

“A New Screening Tool Connects Comorbidities to Sleep Disordered Breathing”

References for the Lamberg Questionnaire: LQ 2.1

Category 1: (the most commonly asked screening questions)

- “STOPBANG” questionnaire: Snoring, Tired, Observed apneas, Pressure (BP), BMI, Age, Neck circumference, Gender) Berlin Questionnaire, ESS.
 - 1) Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008;108:812-21.2) Lavie P, Ben-Yosef R, Rubin AE. Prevalence of sleep apnea syndrome among patients with essential hypertension. *Am Heart J.* 1984;108(2):373–376.
 - 2) Chung F, Yegneswaran B, Liao P, et al. STOP questionnaire: a tool to screen patients for obstructive sleep apnea. *Anesthesiology* 2008;108:812-21.
 - 3) Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. *Ann Int Med* 1999;131:485-91.
 - 4) Johns MJ. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep* 1991;14:540-5.
- Physical: BMI, Sex, Age >50, Neck Size, Tonsil Grade, Oral Pharyngeal Crowding, Tongue level, Hyoid position, Craniofacial characteristics Orthodontic type, Palatal vaulting, Family History of SDB.
- Have you had unexpected weight changes recently?
- Have you ever had a PSG? Titration study? Home sleep test?
- Do you snore loudly enough at night to cause conflict with others?
- Have you been told you have stopped breathing at night?
- Did you ever wake up choking?
- Do you awaken unrefreshed?
- Do you have morning headaches?
- Do you feel sleepy during the day? ESS. (Use Caffeine or Prescription Stimulants)
- Do you feel fatigued during the day?
- Do you have difficulty breathing through your nose?
(Post nasal drip, or dry mouth in morning?)

Category 2: Cardiovascular:

SDB predicts an increased prevalence of CAD, Stroke, Arrhythmias, Hypertension. Endothelial Dysfunction.

- 1) Young T; Finn L; Peppard PE; Szklo-Coxe M; Austin D; Nieto FJ; Stubbs R; Hla KM. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin Sleep Cohort. *SLEEP* 2008;31(8):1071-1078.
- 2) Nieto FJ, Young TB, Lind BK, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. *Sleep Heart Health Study. JAMA.* 2000; 283: 1829–1836.

SDB in CAD patients is twice that of non-CAD patients. An AHI>10/h has been shown in 37% of the patients with CAD.

Moore T, Rabben T, Wiklund U, Franklin KA, Eriksson P. Sleep disordered breathing in men with coronary artery disease. *Chest* 1996;109(3):659–63.

Patients with OSA have higher risk of CAD and need aggressive prevention.

Gami AS et. al., *Chest* 1/2007, 131:118-121

Meta-analysis showed greater likelihood of stroke or CV events with increasing AHI.

Loke, YK MD, et. al. *Circ Cardiovasc Qual Outcomes.* 8/2012;5:00-00

Increase in free radicals (oxidative stress), homocysteine and decrease in nitric oxide leads to damaged endothelium and loss of vessel elasticity, resulting in hypertension.

- 1) Lerman LO, Nath KA, Rodriguez-Porcel M, Krier JD, Schwartz RS, Napoli C, Romero JC. Increased oxidative stress experimental renovascular hypertension. *Hypertension.* 2001; 37: 541–546.
- 2) Reckelhoff JF, Romero JC. Role of oxidative stress induced hypertension. *Am J Physiol.* 2003; 284: R893–R912.

OSA is an independent risk factor for development of hypertension and this relationship is dose-dependent.

- 1) Silverberg DS¹, Oksenberg A. Are sleep-related breathing disorders important contributing factors to the production of essential hypertension? *Curr Hypertens Rep.* 2001 Jun;3(3):209-15.
- 2) Peppard PE, Young T, Palta M, et al. Prospective study of the association between sleep disordered breathing and hypertension. *N Engl J Med* 2000;342(19):1378-1384.

Within OSA population, 50% are hypertensive and within Hypertensive population, 30% have OSA.

- 1) Fletcher ED, DeBehnke RD, Lovoi MS, et al. Undiagnosed sleep apnea in patients with essential hypertension. *Ann Intern Med.* 1985;103(2):190–195.
- 2) Lavie P, Ben-Yosef R, Rubin AE. Prevalence of sleep apnea syndrome among patients with essential hypertension. *Am Heart J.* 1984;108(2):373–376.
- 3) Worsnop CJ, Naughton MT, Barter CE, Morgan TO, Anderson AI, Pierce RJ. The prevalence of obstructive sleep apnea in hypertensives. *Am J Respir Crit Care Med.* 1998;157(1):111–115.
- 4) Durán-Cantolla J, Aizpuru F, Martínez-Null C, Barbélla F. Obstructive sleep apnea/hypopnea and systemic hypertension. *Sleep Med Rev.* 2009;13(5):323–331.

OSA patients have an impairment of resistance-vessel endothelium-dependent vasodilation.(Endothelial Dysfunction) This may be implicated in the pathogenesis of hypertension and heart failure in this condition.

Kato M, Roberts-Thomson P, Phillips BG, et al. Impairment of endothelium-dependent vasodilation of resistance vessels in patients with obstructive sleep apnea. *Circulation* 2000; 102: 2607–2610.

Drug Resistant Hypertension, prevalence of OSA: 96% men, 65% women.

Logan AG, Perlikowski SM, Mente A, Tisler A, Tkacova R, Niroumand M, Leung RS, Bradley TD, High prevalence of unrecognized sleep apnea in drug-resistant hypertension. *J Hypertens*. 2001 Dec;19(12):2271-7.

Hypertensive patients, especially those whose 24 h BP studies that yielded non-dipping, should be screened for occult OSA as a cause of secondary hypertension.

Yasmine A. Ashram, Nashwa H. Abdel Wahab, Iman H. Diab, Non-dipping pattern of nocturnal blood pressure in obstructive sleep apnea syndrome: Possible role of oxidative stress and endothelin-1 precursor. *Alexandria Journal of Medicine* Volume 49, Issue 2, June 2013, Pages 153–161.

If ambulatory blood pressure monitoring indicates that a patient is a “non-dipper”, the chances that the patient has OSA are increased.

Portaluppi F, Provini F, Cortelli P, Plazzi G, Bertozzi N, Manfredini R, et al. Undiagnosed sleep disordered breathing among male nondippers with essential hypertension. *J Hypertens*. 1997;15:1227–33.

In patients who are “non-dipping”, the prevalence OSA was 84%

J.S. Loreda, S. Ancoli-Israel, J.E. Dimsdale, Sleep quality and blood pressure dipping in obstructive sleep apnea *Am J Hypertens*, 14 (2001), pp. 887–892.

**38,000 CV deaths/year linked to OSA National Commission on Sleep Disorders Research
Stroke OR is 3x if AHI>30**

Arzt M, Young T, Finn L, Skatrud JB, Bradley TD., Association of sleep-disordered breathing and the occurrence of stroke. *Am J Respir Crit Care Med*. 2005 Dec 1;172(11):1447-51. Epub 2005 Sep 1.

Heart Failure patients: 12%-53% have OSA

- 1) Sin D, Fitzgerald F, Parker JD, Newton G, Floras JS, Bradley TD. Risk factors for central and obstructive sleep apnea in 450 men and women with congestive heart failure. *Am J Respir Crit Care Med* 1999;160:1101–6.
- 2) Javaheri S. Sleep disorders in systolic heart failure: a prospective study of 100 male patients. The final report. *Int J Cardiol* 2006;106:21–8.
- 3) Ferrier K, Campbell A, Yee B, et al. Sleep-disordered breathing occurs frequently in stable outpatients with congestive heart failure. *Chest* 2005;128:2116 –22.

Presence of OSA was associated with increased odds of having HF.

Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Am J Respir Crit Care Med* 2001; 163:19–25.

Severe OSA patients OR=5.2 for CV mortality

Young T; Finn L; Peppard PE; Szklo-Coxe M; Austin D; Nieto FJ; Stubbs R; Hla KM. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. *SLEEP* 2008;31(8):1071-1078

Within Angina Population (including acute coronary syndrome “ACS”), 30% to 69% had OSA.

- 1) T. Mooe, T. Rabben, U. Wiklund, K. A. Franklin, and P. Eriksson, “Sleep-disordered breathing in men with coronary artery disease,” *Chest*, vol. 109, no. 3, pp. 659–663, 1996
- 2) Y. Peker, H. Kraiczi, J. Hedner, S. Löth, A. Johansson, and M. Bende, “An independent association between obstructive sleep apnea and coronary artery disease,” *European Respiratory Journal*, vol. 14, no. 1, pp. 179–184, 1999.
- 3) T. Konecny, F. H. Sert Kuniyoshi, M. Orban et al., “Under-diagnosis of sleep apnea in patients after acute myocardial infarction,” *Journal of the American College of Cardiology*, vol. 56, no. 9, pp. 742–743, 2010.

Moderate-Severe OSA was independently associated with Angina (odds ratio 9.61)

Akira Tamura, MD et.al., Association between coronary spastic angina pectoris and obstructive sleep apnea, *Journal of Cardiology* Volume 56, Issue 2, September 2010, Pages 240–244, Elsevier.

60% of patients with severe OSA were found to develop cardiac arrhythmias.

Guilleminault, C., Connolly, S.J., and Winkle, R.A. Cardiac arrhythmia and conduction disturbances during sleep in 400 patients with sleep apnea syndrome. *Am J Cardiol.* 1983; 52: 490–494.

Nocturnal Arrhythmias occur in 50% of OSA patients

Virend K. Somers, MD, et.al., Sleep Apnea and Cardiovascular Disease, An American Heart Association/American College of Cardiology Foundation Scientific Statement From the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing In Collaboration With the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health) *J Am Coll Cardiol.* 2008;52(8):686-717.

68% of patients with atrioventricular block have OSA

Virend K. Somers, MD, et.al., Sleep Apnea and Cardiovascular Disease, An American Heart Association/American College of Cardiology Foundation Scientific Statement From the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing In Collaboration With the National Heart, Lung, and Blood Institute National Center on Sleep Disorders Research (National Institutes of Health) *J Am Coll Cardiol.* 2008;52(8):686-717.

Ventricular Arrhythmias in 66% of OSA patients (PVCs)

Tilkian AG, Guilleminault C, Schroeder JS, Lehrman KL, Simmons FB, Dement WC. Sleep induced apnea syndrome: Prevalence of cardiac arrhythmias and their reversal after tracheostomy. *Am J Med.* 1977;63:348–58.

In AFib cohort studies: 42% to 45% to 81% have OSA

- 1) Bitter T, Langer C, Vogt J, Horstkotte D, Oldenburg O. Sleep-disordered breathing in patients with atrial fibrillation and normal systolic left ventricular function. *Dtsch Arztebl Int.* 2009;106:164-170.
- 2) Braga B, Poyares D, Cintra F, et al. Sleep-disordered breathing and chronic atrial fibrillation. *Sleep Med.* 2009;10:212-216.

In Severe OSA cohort, risk of AFib is increased 4x

Mehra R, Benjamin EJ, Shahar E, et al; Sleep Heart Health Study. Association of nocturnal arrhythmias with sleep-disordered breathing: The Sleep Heart Health Study. *Am J Respir Crit Care Med.* 2006;173:910-916.

Patients with AFib may benefit from screening for OSA because OSA is a treatable risk factor for the initiation and recurrence of AFib after ablation.

- 1) A. S. Gami, G. Pressman, S. M. Caples et al., "Association of atrial fibrillation and obstructive sleep apnea," *Circulation*, vol. 110, no. 4, pp. 364–367, 2004.
- 2) R. Mehra, E. J. Benjamin, E. Shahar et al., "Association of nocturnal arrhythmias with sleep-disordered breathing: the Sleep Heart Health Study," *American Journal of Respiratory and Critical Care Medicine*, vol. 173, no. 8, pp. 910–916, 2006.
- 3) T. Tanigawa, K. Yamagishi, S. Sakurai et al., "Arterial oxygen desaturation during sleep and atrial fibrillation," *Heart*, vol. 92, no. 12, pp. 1854–1855, 2006.
- 4) K. Monahan, A. Storfer-Isser, R. Mehra et al., "Triggering of nocturnal arrhythmias by sleep-disordered breathing events," *Journal of the American College of Cardiology*, vol. 54, no. 19, pp. 1797–1804, 2009.
- 5) A. S. Gami, D. O. Hodge, R. M. Herges et al., "Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation," *Journal of the American College of Cardiology*, vol. 49, no. 5, pp. 565–571, 2007.
- 6) I. H. Stevenson, H. Teichtahl, D. Cunnington, S. Ciavarella, I. Gordon, and J. M. Kalman, "Prevalence of sleep disordered breathing in paroxysmal and persistent atrial fibrillation patients with normal left ventricular function," *European Heart Journal*, vol. 29, no. 13, pp. 1662–1669, 2008.
- 7) Adam S. Fein, MD et al; Treatment of Obstructive Sleep Apnea Reduces the Risk of Atrial Fibrillation Recurrence After Catheter Ablation, *J Am Coll Cardiol*. 2013; 62 (4):300-305.

In Pacemaker patients, 59% have OSA..

Stéphane Garrigue, MD, PhD; Jean-Louis Pépin, MD, PhD; Pascal Defaye, MD; Francis Murgatroyd, MD; Yann Poezevara, MS; Jacques Clémenty, MD; Patrick Lévy, MD, PhD, High Prevalence of Sleep Apnea Syndrome in Patients With Long-Term Pacing, The European Multicenter Polysomnographic Study, *Circulation-Arrhythmia/Electrophysiology*, American Heart Association.

Snoring may be a CV Risk Factor. CIMT was significantly thickened compared to healthy non-snorers. Snoring posed a greater risk for abnormal CIMT than smoking obesity, and high cholesterol.

Deeb R, MD et. al. Combined Sections Meeting of the Triological Society
Submitted The Laryngoscope, 1/25/2013.

Patients with OSA appear to have increased dyslipidemia (high total cholesterol, LDL, TG, and low HDL) Sixty-four studies were pooled for analysis; since some studies have more than one dataset, there were 107 datasets with 18,116 patients pooled for meta-analysis.

Nadeem R, Singh M, Nida M, Waheed I, Khan A, Ahmed S, Naseem J, Champeau D, Effect of obstructive sleep apnea hypopnea syndrome on lipid profile: a meta-regression analysis. *J Clin Sleep Med*. 2014 May 15;10(5):475-89. doi: 10.5664/jcsm.3690

Insulin resistance Increases Arterial Inflammation

Kim T N et al. *Circ Cardiovasc Imaging* 2010;3:142-148

The risk of having clogged coronary arteries (the precursor of a heart attack) is more than doubled for people with vitamin D deficiency (less than 20 ng/mL).

Shor R, Tirosh A, Shemesh L, et al. 25 hydroxyvitamin D levels in patients undergoing coronary artery catheterization. *Eur J Intern Med*. 2012 Jul;23(5):470-3.

Patients with hypertension who sleep less than five hours or more than eight hours each night may have significantly higher odds of a stroke, new research suggests. Analyzing data from 203,794 U.S. residents with hypertension, scientists determined that "insufficient" sleepers

logging less than five hours of sleep each night had an 83 percent increased risk of stroke compared to "healthy" sleepers who got seven to eight hours of sleep. "Long" sleepers reporting more than eight hours of nightly sleep experienced a 74 percent higher stroke risk than healthy sleepers, according to the study. Data collected over nine years from the U.S. National Health Interview Survey of 203,794 Americans with hypertension. Overall, the stroke risk was nearly 13.6 percent among "long" sleepers; 11.2 percent among "insufficient" sleepers; 5.7 percent for "short sleepers" logging five to six hours per night; and about 5.4 percent among "healthy" sleepers.

Oluwaseun Akinseye, M.D., a resident in internal medicine at the Icahn School of Medicine of Mount Sinai Hospital in New York City, Presented at the annual meeting of the American Society of Hypertension, May 15, 2015, in New York City.

Category 3: Pulmonary:

In OSA population, 10%-20% have COPD

- 1) Ruth Lee, Walter T. McNicholas, Obstructive Sleep Apnea in Chronic Obstructive Pulmonary Disease Patients, *Curr Opin Pulm Med.* 2011;17(2):79-83.
- 2) Chaouat A., Weitzenblum E., Krieger J., Ifoundza T., Oswald M., Kessler R. Association of chronic obstructive pulmonary disease and sleep apnea syndrome. *Am. J. Respir. Crit. Care Med.* 1995; 151: 82–86.
- 3) De Miguel J., Cabello J., Sánchez-Alarcos J.M., Alvarez-Sala R., Espinós D., Alvarez-Sala J.L. Long-term effects of treatment with nasal continuous positive airway pressure on lung function in patients with overlap syndrome. *Sleep Breath.* 2002; 6: 3–10.

COPD with OSA = "Overlap Syndrome" increased mortality

Jose M. Marin, Joan B. Soriano, Santiago J. Carrizo, Ana Boldova, and Bartolome R. Celli "Outcomes in Patients with Chronic Obstructive Pulmonary Disease and Obstructive Sleep Apnea", *American Journal of Respiratory and Critical Care Medicine*, Vol. 182, No. 3 (2010), pp. 325-331.

Greater than 10% chance of OSA in COPD pop and vice versa. When seeing a patient with either OSA or COPD, it is reasonable to screen for the other.

Robert L Owens, MD and Atul Malhotra, MD, Sleep-Disordered Breathing and COPD: The Overlap Syndrome, *Respir Care.* Oct 2010; 55(10): 1333–1346.

OSA increases BP of Pulmonary Artery leads to Pulmonary Hypertension and possibly COPD.

- 1) Trenton D. Nauser, M.D., and Steven W. Stites, M.D., Diagnosis and Treatment of Pulmonary Hypertension, *Am Fam Physician.* 2001 May 1;63(9):1789-1799.
- 2) Chaouat A, Weitzenblum E, Krieger J, Oswald M, Kessler R. Pulmonary hemodynamics in the obstructive sleep apnea syndrome. Results in 220 consecutive patients. *Chest.* 1996;109:380–6.

COPD causes Nocturnal Oxygen Desats, impairs sleep.

E C Fletcher; J Miller; G W Divine; J G Fletcher; T Miller, Nocturnal oxyhemoglobin desaturation in COPD patients with arterial oxygen tensions above 60 mm Hg., *Chest.* 1987;92(4):604-608.

11% to 20% of those with controlled asthma reported sleep disturbances.

Dr. Braido, *Asian Pac J Allergy Immunol.* 2009;27:27-33.

OSA patients have OR of 2.87 for asthma

Chest. 2010: 138:543-550.

Asthma cohort has 72% inc. risk for developing OSA, each disorder making the other worse.

Teodorescu M, et al "Asthma predicts 8 year incidence of obstructive sleep apnea in the Wisconsin sleep cohort" *Am J Respir Crit Care Med* 2013; 187: A6015

In Asthma cohort, 30%-90% have Rhinitis

- 1) Leynaert B, Neukirch F, Demoly P, Bousquet J. Epidemiologic evidence for asthma and rhinitis comorbidity. *J Allergy Clin Immunol.* 2000;106:S201-5.
- 2) Simons FE. Allergic rhinobronchitis: The asthma-allergic rhinitis link. *J Allergy Clin Immunol.* 1999;104:534-40.
- 3) Sibbald B, Rink E. Epidemiology of seasonal and perennial rhinitis: Clinical presentation and medical history. *Thorax.* 1991;46:895-901.

Category 4: Gastroenterology:

In Western countries, GERD symptoms, such as heartburn and acid regurgitation, occur in about 20% of adults weekly and in about 7% of adults daily.

- 1) Nebel OT, Fornes MF, Castell DO. Symptomatic gastroesophageal reflux: incidence and precipitating factors. *Am J Dig Dis.* 1976;21:953-6.
- 2) A Gallup Organization National Survey: Heartburn Across America. Princeton: The Gallup Organization; 1988.
- 3) Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology.* 1997;112:1448-56.

While the airway obstruction is superior to the junction of the larynx and the esophagus, each "event" will cause increased negative pressure in the esophagus. Pressure gradient across the LES may create aspirations of stomach contents.

Dent J, Dodds WJ, Friedman RH, et al. Mechanism of gastroesophageal reflux in recumbent asymptomatic human subjects. *J Clin Invest* 1980;65:256-257.

In Nocturnal GERD pop, Odds Ratio of having OSA is 2.97.

You, Chan Ran; Oh, Jung Hwan; Seo, Minji; Lee, Hye Yeon; Joo, Hyonsoo; Jung, Sung Hoon; Lee, Sang Haak; Choi, Myung-Gyu, Association Between Non-erosive Reflux Disease and High Risk of Obstructive Sleep Apnea in Korean Population, *PMC* 2014-01-01.

Nocturnal reflux symptoms was increased in OSA patients to (10.2%) versus the general population (5.5%) and is 3 times as likely in severe OSA compared with Mild OSA.

Prevalence of nocturnal reflux symptoms is increased in those with or suspected of having OSA.

Kelly L, SHepherd, Alan L, James, Arthur W. Musk, Michael L. Hunter, David R. Hillman, and Peter R. Eastwood. Gastro-esophageal reflux symptoms are related to the presence and severity of obstructive sleep apnoea. *J. Sleep Res.* (2011) 20, 241-249.

A study of 16 patients with both OSA and GERD found that improving their breathing mechanics with continuous positive airway pressure (CPAP) normalized the esophageal acid exposure in 81%.

Tawk M, Goodrich S, Kinasewitz G, Orr W. The effect of 1 week of continuous positive airway pressure treatment in obstructive sleep apnea patients with concomitant gastro-esophageal reflux. *Chest*. 2006;130(4):1003-1008.

Prevalence of GERD was significantly increased in those with primary snoring and OSAS compared to the general population.

Basoglu OK1, Vardar R, Tasbakan MS, Ucar ZZ, Ayik S, Kose T, Bor S., Obstructive sleep apnea syndrome and gastroesophageal reflux disease: the importance of obesity and gender. *Sleep Breath*. 2014 Aug 31.

Morbid Consequences of GERD include: changes of cells lining the lower esophagus. About 10% of people with chronic symptoms of GERD develop Barrett's esophagus which is a precursor to esophageal adenocarcinoma, a serious and potentially fatal cancer.

Watson A. Barrett's, esophagus - 50 years on. *Br J Surg*. 2000;87:529-531.

In GERD cohort, TMJ disorders are twice as prevalent

Tareq M. Gharaibeh, BDS, MMedSc, FDS RCS,* Khaled Jadallah, MD,† and Fuad Abul Jadayel, BDS, DPH, MSc. Prevalence of Temporomandibular Disorders in Patients With Gastroesophageal Reflux Disease: A Case-Controlled Study, *J Oral Maxillofac Surg* 2010.

Patients with GERD have a significantly higher risk of concurrent asthma compared with patients without GERD

Tsai MC1, Lin HL, Lin CC, Lin HC, Chen YH, Pfeiffer S, Lin HC. Increased risk of concurrent asthma among patients with gastroesophageal reflux disease: a nationwide population-based study. *Eur J Gastroenterol Hepatol*. 2010 Oct;22(10):1169-73.

Less than six hours and more than nine hours of sleep per day are each associated with an increased risk of ulcerative colitis.

Ashwin N. Ananthakrishnan, MD, MPH, Prospective study of women who were enrolled in the Nurses' Health Study (NHS) I since 1976 and (NHS) II since 1989. *American Gastroenterological Association*, October 21, 2014.

13% of patients with IBD had OSA

Keefer L, Stepanski EJ, Ranjbaran Z, Benson LM, Keshavarzian A. An initial report of sleep disturbance in inactive inflammatory bowel disease. *J Clin Sleep Med*. 2006;2(4):409-416.

Category 5: Neurology:

Neurological disorders with primary neurological symptoms are improved by treatment of comorbid OSA include: dementia, stroke, epilepsy and headache.

- 1) Ancoli-Israel S, Palmer BW, Cooke JR, Corey-Bloom J, Fiorentino L, Natarajan L, Liu L, Ayalon L, He F, Loreda JS. Cognitive effects of treating obstructive sleep apnea in Alzheimer's disease: a randomized controlled study. *J Am Geriatr Soc*. 2008;56(11):2076-2081
- 2) Malow BA, Foldvary-Schaefer N, Vaughn BV, Selwa LM, Chervin RD, Weatherwax KJ, Wang L, Song Y. Treating obstructive sleep apnea in adults with epilepsy: a randomized pilot trial. *Neurology*. 2008;71(8):572-577.
- 3) Nath Zallek S, Chervin RD. Improvement in cluster headache after treatment for obstructive sleep apnea. *Sleep Med*. 2000;1(2):135-138.

Intermittent hypoxia in OSA is an independent risk factor for axonal damage of peripheral nerves.

P Lüdemann, R Dzierwas, P Sörös, S Happe, A Frese, Axonal polyneuropathy in obstructive sleep apnea, *J Neurol Neurosurg Psychiatry* 2001;70:685–687.

Strong association between OSA and peripheral neuropathy and sight-threatening retinopathy .

Waller E, Bendel R, Kaplan J. Sleep disorders and the eye. *Mayo Clin Proc.* 2008;83:1251-1261.

60% of patients with diabetes and OSA also have a peripheral neuropathy, which is partly reversible with treatment for sleep apnea.

Dzierwas R, Schilling M, Engel P, et al. Treatment for obstructive sleep apnoea: effect on peripheral nerve function. *J Neurol Neurosurg Psychiatry.* 2007;78:295-297.

Neuropathy prevalence was higher in patients with OSA than those without” (60% vs 27%) ... OSA remained independently associated with diabetic neuropathy (odds ratio, 2.82)

Tahrani AA, Ali A, Raymond NT, et al. Obstructive sleep apnea and diabetic neuropathy: a novel association in patients with type 2 diabetes. *Am J Respir Crit Care Med.* 2012;186:434-441.

In patients with neuromuscular disorders, 42% have OSA.

Labanowski, M, Schmidt-Nowara, W and Guilleminault, C (1966), Sleep and Neuromuscular disease clinic population. *Neurology*, 47(5): 1173-1180 Elsevier.

30%-70% Alzheimer’s patients have SDB

Rongve A, Boeve BF, Aarsland D. Frequency and correlates of caregiver-reported sleep disturbances in a sample of persons with early dementia. *J Am Geriatr Soc.* 2010;58(3):480–486.

Prevalence of OSA in patients with dementia has been estimated to be 70%-80%.

Ancoli-Israel S, Klauber MR, Butters N, et al. Dementia in institutionalized elderly: Relation to sleep apnea. *J Am Geriatr Soc.* 1991;39(3):258–263.

20% Parkinson’s patients have OSA

Arnulf I. Excessive daytime sleepiness in parkinsonism. *Sleep Med Rev.* 2005;9(3):185–200.

Within OSA patients, OR of developing Glaucoma within 5 years is 1.67

AAOJ, Obstructive Sleep Apnea and Increased Risk of Glaucoma. A Population-Based Matched-Cohort Study Ching-Chun Lin, MA, Chao-Chien Hu, MD, Jau-Der Ho, MD, PhD, Hung-Wen Chiu, PhD, Heng-Ching Lin, PhD Published Online: April 17, 2013.

OSA treatment shown to reduce frequency of cluster headache. Patients with severe snoring and cluster headache should be evaluated for OSA.

Nobre ME, Filho PF, Dominici M. Cluster headache associated with sleep apnoea. *Cephalalgia.* 2003;23:276–9.

Population-based studies using the full standard diagnostic criteria for RLS report a prevalence of 5% to 10%.

- 1) Berger K, Luedemann J, Trenkwalder C, John U, Kessler C. Sex and the risk of restless legs syndrome in the general population. *Arch Intern Med.* 2004;164: 196-202.

- 2) Ulfberg J, Nystrom B, Carter N, Edling C. Restless Legs Syndrome among working aged women. *Eur Neurol.* 2001;46:17-19.
- 3) Ulfberg J, Nystrom B, Carter N, Edling C. Prevalence of restless legs syndrome among men aged 18 to 64 years: an association with somatic disease and neuropsychiatric symptoms. *Mov Disord.* 2001;16:1159-1163.

80%-90% of patients with RLS have PLMD

Aurora RN; Kristo DA; Bista SR; Rowley JA; Zak RS; Casey KR; Lamm CI; Tracy SL; Rosenberg RS. The treatment of restless legs syndrome and periodic limb movement disorder in adults—an update for 2012: practice parameters with an evidence-based systematic review and meta-analyses. *SLEEP* 2012;35(8):1039-1062.

40% of subjects with iron and B12 deficiency have RLS symptoms. Patients with symptoms of RLS should be tested for iron deficiency.

Gamaldo CE, Earley CJ. Restless legs syndrome: a clinical update. *Chest.* Nov 2006;130(5):1596-604.

Hyperhidrosis (night sweating), May be related to excessive body movement.

Viera AJ, Bond MM, Yates SW. Diagnosing night sweats. *Am Fam Physician.* 2003;67:1019–1024.

OSAS should be considered as a significant risk factor for Normal-tension glaucoma (NTG). It is advisable to take an accurate sleep history (including questions about snoring, nocturnal gasping-choking, daytime sleepiness and morning headaches) from patients with NTG and refer these patients for PSG test.

Gorkem Bilgin, Normal-tension glaucoma and obstructive sleep apnea syndrome: a prospective study, *BMC Ophthalmology* 2014, 14:27 doi.10.1186/1471-2415-14-27

Category 6: Endocrinology:

Diabetes prevalence in America is 9.3%. CDC, National Diabetes Statistics Report, 2014. Prediabetes (pop >20 yrs old) 35%.

CDC, National Diabetes Statistics Report, 2014.

Within Type 2 Diabetes population, 36%-50% have OSA with AHI >15. (49 percent of male participants with an AHI > 15 have type 2 diabetes.)

Reichmuth, K.J., et al., *Am J Respir Crit Care Med* 2005;172: 1590-1595.

Within Type 2 Diabetes population, 71% have OSA, in the average data from 5 studies including a total number of nearly 1200 type 2 diabetic patients:

What is the Prevalence of OSA in Type 2 Diabetics? Resnick et al., 2003; Einhorn et al., 2007; Foster et al., 2009; Laaban et al., 2009; Aronsohn et al., 2010, *Frontiers in Neurology.* 2012; 3: 126.

In diabetes cohort, the prevalence of OSA may be up to 23%.

West SD, Nicoll DJ, Stradling JR: Prevalence of obstructive sleep apnea in men with type 2 diabetes. *Thorax* 61(11): 945-950, 2006.

In diabetes cohort, prevalence of some form of sleep disordered breathing may be as high as 58%.

Resnick HE, Redline S, Shahar E, Gilpin A, Newman A, Walter R, Ewy GA, Howard BV, Punjabi NM: Diabetes and sleep disturbances: findings from the Sleep Heart Health Study. *Diabetes Care* 26(3): 702-709, 2003.

In patients with diabetes, the prevalence of OSA range from 29% to 63% depending of the criteria adopted for OSA.

- 1) Einhorn D, Stewart DA, Erman MK, Gordon N, Philis Tsimikas A, Casal E. Prevalence of sleep apnea in a population of adults with type 2 diabetes mellitus. *Endocr Pract* 2007;13:355-62.
- 2) Laaban JP, Daenen S, Léger D, Pascal S, Bayon V, Slama G, Elgrably F. Prevalence and predictive factors of sleep apnoea syndrome in type 2 diabetic patients. *Diabetes Metab* 2009;35:372-7.

In OSA cohort, estimates suggest 40% have diabetes.

Meslier N, Gagnadoux F, Giraud P, Person C, Oukssel H Urban T Racineux JL: Impaired glucose insulin metabolism in males with obstructive sleep apnea syndrome. *Eur Respir J* 22(1): 156-160, 2003.

Optimal treatment of sleep apnea with continuous positive airway pressure (CPAP) for two weeks led to significant improvements in glucose levels following an oral glucose challenge without affecting insulin secretion, suggesting an improvement in insulin sensitivity. Treatment of sleep apnea in patients at risk for developing diabetes may lower this risk, and an assessment for sleep apnea may be appropriate as part of the clinical evaluation of patients with prediabetes.

Effective Treatment Of Obstructive Sleep Apnea Improves Glucose Tolerance In Prediabetes: A Randomized Placebo-, Sushmita Pamidi , MD, Magdalena Stepien , BSc , Khalid Sharif-Sidi , BSc , Harry Whitmore , RPSGT, Lisa Morselli , PhD, Kristen Wroblewski , MS , Esra Tasali , MD, Pamidi S. Abstract 39588. Presented at: American Thoracic Society 2013 International Conference; May 17-22, 2013; Philadelphia

Menopause: Decrease in Estrogen and Progesterone leads to weight gain and decrease muscle tone which increases SDB. HRT may help.

Keefe DL, Watson R, Naftolin F, Hormone replacement therapy may alleviate sleep apnea in menopausal women: a pilot study. *Menopause*.1999 Fall;6(3):196-200.

Within obese population, prevalence of OSA 70%.

Lopez PP, Stefan B, Schulman CI, Byers PM, Prevalence of sleep apnea in morbidly obese patients who presented for weight loss surgery evaluation: more evidence for routine screening for obstructive sleep apnea before weight loss surgery. *Am Surg*. 2008 Sep;74(9):834-8.

Within OSA pop, 70% are obese, so 30% aren't obese.

Daltro C, Gregorio PB, Alves E, Abreu M, Bomfim D , Chicourel MH, Araújo L, Cotrim HP. Prevalence and severity of sleep apnea in a group of morbidly obese patients. *Obes Surg*. 2007 Jun;17(6):809-14.

24% of the general population has Metabolic Syndrome , a cluster of conditions (increased blood pressure, a high blood sugar level, excess body fat around the waist,

and abnormal cholesterol levels) that, when occurring in combination, increase your risk of heart disease, stroke and diabetes.

Ford, Earl S., Wayne H. Giles, and William H. Dietz. "Prevalence of the metabolic syndrome among US adults: findings from the third National Health and Nutrition Examination Survey." *Jama* 287.3 (2002): 356-359.

In Metabolic Syndrome cohort, OR for MI is 2.63 compared with normal

B. Isomaa, P. Almgren, T. Tuomi, et al. Cardiovascular morbidity and mortality associated with the metabolic syndrome, *Diabetes Care*, 24 (2001), pp. 683–689.

In Metabolic Syndrome Cohort, prevalence of mod-severe OSA is 60%

Drager LF, Lopes HF, Maki-Nunes C, et al. The impact of obstructive sleep apnea on metabolic and inflammatory markers in consecutive patients with metabolic syndrome. *PLoS One* 2010;5:e12065.

In OSA population, 60% have Metabolic Syndrome.

James M. Parish, M.D., Terrence Adam, M.D., Ph.D., and Lynda Facchiano, R.N.P. Relationship of Metabolic Syndrome and Obstructive Sleep Apnea, *J Clin Sleep Med*. Aug 15, 2007; 3(5): 467–472.

In patients with OSA, prevalence of metabolic syndrome is 40% greater.

Metabolic Syndrome + OSA= Syndrome Z

Coughlin S. Mawdsley, L., Mugarza, JA et al. Obstructive sleep apnoea is independently associated with an increased prevalence of metabolic syndrome. *Eur Heart J* 2004;25:735–41.

Narcolepsy is result of reduction of Hypocretin (orexin) and can be accompanied by: Cataplexy, Hypnogogic Hallucinations, Sleep Paralysis (SP), and Sudden Onset REM Sleep (SOREMS).

Mona Skard Heier, MD, PhD, Tatiana Evsiukova, MD, Steinar Vilming, MD, PhD, Michaela D. Gjerstad, MD, Harald Schrader, MD, PhD, and Kaare Gautvik, MD, PhD. CSF Hypocretin-1 Levels and Clinical Profiles in Narcolepsy and Idiopathic CNS Hypersomnia in Norway. *Sleep*. Aug 1, 2007; 30(8): 969–973.

Incidence of osteoporosis was 2.7 times higher among patients with sleep apnea than their counterparts.

Yu-Li Chen, Shih-Feng Weng, Yuan-Chi Shen, Chien-Wen Chou, Chwen-Yi Yang, Jhi-Joung Wang, Kai-Jen Tien. Obstructive Sleep Apnea and Risk of Osteoporosis: A Population-Based Cohort Study in Taiwan. *The Journal of Clinical Endocrinology & Metabolism*, 2014; jc.2014-1718.

75 percent of the participants who had gestational diabetes also suffered from obstructive sleep apnea.

Sirimon Reutrakul et al. Interactions between Pregnancy, Sleep Apnea and Gestational Diabetes Mellitus. *Journal of Clinical Endocrinology & Metabolism*, Aug. 20, (2013).

Sleep Fragmentation and Deprivation leads to: activation of Hypothalamic Pituitary Adrenal axis and Sympathetic NS stimulation, and increased cortisol release.

Marcella Balbo, Rachel Leproult, and Eve Van Cauter, Impact of Sleep and Its Disturbances on Hypothalamo-Pituitary-Adrenal Axis Activity, *International Journal of Endocrinology* Volume 2010 (2010), Article ID 759234.

Less than 6 hours sleep increases risk of Pre-diabetes 4.7 times.

Lisa Rafalson, PhD. presented at the AHA epidemiology and Prevention Meeting, April 2009.

Sleep duration and quality have emerged as predictors of levels of Hemoglobin A1c, an important marker of blood sugar control. Recent research suggests that optimizing sleep duration and quality may be important means of improving blood sugar control in persons with Type 2 diabetes.

Knutson KL, Ryden AM, Mander VA, Van Cauter E. Role of sleep duration and quality in the risk and severity of type 2 diabetes mellitus. *Arch Intern Med* 2006;166:1768–1764.

Patients with severe OSAS had significantly lower levels of 25(OH)D, vitamin D, as compared with other groups. When the severity of OSAS increases, 25(OH)D deficiency becomes more pronounced. (This study shows association only, not causality.)

Mete T, Yalcin Y, Berker D, Ciftci B, Guven SF, Topaloglu O, Yavuz HC, Guler S. *J Endocrinol Invest*. 2013 Oct;36(9):681-5. doi: 10.3275/8923. Epub 2013 Apr 2

If you have normal blood sugar today, a vitamin D deficiency makes you 91% more likely to progress to insulin resistance, or “pre-diabetes,” and it more than doubles your risk for progressing to active, type II diabetes.

Huang Y, Li X, Wang M, et al. Lipoprotein lipase links vitamin D, insulin resistance, and type 2 diabetes: a cross-sectional epidemiological study. *Cardiovasc Diabetol*. 2013;12:17.

In a study of 50 patients with primary hypothyroidism, OSA (AHI ≥ 5) was present in 15 patients (30%) at baseline and was reversible in 10 of the 12 patients evaluated following thyroxine replacement therapy ($P=0.006$). Thyroxine replacement therapy was associated with improvement in findings that reflect a compromised upper airway, such as macroglossia (4 [33%] vs. 1 [8%]; $P=0.083$), myoedema (5 [42%] vs. 1 [8%]; $P=0.046$) and facial puffiness (10 [83%] vs. 1 [8%]; $P=0.003$). Reversible SDB is common among patients with primary hypothyroidism. Changes in upper airway anatomy resulting from hypothyroidism probably contribute to the development of SDB in these patients.

Thyroxine replacement therapy reverses sleep-disordered breathing in patients with primary hypothyroidism. Jha, Sharma, Tandon, Lakshmy, Kadiravan, Handa, Gupta, Pandey, Chaturvedi, *Sleep Med*, 7, 55-61, 2006

Category 7: Otolaryngology:

Nasal congestion patients are 2x as likely to have OSA.

Diseases and Conditions, Obstructive Sleep Apnea, Risk Factors, Mayo Clinic, Mayo Clinic Staff, June 15, 2013.

Patients with nasal congestion are 1.8 times more likely to have moderate to severe OSA compared to those without symptomatic congestion.

- 1) Gupta N, Goel N, Kumar R. Correlation of exhaled nitric oxide, nasal nitric oxide and atopic status: cross-sectional study in bronchial asthma and allergic rhinitis. *Lung India*. 2014; 31(4): 342-347.
- 2) Michels Dde S, Rodrigues AM, Nakanishi M, Sampaio AL, Venosa AR. Nasal involvement in obstructive sleep apnea syndrome. *Int J Otolaryngol*. 2104. 2014:717419. doi: 10.1155/2014/717419. Epub 2014 Nov 20.

- 3) Fitzpatrick MF, McLean H, Urton AM, Tan A, O'Donnell D, Driver HS. Effect of nasal or oral breathing route on upper airway resistance during sleep. *Eur Respir J.* 2003;22(5):827-832.
- 4) McLean HA, Urton AM, Driver, HS, Tan AK, Day AG, Munt PW, Fitzpatrick MF. Effect of treating severe nasal obstruction on the severity of obstructive sleep apnoea. *Eur Respir J.* 2005;25(3): 521-527.

Nasal obstruction associated with congestion represents a risk factor for respiratory sleep disordered breathing, including snoring, increase of the number of microarousals, episodes of hypopnea, and apnea.

- 1) Young T, Finn L, Palta M. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. *Arch Intern Med.* 2001;161:1514–1519.
- 2) Koinis-Mitchell D, Craig T, Esteban CA, Klein RB. Sleep and allergic disease: a summary of the literature and future directions for research. *J Allergy Clin Immunol.* 2012;130:1275–81.

Nasal Inflammation and sinus problems can result from OSA: Post nasal drip, sinusitis, nasal resistance, rhinitis, deviated septum, dry mouth upon awakening.

Rubinstein I, author. Nasal inflammation in patients with obstructive sleep apnea. *Laryngoscope.* 1995;105:175–7.

Nasal congestion is independently associated with snoring frequency.

Young T, Finn L, Palta M. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. *Arch Intern Med.* 2001;161(12):1514–9.

Nasal congestion is a recognized risk factor for OSA

Young T, Finn L, Palta M. Chronic nasal congestion at night is a risk factor for snoring in a population-based cohort study. *Arch Intern Med.* 2001;161(12):1514–9.

Allergic rhinitis increases risk of asthma 3x.

Settipane RJ, Hagy GW, Settipane GA. Long-term risk factors for developing asthma and allergic rhinitis: a 23-year follow-up study of college students. *Allergy Proc.* 1994;15:21–5.

Otological Symptoms 85% in TMD population (tinnitus 42%, ear pain 42%, dizziness 23% and diminished hearing 18%)

Fricton JR, Kroening R, Haley D, Siegert R: Myofascial pain syndrome of the head and neck: a review of clinical characteristics of 164 patients. *Oral Surg Oral Med Oral Pathol* 60:615-623, 1985.

Category 8: Urology:

In OSA population, reduced bioavailability of endothelially derived nitric oxide and altered endothelially mediated vasodilation.

Ip MS, Lam B, Chan LY, et al. Circulating nitric oxide is suppressed in obstructive sleep apnea and is reversed by nasal continuous positive airway pressure. *Am J Respir Crit Care Med.* 2000; 162: 2166–2171.

Various studies report between 40% and 64.4% of OSA patients have Erectile Dysfunction “ED”

- 1) Seftel AD, Strohl KP, Loye TL, Bayard D, Kress J, Netzer NC. Erectile dysfunction and symptoms of sleep disorders. *Sleep*. 2002;25:643-647
- 2) Shin HW, Rha YC, Han DH, et al. Erectile dysfunction and disease-specific quality of life in patients with obstructive sleep apnea. *Int J Impot Res*. 2008;20:549-553.
- 3) Santos T, Drummond M, Botelho F. Erectile dysfunction in obstructive sleep apnea syndrome--prevalence and determinants. *Rev Port Pneumol*. 2012;18:64-71.

Within ED population, 40% have OSA

- 1) Pressman MR, Diphillipo MA, Kendrick JI, et al., Problems in the interpretation of nocturnal penile tumescence studies: disruption of sleep by occult sleep disorders, *J Urol*, 1986;136(3):595-8.
- 2) Goncalves MA, Guillemineault C, Ramos E, et al., Erectile dysfunction, obstructive sleep apnea syndrome and nasal CPAP treatment, *Sleep Medicine*, 2005;6(4):33-9.

Within ED population, 44% had OSA

Hirshkowitz M, Karacan I, Arcasoy MO, Acik G, Narter EM, Williams RL. Prevalence of sleep apnea in men with erectile dysfunction. *Urology*. 1990;36:232-234.

NO has a role in erectile function and dysfunction. It was recognized as the key mediator of smooth-muscle relaxation in the penis many years ago.

Rajfer J, Aronson WJ, Bush PA, et al., Nitric oxide as a mediator of relaxation of the corpus cavernosum in response to nonadrenergic, noncholinergic, *N Engl J Med*. 1992 Jan 9;326(2):90-4.

Reduction in circulating NO in OSA patients has been observed.

Ip MS, Lam B, Chan LY, et al., Circulating nitric oxide is suppressed in obstructive sleep apnoea and is reversed by nasal continuous positive airway pressure, *Am J Respir Crit Care*, 2000;162(6): 2166-71.

With increased severity of OSA, there is also increased occurrence of: overactive bladder, urgency incontinence.

Kemmer H1, AM, Dilk O, Gröschel A, Grass C, Stöckle M., Obstructive sleep apnea syndrome is associated with overactive bladder and urgency incontinence in men. *Sleep*. 2009 Feb;32(2): 271-5.

Sleep Fragmentation and sympathetic activation from SDB causes inhibition of and decrease in circulating antidiuretic hormone "ADH" which may cause Nocturia or Enuresis. (ADH normally prevents urination at night.)

Ichioka M1, Hirata Y, Inase N, Tojo N, Yoshizawa M, Chida M, Miyazato I, Taniai S, Marumo F. Changes of circulating atrial natriuretic peptide and antidiuretic hormone in obstructive sleep apnea syndrome. *Respiration*, 1992;59(3):164-8.

OSA should be considered whenever a patient reports frequent awakenings from sleep to urinate, even when the symptom was previously attributed to the presence of BPH.

Howard Tandeter, MD, Sammy Gendler, Jacob Dreier, MD, MPH and Ariel Tarasiuk, PhD., Nocturic Episodes in Patients with Benign Prostatic Enlargement May Suggest the Presence of Obstructive Sleep Apnea, *J Am Board Fam Med* March-April 2011 vol. 24 no. 2 146-151.

Nocturia was independently associated with SDB (measured as Apnea Hypopnea index >15 per hour; OR 1.3) Results support sleep screening for SDB in patients with nocturia,

Parthasarathy S1, Fitzgerald M, Goodwin JL, Unruh M, Guerra S, Quan SF. Nocturia, Sleep-Disordered Breathing, and Cardiovascular Morbidity in a Community-Based Cohort. *PLoS One*. 2012; 7(2): e30969.

Nocturia appears comparable to snoring as a screening tool for OSA .

Romero E, Krakow B, Haynes P, Ulibarri V. Nocturia and snoring: predictive symptoms for obstructive sleep apnea. *Sleep Breath*. 2010 Dec;14(4):337-43.

The overall adjusted HR for BPH was 2.35 fold higher in the patients with SA than in the control patients. The patients aged between 51 and 65 had an adjusted HR of 5.59 for BPH in the SA patients compared with the control patients.

PLoS One. 2014; 9(3): e93081. Published online Mar 25, 2014. doi: 10.1371/journal.pone.0093081.

Short-term use of CPAP ameliorates globular hyper filtration in patients with OSA.

Shin-ichi Kinebuchi, Junichiro J. Kazama, Makoto Satoh, Kunihiko Sakai, Hideaki Nakayama, Hirohisa Yoshizawa, Ichiei Narita, Eiichi Suzuki, Fumitake Gejyo, *Clinical Science* Sep 01, 2004, 107 (3) 317-322;

Category 9: Bruxism and TMD:

Sleep Bruxism “SB” reported in 8% of general population

- 1) Lavigne GJ, Montplaisir JY. Restless legs syndrome and sleep bruxism: prevalence and association among Canadians. *Sleep* 1994;17(8):739–43.
- 2) Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. *Chest* 2001;119(1):53–61.

OSA has highest risk factor for SB (OR of 1.8). Approx. twice general pop.

Maurice M. Ohayon, Kasey K. Li and Christian Guilleminault, Risk Factors for Sleep Bruxism in the General Population, *Chest* 2001;119;53-61.

Most RMMA episodes (75%–88%) occur in association with sleep arousals.

Macaluso GM, Guerra P, Di Giovanni G, et al. Sleep bruxism is a disorder related to periodic arousals during sleep. *J Dent Res* 1998;77(4):565–73.

Within adult SB population, 30%-50% of adult patients suffer from headaches.

Lavigne G, Palla S. Transient morning headache: recognizing the role of sleep bruxism and sleep-disordered breathing. *J Am Dent Assoc* 2010; 141(3):297–9.

Within all age SB population, 65 percent of patients report frequent headaches.

- 1) Camparis CM, Siqueira JT. Sleep bruxism: clinical aspects and characteristics in patients with and without chronic orofacial pain. *Oral surgery, oral medicine, oral pathology, oral radiology, and endodontics* 2006;101(2):188-93.
- 2) Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. *Chest* 2001;119(1):53-61.

Within children with SB have OR for headaches of 4.3

Carra MC, Huynh N, Morton P, et al. Prevalence and risk factors of sleep bruxism and wake-time tooth clenching in a 7- to 17-yr-old population. *Eur J Oral Sci* 2011;119(5):386–94.

Within SB population, prevalence of OSA is 4X that of general population so bruxers should be examined for presence of OSA.

C. Martínez, E. Anitua Aldecoa, J. Durán Carro, J. Aguirre, J. Durán Cantolla, Prevalence of sleep apnea-hypopnea syndrome (SAHS) among a bruxism population. Preliminary data. Sleep Medicine, Volume 14, Supplement 1, Page e221, December 2013.

Within OSA population, 25% have SB.,

American College of Chest Physicians, Teeth Grinding Linked To Sleep Apnea; Bruxism Prevalent In Caucasians With Sleep Disorders, Science Daily, November 5, 2009.

In general population, 12% have TMD.

LeResche L, Saunders K, Von Korff MR, Barlow W, Dworkin SF. Use of exogenous hormones and risk of temporomandibular disorder pain. Pain. 1997;69:153-60.

In OSA population, 52% have TMD. (Of these, 75% had chronic pain)

Cunali PA, Almeida FR, Santos CD, Valdrighi NY, Nascimento LS, Dal'Fabbro C, Tufik S, Bittencourt LR, Prevalence of temporomandibular disorders in obstructive sleep apnea patients referred for oral appliance therapy. J Orofac Pain. 2009 Fall;23(4):339-344.

In TMD population, 65% reported Sleep Bruxism "SB" upon questioning.

Chandwani B1, Ceneviz C, Mehta N, Scrivani S, Incidence of bruxism in TMD population. N Y State Dent J. 2011 Aug-Sep;77(5):54-7.

60% of TMD pain patients and 37% of Sleep Bruxism patients report sleep disturbances.

Dao TT, Lund JP, Lavigne GJ. Comparison of pain and quality of life in bruxers and patients with myofascial pain of the masticatory muscles. J Orofac Pain, 1994;8:350-356.

In TMD population, 28%-32% have OSA.

- 1) Michael T. Smith, PhD, Emerson M. Wickwire, PhD, and Jennifer A. Haythornthwaite, PhD, Sleep Disorders and their Association, with Laboratory Pain Sensitivity in Temporomandibular Joint Disorder, Sleep. Jun 1, 2009; 32(6): 779-790.
- 2) Santos-Silva R, Castro LS, Taddei JA, Tufik S, Bittencourt LR. Sleep disorders and demand for medical services: evidence from a population-based longitudinal study. PLoS One. 2012;7(2):e30085.

Within a TMD population, 42% of reported tinnitus, 18% dizziness

Gelb, H., Calderone, J.P., Gross, S.M. & Kantor, M.E. 1967. The role of the dentist and the otolaryngologist in evaluating temporomandibular joint syndromes. J Prosthet Dent, 18, 497-503.

In TMD population up to 85% have Otological Symptoms as compared to 10%-31% In general population.

- 1) Salvetti, G., Manfredini, D., Barsotti, S. & Bosco, M. 2006. Otologic symptoms in temporomandibular disorders patients: Is there evidence of an association-relationship? Minerva Stomatol, 55,627-37.
- 2) Friction JR, Kroening R, Haley D, Siegert R: Myofascial pain syndrome of the head and neck: a review of clinical characteristics of 164 patients. Oral Surg Oral Med Oral Pathol 60:615-623, 1985.

Category 10: Psychology and Psychiatry:

Between 10%-15% general population have chronic insomnia.

Roth T. Insomnia: definition, prevalence, etiology and consequences. *J Clin Sleep Med* 2007;3(Suppl):S7-S10.

Within OSA population, 39%-58% have insomnia symptoms, and Within insomnia population, 29% and 67% have OSA (OSA concurrent with Insomnia is called "SDB+")

Luyster FS; Buysse DJ; Strollo PJ. Comorbid insomnia and obstructive sleep apnea: challenges for clinical practice and research. *J Clin Sleep Med* 2010;6(2):196-204.

In SDB cohort, 50% have some type of insomnia.

Krakow B1, Melendrez D, Ferreira E, Clark J, Warner TD, Sisley B, Sklar D., Prevalence of insomnia symptoms in patients with sleep-disordered breathing. *Chest*. 2001 Dec;120(6):1923-9.

Significant association between the psychiatric disorders (specifically depression) and sleep apnea.

- 1) Flemons Ww, Tsai W. Quality of life consequences of sleep- disordered breathing. *J Allergy Clin Immunol* 1997;99:S750-6.
- 2) Millman RP, Fogel BS, Mcnamara ME, Carlisle CC. Depression as a manifestation of obstructive sleep apnea: reversal with nasal continuous positive airway pressure. *J Clin Psychiatry* 1989;50:348- 51.
- 3) Balan S, Spivak B, Mester R, Leibovitz A, Habet B, Weizman A. Psychiatric and polysomnographic evaluation of sleep disturbances. *J Affect Disord* 1998;49:27-30.
- 4) Reynolds CF, Kupfer DJ, Mceachran AB, Taska LS, Sewitch De, Coble PA. Depressive psychopathology in male sleep apneics. *J Clin Psychiatry* 1984;45:287-90.

In Depressive Cohort 20% have OSA, and in OSA Cohort, 20% have Depression.

Carmen M Schröder and Ruth O'Hara, Depression and Obstructive Sleep Apnea (OSA) *Annals of General Psychiatry* 2005, 4:13.

Within the psychiatric outpatient population the prevalence of OSA is increased.

Suhayl Nasr, MD ,increased incidence of sleep apnea in psychiatric outpatients, *Annals of Clinical Psychiatry* 2010;22(1):29-32.

Within OSA population, the prevalence of Psychiatric comorbid conditions are increased.

In OSA cohort, 21.8% have Depression, as compared to 9% in the general population.

Amir Sharafkhaneh, MD; Nilgun Giray, MD; Peter Richardson, PhD; Terry Young, PhD; Max Hirshkowitz, PhD, Association of Psychiatric Disorders and Sleep Apnea in a Large Cohort, *SLEEP*, Vol. 28, No. 11, 2005.

Subjects with moderate or worse OSA had a 2.6 increase in odds of developing depression. This study further clarified the significant association between OSA and depression.

Peppard PE, Szklo-Coxe M, Hla KM, Young T. Longitudinal association of sleep-related breathing disorder and depression. *Arch Intern Med*. 2006;166:1709–1715.

In OSA cohort, 11.9% have experienced PTSD, as compared to 3.9% in general population.

Amir Sharafkhaneh, MD1,3; Nilgun Giray, MD2,3; Peter Richardson, PhD1; Terry Young, PhD4; Max Hirshkowitz, PhD1-3, Association of Psychiatric Disorders and Sleep Apnea in a Large Cohort, *SLEEP*, Vol. 28, No. 11, 2005.

In OSA cohort, 5.1% experience Psychosis, significantly greater than seen in non-OSA.

Amir Sharafkhaneh, MD1,3; Nilgun Giray, MD2,3; Peter Richardson, PhD1; Terry Young, PhD4; Max Hirshkowitz, PhD1-3, Association of Psychiatric Disorders and Sleep Apnea in a Large Cohort, SLEEP, Vol. 28, No. 11, 2005.

SDB causes increases in: Cognitive Impairment, Mood Swings, ADHD, Difficulty Concentrating, and Circadian Rhythm Disorder in various populations.

Louise M. O'Brien, PhD, The Neurocognitive Effects of Sleep Disruption in Children and Adolescents, Child Adolesc Psychiatric Clin N Am 18 (2009) 813–823.

Depression is reported at a prevalence of 1.8%–3.3% in community-based studies of the general population, but in patients with a sleep disorder, the prevalence of depression has been reported to be 17.6%. In patients with OSA in particular, its prevalence increases to 20% to 40%.

- 1) Sharafkhaneh A, Giray N, Richardson P, et al. Association of psychiatric disorders and sleep apnea in a large cohort. *Sleep*. 2005;28(11):1405–1411.
- 2) Hashmi AM, Giray N, Hirshkowitz M. Sleep-related breathing disorders and mood disorders. *Sleep Med Clin*. 2006;1(4):513–517.
- 3) Schwartz DJ, Karatinos G. For individuals with obstructive sleep apnea, institution of CPAP therapy is associated with an amelioration of symptoms of depression which is sustained long term. *J Clin Sleep Med*. 2007;3(6):631–635.

Progression of OSA has been found to be associated with an increased risk of developing depression. Even patients with mild OSA are 60% more likely to become depressed than individuals without this sleep disorder.

Peppard PE, Szklo-Coxe M, Hla KM, et al. Longitudinal association of sleep-related breathing disorder and depression. *Arch Intern Med*. 2006;166(16):1709–1715.

Many anxiolytic medications affect sleep architecture. Benzodiazepines reduce muscle tone, compromise airway patency, reduce REM sleep, suppress arousal response.

- 1) Borbely AA, Mattman P, Loepfe M, et al. Effect of benzodiazepine hypnotics on all-night sleep EEG spectra. *Hum Neurobiol*. 1985;4:189-194.
- 2) Achermann P, Borbely A. Dynamics of EEG slow wave activity during physiological sleep and after administration of benzodiazepine hypnotics. *Hum Neurobiol*. 1987;6:203-210.

Category 11: Rheumatology:

Sleep abnormalities have been recognized in a number of different rheumatic diseases, including RA, OA, FM, JIA, SS, SLE, scleroderma, SpAs, sarcoidosis and Behçet's syndrome

Abad VC, Sarinas PSA, Guilleminault C. Sleep and rheumatologic disorders. *Sleep Med Rev* 2008;12:211-28.

Patients with rheumatic disorders (particularly RA) may be at increased risk for sleep

disorders, particularly OSA.

Regina M. Taylor-Gjevre, Bindu V. Nair and John A. Gjevre, Obstructive sleep apnoea in relation to rheumatic disease, *Rheumatology Review*, *Rheumatology Advance Access* published August 25, 2012, doi:10.1093/rheumatology/kes210.

Co-existing sleep apnea may contribute to increased pain and fatigue, as well as increased cardiovascular morbidity/mortality, in patients with inflammatory rheumatological disorders.

- 1) Gabriel SE. Cardiovascular morbidity and mortality in rheumatoid arthritis. *Am J Med* 2008; 21:S9-14
- 2) Regina M. Taylor-Gjevre, Bindu V. Nair and John A. Gjevre, Obstructive sleep apnoea in relation to rheumatic disease, *Rheumatology Review*, *Rheumatology Advance Access* published August 25, 2012, doi:10.1093/rheumatology/kes210.

Cohort with Gout had an OR of 2.10 of having OSA, compared with controls.

Edward Roddy, Sara Muller, Richard Hayward and Christian D Mallen, The association of gout with sleep disorders: a cross-sectional study in primary care. *BMC Musculoskeletal Disorders* 2013, 14:119.

Oxygen desaturation in SDB may be associated with subsequent activation of inflammatory pathways, elevating serum uric acid levels.

H. Sahebji, "Changes in urinary uric acid excretion in obstructive sleep apnea before and after therapy with nasal continuous positive airway pressure," *Chest*, vol. 113, no. 6, pp. 1604–1608, 1998.

Uric acid crystallizes in the form of monosodium urate, precipitate in joints, on tendons, and in the surrounding tissues.

Schlesinger N (March 2010). "Diagnosing and treating gout: a review to aid primary care physicians". *Postgrad Med* 122 (2): 157–61.

Acidosis, (associated with hypoxia) is one factor that triggers MSU crystals to precipitate.

- 1) Moyer RA, John DS (2003). "Acute gout precipitated by total parenteral nutrition". *The Journal of rheumatology* 30 (4): 849–50. PMID 12672211.
- 2) Jump up Halabe A, Sperling O (1994). "Uric acid nephrolithiasis". *Mineral and electrolyte metabolism* 20 (6): 424–31. PMID 7783706.

Not previously described is that joint diseases such as arthrosis and gout show a high occurrence in OSA. It is known that intermittent hypoxia during the sleep period increases purine catabolic products of adenosine and uric acid, which may be causative in the arthritic sequelae in OSA.

Lavie L. Obstructive sleep apnoea syndrome—an oxidative stress disorder. *Sleep Med Rev*. 2003;7:35–51.

Braghiroli et al. showed high levels of uric acid in OSA patients and this level was restored by continuous positive airway pressure therapy.

Braghiroli A SC, Erbeta M, Ruga V, Donner CF. Overnight urinary uric acid: creatinine ratio for detection of sleep hypoxemia. Validation study in chronic obstructive pulmonary disease and

obstructive sleep apnea before and after treatment with nasal continuous positive airway pressure. *Am Rev Respir Dis.* 1993;148:173–8.

One-quarter to one-half of patients with obstructive sleep apnea syndrome have been shown to have hyperuricemia.

- 1) Chou YT, Chuang LP, Li HY, Fu JY, Lin SW, Yang CT, Chen NH: Hyperlipidaemia in patients with sleep-related breathing disorders: prevalence & risk factors. *Indian J Med Res* 2010, 131:121-125.
- 2) Pływaczewski R, Bednarek M, Jonczak L, Górecka D, Sliwiński P: Hyperuricaemia in males with obstructive sleep apnoea (osa). *Pneumonol Alergol Pol* 2005, 73:254-259.
- 3) Pływaczewski R, Bednarek M, Jonczak L, Górecka D, Sliwiński P: Hyperuricaemia in females with obstructive sleep apnoea. *Pneumonol Alergol Pol* 2006, 74:159-165.
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PSG data revealed OSA in 46.7% of RA (Rheumatoid Arthritis) patients.

Neven Fouda, Aya Abdel Dayem, Obstructive sleep apnea in patients with rheumatoid arthritis: Correlation with disease activity and pulmonary function tests, *The Egyptian Rheumatologist*, Volume 36, Issue 4, October 2014, Pages 165–171.

More than half of patients with RA report sleep disturbance, a rate of prevalence that is 2–3 times greater than that found in the general population.

R.M. Taylor-Gjevre, B.V. Nair, J.A. Gjevre Obstructive sleep apnoea in relation to rheumatic disease *Rheumatology (Oxford)*, 52 (1) (2013), pp. 15–21.

Co-existence of OSA in RA patients may influence the disease activity and the level of circulating inflammatory markers. Diagnosis and treatment of OSA in RA patients may help in improved clinical care, better prognosis and avoid rheumatoid-associated morbidities.

Neven Fouda, Aya Abdel Dayem, Obstructive sleep apnea in patients with rheumatoid arthritis: Correlation with disease activity and pulmonary function tests, *The Egyptian Rheumatologist*, Volume 36, Issue 4, October 2014, Pages 165–171.

17% of Sarcoid patients were found to have sleep apnea , as compared with a control group at 3%.

Turner GA, Lower EE, Corser BC, Gunther KL, Baughman RP, Sarcoidosis, Vasculitis, and Diffuse Lung Diseases : Official Journal of WASOG / World Association of Sarcoidosis and Other Granulomatous Disorders [1997, 14(1):61-64].

Prevalence of sleep disturbance in Systemic Lupus Erythematosus (SLE) was 62%.

Pradeep Kumar Shenoy Chandrasekhara, Nambiar Veettil Jayachandran, Liza Rajasekhar, Joe Thomas, Gumdal Narsimulu, The prevalence and associations of sleep disturbances in patients with systemic lupus erythematosus. *Modern Rheumatology*, August 2009, Vol. 19, No. 4 , Pages 407-415.

Category 12: Chronic Pain Patients:

Prevalence of Chronic pain ranges from 2% to 55%, depending on the criteria that the researchers set for their definition.

- 1) Crombie IK, Davies HT, Macrea WA. The epidemiology of chronic pain: time for new directions. *Pain* 1994;57(1):1-3.
- 2) Verhaak PF, Kerssens JJ, Dekker J, Sorbi MJ, Bensing JM. Prevalence of chronic benign pain disorder among adults: a review of the literature. *Pain* 1998;77(3):231-239.
- 3) Elliott AM, Smith BH, Penny KI, Smith WC, Chambers WA. The epidemiology of chronic pain in the community. *Lancet* 1999;354:1248-1252.
- 4) Cranenburgh B van. Pijn vanuit een neurowetenschappelijk perspectief [Dutch]. Maarssen: Elsevier gezondheidszorg; 2002.
- 5) Picavet HSJ, Schouten JSAG. Musculoskeletal pain in the Netherlands: prevalences, consequences and risk groups, the DMC3-study. *Pain* 2003;102:167-178.
- 6) Harstall C, Ospina M. How prevalent is chronic pain? *Clinical updates (IASP)* 2003;11(2):1-4.

Chronic pain in elderly increased to 25%–50% and for nursing home residents as high as 70%.

Ferrell BA. Managing pain and discomfort in older adults near the end of life. *Annals of Long-Term Care*; Presented at the American Geriatrics Society Annual Scientific Meeting; May 14, 2003; Baltimore, MD. 2003. February 2004.

44% of patients with chronic pain report insomnia versus 19% subjects without pain. Moldofsky H., Sleep and pain: clinical review. *Sleep Med Rev* 2001;5:387-398.

As many as 50%–88% patients with chronic pain report sleep disturbance.

- 1) Smith MT, Perlis ML, Smith MS, Giles DE, Carmody TP. Sleep quality and presleep arousal in chronic pain. *J Behav Med.* 2000;23:1-13.
- 2) Pilowsky I, Crettenden I, Townley M. Sleep disturbance in pain clinic patients. *Pain.* 1985;23:27-33.

Chronic Pain causes a decrease in Slow Wave Sleep.

- 1) Drewes AM, Nielsen KD, Arendt-Nielsen L, Birket-Smith L, Hansen LM. The effect of cutaneous and deep pain on the electroencephalogram during sleep --an experimental study. *Sleep.* 1997;20:632-640. Abstract
- 2) Smith MT, Perlis ML, Smith MS, Giles DE, Carmody TP. Sleep quality and presleep arousal in chronic pain. *J Behav Med.* 2000;23:1-13.

Awakening headache occurs in 4% to 6% of the general population, 18% of insomniacs, and 15% to 74% of sleep apneics across studies.

Rains JC, Poceta JS. Headache and sleep disorders: Review and clinical implications for headache management. *Headache* 2006;46(9):1344-1361.

24% of patients with OSA had frequent morning headache.

Poceta JS, Dalessio DJ., Identification and treatment of sleep apnea in patients with chronic headache. *Headache.* 1995 Nov-Dec;35(10):586-9.

Within chronic headache population, 80% have OSA

Graff-Radford SB, Newman A, Obstructive sleep apnea and cluster headache. *Headache.* 2004 Jun;44(6):607-610.

OSA was diagnosed in 35%–57% of patients managed in long-term pain clinics.

Guilleminault C, Cao M, Yue HJ, Chawla P. Obstructive sleep apnea and chronic opioid use. *Lung.* 2010;188:459-468.

Orofacial Pain reported in 66%-84% of patients with Sleep Bruxism.

- 1) Johansson A, Johansson AK, Omar R, et al. Rehabilitation of the worn dentition. *J Oral Rehabil* 2008;35(7):548-66.
- 2) Pergamalian A, Rudy TE, Zaki HS, et al. The association between wear facets, bruxism, and severity of facial pain in patients with temporomandibular disorders. *J Prosthe Dent* 2003;90(2):194-200.

SB patients have 4.3x headaches compared with control (7-17 yr olds).

Carra MC, Huynh N, Morton P, Rompré PH, Papadakis A, Remise C, Lavigne GJ., Prevalence and risk factors of sleep bruxism and wake-time tooth clenching in a 7- to 17-yr-old population, *Eur J Oral Sci.* 2011 Oct;119(5):386-94.

In TMD population, 75% have chronic pain.

Cunali PA, Almeida FR, Santos CD, Valdrighi NY, Nascimento LS, Dal'Fabbro C, Tufik S, Bittencourt LR, Prevalence of temporomandibular disorders in obstructive sleep apnea patients referred for oral appliance therapy. *J Orofac Pain.* 2009 Fall;23(4):339-44.

Chronic headache reported in 76% of treatment-seeking fibromyalgia patients.

Dawn A. Marcus , Cheryl Bernstein , Thomas E. Rudy. Fibromyalgia and headache: an epidemiological study supporting migraine as part of the fibromyalgia syndrome. *Clin Rheumatol* (2005) 24: 595–601.

In patients with fibromyalgia, complaints of poor sleep quality and fatigue are more prominent than pain.

Roizenblatt S, Neto NS, Tufik S. Sleep disorders and fibromyalgia. *Curr Pain Headache Rep.* 2011;15:347-355.

Bidirectionality Theory: Pain causes poor sleep and poor sleep lowers pain threshold.

- 1) Lavigne GJ, McMillan D, Zucconi M, Pain and Sleep. In Kryger MH, Roth T, Dement WC (eds). *Principles and Practice of Sleep Medicine*, ed 4 Philadelphia:Saunders, 2005:1246-1255
- 2) Christopher J. Lettieri, MD, The Association of Obstructive Sleep Apnea and Chronic Pain, *Medscape Pulmonary Medicine*, May 24, 2013.

Sleep abnormalities have been recognized in a number of different rheumatic diseases, including RA, OA, FM, JIA, SS, SLE, scleroderma, SpAs, sarcoidosis and Behçet's syndrome.

Abad VC, Sarinas PSA, Guilleminault C. Sleep and rheumatologic disorders. *Sleep Med Rev* 2008;12:211-28.

Co-existence of sleep apnea in rheumatic disease patients may influence the severity of patient-reported symptoms of pain and fatigue, as well as potentially impacting on levels of circulating inflammatory markers and mediators.

- 1) Lui MM, Lam JC, Mak HK, et al. C-reactive protein is associated with obstructive sleep apnea independent of obesity. *Chest* 2009;135:950-6.
- 2) de la Pena Bravo M, Serpero LD, Barceló A, et al. Inflammatory proteins in patients with obstructive sleep apnea with and without daytime sleepiness. *Sleep Breath* 2007;11:177-85.

Category 13: Pediatrics:

Prevalence OSAS in children is estimated to be 1-3%

- 1) Ali NJ, Pitson DJ, Stradling JR. Snoring, sleep disturbance, and behaviour in 4–5 year olds. *Arch Dis Child* 1993;68:360–366.
- 2) Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children: associations with obesity, race, and respiratory problems. *Am J Respir Crit Care Med* 1999;159:1527–1532.
- 3) Lipton AJ, Gozal D., Treatment of obstructive sleep apnea in children: do we really know how? *Sleep Med Rev*. 2003 Feb;7(1):61-80.
- 4) Green MG, Carroll JL. Consequences of sleep disordered breathing in childhood. *Cur Opin Pulm Med* 1997;3:456-463.

Prevalence SDB is as high as 7%-25%

- 1) Halterman JS, Aligne CA, Auinger P, McBride JT, Szilagyi PG. Inadequate therapy for asthma among children in the United States. *Pediatrics*. 2000;105(1 Pt 3):272–276.
- 2) Hultcrantz E, Lofstrand-Tidestrom B, Ahlquist-Rastad J. The epidemiology of sleep related breathing disorder in children. *Int J Pediatr Otorhinolaryngol*. 1995;32(Suppl):S63–66.
- 3) Rosen CL, Storfer-Isser A, Taylor HG, Kirchner HL, Emancipator JL, Redline S. Increased behavioral morbidity in school-aged children with sleep-disordered breathing. *Pediatrics*. 2004;114(6):1640–1648.
- 4) Gottlieb DJ, Vezina RM, Chase C, et al. Symptoms of sleep-disordered breathing in 5-year-old children are associated with sleepiness and problem behaviors. *Pediatrics*. 2003;112(4):870–877.

Prevalence of habitual snoring ranged from 3.2%-12.1% and in some reviews from 8%-27%.

- 1) Schechter MS, Technical report: diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. Apr 2002;(4):e69.
- 2) Lipton AJ, Gozal D., Treatment of obstructive sleep apnea in children: do we really know how? *Sleep Med Rev*. 2003 Feb; 7(1):61-80.

SDB inhibits growth in 1-10% of children by decreasing Insulin Growth Factor.

- 1) Muzaffer Kiris, Togay Muderris, Sezgin Celebi Hakan Cankaya, Sami Bercin. Changes in serum IGF-1 and IGFBP-3 levels and growth in children following adenoidectomy, tonsillectomy or adenotonsillectomy, *International Journal of Pediatric Otorhinolaryngology Volume 74, Issue 5, May 2010, Pages 528–531.*
- 2) Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adenotonsillectomy on serum insulin-like growth factor-1 and growth in children with obstructive sleep apnea syndrome. *J Pediatr* 1999; 135: 76-80.
- 3) Schechter MS, Technical report: diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. Apr 2002;(4):e6.

Childhood onset asthma predicted development of OSA with OR of 2.1

Mihaela Teodorescu, MD, Asthma Tied to Sleep Apnea, medpage, May 21, 2013.

Chervin et al reported that 33% of children with ADHD were habitual snorers.

Chervin RD, Dillon JE, Bassetti C, Ganoczy DA, Pituch KJ. Symptoms of sleep disorders, inattention, and hyperactivity in children. *Sleep*. 1997;20:1185–1192.

10%-30% of children with SDB are misdiagnosed with asthma or allergic rhinitis.

Richards W, Ferdman RM, Prolonged morbidity due to delays in the diagnosis and treatment of obstructive sleep apnea in children. *Clin Pediatr (Phila)*. 2000;39(2):103.

OR for neurobehavioral problems is 2.93

Michael S. Schechter, MD, MPH, and the Section on Pediatric Pulmonology, Technical Report: Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome, *PEDIATRICS* Vol. 109 No. 4 April 2002.

When AHI>10, LV mass index above the 95th percentile OR of 11.2

Amin RS, Kimball TR, Bean JA, Jeffries JL, Willging JP, Cotton RT, Witt SA, Glascock BJ, Daniels SR, Left ventricular hypertrophy and abnormal ventricular geometry in children and adolescents with obstructive sleep apnea, *Am J Respir Crit Care Med*. 2002 May 15;165(10):1395-9.

37% of children with OSAS had evidence of right ventricular dysfunction commensurate with elevated pulmonary artery pressure.

- 1) Tal A, Leiberman A, Margulis G, Sofer S. Ventricular dysfunction in children with obstructive sleep apnea: radionuclide assessment. *Pediatr Pulmonol* 1988; 4: 139-143. Bar A, Tarasiuk A, Segev Y, Phillip M, Tal A. The effect of adenotonsillectomy on serum insulin-like growth factor-1 and growth in children with obstructive sleep apnea syndrome. *J Pediatr* 1999; 135: 76-80.
- 2) Sofer S, Weinhouse E, Tal A, Wanderman KL, Margulis G, Leiberman A, Gueron M. Cor pulmonale due to adenoidal or tonsillar hypertrophy or both in children. Noninvasive diagnosis and follow-up. *Chest* 1988; 93: 119-122.

Changes in left ventricular wall thickness indicative of elevated afterload were found in a high proportion of children with OSAS, systemic blood pressure elevations.

Amin RS, Daniels S, Kimball T, Willging P, Cotton R. Echocardiographic changes in children with obstructive sleep apnea. *Sleep* 2000; 23: A99.

Within "children with OSA" have frequent enuresis up to 7%-32%,

- 1) Topol HI, Enuresis in children with sleep apnea, *J Pediatr*. 2003 May; 142(5):515-8.
- 2) Guilleminault C, Leger D, et al. Recognition of sleep disordered breathing in children *Pediatrics*. 1996;98:871-882.
- 3) Richards W, Ferdman RM, Prolonged morbidity due to delays in the diagnosis and treatment of obstructive sleep apnea in children. *Clin Pediatr (Phila)*. 2000;39(2):103.

Within "children with OSA" have persistent snoring and difficulty breathing 96%-100%

- 1) Guilleminault C, Korobkin R, Winkle R. A review of 50 children with obstructive sleep apnea syndrome. *Lung* 1981;159:275-287. Guilleminault C, Leger D, et al. Recognition of sleep disordered breathing in children *Pediatrics*. 1996;98:871-882.
- 2) Brouillette R, Hanson D, David R, Klemka L, Szatkowski A, Fernbach S, Hunt C. A diagnostic approach to suspected obstructive sleep apnea in children. *J Pediatr* 1984;105:10-14.
- 3) Richards W, Ferdman RM, Prolonged morbidity due to delays in the diagnosis and treatment of obstructive sleep apnea in children. *Clin Pediatr (Phila)*. 2000;39(2):103.

Within "children with OSA" prevalence of mouth breathing is 84%

Richards W, Ferdman RM, Prolonged morbidity due to delays in the diagnosis and treatment of obstructive sleep apnea in children. *Clin Pediatr (Phila)*. 2000;39(2):103.

Mouth breathing has been associated with altered craniofacial growth, including narrow maxillary arch, posterior crossbite, long anterior face height with clockwise mandibular growth rotation, anterior open bite and mandibular retrognathia. SDB in children has been

associated with numerous systemic health consequences including reduced systemic growth, systemic hypertension, and pulmonary hypertension causing right and left ventricular hypertrophy, respectively, as well as behavioral problems such as hyperactivity and attention deficit, aggression, and lower grades in school. Additionally, if left untreated, the altered growth pattern increases the risk of adult OSA. All children should be carefully observed while sleeping and any breathing sounds made, or apparent struggles with breathing, must result in additional diagnostic steps.

- 1) Hultcrantz E, Larson M, Hellquist R, Ahlquist-Rastad J, Savanhholm H, Jakobsson OP. The influence of tonsillar obstruction and tonsillectomy on facial growth and dental archmorphology. *Int J Pediatr Otorhinolaryngol.* Sept 1991;22(2):
- 2) Lipton AJ, Gozal D., Treatment of obstructive sleep apnea in children: do we really know how? *Sleep Med Rev.* 2003 Feb; 7(1):61-80.
- 3) Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. *Sleep.* June 15 2004;27(4):761-766.
- 4) Ozdemir H, Altin R, Sogut A, et al. Craniofacial differences according to Ahi scores of children with obstructive sleep apnea syndrome: Cephalometric study in 39 patients. *Pediatr Radiol.* May 2004;34(5)393-399.
- 5) Linder-Aronson S. Effects of adenoidectomy on dentition and nasopharynx. *Trans Eur Orthod Soc.* 1972:177-186.

Rapid maxillary expansion is an effective treatment option for children with OSA, particularly in cases of malocclusion and without significant adenotonsillar hypertrophy.

- 1) Villa M et al. Rapid maxillary expansion in children with obstructive sleep apnea syndrome: 12-month follow-up. *Sleep Med* 2007; 8:128-34.
- 2) Pirelli P et al. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. *Sleep* 2004; 27:761-6.

The Brouillette questionnaire is an excellent diagnostic questionnaire for OSAS in children with AT hypertrophy.

Michael S. Schechter, MD, MPH, and the Section on Pediatric Pulmonology, Technical Report: Diagnosis and Management of Childhood Obstructive Sleep Apnea Syndrome, *PEDIATRICS* Vol. 109 No. 4 April 2002.

OSA incidence in kids w/ ADHD is 20-30% vs 1-4% in general population. A retrospective study.

Youssef, et al, *Ann Clin Psychiatry.* 2011 Aug;23(3):213-24.

Additional Recommended Reading:

AADSM Board Review Reading List.

Books:

Principles and Practice of Sleep Medicine, Kryger, Roth, and Dement, 4th and 5th Editions, Elsevier, were major resources.

Principles and Practice of Pediatric Sleep Medicine (second edition) Sheldon Ferber, Kryger, Gozal. 2014 Elsevier

Sleep Medicine for Dentists, A practical Overview, Gilles J. Lavigne, DMD, Peter A. Cistulli MBBS PhD, Michael T. Smith PhD., 2009 Quintessence Publishing Co Inc.

Sleep Disorders and Sleep Deprivation, An Unmet Public Health Problem, Harvey R. Colten and Bruce M. Altevogt Editors, Institute of Medicine, National Academies Press, Washington, DC, 2006

Sleep Disorders, Diagnosis, Management and treatment, A handbook for clinicians. Peretz Lavie, Fiora Pillar, Atul Malhotra, Martin Dunitz, 2002

Beat the Heart Attack Gene, "The Revolutionary Plan to Prevent Heart Disease, Stroke and Diabetes", Bradley Bale MD, Amy Doneen ARNP, Lisa Collier Cool. Wiley General Trade 2014