, 2002
Data for 636,095 women
HR for Hypertension, Adjusted

Sleep Duration (hrs) vs. Adjusted HR for Hypertension

- Ages 32 to 86
- Ages 32 to 59
- Ages 60 to 86
Sleep Duration and Incident Coronary Artery Calcification in YOUNG People (King R, JAMA, 2008)

- Actigraphy
- Self-report

<table>
<thead>
<tr>
<th>Sleep, h</th>
<th>&lt;4</th>
<th>4-&lt;5</th>
<th>5-&lt;6</th>
<th>6-&lt;7</th>
<th>7-&lt;8</th>
<th>≥8</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of participants</td>
<td>17</td>
<td>49</td>
<td>148</td>
<td>188</td>
<td>88</td>
<td>5</td>
</tr>
<tr>
<td>Actigraphy</td>
<td>8</td>
<td>22</td>
<td>60</td>
<td>144</td>
<td>175</td>
<td>83</td>
</tr>
</tbody>
</table>
Insomnia Is Not Sleep Deprivation

- Insomnia diagnosis assumes adequate opportunity to sleep
- Sleep deprivation
  - Adequate ability to sleep
  - Inadequate opportunity
  - Generally sleepy
- Insomnia patients
  - Inadequate ability to sleep
  - Adequate opportunity
  - Generally NOT sleepy, though may report fatigue

NIH State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults

National Institutes of Health
State-of-the-Science Conference Statement
June 13–15, 2005
Definition (NIH)

- Difficulty falling asleep (DFA)
- Difficulty maintaining sleep (DMS)
- Waking up too early (WASO, EMA)
- (Nonrestorative or poor-quality sleep)
- May include daytime impact
“Insomnia usually appears in the presence of at least one other disorder. Particularly common comorbidities are major depression, generalized anxiety, substance abuse, attention deficit/hyperactivity in children, dementia, and a variety of physical problems. The research diagnostic criteria for insomnia recently developed by the American Academy of Sleep Medicine indeed share many of the criteria of major depressive disorder. Explaining this overlap requires a study that determines how often insomnia precedes the disorders with which it is associated and continues to exist after the other disorders are cured or go into temporary remission.”
Although chronic insomnia is considered to be common... Conclusive evidence from epidemiologic studies has been limited by their different definitions of chronic insomnia and by the lack of standardized...screening methods. Population-based studies suggest that about 30 percent of the general population has complaints of sleep disruption, while approximately 10 percent has associated symptoms of daytime functional impairment...Not surprisingly, prevalence appears to be greater in clinical practices, where about one-half of respondents report symptoms of sleep disruption.
Epidemiology of Insomnia

• Use of hypnotics increased almost 60% from 2000 to 2006 (Saul S, NYT, Feb 7, 2006), and cost US consumers $45 billion/yr (Saul S NYT, Oct 23, 2007)

• Benefits of hypnotics are elusive (Glass J, BMJ, 2005), and largely subjective (Walsh JK, Sleep 2007)
Relative Prevalence of Insomnia

Zhang B *SLEEP* 2006  
Cases = 1,265,015
INSOMNIA ACROSS THE LIFE SPAN

Ohayon MM, Sleep 1997
Prevalence of Comorbid Insomnia With Psychiatric Disorders

Population (%)

- Major Depression
- Dysthymia
- Anxiety Disorder
- Alcohol Abuse
- Drug Abuse
- Other Psychiatric Disorder

- Insomnia
- No sleep complaint

N=10,534 (≥18 years old)

Ford DE, Kamerow D 1989 JAMA
Insomnia is a PRECEDES (Is Risk Factor for ?) Depression

- Ford and Kamerow, *JAMA*, 1989
- Breslau et al., *Biol Psychiatry*, 1996
- Chang et al., *Am J Epidemiol*, 1997
- Livingston et al., *Br J Gen Practice*, 1993
- Weissman et al., *Gen Hos Psychiatry*, 1997
- Mallon et al., *Int Psychogeriatrics*, 2000
Great moments in evolution
Sleep Disorders Contribute to Weight Gain

July 5, 2010

A new study published in the International Journal of Obesity found that middle-aged women who suffer from sleep disorders are more likely to have problems with their weight than their peers who get the recommended eight hours a night. Although there are studies that have established the link between weight gain and sleep, these findings suggest that sleep problems preceded weight gain in the subjects.

The researchers at the University of Helsinki looked into the sleeping habits and weights of around 7,300 adults aged between 40 and 60 over a seven-year period and found that one in five of the 5,700 women participating in the study with frequent sleep problems gained at least 11 pounds in weight over the course of the study. In comparison, just one in five of those women who slept well through the night gained as much weight.

Lead researcher Pepo Lyttkainen told Reuters Health that this correlation could be down to the fact that sleep disorders could affect the chemicals that dictate appetite. The link in the women persisted even when the investigators accounted for a number of factors that can affect both sleep quality and weight gain — including participants' body weight at the study's start, their exercise habits and their general physical and mental health.

The study concluded that sleep problems likely contribute to weight gain which means that sleep problems need to be taken into account when trying to prevent and manage weight gain and obesity.

Average: Your rating:
Original Article

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Sleep problems and major weight gain: a follow-up study

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Received 11 April 2010; Revised 29 April 2010; Accepted 3 May 2010; Published online 8 June 2010.

Abstract

Objective: To examine the associations between sleep problems and major weight gain during a 5- to 7-year follow-up among middle-aged women and men.

Methods: The Helsinki Health Study prospective cohort baseline survey data from 2000 to 2002 (n=8960, response rate 67%) among 40- to 60-year-old municipal employees and follow-up survey data from 2007 (n=7332, response rate 83%) were used. Logistic regression analysis was used to examine the association between the four-item Jenkins Sleep Questionnaire and major weight gain of 5kg or more over a 5- to 7-year
After Controlling for Mood Disturbance

Table 4. Associations between summary of sleep problems and weight gain in women

<table>
<thead>
<tr>
<th>Summary of sleep problems</th>
<th>Model 1 OR (CI 95%)</th>
<th>Model 2 OR (CI 95%)</th>
<th>Model 3 OR (CI 95%)</th>
<th>Model 4 OR (CI 95%)</th>
<th>Model 5 OR (CI 95%)</th>
<th>Model 6 OR (CI 95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not at all</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1−3 days</td>
<td>1.16 (0.95, 1.42)</td>
<td>1.16 (0.95, 1.43)</td>
<td>1.19 (0.97, 1.46)</td>
<td>1.16 (0.94, 1.43)</td>
<td>1.18 (0.96, 1.45)</td>
<td>1.15 (0.93, 1.41)</td>
</tr>
<tr>
<td>4−14 days</td>
<td>1.25 (1.02, 1.54)</td>
<td>1.22 (0.99, 1.50)</td>
<td>1.25 (1.01, 1.54)</td>
<td>1.24 (1.01, 1.53)</td>
<td>1.24 (1.01, 1.53)</td>
<td>1.16 (0.94, 1.43)</td>
</tr>
<tr>
<td>15−28 days</td>
<td>1.41 (1.13, 1.75)</td>
<td>1.35 (1.08, 1.69)</td>
<td>1.35 (1.08, 1.69)</td>
<td>1.36 (1.09, 1.70)</td>
<td>1.36 (1.09, 1.71)</td>
<td>1.25 (0.99, 1.58)</td>
</tr>
</tbody>
</table>

Odds ratios (OR) and their 95% confidence intervals (CI).

Model 1: Adjusted for age.
Model 2: Model 1+baseline body mass index.
Model 3: Model 2+physical activity+smoking+alcohol consumption.
Model 4: Model 2+marital status+educational level+work arrangements.
Model 5: Model 2+sleep duration.
Model 6: Model 2+common mental disorders.
Sleep Disorders (eg, insomnia, in this case) Don’t Contribute to Weight Gain

• They are ASSOCIATED with weight gain
• But only in women
• Who have problems sleeping more than half the time
• But not if you control for mental health problems
• (much less physical activity, smoking, alcohol, education, or work)
Beware the Hype....

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A new study published in the International Journal of Obesity found that middle-aged women who suffer from sleep disorders are more likely to have problems with their weight than their peers who get the recommended eight hours a night. Although there are studies that have established the link between weight gain and sleep, these findings suggest that sleep problems preceded weight gain in the subjects.

The researchers at the University of Helsinki looked into the sleeping habits and weights of around 7,300 adults aged between 40 and 60 over a seven-year period and found that around one in three of the 5,700 women participating in the study with frequent sleep problems gained at least 11 pounds in weight over the course of the study. In comparison, just one in five of those women who slept well through the night gained as much weight.

Lead researcher Pepsi Lytkarinen told Reuters Health that this correlation could be due to the fact that sleep disorders could affect the chemicals that dictate appetite. The link in the women persisted even when the investigators accounted for a number of factors that can affect both sleep quality and weight gain – including participants' body weight at the study's start, their exercise habits and their general physical and mental health.

The study concluded that sleep problems likely contribute to weight gain which means that sleep problems need to be taken into account when trying to prevent and manage weight gain and obesity.
Does Insomnia Kill?
Barbara Phillips, MD, MSPH; David M. Mannino, MD

Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Internal Medicine, University of Kentucky College of Medicine, Lexington, KY

Study Objectives: We investigated the prevalence and hazard ratios for insomnia complaints in a large cohort of middle-aged men and women.

Design: The Atherosclerosis Risk in Communities Study is a prospective study of cardiovascular disease. Using multivariate regression analysis, we predicted the likelihood of endorsing the insomnia complaints by age, sex, alcohol intake, smoking, diabetes, heart disease, menopausal status, use of hypnotics, hypertension, depressive symptoms, education level, body mass index, respiratory symptoms, and pulmonary function status. We predicted the hazard ratios (HR) of death at 6.3 ± 1.1 year by endorsement of insomnia complaints and by hypnotic use controlling for covariates.

Setting: North American communities.

Participants: 13563 participants aged 45 to 69 years at baseline

Interventions: None.

Measurements and Results: The prevalence of insomnia complaints in this cohort was 23%. Predictors of insomnia complaints were female sex (odds ratio [OR] 0.56, 95% confidence interval [CI] 0.45-0.70 for men), annual family income below $50,000 (OR 1.23, CI 1.09-1.40), age 40 to 49 years (OR 1.29, CI 1.11-1.50), depressive symptoms (OR 5.05, CI 4.60-5.55), heart disease (OR 1.89, CI 1.67-2.14), severe airflow obstruction (OR 1.61, CI 1.17-2.22), pulmonary symptoms (OR 1.71, CI 1.5-1.95), and restrictive lung disease (OR 1.27, CI 1.10-1.47). After controlling for covariates, insomnia complaints were not associated with an increased risk for death (OR 1.01, CI 0.85-1.21), nor was the use of hypnotics (OR 1.38, CI 0.90-2.13).

Conclusions: In this cohort, the prevalence of insomnia complaints was 23%. After controlling for confounders, neither insomnia complaints nor hypnotic use predicted increased mortality over 6.3 years.

Keywords: Sleeping pills, lifestyle, nonrestorative sleep, benzodiazepines, sleep continuity, depression, women, aging, ARIC

Citation: Phillips B; Mannino DM. Does insomnia kill? SLEEP 2005;28(8):965-971.
Methods: Population

- The Atherosclerosis Risk in Communities (ARIC) participants
- Multicenter cohort, aged 44-69 years
- Examinations, interviews, questionnaires at intake (1987-1989) and approximately every 3 years afterward
- We used data from 2nd visit as baseline, and survival at follow-up (mean, 6.3 ± 1.1 years) as a dependent variable.
Methods: Variables

• Three sleep complaints were available as part of the Maastricht questionnaire:
  – “Do you often have trouble falling asleep?” (difficulty falling asleep, DFA)
  – “Do you wake up repeatedly during the night?” (sleep continuity disturbance, SCD)
  – “Do you ever wake up with a feeling of exhaustion and fatigue?” (nonrestorative sleep, NRS)

• We defined insomnia as difficulty falling asleep or staying asleep, plus nonrestorative sleep.
## Results: 13,564 Participants

<table>
<thead>
<tr>
<th>Age</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-49:</td>
<td>1477</td>
<td>(10.9)</td>
</tr>
<tr>
<td>50-54:</td>
<td>3670</td>
<td>(27.1)</td>
</tr>
<tr>
<td>55-59:</td>
<td>3515</td>
<td>(25.9)</td>
</tr>
<tr>
<td>60-65:</td>
<td>3181</td>
<td>(23.5)</td>
</tr>
<tr>
<td>65-69:</td>
<td>1720</td>
<td>(12.7)</td>
</tr>
<tr>
<td>Sex: Female</td>
<td>7482</td>
<td>(55.2)</td>
</tr>
<tr>
<td>Premenopausal:</td>
<td>774</td>
<td>(5.7)</td>
</tr>
</tbody>
</table>

### Race

<table>
<thead>
<tr>
<th>Race</th>
<th>n</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black:</td>
<td>3213</td>
<td>(23.7)</td>
</tr>
<tr>
<td>White:</td>
<td>10350</td>
<td>(76.3)</td>
</tr>
</tbody>
</table>
Insomnia Complaints %

- Difficulty falling asleep 21.5
- Waking up repeatedly 38.5
- Nonrestorative sleep 35.0
- All of the above 9.6
- Insomnia * 23.0

(DFA OR SCD PLUS NRS)
<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>OR (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female gender (vs. male)</td>
<td>1.7 (1.42-2.22)</td>
</tr>
<tr>
<td>Annual income: &lt; $50,000</td>
<td>1.23 (1.09-1.40)</td>
</tr>
<tr>
<td>Depression</td>
<td>5.05 (4.60-5.55)</td>
</tr>
<tr>
<td>Heart disease</td>
<td>1.89 (1.67-2.14)</td>
</tr>
<tr>
<td>Severe airflow obstruction</td>
<td>1.61 (1.17-2.22)</td>
</tr>
<tr>
<td>Pulmonary symptoms</td>
<td>1.71 (1.5-1.95)</td>
</tr>
<tr>
<td>Restrictive lung disease</td>
<td>1.27 (1.10-1.47)</td>
</tr>
</tbody>
</table>
“God, Collings, I hate to start a Monday with a case like this.”
Risk Factors for Death at 6 Years (N=709)

- Age
- Male gender
- Less than high school education
- BMI < 20
- Diabetes
- Depression
- Heart disease
- Severe pulmonary disease or symptoms
- Current or former cigarette smoking
- Former or never alcohol use
Does Insomnia Kill?
(Phillips and Mannino, Sleep 2005)

• After controlling for covariates, insomnia was not associated with an increased risk of death at 6.3 year follow-up.

• After controlling *only* for depression, insomnia was not associated with an increased risk of death.
Insomnia Did Not Predict Incident Hypertension in Older Adults in the Cardiovascular Health Study

Barbara Phillips, MD, MSPH¹; Petra Bůžková, PhD²; Paul Enright, MD³; On behalf of the Cardiovascular Health Study Research Group

¹Department of Internal Medicine, University of Kentucky College of Medicine, Lexington, KY; ²Department of Biostatistics, University of Washington, Seattle, WA; ³The University of Arizona, Tucson, AZ

Study Objective: We hypothesized that the sleep complaints of insomnia predict incident hypertension, particularly in African Americans. The purpose of this study was to analyze insomnia complaints as predictors of incident hypertension in the Cardiovascular Health Study (CHS), stratifying by gender and allowing for race and sleep variable interaction.

Design: This is a prospective cohort study over a 6-year period of follow-up.

Setting: This is a community-based study of participants in Forsyth County, North Carolina; Pittsburgh, Pennsylvania; Sacramento County, California; and Washington County, Maryland.

Participants: The study analyzed data from 1419 older individuals (baseline mean age 73.4 ± 4.4 years) from the Cardiovascular Health Study who were not hypertensive at baseline.

Interventions: none

Measurements: We constructed relative risks of incident hypertension over a 6-year period for insomnia complaints singly and in combination.

Results: Difficulty falling asleep, singly or in combination with other sleep complaints, predicted a statistically significant reduction of risk for incident hypertension for non-African American men in 6 years of follow-up. Insomnia complaints did not predict incident hypertension in 6 years of follow-up in women or in African Americans, although there may not have been enough power to show a significant association for African Americans.

Conclusions: Insomnia did not predict hypertension in this older cohort which was free of hypertension at baseline. Difficulty falling asleep was associated with reduced risk of hypertension in non-African American men.

Keywords: Aging, sleep complaints, cardiovascular disease, epidemiology, African American

Citation: Phillips B; Bůžková P; Enright P. Insomnia did not predict incident hypertension in older adults in the cardiovascular health study. SLEEP 2009;32(1):XXX-XXX.
The CHS Study

• Hypothesis: Sleep complaints predict incident hypertension.

• *Design*: Secondary analysis of an existing dataset (the Cardiovascular Health Study, CHS)

• *Setting*: Community-based study over a 6 year period of follow-up.
Table 4. Relative Risks of Incident Hypertension in 6 Years Associated with Sleep Complaints, Model II.

<table>
<thead>
<tr>
<th>Model II</th>
<th>RR (p-value) 95% CI</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td>Women</td>
</tr>
<tr>
<td></td>
<td>Non-AAs</td>
<td>AAs</td>
<td>Non-AAs</td>
</tr>
<tr>
<td>DFA</td>
<td>0.47 (0.02)</td>
<td>0.79 (0.63)</td>
<td>1.23 (0.08)</td>
</tr>
<tr>
<td></td>
<td>0.25-0.87</td>
<td>0.3-2.08</td>
<td>0.98-1.54</td>
</tr>
<tr>
<td>EMA</td>
<td>1.13 (0.44)</td>
<td>1.89 (0.13)</td>
<td>0.99 (0.96)</td>
</tr>
<tr>
<td></td>
<td>0.82-1.56</td>
<td>0.83-4.32</td>
<td>0.79-1.25</td>
</tr>
<tr>
<td>SCD</td>
<td>1.19 (0.26)</td>
<td>1.25 (0.61)</td>
<td>1 (0.99)</td>
</tr>
<tr>
<td></td>
<td>0.98-1.62</td>
<td>0.53-2.97</td>
<td>0.81-1.24</td>
</tr>
<tr>
<td>DFA &amp; SCD</td>
<td>0.36 (0.01)</td>
<td>0.42 (0.32)</td>
<td>1.19 (0.16)</td>
</tr>
<tr>
<td></td>
<td>0.17-0.76</td>
<td>0.08-2.31</td>
<td>0.94-1.52</td>
</tr>
<tr>
<td>DFA &amp; EMA</td>
<td>0.49 (0.07)</td>
<td>0.69 (0.56)</td>
<td>1.08 (0.6)</td>
</tr>
<tr>
<td></td>
<td>0.23-1.05</td>
<td>0.19-2.43</td>
<td>0.81-1.46</td>
</tr>
<tr>
<td>DFA &amp; EMA &amp; SCD</td>
<td>0.41 (0.04)</td>
<td>0.6 (0.56)</td>
<td>1.09 (0.59)</td>
</tr>
<tr>
<td></td>
<td>0.17-0.95</td>
<td>0.11-3.37</td>
<td>0.81-1.46</td>
</tr>
</tbody>
</table>

Adjusted for age, education, income, BMI, smoking status, alcohol intake, FEV1, CHD, diabetes stage, height and estrogen, using interaction of race and sleep complaint.

AAs = African Americans
EMA = Early morning awakening; DFA = Difficulty falling asleep; SCD = Sleep continuity disturbance
The CHS Study

• *Results.* Difficulty falling asleep, singly or in combination with other sleep complaints, predicted a statistically significantly reduced risk of incident hypertension for non-African American men in 6 years of follow-up.

• Insomnia complaints did not predict hypertension in women or in African Americans, although there may not have been enough power to show a significant association for African Americans.
Consequences of Insomnia?

• VERY few studies are done in “drug-free” insomniacs
• Patients complain of poor daytime functioning due to their insomnia
  – Poor functioning at work
  – Memory difficulties
  – Problems concentrating
  – Drowsiness during driving
• Studies show conflicting data on objective testing in insomniacs
• Most insomniacs are not objectively sleepy when tested
Insomnia with Short Sleep Duration and Mortality: The Penn State Cohort. SLEEP 2010;33(9):1159-1164. Vgontzas AN, Liao D, Pejovic S et. al.

“Insomnia with objective short sleep duration in men is associated with increased mortality, a risk that has been underestimated. “
Methods

• 14 year follow-up of population-based sample of 1741 after objectively-measured sleep duration.

• “Insomnia” was self-defined and had to have lasted at least a year

• “Short sleep” was < 6 hours measured in the sleep laboratory.
## Mortality Risk, WOMEN

Adjusted for age, race, education, BMI, smoking status, alcohol use, depression, SDB, and sampling weight.

<table>
<thead>
<tr>
<th></th>
<th>Number</th>
<th>BMI Kg/m²</th>
<th># Depression</th>
<th>Death (OR)</th>
<th>* P &lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 6 h, no insomnia</td>
<td>437</td>
<td>27.3</td>
<td>79 (18%)</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>≥ 6 h, insomnia</td>
<td>64</td>
<td>31.6</td>
<td>31 (48%)</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>≤ 6 h, no insomnia</td>
<td>419</td>
<td>28.4</td>
<td>80 (19%)</td>
<td>1.4</td>
<td></td>
</tr>
<tr>
<td>≤ 6 h, insomnia</td>
<td>80</td>
<td>27.3</td>
<td>24 (30 %)</td>
<td>0.4</td>
<td></td>
</tr>
</tbody>
</table>
### Mortality Risk, MEN

<table>
<thead>
<tr>
<th>Condition</th>
<th>Number</th>
<th>BMI Kg/m²</th>
<th># Depression</th>
<th>Death (OR) if NOT hypertensive or diabetic * P &lt;0.05</th>
<th>Death (OR) if hypertensive or diabetic * P &lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 6 h, no insomnia</td>
<td>342</td>
<td>26.9</td>
<td>45 (13%)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>≥ 6 h, insomnia</td>
<td>22</td>
<td>27.4</td>
<td>9 (41%)</td>
<td>1.2</td>
<td>0.6</td>
</tr>
<tr>
<td>≤ 6 h, no insomnia</td>
<td>344</td>
<td>27.6</td>
<td>38 (11%)</td>
<td>1.0</td>
<td>1.9</td>
</tr>
<tr>
<td>≤ 6 h, insomnia</td>
<td>33</td>
<td>28.4</td>
<td>18 (55%)</td>
<td>1.5</td>
<td>7.2*</td>
</tr>
</tbody>
</table>

Adjusted for age, race, education, BMI, smoking status, alcohol use, depression, SDB, and sampling weight.
Results/Conclusions

• In women, insomnia was not associated with increased risk of death, regardless of sleep duration.

• In men, mortality risk was significantly increased only in insomniacs who slept < 6 hours (there were only 33 of these) and who were diabetic or hypertensive at baseline.

• In these 33 short sleeping, insomniac men, 23 had hypertension and 19 had diabetes.

• Male short sleeping insomniacs are rare, but those with have diabetes or hypertension may be at increased risk for death.
Management of Insomnia

- Pharmacologic
- Non-pharmacologic
Drugs FDA-Approved to Treat Insomnia

• Benzodiazepines
  – Estazolam (Prosom)
  – Flurazepam (Dalmane)
  – Quazepam (Doral)
  – Temazepam (Restoril)
  – Triazolam (Halcion)

• Benzodiazepine Receptor Agonists (BZRA’s)
  – Eszopiclone (Lunesta)
  – Zaleplon (Sonata)
  – Zolpidem (Ambien)

• Melatonin Agonists
  – Ramelteon (Rozerem)
Benefits of Hypnotic Treatment for Insomnia

- Improved measured sleep parameters (eg, WASO, TST).
- Sometimes improved subjective daytime function. (Hajak G Sleep Medicine 2009).
- Sometimes improved mood
- But not:
  - Improved objective sleepiness
  - Psychomotor vigilance
  - Cardiovascular measures
  - Life expectancy

- **Rationale:** short sleep and insomnia complaints are assoc with death, but don’t usually control for hypnotics.

- **Methods**
  - Mailed questionnaire to 5102 random subjects
  - Response was 70%, mean age 46 years
  - Follow-up in national death registry over 20 yrs
Fig. 1. Survival in men using hypnotics sometimes or regularly compared to men not using hypnotics. (—) No hypnotic usage; (-----) Hypnotic usage sometimes; (----) Regular hypnotic usage.
Hypnotics and Survival in Women
(Mallon, Sleep Med 2009)

Fig. 2. Survival in women using hypnotics sometimes or regularly compared to women not using hypnotics. (—) No hypnotic usage; (-----) Hypnotic usage sometimes; (——) Regular hypnotic usage.
### Hypnotics and Crash

Gustavsen I, Sleep Medicine, 2008

<table>
<thead>
<tr>
<th>Hypnotic</th>
<th>Zopiclone</th>
<th>Zolpidem</th>
<th>Nitrazepam</th>
<th>Flunitrazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number crashes</strong></td>
<td>129</td>
<td>21</td>
<td>27</td>
<td>18</td>
</tr>
<tr>
<td><strong>Standardized Incidence Ratio for Crash</strong></td>
<td>2.3*</td>
<td>2.2*</td>
<td>2.7*</td>
<td>4.0*</td>
</tr>
</tbody>
</table>
Off-Label Medications

- Antidepressants
- Antihistamines
- Antipsychotics
- OTC’s
“In short-term use, trazodone is sedating and improves several sleep parameters. These initial effects may not last beyond 2 weeks. However, there are no studies of long-term use of trazodone for treatment of insomnia... All antidepressants have potentially significant adverse effects, raising concerns about the risk-benefit ratio.”
Insomnia, Outcomes and Hypnotics

- The evidence that chronic use of hypnotics is dangerous is much more compelling than the evidence that hypnotics improve any important objective outcome.
Management of Insomnia

- Pharmacologic
- Non-pharmacologic
“Behavioral and cognitive-behavioral therapies (CBTs) have demonstrated efficacy in RCTs. ... When these cognitive methods have been added to the behavioral methods to compose a cognitive-behavioral treatment package, it has been found to be as effective as prescription medications are for brief treatment of chronic insomnia. Moreover, there are indications that the beneficial effects of CBT, in contrast to those produced by medications, may last well beyond the termination of treatment.”
Behavioral Model of Insomnia

• A state of “conditioned arousal” may develop in which situations associated with sleep become alerting rather than relaxing- further impairing sleep.

• (In other words, the patient fears that insomnia will kill).
Conditioned Arousal Explained

When Falling Asleep Feels the Easiest

<table>
<thead>
<tr>
<th>Circumstance</th>
<th>Ease of Falling Asleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>In Class</td>
<td>100</td>
</tr>
<tr>
<td>At Work</td>
<td>80</td>
</tr>
<tr>
<td>In bed actually trying to sleep</td>
<td>10</td>
</tr>
</tbody>
</table>
Cognitive-Behavioral Therapy (CBT)

- Often used to treat other psychological disorders
- Usually 8-10 weekly sessions
- CBT seeks to change poor sleep habits and faulty beliefs about sleep and promote good sleep hygiene.
- CBT principles include sleep restriction, stimulus control, relaxation techniques, education and sleep hygiene.
The purpose of this study was to assess objective and subjective sleep in chronic insomniacs treated with CBT alone vs CBT plus a hypnotic.
Randomization and Attrition (Morin CM JAMA 2009)

486 Patients assessed for eligibility

244 Excluded or declined to participate

242 Completed clinical evaluation

82 Excluded
26 Declined to participate
24 Had psychiatric disorder
10 Had other sleep disorder
9 Did not meet insomnia criteria
5 Had hypnotic drug use
4 Had alcohol or substance abuse
4 Had medical condition

160 Randomized

80 Randomized to receive cognitive behavioral therapy (CBT) for 6 wk
5 Dropped out

75 Randomized

38 Randomized to extended CBT for 6 mo
1 Dropped out
4 Lost to follow-up
33 Patients followed up at 6 mo

37 Randomized to no treatment for 6 mo
2 Dropped out
35 Patients followed up at 6 mo

80 Randomized to receive CBT plus 10 mg/d of zolpidem for 6 wk
6 Dropped out

74 Randomized

37 Randomized to extended CBT alone for 6 mo
1 Dropped out
6 Lost to follow-up
30 Patients followed up at 6 mo

37 Randomized to extended CBT plus zolpidem as needed for 6 mo
4 Dropped out
4 Lost to follow-up
29 Patients followed up at 6 mo

80 Included in analysis for 6-wk treatment
75 Included in analysis for 6-mo treatment and 6-mo follow-up
Remission Rates at 1 Year
(Based on ISI)

• CBT alone acutely (6 weeks)
  – CBT alone for 6 more months 44%
  – No additional CBT 40%

• CBT + zolpidem acutely (6 weeks)
  – CBT alone for 6 more months 68%
  – CBT + zolpidem prn for 6 more months 42%
The National Institutes of Health (NIH) State of the Science conference on insomnia concluded that behavioral therapy may be more effective and the effect may last longer than that of medications. {Evidence level C, nonquantitative systematic review}

Why Don’t More Patients Receive CBT?

• Not consistently reimbursed
• Few practitioners available
• Many patients want a “medical” diagnosis, not a behavioral or psychological one
• Medications are readily available and well-advertised.
• CBT takes time.
Our Patient

• A 58 year old woman, who is married and whose husband has retired
• Gets up at 08:30
• Goes to church, reads, plays bridge
• Goes to bed about 10:00
  – Sleeps until 1:30
  – Is “up and down” the rest of the night
  – Finally gets out of bed about 08:30
• Sometimes naps
• She gets about 6 ½ hours of sleep a night
Intitial Rx

• Let her know that insomnia doesn’t kill!
• Restrict time in bed to about 6½ hours (midnight to 6:30)
• Tell her to get out of bed and do something else if she lies there longer than 20-30 minutes without sleeping.
• No napping!
• Consider referral for CBT
Summary

• Insomnia and sleep deprivation are not the same thing.
• Sleep deprivation MAY kill, but insomnia doesn’t.
• Younger people are more susceptible to the effects of sleep deprivation than are older people.
• The treatment of choice for chronic insomnia is CBT.
• The treatment of choice for sleep deprivation is...sleep.