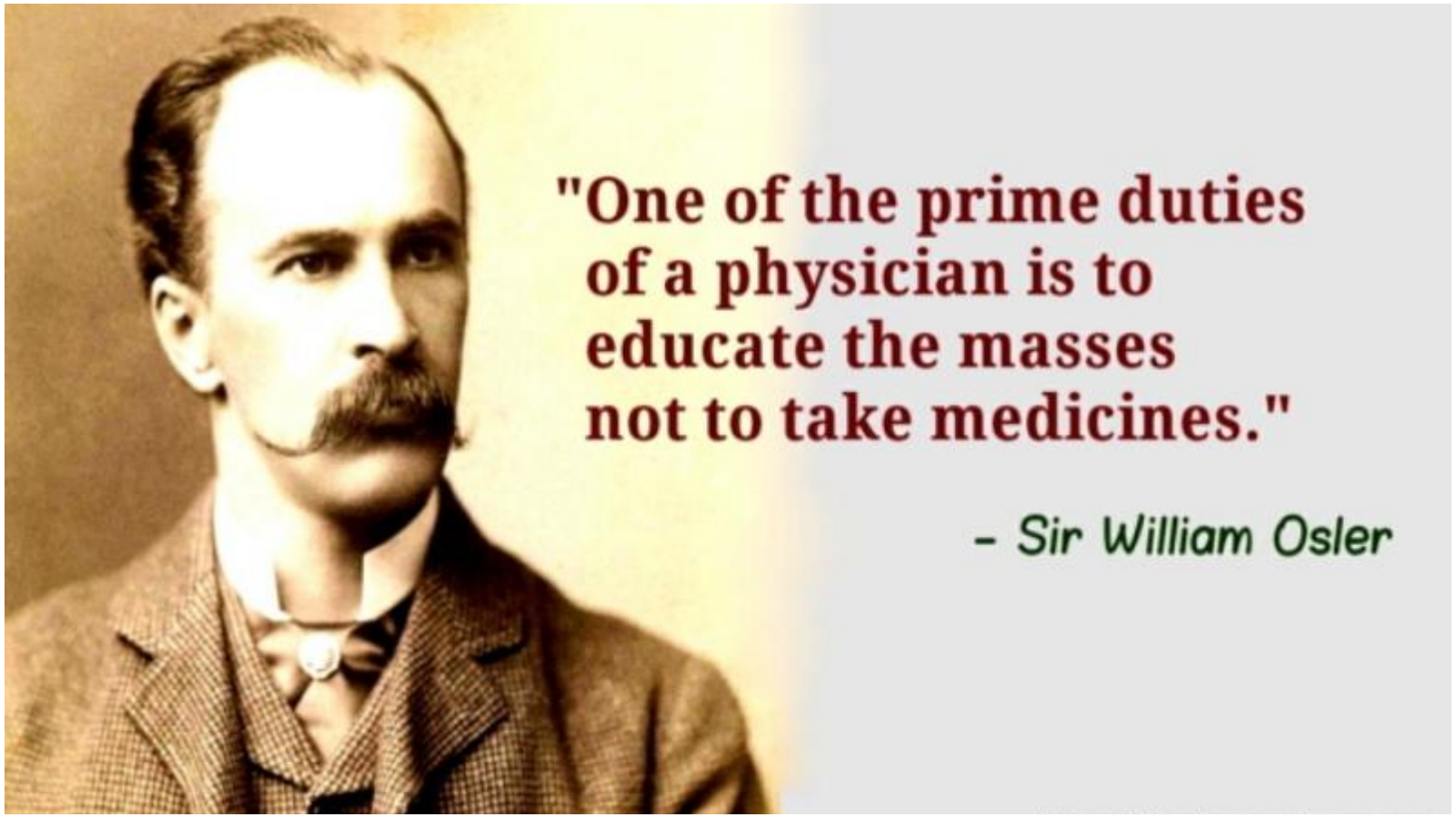

"One of the prime duties
of a physician is to
educate the masses
not to take medicines."
- Sir William Osler

Obstructive Sleep Apnea -Beyond Snoring

Medical Grand Rounds

St. Vincent East

January 26, 2021

Patricia E. Patterson, MD, FCCP, FAASM

Clinical Associate Professor

UAB Sleep/Wake Disorders Center

CONFLICT OF INTEREST DISCLOSURES

- ❑ 1. I do not have any relationships with any entities producing, marketing, re-calling, or distributing health care goods or services consumed by, or used on, patients, OR

- ❖ 2. I have the following relationships with any entities producing, marketing, re-calling, or distributing health care goods or services consumed by or used on, patients.

TYPE OF POTENTIAL CONFLICT	
Consultant	Inspire Medical System
Speakers' Bureaus	Inspire Medical System

- ❖ 3. The material presented in this lecture has no relationship with any of these potential conflicts.

Objectives

- Concise review of OSA - Symptoms, pathophysiology, work up
- Review consequences of untreated OSA
- Discuss options for treatment of OSA - old and newer

Ms. SD…

- 38 y/o female, presents for routine follow up of DM, hypothyroidism.

- Her main complaint -“I’m so tired –I just can’t keep on like this—I fall asleep most nights but can’t stay asleep – I have to go to bathroom or my husband is shoving me to roll over because I am snoring. Then, when I get up -I have a headache, mouth is parched. I am miserable all day.”

- PMH: Type 2 Diabetes Mellitus, Hypothyroidism, Fibromyalgia, Depression

Laugh and the world laughs with you;
snore,
and you sleep alone!

Anthony Burgess

Sleep

- A rapidly reversible behavioral state of perceptual disengagement from and reduced responsiveness to the environment.
- A very complex amalgam of physiologic and behavioral processes.
- Unlike coma—SLEEP IS physiologic, recurrent, and reversible

Normal Sleep

- Humans spend approximately 1/3 of life sleeping (~8hrs/night)

- Purpose poorly understood- numerous theories
  - Restoration
  - Energy conservation
  - Memory consolidation

Normal Sleep -Physiologic changes

❖ <u>NREM sleep</u>

- Enhanced parasympathetic tone
- Reduced and regular HR
  Reduced BP *cardioprotective
- Mild decr in ventilatory drive in response to hypoxia /hypercapnia

  Decreased and Regular RR
- Decr hypothalamic temp set point

❖ <u>REM sleep</u>

- Unstable, brief surges in both

sympathetic and parasympathetic activity

- More irregular HR

  Transient increases BP
- Signif decr in ventilatory drive
  Increased and Irreg RR
- Decr thermoregulatory mech

Ms. SD - Perceived poor sleep quality

- Usual starting point –
  - History - - ->>> Differential diagnosis
  - Physical (difficult on telehealth videos)
  - Screening
  - Evaluation

Ms. SD MORE history --when she is asleep…

- Husband (when he is there) reports heroic snoring, pauses in breathing, teeth grinding, thrashing and kicking at times, tossing and turning all night to the point he sleeps on the couch leaving her in the bed with the 2 youngest kids and 2 dogs
- Nocturia x 2-33
- When up to the bathroom –occasionally finds it difficult to return to sleep
- Occasionally pain in lower back and legs
- Wakes up with choking 2-3 x a week

Common Causes of **Sleep-Related** Fatigue

- Sleep Disorders Nonrestorative Sleep
  - Sleep Disordered Breathing – **OSA**, Snoring, UARS, CSA
  - Insomnia – Initiation, Maintenance
  - PLMD, Bruxism
  - Sleep-Wake Timing – Shift work, Circadian rhythm disorders
  - Medication - Prescribed, OTC
  - Medical disorders –GERD, Chronic Pain, Asthma/COPD, CHF
  - Inadequate Sleep Hygiene - Bed partner, children, pets, screens
  - Rare- REM Behavior Disorder, Somnambulism, Sleep terrors, Sleep-related eating disorders

Obstructive Sleep Apnea

- Recurrent, sleep state dependent collapse of upper airway resulting in functional obstruction of the pharyngeal airway causing substantially reduced airflow(hypopnea) or complete cessation of airflow (apnea) despite ongoing breathing effort
- Resulting in either arousals from sleep and/or oxygen desaturation

Fragmented sleep and NONRESTORATIVE Sleep

OSA: Symptoms

- Non-restorative sleep
- Snoring, snorting
- Apnea
- Nocturia
- Gasping/choking ****
- Sleep maintenance insomnia ***
- Night sweats
- Bedwetting
- Excessive wake time sleepiness
- Fatigue
- Morning headache
- Dry mouth
- Reduced memory/concentration
- Loss or reduced libido
- Irritability
- Brain fog

OSA: Prevalence

- Most common sleep related breathing disorder in North America
  - >20 million Americans
- Underestimated and underdiagnosed

- 14-15% Men/ 5% Women AHI >5/hr **+** symptoms or comorbidity

OR AHI > 15/hr

- 20-30% Men/10-15% Women AHI >5/hr

OSA: Risk Factors

- **Unmodifiable**

Male sex

Age

Race

Genetic predisposition

Family history of OSA

Craniofacial anatomy*

- **Modifiable**

Obesity- BMI>30kg/m2

Medication

Endocrine disorders

- Hypothyroidism
- PCOD
- Acromegaly
- Menopause

Smoking

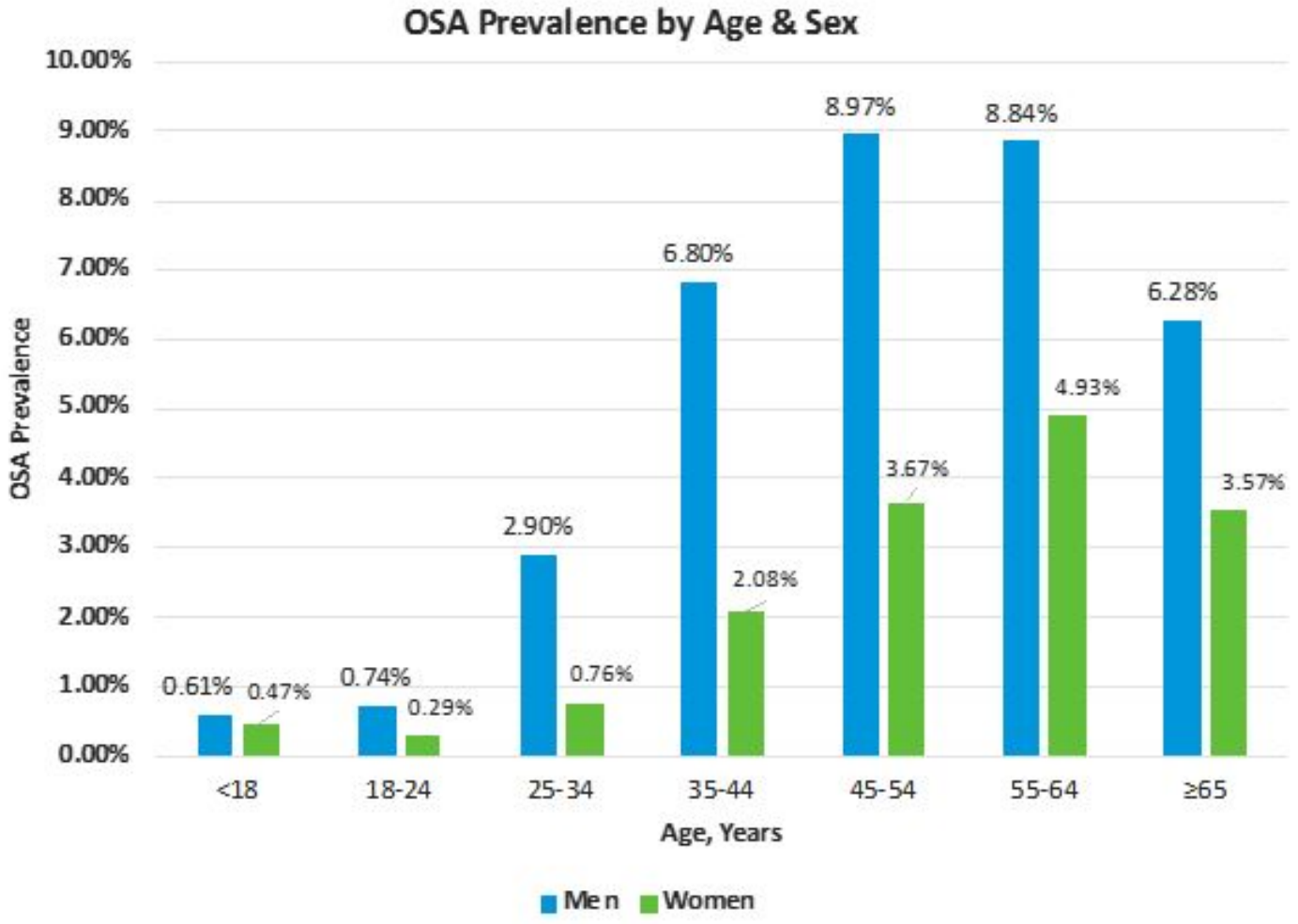
Nasal congestion/obstruction

Craniofacial anatomy

OSA: Differences in the sexes

- Incidence: Men>women until menopause(unless treated with HRT)
- Sleep State: REM-women>
- Position: Supine-Men>
- Severity of OSA: Men>women similar BMI
- Symptoms: Men-Snoring, witnessed apnea
    - Women- Hypersomnia, insomnia - sleep maintenance insomnia

OSA: Age



Suomi, J. *Journal of Current Medical Research and Opinion*, *3*(06), 478-486. https://doi.org/10.15520/jcmro.v3i06.301

OSA: Race

- Increased risk of OSA
  - Black 20%*-32%^
  - American Indians 23%*
  - White 17%*-30%^
  - Hispanics 38%^
  - Chinese 39%^
- *Sleep Heart Health Study – Incr risk of mod-sev OSA in Blacks, American Indians compared to whites
- ^Data from the 2015 Multi-Ethnic Study of Atherosclerosis (MESA)

Chen X. Sleep 2015;38(6):877-888
*Young T. Arch Intern Med2002;162(8):893-900

OSA – Risk factors/Comorbid conditions

- Congestive Heart Failure
- Atrial Fibrillation
- Refractory Hypertension
- Myocardial infarction
- Nocturnal dysrhythmias
- Stroke
- Pulmonary Hypertension
- Type 2 Diabetes/glucose intolerance
- Depression
- Down syndrome

OSA and Comorbid conditions

- Patients with cardiovascular disease ->high prevalence of OSA

- Hypertension – mild OSA 83% // moderate to severe OSA 30%
- CHF – mild OSA 55% // moderate to severe OSA 12%
- Arrhythmias – mild OSA 50% // moderate to severe OSA 20%
- Stroke - mild OSA 75% // moderate to severe OSA 57%
- Coronary Artery Disease -mild OSA 65% //moderate to severe OSA 38%

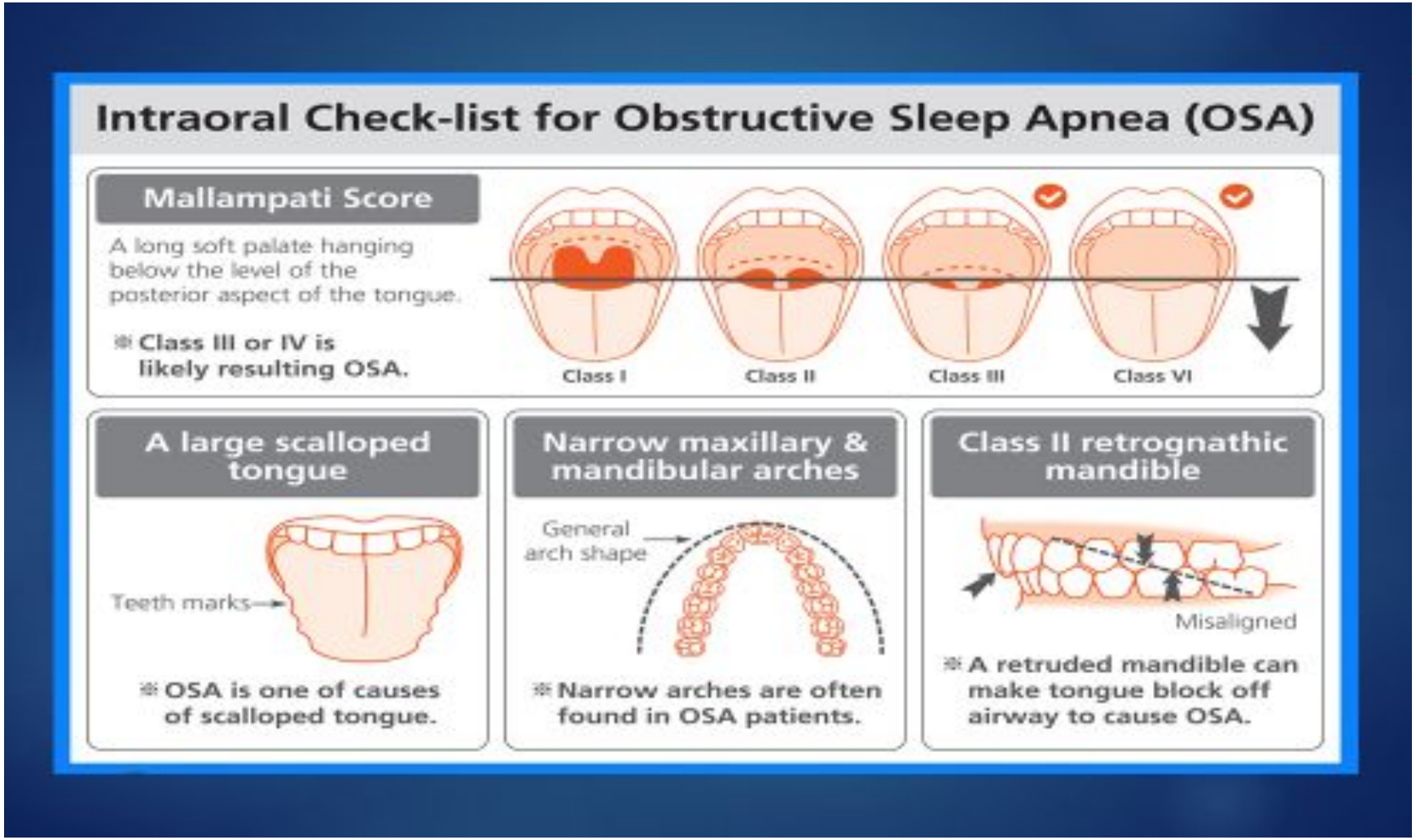
Javaheri S. J Am Coll Cardiol 2017;69(7):841-858

OSA – Comorbidities/Insurance*

- Hypersomnia
- Insomnia
- Mood disturbance
- Hypertension
- Heart disease

OSA – Physical Exam

- Obesity – BMI >30
- Increased neck circumference Men>17in, women >16in
- Oropharyngeal exam - soft palate, tongue, tonsils
- Skeletal features - jaw structure - retrognathia
- Nasal exam - deviated septum, turbinate hypertrophy

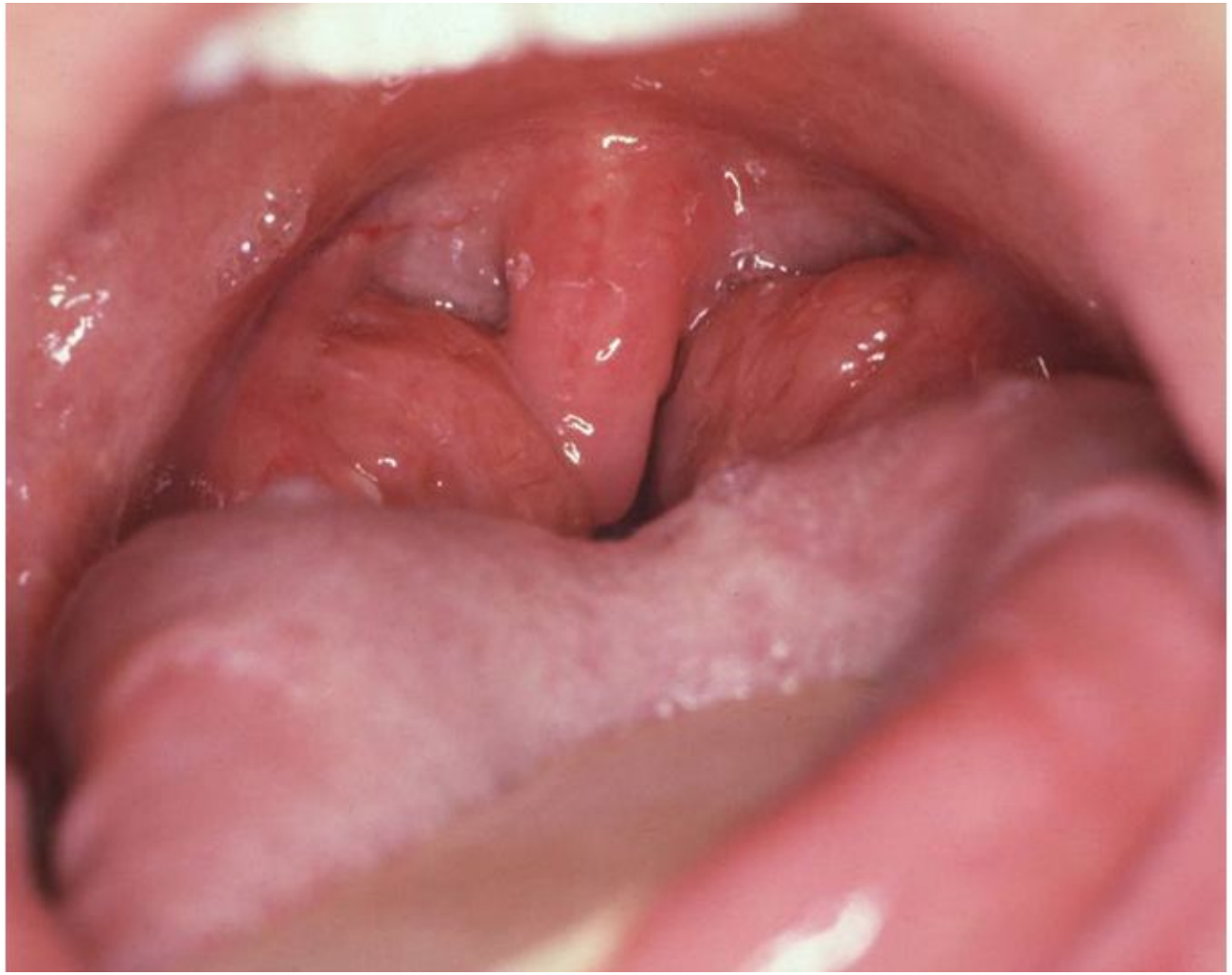


https://raphaelsondentalsleepcenter.com/category/sleep-apnea/

5’2” 165lbs BMI 30.2
142/84 **88** 98%

http://www.healthcaretip.com/2017/09/Retrognathia-Pictures-Symptoms-Causes-Treatment.html

Tonsillar hypertrophy
Prolonged uvula
Mild macroglossia



OSA- Screening tools

- Stop Bang
- Epworth Sleepiness Scale
- Berlin Questionnaire

STOP-BANG Questionnaire

1. S**noring** Do you snore loudly (louder than talking or loud enough to be heard through closed doors)? Yes No
2. **Tired** Do you often feel tired, fatigued, or sleepy during daytime? Yes No
3. **Observed** Has anyone observed you stop breathing during your sleep? Yes No
4. **Blood Pressure** Do you have or are you being treated for high blood pressure? Yes No
5. B**MI** more than 35 kg/m2? Yes No
6. **Age** over 50 yr old? Yes No
7. **Neck circumference** greater than male/female17”/16”? Yes No
8. **Gender** Male? Yes No

High risk of OSA: Yes 5-8 // Intermediate risk: Yes 3-4 // Low risk: Yes 0-2

93% sensitivity

Chung F et al. Anesthesiology 2008; 108:812–21

Epworth Sleepiness Scale

- Sitting and reading
- Watching TV
- Sitting inactive in a public place (e.g. theater, meeting)
- As a passenger in a car for >1hr without a break
- Lying down to rest in afternoon when circumstances permit
- Sitting talking to someone
- Sitting quietly after lunch without alcohol
- In a car, stopped for a few minutes in traffic

0-3 No chance to high chance of falling asleep

≥10 - Abnormal

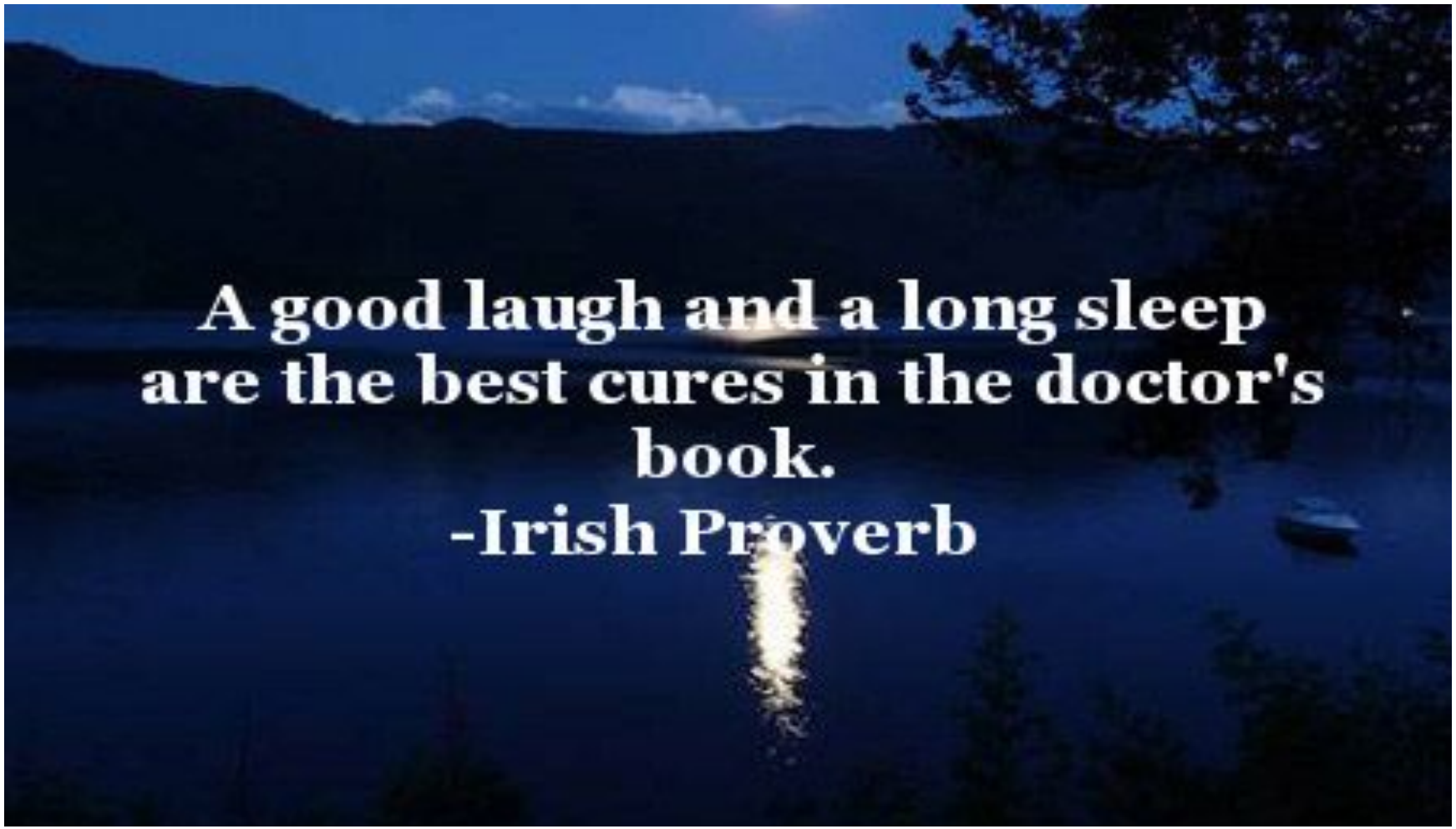
Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep, 1991; 14: 50-55.

Berlin Questionnaire

- Developed for primary care population
- 10 questions-
  - Severity of snoring
  - Witnessed apnea
  - Significance of daytime sleepiness
  - Presence of obesity and HTN

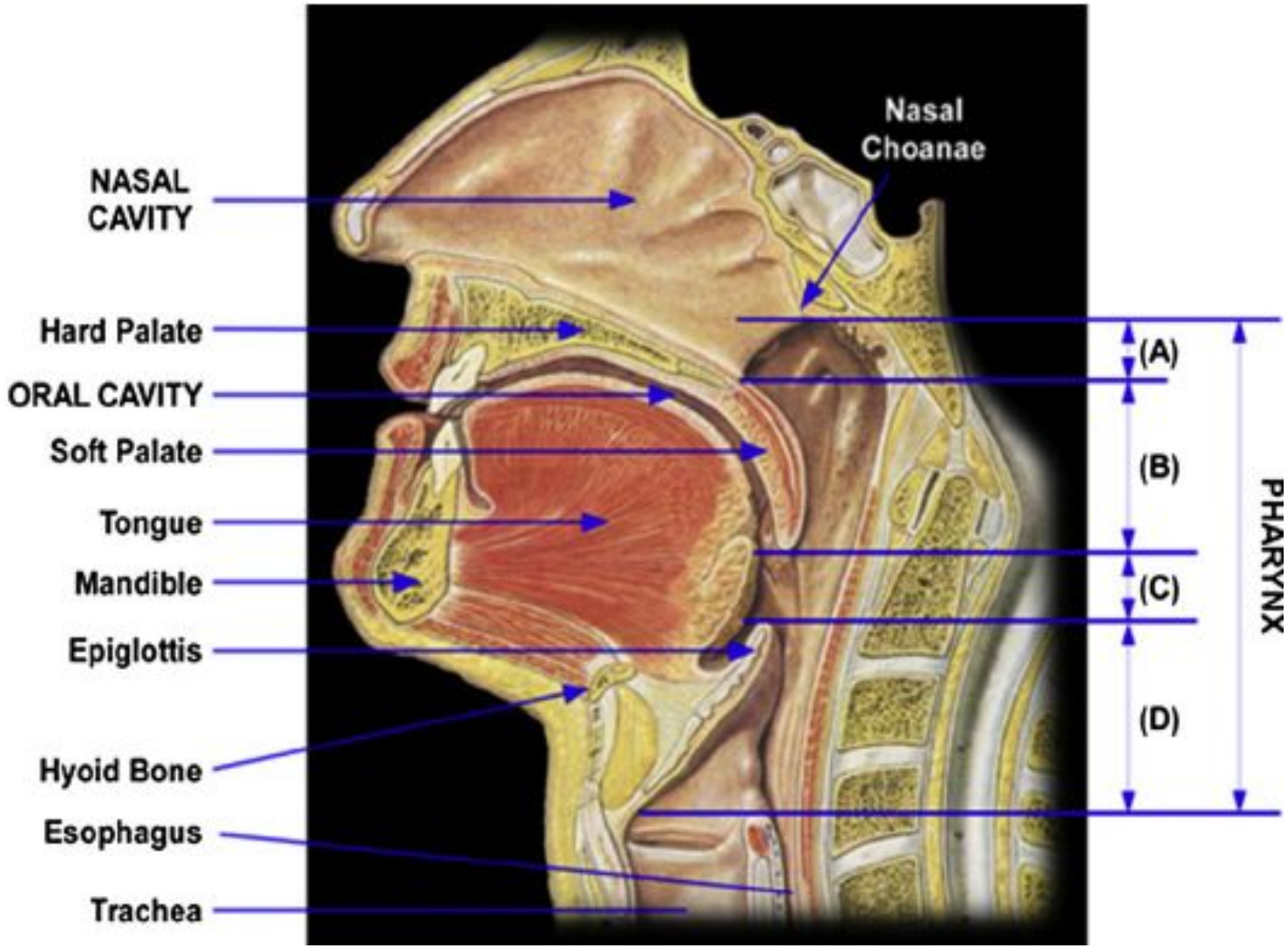
- In primary care setting - 1in 3 patients were high risk for OSA
  - Sensitivity was 86%

Netzer NC Ann Int Med 1999;131:485-491.



https://quotesblog.net/a-good-laugh-and-a-long-sleep-quote/

Components of the Upper Airway



A-Nasopharynx

B- Retropalatal space

C- Retroglossal region

D- Hypopharynx

Sleep– Upper Airway Patency

Determinants of UA patency - 2 categories -

- STRUCTURAL FACTORS
  - Craniofacial structure
  - Soft Tissue Structure
  - Vascular Structures
  - Mucosal Factors
- NEUROMUSCULAR FACTORS
  - Upper Airway Muscle Activity
  - Ventilatory motor output
  - Thoracic-upper airway link via caudal traction

Normal Sleep– Upper Airway Mechanics

- Decreased upper airway muscle activity
  - UA narrowing
- Changes in caliber and compliance
  - ↓ pharyngeal caliber - UA narrowing
  - ↑ UA resistance
  - ↑ UA compliance
    - ❖ ------>>>Small UA lumen and more pliable airway walls
    - ❖ THUS UA more susceptible to closure in presence of collapsing transmural pressure

Normal Sleep– Upper Airway Mechanics

- UA narrowing □incr turbulent flow
- Incr UA resistance □incr turbulent flow, inspiratory flow limitation and fluttering of soft palate and UA soft tissue **Snoring
- Snoring and flow limitation increase propensity for UA collapse during sleep

Normal Sleep – Loss of load compensation

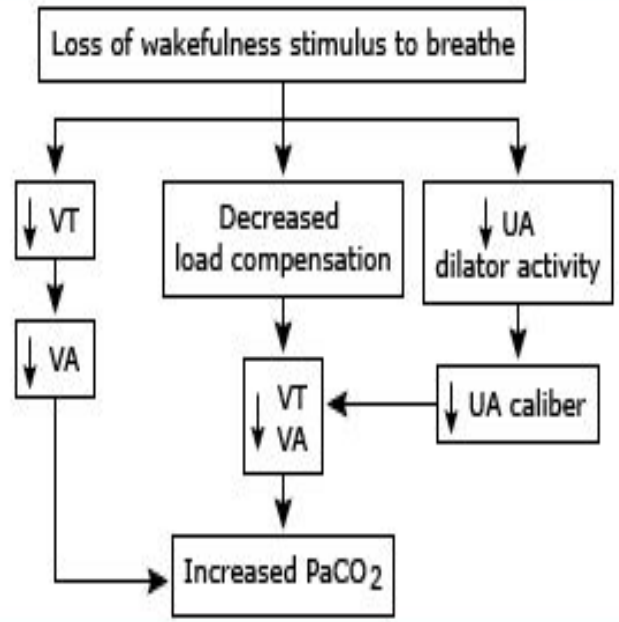
- Sleep-related UA narrowing and increased resistance to flow represents added internal load on respiratory system
  - THE ABILITY TO RESPOND TO ADDED LOADS IS CRITICAL TO PRESERVE ALVEOLAR VENTILATION
- WAKE: Breathe through a Straw □ ↑RR and effort-> ↑ ventilation

  Maintain alveolar ventilation and Pa CO2

- SLEEP: Breathe through a straw-->No compensation--□ ↓ventilation

  Do not perceive load – normal pt –mild PaCO2 increases

Effect of sleep on upper airway mechanics and alveolar ventilation



Note that several sleep-related changes contribute to decreased alveolar ventilation and increased arterial $PaCO_2$.

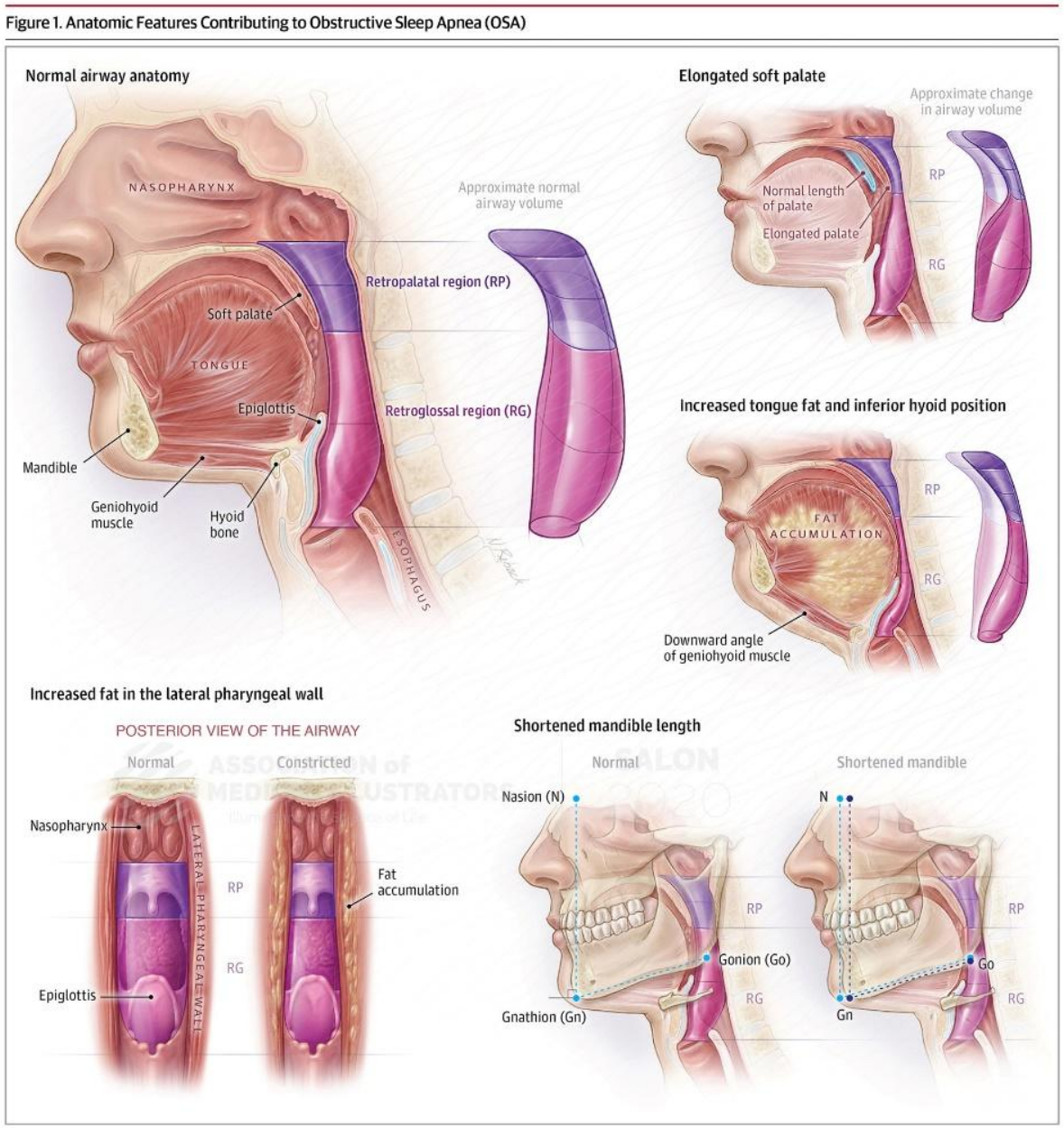
VT: tidal volume; UA: upper airway; VA: alveolar ventilation.

Obstructive Sleep Apnea

- Recurrent, sleep state dependent collapse of upper airway resulting in functional obstruction of the pharyngeal airway causing substantially reduced airflow(hypopnea) or complete cessation of airflow (apnea) despite ongoing breathing effort
- Resulting in either arousals from sleep and/or oxygen desaturation
- Fragmented sleep

Normal airway anatomy

Increased fat in lateral pharyngeal wall



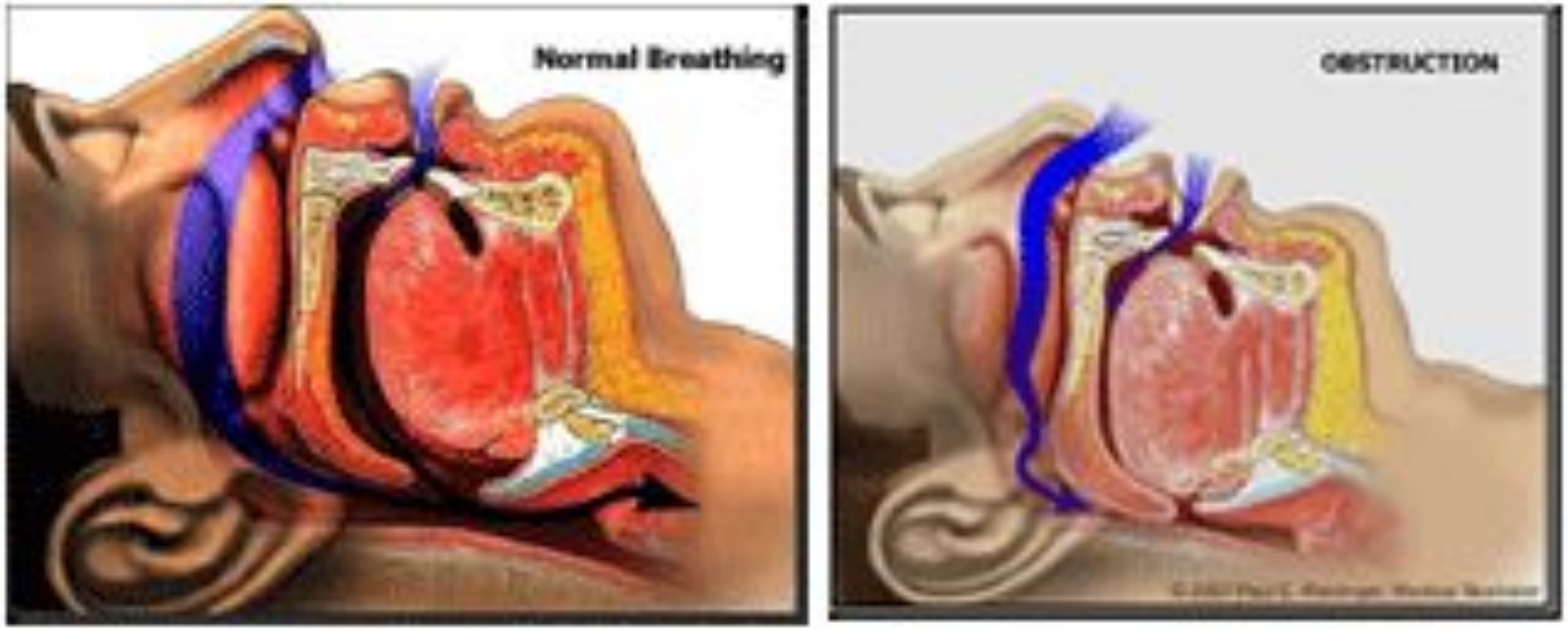
Diagnosis and Management of Obstructive Sleep Apnea. A Review JAMA. 2020;323(14):1391. © American Medical Association

Elongated soft palate

Increased tongue fat and inferior hyoid position

Retrognathia short mandible

Normal vs OSA – Upper Airway



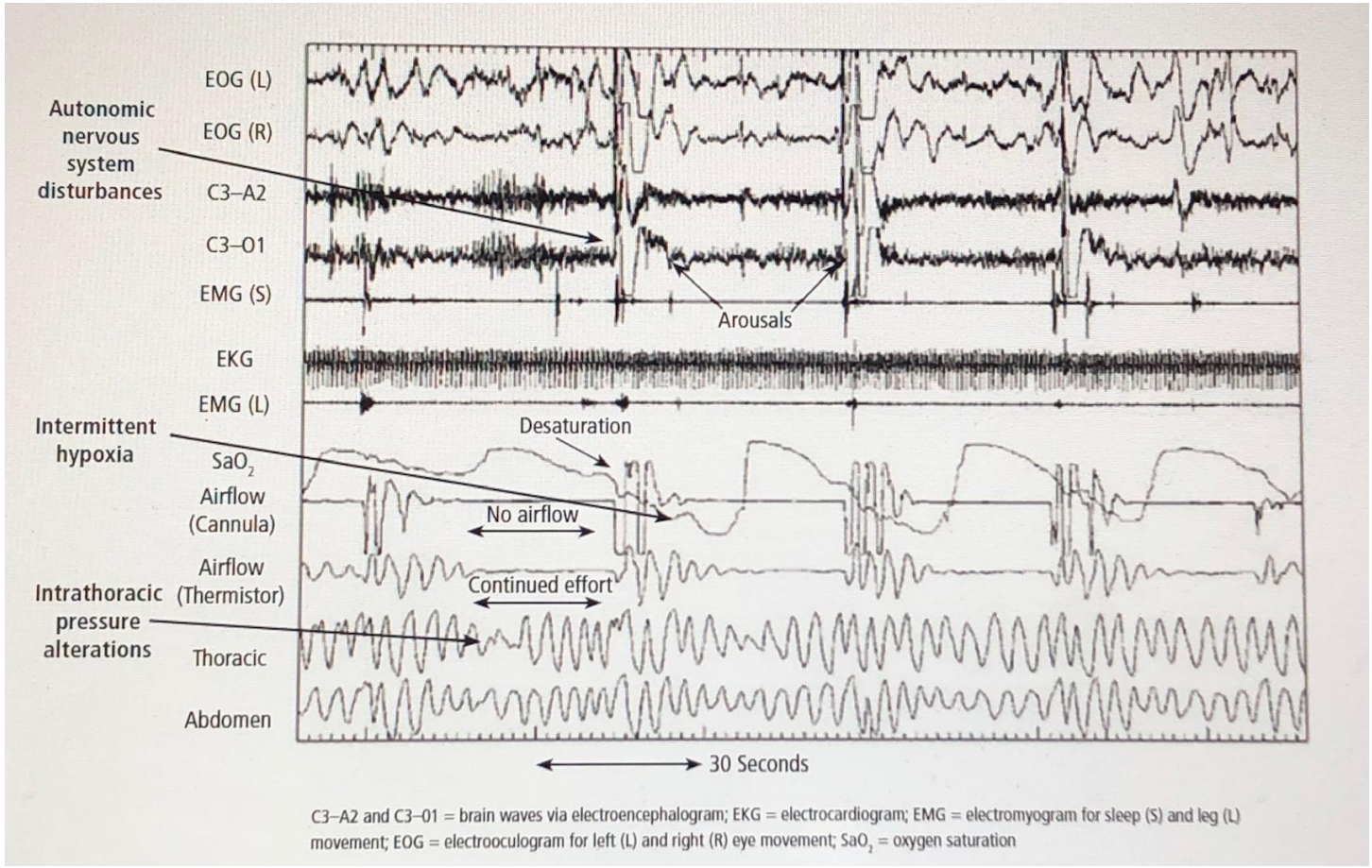
Normal Airway

Obstructed Airway

OSA - Pathophysiology

- Autonomic nervous system disturbances
- Gas exchange disturbance
  - Intermittent hypoxia, increased carbon dioxide
    - Due to Airflow obstruction despite persistent effort
- Intrathoracic pressure alterations
  - Results in systemic inflammation and oxidative stress

OSA - Pathophysiology



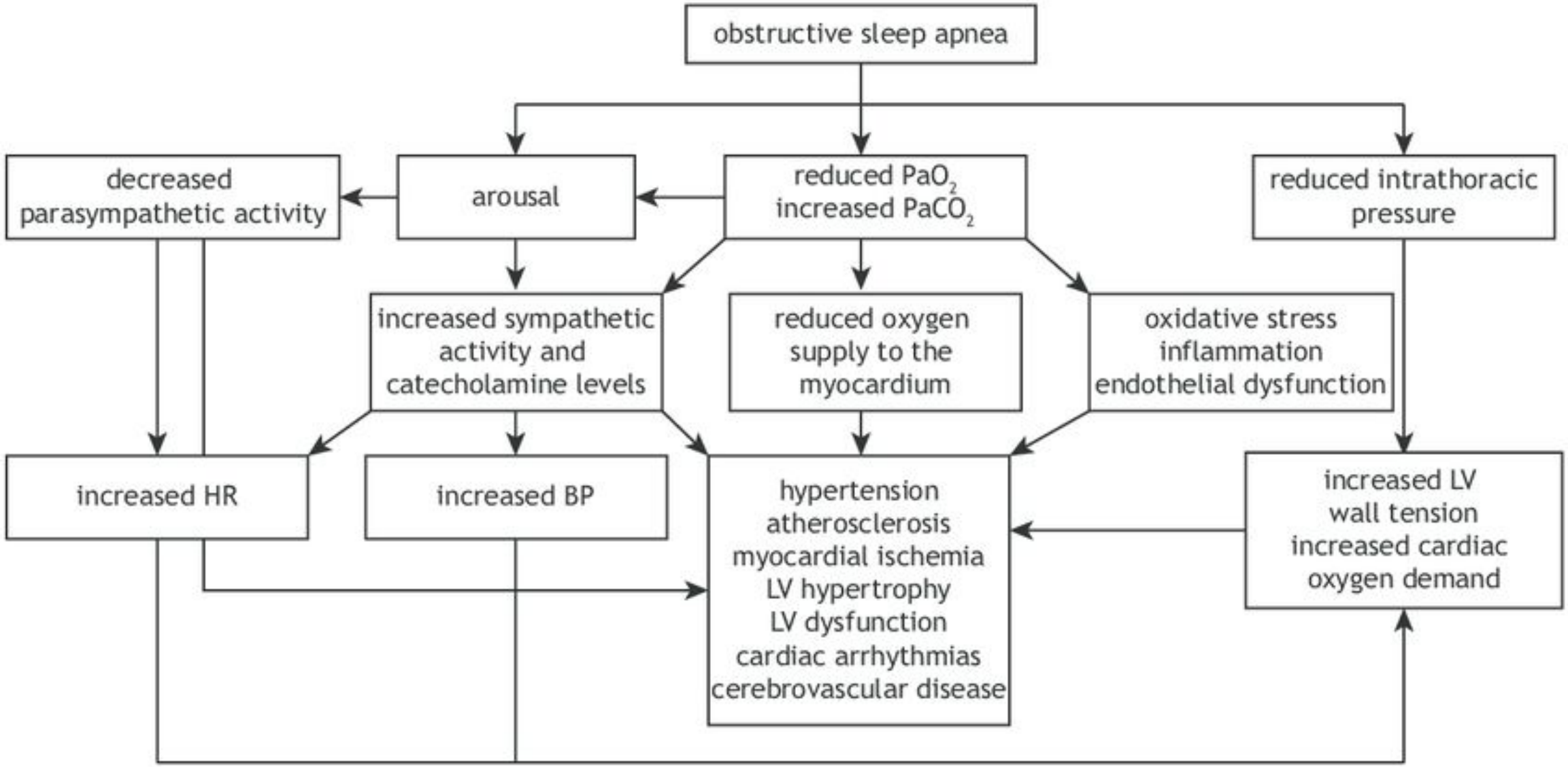
Mehra R. Clev Clin J Med 2019; 86(suppl 1):10-17.

OSA- Pathophysiology

- During obstructive episode –
- Increased cardiac load
- Intrathoracic pressure swings contribute to
  - Impaired diastolic function
  - Atrial and aortic enlargement
  - Shift of interventricular septum reduced cardiac output
- Hypoxia leads to
  - Constriction of the pulmonary vasculature ->elev pressure in pulmonary vasculature incr mean pulmonary artery pressure

OSA - Pathophysiology

- Systemic inflammation and oxidative stress due to
  - Intrathoracic pressure variations
  - Hypercapnia
  - Hypoxia
  - Autonomic nervous system disturbances
- Upregulation of markers of systemic inflammation and prothrombotic markers -
  - IL-6, plasminogen activation inhibitor 1
- Oxidative stress due to lower oxygen oxidation of serum proteins and lipids
- Endothelial dysfunction as well as insulin resistance and dyslipidemia
- Taken together pathways can increase cardiovascular or atherogenic risk


obstructive sleep apnea
decreased parasympathetic activity
arousal
reduced PaO_2 increased $PaCO_2$
reduced intrathoracic pressure
increased sympathetic activity and catecholamine levels
reduced oxygen supply to the myocardium
oxidative stress inflammation endothelial dysfunction
increased HR
increased BP
hypertension atherosclerosis myocardial ischemia LV hypertrophy LV dysfunction cardiac arrhythmias cerebrovascular disease
increased LV wall tension increased cardiac oxygen demand

Diagnostic Tools

- Polysomnography
- Home Sleep Apnea Testing

Diagnostic Tools: Polysomnography (PSG)

- GOLD STANDARD
- Standard or sleep-disordered breathing montage
  - Sleep Staging (EEG, EOG, chin EMG)
  - Respiration
    - Respiratory effort – thoraco-abdominal
    - Airflow / Nasal pressure
    - Pulse oximetry
    - Snore microphone
    - CPAP, bilevel PAP, or oxygen settings if used
  - ECG
  - Anterior tibialis EMG
  - Sleep position
  - Videotape (synchronized)

Diagnostic Tools: Home Sleep Apnea Test (HSAT)

- Specific Use –High probability of OSA without comorbidities

- Records 4-7 parameters
  - Oximetry - Oxygen saturation and heart rate
  - Position channel
  - Respiratory effort
  - Air Flow- thermal and nasal pressure
  - +/- crude EEG
  - *WatchPat – Peripheral arterial tomography

Diagnostic Tools

- HSAT are NOT to be used in patients with
  - Cardiopulmonary Disease
  - CHF
  - COPD/or disorders causing awake hypoventilation
  - Neuromuscular Disease
  - Chronic Opiate Use
  - Stroke
  - Concern for other sleep disorders
    - Severe insomnia…
    - Parasomnias / RBD
  - Poor environment
  - Inability to self-apply equipment

Diagnostic Tools

PSG

- **Advantages**
  - Diagnose other sleep disorders
    - Seizure
    - Parasomnia
  - True sleep staging
  - Hands on to intercede for equipment issues
  - Ability to initiate therapy
    - Oxygen, PAP, positional
  - ETCO2 - hypoventilation

HSAT

- **Advantages**
  - Cost
  - Access
  - COVID

Diagnostic Tools

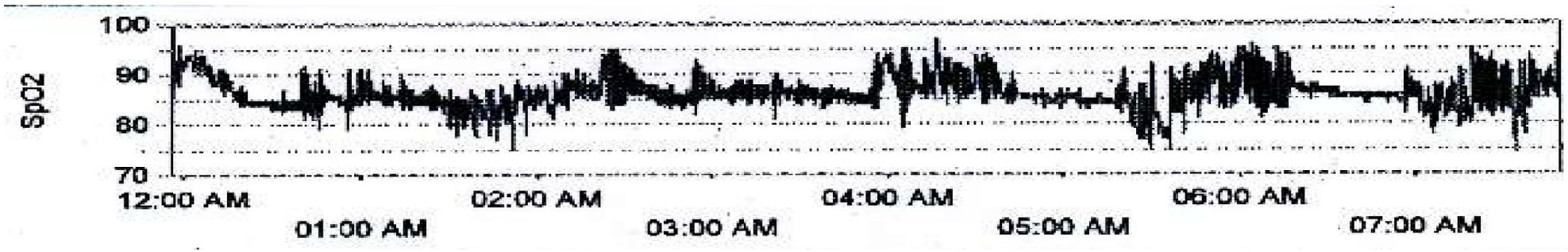
PSG

- **Disadvantages**
  - Cost
  - Access
  - COVID
  - Only 1 night
  - Insurers

HSAT

- **Disadvantages**
  - Fewer physiologic parameters measured
  - Sensor failures
  - Cannot truly define sleep vs wake
  - Use recording time vs sleep time
  - Underestimate true AHI
  - Negative/inconclusive PSG
  - Insurers

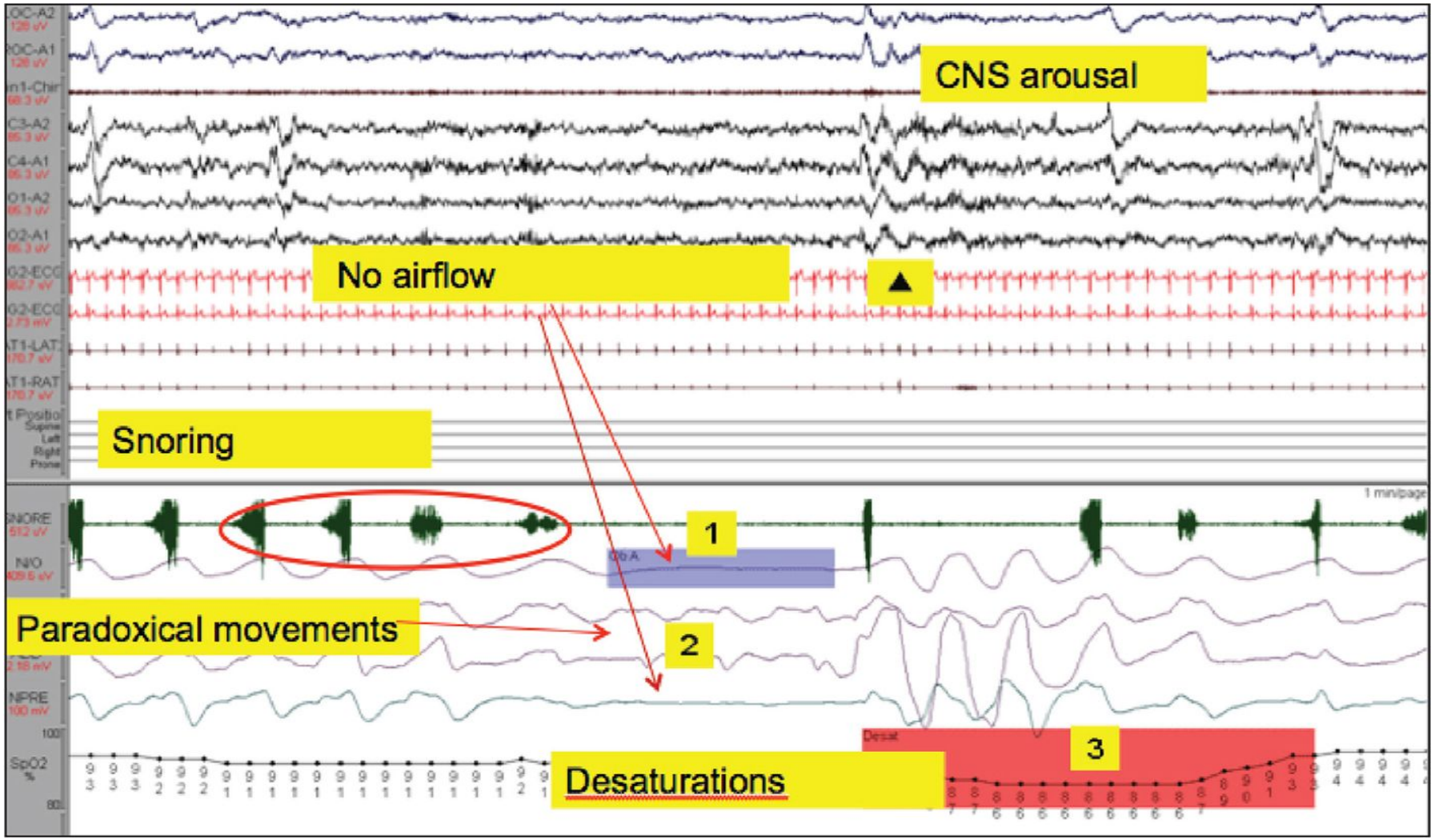
Pulse Oximetry



OSA - Terms

- Obstructive Apnea - Respiratory event >90% near cessation of airflow for ≥10 secs in sleep with continued respiratory effort
  - Central apnea – no airflow and no effort
- Obstructive Hypopnea - >30% reduction in airflow for ≥10secs in sleep associated with ≥3% oxygen desaturation (≥4%-Medicare) or EEG arousal

- AHI – Apnea Hypopnea Index - # events/hr of total sleep time(PSG)
- REI- Respiratory Event Index - # events/hr total monitoring time (HSAT)
- Time ≤ 88%
- ODI-Oxygen desaturation Index - # desats <90%/hr of sleep/monitoring time



https://m4.healio.com/~/media/journals/psycann/2015/1_january/10_3928_00485713_20150106_05/fig1.jpg

OSA - Apnea Hypopnea Index

Normal 0-5/hr
Mild OSA 5-15/hr
Moderate OSA 15-30/hr
Severe OSA ≥30/hr

Influencers to AHI
- Weight
- Position while sleeping
- Age
- Alcohol or sedatives
- Fluid balance

OSA – Who to treat

- Symptomatic patients
  - Sleepy patients regardless of severity of OSA

    Patil SP J Clin Sllep Med 2019;15:335-43

- Patients with comorbidities

- Patients that have a high-risk occupation

OSA: Consequences if Untreated

- Increased risk- Hypertension
  - Pulmonary Hypertension
  - Cardiac arrhythmias
  - CHF
  - CVA
  - Metabolic Dysregulation – insulin resistance // Type 2 DM
  - Nonalcoholic Fatty Liver
  - Sexual Dysfunction
  - Nocturia
  - Depression, Anxiety

OSA- Consequences-Cardiovascular

- MI - likelihood in am - 3 fold incr risk first 3 hrs of awakening -peak 9a
- Sudden Cardiac Death - highest risk in am hours 6-9a

  Unclear reason for am predisposition

    Autonomic fluctuations in REM - Incr REM in early am

      Diurnal changes in BP, cortisol levels, systemic inflammatory and thrombotic markers- plasminogen activator inhibitor 1

- Arrhythmias – diurnal pattern –
- Atrial fibrillation - particularly P Afib - in those patients (10-25%) that are believed to be vagally-mediated - increase risk in sleep

OSA and Hypertension

- Increased risk and incidence of HTN in patient with OSA
- Peppard's prospective, population-based study of 709 pts over 4 yrs
  - Dose response relationship between OSA and newly diagnosed HTN
  - Moderate to severe OSA - Odds ratio of 2.89 developing HTN
    - Peppard PE N Engl J Med 2000;342(19):1378-1384
- Marin's study of 1889 pts over 12 yrs
  - Severity of OSA dose-response developing HTN
  - Poor adherence to CPAP 80% Incr incidence of HTN
  - Good adherence to CPAP 30% decr incidence of HTN
    - Marin JM JAMA 2012;30(20):2169-2176

OSA and Hypertension

- Treatment of OSA with either CPAP or Mandibular Advancement Device –
  - Modest reduction in BP
  - Degree of adherence correlate with response
    - Haentigens P Arch Intern Med 2007;167:757-64
- CPAP –Greater effect on treatment resistant HTN
    - Navarro-Soriano C J Hypertens 2019;37:1269-75
- CPAP is additive to other treatment for HTN
    - Chirinos JA N Engl J Med 2014;370:2265-75
    - Pepin JL AmJ Respir Crit Care Med 2010;182:954-60

OSA and Hypertension

- Randomized controlled trial ~300 pt
  - Improvement in 6 BP parameters CPAP vs sham after 12 weeks
    - Duran-Cantolla J BMJ 2010;341:c5991
- Meta-analysis of RCTs on effectiveness of CPAP on HTN –
  - Reductions 2-3 mmHg in BP
    - Montesi SB J Clin Sleep Med 2012;8(5):587-596
- Meta-analysis of RCTs on CPAP and resistant HTN -
  - Reductions in mean SBP 5.4mmhg and DBP 3.86mmHg
    - Lei Q J Bras Pneumol 2017;43(5):373-379

OSA and Heart Failure

- Prevalent in patients with CHF
- May be associated with progression of CHF
- Contributing factor in relationship OSA and CHF
  - Rostral shifts in fluid
    - To the neck □parapharyngeal edema□OSA
    - To pulmonary receptors in alveoli□pulmonary edema□CSA

      Kasai T. Circulation 2012;126(12):1495-1510.
- Untreated sleep apnea- increased post-discharge mortality and readmissions in setting of acute CHF

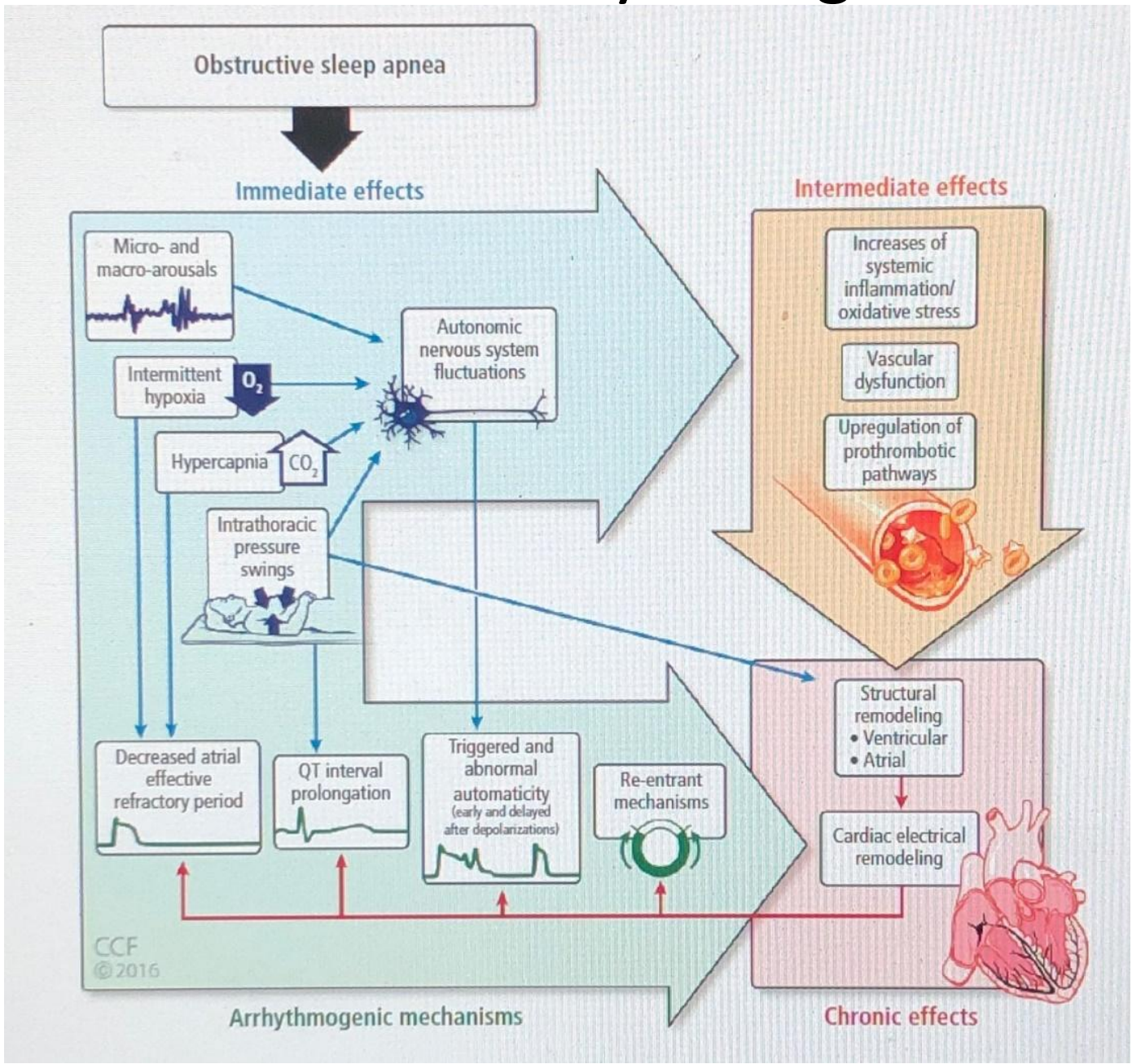
  Khayat R. Eur Heart J 2015;36(23):1463-1469.

OSA- Atrial fibrillation

- Shared risk factors – Obesity / Increased age
- OSA is associated with 58% increased risk afib in African Americans
- Nocturnal hypoxia associated increased risk afib in Asians
- Plausible pathophysiology: Increased inflammation and oxidative stress alter the cardiac electrophysiology and contribute to structural remodeling (evidenced by atrial size, electrical silence, and atrial voltage conduction velocity) that increases risk cardiac arrhythmia

May AM. Chest 2017; 151(1):225-241.

OSA and Arrhythmogenesis



Mehra R. Clev Clin J Med 2019; 86(suppl 1) 10-17.

OSA- Atrial fibrillation

- Clinic based cohort study –Association OSA and afib
  - Increased severity of sleep apnea incr prevalence afib
  - Increased degree oxygen desaturation increased incidence afib

Gami AS. J Am Coll Cardiol 2007;49(5):565-571.

Longitudinal examination of 2 epidemiologic studies

Sleep Heart Health Study and Outcomes of Sleep Disorders Study in Older Men

Central sleep apnea may pose greater risk for development afib

May AM Am J Respir Crit Care 2016; 193(7):783-791.

Post cardiac surgery afib risk higher in patients with OSA and obesity

Kaw R. Chest 2017;151(6):1279-1287.

OSA and Atrial fibrillation

- Treating OSA
  - may improve arrhythmic burden
  - Case-based studies: Treating OSA -Reduced burden and resolution of baseline arrhythmia
  - Retrospective studies: Treating OSA after ablation and after cardioversion reduced recurrence of afib
    - Kanagala Circulation 2003;107(20):2589-94

OSA and Stroke

- OSA Intermittent hypoxia-mediated elevation of oxidative stress and systemic inflammation, hypercoaguability, and impairment of cerebral autoregulation causes increased risk for stroke
- Outcomes of Sleep Disorders Study in Older Men –
  - Severe hypoxia-increased incidence of stroke
  - May be a predictor of newly diagnosed stroke on older men

    May AM Am J Respir Crit Care 2016; 193(7):783-791
- Post-hoc propensity-score matched analysis from the Sleep Apnea Cardiovascular Endpoints (SAVE)- Lower stroke risk in those adherent to CPAP

  McEvoy RD. N Engl J Med 2016;375(10):919-931.

OSA and Coronary Artery Disease

- Marin et al - Spanish study of 1,500 patients followed 10 yrs
  - OSA – Increased risk of fatal MI or stroke
  - CPAP Rx reduced cardiac events
  - Survival of treated OSA patients approached that of patients without OSA

    Marin JM. Lancet 2005;365(9464):1046-1053.

- MESA study-Diagnosed OSA – 2-3-fold increase in various cardiovascular outcomes and all-cause mortality

  Yeboah J. Atherosclerosis 2011;219(2):963-968.

- Sleep Heart Health Study >6,000 patients- progressive worsening of OSA poorer survival after accounting for confounding factors
  - Decreased survival mainly affected men and patients <70

    Punjabi NM. PLoS Med 2009; 6(8):e10000132.

OSA - Negative consequences -QOL

- Reduced Quality of life
  - Excessive daytime sleepiness
  - Inattention
  - Fatigue

→ Increased risk of accidents
→ Medical disability

***Improved QOL – Central goal of OSA treatment

-Best indicator of effectiveness of treatment

Treatment of 2,027 patients OSA – adherent to PAP therapy

FOSQ, EQL-5D scores in patients with most impaired QOL

Improved QOL when adherent to PAP

Walia HK. J Clin Sleep Med2017;13(11):1255-1263.

OSA- Negative consequences- Drowsy Driving

- 2 main reasons OSA increases risk and incidence of MVA
  - Changes in attention and vigilance resulting from sleep deprivation and fragmentation
  - Changes in global cognition and function may be due to intermittent hypoxia

- NHTSA stats - 2017
  - Death due to drowsy driving in 2017 - 795
  - Fatalities due to drowsy driving 2013-2017 – 4,111
  - Motor vehicle crashes in 2017 - 91,000

OSA-Negative consequences- Drowsy Driving

- Treatment of OSA – reduces incidence of MVA
- Early study in 2001 - George found that the treatment of OSA with CPAP eliminated MVAs

  George CFP. Sleep 2007;20(8):608-613.

- Walia et al - 2,000 patients with OSA self-reported near-accident incidents
  - Pre PAP 14%
  - Post PAP 5.3%

  Walia HK. J Clin Sleep Med 2019;15(11):1613-1620.

OSA-Negative consequences-Depression

- Prevalence of depression in OSA patients –5-63%
- Potential mechanisms to explain link
  1. Poor sleep quality, frequent arousals, sleep fragmentation

     Frontal lobe emotional modulation changes
  2. Intermittent hypoxia neuronal injury and disruption of noradrenergic and dopaminergic pathways
  3. Increased pro-inflammatory substances-IL-6, IL-1 –in both OSA and depression
  4. Serotonin –may be impeded in depression-could influence the UA dilator motor neurons
- Treatment of OSA improves symptoms and incidence of depression
  - Zheng D EClinicalMedcine 2019;11:89-96

OSA and Metabolic Syndrome

- Syndrome Z

  OSA and Metabolic Syndrome

  - Waist circumference Men>40 in Women >35in
  - Triglycerides > 150 mg/dl or treatment for hypertriglyceridemia
  - HDL Men <40mg/dl Women <50mg/dl or treatment for cholesterol
  - BP >130/85 or treatment for HTN
  - Fasting blood glucose > 100mg/dl or treatment for hyperglycemia
- Incr risk of cardiovascular morbidity and mortality
- Higher risk atherogenic burden and presence of atheroma
  - Nock NL Sleep 2009;32(5):615-622

OSA and Metabolic Syndrome

- Mechanisms implicated in abnormal metabolic regulation…
- Intermittent hypoxia
  - Sympathetic nervous system activation affecting pancreas, skeletal muscle, liver and fat cells altered insulin secretion, lipid-bile synthesis, glucose metabolism, and lipoprotein metabolism
    - Braincon-Marjollet A Diabetol Metab Syndr 2015;7:25
- Sleep fragmentation and glucose homeostasis
  - Reduced insulin sensitivity, incr am cortisol, incr sympathetic nervous sys activation
    - Spiegel K J Appl Physiol (1985)2005;99(5):2008-2019
- Obesity
  - Fatty tissue higher systemic inflammation and inflammatory markers
    - Framnes SN Front Endocrinol 2018;9:440

OSA and Metabolic Syndrome

- Need large-scale clinical trials with longer duration and good CPAP compliance
- Harsch et al studied 40 men with moderate OSA and ≥5hrscompliance
  - Incr insulin sensitivity index after 2 days and even more after 3 mo
    - Harsch IA Am J Respir Crit Care Med 2004;169(2):156-162
- Meta- analysis reported improves insulin resistance but no change in HgA1c, fasting insulin and glucose levels
    - Iftikhar IH J Clin Sleep Med 2015;11(4):475-485

OSA and Cognitive Impairment

- Data suggests OSA linked with cognitive impairment, may advance cognitive decline, bidirectional relationship
- Women with OSA >>to develop mild cognitive impairment than those without OSA
    - Yaffe K JAMA 2011;306(6):613-619
- OSA independent RF for cerebral white matter changes in middle-age and older adults
    - Mod- severe OSA imparted 2x higher risk of white matter changes than those without OSA
        - Kim H Sleep 2013;35(5):709-715b

OSA and Cognitive Impairment

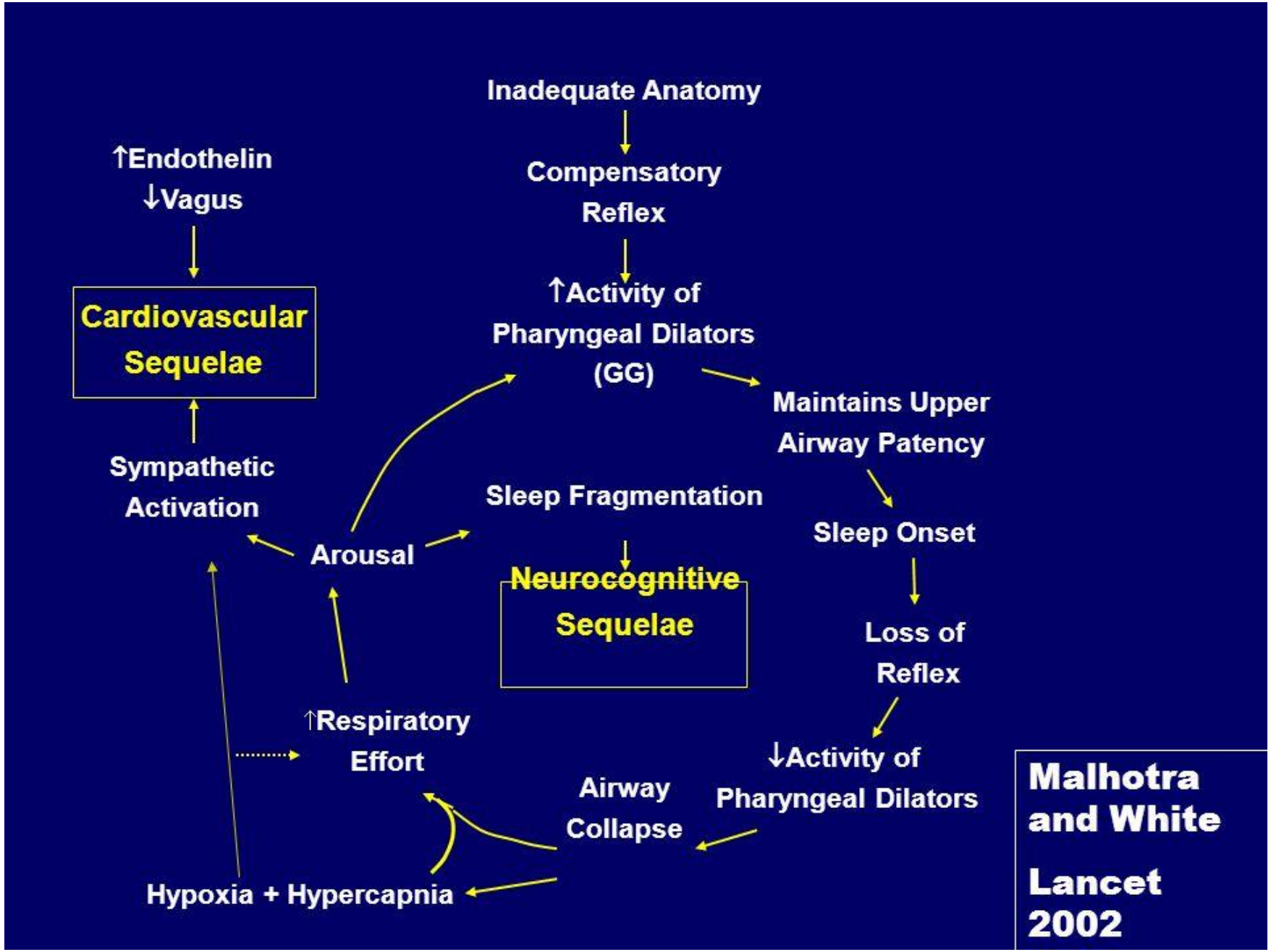
- Osorio reported sleep-disordered breathing patients were more likely to develop mild cognitive impairment and Alzheimer disease at an earlier age than those without sleep-disordered breathing
    - Osorio RS Neurology 2015;84(19): 1964-1971
- Bu's study of 45 cognitively normal patients with OSA compared to 49 age and sex-matched controls
    - OSA patients had incr serum amyloid beta levels
    - Incr levels correl with increasing severity of OSA
        - Bu X-L Sci Rep 2015;5:13917

OSA and Cognitive Impairment

- Interesting possible mechanism linking sleep quality and cognitive impairment or Alzheimer disease Fragmented sleep
- Unfragmented sleep attenuates the apolipoprotein E e4 allele on the incidence of Alzheimer
    - Lim ASP JAMA Neurol 2013;70(12):1544-1551
- Beta amyloid is released during synaptic activity which is decreased in normal sleep
- Disrupted sleep could increase beta amyloid release
    - Lucey BP Neurobiol Aging 2014;35(suppl 2):529-534

OSA and Cognitive Impairment

- Effect of treatment in 1 study -
- 15 pts with OSA before and after treatment with CPAP
- 15 matched controls
- Over 12 months – near complete reversal of white matter abnormalities
  - Improvement in memory, attention, executive function paralleled white matter improvement
    - Castronovo V Sleep 2014;37(9):1465-1475

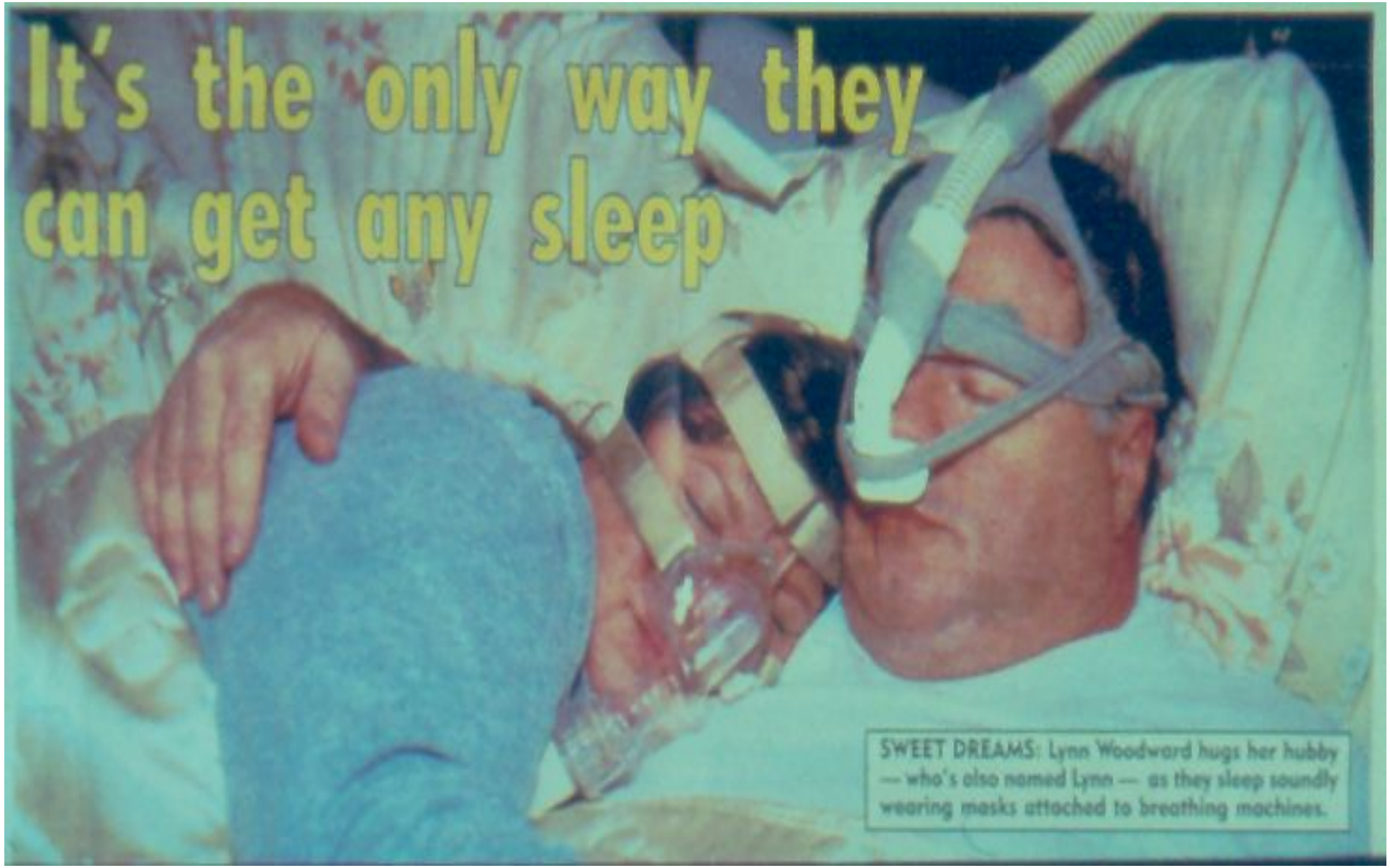

Inadequate Anatomy
↑Endothelin
↓Vagus
Compensatory Reflex
Cardiovascular Sequelae
↑Activity of Pharyngeal Dilators (GG)
Maintains Upper Airway Patency
Sympathetic Activation
Sleep Fragmentation
Sleep Onset
Arousal
Neurocognitive Sequelae
Loss of Reflex
↑Respiratory Effort
↓Activity of Pharyngeal Dilators
Airway Collapse
Hypoxia + Hypercapnia
Malhotra and White
Lancet 2002

OSA – Negative consequences -Perioperative

- Surgical patients – Untreated OSA in perioperative setting assoc with higher rate of cardiopulmonary complications and ICU transfer
  - Kaw R Chest 2012;141:436-41
- Amer Assoc of Anesthesiologists rec in OSA patients
  - Moderate sedation—>monitor ventilation with continuous oximetry and capnography

OSA: Treatment

- Continuous Positive Airway Pressure (CPAP)
- Bilevel Positive Airway Pressure (BIPAP)
- Positional Therapy
- Oral Appliance
- Surgery
- Upper Airway Stimulation (Hypoglossal Nerve Stimulation)
- Combination
- Lifestyle Modification – Weight loss, avoidance of substances that promote relaxation of UA


It's the only way they can get any sleep
SWEET DREAMS: Lynn Woodward hugs her hubby — who's also named Lynn — as they sleep soundly wearing masks attached to breathing machines.

OSA – PAP therapy

- PAP - pneumatic stint to the upper airway
- APAP (autotitrating CPAP) detects airflow limitation as a surrogate marker for upper airway narrowing and automatically adjusts pressure
- Goal - Use all night
- CMS- Adequate - 4+ hrs 70% of nights
  - 75% of patients achieve this threshold

OSA – Mandibular Advancement Device (MAD)

Prevent upper airway collapse by protruding the mandible forward, thus altering the jaw and tongue position.

Predominantly increases the volume of the airway at the level of the velopharynx .

The airway space is mostly enlarged laterally, thought to be due to traction on soft tissue connections between the pharynx and the mandibular ramus

OSA- MAD

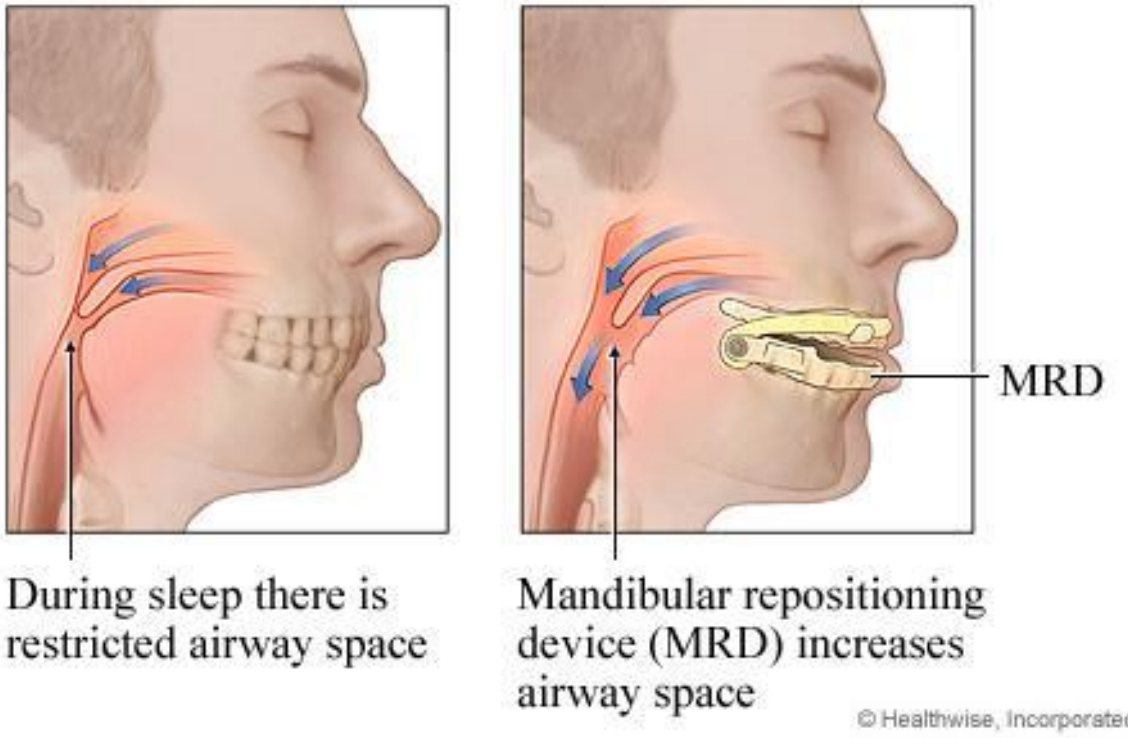
- **Indications**
- Lower AHI
- Younger age
- Lower BMI
- Smaller neck size
- Positional OSA
- Retrognathia
- Good ability to advance mandible

- **Contraindications**
- Recent/active orthodontics
- Compromised dentition
- Acute TMJ dysfunction
- Unrealistic expectations
- Uncontrolled seizure disorder
- Growth potential
- Limited ability to advance mandible

OSA – MAD

Oasys Hinge - Glidewell Dental

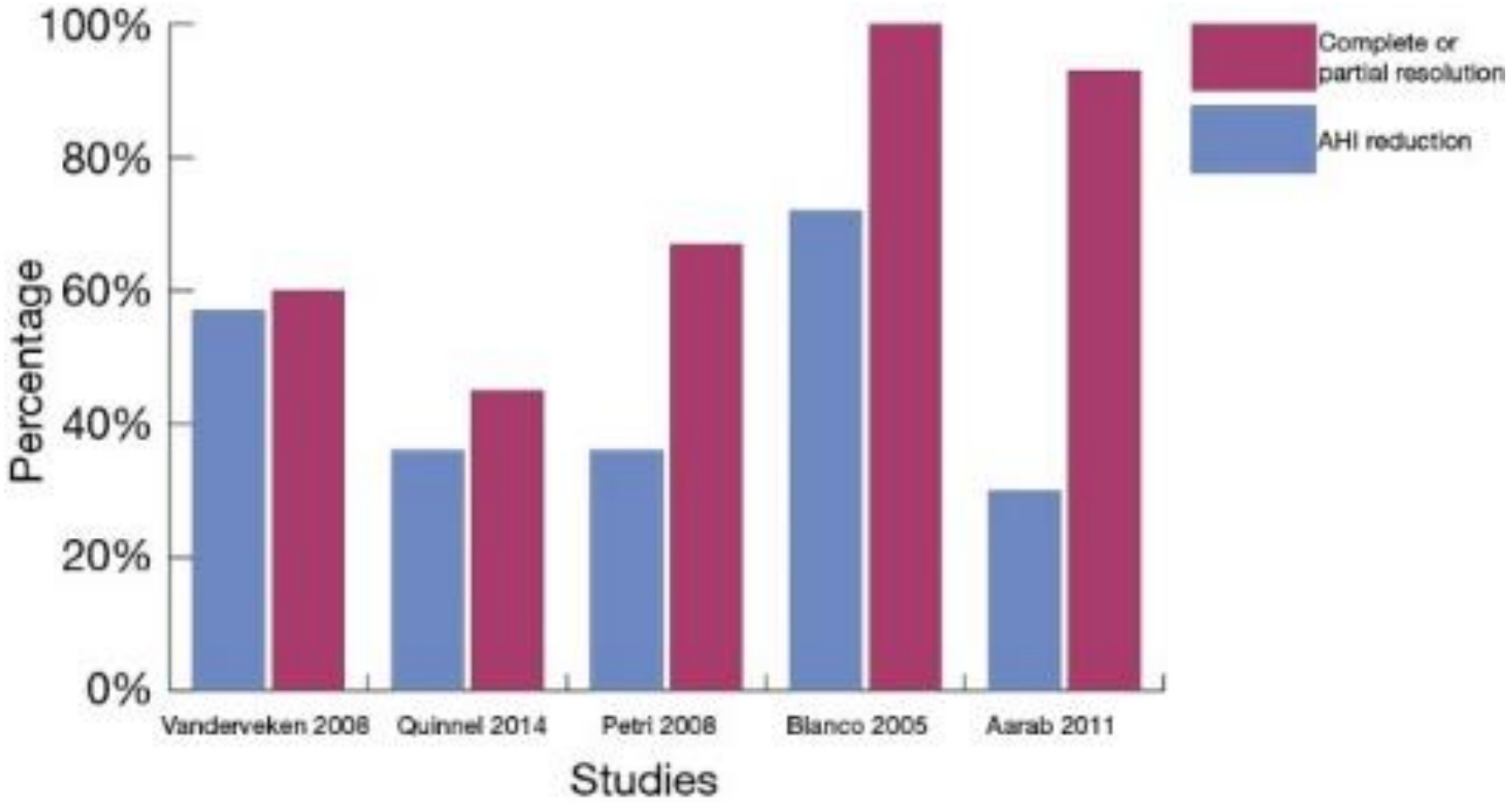
Action of treatment



OSA - MAD

- Offer to patients with mild to moderate OSA
- Moderate to severe OSA if cannot tolerate CPAP
- Possible combination therapy with patients who cannot tolerate high pressures on PAP

OSA – MAD efficacy



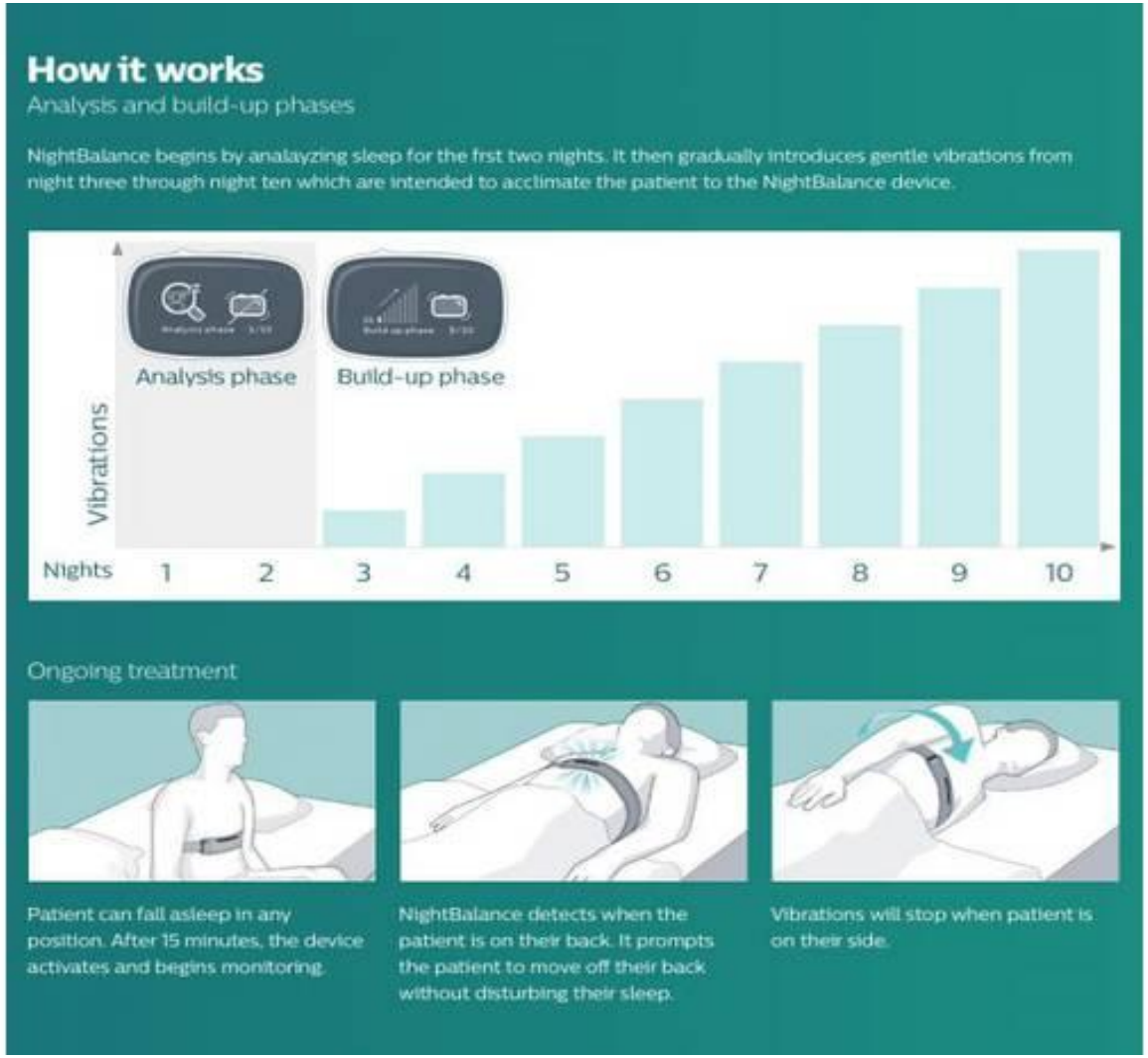
OSA – MAD vs CPAP

- CPAP more effective treatment of OSA
- MAD -increased compliance
- Similar effect of sleepiness and QOL
- Side effects -
  - Short term – dry mouth or hypersalivation, dental pain, gingival irritation
  - Long term – dentofacial changes, occlusal alteration, TMJ issues
- Made by qualified dentists who have had appropriate training in the field.

OSA: Positional Therapy

Positional therapy for OSA

OSA –Positional therapy



Nightbalance –Respironics

OSA: Surgery

- PAP facilitator surgery
  - Nasal Procedures: Intra nasal // Extra nasal procedures

- PAP Alternatives (or even in combination)
  - Upper pharyngeal Procedures
  - Lower pharyngeal Procedures
  - Upper Airway Surgery (Hypoglossal nerve stimulation)
  - Skeletal surgery
  - Tracheostomy
  - Bariatric Surgery

OSA –-Nasal procedures

- Intranasal - Facilitator surgery
  - 2/3 of PAP intolerant patients - moderate to severe nasal obstruction
  - Deviated septum - septoplasty
  - Inferior turbinate hypertrophy – Inf turbinate reduction
- Extranasal
  - Narrow upper jaw, high arching palate – palate expander
    - DOME - Distraction Osteogenesis Maxillary Expansion
      - Reduces nasal airway velocity decreased pharyngeal and nasal pressure

OSA- Alternative Treatment-Soft tissue Surgery

- Upper Pharyngeal Surgery
  - Palantine tonsillectomy
  - Palatopharyngoplasty
  - Partial uvulectomy
  - Expansion pharyngoplasty
- Lower Pharyngeal Surgery
  - Lingual tonsillectomy
  - Tongue base surgery
  - Epiglottis Correction

OSA: Alternative treatment -Skeletal Surgery

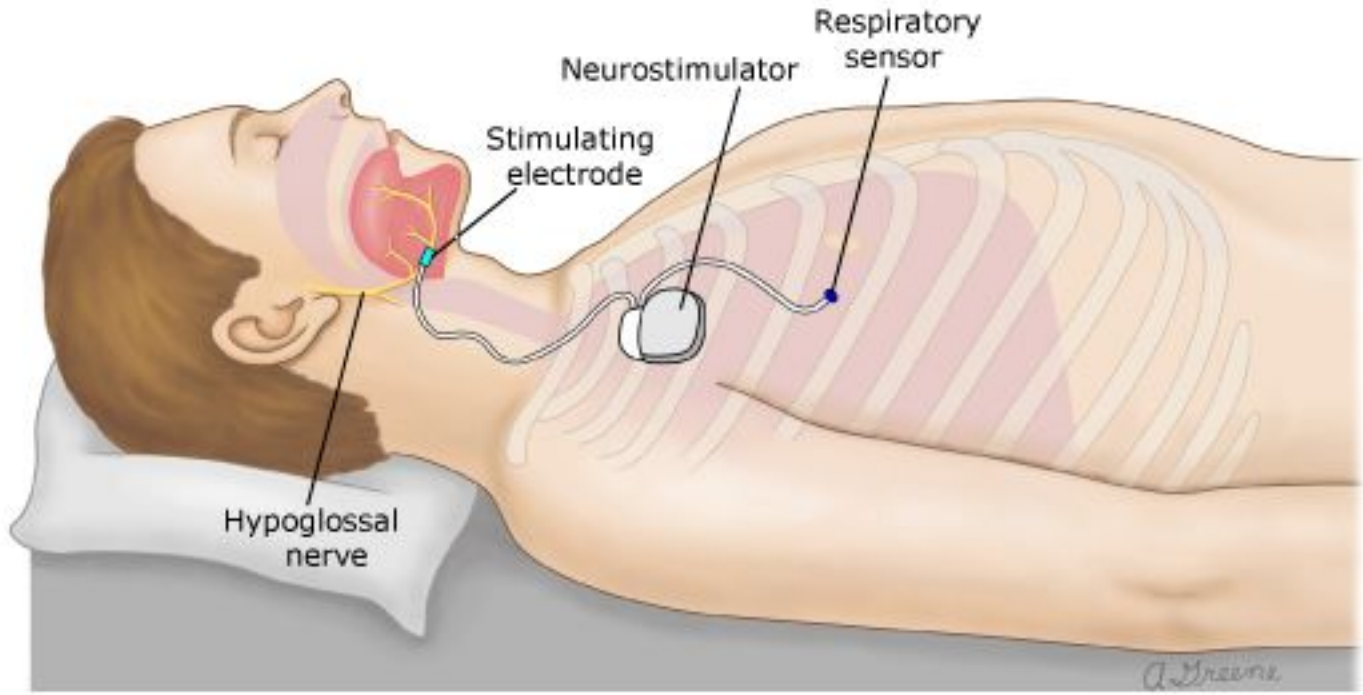
- Skeletal/ Global Airway Procedures
  - Maxillomandibular Advancement
  - Maxillary expansion
  - Tongue Advancement/Stabilization
    - Genioglossus advancement
    - Hyoid suspension
    - Tongue suspension
  - Tracheostomy

OSA – Upper Airway Stimulation

- Respiratory sensing lead
- Programmable implanted pulse generator (IPG)
- Stimulating electrode encircles the anterior branches of the HGN with an electrode cuff

- FDA approved in 2014

Upper airway stimulation device for obstructive sleep apnea



OSA- Upper Airway Stimulation

- Sensing lead monitors breathing during sleep and detects pressure changes in respiratory cycle and sends info to IPG
- IPG receives info from sensing lead, operates timing and output algorithms, delivers energy synchronized with respiratory cycle to stimulation lead
- Stimulation lead - stimulation delivered to key airway muscles (primarily controlled by the HGN– genioglossus muscle) causes tongue protrusion- opening oropharyngeal airway directly BUT also affects retropalatal airway by palatoglossal coupling action

OSA- Upper Airway Stimulation

- Upper Airway Stimulation: Indications
  - >18 yrs old
  - AHI Moderate-Severe 15-65/hr with ≤25% Central/mixed apnea
  - BMI <32 (35kg/m2)
  - Unable to tolerate airway pressure (PAP) treatments
  - Acceptable airway closure – DISE – no complete concentric collapse at the soft palate level.

OSA- Upper Airway Stimulation

- Upper Airway Stimulation: Contraindications
  - >25% central/mixed apneas
  - Anatomic findings that compromise performance- concentric collapse
  - Pre-existing conditions that compromise neurologic function of upper airway
  - Inability to operate system
  - Pregnancy or plan to become pregnant
  - Require MRI (in some cases)

OSA – Upper Airway Stimulation - DISE

- Drug-induced sleep Endoscopy - DISE
- Locates level of airway obstruction
  - Palate, oropharynx, base of tongue, hypopharynx/epiglottis, multilevel
- Direction of collapse
  - Anteroposterior, lateral, concentric
- Degree of collapse
  - None, partial, complete

❖ Prevalence of complete collapse, multilevel collapse, and hypopharyngeal collapse incr with incr severity of OSA
  - Vroegop AV Laryngoscope 2014;124(3):797-802
- Anteroposterior collapse - most likely to benefit from UAS

OSA – UAS - ADHERE Registry -6,12 months

- ADHERE registry -ongoing international, multicenter prospective observational study of UAS outcomes after implantation

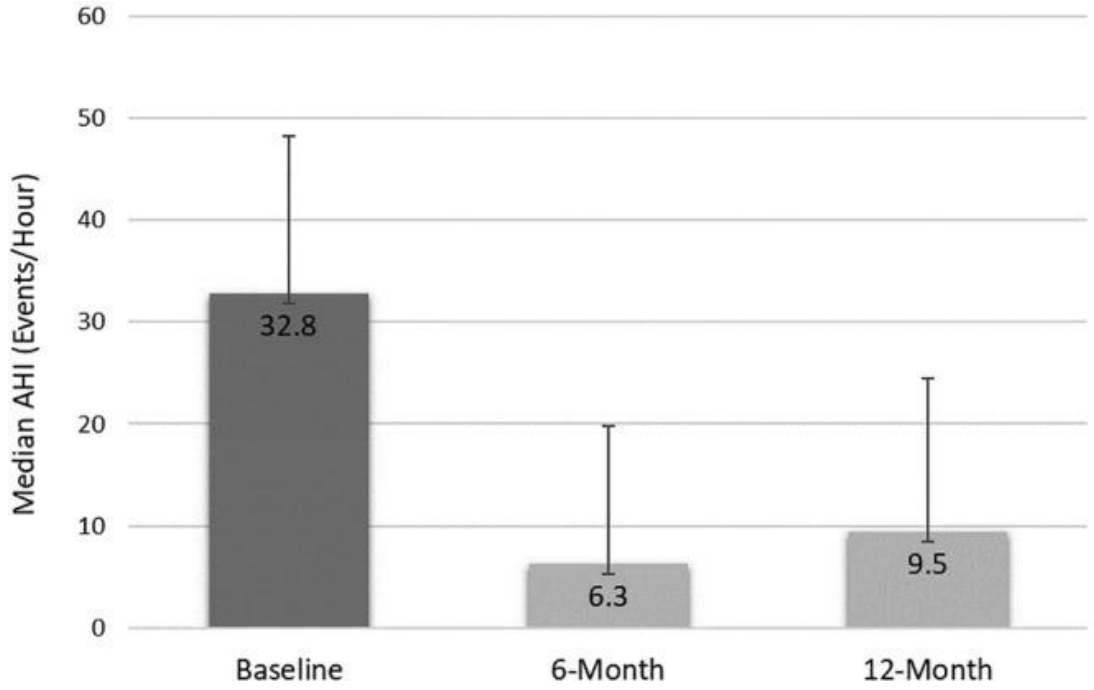
  10/2016-2/2019 -1017 patients

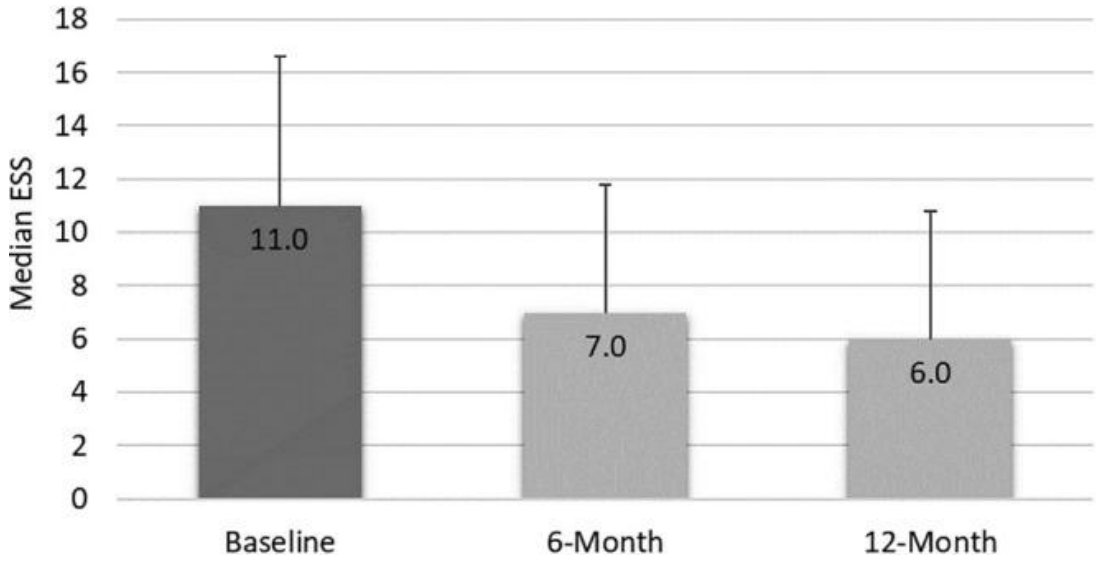
  6mo- 640 pts // 12 mo 382 pts

Endpoints - AHI, ESS, Time of use

Baseline , 6 mo, 12 mo

OSA – UAS – ADHERE Registry





OSA – UAS – ADHERE Registry

- Time device therapy – 12months
  - Median 5.7hrs (IQR 4.1—7.1hrs)
  - Mean 5.6+/-2.1hrs

- 93% pts reported overall satisfaction
- 95% UAS>>PAP
- 94% Would do it again
- 96% recommend to family and friends

OSA – UAS – ADHERE Registry

- Adverse events at 12 months

- Stimulation discomfort 12% at 6 mo 8% at 12 mo

- Tongue abrasion 3% at 6 mo 4% at 12 mo
- Insomnia/arousal 3% at 6 mo 5% at 12 mo

- Surgical device revision in 3 cases - stimulation electrode

UAB 2018-2019 -UAS Experience (Inspire)

- 2018 – 40 implants (2-late2017)
  - Age 37-80yrs avr 62yrs
  - Race 38 W // 2 AA
  - Sex 25 M // 15 F
  - BMI 23.2-39.7 avr 28.6
- 2019 – 39 implants
  - Age 30-74yrs avr 54yrs
  - Race 39 W
  - Sex 25 M // 14 F
  - BMI 24-39.7 avr 28.6

UAB 2018-2020 UAS Experience

- Pre implant AHI 2018: 13.1-76.8/hr

  2019: 9.3-87/hr

- Post implant AHI (at MTA) 2018: 0-9.4/hr (ex-76.8/hr□0/hr)

  2019: 0-30.4/hr (ex- 87/hr□27/hr)

  (ex- 52.5/hr 70% □ 30.4/hr 83%)

- Pre implant min O2 sat 2018: 47-91%
- Post implant min O2 sat 2018: 74%-91% (ex- 47%□85%)

UAB 2018-2019 UAS Experience

- Quality of life? **Better**
- Would you do it again? **Resounding –yes**
- Interesting :
  - Prior upper airway surgery
    - 2018: 15/40 37.5%
    - 2019: 14/39 38.4%
  - Comorbidities such as HTN, CHF, AFib, DM, Asthma/COPD
    - 2018: 12/40 30%
    - 2019: 21/39 53.8%

UAB Experience - UAS

- Challenges –
  - Tongue soreness/irritation - poor dentition
  - Some patients more sensitive to voltage changes than others
    - From “no sensation” - to “a jolt”
  - Need for repeated studies on some patients after adjustments- insurance limitations

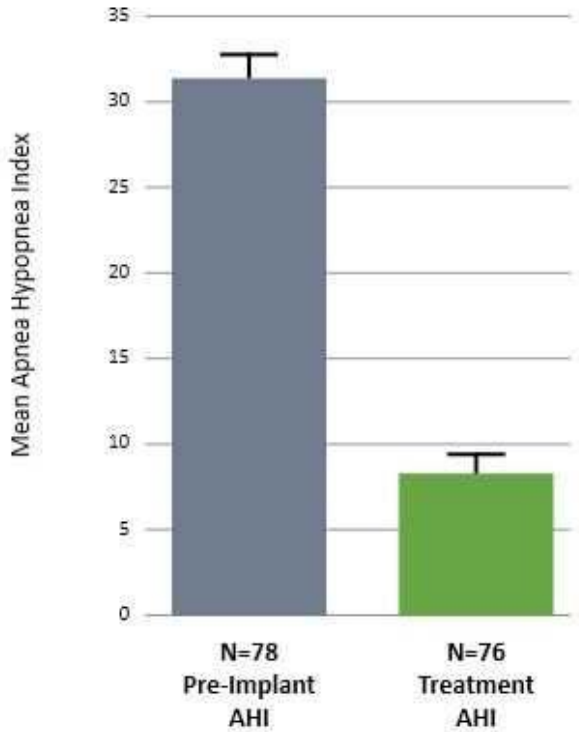
- **Inspire does not ‘fix’ underlying insomnia/ RLS/ poor sleep hygiene**

OSA - Hypoglossal Nerve Stimulation UAB Experience –

Practice AHI Outcomes

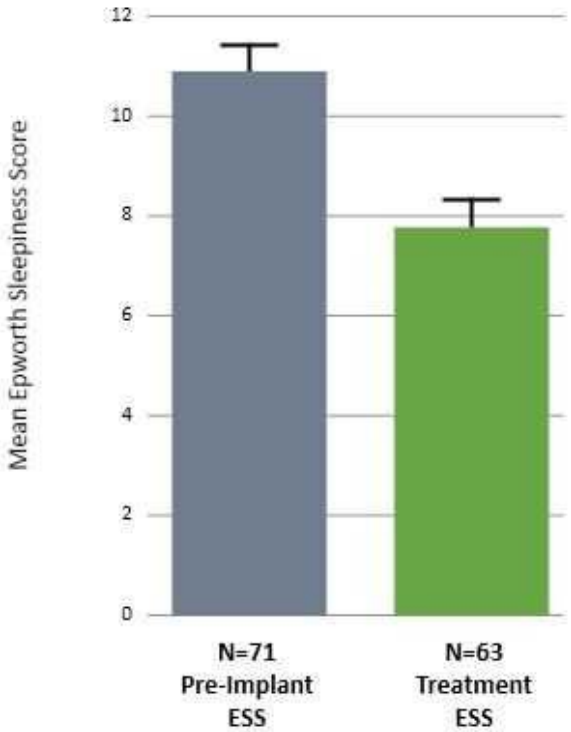
Mean Treatment AHI: 8.4 (N=76)

Treatment AHI < 15: 77.6%



Practice ESS Outcomes

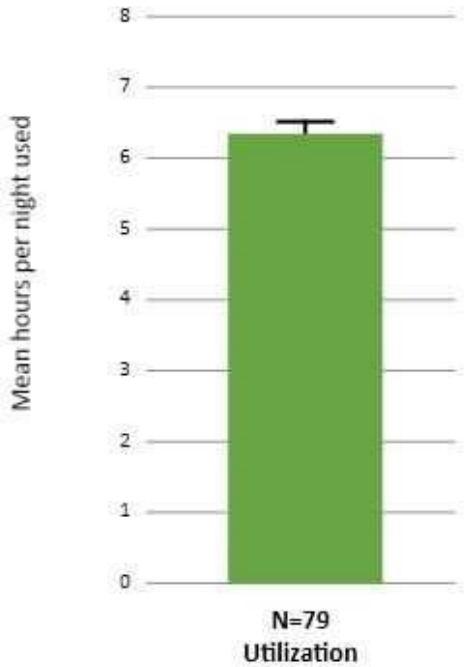
Mean Treatment ESS: 7.8 (N=63)



Practice Utilization

Mean Utilization: 6.4 (N=79)

Nights Used >= 4 Hours: 76.0%



UAB Experience- TEAMWORK IS KEY

- Team
  - ENT and support staff
    - **Kirk Withrow, MD, Jaime Sandlin, PA**
  - Sleep clinic/lab - Activation, Titration, Follow up, Troubleshooting
    - **David Moore, RPSGT**
    - **Josh Warren, CRNP**
    - **Melissa Butler, RPSGT, RST, CCSH; William Mathis, RST; Alisha Hays, RPSGT**
  - Inspire- Support team (AWESOME) – **Michael, Jeff, Scott, Wynne**
    - Inspire cloud

OSA: Therapeutic Benefit

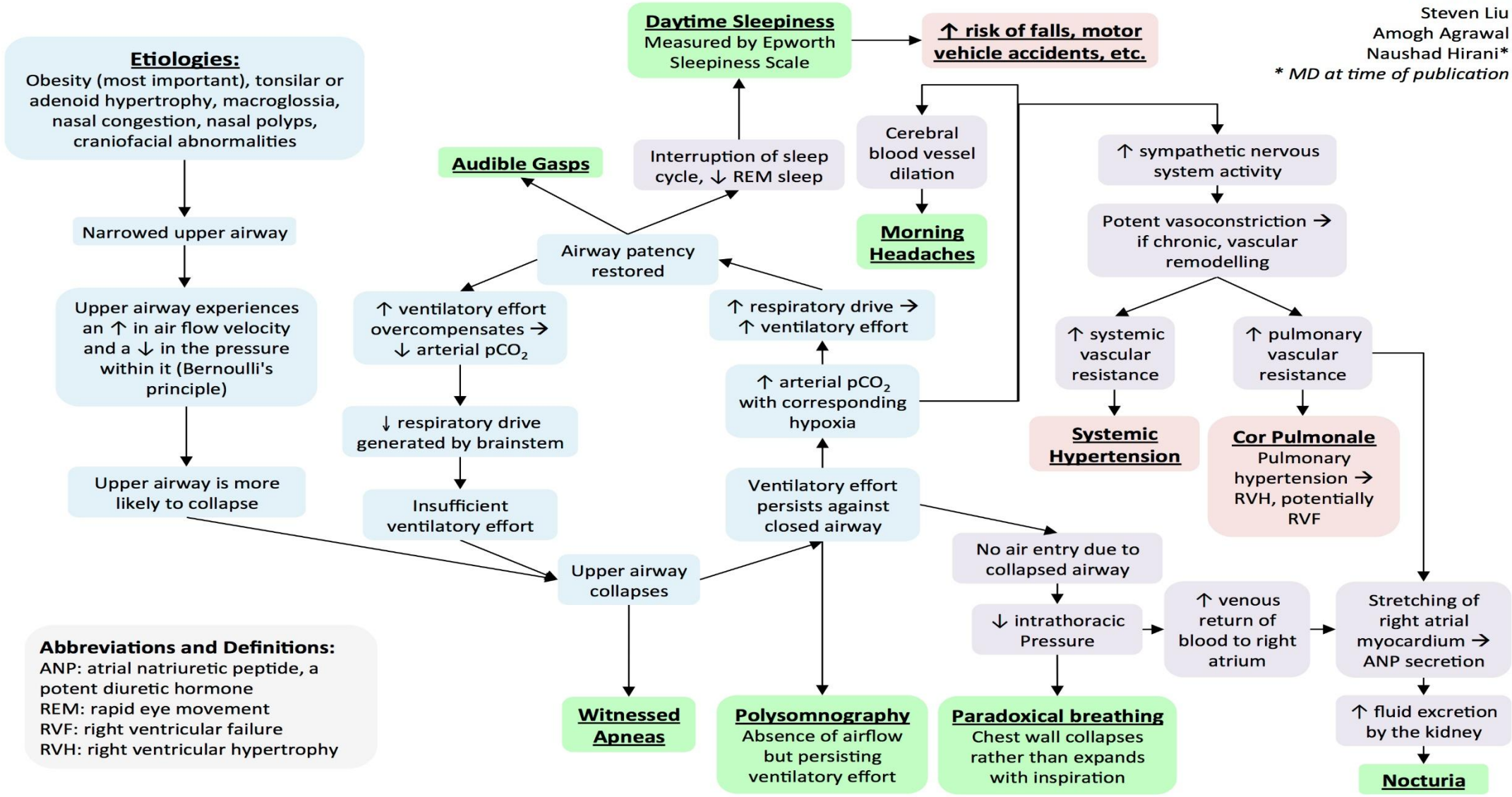
- Improved Quality of Life
- Improved Hypertension
- Reduced cost and healthcare utilization
- Reduced morbidity and mortality
- Reduced risk of MVA
- Reduced risk of chronic health consequences

“If sleep does not serve an absolutely vital function, then it is the biggest mistake the evolutionary process has ever made.”

A. Rechtschaffen - 1970

Obstructive Sleep Apnea: *Pathogenesis and clinical findings*

Author:
Alexander Arnold
Reviewers:
Steven Liu
Amogh Agrawal
Naushad Hirani*
** MD at time of publication*



Legend: Pathophysiology | Mechanism | Sign/Symptom/Lab Finding | Complications

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There is only one thing people like that is good for them;
a good night's sleep.
-Edgar Watson Howe