The New Imitator: Obstructive Sleep Apnea in Psychiatry

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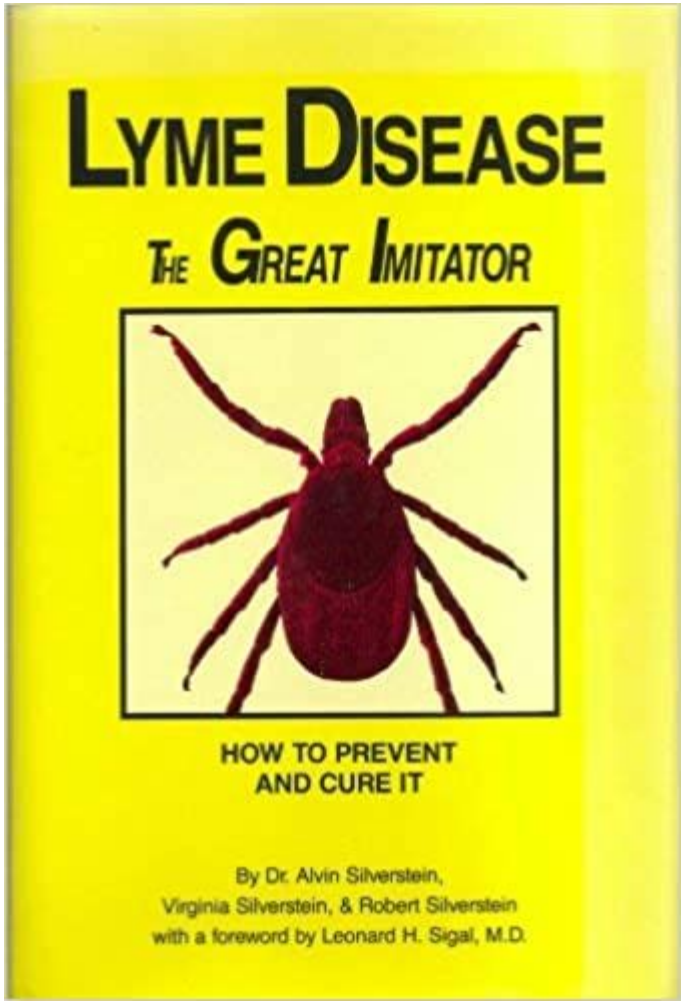


Disclosure Statement:

- I have no relationship with any industry or person(s) that could be construed as a conflict of interest in presenting this material

- No off label therapies or products will be discussed in this presentation.

My objectives, are to demonstrate:

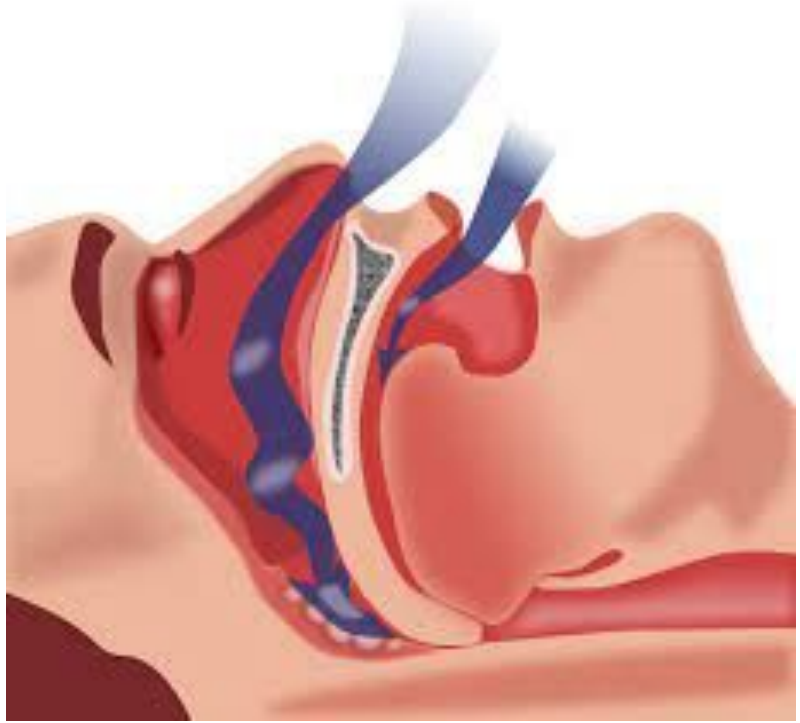
1. Obstructive sleep apnea (OSA) commonly presents with or as psychiatric symptoms
2. OSA commonly occurs in all age groups, and both sexes
3. Treatment of OSA will improve psychiatric outcomes and quality of life.

Defining Obstructive Sleep Apnea (OSA)

OSA refers to the obstruction of the upper airway during sleep causing an arousal, which may be conscious or unconscious.

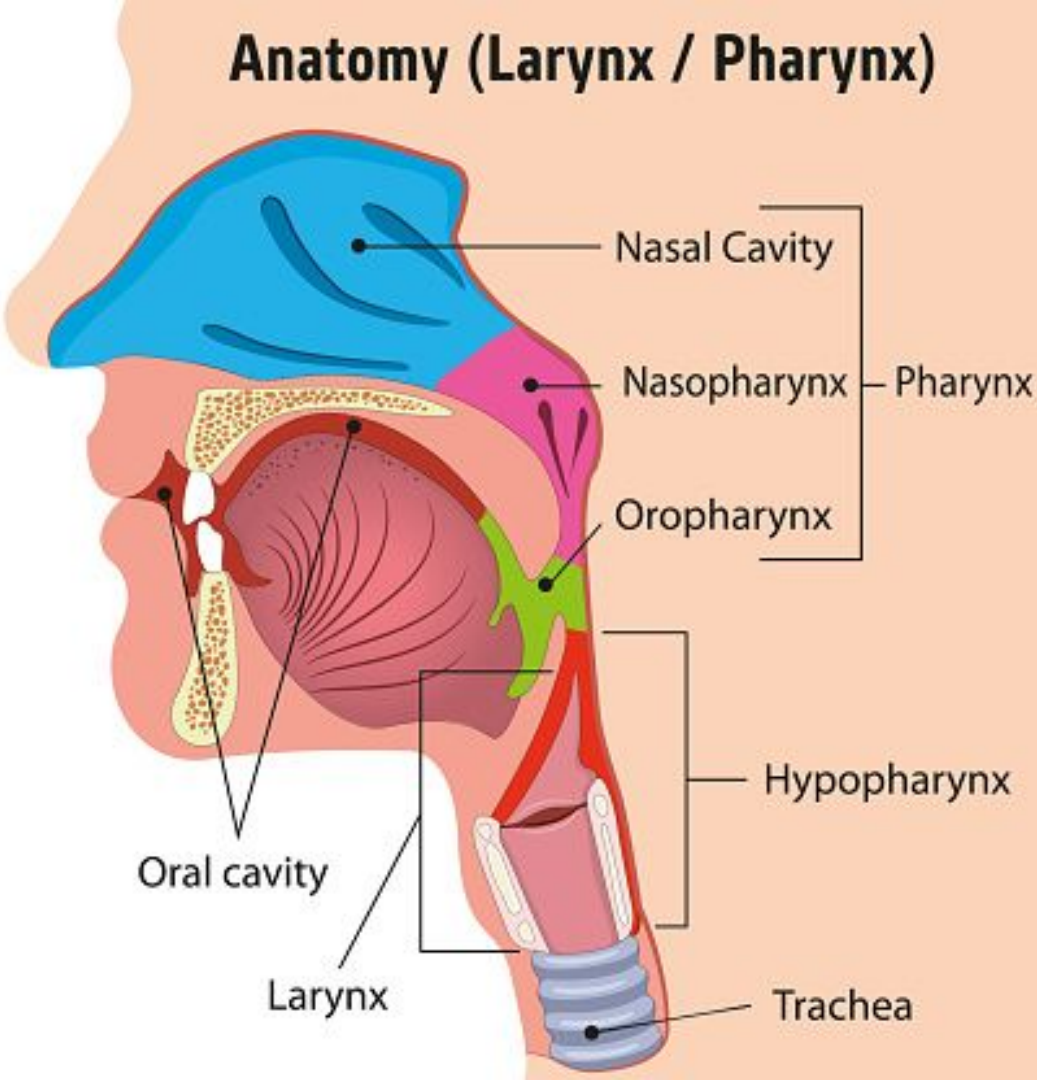
This can lead to oxygen desaturation, hypercapnia, and sleep fragmentation.

Nasal airflow determines if it is apnea (no flow) or hypopnea (reduced flow).

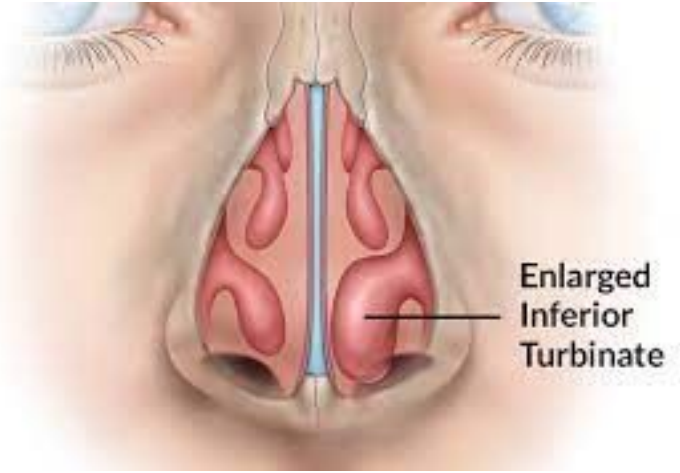


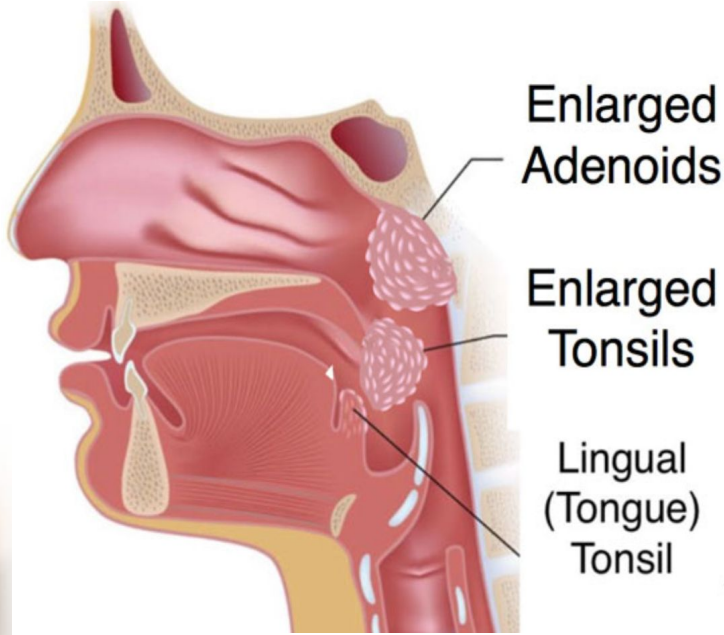
Locations

Obstructions can occur at the nares, nasal passage, nasopharynx, oral cavity, or, oropharynx. Either a blockage or collapse of the airway due to compromise of the airway wall.

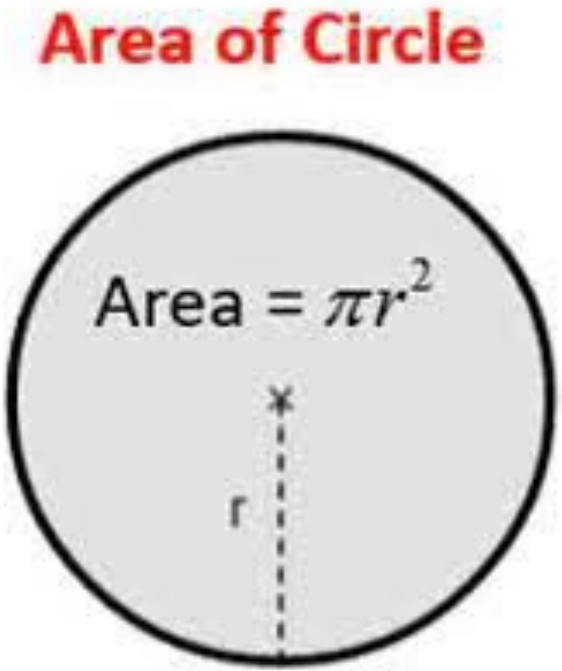


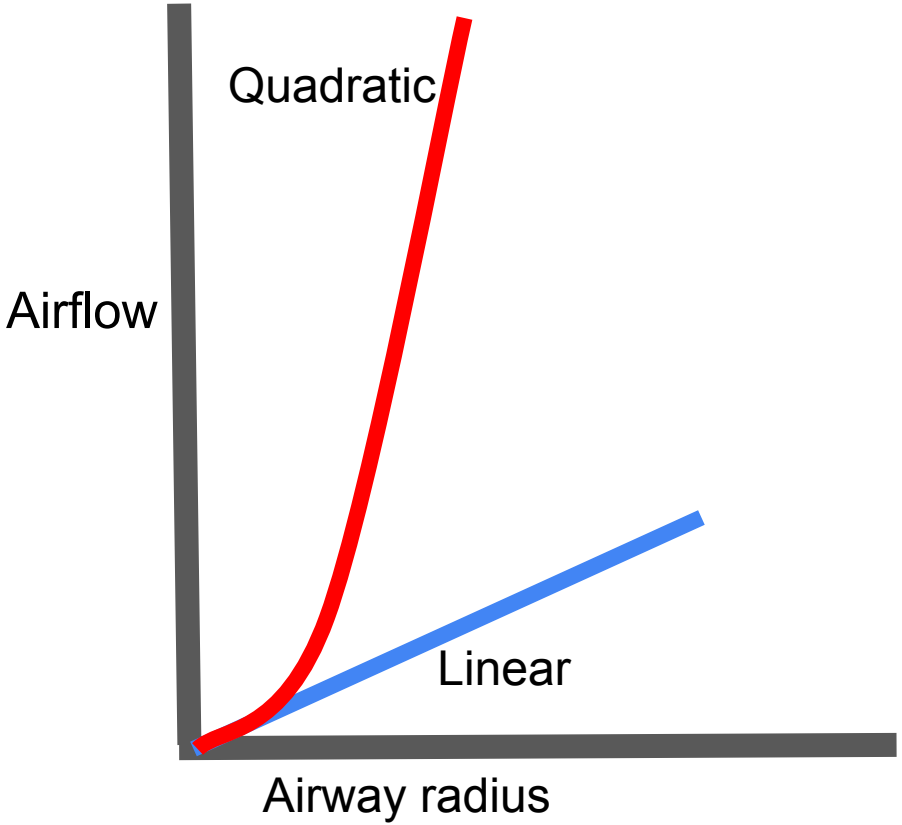
Possible causes of obstructions





Small change in airway = big impact





Prevalence

OSA in Adults: Wisconsin Sleep Study Cohort

- age 30-49: 10% of men and 3% of women at least moderate OSA
- age 50-70: 17% of men and 9% of women have at least moderate OSA.

- It is estimated that 82% of men and 93% of women in the United States with OSA are undiagnosed.

Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol 2013; 177(9):1006–1014.
Young T, Evans L, Finn L, Palta M. Estimation of clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 1997; 20(9):705–706.

OSA in Non-Obese Adults w Serious Mental Illness (SMI)

- 2016; Meta-analysis of 12 studies; n= 570,121 participants with SMI (mean age=38.3+/-7.5 years), 45.8% male (range=32-80.4) and mean BMI 25.9+/-3.7

- OSA in clinical studies:
  - SMI: **25.7%** (95% CI 13.9 to 42.4%, n=1,535)
  - MDD **36.3%** (95% CI 19.4-57.4%, n=525)
  - Bipolar Disorder **24.5%** (95% CI 10.6-47.1, n=681)
  - Schizophrenia **15.4%** (95% CI 5.3-37.1%, n=329).

- OSA in population cohort studies:
  - SMI: **10.7%** (95% CI 2.4-37.0%) in 568,586 people
  - MDD: **19.8%** (95% CI 2.5-70.0%) in 358,853 people

OSA in Children

General child population: 5-6%

Children w syndromic conditions: 50-100%

Systematic Review of 33 studies, in 2011 - major findings:

(1) Children in racial/ethnic and socioeconomic minorities may have higher prevalence and greater risk for Sleep Disordered Breathing, and

(2) In the U.S., white children or children with private insurance are more likely to undergo adenotonsillectomy.

Nature vs Nurture of OSA and Psychiatric Symptoms

Twin/sibling study, 1521 subjects

- Genes influence 40% of the variance in sleep apnea symptoms.
- Association between depression, anxiety and externalizing behaviors with apnea symptoms (ranging from r = 0.22-0.29).
- Genetic covariation between symptoms of sleep apnea and symptoms of:
  - Depression is 95%
  - Anxiety is 53%
  - Externalizing behavior is 57%

Psychiatric Symptoms & OSA

Depression & Anxiety

CPAP improved depression in OSA

Same effect size as antidepressants

- 2020; Meta-analysis of 9 RCTs w 1,052 patients
- **The pooled standard mean difference of CPAP on depression was 0.31** (95% CI 0.18, 0.43).
    - If use was **> 4hr/night**, it tended to be effective in improving patients' mood symptoms (SMD = 0.38; confidence interval 0.23, 0.54).

CPAP adherence improves depression

Secondary analysis of the RICCADSA (Randomized Intervention with CPAP in CAD and Sleep Apnea) trial.

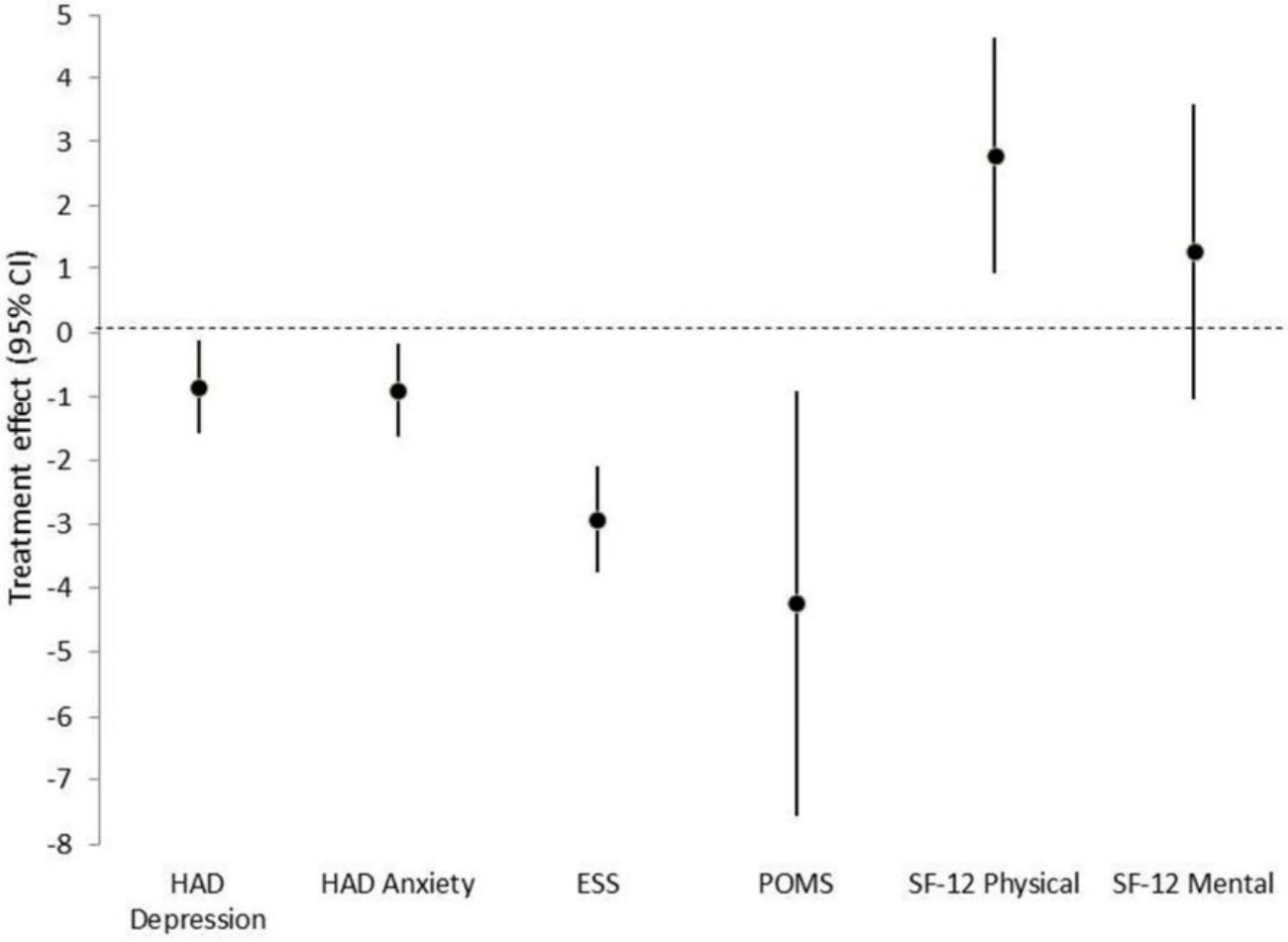
Depression Scores (n=203), p=0.001		
	CPAP	No CPAP
baseline	30.3%	25.0%
3mos	16.2%	23.1%
12mos	13.1%	24.1%

→ CPAP use (h/night) associated w decline in depression score ($r = 0.46$; $P < 0.001$).

→ Depression improvement (Odds Ratio): 3.92 w 3hr/night, 4.45 w 4hr/night, and 4.89 w 5hr/night

Substantial benefi in women

2016, 300 women w moderate to severe OSA, randomized to CPAP or conservative tx for 3 mos



Suicidality

- 125 acutely suicidal adults w MDD and no prior OSA dx.
- Polysomnogram revealed 21% positivity
- Daytime sleepiness or degree of insomnia did not predict OSA.
- Although, obese, male, and older were associated risk factors, 6 women w healthy BMI were found positive.

McCall WV, Benca RM, Rumble ME, Case D, Rosenquist PB, Krystal AD. Prevalence of obstructive sleep apnea in suicidal patients with major depressive disorder. J Psychiatr Res. 2019 Sep;116:147-150. doi: 10.1016/j.jpsychires.2019.06.015. Epub 2019 Jun 19. PMID: 31238203; PMCID: PMC6606377.

Late life depression responds worse w a h/o OSA

Multicenter, open-label study of 468 subjects >60y/o w depression, on 300mg of venlafaxine for 12wks and baseline PSG. **40.8% responded** to treatment.

	OSA	**No OSA**
Venlafaxine response	27.5% (22 of 80)	43.6% (169 of 388)
Hazard Ratio	1.79 (95% CI 1.13-2.86, p<0.05)	

“**depressed older adults with comorbid OSA were more likely to experience longer episodes of depression and have been exposed to more treatments** during the index episode of depression than those without OSA.”

Children: similar pattern as adults

2013; Meta-analysis

11 studies for depressive symptoms in children diagnosed with OSA (n = 894) and a comparison group (n = 1,096).

➢ **A medium relationship was found between depressive symptoms and OSA** (Hedges' g = 0.43, 95% CI: 0.22-0.64; p = 0.0005).

9 studies (n = 379 children) examined depressive symptoms pre- and post-Adenotonsillectomy.

➢ **A medium improvement in depressive symptoms** was found at follow-up (Hedge's g = 0.41, 95% CI: 0.20-0.62; p ≤ 0.001).

Cognition in Adults

Cognitive Dysfunction w Adults

19 studies on neuropsych assessments found:

- 3 studies totalling 231 subjects (largest n=140) found no evidence of deficits
- 16 studies totalling 1110 subjects (largest n= 157, 190, 197) found deficits
- most common impairments: **working memory > executive function, attention**

ADHD & MCI mimic

10 neuroimaging studies totalling 425 subjects all found brain related changes

- Includes MRI, MRS, DTI-MRI, PET, fMRI
- White & grey matter damage
- Structures most affected: PFC, hippocampus, and striatum
- **Persistent & recurrent cerebral hypoxia postulated to be the culprit**

Beneficial for eldely with severe OSA

224 subjects 75.5±3.9 years, w AHI >30

Intention to Treat Analysis, CPAP superior to no-CPAP for:

- **all quality-of-life domains (p<0.001; effect size: 0.41-0.98**)
- sleep-related symptoms (p<0.001; effect size 0.31-0.91)
- **anxiety (p=0.016; effect size 0.51)**
- depression (p<0.001; effect size: 0.28)
- neurocognitive tests (digit symbol test (p=0.047; effect size: 0.20) and Trail Making Test A (p=0.029; effect size: 0.44))

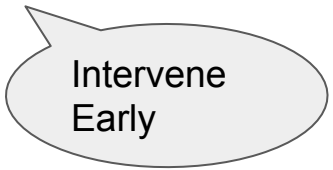
Sleep improves for elderly w moderate OSA populations

n=124, 74.9±4.6 years, w AHI 15 to 30

Intention to Treat Analysis, CPAP superior to no-CPAP for:

- Epworth Sleepiness Scale score (adjusted difference of 2.6 (95% CI 3.6-1.6) points; effect size 1)
- QoL scale for nocturnal symptoms: -0.7 (95% CI -0.3 to -1.0) points; p<0.0001
- QoL scale for emotions: -0.4 (95% CI -0.1 to -0.7) points; p=0.023).

CPAP did not demonstrate benefit for neurocognitive, anxiety & depression measures



Ponce S, Pastor E, Orosa B, Oscullo G, Catalán P, Martinez A, Hernández L, Muriel A, Chiner E, Martínez-García MÁ; on behalf the Sleep Respiratory Disorders Group of the Sociedad Valenciana de Neumología. The role of CPAP treatment in elderly patients with moderate obstructive sleep apnoea: a multicentre randomised controlled trial. Eur Respir J. 2019 Aug 22;54(2):1900518. doi: 10.1183/13993003.00518-2019. PMID: 31164429.

Neurodevelopmental Disorders in Youth

Cognitive Dysfunction in Children w OSA

15 studies all demonstrating some impairment detected w various neuropsychological measurements

- 3-5y/o: 1 study of 92 subjects
- 5-12y/o: 9 studies, 659 subjects
- 12-18: 5 studies, 260 subjects

-cognitive impairment in domains for **behavioral & educational aspects**

-problems w phonological processing & visual attention required for intellectual development

Childhood ADHD

2009; meta-analysis of 16 studies; 722 w ADHD vs 638 controls

Subjective items (questionnaires):

- **More sleep disordered breathing (z = 2.05, p =.040)**
- More daytime sleepiness (z = 1.96, p =.050)

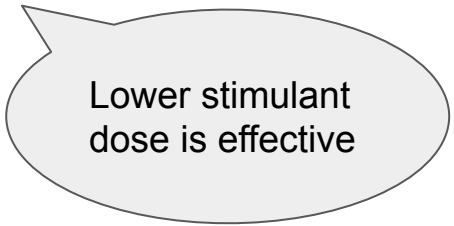
Objective parameters:

- **Higher apnea-hypopnea index** (**z = 3.47, p =.001**)
- lower sleep efficiency (z = 2.26, p =.024)
- Less sleep time (z = 2.85, p =.004),
- Longer times to fall asleep (z = 6.37, p <.001)

Childhood Adenotonsillectomy Trial (CHAT) in 2013

n=464 w OSA, 5-9y/o, randomized to adenotonsillectomy or watchful waiting

- After 1yr: intervention didn’t improve attention or executive function on neuropsych testing
- Did improve behavior, QoL, and polysomnogram findings



Autism Spectrum Disorder

2016; 965 community vs 193 ASD preschoolers from Japan

- ASD preschoolers: more sleep problems, including OSA and parasomnias.
- ASD preschoolers with sleep problems had more behavioral problems than those without
- The severity of sleep problems was significantly correlated with behavioral problems in ASD preschoolers.

Breathing issues, not sleep duration, was associated with more behavioral problems

Table 3
Number of children with scores above the cutoff values for JSQ-P subscales.

Variables	Community group ($n = 965$) Above cutoff value n (%)	ASD group ($n = 193$)	X^2 p	Odds ratio
RLS-sensory	227 (23.52)	40 (20.73)	0.57 0.45	0.84
RLS-motor	208 (21.55)	48 (24.87)	0.85 0.36	1.20
OSA	142 (14.72)	54 (27.98)	19.63 <0.0001*	2.34
Morning symptoms	473 (49.02)	81 (41.97)	2.93 0.087	0.75
Parasomnias	361 (37.40)	95 (49.22)	8.94 0.0028*	1.60
I/CRD	244 (25.28)	56 (29.02)	1.00 0.32	1.21
DES	223 (23.11)	76 (39.38)	21.70 <0.0001*	2.17
Daytime behaviors	325 (33.68)	118 (61.14)	51.27 <0.0001*	3.23
Sleep habit	275 (28.50)	74 (38.34)	7.07 0.0078*	1.58
Insufficient sleep	309 (32.02)	56 (29.02)	0.53 0.47	0.87
JSQ-P total	307 (31.81)	83 (43.01)	8.75 0.0031*	1.61

Note: RLS, restless legs syndrome; OSA, obstructive sleep apnea; I/CRD, insomnia/circadian rhythm disorder; DES, daytime excessive sleepiness.

* $p < 0.05$.

Adenotonsillectomy improves behavior in ASD

- 2017 clinical trial; ASD aged 5-14 years; 30 w OSA, 24 w/out OSA
- After AT, behavioral scales (CBCL) were significantly improved in the OSA group, but no change was observed in the control.
- Those improving w AT had significantly more behavioral problems pre-AT than the unchanged/deteriorated group w ASD.

Murata E, Mohri I, Kato-Nishimura K, Iimura J, Ogawa M, Tachibana M, Ohno Y, Taniike M. Evaluation of behavioral change after adenotonsillectomy for obstructive sleep apnea in children with autism spectrum disorder. Res Dev Disabil. 2017 Jun;65:127-139. doi: 10.1016/j.ridd.2017.04.012. Epub 2017 May 14. PMID: 28514706.

Intellectual Disabilities

- 39 patients with ID, 87% after 8-10 weeks and 70% at 8 months still used CPAP, of whom 74% and 77% showed acceptable adherence (≥ 4 h/night during ≥ 70% of the nights).
- **AHI decreased from 41 to 5 after 8-10 weeks, and 4 after 8 months**
- At 8-10 weeks and after 8 months, there was a significant **improvement in the most restrictive reported complaint, difficulty waking up, handling behavior, presence of irritability, and sleepiness.**
- The expectation that CPAP would not be tolerated was the main reason for not starting. CPAP use in the first 2 weeks predicted adherence at 8-10 weeks and 8 months.

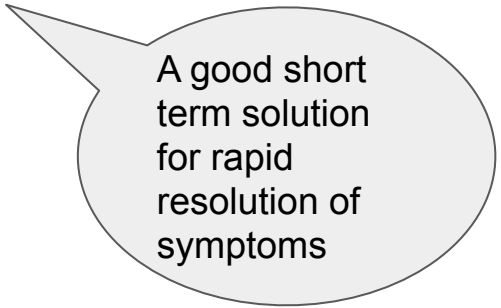
Down Syndrome

Meta-analysis of 18 studies (1,200 children) were included (mean age: 7.7 years; 56% boys; mean sample size: 67 patients).

AHI	Prevalence
>1	69%
>1.5	76%
>2	75%
>5	50%
>10	34%

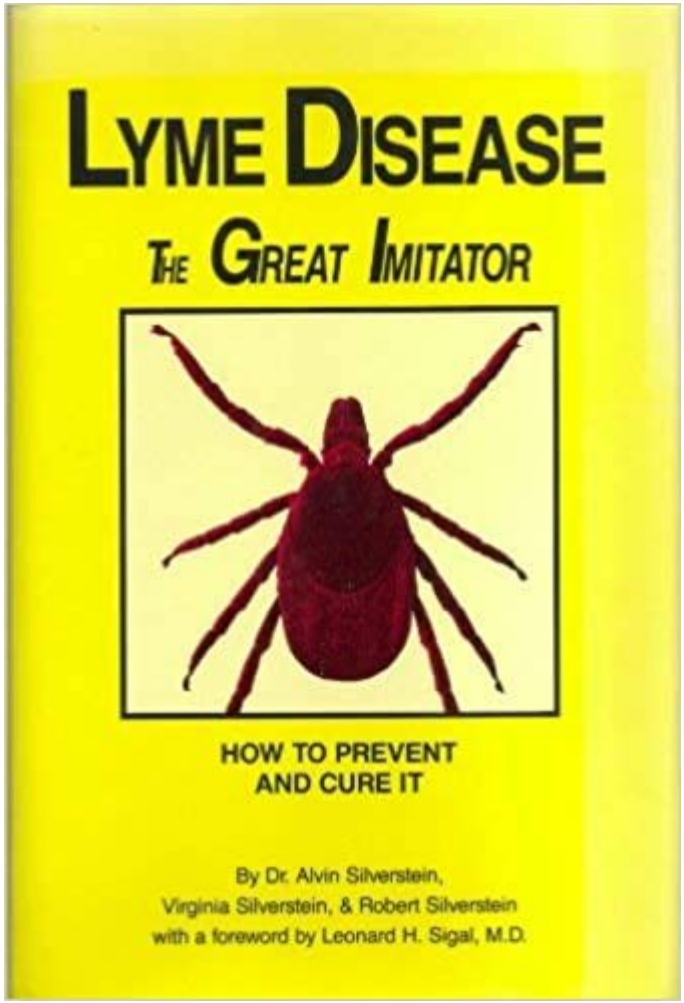
Genetic Syndromes

- 124 kids w down syndrome or mucopolysaccharidosis, 6-12y/o
- Randomized to CPAP or T&A
- After 1yr, both demonstrated similar improvements in sleepiness, QoL, & AHI
- CPAP demonstrated faster results



Making sense of the New Imitator

1. Obstructive sleep apnea commonly presents as psychiatric symptoms.
2. OSA is a reversible cause of psychiatric symptoms.
3. Non-obese, female, young, & patients w neurodevelopmental disorders are all cohorts at risk of OSA.
4. ADHD, depression, anxiety, fatigue, intellectual disabilities, mental illness are all reasons to refer for sleep studies. And insurance companies (including HMSA) acknowledge this.
5. Refer early (on intake appt if sx evident)



Thank You - questions or cases?

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