Diagnosis and Management of Insomnia

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Massachusetts General Hospital

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Harvard Medical School
## Disclosure Information

<table>
<thead>
<tr>
<th>Type of Affiliation</th>
<th>Commercial Entity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consultant</td>
<td>Flex Pharma, Merck</td>
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<tr>
<td>Stock Options</td>
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<td>Royalties</td>
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<tr>
<td>Travel Support</td>
<td>Otsuka</td>
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<tr>
<td>Research Support</td>
<td>NIMH, UCB Pharma, Neurometrix, Luitpold Pharma, RLS Foundation</td>
</tr>
</tbody>
</table>
Sleep disorders

• Insomnias
  – Insomnia, psychiatric/medical disorders, RLS, medications

• Hypersomnias
  – Sleep apnea, medications, Periodic leg movements of sleep

• Parasomnias
  – Sleepwalking, sleep terrors, REM sleep behavior disorder

• Circadian rhythm disorders
  – Shift work sleep disorder, Delayed sleep phase disorder
DSM-5 Insomnia disorder

• Dissatisfaction with sleep quality or quantity associated with (at least one of):
  – difficulty initiating sleep
  – difficulty maintaining sleep
  – early morning awakening

• Distress or dysfunction related to sleep disturbance

• Minimum of 3x/wk for 3 months

• The insomnia does not co-occur with another sleep disorder

• The insomnia is not *explained* by coexisting mental disorders or medical conditions
Chronic Insomnia Requires a Thorough Evaluation

Symptoms → Differential Diagnosis

Treatment ← Diagnosis
Sleep quality is only as strong as the weakest link and many insomniacs have many sleep-related issues.

All contributing factors must be treated to achieve maximum benefit.
Our understanding of the regulation of sleep informs insomnia treatment approaches

Two processes control sleep timing, quality and quantity

1. Homeostatic Drive
   - Increases with the duration of waking and dissipates with sleep

2. Circadian Rhythms
   - Confines sleep and waking to different phases of the 24-hour day
   - Entrained to the light-dark cycle
   - Sleep-independent
Insomnia tips the scales of sleep

High Arousal
(physiological/psychological)
eg pain, worry, dyspnea

Low Homeostatic drive
To treat insomnia:
1) increase sleep drive and decrease arousal

Arousal
(physiological/psychological)
eg pain, worry, dyspnea

Homeostatic drive
To treat insomnia:
2) attempt sleep at optimal time of day
To treat insomnia:
2) match time in bed to optimal circadian time for sleep
Differential diagnosis of chronic insomnia

- Primary psychiatric disorders
- Medications
- Substances
- Medical disorders
- Restless Legs Syndrome (RLS)
- Sleep schedule disorders
- Obstructive sleep apnea
Common cognitive and behavioral issues which can produce/worsen insomnia

• Inconsistent bedtimes and wake times
• “Dozing” in evening before bed
• Excessive time in bed
• Sleep-related anxiety (“insomnia phobia”)
• Unrealistic expectations of total sleep time, sleep onset and number of awakenings
• Clock watching
• Use of electronics in bedroom
• Inappropriate attributions of daytime issues to sleep
Indications for polysomnography

- Suspicion of sleep apnea (loud snoring *PLUS one of the following*):
  - daytime sleepiness
  - witnessed apneas
  - refractory hypertension

- Abnormal behaviors or movements during sleep
- Unexplained excessive daytime sleepiness
- Refractory sleep complaints, particularly repetitive brief awakenings
Conditioned or Psychophysiological Insomnia

Many people with insomnia, regardless of the cause, develop negative associations and anxiety regarding sleep initiation ("insomnia phobia") which perpetuate insomnia.
Treatment of Conditioned Insomnia

• Improve sleep-related habits and beliefs
• Cognitive Behavioral Therapy (CBT-I)
• Hypnotics, intermittently or chronically, if CBT-I fails
## Table 2. Components of Cognitive Behavioral Therapy for Insomnia.

<table>
<thead>
<tr>
<th>Component</th>
<th>Intended Effect</th>
<th>Specific Directions for Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep restriction</td>
<td>Increase sleep drive and stabilize circadian rhythm</td>
<td>Reduce time in bed to perceived total sleep time (not less than 5–6 hours), choose specific hours on the basis of personal preference and circadian timing, increase time in bed gradually as sleep efficiency improves</td>
</tr>
<tr>
<td>Stimulus control</td>
<td>Reduce arousal in sleep environment and promote the association of bed and sleep</td>
<td>Attempt to sleep when sleepy, get out of bed when awake and anxious at night, use the bed only for sleep or sexual activity (e.g., no watching TV in bed)</td>
</tr>
<tr>
<td>Cognitive therapy</td>
<td>Restructure maladaptive beliefs regarding daytime and health consequences of insomnia</td>
<td>Maintain reasonable expectations about sleep; review previous insomnia experiences, challenging perceived catastrophic consequences</td>
</tr>
<tr>
<td>Relaxation therapy</td>
<td>Reduce physical and psychological arousal in sleep environment</td>
<td>Practice progressive muscle relaxation, breathing exercises, or meditation</td>
</tr>
<tr>
<td>Sleep hygiene</td>
<td>Reduce behaviors that interfere with sleep drive or increase arousal</td>
<td>Limit caffeine and alcohol, keep bedroom dark and quiet, avoid daytime or evening napping, increase exercise (not close to bedtime), remove bedroom clock from sight</td>
</tr>
</tbody>
</table>
CBT-I treatment of insomnia with medical and psychiatric comorbidity

Figure 2. Remission From Insomnia at Posttreatment

<table>
<thead>
<tr>
<th>Source</th>
<th>OR</th>
<th>95% CI</th>
<th>z Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol dependence: Arnedt et al., 2011</td>
<td>ISI</td>
<td>5.00</td>
<td>0.27-91.52</td>
<td>1.09</td>
</tr>
<tr>
<td>Chronic pain: Currie et al., 2000</td>
<td>PSQI</td>
<td>7.56</td>
<td>0.87-65.87</td>
<td>1.83</td>
</tr>
<tr>
<td>Alcohol dependence: Currie et al., 2004</td>
<td>PSQI</td>
<td>8.14</td>
<td>0.88-75.48</td>
<td>1.85</td>
</tr>
<tr>
<td>Breast cancer: Dirlsen and Epstein, 2008</td>
<td>ISI</td>
<td>1.73</td>
<td>0.71-4.17</td>
<td>1.21</td>
</tr>
<tr>
<td>Mixed psychiatric: Edinger et al., 2009</td>
<td>PSQI</td>
<td>0.88</td>
<td>0.19-4.16</td>
<td>-0.16</td>
</tr>
<tr>
<td>Hearing impairment: Jansson-Frajmark, 2012</td>
<td>ISI</td>
<td>3.96</td>
<td>0.97-16.27</td>
<td>1.91</td>
</tr>
<tr>
<td>COPD: Kapella et al., 2011</td>
<td>PSQI</td>
<td>2.63</td>
<td>0.39-17.46</td>
<td>1.00</td>
</tr>
<tr>
<td>Depression: Manber et al., 2008</td>
<td>ISI</td>
<td>6.26</td>
<td>1.27-30.80</td>
<td>2.26</td>
</tr>
<tr>
<td>PTSD: Margolies et al., 2013</td>
<td>Combined</td>
<td>4.45</td>
<td>0.29-67.55</td>
<td>1.07</td>
</tr>
<tr>
<td>Chronic pain: Pigeon et al., 2012-1</td>
<td>ISI</td>
<td>143.00</td>
<td>2.42-8467.01</td>
<td>2.38</td>
</tr>
<tr>
<td>Chronic pain: Pigeon et al., 2012-2</td>
<td>ISI</td>
<td>16.20</td>
<td>0.59-441.68</td>
<td>1.65</td>
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<tr>
<td>Cancer: Ritterband et al., 2012</td>
<td>ISI</td>
<td>6.00</td>
<td>0.97-37.30</td>
<td>1.92</td>
</tr>
<tr>
<td>PD: Rios Romenets et al., 2013</td>
<td>ISI</td>
<td>0.30</td>
<td>0.02-4.91</td>
<td>-0.84</td>
</tr>
<tr>
<td>Breast cancer: Savard et al., 2005</td>
<td>ISI</td>
<td>10.38</td>
<td>2.55-42.33</td>
<td>3.26</td>
</tr>
<tr>
<td>PTSD: Talbot et al., 2014</td>
<td>ISI</td>
<td>23.57</td>
<td>1.29-430.80</td>
<td>2.13</td>
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<tr>
<td>Chronic pain: Tang et al., 2012</td>
<td>ISI</td>
<td>3.50</td>
<td>0.55-22.30</td>
<td>1.33</td>
</tr>
<tr>
<td>PTSD: Ulmer et al., 2011</td>
<td>ISI</td>
<td>2.48</td>
<td>0.09-68.14</td>
<td>0.54</td>
</tr>
<tr>
<td>Osteoarthritis: Vitiello et al., 2013</td>
<td>Combined</td>
<td>1.00</td>
<td>1.43-4.30</td>
<td>3.22</td>
</tr>
<tr>
<td>Depression: Wagley et al., 2012</td>
<td>PSQI</td>
<td>3.17</td>
<td>0.23-4.37</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Wu et al. JAMA Int Med 2015
Psychiatric outcomes using CBT-I for insomnia

<table>
<thead>
<tr>
<th>Psychiatric</th>
<th>Combined</th>
<th>2.48</th>
<th>0.85</th>
<th>0.72</th>
<th>0.82 to 4.15</th>
<th>2.92</th>
<th>.003</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alcohol dependence: Arnedt et al,25 2011</td>
<td>Combined</td>
<td>2.48</td>
<td>0.85</td>
<td>0.72</td>
<td>0.82 to 4.15</td>
<td>2.92</td>
<td>.003</td>
</tr>
<tr>
<td>Alcohol dependence: Currie et al,26 2004</td>
<td>BDI</td>
<td>0.66</td>
<td>0.35</td>
<td>0.12</td>
<td>-0.03 to 1.34</td>
<td>1.88</td>
<td>.06</td>
</tr>
<tr>
<td>Depression: Manber et al,28 2008</td>
<td>HRSD</td>
<td>0.29</td>
<td>0.38</td>
<td>0.14</td>
<td>-0.45 to 1.02</td>
<td>0.77</td>
<td>.44</td>
</tr>
<tr>
<td>Depression: Wagley et al,33 2013</td>
<td>PHQ-9</td>
<td>0.76</td>
<td>0.39</td>
<td>0.15</td>
<td>-0.00 to 1.52</td>
<td>1.95</td>
<td>.05</td>
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<tr>
<td>Depression: Watanabe et al,34 2011</td>
<td>HRSD</td>
<td>0.83</td>
<td>0.34</td>
<td>0.11</td>
<td>-0.17 to 1.49</td>
<td>2.46</td>
<td>.01</td>
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<tr>
<td>Hypnotic dependence: Morgan et al,30 2004</td>
<td>Abstinent d/wk</td>
<td>0.69</td>
<td>0.17</td>
<td>0.03</td>
<td>0.35 to 1.03</td>
<td>4.02</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>PTSD: Margolies et al,29 2013</td>
<td>Combined</td>
<td>0.96</td>
<td>0.40</td>
<td>0.16</td>
<td>0.18 to 1.74</td>
<td>2.40</td>
<td>.02</td>
</tr>
<tr>
<td>PTSD: Talbot et al,31 2014</td>
<td>Combined</td>
<td>0.26</td>
<td>0.31</td>
<td>0.09</td>
<td>-0.34 to 0.86</td>
<td>0.85</td>
<td>.40</td>
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<tr>
<td>PTSD: Ulmer et al,32 2011</td>
<td>PCL-M</td>
<td>1.89</td>
<td>0.56</td>
<td>0.32</td>
<td>0.79 to 3.00</td>
<td>3.36</td>
<td>.001</td>
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<tr>
<td>Subtotal</td>
<td></td>
<td>0.76</td>
<td>0.15</td>
<td>0.02</td>
<td>0.46 to 1.05</td>
<td>5.03</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Wu et al. JAMA Int Med 2015
Brief Behavioral Therapy for Insomnia (BBTI)

- Limit time in bed to estimated sleep time + 30 min
  - Minimum of 6 hours
- Keep the same rise time EVERY day regardless of sleep duration
- Only go to bed when sleepy
- Do not stay in bed unless asleep; avoid naps

- Developed to be shorter duration than traditional CBTI
- A single 45-60 min RN-led session, a single 30 min follow-up 2wks later, followed by two 20 min phone calls 1 & 3 wks after treatment

Buysse DJ Arch Intern Med 2011
“A story? Honey, wouldn’t you rather a mild sedative?”
The complex neurochemistry of sleep provides many treatment options.

- **Ascending arousal pathways**
- **Descending inhibitory pathways**
Pharmacologic Treatments for Insomnia

- Benzodiazepine receptor agonists (BzRAs)
- Melatonin agonists
- Orexin antagonist
- Sedating antidepressants
- Anticonvulsants
- Dopaminergic antagonists (eg antipsychotics)
- Miscellaneous (eg prazosin, clonidine, hydroxyzine)
Benzodiazepine-Receptor Agonists (BzRA) Commonly Used as Hypnotics

<table>
<thead>
<tr>
<th>Agent (brand name)</th>
<th>Dose range</th>
<th>Half-life</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonazepam (Klonopin)</td>
<td>0.25 -1.0 mg</td>
<td>40 hr</td>
</tr>
<tr>
<td>Temazepam (Restoril)*</td>
<td>7.5-30 mg</td>
<td>4-18 hr</td>
</tr>
<tr>
<td>Lorazepam (Ativan)</td>
<td>0.5-2.0 mg</td>
<td>10-20 hr</td>
</tr>
<tr>
<td>Oxazepam (Serax)</td>
<td>10-30 mg</td>
<td>5-10 hr</td>
</tr>
<tr>
<td>Eszopiclone (Lunesta)*</td>
<td>1-3 mg</td>
<td>5.5-8 hr</td>
</tr>
<tr>
<td>Triazolam (Halcion)*</td>
<td>0.125-0.25 mg</td>
<td>2-3 hr</td>
</tr>
<tr>
<td>Zolpidem (Ambien)*</td>
<td>3.75-12.5 mg</td>
<td>2-3 hr (CR extends duration of action)</td>
</tr>
<tr>
<td>Zaleplon (Sonata)*</td>
<td>5-10 mg</td>
<td>1-2 hr</td>
</tr>
</tbody>
</table>

*FDA approved for insomnia.
Do z-drugs work for insomnia?

### Table 3: Weighted mean raw differences in effect of Z drugs (treatment) or placebo on insomnia

<table>
<thead>
<tr>
<th></th>
<th>Within groups</th>
<th>Between groups</th>
<th>Homogeneity of effect sizes I² (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No*</td>
<td>Treatment</td>
<td>Control</td>
</tr>
<tr>
<td><strong>Primary outcome-sleep latency</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PSG</td>
<td>14</td>
<td>-42 (-60 to -23)</td>
<td>-20 (-28 to -11)</td>
</tr>
<tr>
<td>Subjective</td>
<td>2</td>
<td>-24.99 (-30.06 to -19.92)</td>
<td>-19.43 (-26.61 to -12.25)</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wake after sleep onset (PSG)</td>
<td>2</td>
<td>-20 (-59 to 18)</td>
<td>-13 (-34 to 7.89)</td>
</tr>
<tr>
<td>No of awakenings (PSG)</td>
<td>2</td>
<td>1.24 (-6.34 to 3.89)</td>
<td>-0.94 (-12 to 9.99)</td>
</tr>
<tr>
<td>No awakenings (subjective)</td>
<td>2</td>
<td>2.88 (-7.15 to 1.39)</td>
<td>-1.05 (-4.86 to 2.76)</td>
</tr>
<tr>
<td>Total sleep time (PSG)</td>
<td>2</td>
<td>49.15 (-60 to 16)</td>
<td>35.10 (-34 to 10)</td>
</tr>
<tr>
<td>Sleep efficiency (PSG)</td>
<td>1</td>
<td>4.27 (2.01 to 6.52)</td>
<td>0 (-2.52 to 2.52)</td>
</tr>
</tbody>
</table>

Effects modified by higher dose, younger age, female sex

Huedo-Medina et al, BMJ, 2012
Do benzodiazepines work for insomnia?

Buscemi et al, JGIM, 2007

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of Studies</th>
<th>Point Estimate (95% CI)</th>
<th>Heterogeneity (I²) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sleep onset latency (WMD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>11</td>
<td>-10.0 min (-16.6, -3.4)</td>
<td>72.6</td>
</tr>
<tr>
<td>Polysomnography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>26</td>
<td>-19.6 min (-23.9, -15.3)</td>
<td>55.5</td>
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<tr>
<td>Non-benzodiazepines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysomnography</td>
<td>12</td>
<td>-12.8 min (-16.9, -8.8)</td>
<td>39.3</td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>34</td>
<td>-17.0 min (-20.0, -14.0)</td>
<td>64.8</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysomnography</td>
<td>4</td>
<td>-7.0 min (-10.7, -3.3)</td>
<td>34.1</td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>2</td>
<td>-12.2 min (-22.3, -2.2)</td>
<td>0</td>
</tr>
<tr>
<td>Wakefulness after sleep onset (WMD)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine</td>
<td>5</td>
<td>-16.7 min (-25.3, -8.1)</td>
<td>0</td>
</tr>
<tr>
<td>Polysomnography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>4</td>
<td>-39.9 min (-71.0, -8.8)</td>
<td>68.2</td>
</tr>
<tr>
<td>Non-benzodiazepines</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysomnography</td>
<td>3</td>
<td>-7.0 min (-14.6, 0.7)</td>
<td>0</td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>12</td>
<td>-15.0 min (-22.3, -7.7)</td>
<td>66.5</td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polysomnography</td>
<td>2</td>
<td>-12.2 min (-17.5, -7.0)</td>
<td>0</td>
</tr>
<tr>
<td>Sleep Diary</td>
<td>1</td>
<td>-7.1 min (-19.1, 4.9)</td>
<td>NA</td>
</tr>
</tbody>
</table>
“Are sleeping pills addictive?”

“Substance use disorders occur when their recurrent use causes clinically and functionally significant impairment, such as health problems, disability, and failure to meet major responsibilities at work, school, or home.”- DSM 5

• Tolerance
• Physiological dependence
• Psychological dependence
• Non-medical diversion
The Current Status of BzRA Risks in the Treatment of Insomnia

- Motor vehicle accidents in elderly: long T$_{1/2}$ agents
- Hip fractures in elderly: long T$_{1/2}$ agents?
- Anterograde amnesia: T$_{1/2}$ dependent
- Abuse: unusual outside of other substance abusers
- Tolerance: no evidence from 12- and 26-week studies
- Rebound insomnia: depends upon dose, duration of use, and speed of taper

Benzodiazepines do increase risk for dementia

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Risk of Alzheimer’s disease associated with benzodiazepine use (variables assessed five to up to 10 years before diagnosis) in people with Alzheimer’s disease (cases) and controls</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No (%) of cases (n=1796)</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Benzodiazepine ever use:</td>
<td></td>
</tr>
<tr>
<td>Non-users</td>
<td>902 (50.2)</td>
</tr>
<tr>
<td>Users</td>
<td>894 (49.8)</td>
</tr>
<tr>
<td>Benzodiazepine density exposure (No of prescribed daily doses):</td>
<td></td>
</tr>
<tr>
<td>Non-users</td>
<td>902 (50.2)</td>
</tr>
<tr>
<td>1-90</td>
<td>234 (13.0)</td>
</tr>
<tr>
<td>91-180</td>
<td>70 (3.9)</td>
</tr>
<tr>
<td>&gt;180</td>
<td>590 (32.9)</td>
</tr>
<tr>
<td>Benzodiazepine elimination half life:</td>
<td></td>
</tr>
<tr>
<td>Non-users</td>
<td>902 (50.2)</td>
</tr>
<tr>
<td>Short half life (&lt;20 h)</td>
<td>585 (32.6)</td>
</tr>
<tr>
<td>Long half life (≥20 h)</td>
<td>309 (17.2)</td>
</tr>
</tbody>
</table>

*Matched for age, sex, and follow-up length.
†Adjusted for high blood pressure (diagnosis or treatment), myocardial infarction (diagnosis), stroke (diagnosis), platelet inhibitors or oral anticoagulant treatment, diabetes mellitus (diagnosis or treatment), hypercholesterolaemia (diagnosis or treatment), comorbidity (diagnosis).
‡Further adjusted for anxiety, depression, and insomnia diagnosis.
Benzodiazepines do not increase risk for dementia

Gray et al, BMJ, 2016
Melatonin in the treatment of insomnia

Figure 1. Efficacy of Melatonin in Reducing Sleep Latency. Forest plot depicting reduction of sleep latency in melatonin compared to placebo. Meta-analysis demonstrated a significant benefit of melatonin in reducing sleep latency. WMD = weighted mean difference; CI = confidence interval.

Figure 2. Efficacy of Melatonin in Increasing Total sleep Time. Forest plot depicting change in total sleep time with melatonin compared to placebo treatment. Meta-analysis demonstrated a significant benefit of melatonin in increasing total sleep time. WMD = weighted mean difference;

Figure 3. Effect of Melatonin on Sleep quality. Forest plot depicts sleep quality with melatonin compared to placebo. Meta-analysis demonstrated a significant benefit of melatonin in improving sleep quality. SMD = standardized mean difference; CI = confidence interval.
Orexin antagonist in the treatment of insomnia

Suvorexant

- Advantages: little abuse liability, 1-year efficacy data (at 40 mg), few side effects
- Disadvantages: unclear efficacy vs BzRAs, prior authorization
Antidepressants in the treatment of insomnia

Mirtazapine, Trazodone, Amitriptyline, Doxepin

• Advantages: little abuse liability
• Disadvantages: probably not as effective as BzRAs, daytime sedation, weight gain, anticholinergic side effects, switch into mania in bipolar disorder
Atypical antipsychotics in the treatment of insomnia

Quetiapine

- Advantages: anxiolytic, mood stabilizing in bipolar disorder, little abuse liability
- Disadvantages: less effective than BzRAs, daytime sedation, weight gain, risks of extrapyramidal symptoms and glucose + lipid abnormalities
Anticonvulsants in the treatment of insomnia

*Gabapentin*

- Advantages: little abuse liability, efficacy in ETOH
- Disadvantages: less effective than BzRAs, cognitive impairment, daytime sedation, dizziness, weight gain
Issues with non-BzRA hypnotics in the treatment of insomnia
(eg antidepressants, anticonvulsants, antipsychotics)

- Paucity of short-term efficacy data
- Absence of long-term efficacy data
- Assumptions of lack of tolerance and rebound insomnia are unsubstantiated
- Anecdotally less effective hypnotics than BzRAs
- May have deleterious side effects
All psychiatric disorders produce insomnia

Mania > Schizophrenia > Depression and Anxiety Disorders
However, psychiatric disorders are present in only 30-40% of those with insomnia.

- Drug Abuse: 4.2%
- Other Psychiatric Disorder: 5.1%
- Alcohol Abuse: 7.0%
- Dysthymia: 8.6%
- Major Depression: 14.0%
- Anxiety Disorders: 23.9%
- No Psychiatric Disorder: 59.5%

Independent treatment of insomnia in MDD improves depression treatment outcome
**Sleep disturbance is the most common persistent symptom in treated MDD**

**25% had treatment-emergent onset of nocturnal awakenings (Nierenberg et al, 2012)**

MDD = Major depressive disorder.
Persistent insomnia in treated MDD: sleep disorder or mood disorder?

- Fatigue
- Loss of interest
- Sleep disturbance
- Depressed mood
- Impaired concentration
- Worry
- Agitation
- Irritability
- Suicidality

- inadequately treated MDD
- treatment-induced insomnia
- pre-existing independent (or primary) insomnia
- combination of above
PTSD is a disorder with an essential difficulty maintaining states of decreased vigilance.

PTSD will therefore nearly always interfere with sleep.

Specific questions as to the circumstances of traumatic episodes (e.g., night, bedroom) may shed light on sleep disturbance.

Treatments:
- Education as to relationship of PTSD to sleep disturbance
- Safety of sleep environment
- Judicious use of hypnotics
- Prazosin or Image Rehearsal Therapy for nightmares
Insomnia related to medications

• Antidepressants
• Stimulants
• Steroids, bronchodilators
• Decongestants
• Dopaminergic antagonists (akathisia)
No evidence of any distinctions between SSRIs in degree of benefit or worsening of sleep complaints in patients treated for depression

Fava et al., 2002
Stimulant pharmacokinetics are not kind to sleep
Insomnia in the elderly is not related to age, but to medical illness

- **Cardiac**: angina, PND
- **Pulmonary**: COPD, coughing
- **GI**: Nocturnal reflux
- **Musculoskeletal pain**
- **Endocrine**: Hypo/hyperthyroidism, diabetes, menopause
- **Neurologic**: Dementia, Parkinson’s, CVA, migraine
- **Urinary**: Nocturia, renal failure
Licit substances

• Caffeine
  – Sleepiness can overcome stimulant effects, but awakenings are common

• Alcohol
  – produces 3-4 hours of good sleep, followed by increased wakefulness in 2nd half of night
Treatment of RLS

• Modify reversible causes
  – Iron Deficiency (keep Ferritin > 50)
  – Medication-Induced (SRIs, DA antagonists, antihistamines)

• Pharmacologic approaches
  – Dopaminergic agonists (pramipexole, ropinirole, rotigotine patch) but watch for iatrogenic worsening of RLS
  – Alpha 2 delts ligands (gabapentin, pregabalin)
  – Opioids (oxycodone, methadone)
Sleep schedule disorders

• Delayed Sleep Phase Syndrome
  – Most common in adolescents
  – Initial insomnia and difficulty awakening in AM
  – Daytime sleepiness

• Advanced Sleep Phase Syndrome
  – Most common in the elderly
  – Early AM awakening
Insomnia is more common than daytime sleepiness in those with sleep apnea (AHI>15)

All patients while untreated (n = 705)

- No insomnia = 32%
- Initial insomnia = 15%
- Late insomnia = 28%
- Middle insomnia = 59%
- 15% overlap
- 7% overlap
- 5% overlap
- 1% overlap

Bjornsdottir et al Sleep 2013
Physical exam (kind of) predicts likelihood of sleep apnea
Berlin questionnaire (kind of) predicts sleep apnea

1. Complete the following:
   height ________ age ________
   weight ________ male/female ________

2. Do you snore?
   ☐ Yes
   ☐ No
   ☐ Don’t know

If you snore:
3. Your snoring is?
   ☐ Slightly louder than breathing
   ☐ As loud as talking
   ☐ Louder than talking
   ☐ Very loud...can be heard in adjacent rooms

4. How often do you snore?
   ☐ Nearly every day
   ☐ 3-4 times a week
   ☐ 1-2 times a week
   ☐ 1-2 times a month
   ☐ never or nearly never

5. Has your snoring ever bothered other people?
   ☐ Yes
   ☐ No

6. Has anyone noticed that you quit breathing during your sleep?
   ☐ Nearly every day
   ☐ 3-4 times a week
   ☐ 1-2 times a week
   ☐ 1-2 times a month
   ☐ never or nearly never

7. How often do you feel tired or fatigued after your sleep?
   ☐ Nearly every day
   ☐ 3-4 times a week
   ☐ 1-2 times a week
   ☐ 1-2 times a month
   ☐ Never or nearly never

8. During your wake time, do you feel tired, fatigued or not wake up to par?
   ☐ Nearly every day
   ☐ 3-4 times a week
   ☐ 1-2 time a month
   ☐ Never or nearly never

9. Have you ever nodded off or fallen asleep while driving a vehicle?
   ☐ Yes
   ☐ No

   If yes, how often does it occur?
   ☐ Nearly every day
   ☐ 3-4 times a week
   ☐ 1-2 times a week
   ☐ 1-2 times a month
   ☐ Never or nearly never

CATEGORY 3

10. Do you have high blood pressure?
    ☐ Yes
    ☐ No
    ☐ Don’t know

BMI = ________

Scoring Questions: Any answer within highlighted box outline is a positive response
Scoring Categories: Category 1 is positive with 2 or more positive responses to questions 2-6
                   Category 2 is positive with 2 or more positive responses to questions 7-9
                   Category 3 is positive with 1 or more positive responses and/or a BMI > 30
Final Results: 2 or more categories indicate a high likelihood of sleep disordered breathing
OSA treatments

Positive Airway Pressure (PAP)

Auto-PAP is allowing both diagnostic and titration to be performed in the home (no sleep lab necessary)

Weight loss, upper airway surgery, positional treatment
Sleep disorders

• Insomnias
  – Insomnia, psychiatric/medical disorders, RLS, medications

• Hypersomnias
  – Sleep apnea, medications, Periodic leg movements of sleep

• Parasomnias (4%)
  – Sleepwalking, sleep terrors, REM sleep behavior disorder

• Circadian rhythm disorders
  – Shift work sleep disorder, Delayed sleep phase disorder
Differential diagnosis of hypersomnia

• “Tired”:
  – excessive daytime sleepiness (EDS)
  – fatigue
  – apathy

• *If* EDS:
  – inadequate sleep time
  – impaired sleep quality
  – excessive sleep drive
Treatment of parasomnias

- Night terrors/sleepwalking
  - Short-acting benzodiazepines (e.g., triazolam)

- REM behavior disorder
  - Discontinue serotonergic antidepressant (if present)
  - Benzodiazepines (short, long)
  - Melatonin (6-10 mg)
  - +/- pramipexole

- Sleep-related eating disorder
  - Treat RLS, if present
  - SSRRI or topiramate