

The Talk

1. Clinical Assessment & Classification
2. Insomnia
3. Mood Disorders

Assessment & Overview of Sleep Disorders

Introduction

Normal human sleep comprises two states-non-rapid eye movement (NREM) and REM sleep-that alternate cyclically across a sleep episode.

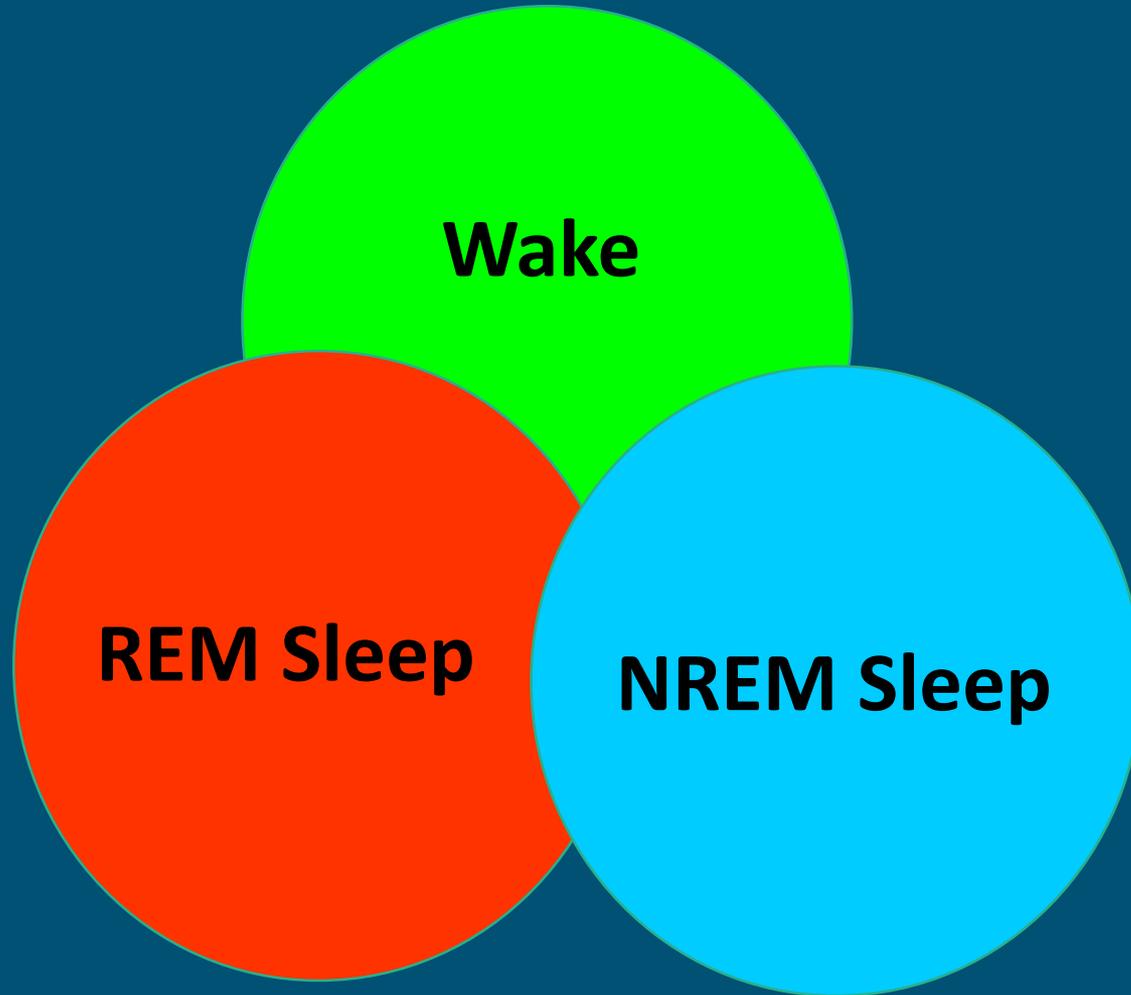
NREM sleep includes a variably synchronous cortical electroencephalogram (EEG; including sleep spindles, K-complexes, and slow waves) associated with low muscle tones and minimal psychological activity;

In REM sleep the EEG is desynchronized, muscles are atonic, and dreaming is typical.

In adult humans sleeping on a regular schedule the nightly cycle includes several reliable characteristics:

- Sleep begins in NREM and progresses through deeper NREM stages (stages 2, 3, and 4) before the first episode of REM sleep approximately 80 to 100 minutes later.
- Thereafter, NREM sleep and REM sleep cycle with a period of approximately 90 minutes.
- NREM stages 3 and 4 concentrate in the early NREM cycles, and REM sleep episodes lengthen across the night.

States of Being

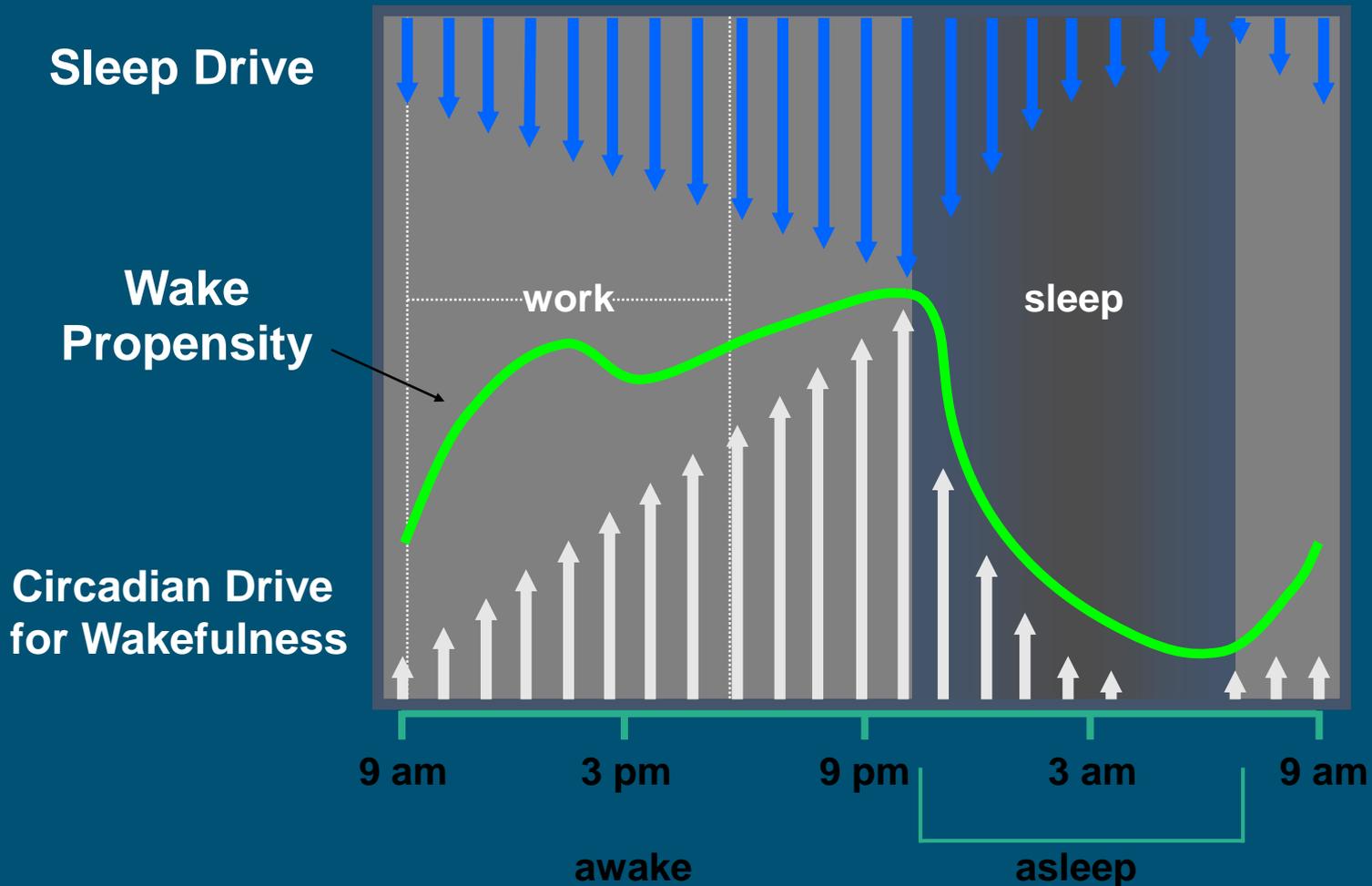


REM vs. NREM Sleep

<u>Physiologic Variable</u>	<u>NREM</u>	<u>REM</u>
• Heart rate	Regular	Irregular
• Respiratory rate	Regular	Irregular
• Blood pressure	Regular	Variable
• Skeletal muscle tone	Preserved	Absent
• Brain O ₂ consumption	Reduced	Increased
• Response to CO ₂	Same as W	Depressed
• Response to O ₂	Same as W	Same as W
• Temperature	Homeothermic	Poikilothermic
• Penile tumescence, Vaginal engorgement	Infrequent	Frequent

Physiologic Determinants of Sleepiness

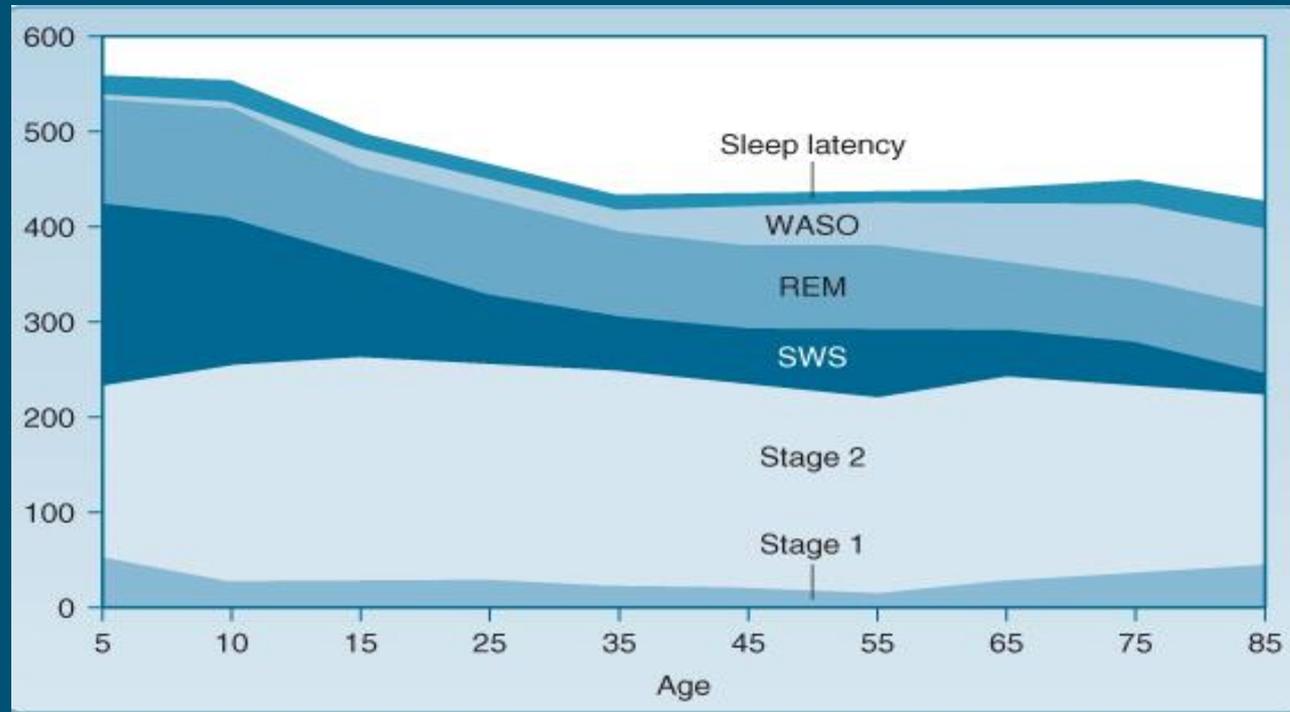
Normal Sleepiness



In Summary

- Sleep is entered through NREM sleep.
- NREM sleep and REM sleep alternate with a period near 90 minutes.
- SWS predominates in the first third of the night and is linked to the initiation of sleep.
- REM sleep predominates in the last third of the night and is linked to the circadian rhythm of body temperature.
- Wakefulness in sleep usually accounts for less than 5% of the night.
- Stage 1 : 2% to 5% of sleep.
- Stage 2 : 45% to 55% of sleep.
- Stage 3 : 3% to 8% of sleep.
- Stage 4 : 10% to 15% of sleep.
- NREM sleep is therefore 75% to 80% of sleep.
- REM sleep is usually 20% to 25% of sleep, occurring in four to six discrete episodes

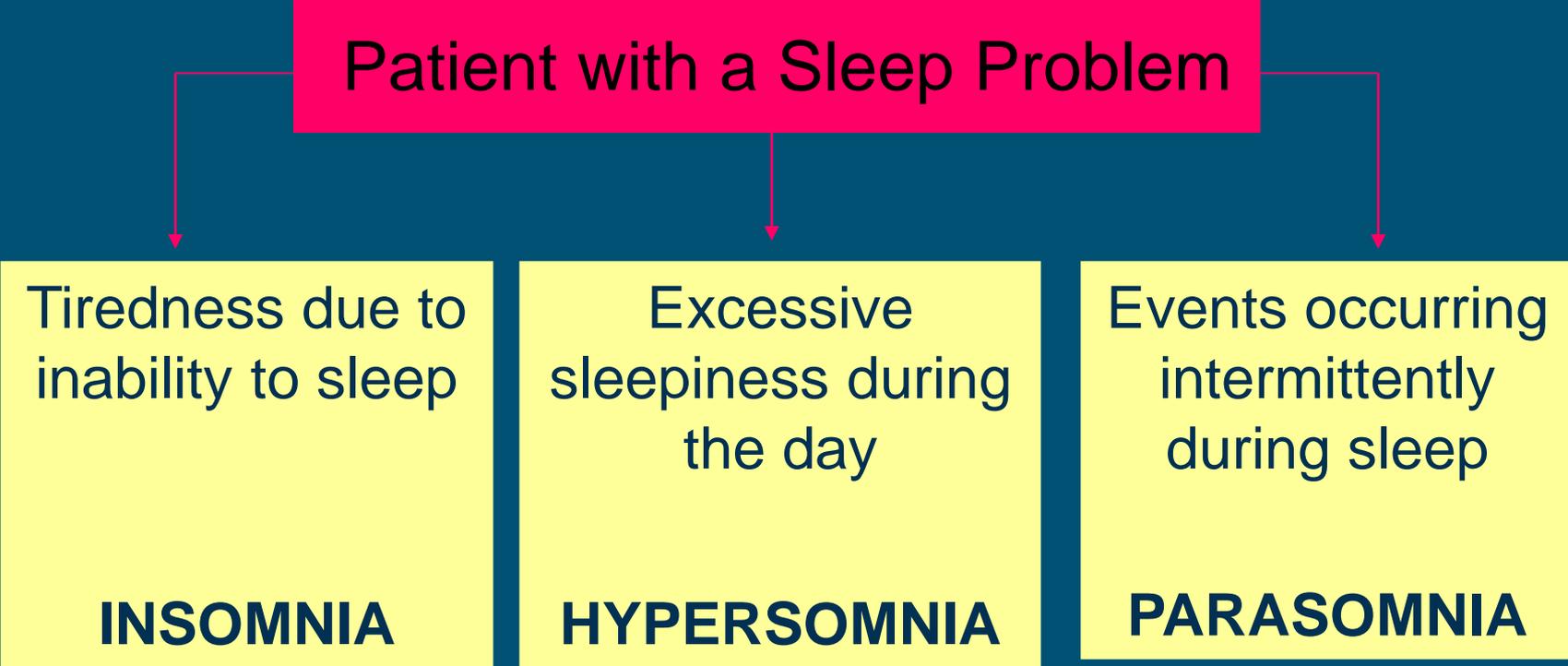
Changes with Age



Time (in minutes) for sleep latency and wake time after sleep onset (WASO) and for rapid eye movement (REM) sleep and NREM sleep stages 1, 2, and slow wave sleep (SWS). Summary values are given for ages 5 to 85 years. (Ohayon M, et al. Sleep 2004;27:1255-1273.)

Assessment of Sleep Disorders

Patient with a Sleep Problem



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graph TD; A[Patient with a Sleep Problem] --> B[Tiredness due to inability to sleep]; A --> C[Excessive sleepiness during the day]; A --> D[Events occurring intermittently during sleep]; B --- E[INSOMNIA]; C --- F[HYPERMOMNIA]; D --- G[PARASOMNIA];
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Tiredness due to inability to sleep

INSOMNIA

Excessive sleepiness during the day

HYPERMOMNIA

Events occurring intermittently during sleep

PARASOMNIA

The Patient Pathway

1. Medical Assessment
2. Subjective Questionnaire Based Evaluation
3. Sleep Studies and Investigations
4. Diagnostic Review
5. Therapeutic Intervention

Taking a History from the Sleep Patient

- Nature of Sleep problem:
- EDS
- Fragmented Sleep
- Difficulty waking
- Difficulty maintaining sleep
- ESS Score ___/24

Nocturnal Symptoms:

- Snoring
- Pauses in breathing
- PLM's
- Sleep walk/talk
- Vivid dreams/nightmares
- Hypnagogic hallucinations

Daytime Symptoms

- Poor concentration
- Irritable
- Memory loss
- Sleep Paralysis
- Cataplexy

• Duration of Sleep Problem

- (? Trigger event)

• Progression:

• Family Hx?

• Timing:

- Bedtime Get up time (w/days)

- Bedtime Get up time (w/ends)

- How long to drop off?

- Daytime napping? (Refreshing/unrefreshing?)

• Bedroom environment?

• Lifestyle:

- Smoking caffeine

- Alcohol Exercise

- PMH Physical Exam:

- Meds Mental state

Investigations to order:

Sleep studies:

Bloods:

Chem pathology:

Radiology:

Taking a History from the Sleep Patient

YOUR SLEEP SYMPTOMS (Please tick all that apply)

- | Sleep Loss | Daytime Symptoms | Nighttime Disturbances
(Self reported or by partner) |
|--|--|---|
| <input type="checkbox"/> Find it difficult to fall asleep | <input type="checkbox"/> Fall asleep at inappropriate times | <input type="checkbox"/> Stop breathing during sleep |
| <input type="checkbox"/> Wake often during the night | <input type="checkbox"/> Tiredness interferes with life | <input type="checkbox"/> Legs jerk before or during sleep |
| <input type="checkbox"/> Have trouble returning to sleep | <input type="checkbox"/> Sleep more than 9 hours in one day | <input type="checkbox"/> Vivid dreams/nightmares |
| <input type="checkbox"/> Feel tired upon waking in the morning | <input type="checkbox"/> Driving accidents or other accidents | <input type="checkbox"/> Very loud snorer |
| <input type="checkbox"/> Sleep routine differs each day | <input type="checkbox"/> Fall asleep unintentionally during the day | <input type="checkbox"/> Grind teeth in sleep |
| <input type="checkbox"/> Travel disrupts sleep | <input type="checkbox"/> Irritable during the day | <input type="checkbox"/> Jaws ache in the morning |
| <input type="checkbox"/> Shift work or night work disrupts sleep | <input type="checkbox"/> Nap intentionally | <input type="checkbox"/> Nocturnal seizures (fits) |
| <input type="checkbox"/> Sleep with light on | <input type="checkbox"/> Awaken with headaches | <input type="checkbox"/> Get out of bed whilst dreaming |
| <input type="checkbox"/> Sleep with the light on or in a noisy environment | <input type="checkbox"/> Sudden feeling of weakness in the knees or legs | <input type="checkbox"/> Kick or twitch during sleep |
| <input type="checkbox"/> Bed partner disrupts sleep | <input type="checkbox"/> Can't concentrate or remember | <input type="checkbox"/> Wake suddenly with intense anxiety or dread |
| <input type="checkbox"/> Exercise within 2 hours of going to bed | <input type="checkbox"/> Dreams or hallucinations while awake | <input type="checkbox"/> Snore loudly and stop breathing during sleep |
| <input type="checkbox"/> Drink tea-coffee after 2pm | | <input type="checkbox"/> Night sweats |
| <input type="checkbox"/> Stay awake/can't sleep due to worry | | <input type="checkbox"/> Sleepwalking |
| <input type="checkbox"/> Sleep better in unfamiliar setting | | <input type="checkbox"/> Waking gasping or choking |
| <input type="checkbox"/> Trouble sleeping due to hot | | |
| <input type="checkbox"/> Trouble sleeping due to pain | | |

Questionnaire Based Evaluation

- ESS
- FSS
- RLS Criteria

The Epworth Sleepiness Scale

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 the things recently, try to work out how they would have affected you. Use the following scale to choose the appropriate number for each situation:

- 0 = Would NEVER Doze
- 1 = SLIGHT CHANCE of dozing
- 2 = MODERATE chance of dozing
- 3 = HIGH chance of dozing

SITUATION	CHANCE OF DOZING
Date	
Sitting and Reading	
Watching Television	
Sitting inactive in a public place	
As a passenger in a car for one hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after lunch without alcohol	
In a car while stopped for a few minutes in traffic	
Total Score:	

Fatigue Severity Scale

The Fatigue Severity Scale (FSS)

This questionnaire contains nine statements that rate the severity of your fatigue symptoms. Read each statement and circle a number from 1 to 7, based on how accurately it reflects your condition during the past week and the extent to which you agree or disagree that the statement applies to you. A low value (e.g. 1) indicates strong disagreement with the statement, whereas a high value (e.g. 7) indicates strong agreement.

During the past week I have found that:	DISAGREE: _____						
	AGREE: _____						
1. My Motivation is lower when I am fatigued	1	2	3	4	5	6	7
2. Exercise brings on my fatigue	1	2	3	4	5	6	7
3. I am easily fatigued	1	2	3	4	5	6	7
4. Fatigue interferes with my physical functioning	1	2	3	4	5	6	7
5. Fatigue causes frequent problems for me	1	2	3	4	5	6	7
6. My fatigue prevents sustained physical functioning	1	2	3	4	5	6	7
7. Fatigue interferes with carrying out certain duties and responsibilities	1	2	3	4	5	6	7
8. Fatigue is among my three most disabling symptoms	1	2	3	4	5	6	7
9. Fatigue interferes with my work, family or social life	1	2	3	4	5	6	7
TOTAL SCORE:							

IRLSSG Criteria

RLS CRITERIA

	Yes	No
Question 1 Do you have, or have you ever had, an urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs?	<input type="checkbox"/>	<input type="checkbox"/>
Question 2 Do you have, or have you ever had, the urge to move or unpleasant sensations in the legs that begin or worsen during periods of rest or inactivity, such as lying down or sitting?	<input type="checkbox"/>	<input type="checkbox"/>
Question 3 Do you have, or have you ever had, an urge to move or unpleasant sensations in the legs that are partially or totally relieved by movement, such as walking or stretching, for at least as long as the activity continues?	<input type="checkbox"/>	<input type="checkbox"/>
Question 4 Do you have, or have you ever had, an urge to move or unpleasant sensations in the legs that are worse during the evening or night than they are during the day or that only occur during the evening or night?	<input type="checkbox"/>	<input type="checkbox"/>

TOTAL SCORE:

/4

Sleep Studies & Investigations

- Screening Tests
 - Oximetry
 - Actigraphy
- Diagnostic Tests
 - Sleep Apnoea Diagnostic Study
 - Nocturnal Polysomnography (NPSG)
 - NPSG + MSLT
- Therapeutic Testing
 - CPAP Titration

Screening Oximetry

- Useful as a screening utility
- Low Sensitivity for Mild to Moderate OSA
- High Sensitivity for Severe OSA

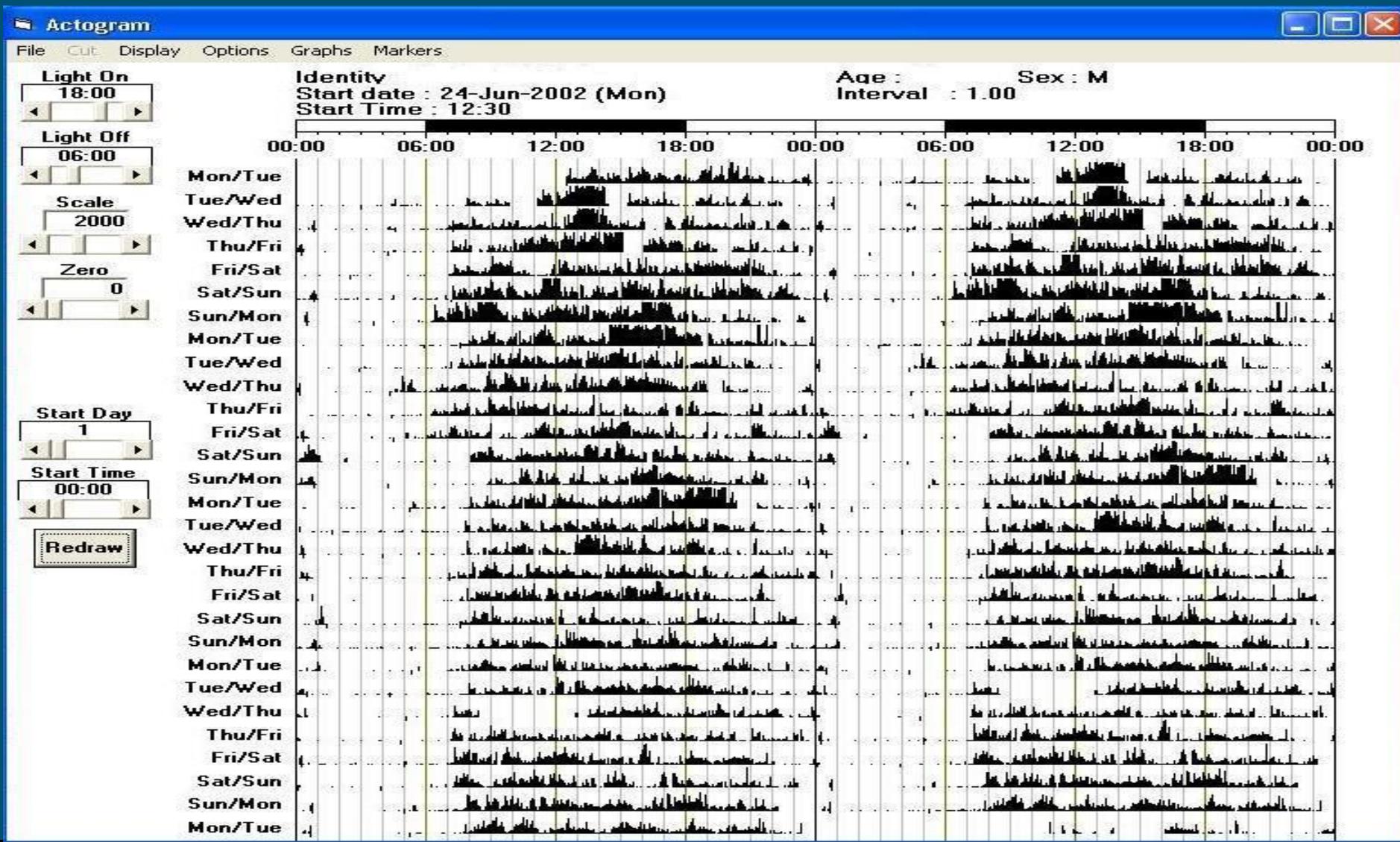


Screening - Actigraphy

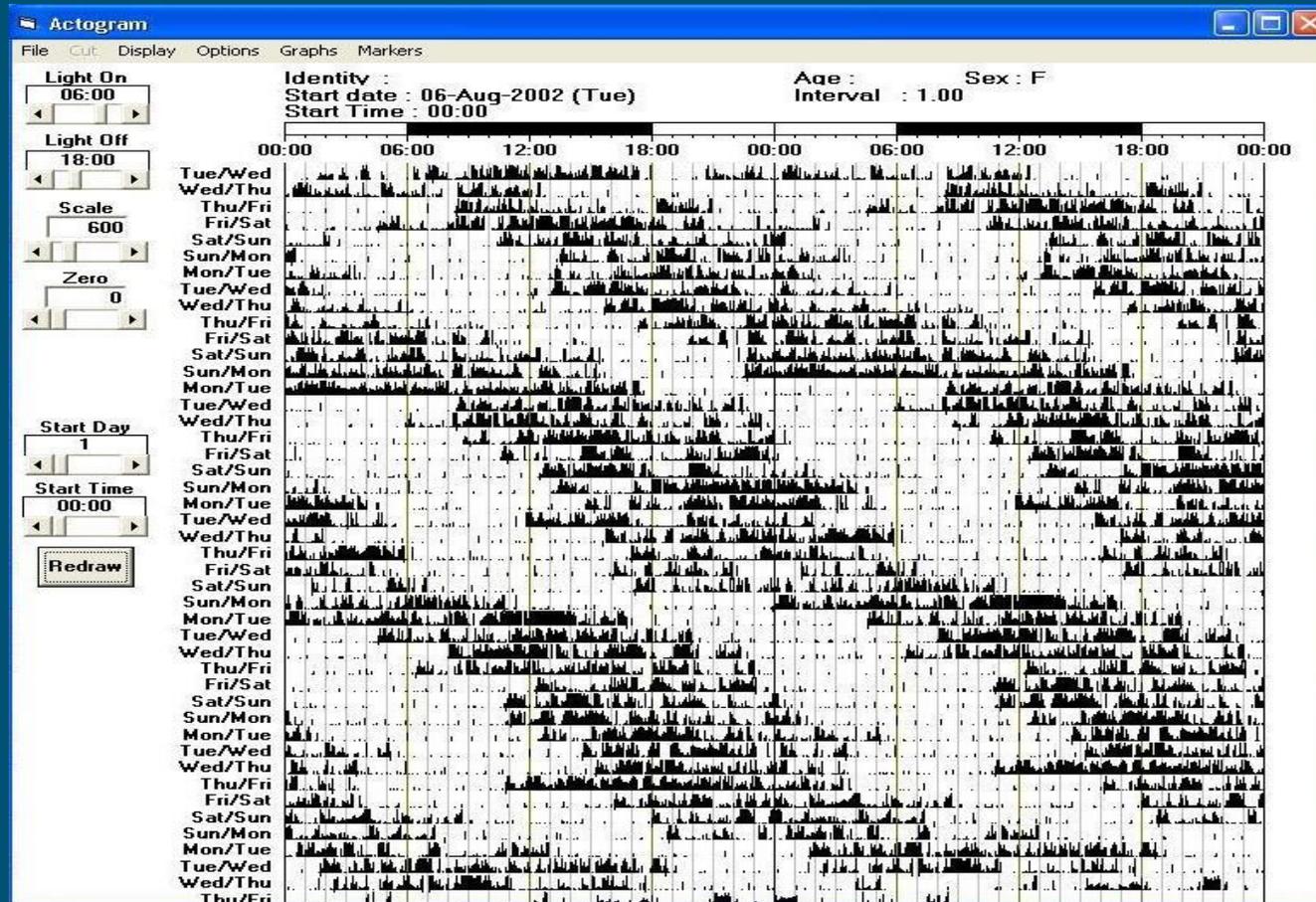
- Useful for assessing Circadian Rhythm Disorders
- Some utility in the screening of Insomnia and for monitoring response to treatment



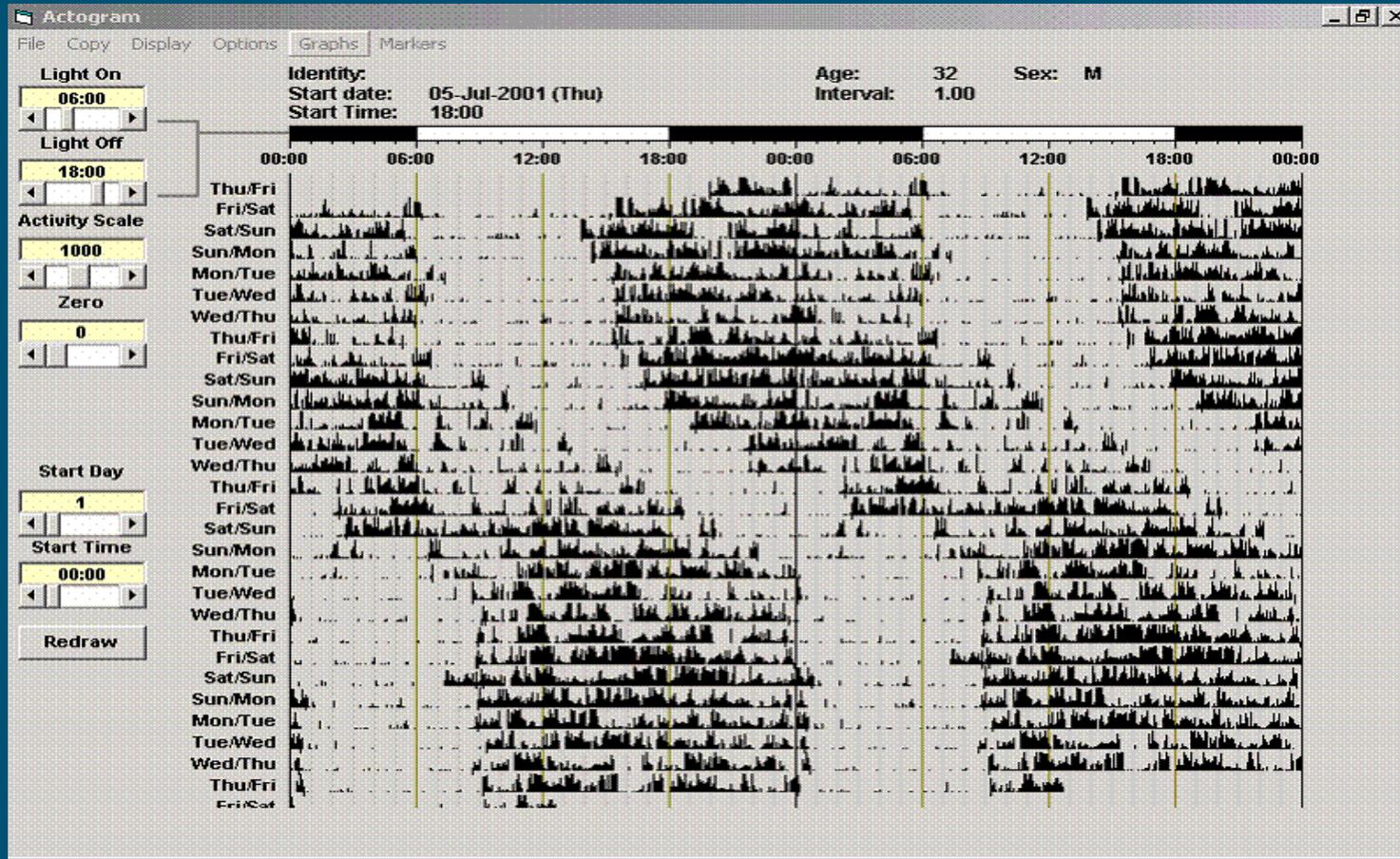
Normal Actogram



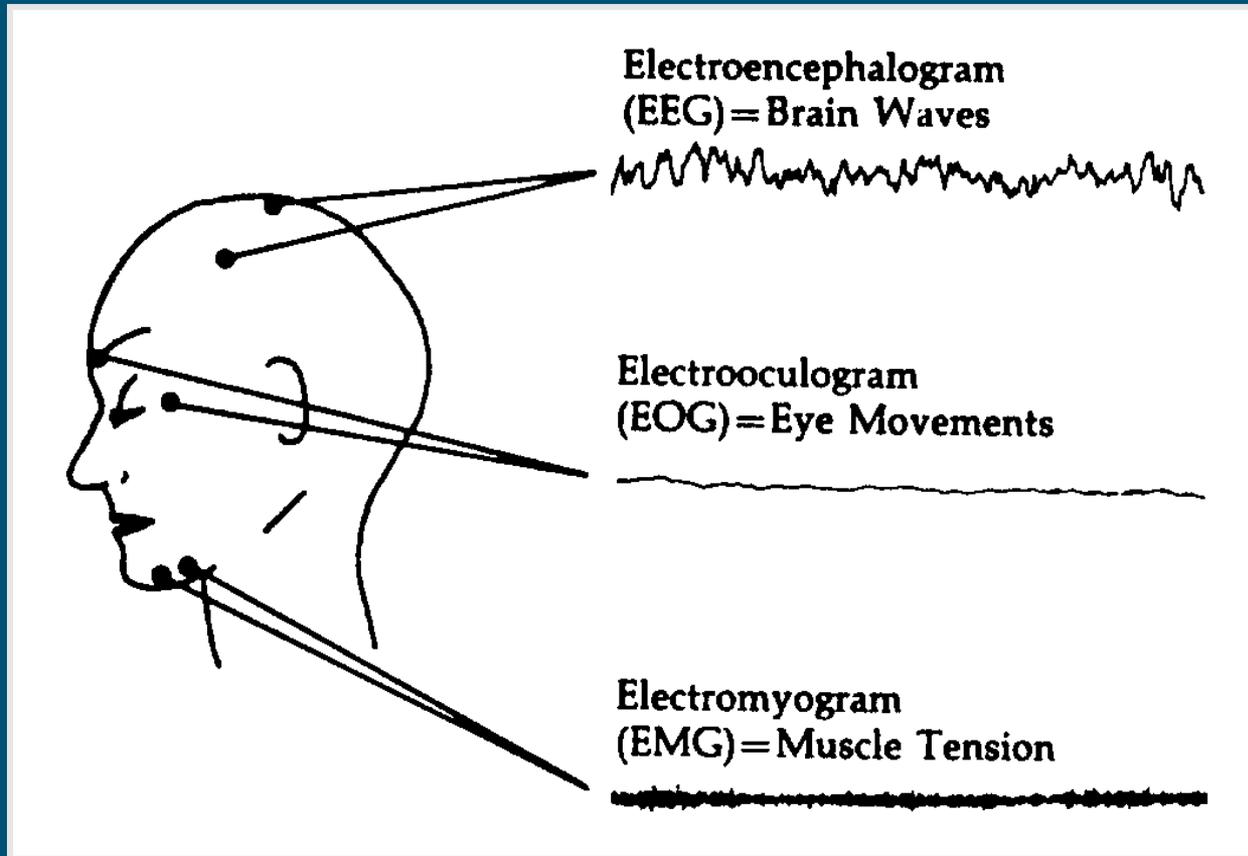
Abnormal Actogram



Light Therapy to Entrain Sleep Pattern



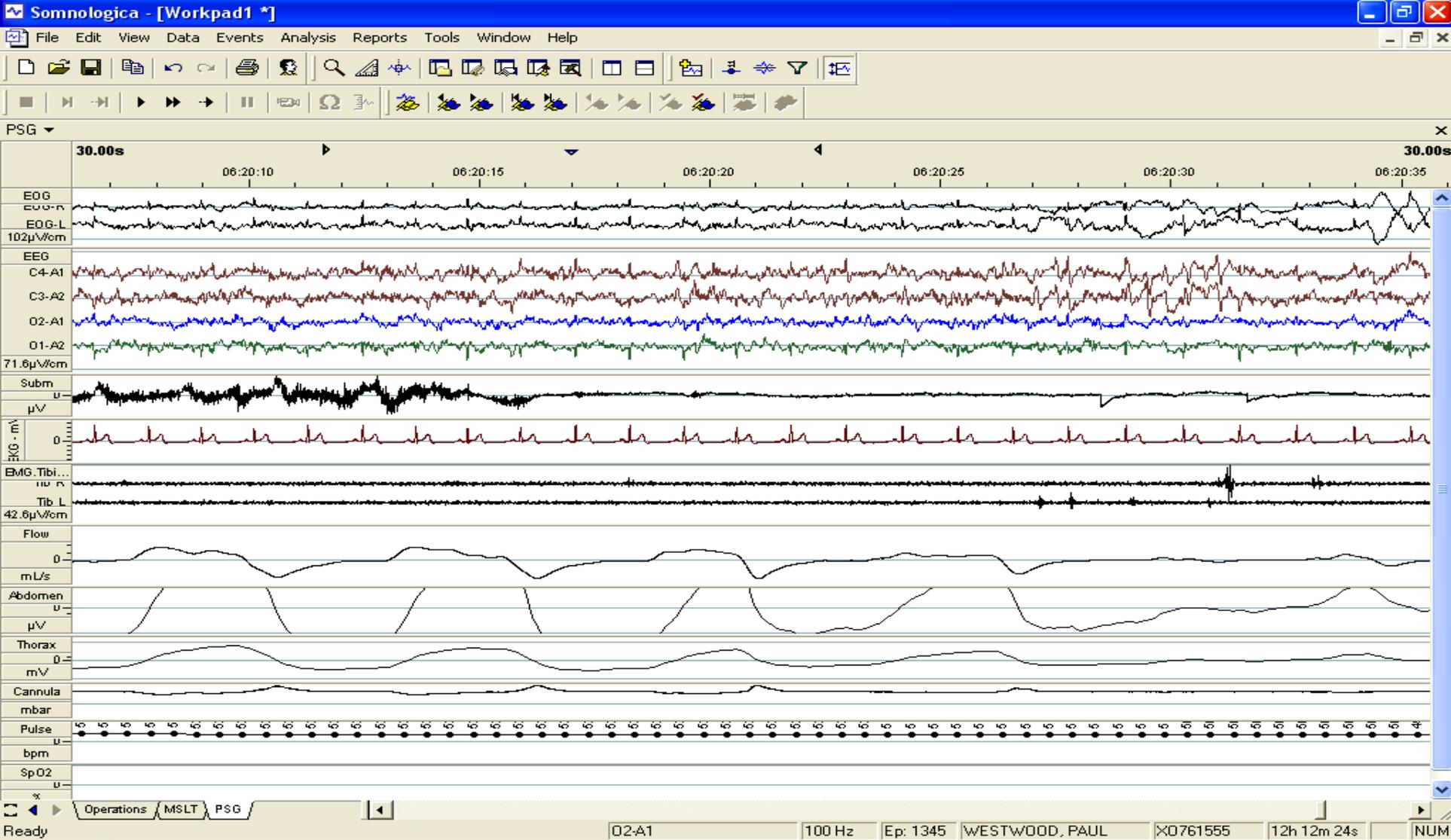
Diagnostic Sleep Studies



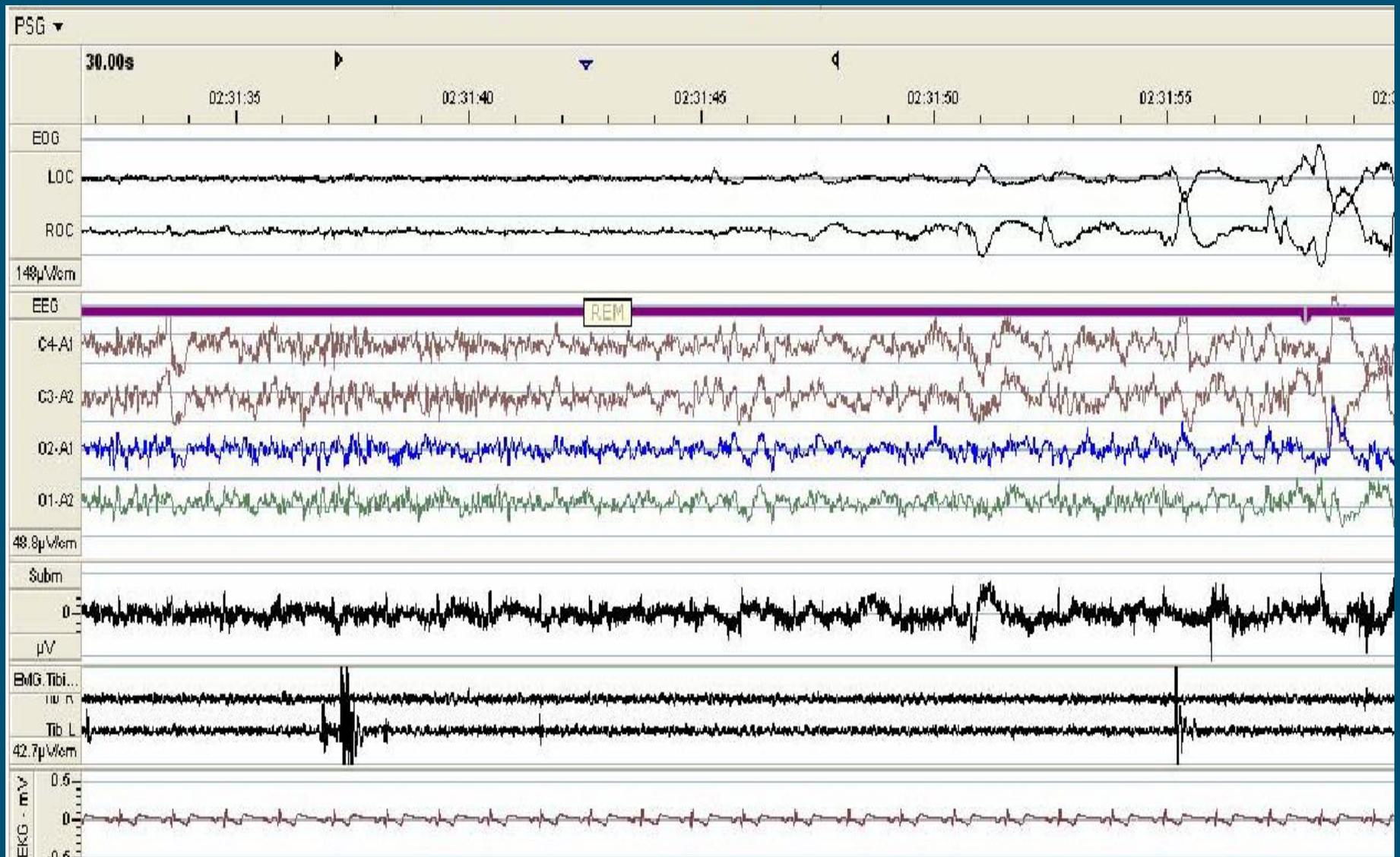
Diagnostic Sleep Studies - PSG

- EEG
- EMG – Submental, Tibial
- Eye movements
- Pulse Oximetry
- Airflow
- Thoracic and Abdominal movements
- Sound
- Digital Video

Normal SWS – REM Transition



Loss of REM Atonia

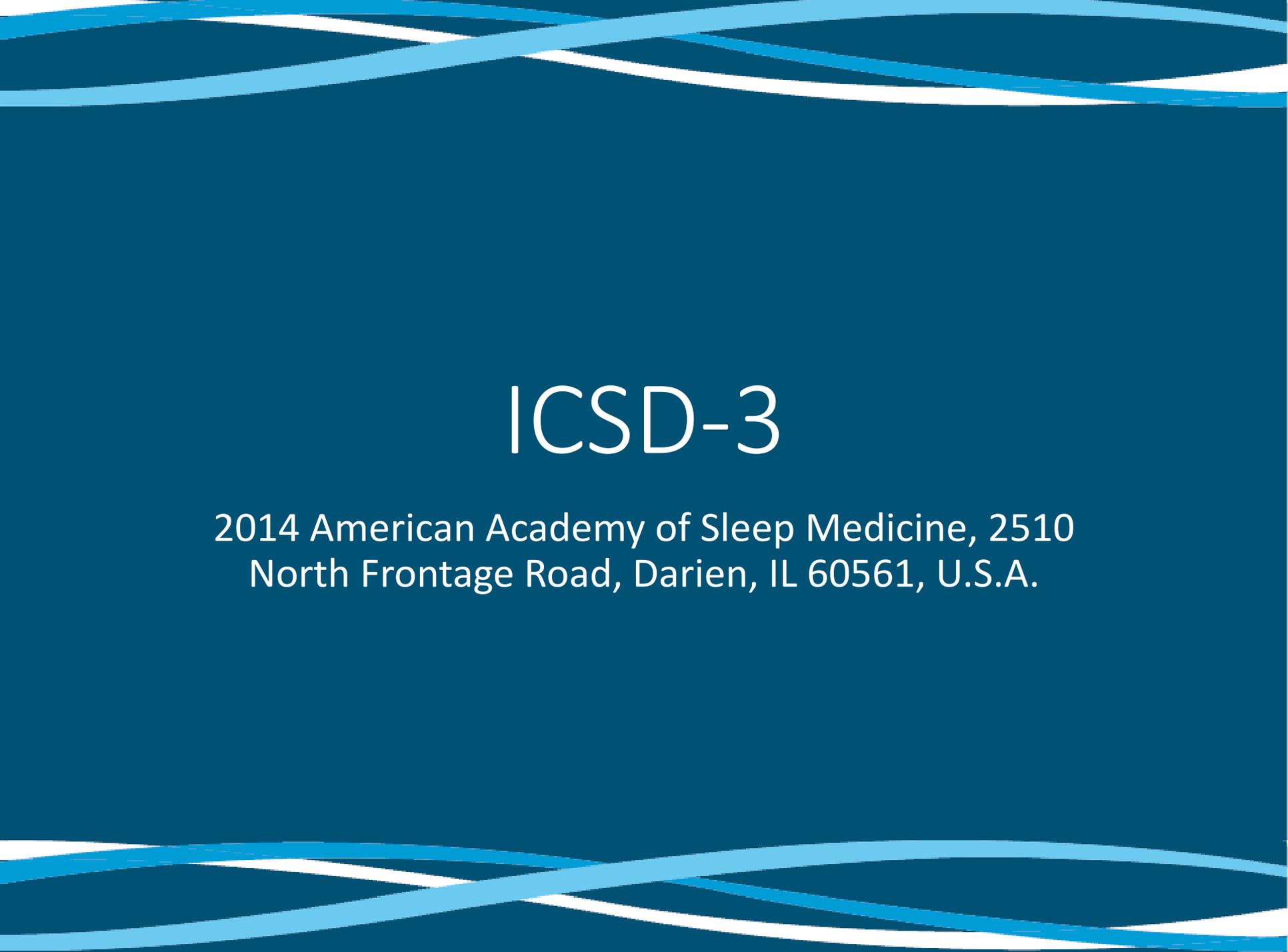


Diagnostic Review & Therapeutic Interventions

- The primary influence on diagnosis is the Clinical presentation of the PATIENT combined with objective data from Sleep Studies and other Investigations.
- Our Diagnostic Formulation includes a thorough evaluation of all Biological – Psychological – and – Social influences on the patient.
- Therapeutic Intervention is therefore geared at all these levels to provide a positive outcome and improve the prognosis

ICSD-2: Hypersomnias of Central Origin

- Narcolepsy with cataplexy (Type 1 – ICSD-3)
- Narcolepsy without cataplexy (Type 2 – ICSD-3)
- Narcolepsy due to a medical condition i.e. symptomatic e.g. tumor(29%), MS(10%), head trauma(17%)
- Idiopathic hypersomnia with long sleep time
- Idiopathic hypersomnia without long sleep time
- Hypersomnia due to drug or substance



ICSD-3

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ICSD-3 Categories

- Insomnia
- Sleep Related Breathing Disorders
- Central Disorders of Hypersomnolence
- Circadian Rhythm Sleep-Wake Disorders
- Parasomnias
- Sleep Related Movement Disorders

Sleep Related Breathing Disorders

- OSA
- CSA
- Sleep Related Hypoventilation Disorders
- Sleep Related Hypoxemia Disorder
- Isolated Symptoms and Normal Variants

OSA

- **Diagnostic Criteria: (A and B) or C satisfy the criteria**

- A. The presence of one or more of the following:

- 1. The patient complains of sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms.
- 2. The patient wakes with breath holding, gasping, or choking.
- 3. The bed partner or other observer reports habitual snoring, breathing interruptions, or both during the patient's sleep.
- 4. The patient has been diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus.

- B. Polysomnography (PSG) or OCST1 demonstrates:

- 1. Five or more predominantly obstructive respiratory events² (obstructive and mixed apneas, hypopneas, or respiratory effort related arousals [RERAs])³ per hour of sleep during a PSG or per hour of monitoring (OCST).¹
- OR

- C. PSG or OCST1 demonstrates:

- Fifteen or more predominantly obstructive respiratory events (apneas, hypopneas, or RERAs)³ per hour of sleep during a PSG or per hour of monitoring (OCST).

CSA Syndromes

- Central Sleep Apnea with Cheyne-Stokes Breathing
- Central Apnea Due to a Medical Disorder without Cheyne-Stokes Breathing
- Central Sleep Apnea Due to High Altitude Periodic Breathing
- Central Sleep Apnea Due to a Medication or Substance
- Primary Central Sleep Apnea
- Primary Central Sleep Apnea of Infancy
- Primary Central Sleep Apnea of Prematurity
- Treatment-Emergent Central Sleep Apnea

Central Sleep Apnea with Cheyne-Stokes Breathing

Diagnostic Criteria: (A or B) + C + D satisfy the criteria

A. The presence of one or more of the following:

- 1. Sleepiness.
- 2. Difficulty initiating or maintaining sleep, frequent awakenings, or nonrestorative sleep.
- 3. Awakening short of breath.
- 4. Snoring.
- 5. Witnessed apneas.

B. The presence of atrial fibrillation/flutter, congestive heart failure, or a neurological disorder.

C. PSG (during diagnostic or positive airway pressure titration) shows all of the following:

- 1. Five or more central apneas and/or central hypopneas per hour of sleep.
- 2. The total number of central apneas and/or central hypopneas is > 50% of the total number of apneas and hypopneas.
- 3. The pattern of ventilation meets criteria for Cheyne-Stokes breathing (CSB).

D. The disorder is not better explained by another current sleep disorder, medication use (e.g., opioids), or substance use disorder.

Central Disorders of Hypersomnolence

- Narcolepsy Type 1 (NC)
- Narcolepsy Type 2 (N)
- Idiopathic Hypersomnia
- Kleine-Levin Syndrome
- Hypersomnia Due to a Medical Disorder
- Hypersomnia Due to a Medication or Substance
- Hypersomnia Associated with a Psychiatric Disorder
- Insufficient Sleep Syndrome

The Narcoleptic Syndrome

Narcolepsy is a primary disorder of alertness with an estimated prevalence of 0.03 - 0.05%. Onset may occur at any age with a peak onset in adolescence and a secondary peak in the fourth decade.

The presenting symptom is usually **Excessive Daytime Sleepiness (EDS)**, with irresistible sleep attacks during the day.

Other symptoms of this syndrome are **cataplexy** (brief episodes of muscle weakness or paralysis precipitated by strong emotion, such as laughter or surprise),

sleep paralysis which is a symptom due to the persistence of REM sleep atonia on waking and,

hypnagogic hallucinations or dream like images, which characteristically occur at sleep onset.

Periods of brief automatic behaviour may also occur, a reflection of brief intrusions of sleep ('micro-sleeps') into the drowsy state

Disrupted night-time sleep is becoming accepted as a further cardinal manifestation

Narcolepsy

- A: The patient has a complaint of EDS occurring almost daily for at least 3 months
- B: A definite history of Cataplexy, defined as sudden and transient episodes of loss of muscle tone triggered by emotions
- C:
- NPSG/MSLT: Nocturnal Sleep of at least 6 hours followed by MSLT that shows a mean Sleep Latency of < 8minutes and at least two Sleep Onset REM Periods OR a SOREM on the PSG and a Minimum of 1 SOREM on MSLT
- OR**
- CSF Hypocretin levels < 110pg/ml
- D: Absence of medical or other sleep condition

ICSD-3 Criteria For Narcolepsy

- International Classification of Sleep Disorders Third Edition (ICSD-3). DSM-5 criteria require EDS in association with any one of the following: (1) cataplexy; (2) CSF hypocretin deficiency; (3) REM sleep latency ≤ 15 minutes on nocturnal polysomnography (PSG); or (4) mean sleep latency ≤ 8 minutes on multiple sleep latency testing (MSLT) with ≥ 2 sleep-onset REM-sleep periods (SOREMPs).

ICSD-3 Criteria For Narcolepsy

- ICSD-3 relies more upon objective data in addition to EDS:
- 1) cataplexy and either positive MSLT/PSG findings or CSF hypocretin deficiency;
- 2) MSLT criteria similar to DSM-5 except that a SOREMP on PSG may count as one of the SOREMPs required on MSLT; and
- 3) distinct division of narcolepsy into **type 1**, which requires the presence of cataplexy or documented CSF hypocretin deficiency, and **type 2**, where cataplexy is absent, and CSF hypocretin levels are either normal or undocumented.

NREM Parasomnias

Disorders of Arousal (From NREM Sleep)

- Confusional Arousals – (NOT in DSM-5)
- Sleepwalking
- Sleep Terrors
- Sleep Related Eating Disorder (Sleep Related Sexual Behaviour – IN DSM-5)



REM-Related Parasomnias

- REM Sleep Behavior Disorder
- Recurrent Isolated Sleep Paralysis
- Nightmare Disorder

Other Parasomnias

- Exploding Head Syndrome
- Sleep Related Hallucinations
- Sleep Enuresis
- Parasomnia Due to a Medical Disorder
- Parasomnia Due to a Medication or Substance
- Parasomnia, Unspecified

Sleep Related Movement Disorders

- Restless Legs Syndrome
- Periodic Limb Movement Disorder
- Sleep Related Leg Cramps
- Sleep Related Bruxism
- Sleep Related Rhythmic Movement Disorder
- Benign Sleep Myoclonus of Infancy
- Propriospinal Myoclonus at Sleep Onset
- Sleep Related Movement Disorder Due to a Medical Disorder
- Sleep Related Movement Disorder Due to a Medication or Substance
- Sleep Related Movement Disorder, Unspecified

Restless Legs Syndrome

- Neurological sensorimotor disorder
- Evidence of central dopaminergic dysfunction
- Characterised by an irresistible urge to move the legs, with uncomfortable:
 - Dysaesthesiae
 - Paraesthesiae
- Symptoms are:
 - **Worse in the evening/night**
 - Relieved by movement
 - Worse at rest
- Important cause of sleep disturbance

RLS Diagnostic Criteria

- A: The patient reports and urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs
- B: The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting
- C: The urge to move or unpleasant sensations are partially or totally relieved by movement such as walking or stretching, at least as long as the activity continues
- D: The urge to move or the unpleasant sensations are worse or occur only in the evening or night

Underlying Pathophysiology

- Primary – most common
- Secondary to another cause:
 - Iron deficiency anaemia
 - Pregnancy
 - End-stage renal failure
 - Polyneuropathy
 - Drugs e.g. **neuroleptics**, lithium, β -blockers, **antidepressants**, anticonvulsants, antihistamines, caffeine, alcohol
 - Withdrawal from sedatives

1. Silber MH. *Mayo Clin Proc* 1997; **72**: 261–4.

2. Evidente VGH *et al. Postgrad Med* 1999; **105**: 59–74.

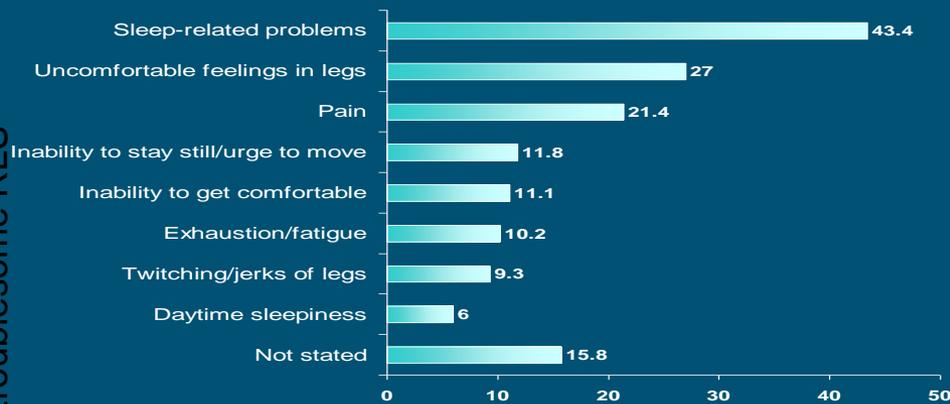
3. O'Keeffe ST. *Arch Intern Med* 1996; **156**: 243–8. www.sleepcentre.co.za

4. Amar K. *Hosp Med* 2001; **62**: 487–9.

How RLS presents

- In any patient presenting with sleep complaints, a diagnosis of RLS should be considered
- Patients complain of a multitude of sleep symptoms

Symptoms of RLS considered most problematic by those with troublesome RLS



Impact of RLS on sleep

Sleep latency

- Over 70%* take >30 min to get to sleep¹
- 15%* take ≥2 hours to fall asleep¹

Night-time awakening

- ~60%* wake 3 or more times per night¹
- ~80% experience PLMS which can disrupt sleep^{2,3}

RLS
sufferers

Poor-quality sleep

- PLMS associated with arousals decrease sleep quality^{2,3}
- Patients can have 40–100 PLMS per hour⁴

Quantity of sleep

- Those with moderate/severe RLS may sleep <5 hours per night²

1. Hening W *et al. Sleep Med* 2004; 5: 237–46.

2. Allen RP *et al. Sleep Med* 2003; 4: 101–19.

3. Allen RP *et al. J Clin Neurophysiol* 2001; 18: 128–47. www.sleepcenter.tufts.edu

4. Allen RP *et al. Sleep* 2003; 26 (Abstract Suppl): A341: 0858.N. quality of life)

*From the REST primary care study; consists only of patients who are likely to present for medical treatment (RLS symptoms at least twice weekly and some or high negative impact on quality of life)

RLS vs. PLMD

- RLS is a symptom
- RLS is diagnosed in the physician's office
- 80% of people who have RLS will have PLM's
- PLM's are an electromyographic finding
- PLM's are diagnosed in the sleep laboratory
- 30% - 80% of individuals who have PLM's have RLS symptoms
- PLM's are neither necessary nor sufficient to make the diagnosis of RLS

PLMD Diagnostic Criteria

A: PSG demonstrates repetitive, highly stereotyped, limb movements that are:

- 0.5 – 5 seconds duration
- Amplitude \geq 25% of baseline toe dorsiflexion
- In a sequence of \geq 4
- Separated by an interval of $>$ 5 seconds (from LM onset to LM onset) and $<$ 90 seconds (average interval 20 – 40 seconds).

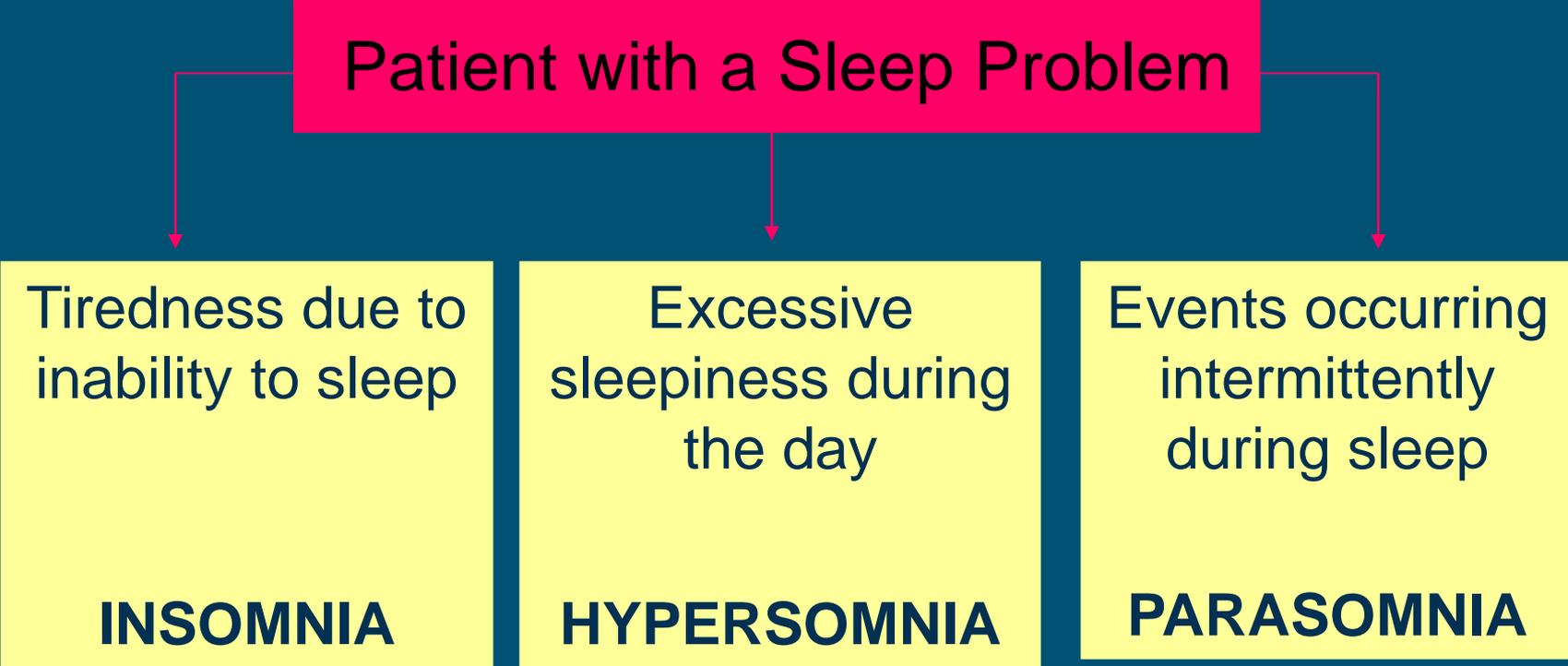
B: The PLMS Index $>$ 15 in adults ($>$ 5 in children)

C: There is clinical sleep disturbance or a complaint of daytime fatigue

D: No other disorder

Assessment of Sleep Disorders

Patient with a Sleep Problem



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graph TD; A[Patient with a Sleep Problem] --> B[Tiredness due to inability to sleep]; A --> C[Excessive sleepiness during the day]; A --> D[Events occurring intermittently during sleep]; B --- E[INSOMNIA]; C --- F[HYPERMOMNIA]; D --- G[PARASOMNIA];
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Tiredness due to inability to sleep

INSOMNIA

Excessive sleepiness during the day

HYPERMOMNIA

Events occurring intermittently during sleep

PARASOMNIA



Insomnia

AASM Research Diagnostic Criteria

- ONE OR MORE:
- Difficulty initiating/maintaining sleep/waking too early/non-restorative sleep
- *DESPITE ADEQUATE OPPORTUNITY*
- AT LEAST ONE OF THE FOLLOWING DAYTIME CONSEQUENCES:
- Fatigue/poor concentration/social dysfunction/sleepiness/accidents/concerns about sleep

Insomnia ruins both night and day



Difficulty initiating sleep
Difficulty maintaining sleep
Non-restorative
(poor quality) sleep

+

Significant
daytime impairment

>1 month

Sleep restriction versus insomnia

Sleep restriction

- Short term
- Usually self-inflicted (social behaviour or demands)
- Quantity of sleep
- Daytime sleepiness
- Long-term consequences?

Insomnia

- Long-term suffering
- A disorder (not self-inflicted)
- Quantity and *quality* of sleep
- **Daytime hyperarousal**
- Long-term risk of depression, poor quality of life...

Pathogenesis of Primary Insomnia

- State of Hyperarousal:
- Increased cerebral glucose metabolism
- Increased Beta, reduced Delta activity
- Increased 24hr metabolic rate
- Increased ACTH/Cortisol

Insomnia is a *prevalent* disorder

- 30% report transient insomnia symptoms
- 5–10% fulfil criteria for chronic insomnia
 - Chronic course
 - Daytime impairment
- Insomnia is more common in women
- Insomnia increases with age

Insomnia Symptoms and Diagnosis

>50 studies community-dwelling samples:

Insomnia symptoms present in 30-48%, present nightly in 16-21%, severe in 10-28% **or 30%**

- Insomnia symptoms with daytime consequences 9-15%
- Symptoms with consequences and dissatisfaction with sleep quantity/quality
8-18% **or 10%**
- Insomnia Dx (DSM-IV, ICSD) 6% **or 5%**

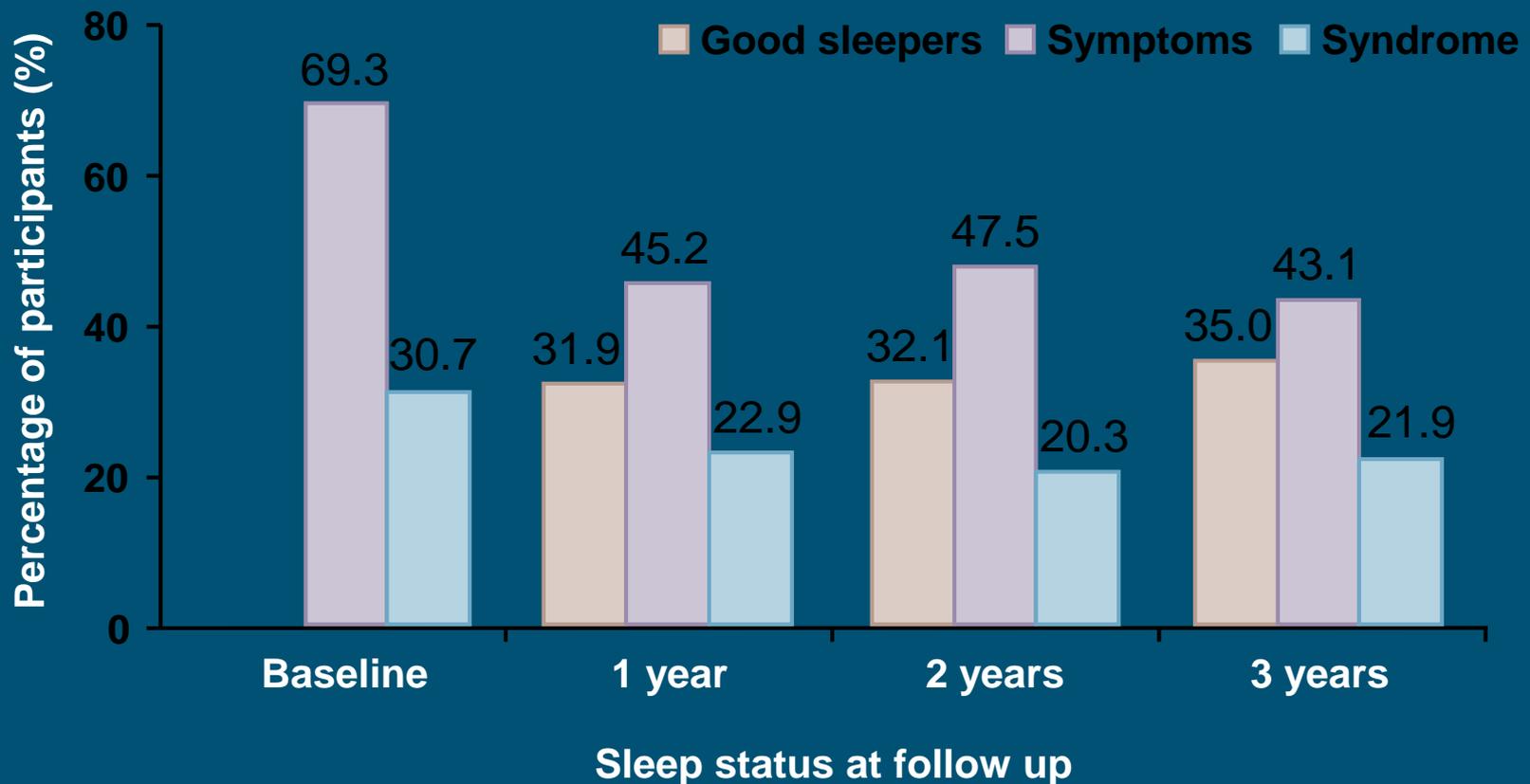
Ohayon MM, Sleep Med Rev 2002:6:97-111

When these distinctions are made

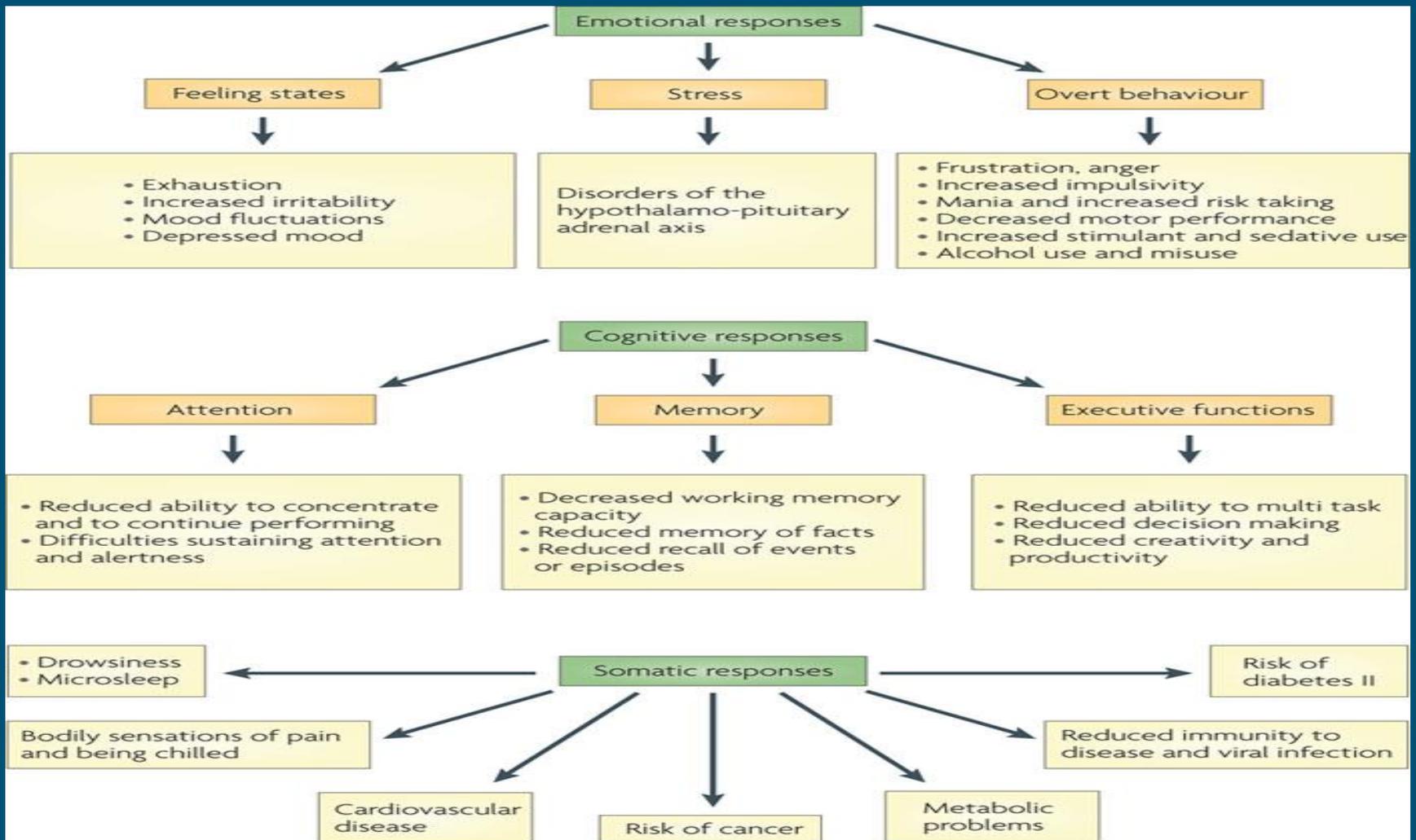
- Patients with Insomnia with daytime consequences and/or dissatisfied with quantity/quality:
- Greater healthcare consumers
- More often present with mental disorders
- and organic disease

Insomnia is a *persistent* disorder

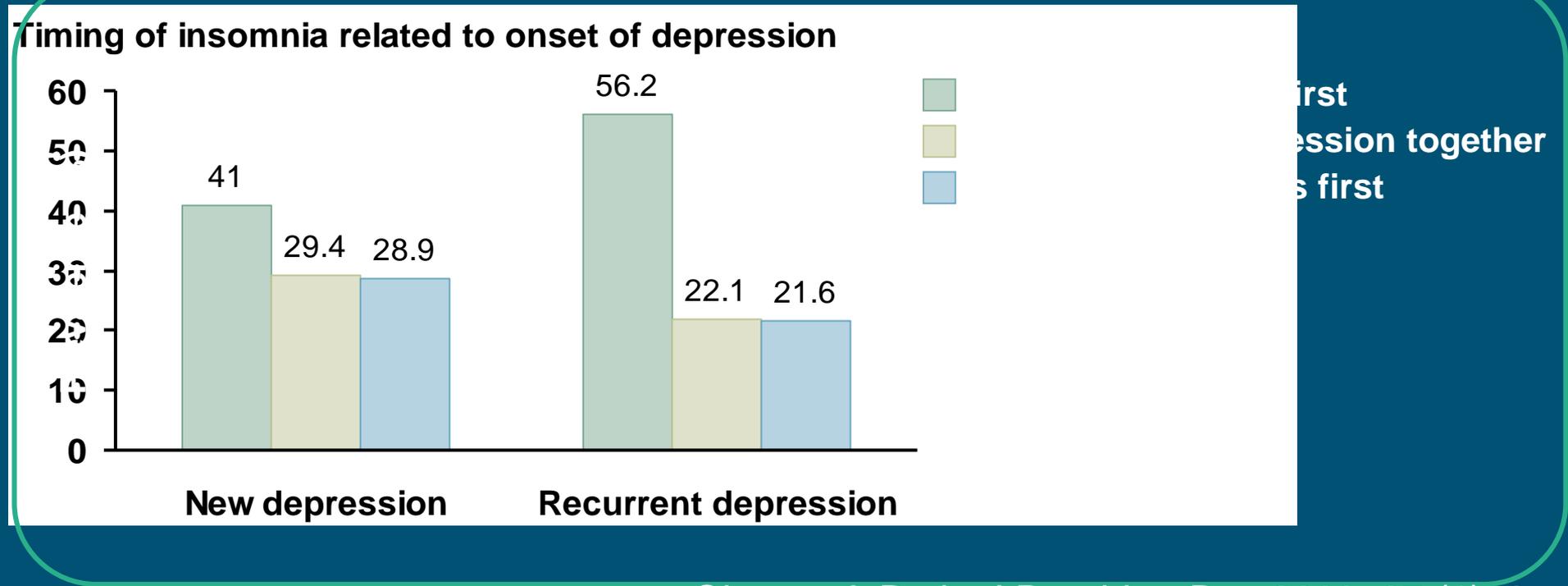
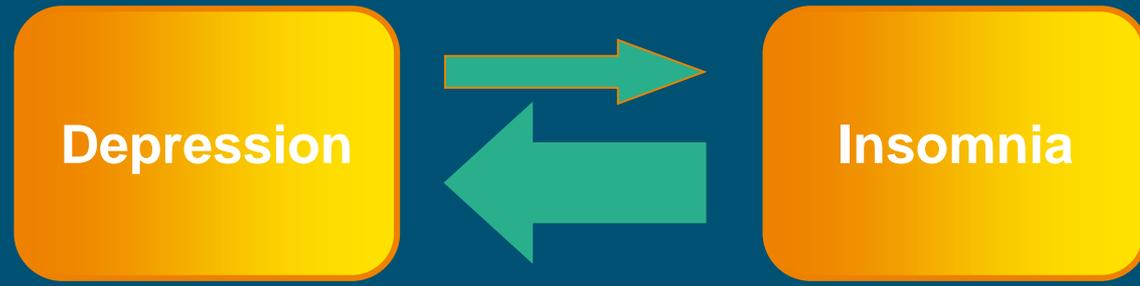
Natural history of insomnia



Consequences of Decreased Sleep

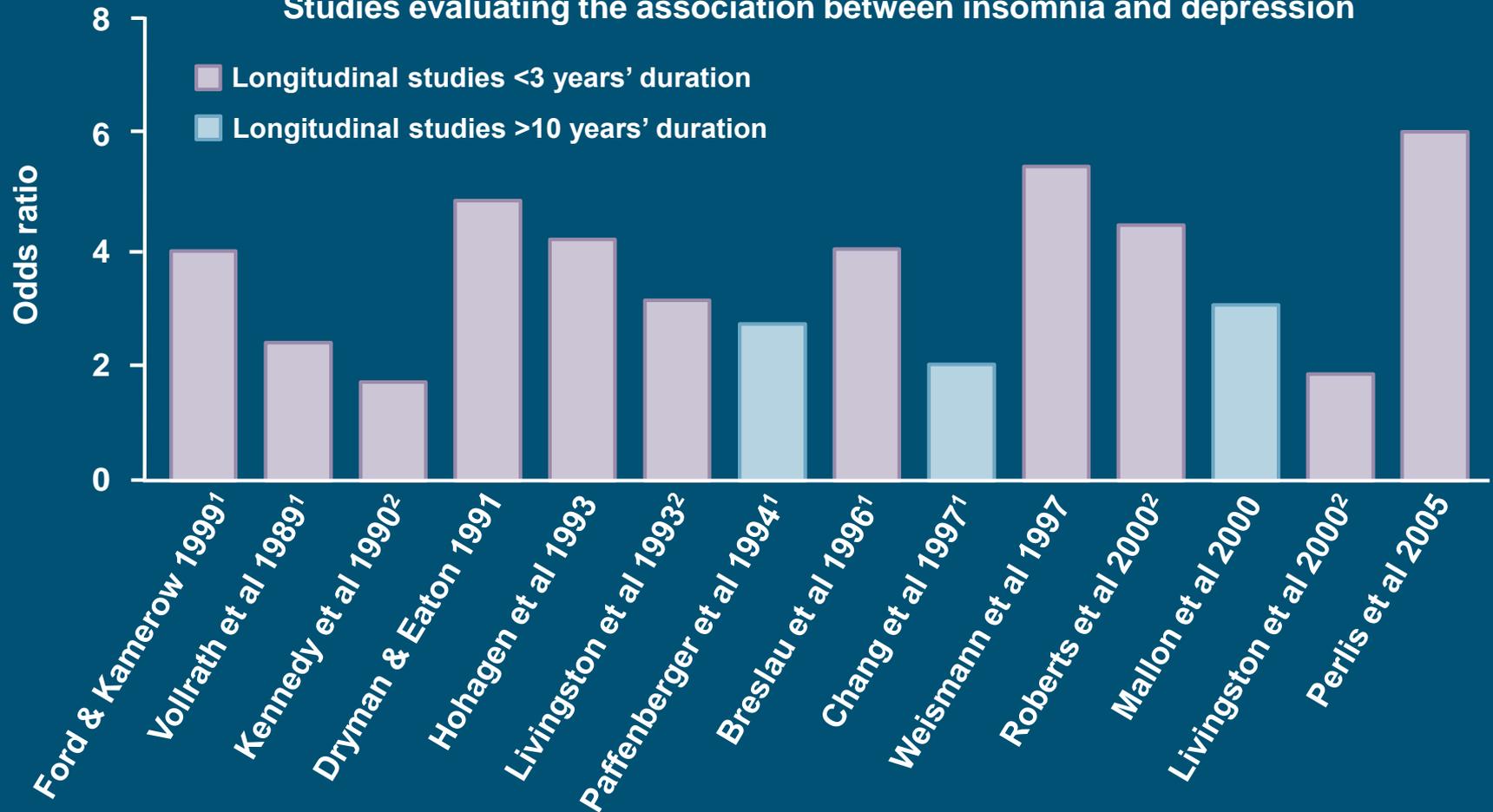


Insomnia and depression



Insomnia as Risk Factor of Depression

Studies evaluating the association between insomnia and depression



Insomnia as Predictor

	Mood Disorder		Anxiety Disorder	
	First Episode (%)	Relapse (%)	First Episode (%)	Relapse (%)
Insomnia appears before	41%	56.2%	18%	23.2%
Insomnia appears with	29.4%	22.1%	38.6%	42.5%
Insomnia appears after	28.9%	21.6%	43.5%	34.5%

Insomnia – is it important?

- Insomnia is a highly prevalent and chronic disorder with daytime impairment
- Poor sleep poses a health risk to the individual
 - Depression
 - Quality of life
- Insomnia is a cause of absenteeism and poor work performance
- Insomnia compares to depression on worsening QoL and work disability

Treatments

- Universal- sleep hygiene
- Disease specific- RLS; Circadian; depression
- Behavioural- stimulus control; sleep restriction; relaxation
- Hypnotics

Determinants of treatment seeking (265 respondents who consulted for insomnia)

- Fatigue (48%)
- Psychological distress (40%)
- Physical discomfort (22%)
- Suggestion by a significant other (14%)
- Reduced work productivity (13%)
- Suggestion by another health professional (11%)
- Significant sleep loss (11%)

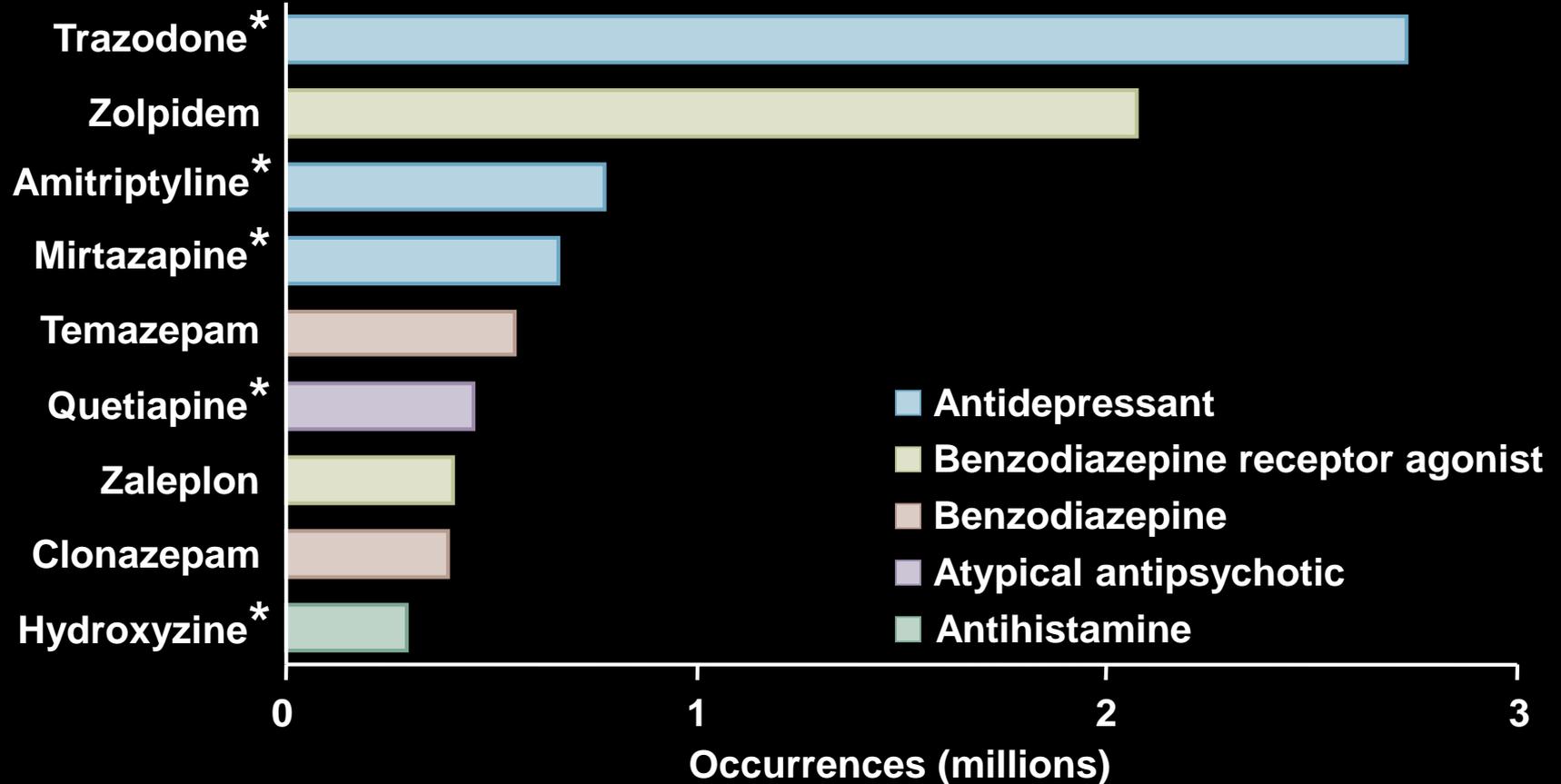
Current treatment options for insomnia

- Pharmacotherapy
- Cognitive–behavioural therapy (CBT)
- Complementary/alternative therapies
 - herbal/dietary supplements
 - acupuncture

Treatments for chronic insomnia (US)

- Treatments endorsed for chronic insomnia
 - CBT
 - FDA-approved benzodiazepine receptor agonists (at least for short-term use)
- Treatments not endorsed for insomnia (due to limited efficacy evidence and/or safety concerns)
 - Unmonitored long-term use of benzodiazepine receptor agonists
 - Complementary and alternative preparations
 - Antihistamines (OTC and prescription)
 - Antidepressants
 - Antipsychotics
 - Sleep hygiene advice alone

Drugs used to treat insomnia



*Not FDA-approved for this use

Efficacy of traditional hypnotics

- Benzodiazepines (BZDs) and Z-drugs:
 - Most BZDs prescribed to the elderly
 - Restricted to short-term use, but often used for years – even decades, in spite of no efficacy data
 - Approval based on improvement in quantitative sleep parameters
 - Subjective experience of sleep rarely improves

“Although a 15 minute group difference on sleep-onset latency may be sufficient to reach statistical significance, such a difference may be of little clinical significance in the patient’s life”

If total sleep time improves, but the patient still complains of daytime dysfunction – has the treatment goal been reached?

Safety of traditional hypnotics

- Well known adverse events are of particular concern in the elderly and include:
 - Daytime sedation/sleepiness/fatigue
 - Memory impairment
 - Worsening of sleep apnea
 - Ataxia
 - Falls
 - Tolerance and dependency
 - Rebound insomnia

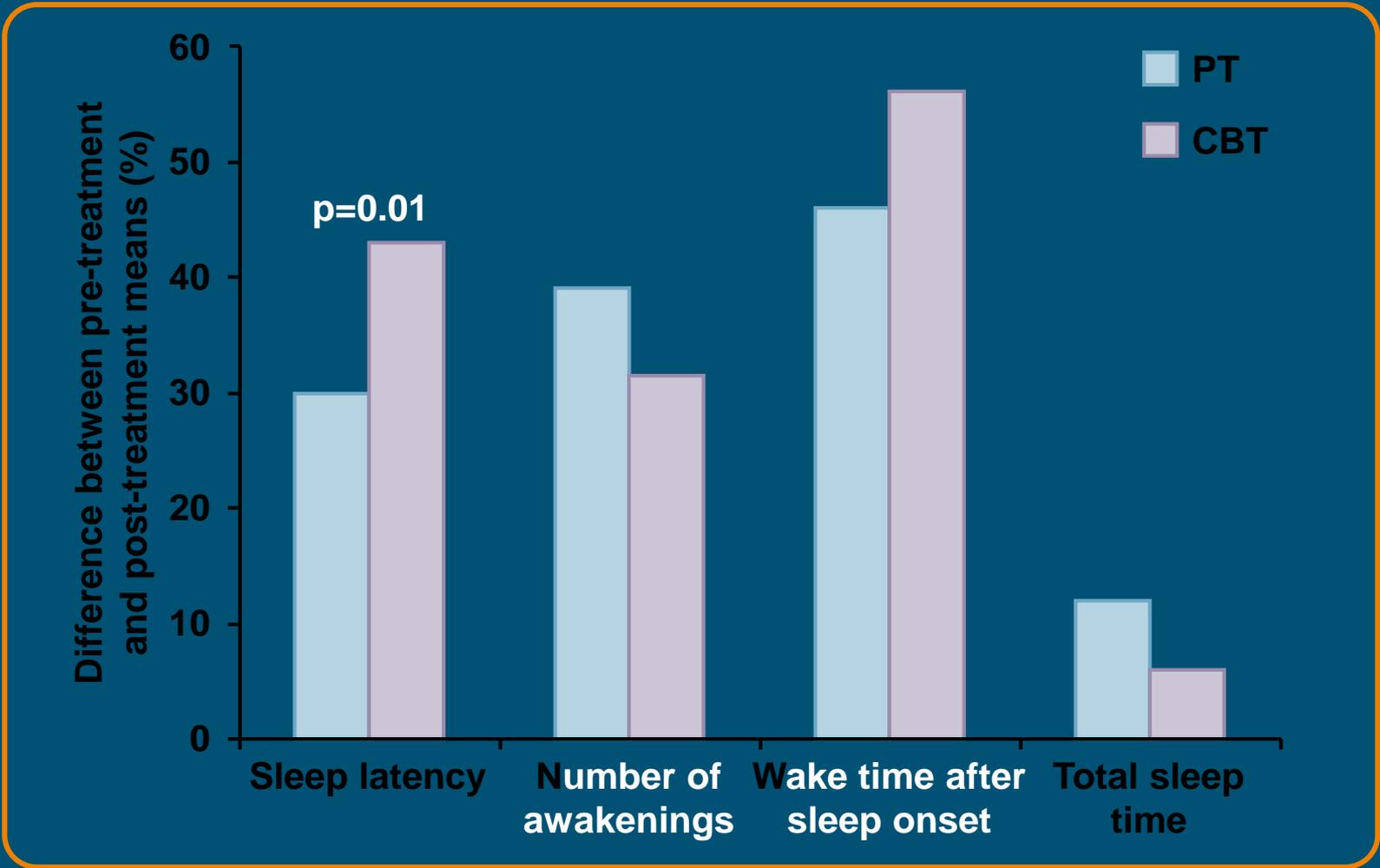
“...an adverse event is more than twice as likely as enhanced quality of sleep”

“...the clinical benefits may be modest at best. The added risk of an adverse event may not justify these benefits, particularly in a high risk elderly population”

Results of the review

- *“Well-established treatment”* – based on criteria defined by the APA:
 - ✓ Stimulus control
 - ✓ Relaxation training
 - ✓ Paradoxical intention
 - ✓ Sleep restriction
 - ✓ CBT

Comparing pharmacotherapy (PT) with cognitive-behavioural therapy (CBT)



Advantages and limitations of medication and CBT for insomnia

- Medication (BZDs and Z-drugs)
 - Efficacious on quantitative sleep parameters
 - Rapid symptomatic relief
 - Limited evidence of long-term efficacy
 - Potential risks for side effects and dependency
 - Readily available
- CBT
 - Efficacious, long-term improvements
 - Well accepted, no known adverse effects
 - Requires time and motivation
 - Not widely available

Need for new treatment options

- Insomnia must be recognised as a disorder with serious health consequences, that is **worth treating**
- CBT has shown to be effective on quantitative parameters but is not widely available
- Treatment options are needed that
 - Address the subjective aspect of sleep complaint
 - Don't cause dependency
 - Incorporate additional endpoints (daytime functioning, QoL, falls and accidents)
 - Focus on elderly
 - Optimise long-term outcomes, not just initial therapeutic response

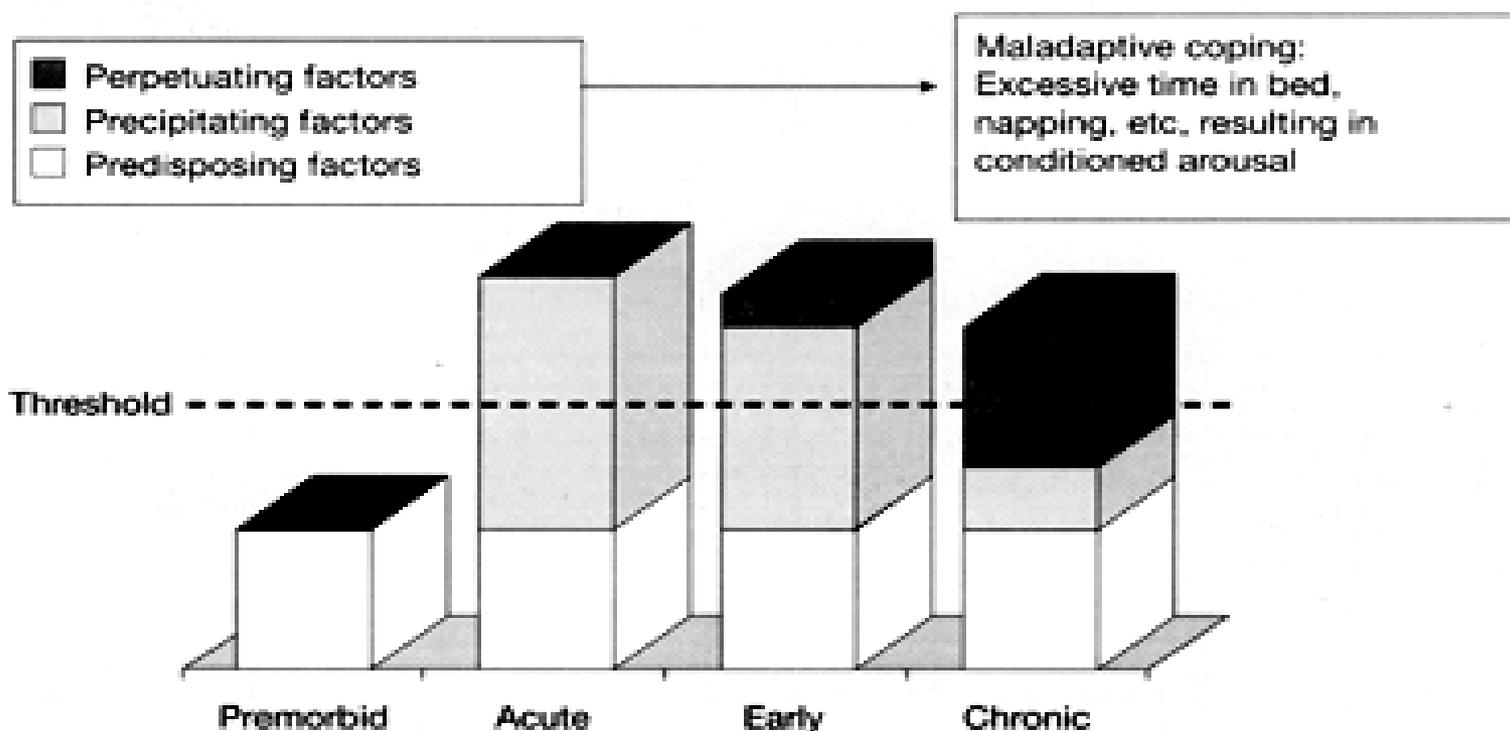
Emerging Trends

- **GABA agonists**
- **Melatonin receptor agonists**
- **Hypocretin antagonists**
- **Histaminergic drugs**
- **Adenosine compounds**

The Rationale of CBT

Medscape®

www.medscape.com



Source: Clin Cornerstone © 2003 Excerpta Medica, Inc.

CBT Interventions

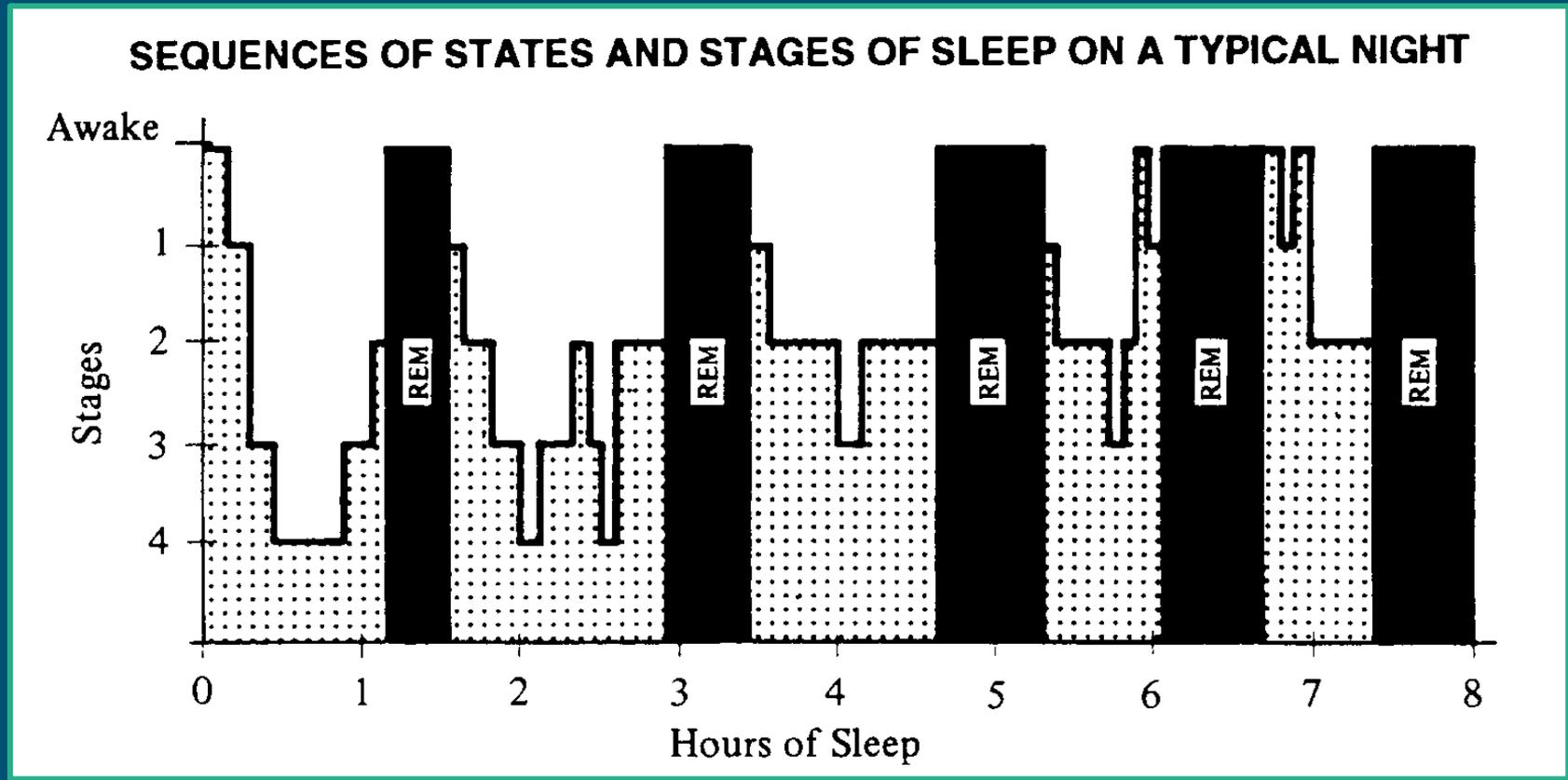
The primary cognitive-behavioural interventions for chronic insomnia are

1. Stimulus control
2. Sleep restriction
3. Relaxation training
4. Sleep hygiene education
5. Cognitive therapy, and,
6. Combination or multi-component therapy.

The Evidence

- **Health Technology Assessment**
- 2004; Morgan K; Sheffield
- 23 General Practices
- 209 patients (31-92yrs) on hypnotics >1mth (m 13yr)
- 6x50' - intro/hygiene/SC;SR/relax/cogn/review
- **Outcomes at 3 and 6 mths**
- Improved PSQI and SF36
- Reduced hypnotic use with 30% off
- The improvement in PQSI & HAD

Normal Sleep Histogram



Mood Disorders

- Mood disorders - second most common category of psychiatric disorders after anxiety disorders,
- Major Depression - affects at least 121 million persons worldwide
- In 2000, bipolar disorder was in the top 10 causes of disability,
- Depression was the leading cause of disability and the fourth leading contributor to the global burden of disease.



Mood Disorders

Mood Disorders

- By 2020, depression is projected to be the second leading contributor to global burden of disease for all ages and both sexes.
- The impact of mood disorders includes eventual suicide in 15% of those affected, as well as increased morbidity and mortality from other illnesses – including Sleep Disorders!

Mood Disorders

- Major depression is a common disorder and is reported to have a lifetime prevalence of 16.2%
- Prevalence of 6.6% for the past 12 months in U.S. adults, with an increased risk: OR =1.7 in women
- Bipolar I and II disorders each affect about 1% of the population (lifetime) and show no sexual predilection
- Median age of Onset for major depression is 32 years and for bipolar disorders 18 to 20 years

Association between Sleep and Mood

- 14% to 20% of persons with significant complaints of insomnia and about 10% of those with hypersomnia show evidence of major depression
- WHEREAS, rates of depression were less than 1% in those without sleep complaints
- The degree and duration of insomnia are positively correlated with more severe or recurrent major depression, or both
- 3.8 X Lifetime Risk of Depression in young people with Insomnia

Subjective Sleep Complaints

- Specific sleep complaints include:
 - difficulty falling asleep,
 - frequent nocturnal awakenings,
 - early morning awakening,
 - Non-restorative sleep,
 - decreased or increased total sleep, and,
 - Disturbing dreams.

Subjective Sleep Complaints

- Insomnia, hypersomnia, or both are reported by approximately 75% of adults, children, and adolescents with major depression.
- Patients with bipolar disorder also often report insomnia or hypersomnia when they are depressed, but they are more likely to exhibit hypersomnia than unipolar patients.
- During (hypo)manic episodes - diagnostic criteria includes a decreased need for sleep, usually accompanied by decreased sleep time.

Objective Sleep Disturbance in Depression

Sleep continuity disturbances

- Prolonged sleep latency
- Increased wake time during sleep
- Increased early morning wake time
- Decreased total sleep time

Objective Sleep Disturbance in Depression

SWS (NREM) deficits

- Decreased SWS amount
- Decreased SWS percentage of total sleep
- Decreased SWS, both as a fraction of total sleep and as SWS minutes
- Predominant loss of SWS is in the First NREM Period

Quantitative EEG (Power Spectral Analysis)

- Reduced Delta Power throughout the night
- Increased Delta Power (SWA) in responders vs. Non-responders

Objective Sleep Disturbance in Depression

REM sleep abnormalities

- Reduced REM sleep latency
- Prolongation of the first REM sleep period
- Increased REM activity (total number of eye movements during the night)
- Increased REM density (REM activity/total REM sleep time)
- Increased REM sleep percentage of total sleep
- ? False + MSLT?

Sleep during Remission in Mood Disorders

- Sleep disturbances are not limited to periods of acute depression or mania
- Reduced REM sleep latency and decreased SWS can persist for prolonged periods in otherwise asymptomatic persons - ? Trait Marker
- The persistence of sleep abnormalities suggests that:
 - a. Sleep disturbance might indicate a biological susceptibility for depression and predate the illness, or,
 - b. sleep changes may be caused by depression and persist much longer than other affective symptoms.

Familial Patterns

- First-degree relatives of subjects with major depression also show reduced REM sleep latency and SWS deficits, **whether or not** they have a personal history of a mood disorder,
- Hence - Sleep changes in depression include a hereditary component.