Updates on the Diagnosis and Treatment of Insomnia

Charles M. Morin, PhD
Professor of Psychology
Canada Research Chair (Behavioral Sleep Medicine)
Quebec City, Canada
cmorin@psy.ulaval.ca

UNIVERSITÉ LAVAL

Disclosures

Nature of Relationship	**Organization**
Grant/Research Support	Canadian Institutes of Health Research, National Institutes of Health, Fonds de Recherche en Santé du Québec, Novartis
Consultant/Advisory Board	Novartis, Merck, Valeant
Speaker	
Other	BeHealth Solutions

Learning Objectives

- Recognize clinical/diagnostic features of insomnia
- Identify approved medications for insomnia
- Learn cognitive-behavioral therapy principles
- Gain knowledge about benefits, risks, indications, and limitations of behavioral and pharmacological therapies for insomnia

Key Messages

- Insomnia is characterized by sleep dissatisfaction, difficulties initiating or maintaining sleep, and significant impairments of daytime functioning
- Drug therapy produces rapid relief of symptoms, but there is limited evidence of long-term benefits; it is best indicated for short-term insomnia.
- CBT is the treatment of choice for chronic insomnia. Sleep improvements take more time than with medication, but they are well sustained over time.

Diagnostic Criteria

Insomnia Disorder

- Dissatisfaction with sleep quality or duration
- Subjective difficulties initiating/maintaining sleep
- Insomnia (or daytime consequences) causes marked distress or significant impairment in social or occupational functioning
- Sleep difficulties are present 3 nights or more per week and for more than 3 months

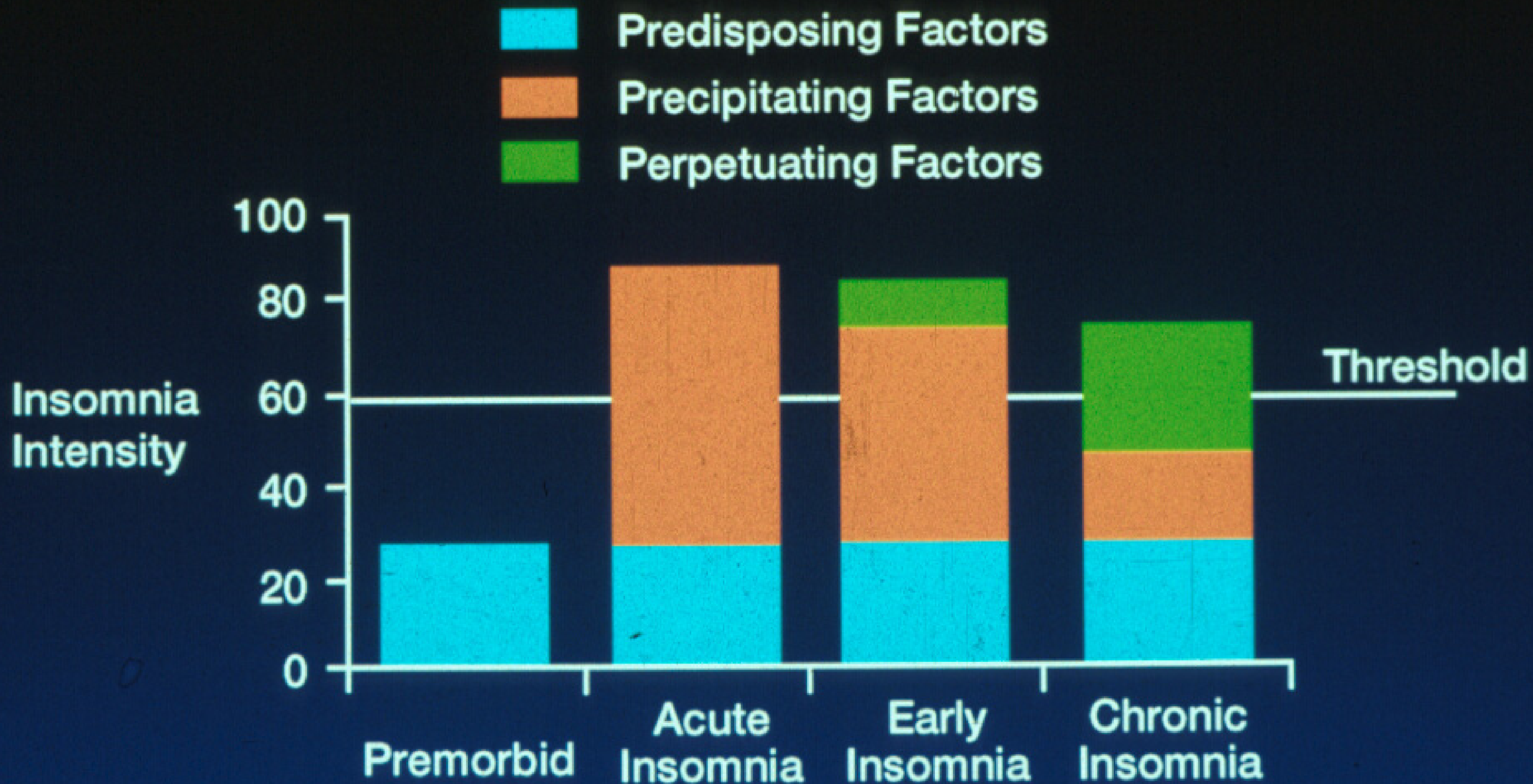
DSM5 no longer makes a distinction between primary and secondary insomnia

Burden of Persistent Insomnia

- Psychiatric – Increased risks of depression and suicide
- Health – Reduced QoL and increased risks of hypertension
- Occupational - Decreased job performance and increased absenteeism and risks of disability
- Economic - Increased use of health care services/costs
- Public Safety - Increased risks of accidents

Baglioni C et al. J Affect Disord 2011; 135:10-19; Laugsand et al. Circulation 2011; 124:2073-81.
Daley M et al. Economic burden of insomnia. Sleep 2009; 32:55-64.
Kyle S et al. Insomia and health-related quality of life. Sleep Med Rev 2010; 14:69-82.
Sivertsen et al. The long-term effect of insomnia on work disability. Am J Epidemiol 2006 163:1018–1024

The Natural History of Insomnia



Spielman AJ, Glovinsky P, 1991.

Treatment Options for Insomnia

- Pharmacotherapy
  - Benzodiazepine receptor agonists
  - Melatonin receptor agonists
  - Antidepressants
  - Antihistamines
- Cognitive Behavioral Therapy
- Complementary/alternative medicines (herbal, dietary supplements)

Current State of Evidence on Insomnia Therapies

NIH State of the Science Conference (2005)
British Association for Psychopharmacology Consensus Statement (2009)

- Treatments endorsed for chronic insomnia:
  - Cognitive Behavioral Therapy
  - Benzodiazepine Receptor Agonists (at least for short-term use)
  - Melatonin-Receptor Agonists (especially for older adults)
- All other treatments not endorsed due to limited evidence of efficacy and/or safety concerns:
  - Complementary and alternative preparations
  - Antihistamines (OTC and prescription)
  - Antidepressants
  - Antipsychotics

- NIH State-of-the-Science Conference Statement on Manifestations and Management of Chronic Insomnia in Adults (2005).
- British Association for Psychopharmacology Consensus Statement on Evidence-based Treatment of Insomnia, Parasomnias and Circadian Rhythm Disorders (2009).

What is Cognitive Behavioral Therapy (CBT)?

- CBT is a psychotherapeutic method aimed at changing behaviors (sleep schedules/habits) and cognitions (sleep worries, beliefs) that perpetuate insomnia
- CBT is brief (4-6 consultation visits), directive, and sleep-focused; it involves education and prescription for behavior changes
- CBT is based on a collaborative patient-therapist relationship (problem-solving focus)

Cognitive Behavioral Therapy

(Treatment Targets)

Behavioral

Sleep Restriction
Stimulus Control
Relaxation

Excessive time in bed
Irregular sleep schedules
Sleep incompatible activities
Hyperarousal

Cognitive

Cognitive Therapy
Paradoxical Intention

Unrealistic sleep expectations
Misconceptions about sleep
Sleep-related worries
Poor coping skills

Educational

Sleep Hygiene Education
Sleep Information

Inadequate sleep hygiene (caffeine, alcohol, exercise, environmental factors)

Behavioral/Sleep Scheduling Prescriptions

- Restrict time in bed to actual sleep time
- Go to bed only when sleepy
- Use the bed/bedroom for sleep only
- Get out of bed when unable to sleep
- Get up at the same time every morning
- Do not nap during the day

Objectives:

1) Reinforce the association between sleep and bedroom stimuli

2) Establish a regular sleep-wake rhythm and strenghten the homeostatic drive

Sleep Restriction

- Restrict time in bed (TIB) to actual sleep time
- Alter TIB based upon SE (by block of 15-20 min)
- Increase TIB if SE >90%; decrease TIB if SE <80%
- Modify the sleep window until optimal sleep duration is achieved
- Caution: do not use with patients presenting daytime sleepiness, seizures, bipolar disorder

SE=sleep efficiency; TIB = Time in Bed;

Cognitive Therapy Principles for Insomnia

- Identify faulty beliefs and attitudes about sleep and excessive worries about insomnia and its consequences
  - Unrealistic expectations (I must get 8 hours of slep)
  - Etiologic misconceptions (Insomnia is due to chemical imbalance)
  - Amplification of consequences (Unable to function if less than 8 hours sleep; insomnia may be detrimental to health)
  - Sleep promoting behaviors (Should stay in bed if can't sleep)
- Challenge validity of those beliefs with socratic dialogue and behavioral experiments
- Replace with more adaptive substitutes/perceptions

Summary of Outcome Evidence

- Benefits
  - 80% of patients benefit from CBT
  - 50%-60% symptom reductions (SOL, WASO)
  - 40% remission and 60% response rates (ISI)
  - Sleep changes well sustained over time
- Indications
  - Persistent insomnia, both primary and comorbid
  - Younger and older adults
  - Singly or as augmentation therapy to hypnotics

Morin et al. Cognitive-behavioral therapy, singly and combined with medication, for persistent insomnia. JAMA 2009; 301: 2005-15.
Morin CM, Benca R. Chronic insomnia. The Lancet 2012; *379;*1129-1141

Pharmacological Treatments

- Benzodiazepines/BzRAs
- Sedating antidepressants
- Antihistamines
- Melatonin receptor agonists
- Orexin receptor antagonists

Medications Indicated for the Treatment of Insomnia

Medication Class	Agent	$T_{1/2}$ (Hour)	Dose (mg)	
Benzodiazepines	Flurazepam	48-120	15-30	
	Temazepam	8-20	15-30	
	Triazolam	2-6	0.125-0.25	
	Estazolam	8-24	1-2	
	Quazepam	48-120	7.5-15	
Non-BZD	Zolpidem IR MR	1.5-2.4	5-12.5	
	Zaleplon	1	5-20	
	Eszopiclone	5-7	1-3	
Melatonin Agonist	Ramelteon	1.5-5	8	
Orexin Antagonist	Suvorexant	0.5-6	12-13	
Antidepressant	Doxepin	1.5-4	3-6	

Medications Used Off-Label for Insomnia

Medication Class	Agent	$T_{1/2}$ (h)	Dosage (mg)
Benzodiazepines	Alprazolam	12-24	0.25-2
	Clonazepam	35-40	0.25-2
	Lorazepam	12-15	0.5-2
Antidepressants	Amitriptyline	20-30	10-75
	Mirtazapine	20-40	15-45
	Trazodone	5-9	50-150
Antipsychotics	Olanzapine	21-54	5-10
	Quetiapine	6	25-200
	Risperidone	3-20	1-8
Anticonvulsants	Gabapentin	5-7	300-600
	Pregabalin	1	150-300

Effects of Benzodiazepine-Receptor Agonists on Sleep

- Sleep Continuity
  - Shorten SOL and WASO
  - Decrease number of awakening and stage shifts
  - Increase total sleep time
- Sleep Architecture
  - Decrease Stage 1 and increase Stage 2
  - Decrease Stages 3-4, REM Sleep
- Improve Subjective Sleep Quality

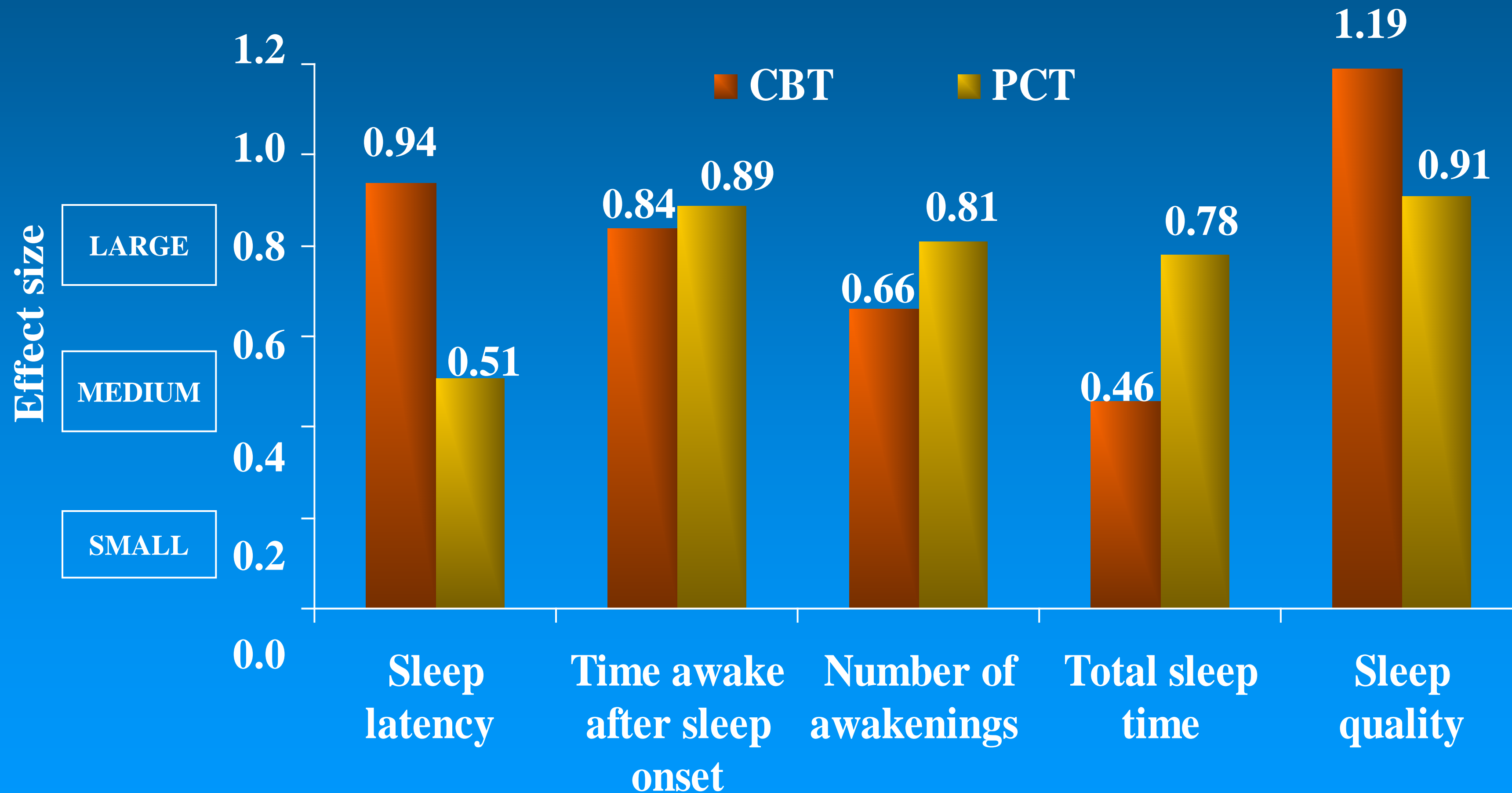
Krystal AD. A compendium of placebo-controlled trials of the risks/benefits of pharmaceutical treatments for insomnia: The empirical basis for U.S. clinical practice. Sleep Med Rev 2009; 13 265-74.

Risks/Limitations of BzRAs

- Next day residual sedation
- Cognitive and psychomotor impairments
- Tolerance
- Dependence (psychological)
- Rebound insomnia

These effects vary as a function of several factors: dose, half-life, duration of use, age and gender, and some psychological factors

Efficacy of Behavioral and Pharmacological Therapies



Morin et al., 1994; Murtagh & Greenwood, 1995; Nowell et al., 1997; Smith et al., 2002

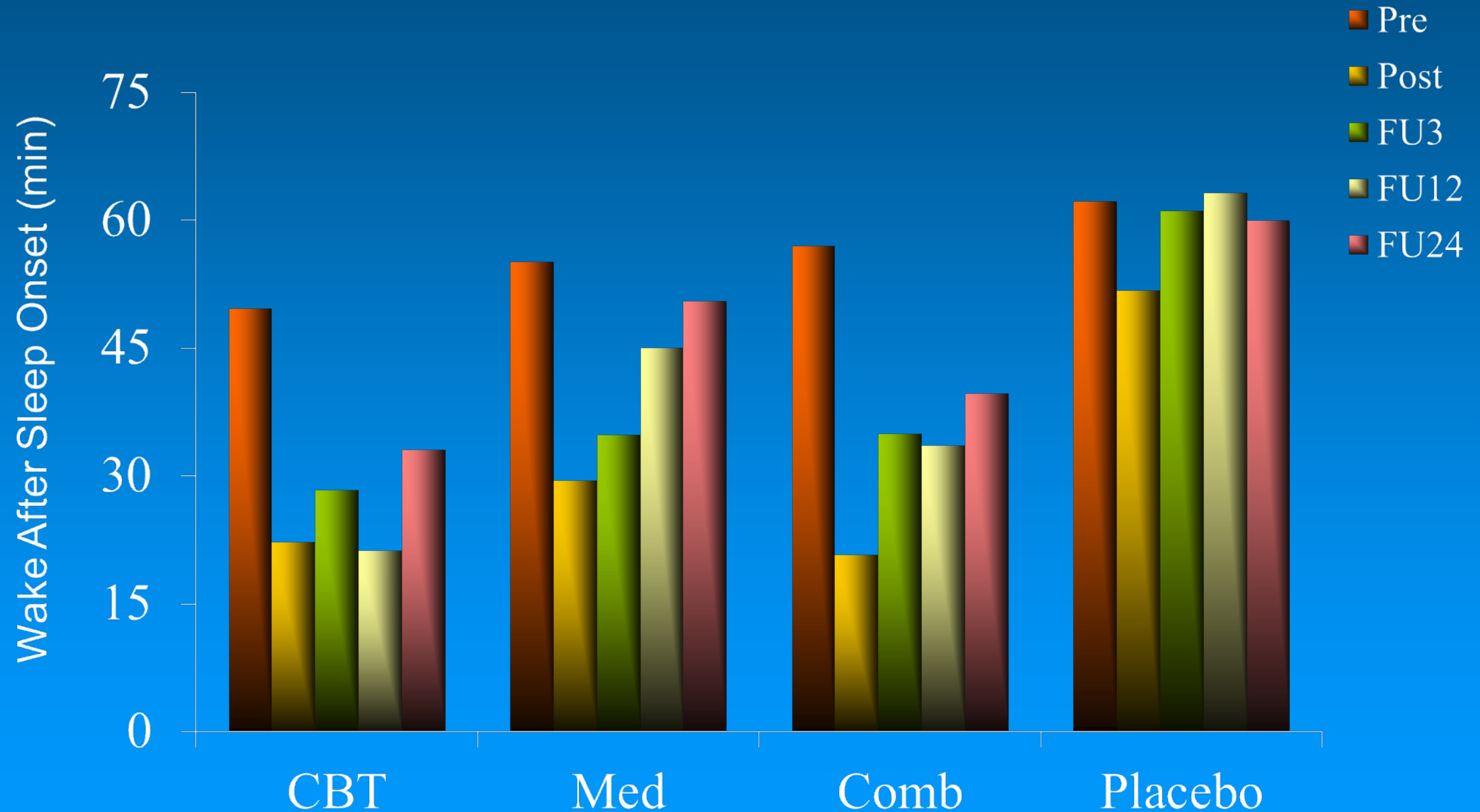
Benefits and Limitations of CBT and Medication for Insomnia

- Cognitive Behavioral Therapy
  - Efficacious, sustained improvements over time
  - Well accepted, few adverse effects
  - Requires time and motivation
  - Compliance may be a problem
- Medication
  - Efficacious, rapid symptomatic relief
  - Limited evidence of long-term efficacy
  - Potential risks for side effects
  - Concerns about dependency

No single treatment is effective or acceptable for all patients with insomnia

CBT, Medication, and Combined Therapies

(N = 76, mean age 66 y/o)



Morin et al. JAMA 1999; 281:991-999.

Combined/Sequential Therapies

- Potential advantages
  - Combines the rapid action of medication and the durability of CBT
  - Takes into account patient's preferences and potential impact of different insomnia phenotypes
- Disadvantages
  - Risk for attribution of sleep improvements to medication alone
  - May undermine compliance with CBT and the development of beneficial self-management skills
  - Risk of dependency on medication

What are the Essential Components ?

- Sleep diary monitoring
- Behavioral/sleep scheduling strategies
  - Restriction of time spent in bed
  - Postponing bedtime until sleep is imminent
  - Regular arising time regardless of sleep duration
  - Getting out of bed when not sleeping
- Education/information about sleep/insomnia
  - Appropriate age-related sleep expectations
  - Sleep-related worries
  - Misconceptions about sleep and insomnia

Key Points/Conclusions

- Insomnia is a prevalent clinical complaint that often presents with other medical and psychiatric disorders
- Persistent insomnia carries significant long-term morbidity
- Approved medications for insomnia provide rapid symptomatic improvements, but there is limited evidence of sustained benefits after drug discontinuation or sustained benefits with prolonged use
- CBT is efficacious, produces sustained benefits, and is well accepted by patients