Sleep Medicine and the role of Sleep Studies in Sleep Assessment

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Breathe West

Mr RS

- 56y.o male, truck driver
- PHx of HTN (Rx with coversyl)
- BMI 32kg/m2
- Snorer
- worked for 30 years with excellent driving record and no “red flags”
- Referred to local sleep diagnostics group for a sleep study at request of employer
- Refreshing sleep
- Occasionally tired in pm (ESS 8/24)

Mr RS

- Home based level 2 study
  - AHI 20 per hour (mainly hypopnoeas in supine position)
  - REM AHI 33 per hour
  - 4%ODI – 8 per hour
  - Cortical arousal index 15 per hour
  - Sleep efficiency 83% with REM 17% and SWS 14%
  - SpO2 nadir 81% and TST with SpO2< 90% is 2 minutes

MR RS

- “There is severe obstructive sleep apnoea in REM. Significant oxygen desaturations occurred. Sleep appeared fragmented. Periodic leg movements were not present.”
- “Recommend CPAP and if CPAP is not tolerated consider oral appliance therapy. Sleep physician referral could be considered. “
- “Untreated sleep apnoea is associated with increased risk of cardiovascular events, stroke and motor vehicle accidents. Driving should be avoided in untreated sleep apnoea”

Treatment

- ?Referral for CPAP
- ?Referral for Oral Appliance Therapy
- ?Reassurance
- ?Report to Vicroads/ Advise that cannot drive unless OSA is effectively treated

Mr RS

- Mr RP purchased Autotitrating PAP device (and mask) – paid $2400
- Device used less than 1 hour per night and subsequently ceased use
- Underwent a repeat sleep study at an accredited service – snoring without significant sleep disordered breathing
- I advised to cease CPAP, focus on weight loss and consider positional aid. Wife happy to trial ear plugs.

WHERE WERE THESE PATIENTS LET DOWN

- ABSENCE OF CLINICAL ASSESSMENT
- MODEL OF CARE
- ? QUALITY OF SLEEP STUDY
- LACK OF EVIDENCE BASED CARE AND ADVICE
- ? COMMERCIAL INTERESTS
- SLEEP APNOEA CENTRIC CARE

OUTLINE

- Overview of Sleep Neurobiology
- Sleep Assessment
- Sleep Investigations
- OSA – when to treat and when not to treat
- What to do with the non-compliant at risk patient

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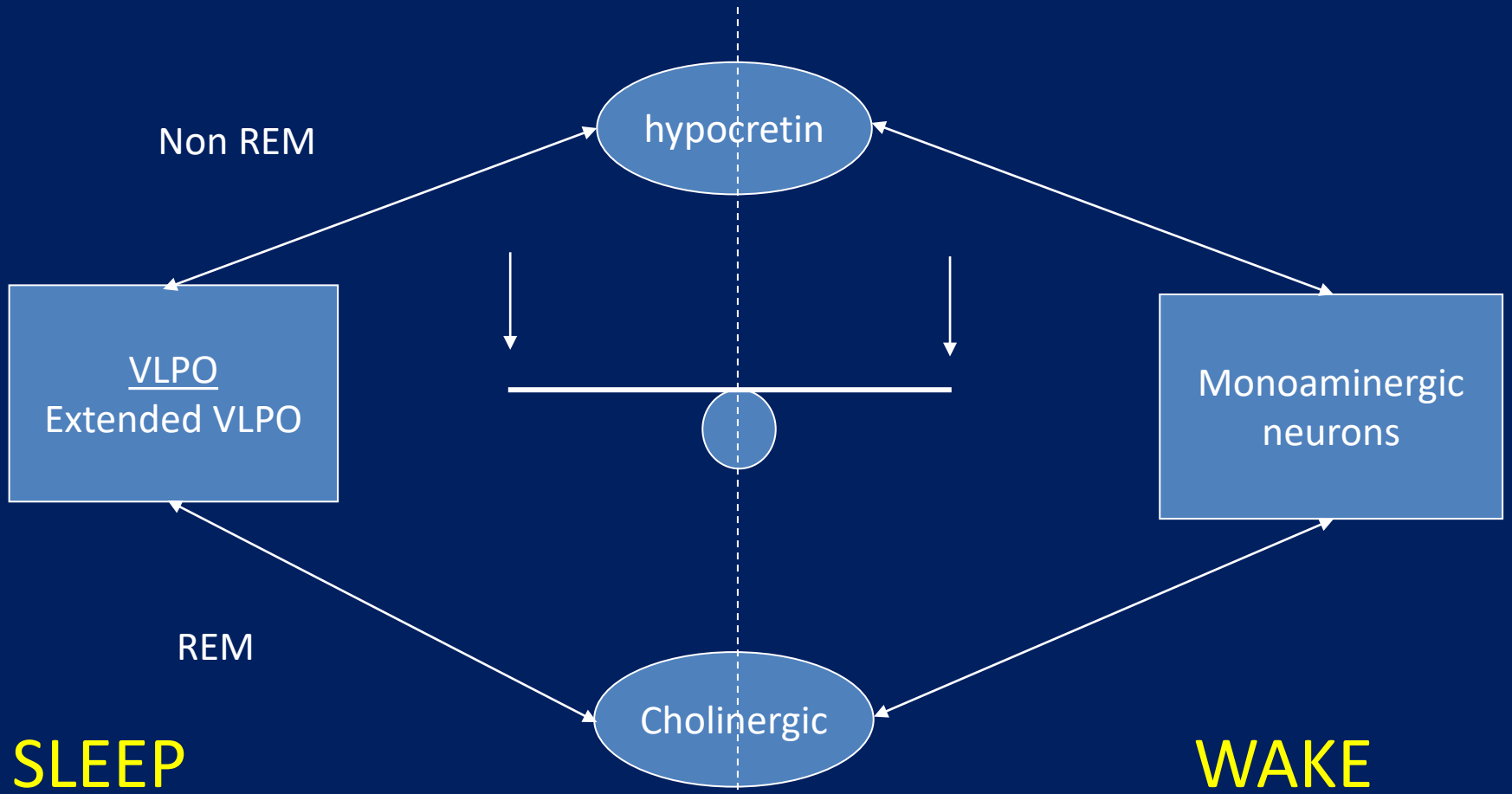
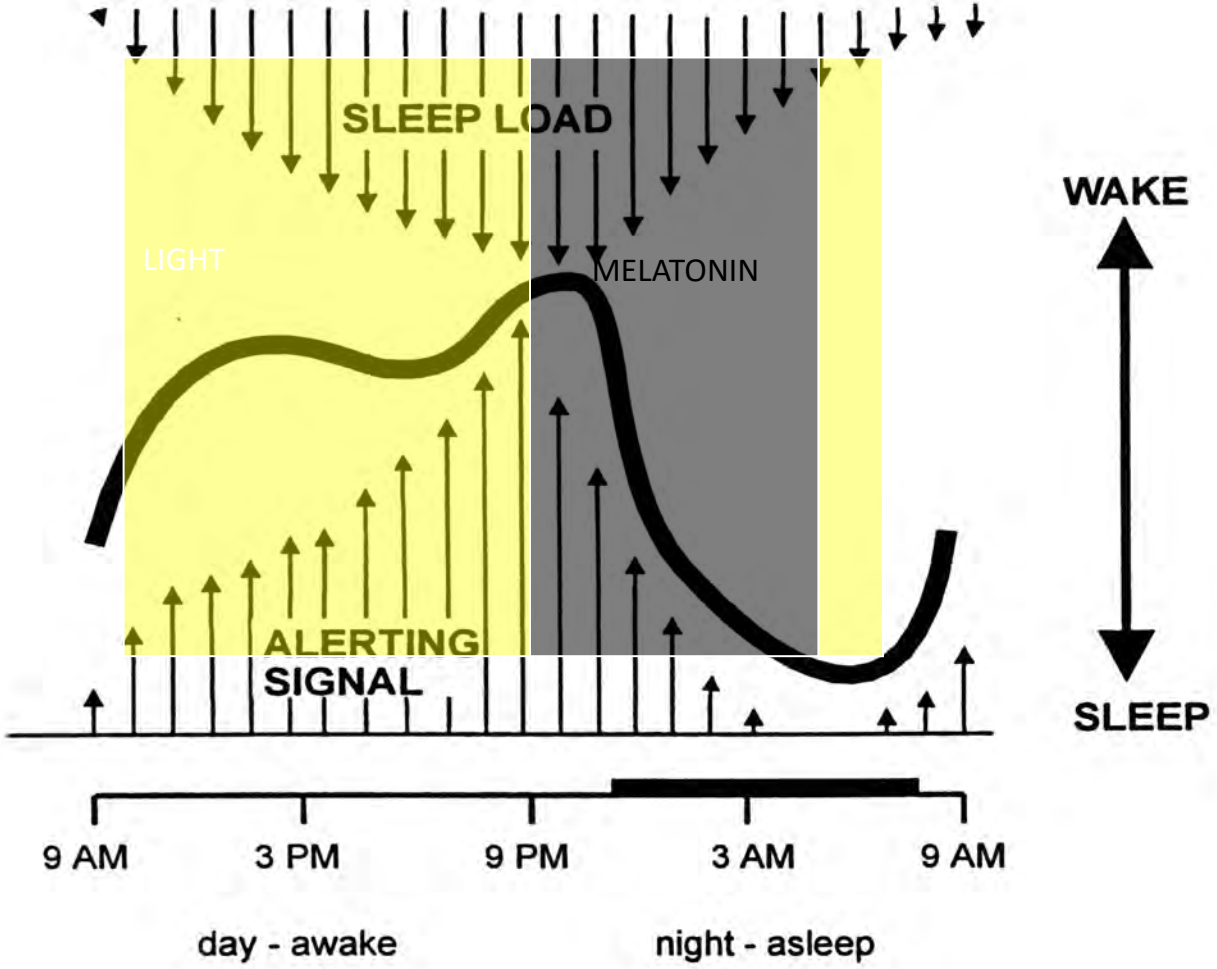
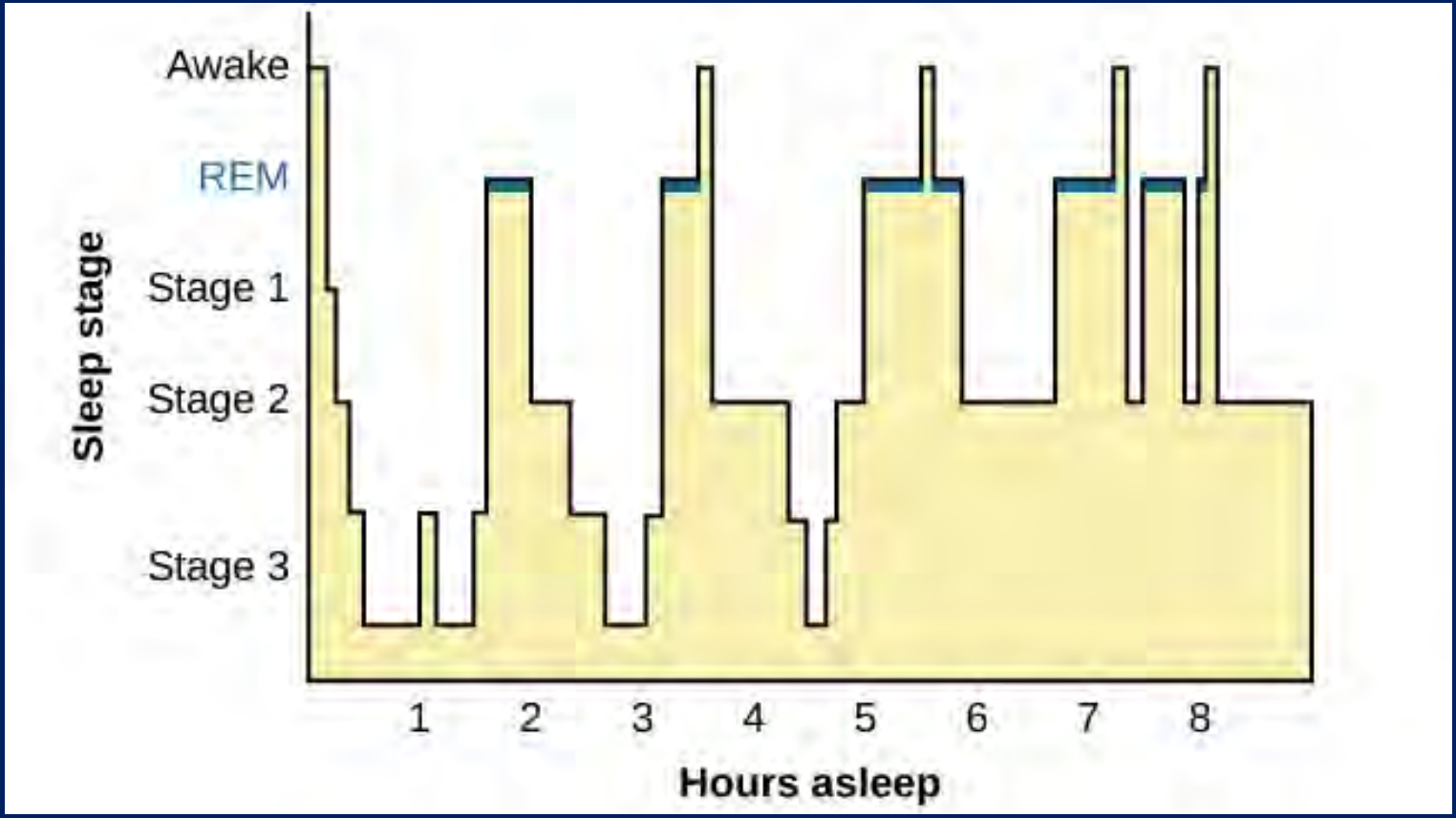
SLEEP REGULATION – OVERVIEW





https://www.medscape.com/answers/1187829-70500/what-are-the-homeostatic-and-circadian-processes-regulating-sleep



Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem. Institute of Medicine (US) Committee on Sleep Medicine and Research; Colten HR, Altevogt BM, editors. Washington (DC): National Academies Press (US); 2006.

Circadian Rhythm Abnormalities

- Jet lag
- Shift work
- Delayed sleep-phase syndrome (DSPS)
- Advanced sleep-phase syndrome (ASPS)
- Irregular sleep–wake pattern
- Non-24-hour sleep–wake syndrome

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Daytime sleepiness

Not enough sleep

- Lifestyle
- Shift work
- Jet lag
- Sleep interruptions
  - Eg young children

Sleep Disorders

- Sleep Breathing Disorders
- RLS/PLMD
- Narcolepsy/ Idiopathic hypersomnia
- Others
  - Circadian Rhythm Disorders
  - Drugs/Alcohol/pain syndromes
  - Neurological Disease
  - Chronic Medical Disease
  - Insomnia.
  - Parasomnias
  - psychiatric disorders

EPWORTH SLEEPINESS SCALE

Use the following scale to choose the **most appropriate number** for each situation:

0 = would **never** doze

1 = **slight chance** of dozing

2 = **moderate chance** of dozing 3 = **high chance** of dozing

Chance of Dozing (0-3)

Sitting and reading

Watching TV

Sitting, inactive in a public place (e.g. a theatre or a meeting)

As a passenger in a car for an hour without a break

Lying down to rest in the afternoon when circumstances permit

Sitting and talking to someone

Sitting quietly after a lunch without alcohol

In a car, while stopped for a few minutes in the traffic

? **M.W. Johns 1990-97**

0-5 Lower Normal Daytime Sleepiness
6-10 Higher Normal Daytime Sleepiness
11-12 Mild Excessive Daytime Sleepiness
13-15 Moderate Excessive Daytime Sleepiness
16-24 Severe Excessive Daytime Sleepiness

TABLE 2.
Risk factors for EDS based on multiple logistic regression
ES, Effect size.

Parameter	ES	*P*	OR
Depression	10.6	<0.001	6.85
Log BMI (kg/m^2)	4.3	<0.001	
+1 SD			1.45
+2 SD			2.10
Age	3.6	<0.001	
+1 SD			0.61
+2 SD			0.38
Typical sleep duration	3.2	0.001	
+1 SD			0.76
+2 SD			0.58
Diabetes (glucose > 126)	2.3	0.019	1.87
Smoke	1.9	0.060	1.53
OHI > 15	1.2	0.255	1.70

Bixler et al. JCEM 2005

SLEEP SYMPTOMS ARE COMMON AND OFTEN NOT SPECIFIC

- Snoring is common – 50-80% of adult population
- Excessive daytime sleepiness has a wide differential diagnosis
- Apnoeic Events are commonly observed
- Nocturnal Awakenings may increase with age
- Nocturnal Choking – asthma, GORD, apnoeic event, nocturnal panic attacks

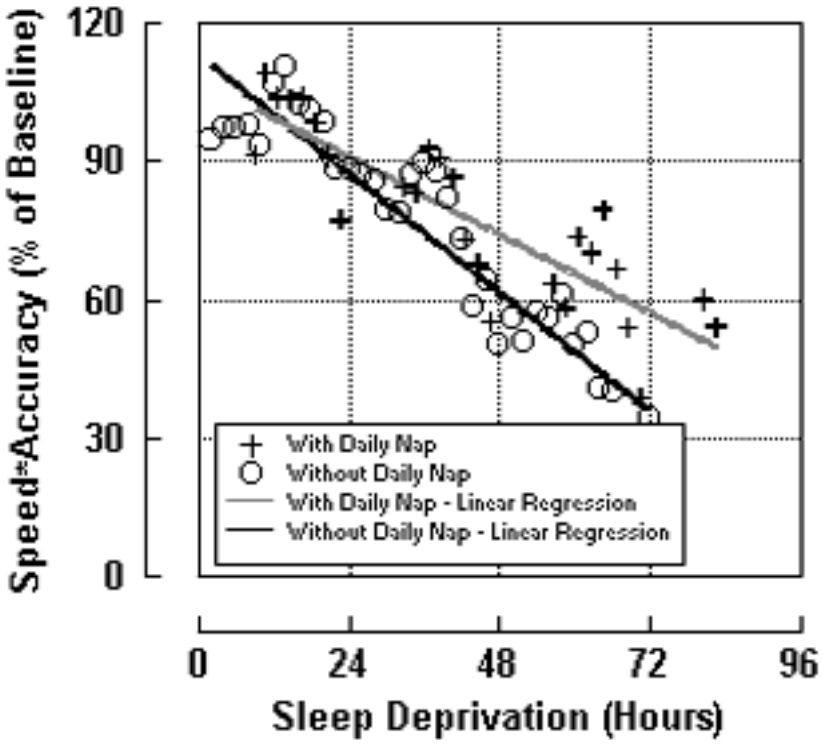
Snoring + EDS

≠

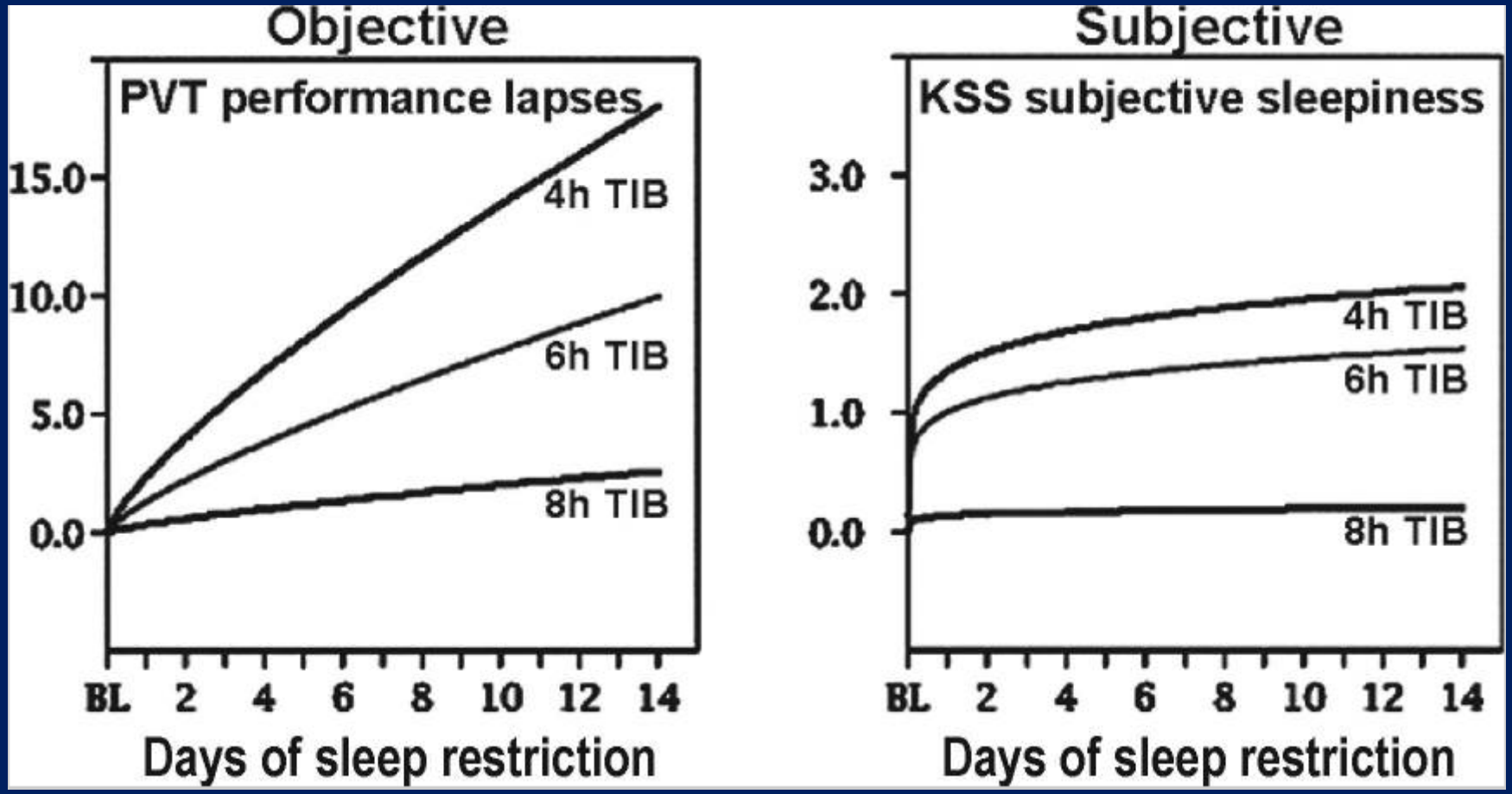
OSA

Degradation in Cognitive Performance
in Sleep Deprivation
With and Without Daily Nap (30 minutes)

- **Sleep deprivation degrades cognitive performance.**
- **The sleep/performance system is sensitive to even brief amounts of sleep.**
- **A daily 30 minute nap improves performance when compared to total sleep deprivation.**



People Get Used to the Impairment

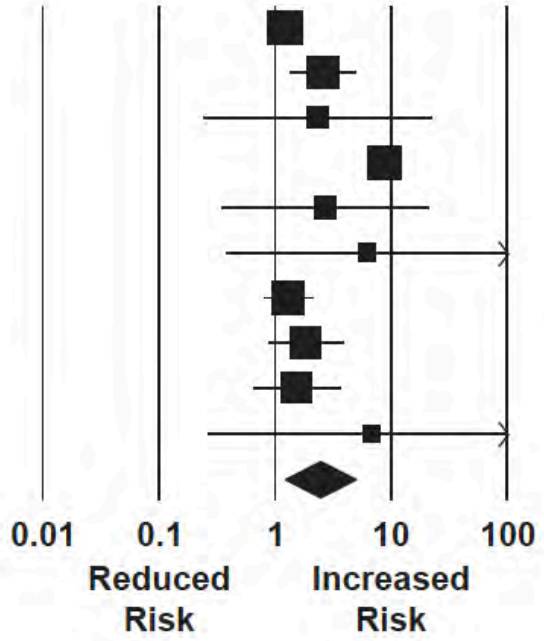


Banks et al J Clin Sleep Med. 2007; 3: 519–528.

OSA AND CRASH RISK

Study name	Rate ratio	Lower limit	Upper limit	Z-Value	p-Value
Mulgrew	1.220	0.920	1.618	1.381	0.167
Barbe	2.570	1.304	5.065	2.727	0.006
Shiomi	2.342	0.237	23.151	0.728	0.467
Horstmann	8.719	6.179	12.303	12.326	0.000
Lloberes	2.720	0.342	21.645	0.946	0.344
Findley 2000	6.195	0.373	102.896	1.272	0.203
George	1.306	0.791	2.157	1.043	0.297
Stoohs	1.848	0.865	3.948	1.586	0.113
Haraldsson	1.551	0.641	3.754	0.973	0.331
Findley 1988	6.833	0.257	181.683	1.148	0.251
	2.427	1.205	4.890	2.480	0.013

Statistics for each study



Tregear et al. JCSM 2009

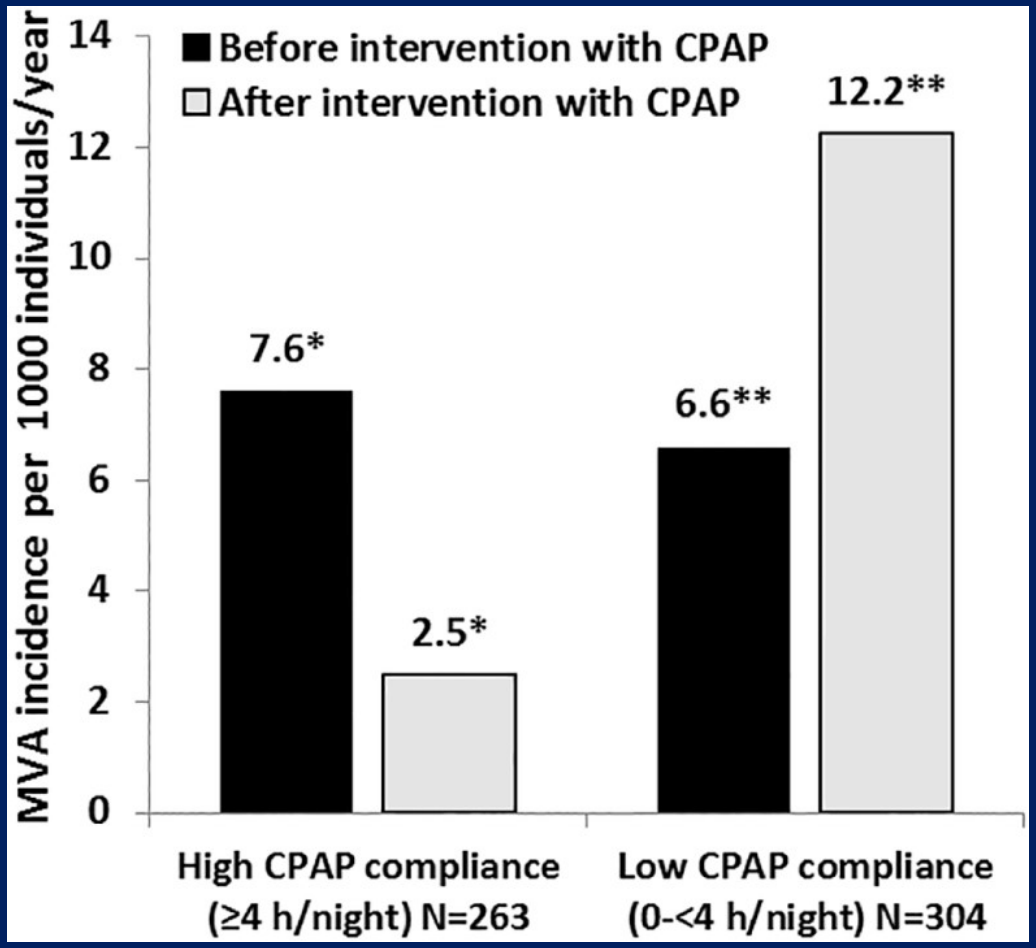
Factors that may increase crash risk in OSA

- Excessive Daytime Sleepiness
- Elevated BMI
- Sleep Restriction
- Shift Work
- Older Age
- Use of Hypnotics

Factors that may increase crash risk in OSA

- Excessive Daytime Sleepiness
- Elevated BMI
- Sleep Restriction
- Shift Work
- Older Age
- Use of Hypnotics
- ? AHI Value – although many studies have NOT found a correlation between AHI size and crash risk

Figure 3 Incidence of motor vehicle accidents (MVAs) per 1,000 individuals per year before and after continuous ...



Sleep, Volume 38, Issue 3, 1 March 2015, Pages 341–349, https://doi.org/10.5665/sleep.4486

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SLEEP ASSESSMENT

- Clinical Assessment is more important than the results of the sleep study.
- Treatment decisions in most cases can be determined either by the clinical assessment alone or together with the results of the sleep study.
- A sleep study alone in the majority of cases cannot drive treatment decisions.

HISTORY AND EXAMINATION

- Age and Gender
- Work – shift work, retired, regular day shift
- Do you have a problem with sleep?
- Comorbidities (HTN, DM, CVD, Thyroid disease etc…)
- Medications/ Smoking/ Etoh/ Caffeine
- Sleep/Wake times – sleep onset, sleep duration
- Nocturnal Awakenings and Cause (?Nocturia)
- Refreshing sleep
- Morning Headaches
- Snoring/ Observed Apnoeas/ Choking/ Dry Mouth
- Restless Legs/ Periodic Leg Movements/ Parasomnia
- Sleep paralysis/ hypnogogic hallucinations/ cataplexy
- Sleep Environment
- Menopause Status
- Mood/ Hx of Depression?
- Constipation, anosmia (if considering RBD)
- Epworth Sleepiness Score

HISTORY AND EXAMINATION

- BMI
- Mallampati Score
- ? Retrognathia
- ? Nasal Obstruction
- Neck Circumference
- Signs of Parkinsonism (RBD)
- Signs of Anaemia
- Signs of Thyroid Disease

STOP-BANG Sleep Apnea Questionnaire

Chung F et al Anesthesiology 2008 and BJA 2012

High risk of OSA: Yes 5 - 8

Intermediate risk of OSA: Yes 3 - 4

Low risk of OSA: Yes 0 - 2

STOP		
Do you **S**NORE loudly (louder than talking or loud enough to be heard through closed doors)?	Yes	No
Do you often feel **T**IRED, fatigued, or sleepy during daytime?	Yes	No
Has anyone **O**BSERVED you stop breathing during your sleep?	Yes	No
Do you have or are you being treated for high blood **P**RESSURE?	Yes	No

BANG		
BMI more than 35kg/m2?	Yes	No
AGE over 50 years old?	Yes	No
NECK circumference > 16 inches (40cm)?	Yes	No
GENDER: Male?	Yes	No

TOTAL SCORE		

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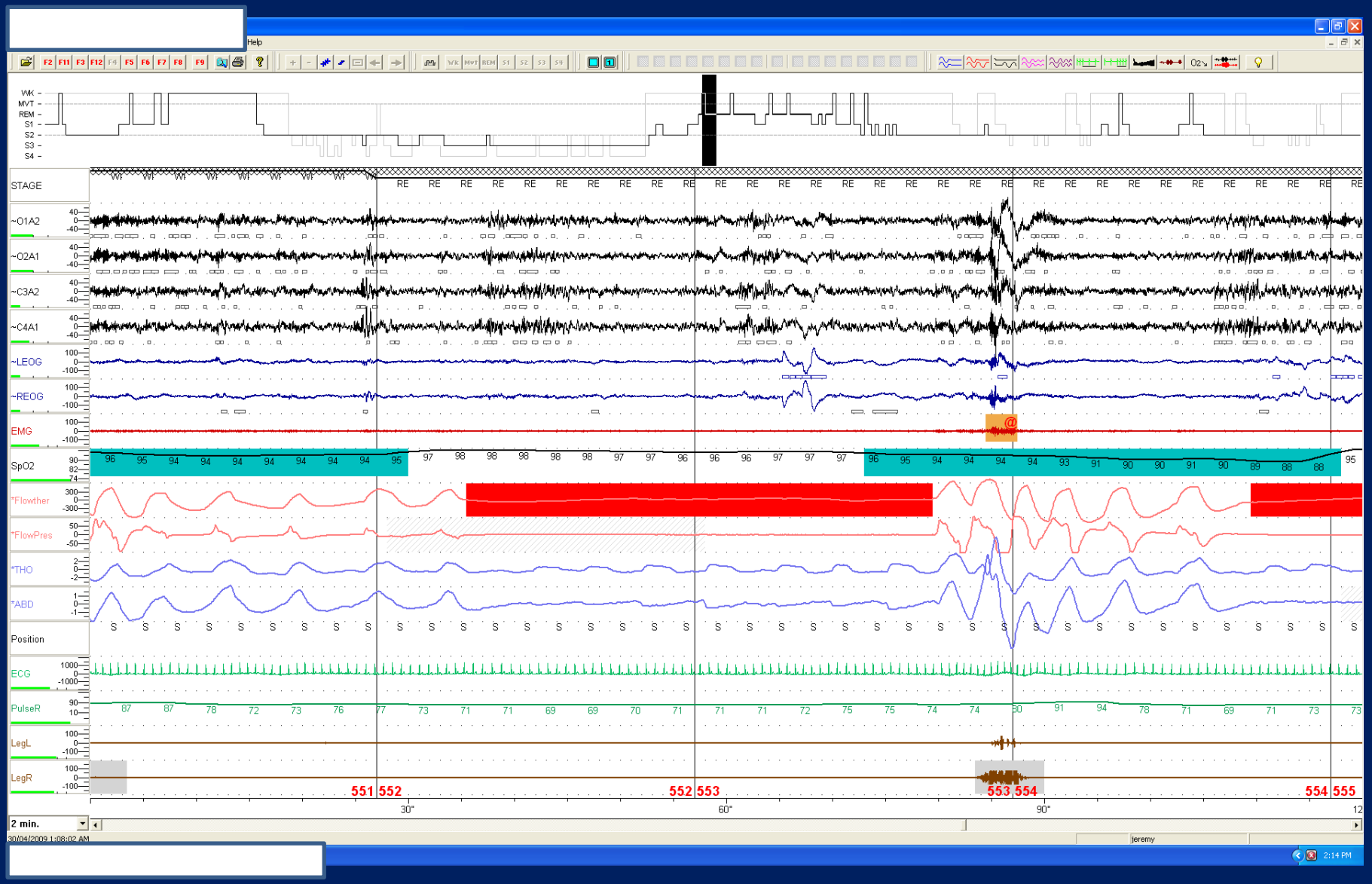
SLEEP STUDIES

- There are 4 levels of sleep studies – choosing the wrong sleep study may result in poor patient outcome
- Sleep Studies consist of multiple signals all of which are prone to artefact. Artefact can significantly alter the results leading to incorrect diagnosis.
- Different models of care may produce very different results and different recommendations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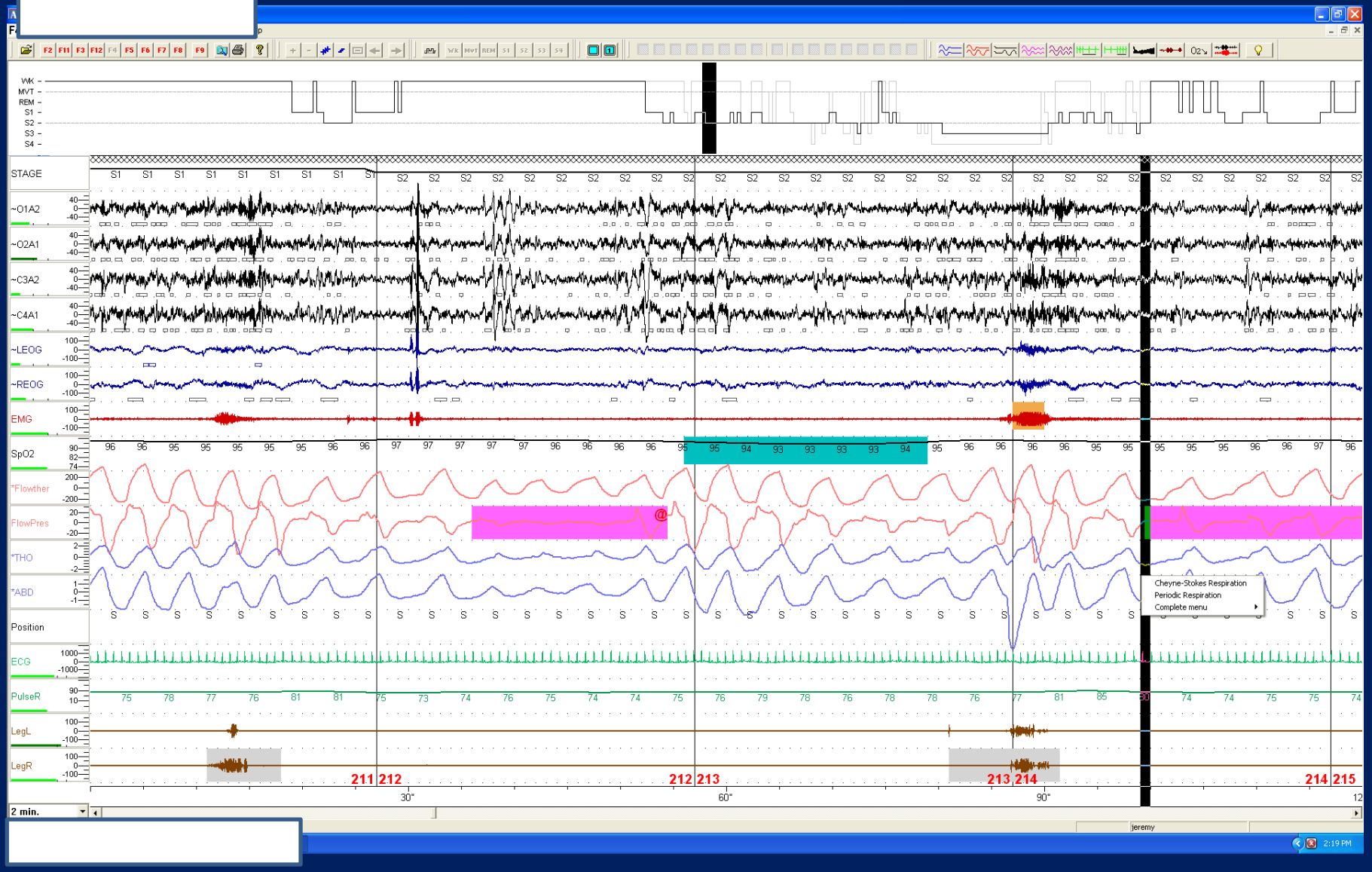
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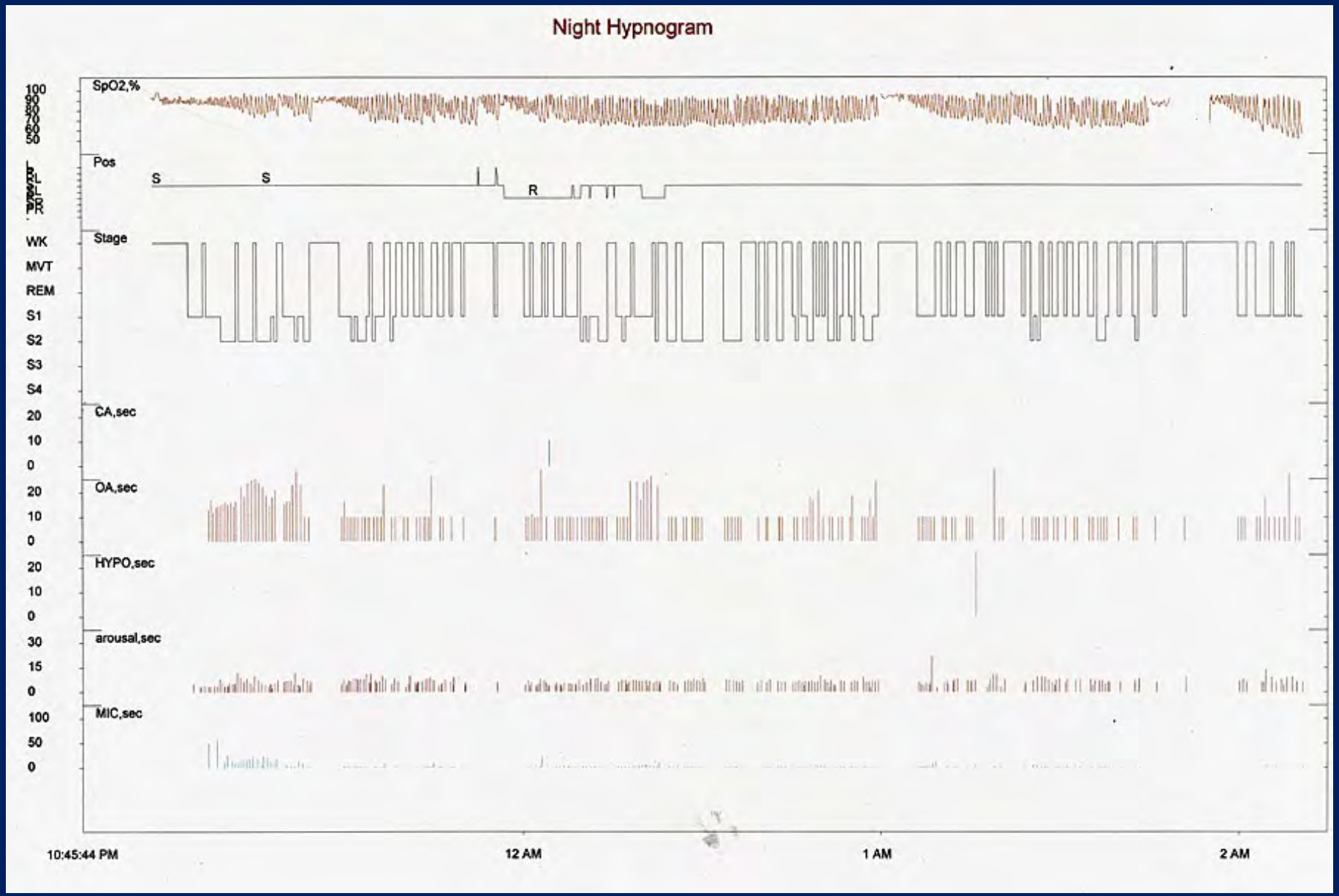
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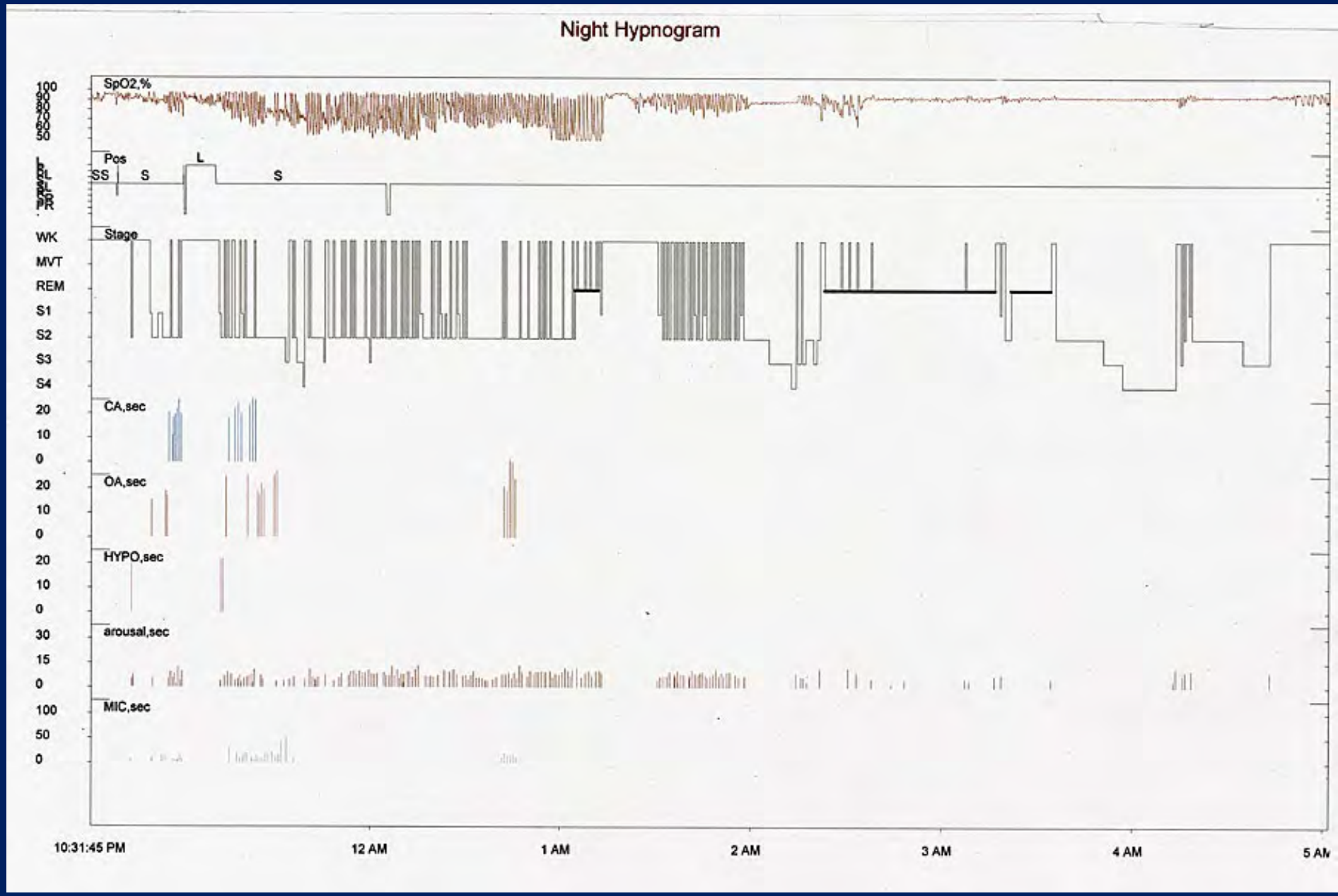
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Portable vs In-Lab Studies

Portable Studies

- PROS
  - more accessible and cheaper
  - performed at home
  - High sensitivity in diagnosing severe OSA in moderate-high risk individual
- CONS
  - variability in quality control and models of care
  - signal loss and artefact
  - many providers are not ASA/NATA accredited

Portable vs In-Lab Studies

In-Lab Studies

- PROS
  - attended studies – signal loss infrequent and artefact better controlled
  - most labs are ASA/NATA accredited
  - can identify a range of sleep abnormalities
- CONS
  - less accessible and more expensive
  - requirement for overnight hospital stay

PROBLEMS WITH AHI

- Increased sensitivity of nasal pressure signal has resulted in increase number of events present
- Inter and Intra-laboratory Variability – technology used, experience of staff, time saving measures (automatic analysis), signal quality
- Intra-patient variability – night to night. Position, percentage REM, effects of alcohol, medication, smoking, weight

IMPLICATIONS

- Over diagnosis of OSA
  - Inappropriate prescription of CPAP therapy
  - Failure to recognise other sleep related problems that are the cause for the patient's symptoms
- Clinical trials may lack validity

MSLT and MWT

- Multiple Sleep Latency Test (MSLT) – test to assess for pathological hypersomnolence (mean sleep latency < 8minutes)
- Maintenance of Wakefulness Test (MWT) – test to assess ability to maintain vigilance (mean sleep latency > 25 minutes *)

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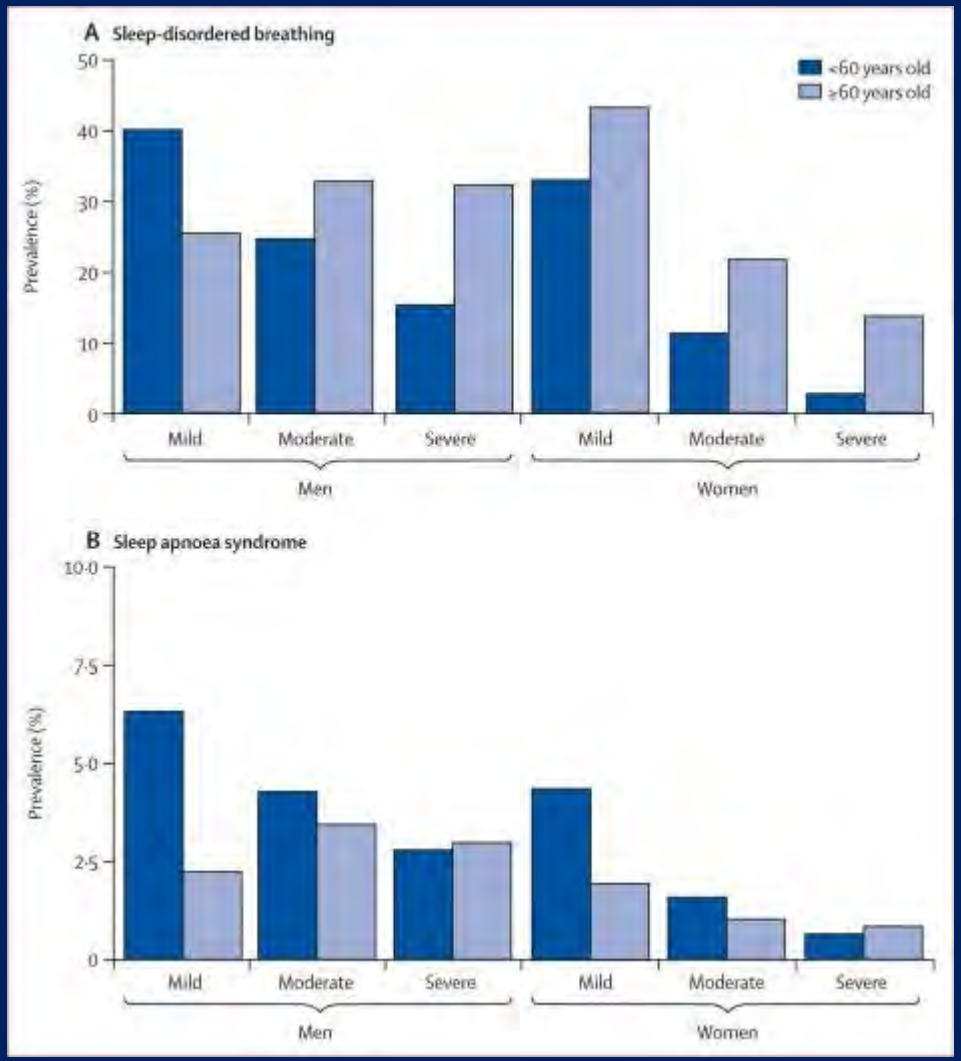
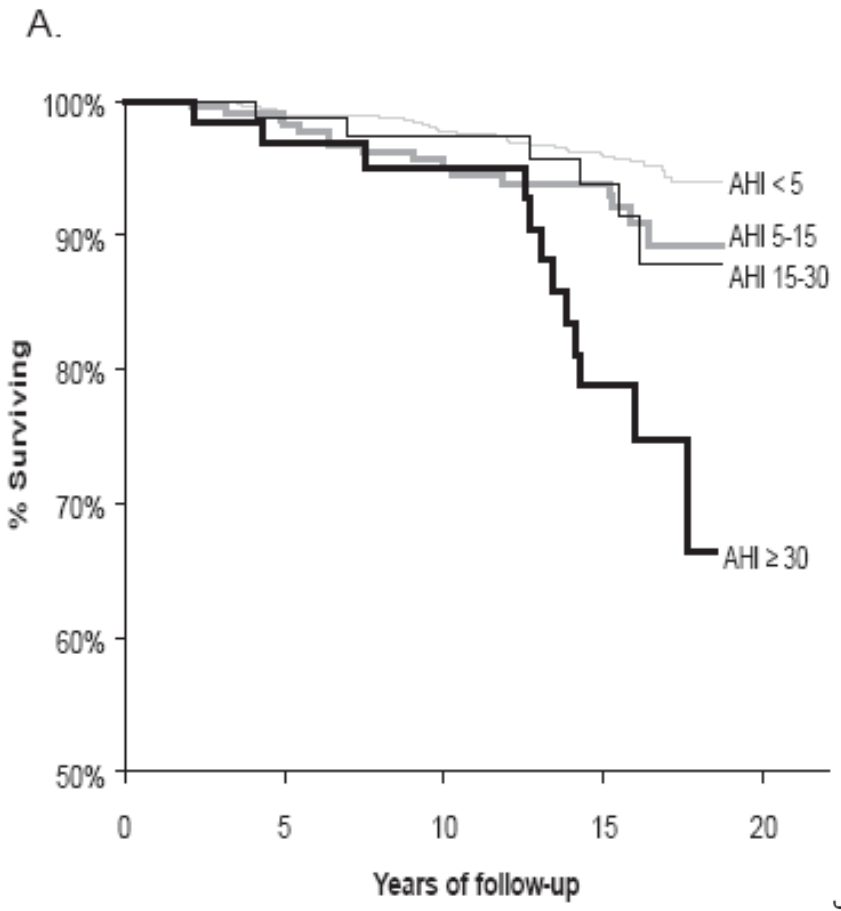
WHAT IS OSA?

Obstructive Sleep Apnoea (OSA) is the repetitive complete or partial cessation of respiration due to obstruction of the upper airway leading to changes in arterial oxygen saturations and/or sleep micro-architecture

- The consequences and management of OSA may differ in childhood, adulthood and the elderly
- OSA often co-exists with other sleep conditions (>50% of cases diagnosed) and in many instances may not cause symptoms or long term sequelae and therefore may not require active treatment

Lancet Resp Med 2015 Apr;3(4):310-8. **Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study.**
Heizner et al.



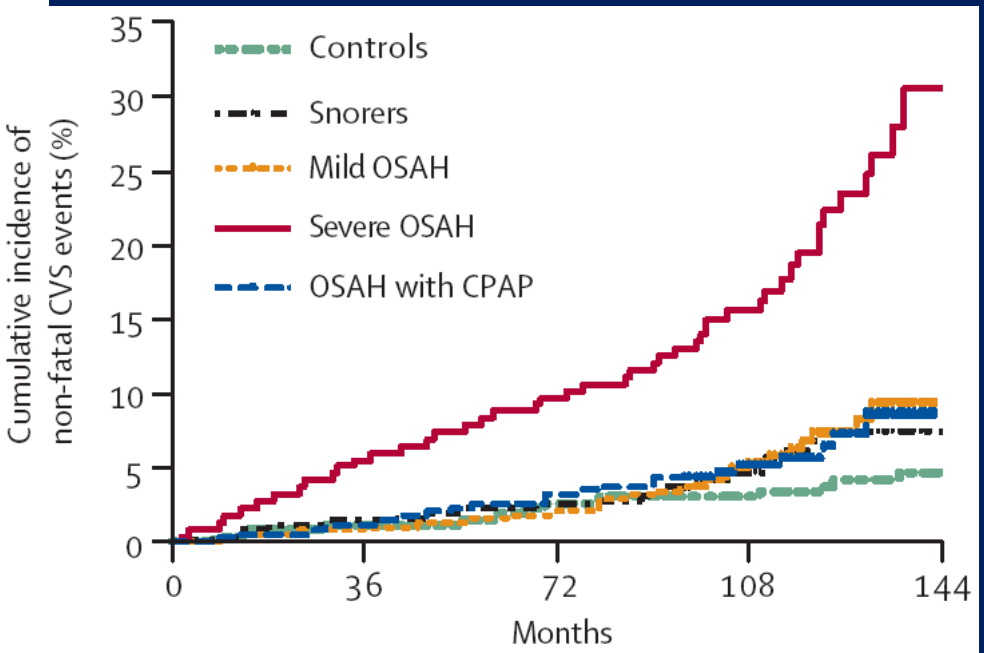


OSA and MORTALITY

Young et al. Sleep 2008;31(8):1071-1078

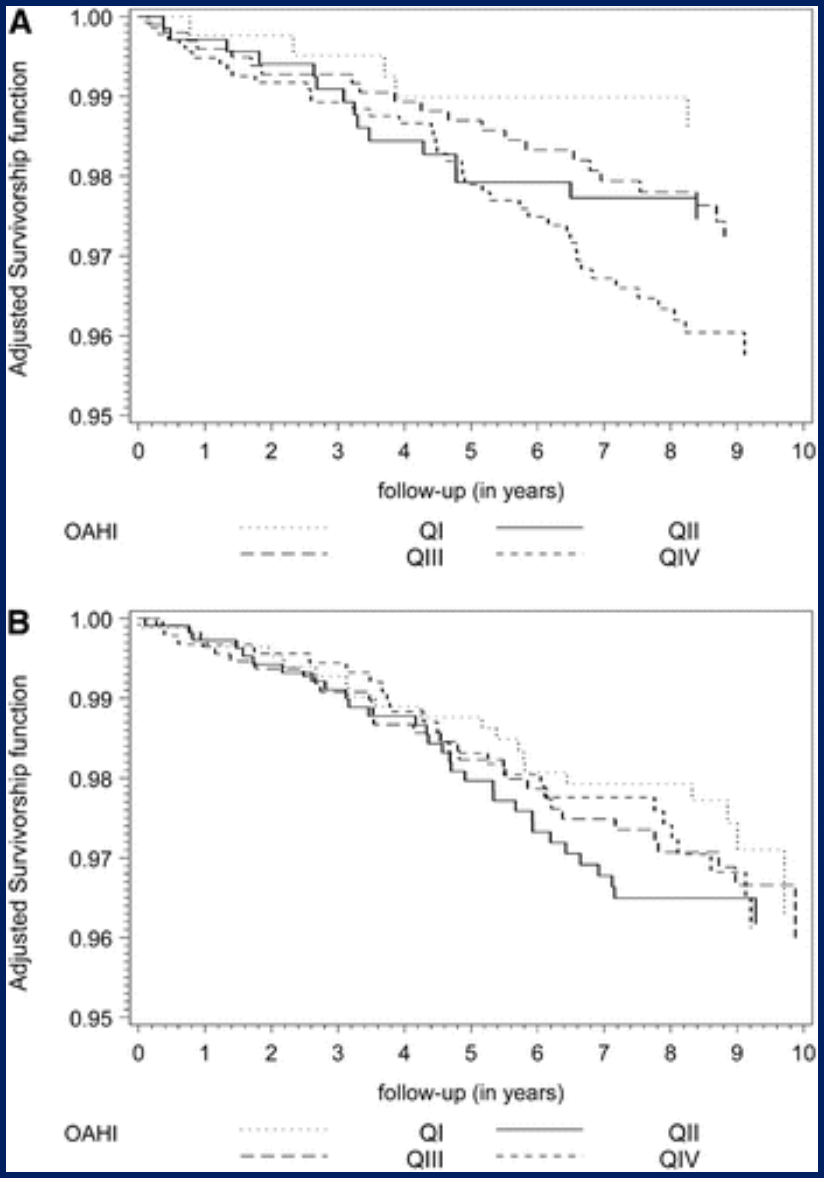
Non-fatal cardiovascular events increased in patients with severe untreated OSA : 12 year clinic follow-up

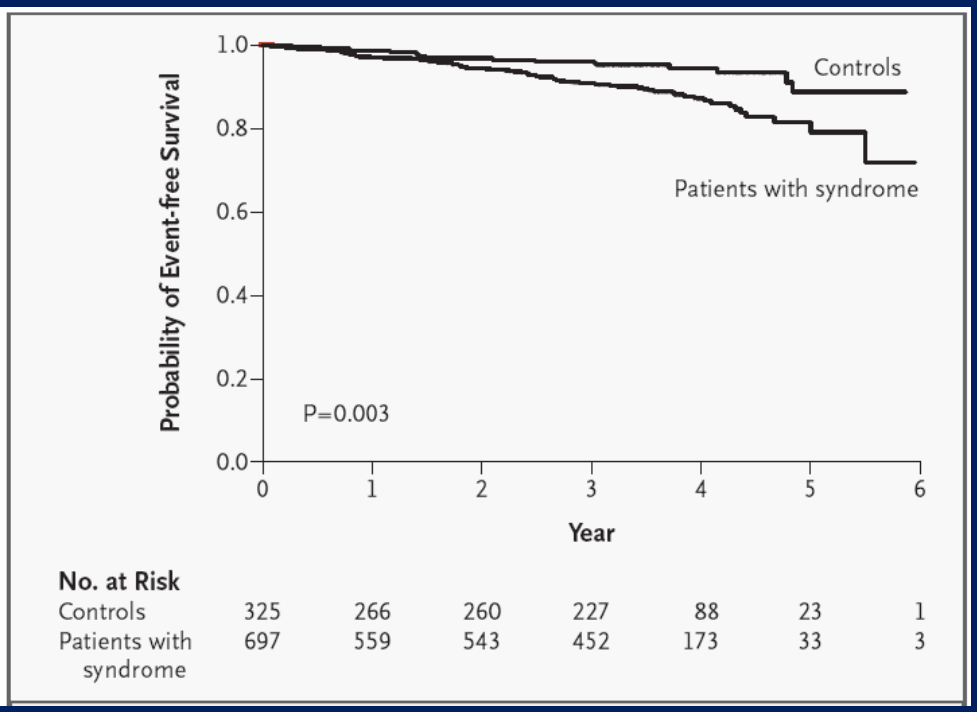
Marin et al LANCET 2005



SHHS STROKE

Redline et al. AJRCCM 2010

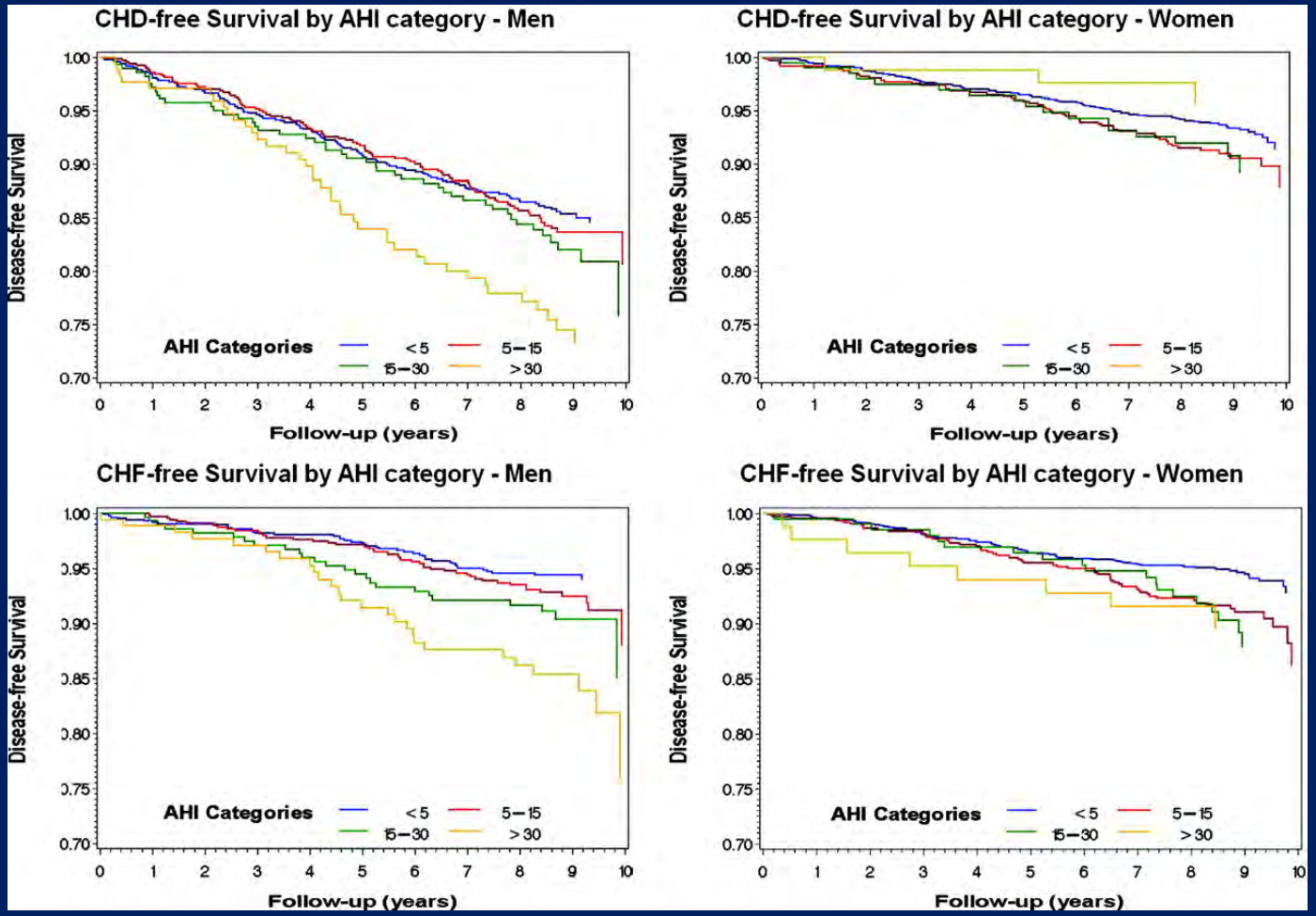




Higher rate of stroke and death in clinic patients with OSA than those without OSA

Yaggi et al NEJM 2005

Unadjusted Kaplan-Meier survival curves for AHI clinical categories, by sex and event type



Gottlieb, D. J. et al. Circulation 2010;122:352-360

Circulation

OSA and DM

TABLE 2. Adjusted odds ratios for glucose intolerance based on fasting and 2-hour glucose levels, Sleep Heart Health Study, 1994–1999*,†

Predictor	Fasting glucose level (n = 2,656)		2-hour glucose level (n = 1,930)	
	Odds ratio	95% confidence interval	Odds ratio	95% confidence interval
Respiratory disturbance index (no. of events/hour)				
<5.0	1.00		1.00	
5.0–14.9	1.27	0.98, 1.64	1.09	0.88, 1.35
≥15.0	1.46	1.09, 1.97	1.44	1.11, 1.87
p for linear trend	0.0090		0.0096	
Average oxyhemoglobin saturation during sleep (%)				
≥95.72	1.00		1.00	
94.57–95.71	1.52	1.05, 2.20	1.16	0.88, 1.53
93.32–94.56	1.75	1.21, 2.53	1.14	0.86, 1.52
<93.32	1.95	1.34, 2.84	1.40	1.05, 1.88
p for linear trend	0.0007		0.0321	
Percentage of sleep time with oxyhemoglobin saturation <90%				
<0.01	1.00		1.00	
0.01–0.25	1.14	0.80, 1.61	1.08	0.83, 1.41
0.26–2.16	1.41	1.01, 1.98	1.32	1.01, 1.74
≥2.17	1.56	1.10, 2.20	1.32	1.00, 1.75
p for linear trend	0.0053		0.0246	
Arousal index (no. of events/hour)				
<12.36	1.00		1.00	
12.36–17.12	0.92	0.66, 1.28	0.87	0.67, 1.14
17.13–24.17	1.23	0.90, 1.69	1.00	0.76, 1.30
≥24.18	1.25	0.91, 1.71	1.23	0.94, 1.61
p for linear trend	NS‡		NS	

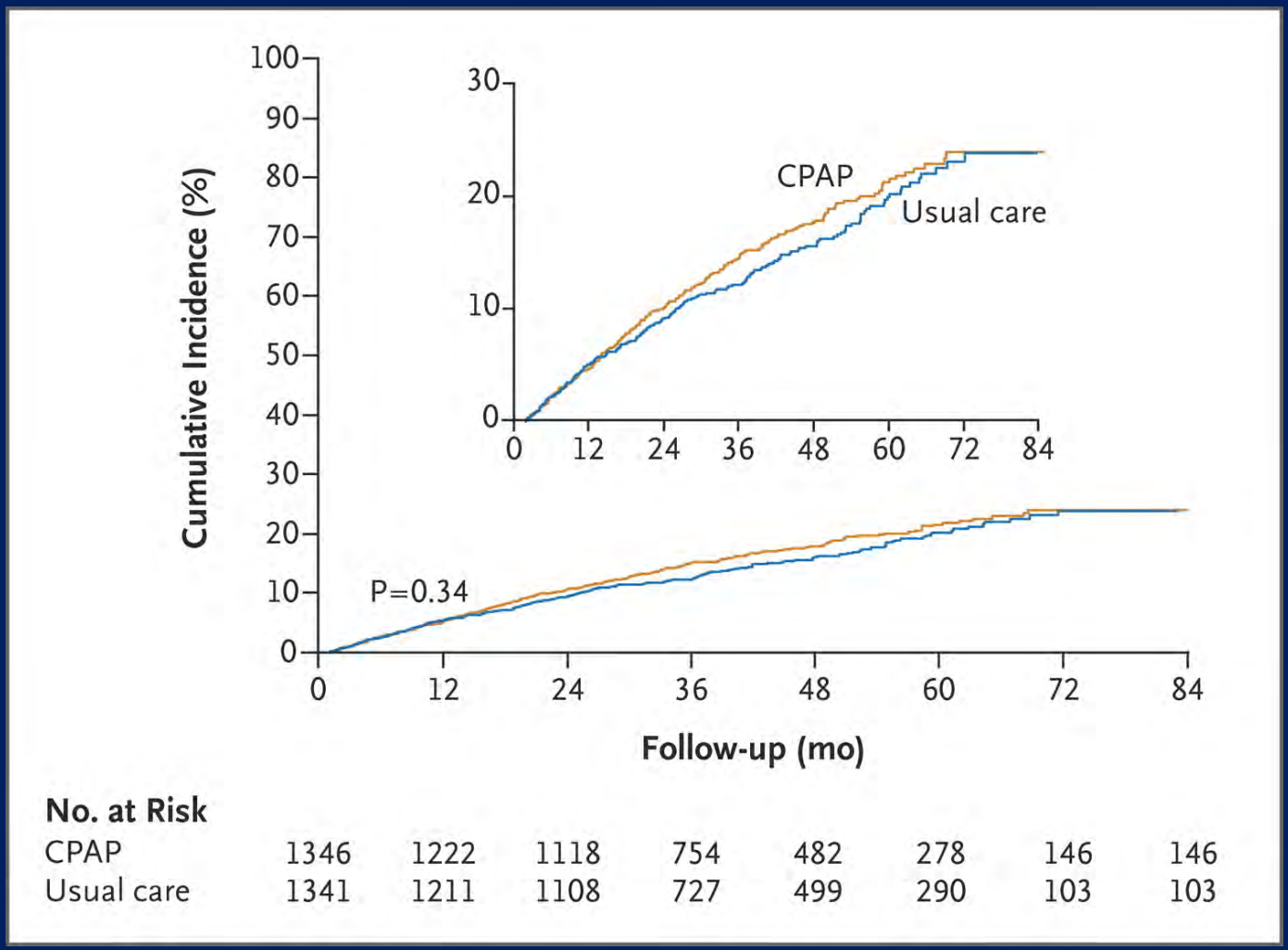
Punjabi et al. Am J Epidemiology 2004;160: 521-530

OSA – Systemic Hypertension

- Nieto et al. JAMA 2000; 283: 1829 – 1836
  - Cross sectional analysis of participants in SHHS – 6132 subjects
  - Mean sBP and dBP and prevalence of HTN increased significantly with increasing SDB measures
  - AHI > 30 – OR 1.37 (1.03 – 1.83)
  - TST with SpO2 < 90% - OR 1.46 (1.12 – 1.88)

- Peppard et al. NEJM 2000; 342(19): 1378 – 1384
  - Wisconsin Sleep Cohort Study – 709 patients
  - AHI > 15 – OR 2.89 (1.46 – 5.64)
  - Dose response relationship between SDB and the presence of HTN 4 years later independent of any known confounding factors.

Cumulative Event Curve of the Primary End Point.



No. at Risk

CPAP	1346	1222	1118	754	482	278	146	146
Usual care	1341	1211	1108	727	499	290	103	103

McEvoy RD et al. N Engl J Med 2016;375:919-931.

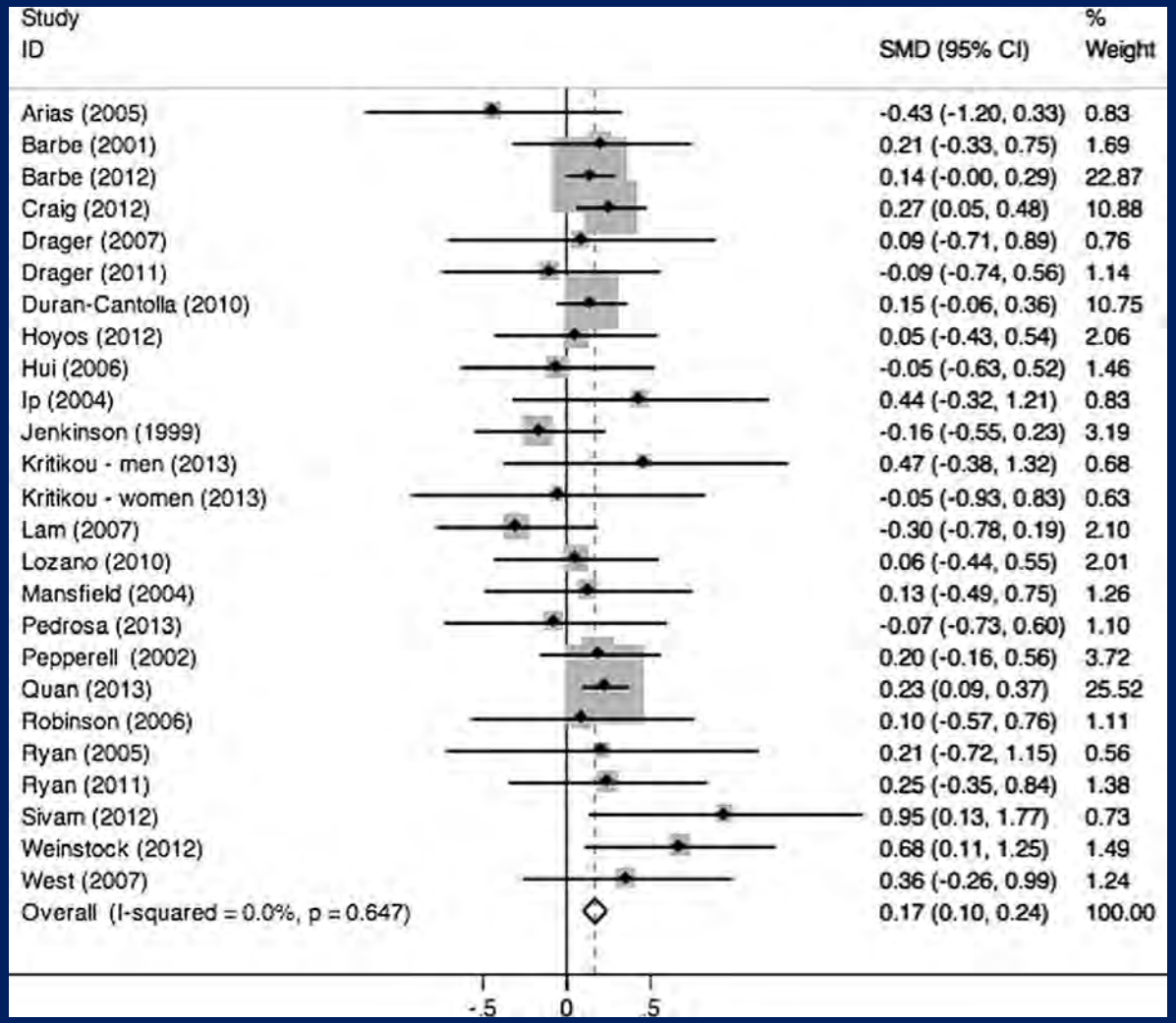
The NEW ENGLAND JOURNAL of MEDICINE

Effects of Continuous Positive Airway Pressure on Neurocognitive Function in Obstructive Sleep Apnea Patients: The Apnea Positive Pressure Long-term Efficacy Study (APPLES)
Kushida et al. Sleep 2012

Conclusions:

CPAP treatment improved both subjectively and objectively measured sleepiness, especially in individuals with severe OSA (AHI > 30). CPAP use resulted in mild, transient improvement in the most sensitive measures of executive and frontal-lobe function for those with severe disease, which suggests the existence of a complex OSA-neurocognitive relationship.

Forest plot for weight.

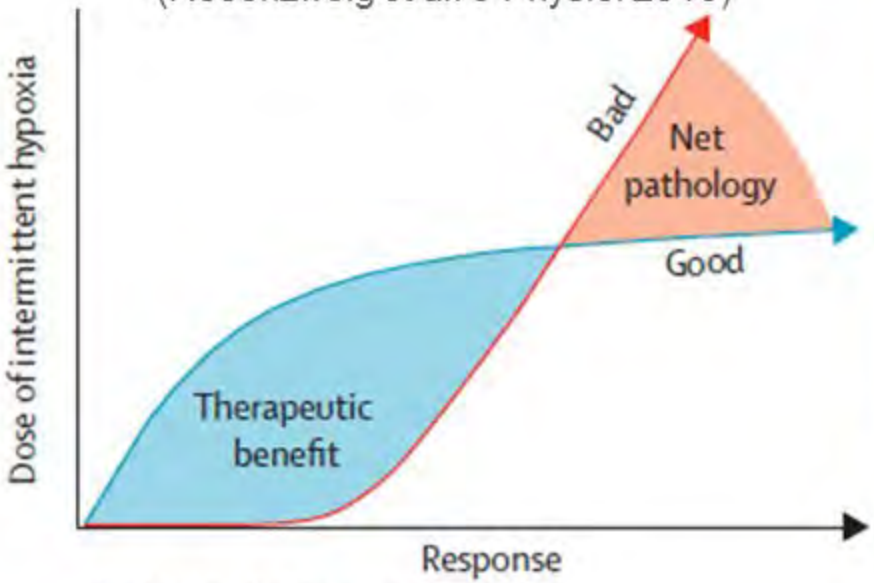


Luciano F Drager et al. Thorax 2015;70:258-264

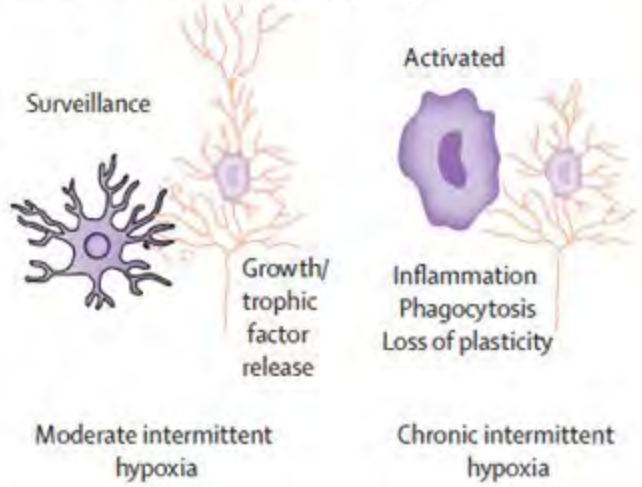
THORAX

Adaptive and Maladaptive processes induced by intermittent hypoxia

(Rosenzweig *et al.* J Physiol 2013)



(Dale *et al.* Physiology 2014)



Model of Sleep Apnoea

- Transgenic TLR2-luc-GFP C57Bl6 mice (backcrossed to an albino background for more precise quantification)
- Imaging bioluminescence directly after intermittent hypoxia every 2 days
- To investigate Toll-like-receptors (TLR) implicated in neurogenesis and neuroinflammation (recently in Alzheimer's dementia)

Sleep apnea may offer unusual protection for heart attack patients

Date: January 2, 2013

Source: American Technion Society

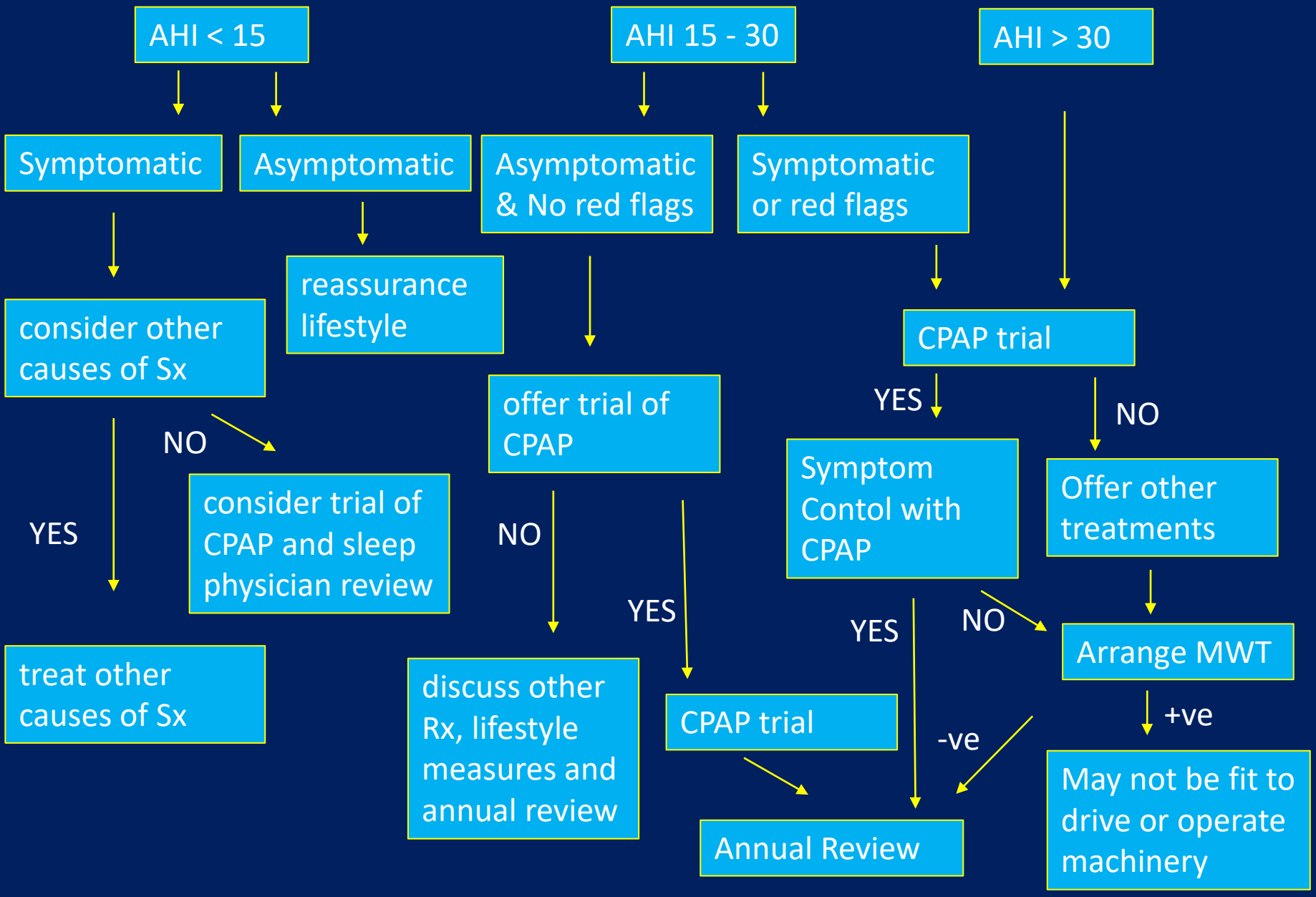
Summary: Researchers at the Technion have found that heart attack patients with breathing disorders such as sleep apnea may benefit from mild-moderate sleep-disordered breathing. The findings could suggest ways to rebuild damaged heart tissue.

OSA CHALLENGES

- Determining whether OSA is a bystander or part of the problem/ presentation
- Asymptomatic individuals where the main issue is the noise pollution of snoring
- OSA in the elderly – often a bystander and it is unknown its significance

Taking a Pragmatic Approach in an Occupational Setting

RED FLAGS – ESS>10, BMI>35Kg/m2, average sleep time <6 hours, night shifts, age>60y.0



OUTLINE

- Overview of Sleep Neurobiology
- Hypersomnolence and OSA Driving Risk
- Sleep Assessment
- Sleep Investigations
- OSA – when to treat and when not to treat
- What to do with the non-compliant at risk patient

Medico-Legal Responsibilities

- Are our “rules” generalizable to every case
- Variability in quality in models of care – who takes on the medico-legal risk for the patient and for the community
- Diagnostic Accuracy and Cost of Treatments
- Non-compliant or poorly complaint patients – who is responsible (company, clinician or individual

CONCLUSIONS

- OSA is a risk factor for MVA, however it is more complex than AHI
- Role of Sleep Studies is to add to the clinical assessment and they should NOT be used alone to make treatment decisions
- Not all sleep studies are the same – quality and models of care differ and that has consequences
- Treat severe OSA and those with moderate OSA who are either symptomatic (from their OSA) or have ”red flags” with CPAP

- Non-compliant (sub-optimally compliant) or untreated “at risk” patients should be followed up with Maintenance of Wakefulness Test (MWT)
- Always consider other causes for patient’s symptoms
- Do you “ground” patients while they are waiting for their appointments/ sleep studies?

QUESTIONS?