

Sleep loss – quality, quantity, timing

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Conflicts

- Patents
 - ECG cardiopulmonary coupling (MyCardio LLC)
 - Positive Airway Pressure Gas Modulator
 - Auto CPAP algorithm (DeVilbiss-Drive)
- Consulting: GLG Councils, Jazz Pharmaceuticals
- Grants: DeVilbiss-Drive, Jazz Pharmaceuticals, American Sleep Medicine Foundation, NHLBI, NINDS

Sleep is a Biological Imperative

Multi-system effects of sleep

- Brain “housekeeping”
 - Attention, executive function, memory, affective regulation
- Cardiovascular and autonomic resetting
- Metabolic regulation
 - Appetite regulation
- Inflammation control
 - Neuroendocrine and neuroimmune modulation
- Motor / musculoskeletal rest
 - Intuitive

Some new facts about sleep

- Highly local process
 - Slow waves, UP/DOWN states, traveling waves
- Use-dependent features
- Complex network dynamics
 - Ocean waves
- Complex synaptic dynamics
 - Worm-like
 - Synaptic homeostasis model

How Much Sleep?

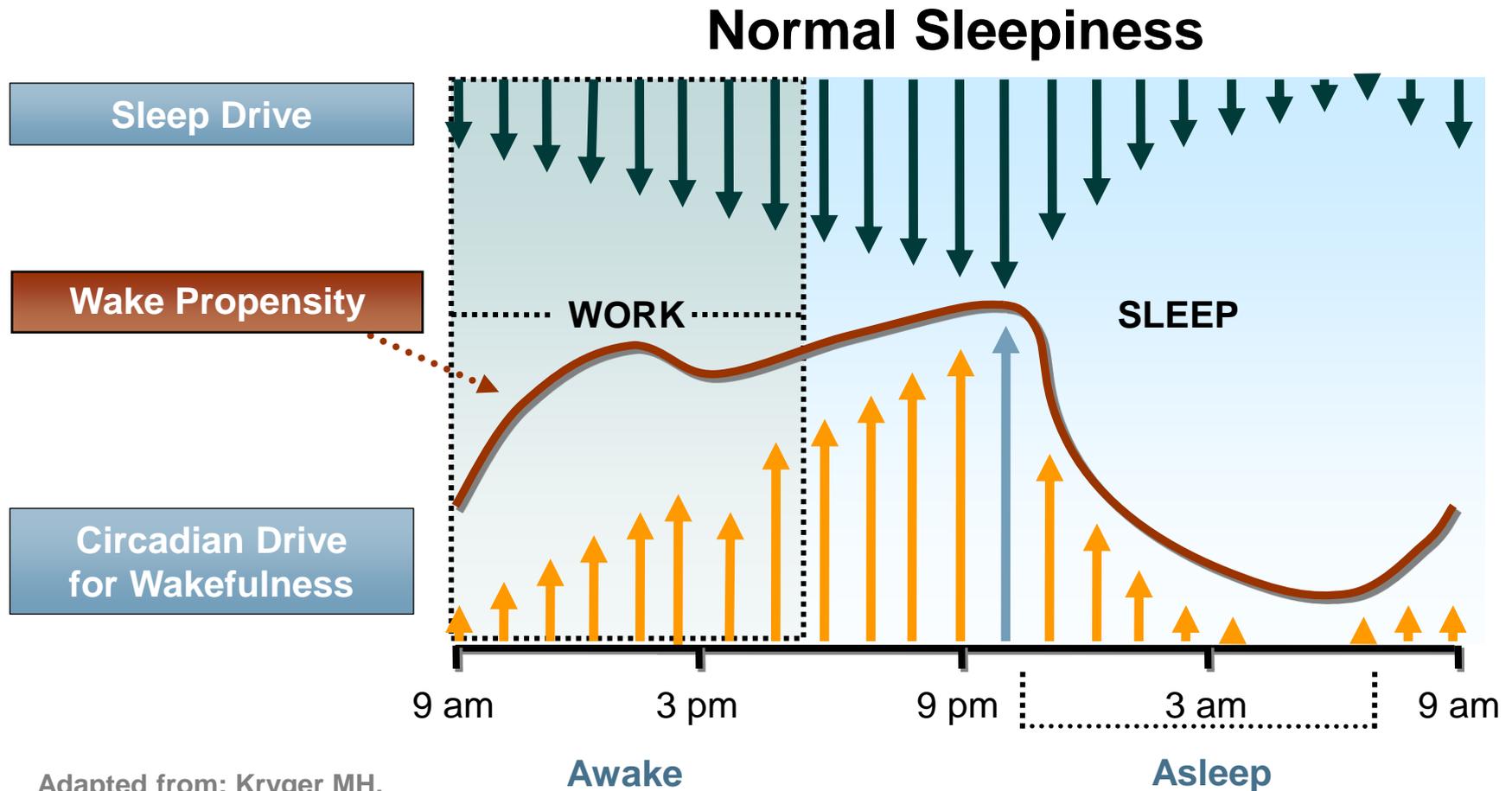
- A) 6 hours
- B) 7 hours
- C) 8 hours
- D) 9 hours

“It depends, but super-humans are rare outside the movies.....”

Common disruptors of sleep

- Pain
- Anxiety/depression
- Stress
- Sleep apnea (public enemy #1 for sleep)
- Circadian misalignment
- Drugs
- Medical training!

Physiologic Determinants of Sleepiness



Adapted from: Kryger MH,
et al. Principles and
Practices of Sleep Medicine.
2000.

Neurobiologic Effects of Sleep Loss

Alertness and vigilance become unstable and unreliable

Cognitive slowing occurs and time pressure increases errors

Tasks may be begun well, but performance declines with increasing rapidity

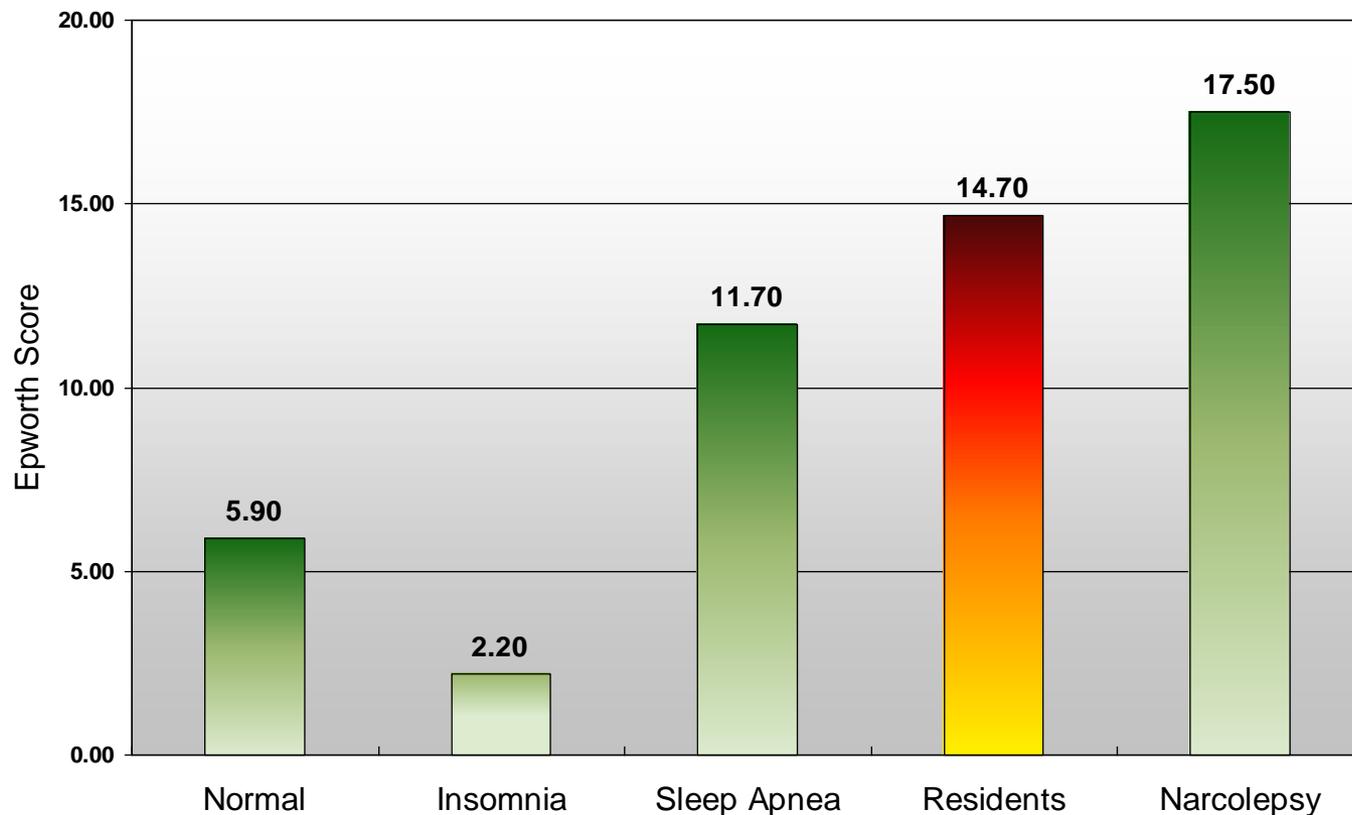
There is growing neglect of activities judged to be nonessential (loss of situational awareness)

Involuntary sleep attacks begin to occur

Risks of accidents and crashes increase

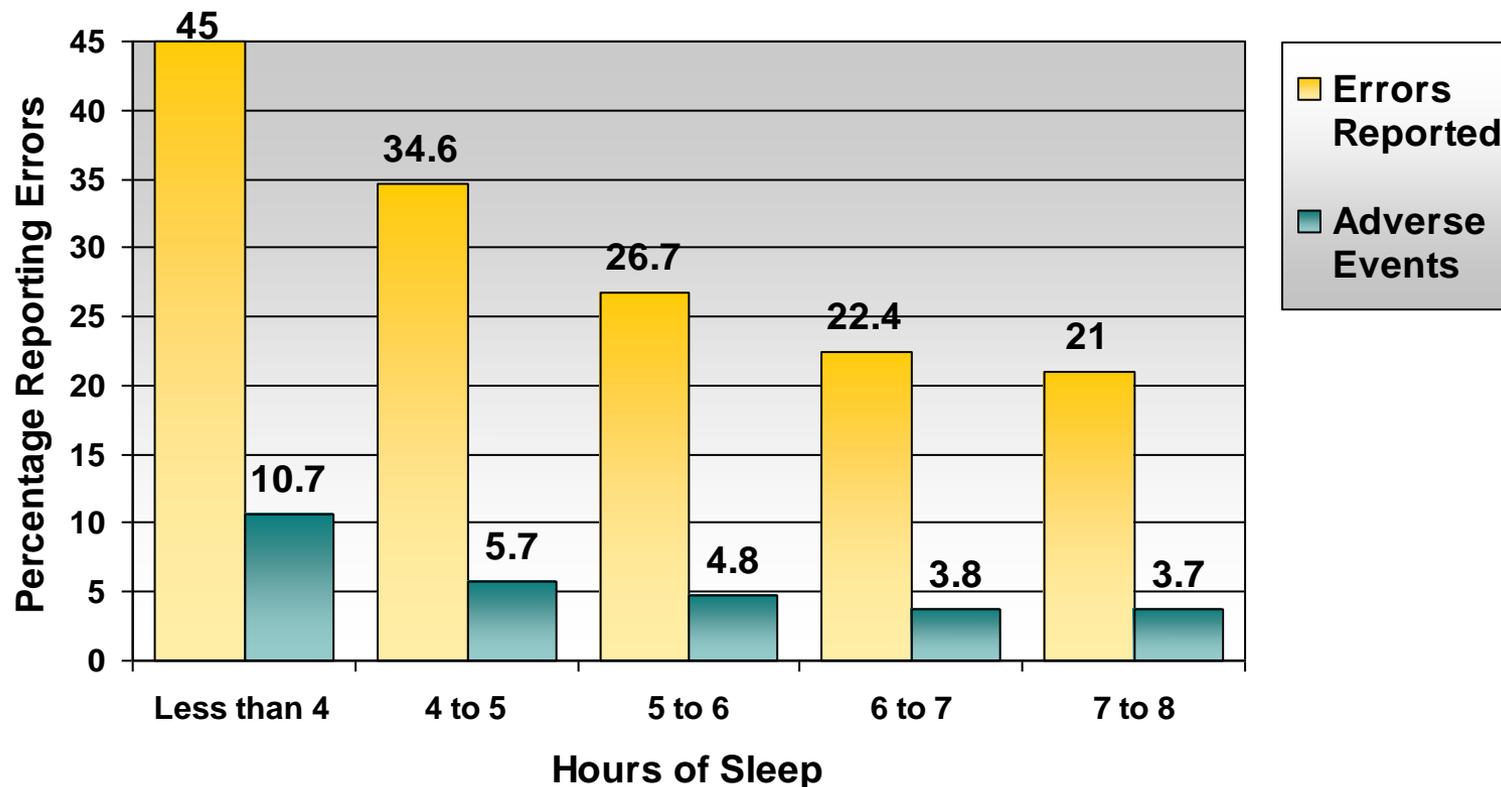
Sleepiness in Residents

Sleepiness in residents is equivalent to that found in patients with serious sleep disorders.



Papp et al, Academic Medicine, 2002
Mustafa et al, Sleep and Breathing, 2005

Resident Self-reported Errors by Average Daily Hours of Sleep



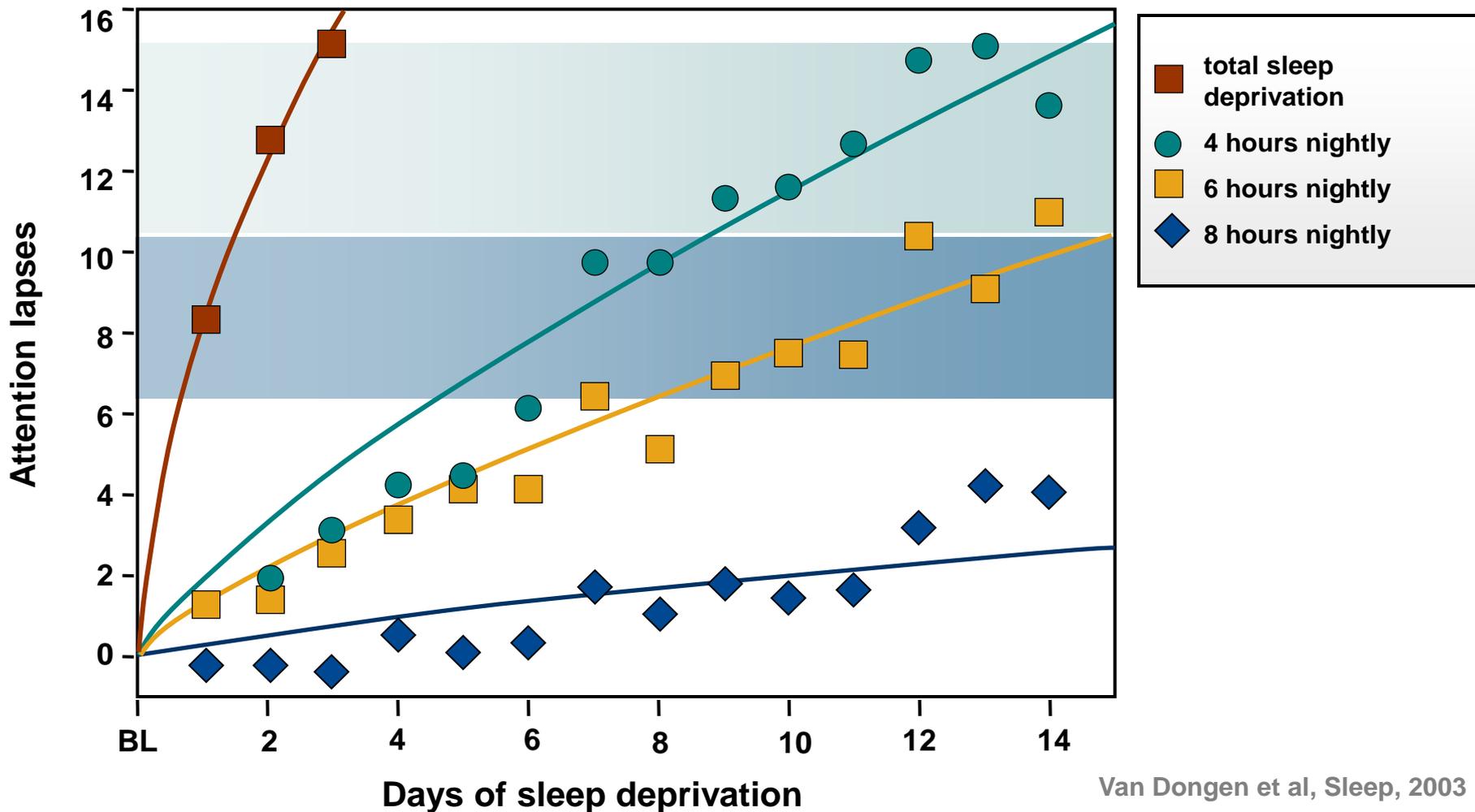
Baldwin & Daugherty, Sleep, 2004

Residents Averaging Less Than Five Hours of Sleep per Night

<i>Were significantly more likely to report:</i>	Odds Ratio
Involvement in a malpractice suit	2.02
Use of medication to stay awake	1.91
Serious conflict with other residents	1.86
Accidents/injuries	1.84
Making a serious medical error	1.74
Noticeable weight change	1.59
Increased use of alcohol	1.52
Serious conflict with nursing staff	1.47

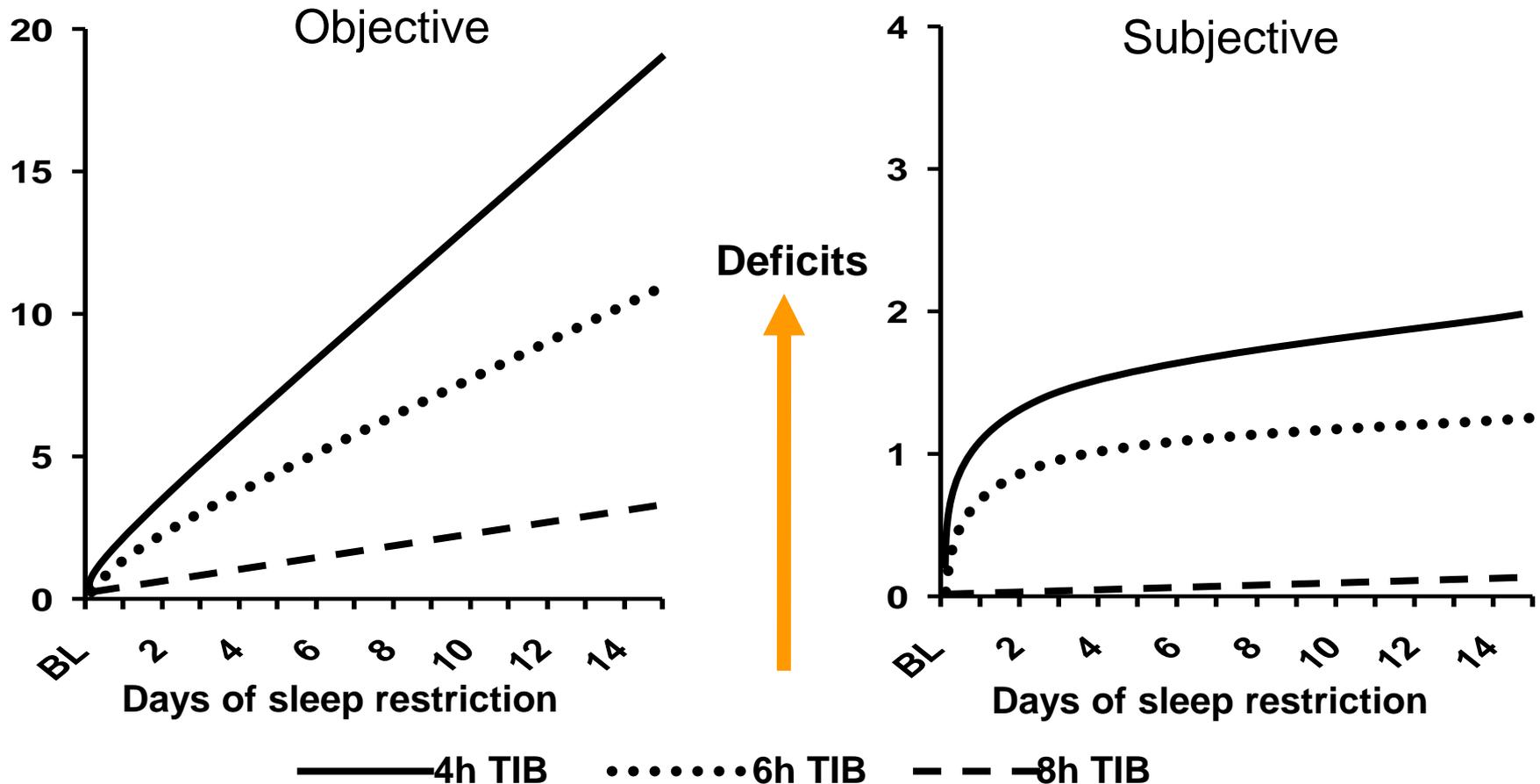
Baldwin & Daugherty, Sleep, 2004

Sleep Deprivation Decreases Attention

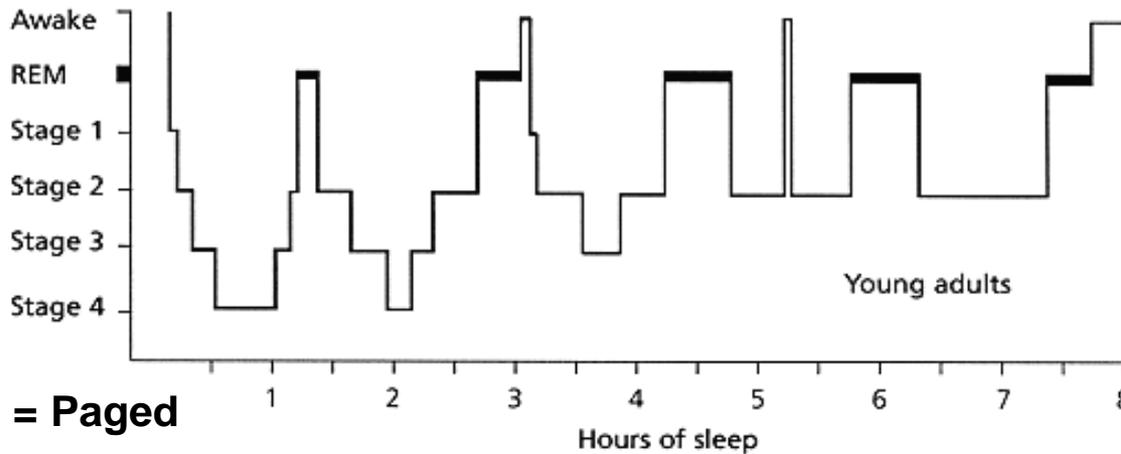


Van Dongen et al, Sleep, 2003

Cumulative adverse effects of chronic partial sleep restriction are greater in objective than subjective measures

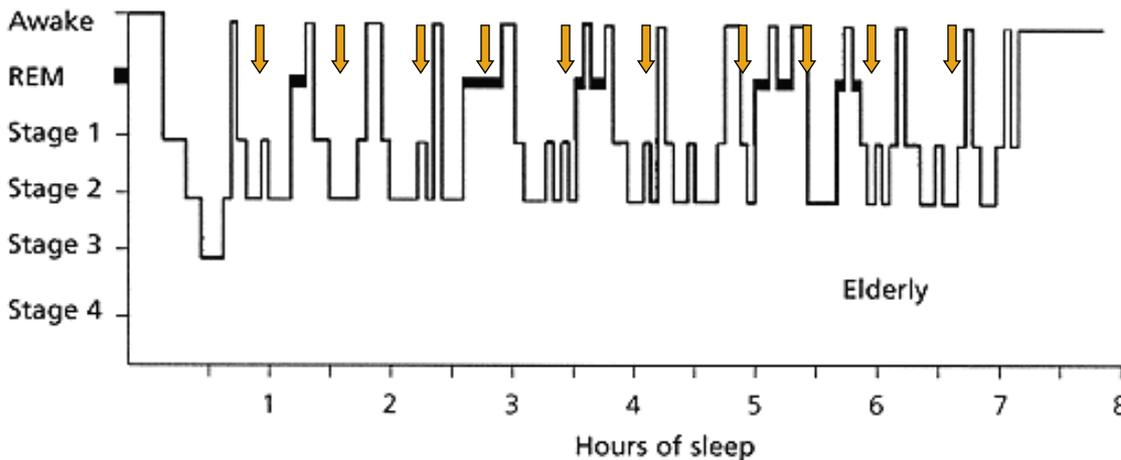


Sleep Fragmentation Affects Sleep Quality



NORMAL SLEEP

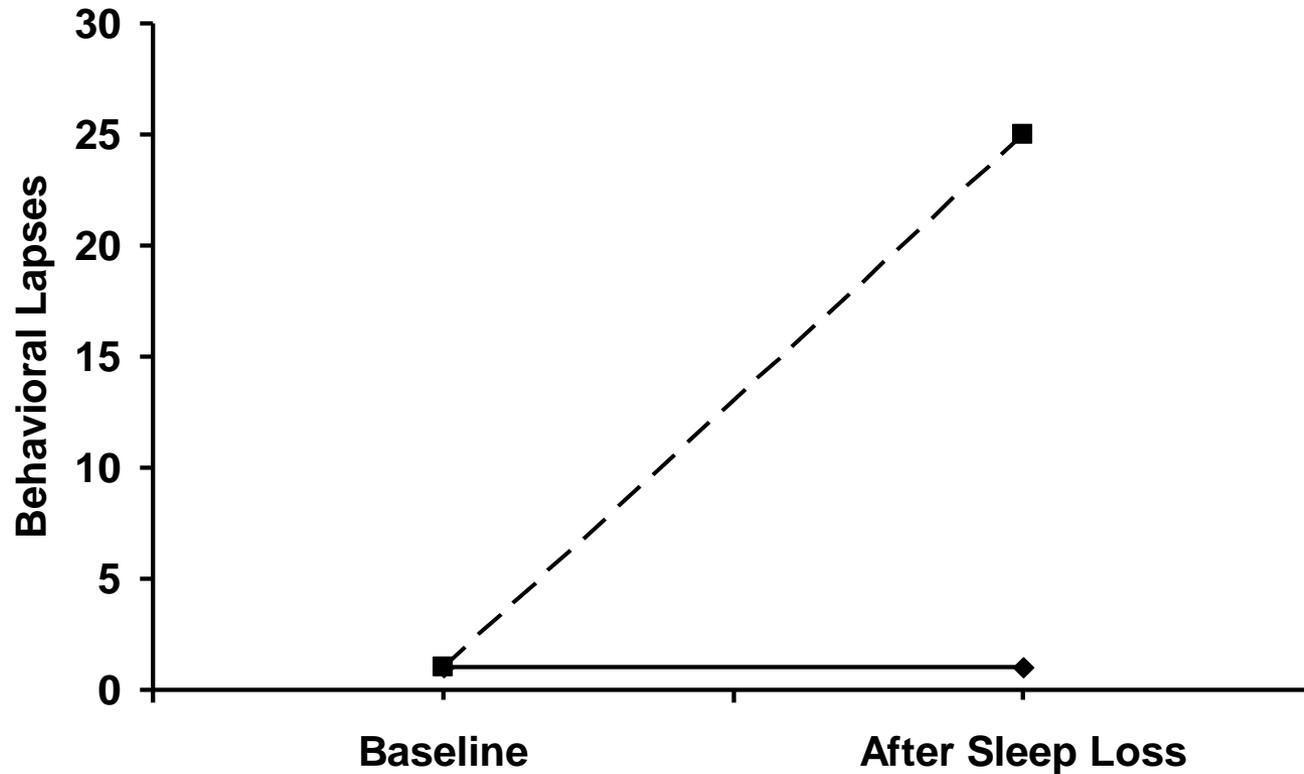
↓ = Paged



ON CALL SLEEP

Morning Rounds

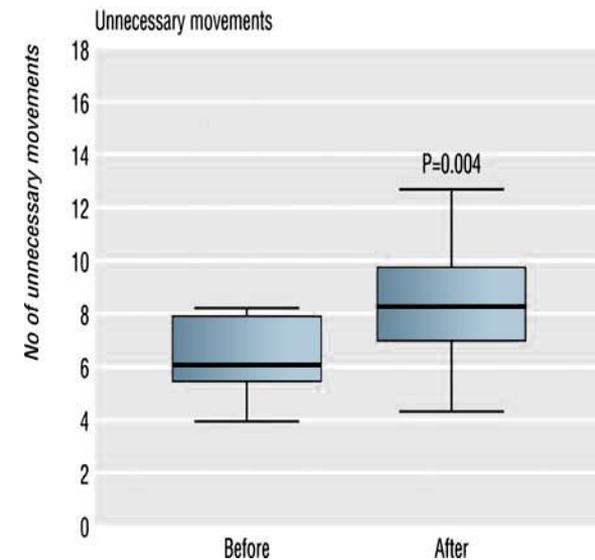
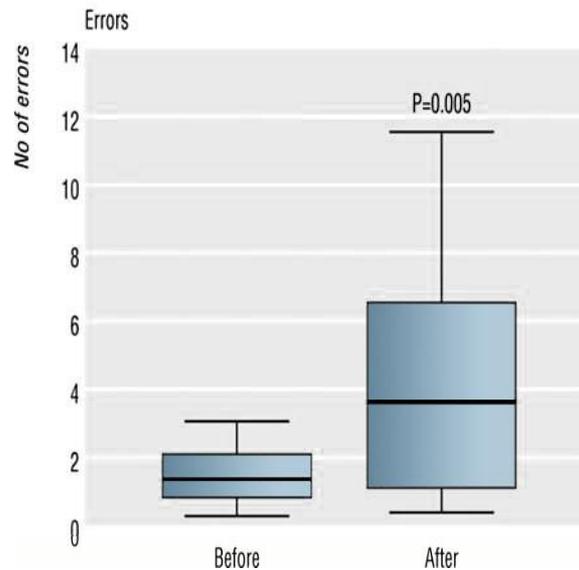
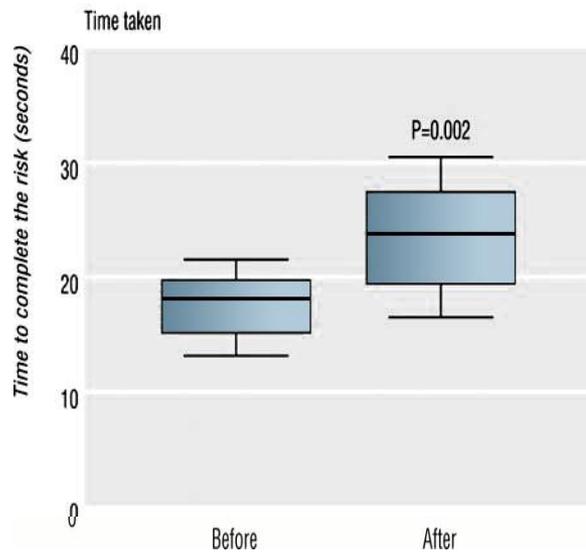
Intra-individual variation



Subject 1 (dotted line) is more vulnerable to sleep loss than subject 2 (solid line)

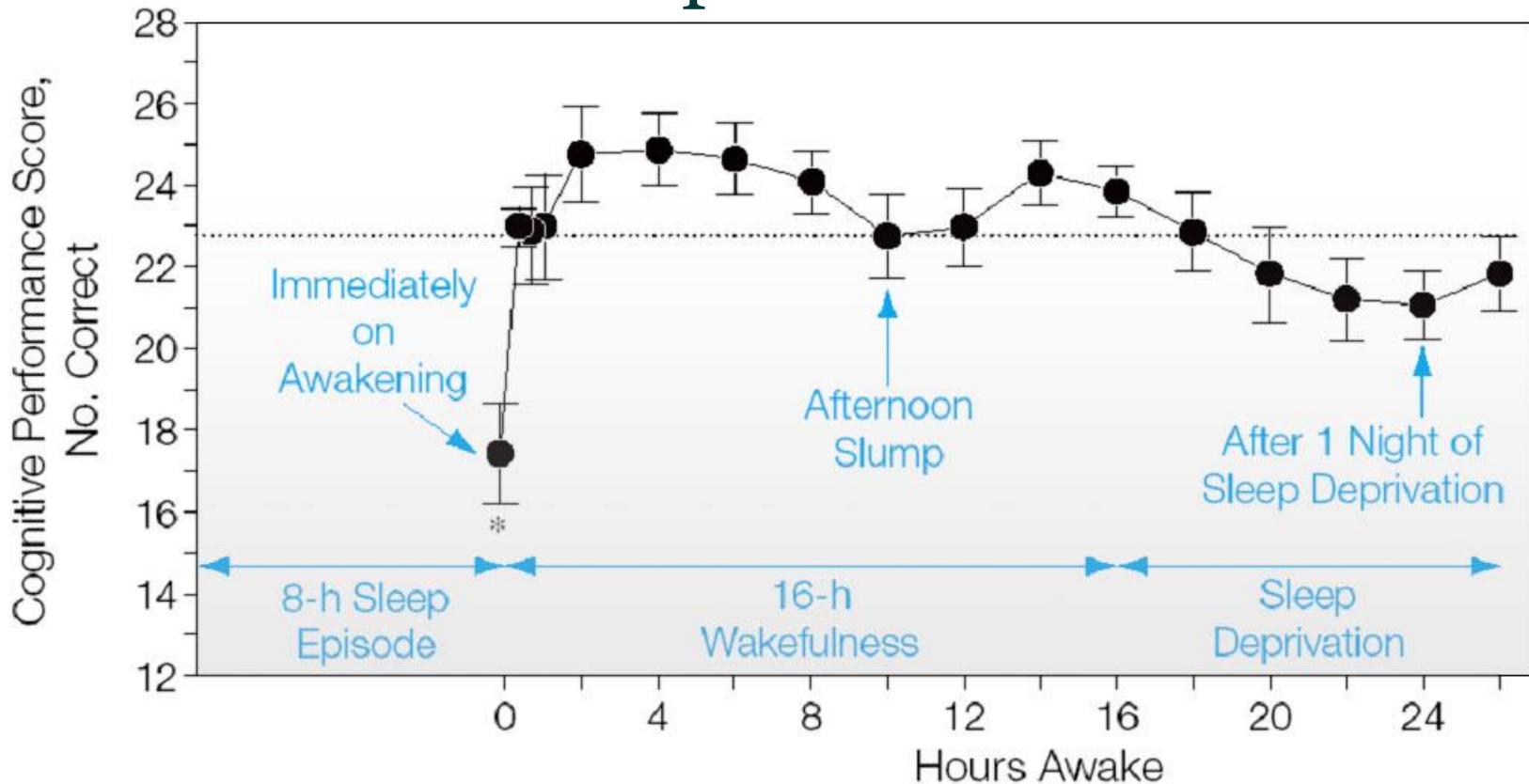
Impaired Speed and Errors in Performance: Laparoscopic Surgical Simulator

Pre and post 17-hour overnight call duty in a surgical department
(median reported sleep time 1.5 h; range 0-3 h)



Grantcharov TP et al, BMJ, 2001

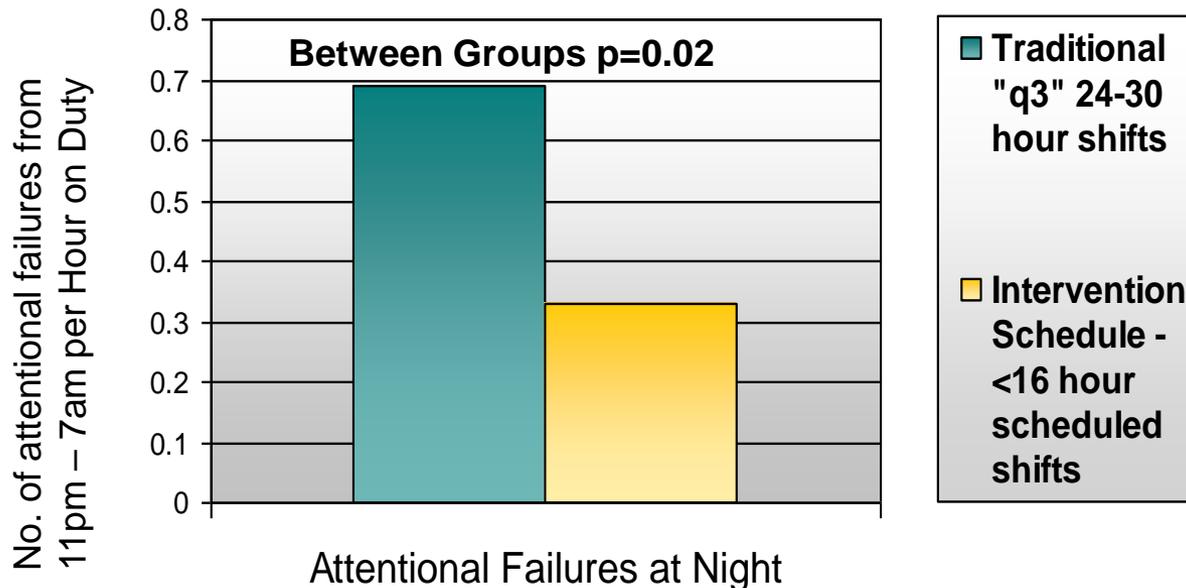
Cognitive Performance on Awakening From Sleep Compared with Subsequent Sleep Deprivation



Wertz et al, JAMA, 2006

Intern Sleep and Patient Safety Study

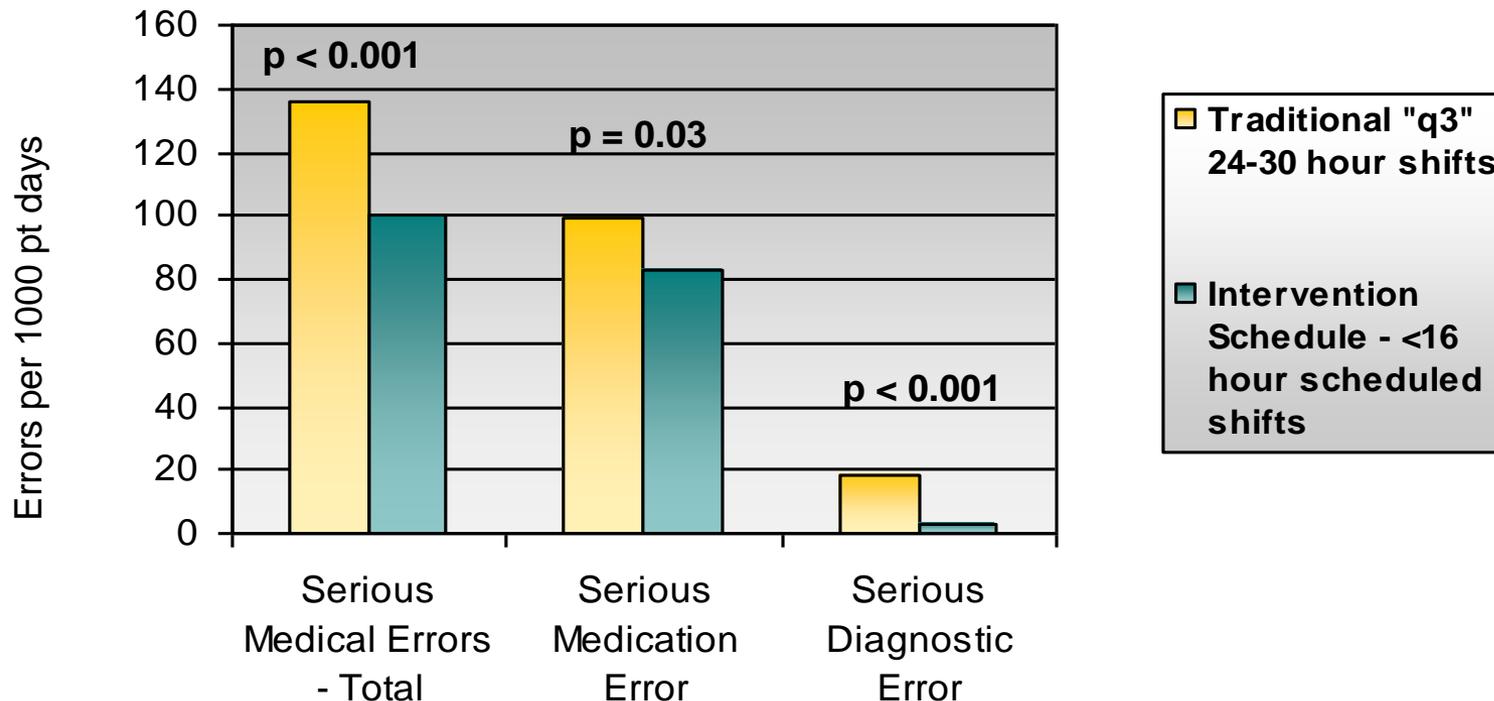
- Randomized trial comparing interns' alertness and performance on traditional "q3" schedule with 24-30 hour shifts (ACGME-compliant) vs. 16 hr max schedule
- Results: *Twice as many* EEG-documented attentional failures at night on traditional schedule



Lockley et al. N Engl J Med 2004

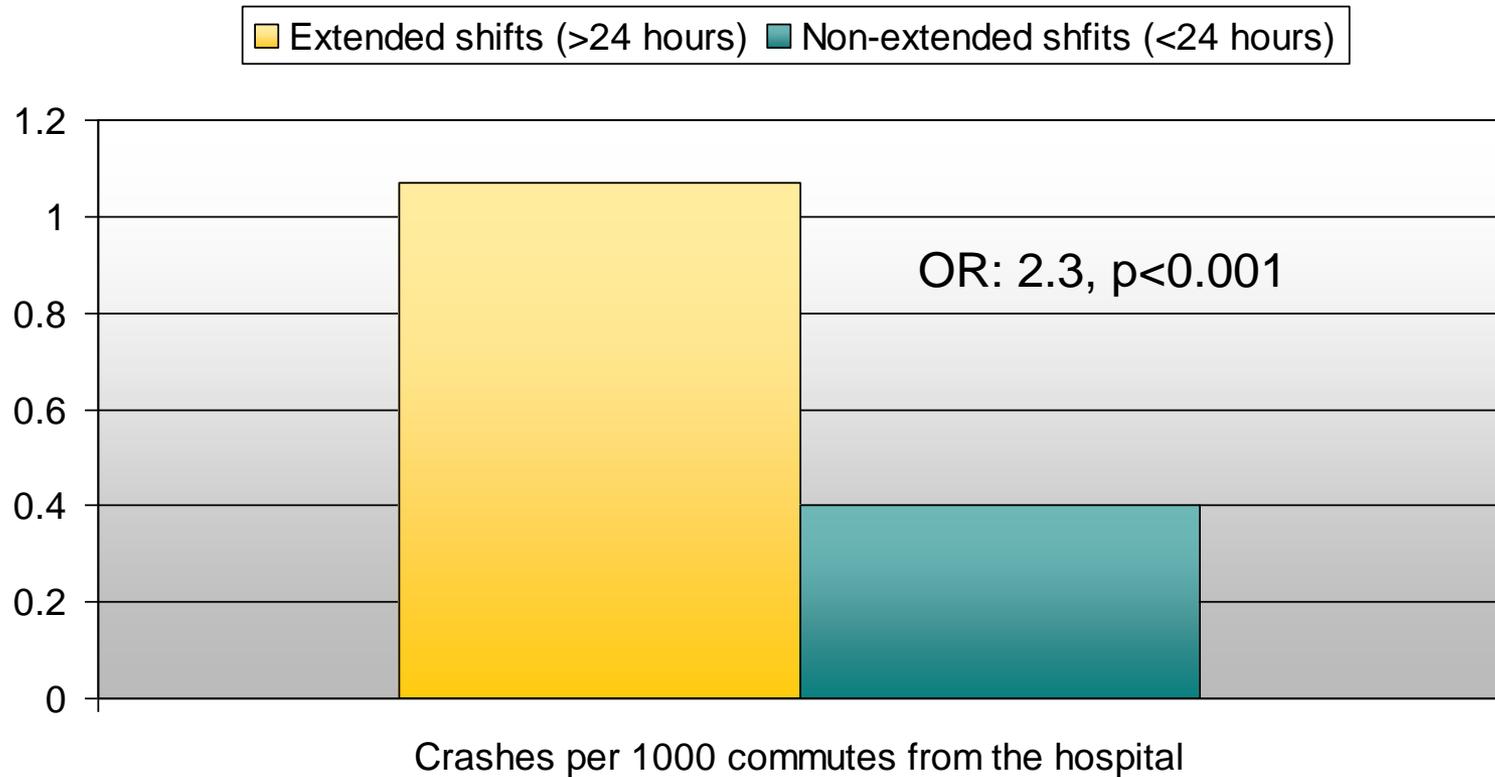
Intern Sleep and Patient Safety Study

Results: 36% more serious errors on traditional schedule, including *five times* as many serious diagnostic errors



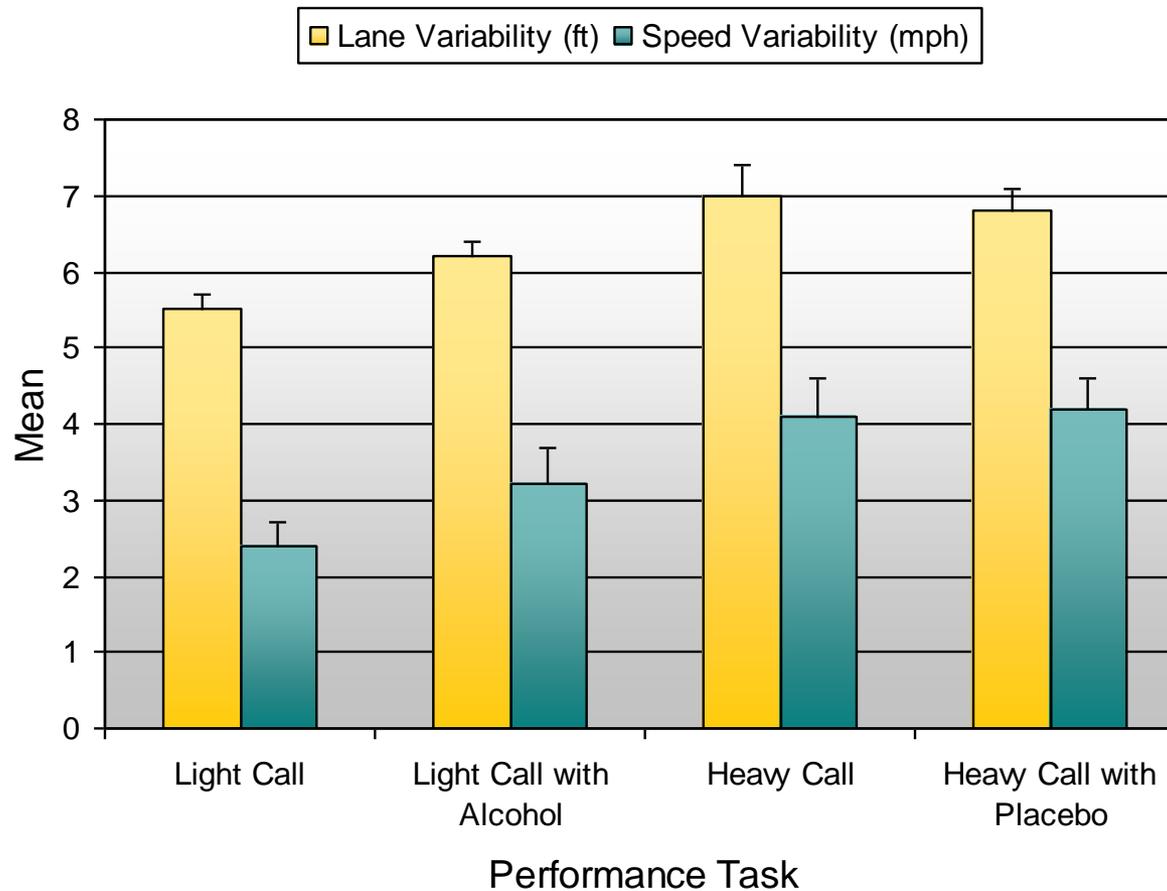
Landrigan et al. N Engl J Med 2004

Harvard Work Hours, Health, and Safety Study: Motor Vehicle Crash Risk in Interns on Commute Home from Hospital



Barger, L. K. et al. N Engl J Med 2005

Driving Simulator

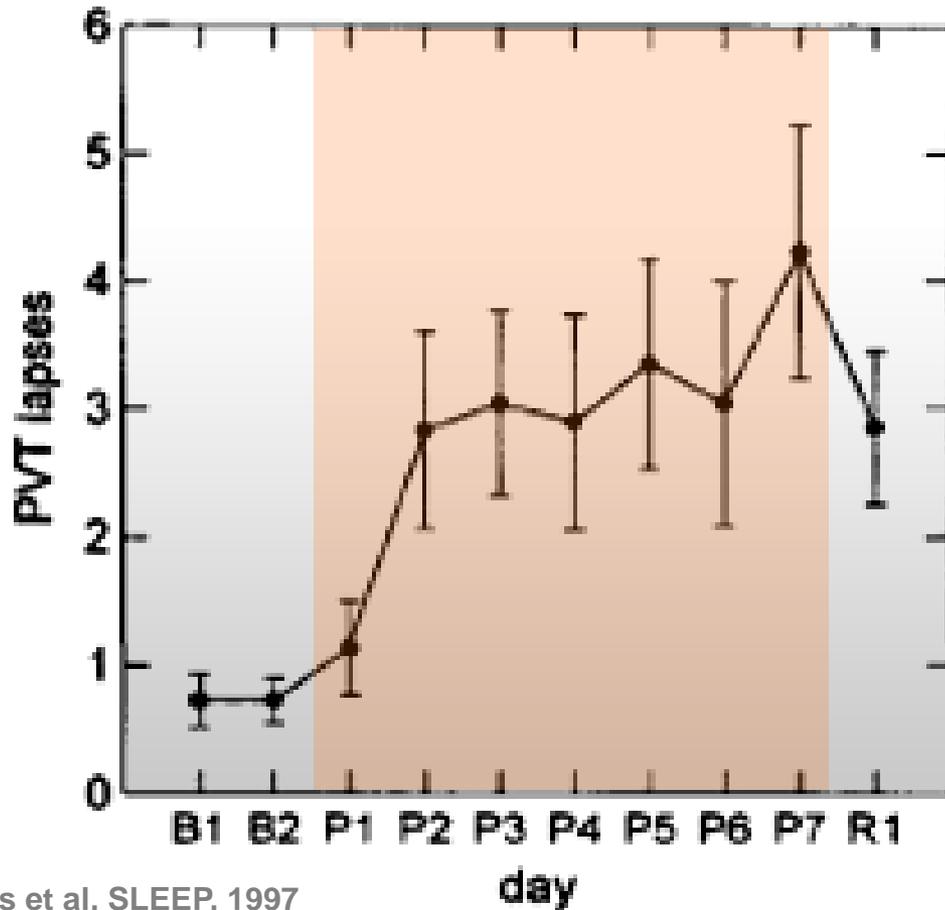


Condition effects:
 $P < 0.001$

No effect of sex or
training year

Arnedt et al. JAMA 2005

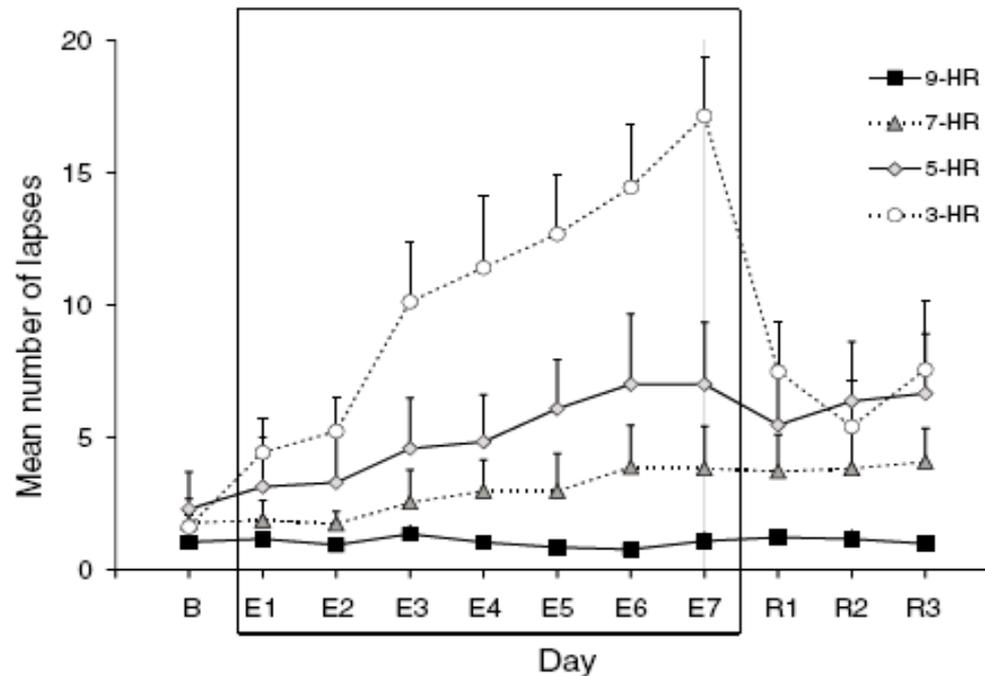
The Effects of Sleep Loss are Cumulative



Psychomotor
vigilance task
(PVT)
performance
during baseline
(B), sleep
restriction (P) and
recovery (R)

Dinges et al, SLEEP, 1997

Recovery Sleep and Attention



Belenky et al, J. Sleep Research, 2003

Hmm....

- In rats, chronic partial sleep loss shows neuronal stress signals which do not seem to resolve over weeks
- Sleep deprivation/fragmentation increases amyloid/tau
- Sleep (undisturbed, good) needed for gunk clearance from brain
- Sleep deprivation damages locus ceruleus and other wake promoting structures

Sleep Inertia

- State of impaired cognition, grogginess, disorientation experienced upon waking from sleep
 - Increased if awakened from slow wave sleep
- Studies suggest severe cognitive impairments lasting up to 10 minutes after awakening*
 - Worse than performance after 26 hr sleep deprivation
 - Residual effects up to two hours

*Wertz, JAMA, 2006

Tassi and Muzet, Sleep Med Rev, 2000

Impact of sleepiness on behavior

- Emotional flattening (perceptive)
- Emotional flattening (expressive)
 - Voice analysis can detect
- Irritability
- Loss of humor perception
- Social cognitive skills including reading emotions
 - Brain imaging (e.g., fMRI) shows substantial and consistent neural network modifications following sleep deprivation

Randomized Trials

- No impact of shortened hours on risk
- Impact of shortened hours on “happiness”
- Thus, ACGME has moved back to 24 hours for Interns
- Supervision and system redundancy likely reduce impact of sleep loss
 - Nocturnists
 - On call Attending Physicians are actually called
 - Computer assistance
 - Team work (nursing, pharmacy)
 - Caffeine

Countermeasures

- Sleep is the BEST countermeasure
- Recovery sleep process not well understood
 - After 7 days PSD (3 or 5 hrs TIB), 3 nights insufficient
 - After 64 hours TSD, 2 nights mostly sufficient
 - Objective residual impairment persists for unknown durations



Countermeasures

- Naps
- Serve as effective, short-term countermeasure
 - 45 min may be minimum length during SD
 - 10 minute naps after 1 night PSD?
 - Particularly useful when taken prior to onset of SD
- Can help even when well-rested



Caffeine

- Reduces some sleep-related deficits at doses of 75-150 mg
- *Strategic* consumption is key
- Effects within 15 – 30 minutes; half-life 3 to 7 hours
- Use for temporary relief of sleepiness
- Cons:
 - Can disrupt subsequent sleep (more arousals)
 - Tolerance may develop
 - Diuretic effects

*Bonnet et al SLEEP 2005

Caffeine Content

Product	Serving Size	Caffeine (mg)
Cola	8 oz	30 -- 45
Tea	8 oz	10 – 70
Orange soda	8 oz	0 – 40
Mountain Dew	8 oz	57
Red Bull	330 ml	80
Drip Coffee	7 oz	110 – 175
Starbucks Grande	16 oz	260
No-Doze	1 tab	100
Vivarin	1 tab	200

Countermeasures

- **Bright Light**
 - Effective for sleepiness and subjective measures
 - Objective measures less clear
- **Exercise**
 - Only very short-term benefit, but longer-term
- **Posture**
 - Temporarily effective, at least for attention
- **“Driving” strategies**
 - Completely ineffective



Dealing with shift work

- Large inter-individual differences
- Different strategies for random vs. clustered/block shift-work
- Light, sleep, activity, drug, avoid naps if likelihood of rapid action post-awakening

Residents Report Using:

Melatonin: minimal effect in ER resident studies

Amphetamines/MPH*: can improve psychomotor performance and promote subjective alertness at 10-20 mg; adverse effects sleep, CV and metabolic/ neuroendocrine measures, high abuse potential

Modafinil (Provigil)* and Armodafinil (Nuvigil): Variable improvement performance, alertness, mood at doses 100-400mg; may result in subjective “overconfidence,” disrupted sleep

*Bonnet et al SLEEP 2005

Summary

- Sleep is necessary for brain and body
- Sleep loss has biological consequences
- Only sleep (maybe some forms of anesthesia) can combat sleepiness
- Sleep loss will ultimately result in “brain failure”
- Sleep loss has implications for “everyone”
- Professional duty hours are under increasing scrutiny
 - Transportation, air-traffic controllers, pilots, medical trainees
- Understanding sleepiness biology increased respect for sleep and sleepiness