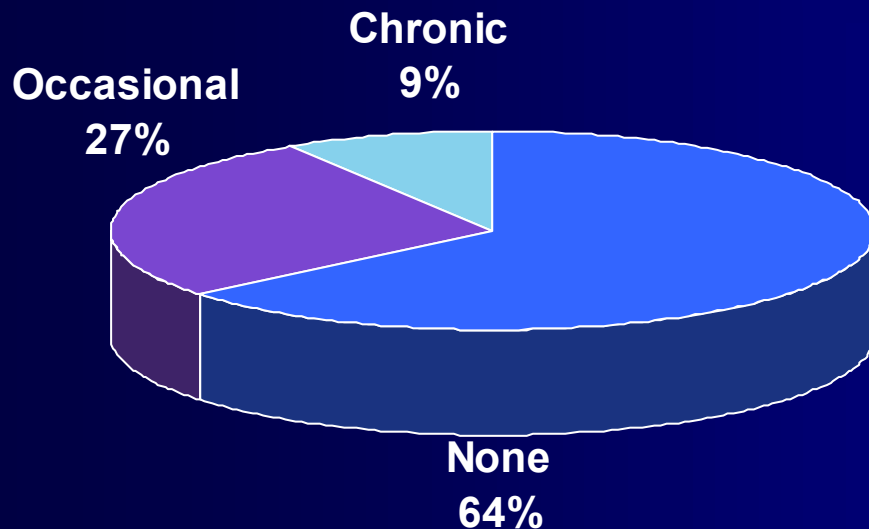


# **Patient Identification and Insomnia Treatment Rationale**

# Insomnia in the US: Prevalence and Detection

---

## Insomnia Prevalence By type

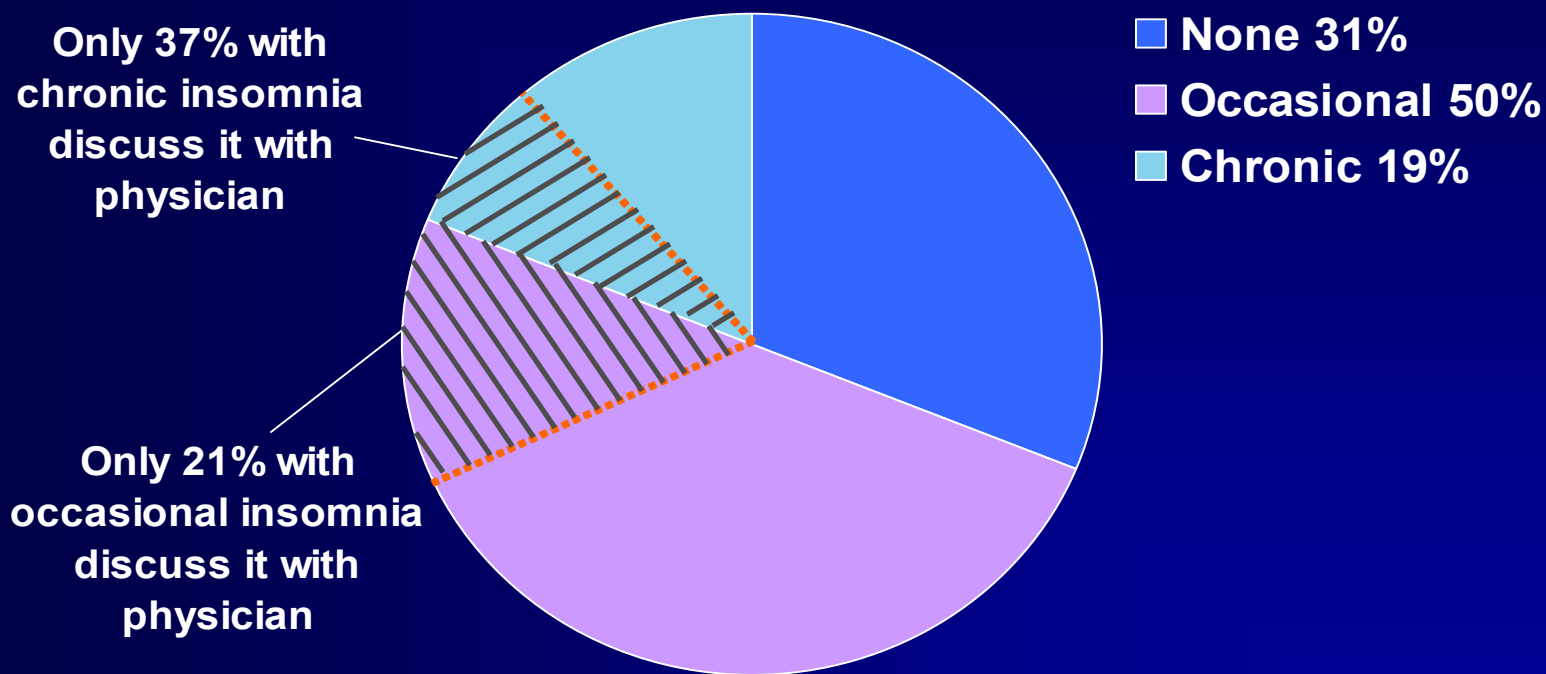


## Insomnia Detection When insomnia discussed with physician



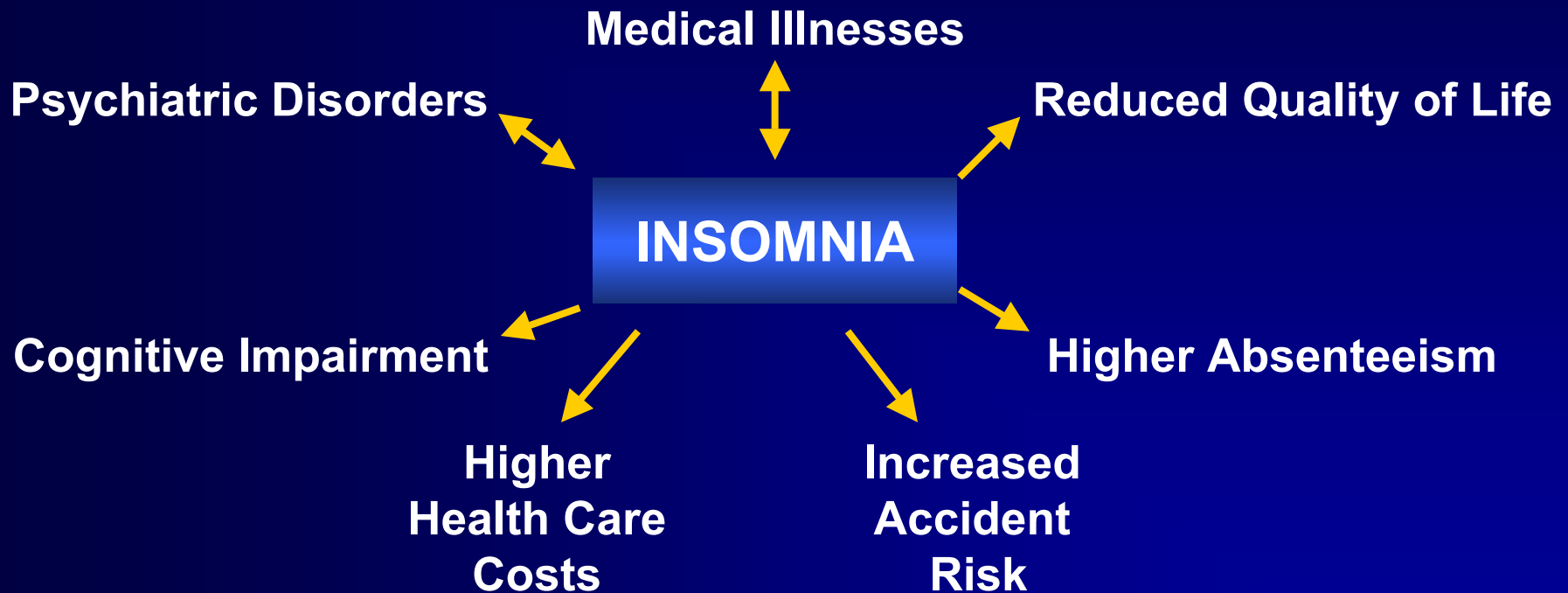
# The “Secret Symptom” in Primary Care

Prevalence of Insomnia in Three Primary Care Offices (n = 286)



# Why Diagnose Insomnia?

---



# Economic Impact of Insomnia

---

## Direct Costs<sup>1</sup>

- Drugs: \$1.97 billion (41% prescription)
- Services: \$11.96 billion

## Indirect Costs<sup>1</sup>

- Decreased productivity
- Higher accident rate
- Increased absenteeism
- Increased comorbidity

## Total Annual Cost Estimates

- Range from \$30 to \$107.5 billion<sup>2,3</sup>

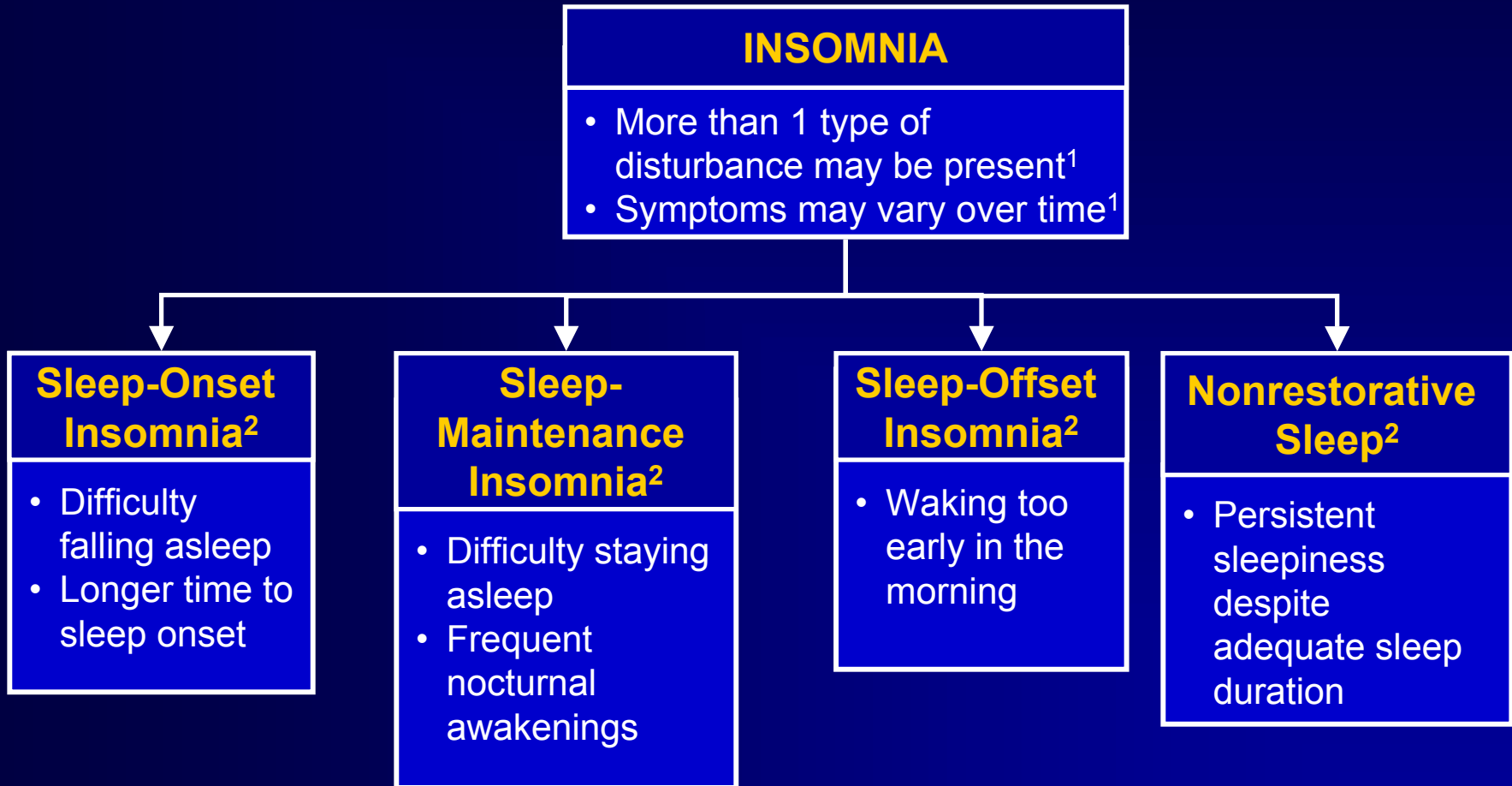
1. Walsh JK, Engelhardt CL. *Sleep*. 1998; 22(suppl 2):S386-S393.  
2. Chilcott LA, Shapiro CM. *Pharmacoeconomics*. 1996;10(suppl 1):1-14  
3. Stoller MK. *Clin Ther*. 1994;16:873-897.

# Recognizing Insomnia in Primary Care

---

- Ask about sleep in all examinations
  - “How have you been sleeping lately?”
- If patient complains of sleep problem, ascertain
  - Sleep pattern
  - Duration of insomnia
  - Sleep hygiene
  - Associated medical/psychiatric condition
  - Medications/substances

# Sleep Patterns in Insomnia



1. American Psychiatric Association. *DSM-IV-TR*<sup>TM</sup>. 2000:597-661.

2. Czeisler CA et al. In Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 15th ed. 2001:155-163.

# Duration of Insomnia

Type	Duration	Pattern	Causes
<b>Transient Insomnia</b>	Episodic—1 to several nights per episode <sup>1</sup>	Typically onset, maintenance, or offset <sup>1</sup>	<ul style="list-style-type: none"> <li>➤ Acute illness<sup>1</sup></li> <li>➤ Social stress/life event<sup>1,2</sup></li> <li>➤ Jet lag<sup>1,2</sup></li> <li>➤ Shift change<sup>2</sup></li> <li>➤ Environment<sup>1,2</sup></li> <li>➤ Meds<sup>2</sup></li> <li>➤ Primary<sup>3</sup></li> </ul>
<b>Short-Term Insomnia</b>	Few days to 3 weeks	Any pattern	<ul style="list-style-type: none"> <li>➤ Major life event<sup>2</sup></li> <li>➤ Illness/surgical recovery<sup>1</sup></li> <li>➤ Meds/substance abuse<sup>2</sup></li> <li>➤ Primary<sup>3</sup></li> </ul>
<b>Chronic Insomnia</b>	>3 weeks, often months or years	Any pattern Waxes and wanes <sup>1</sup>	<ul style="list-style-type: none"> <li>➤ Medical/psych illness<sup>2,4</sup></li> <li>➤ Meds/substance abuse<sup>4</sup></li> <li>➤ Primary<sup>3</sup></li> </ul>

1. Czeisler CA et al. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine*. 15th ed. 2001:155-163.

2. Lippmann S et al. *South Med J*. 2001;94:866-873.

3. NHLBI. NIH Publication No. 98-4088, 1998.

4. Fry JM. In: Rowland LP, ed. *Merritt's Neurology*. 10th ed. 2000:839-846.

# Primary Insomnia

---

- *DSM-IV* diagnostic criteria
  - Predominant complaint: sleep onset/maintenance problem or NRS  $\geq 1$  month
  - Significant daytime fatigue
  - No other sleep disorder (eg, narcolepsy)
  - No other psychophysical disorder (eg, depression)
  - Not caused by substance or medical condition

NRS = nonrestorative sleep.

American Psychiatric Association. *DSM-IV-TR*<sup>TM</sup>. 2000:597-661.

# Sleep Hygiene

---

<b>Good</b>	<b>Poor</b>
Same waking time each day	Waking time varies
Minimal caffeine	High caffeine use
No nicotine	Smoker/on nicotine med
No alcohol in evening	Evening drinker
Light meals at night	Heavy meals at night
Exercise in afternoon	Sedentary; exercise at night
Serene sleep environment	Disruptive sleep environment

# Conditions Associated With Insomnia

---

## Medical

- COPD, asthma<sup>1-3</sup>
- GERD, PUD<sup>2-4</sup>
- Pain syndrome<sup>3,4</sup>
- CVD, CHF<sup>1-3</sup>
- Hyperthyroidism<sup>1</sup>
- BPH<sup>2,3</sup>
- Sleep disorder (apnea, RLS, PLM)<sup>5</sup>

## Psychiatric

- Depression<sup>1-3</sup>
- Panic/other anxiety<sup>1,2</sup>
- PTSD<sup>6</sup>
- Substance/alcohol abuse<sup>1,2,4</sup>

1. Holbrook AM et al. *Can Med Assoc J.* 2000;162:216-200.

2. Lippmann S et al. *South Med J.* 2001;94:866-873.

3. Katz DA, McHorney CA. *Arch Intern Med.* 1998;158:1099-1107.

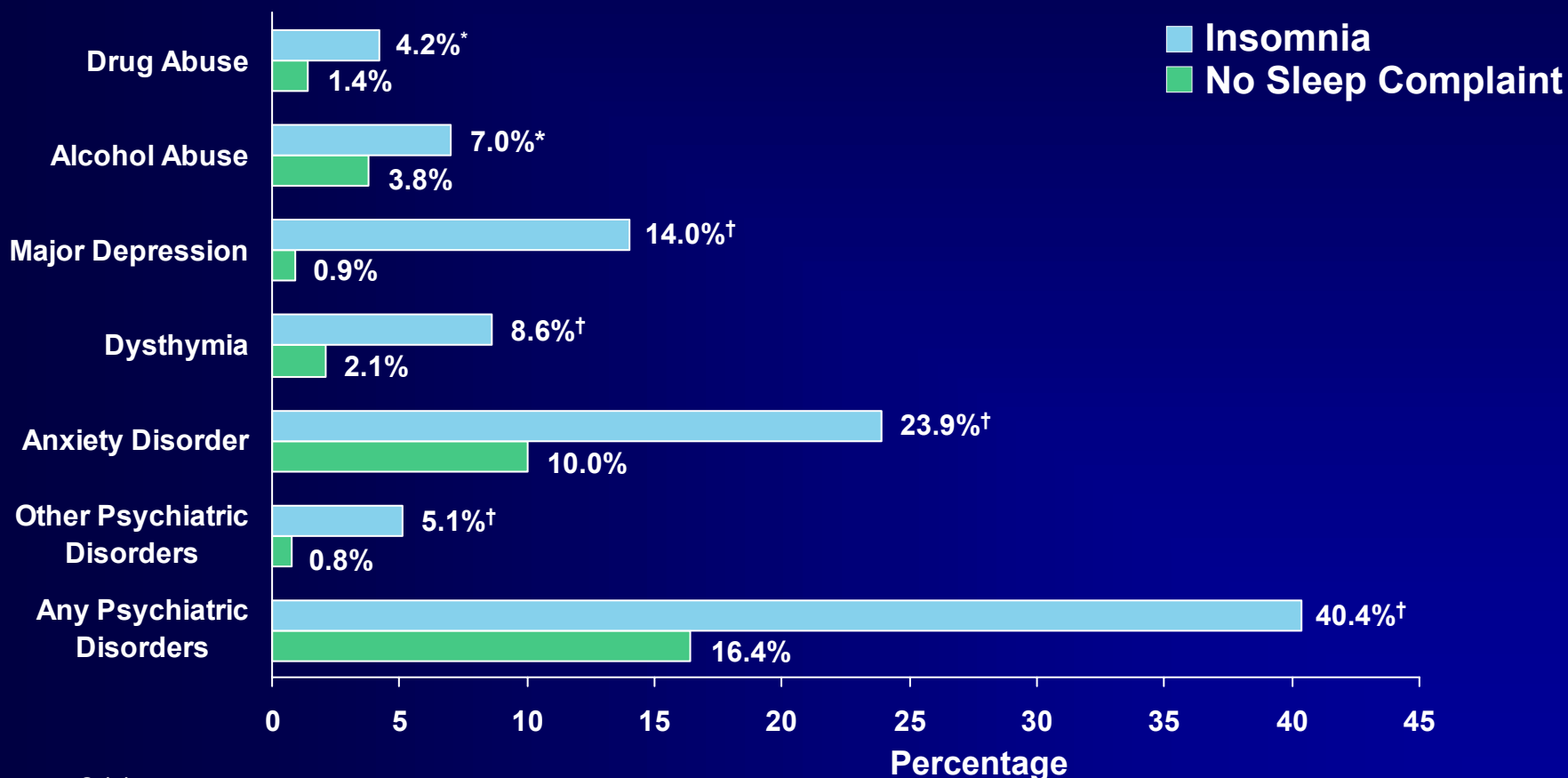
4. Fry JM. In: Rowland LP, ed. *Merritt's Neurology.* 10th ed. 2000:839-846.

5. Czeisler CA et al. In: Braunwald E et al, eds. *Harrison's Principles of Internal Medicine.* 15th ed. 2001:155-163.

6. Mellman TA et al. *Am J Psychiatry.* 1995;152:110-115.

# Comorbid Psychiatric Disorders in Patients With Insomnia

Significantly More Respondents With Insomnia Had  $\geq 1$  Psychiatric Disorder vs Those With No Sleep Complaints



n = 811.

\* $P < .05$  vs no sleep complaint; † $P < .001$  vs no sleep complaint.

Ford DE, Kamerow DB. *JAMA*. 1989;262:1479-1494.

# Medications/Substances That Cause Insomnia

---

- Anticholinergics<sup>1-3</sup>
- Antidepressants<sup>2,3</sup>
- Histamine<sub>2</sub> blockers<sup>2,4</sup>
- Antihypertensives<sup>1-4</sup>
- CNS stimulants/  
sympathomimetic  
amines<sup>1-3</sup>
- Hormones/steroids<sup>1,2,4</sup>
- Anticancer agents<sup>1,2</sup>
- Misc: Phenytoin, levodopa,  
quinidine<sup>1</sup>
- Caffeine, alcohol,  
nicotine<sup>1,2,3,5</sup>
- Cocaine<sup>3,5</sup>

1. Kupfer DJ, Reynolds CF. *N Engl J Med*. 1997;336:341-346.

2. Becker PM et al. *Postgrad Med*. 1993;93:66-79,85.

3. Ashton H. In: Cooper R, ed. *Sleep*. London, England: Chapman & Hall Medical; 1994:175-211.

4. Keck PE. *Modern Med*. 1992;60:79-86.

5. Lippman MD et al. *South Med J*. 2001;94:886-873.

# Treatment of Insomnia: Goals in Primary Care

---

- Remove/reduce underlying causes<sup>1</sup>
- Prevent progression from transient/short-term to chronic insomnia<sup>1,2</sup>
- Enhance quality of life<sup>1</sup>

1. Kupfer DJ, Reynolds CF. *N Engl J Med*. 1997;336:341-346.

2. NHLBI. NIH Publication No. 98-4088, 1998.

# Successful Treatment Integrates Three Approaches

<b>Medical/ Psychiatric Management<sup>1</sup></b>	<b>Educational/ Behavioral Intervention<sup>1,2</sup></b>	<b>Pharmacology for Insomnia<sup>1</sup></b>
<ul style="list-style-type: none"><li>➤ Medical/surgical care of contributory disease</li><li>➤ Mental health care for contributory psychiatric disorder</li></ul>	<ul style="list-style-type: none"><li>➤ Stimulus-control therapy</li><li>➤ Sleep-restriction therapy</li><li>➤ Good health practices</li><li>➤ Cognitive-behavioral therapy (referral)</li></ul>	<ul style="list-style-type: none"><li>➤ First-line hypnotic agents:<ul style="list-style-type: none"><li>– Benzodiazepines (eg, estazolam)</li><li>– Non-benzodiazepines (eg, zolpidem)</li></ul></li><li>➤ Other choices:<ul style="list-style-type: none"><li>– Antidepressants (eg, tricyclics, trazodone)</li><li>– Melatonin</li></ul></li></ul>

1. Kupfer DJ, Reynolds CF. *N Engl J Med*. 1997;336:341-346.

2. NHLBI. NIH Publication No. 98-4088, 1998.

# Pharmacologic Treatment of Insomnia: Basic Principles

---

- Lowest effective dose
- Intermittent dosing (2-4 times per week)
- Prescribe short term (regular use for no longer than 3-4 weeks)
- Taper off gradually
- Watch for rebound insomnia

# Hypnotic Agents: BZ1-Receptor Selectivity

---

- Non-benzodiazepines—highly selective for BZ1-receptors<sup>1</sup>
- Benzodiazepines—bind nonselectively to all BZ subtypes<sup>1</sup>
- Selectivity
  - Reduces muscle-relaxant, anticonvulsant, anxiolytic activity and cognitive/psychomotor effects<sup>1-5</sup>
  - May preserve sleep architecture<sup>1,2,4,5</sup>
  - Does not eliminate abuse potential<sup>6,7</sup>

1. Mitler MM. *Sleep*. 2000; 23(suppl 1):S39-S47.

2. Ambien Full Prescribing Information.

3. Sonata Full Prescribing Information.

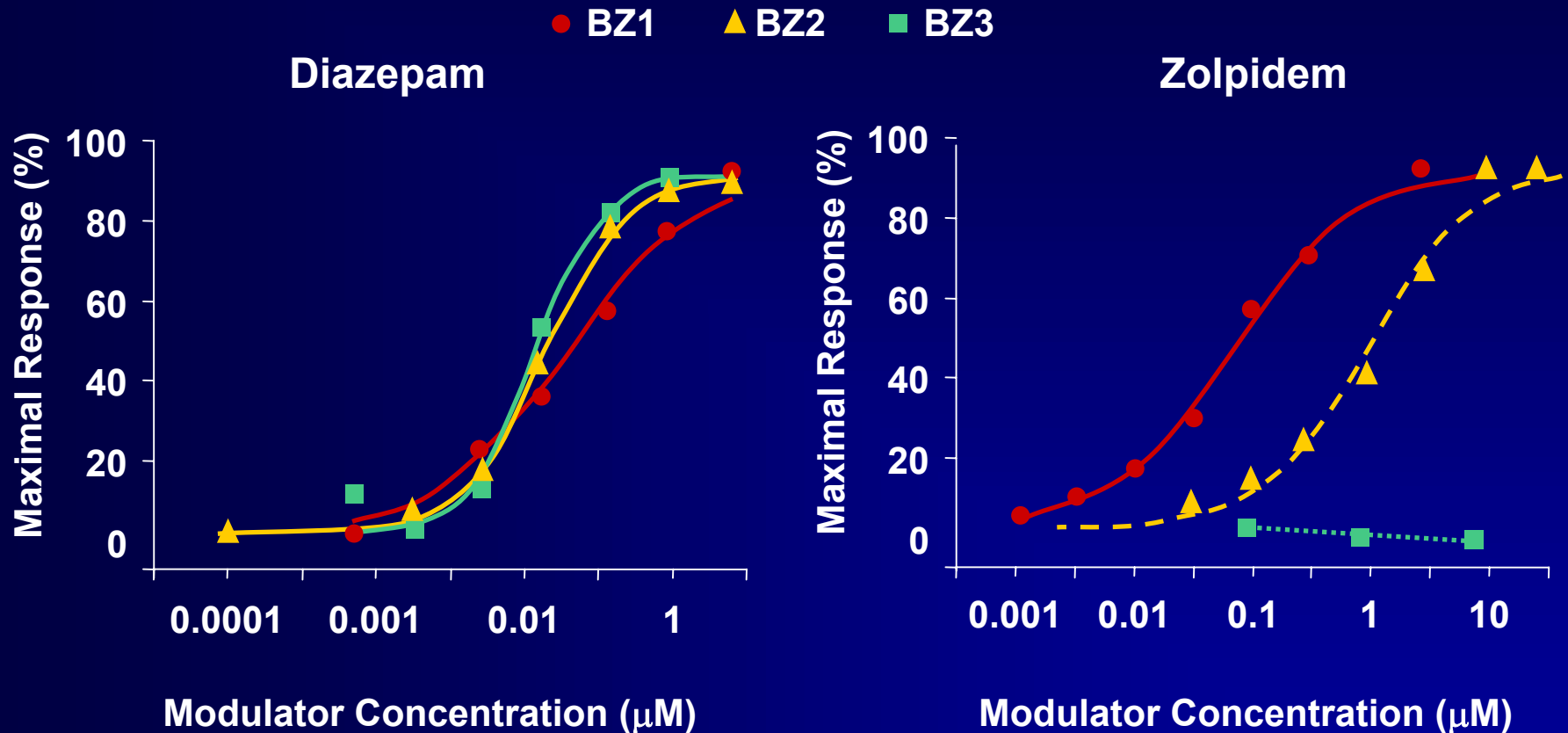
4. Holm KJ, Goa KL. *Drugs*. 2000;59:865-889

5. Kupfer DJ, Reynolds CF. *N Engl J Med*. 1997;336:341-346.

6. Jasinski DR, Preston DR. [citation TBD]; A189, abstract PP 06.04.

7. Soyka M et al. *Pharmacopsychiatry*. 2000;33:138-141.

# BZ1 Selectivity: Results With Zolpidem In Vitro



# Hypnotic Agents: Clinically Relevant Pharmacokinetics

---

- Short elimination half-life
  - Minimizes daytime sedation<sup>1,2</sup>
- Rapid onset
  - Helpful in sleep-onset insomnia<sup>1</sup>
- Absence of active metabolites
  - No metabolite accumulation/next-day effects<sup>1</sup>

1. Mitler MM. *Sleep*. 2000; 23(suppl 1):S39-S47.

2. Kupfer DJ, Reynolds CF. *N Engl J Med*. 1997;336:341-346.

# Benzodiazepines: Pharmacokinetics

Generic Name	Trade Name	Dose (mg) [elderly]	Half-Life (h)	Onset of Action (min)	Active Metabolites
Triazolam	Halcion®	0.125-0.25 [0.125]	2-5	15-30	No
Estazolam	ProSom™	1-2 [0.5-1]	8-24	15-60	No
Temazepam	Restoril®	15-30 [7.5-15]	8-20	45-60	No
Quazepam	Doral®	7.5-15 [7.5]	14-40*	20-45	Yes
Flurazepam	Dalmane®	15-30 [7.5]	47-100*	30-60	Yes

\*Half-life includes metabolites.

Mitler MM. *Sleep*. 2000;23(suppl 1):S39-S47.  
Doghramji K. *Sleep*. 2000;23(suppl 1):S16-S20.

# Non-benzodiazepines: Clinical Effects of Half-life

## Key Pharmacokinetics<sup>1</sup>

	Zolpidem	Zaleplon
Dose mg [elderly]	5-10 [5]	5-20 mg [5 mg]
Half-life (h)	1.5 - 4.5 hours	1
Onset (min)	30	15-30
Metabolites	No	No

## Clinical Findings<sup>2,3</sup>

	Zolpidem	Zaleplon
Sleep latency	↓	↓
Number of awakenings	↓	0
Total sleep time	↑	0

1. Mitler MM. *Sleep*. 2000; 23(suppl 1):S39-S47.

2. Ambien Full Prescribing Information.

3. Sonata Full Prescribing Information.