Asthma & Obstructive Sleep Apnea

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Accreditation Statement

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Conflict of Interest Disclosures for Speakers

Sushma Dharia, MD, FCCP, FAASM, ATSF has no relevant financial relationships with ineligible companies to disclose.

Learning Objectives

Upon completion of this course, attendees should be able to …

1. Describe mechanisms for Asthma and Obstructive Sleep Apnea
2. Understand link between OSA and Asthma
3. Evaluate treatment and management options

Agenda

- Definitions (OSA, OLD, Asthma)
- Prevalence
- Pathophysiology
- Overlap syndrome (OSA-OLD)
  - Bi-directional relationships
  - Predispositions
- Alternative overlap syndrome (OSA-Asthma)
  - Bi-directional relationships
  - Bi-directional Impact
  - Rx effects
- Findings from select studies
- Summary & Recommendations

Obstructive Respiratory Events

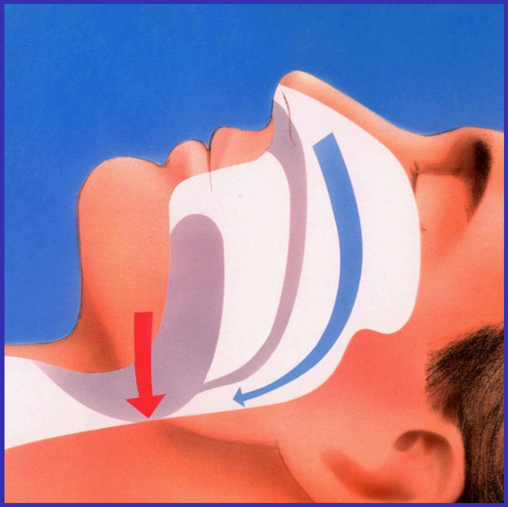
- Apnea
  - cessation of ventilation for 10 seconds or longer
- Hypopnea
  - decrease in ventilation, <u>and</u>
  - oxyhemoglobin desaturation

    <u>or</u>
  - terminated by arousal
- "Upper Airway Resistance Event" or "Respiratory Effort Related Arousal" (obstructive)
  - increased respiratory effort
  - no change in ventilation
  - terminated by arousal
- Snoring: *The sound produced by the soft tissues of the upper airway, primarily the pharynx, soft palate, and uvula, when turbulent airflow causes these tissues to vibrate*

What is OSA?

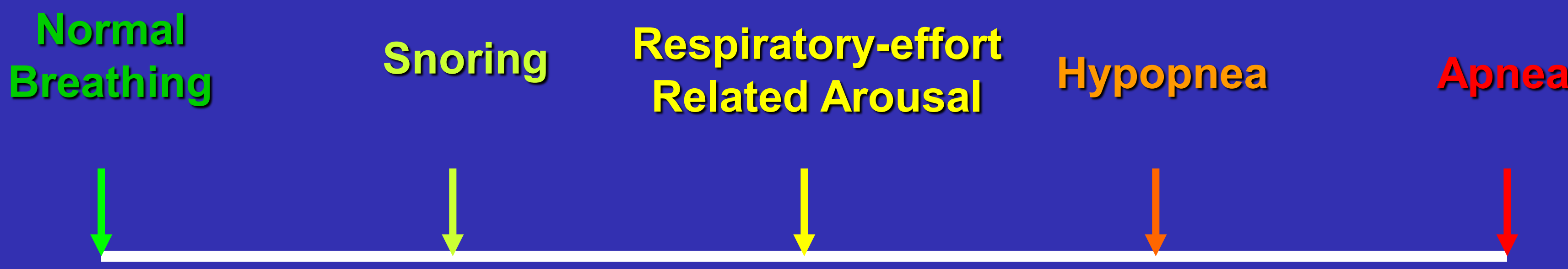
- Obstructive Apneas, Hypopneas
  - Repeated episodes of collapse of pharyngeal airway, usually a result of obstruction by soft tissue in the rear of throat

Normal Airway



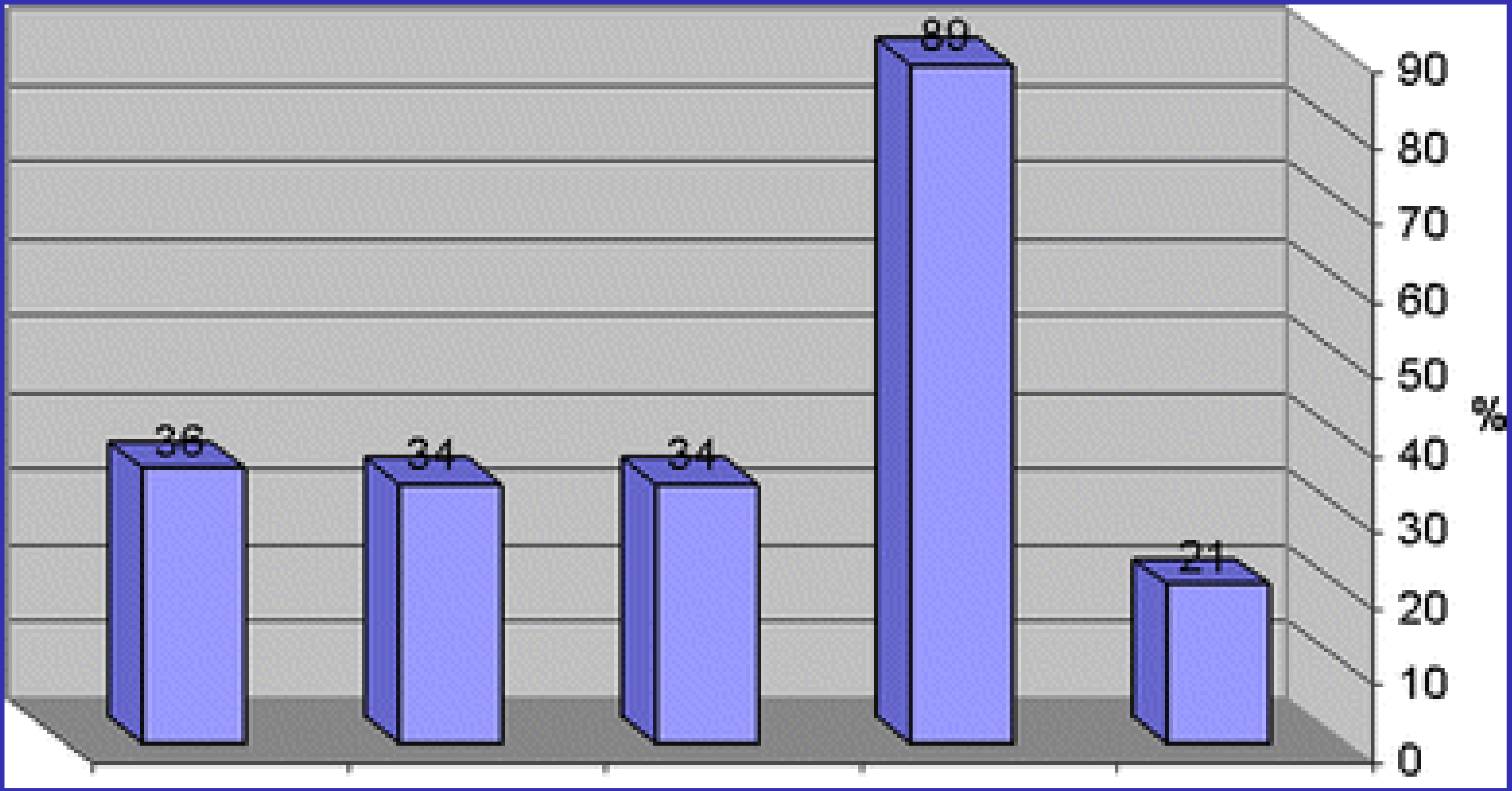
Obstructed Airway

Obstructive Events: The Continuum



Worsening Disease →
Decreasing Airway Caliber →

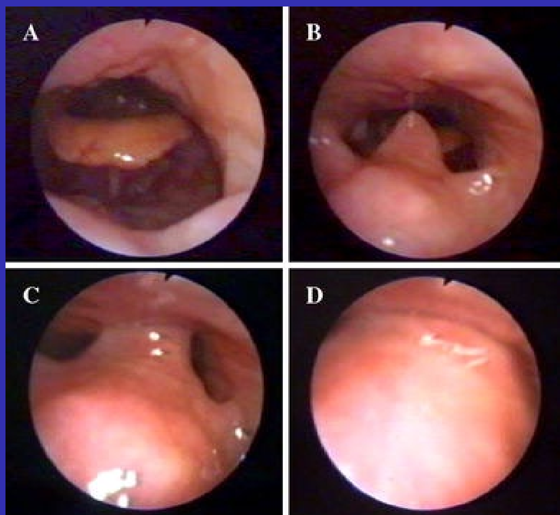
Site of Obstruction in OSA by Sleep Endoscopy



Hypopharyngeal Laryngeal Retroglossal Oropharyngeal Nasopharyngeal

Adapted from Bachar G et al. Eur Arch Otorhinolaryngol 2008; 265:1397-402

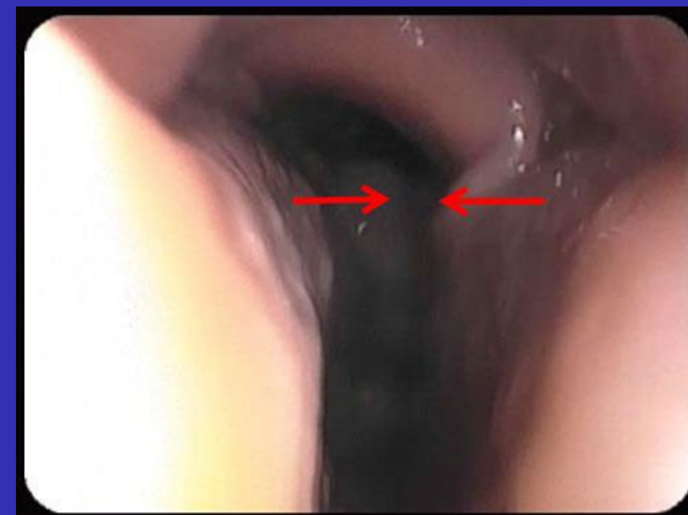
Endoscopic Appearance of Oropharyngeal Collapse



Antero-posterior

Bachar G et al. Eur Arch Otorhinolaryngol 2008

Lateral



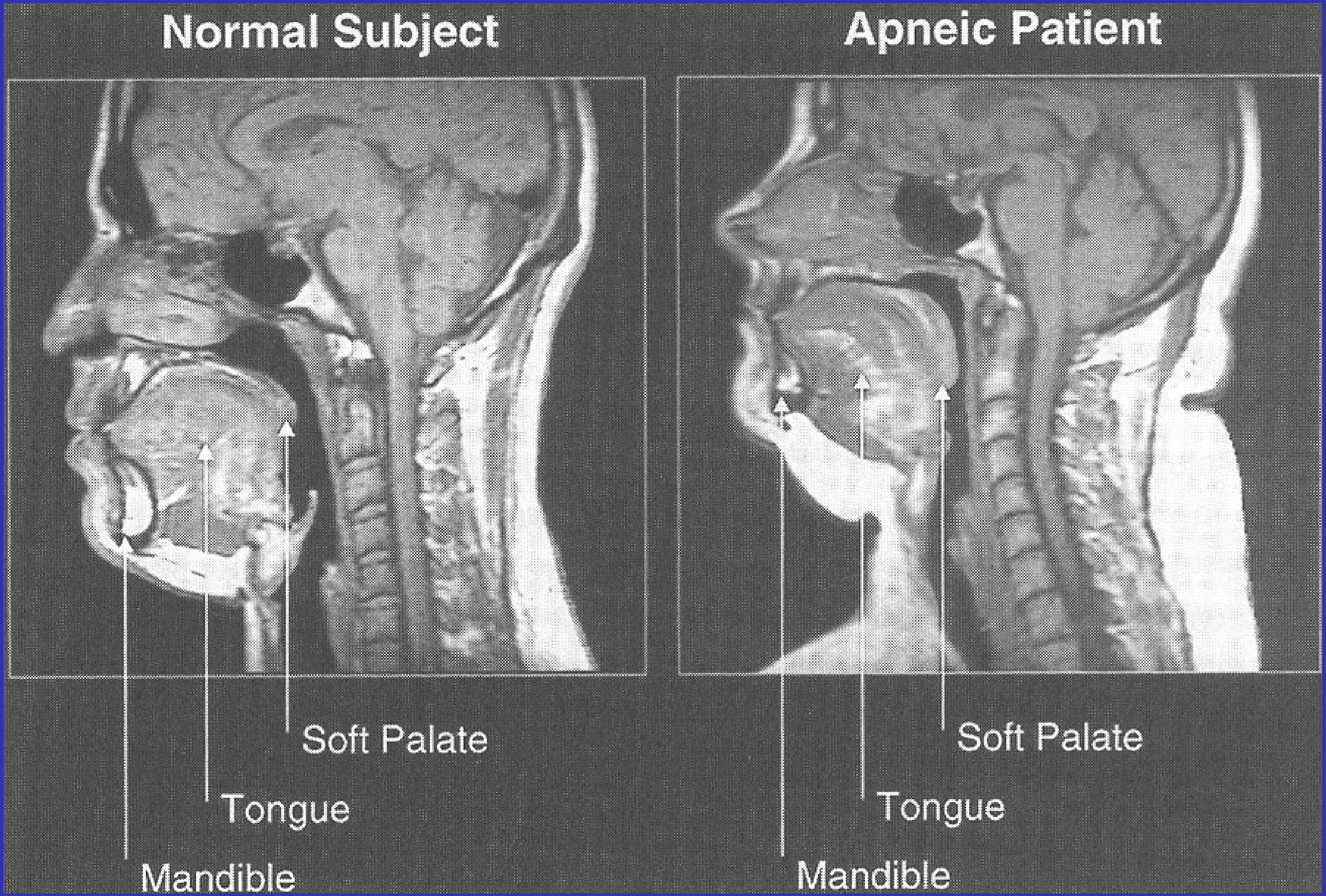
Antero-posterior

Vicini C et al. Eur Arch Otorhinolaryngol 2012

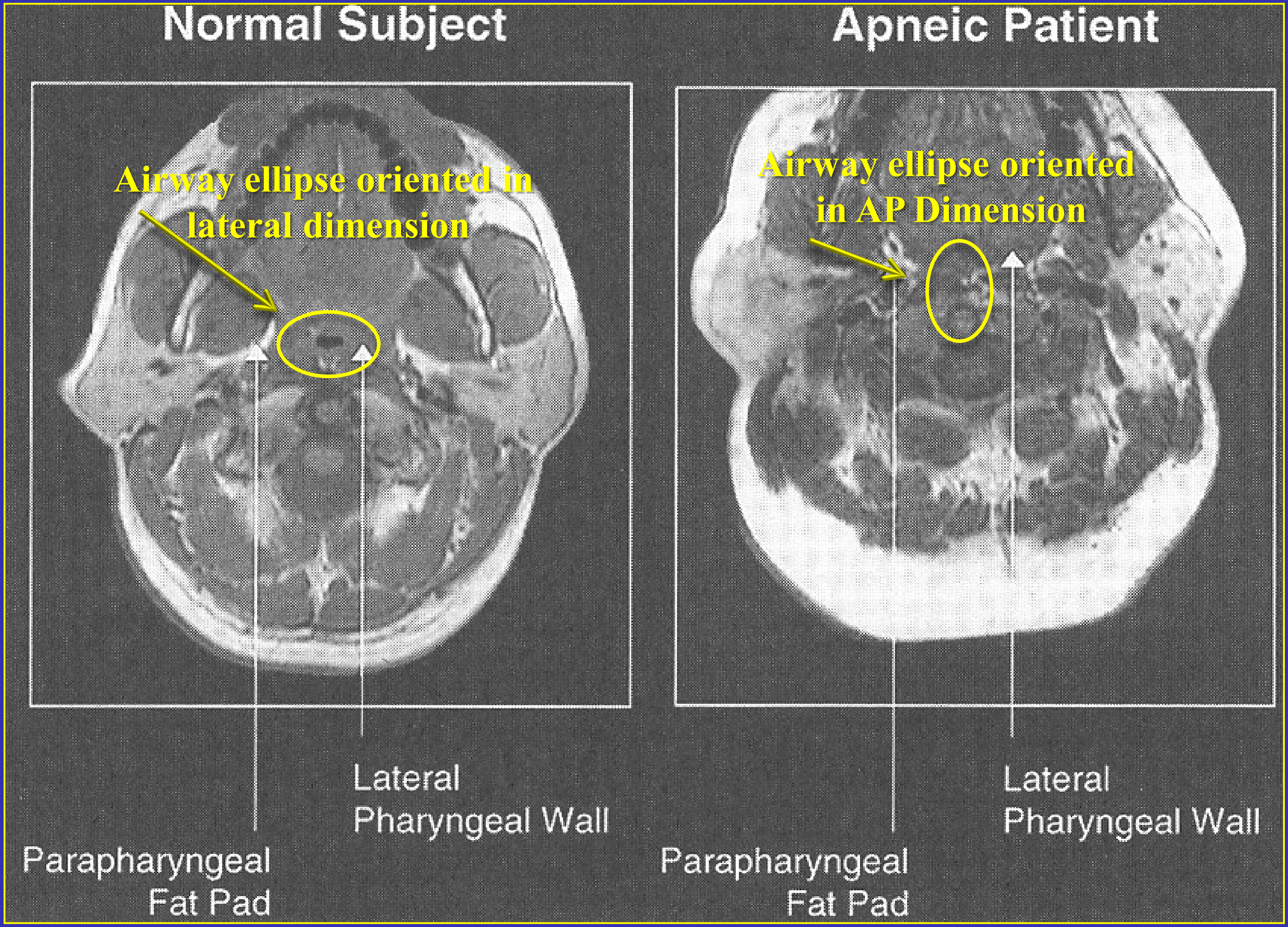
Concentric

Vicini C et al. Eur Arch Otorhinolaryngol 2012

Normal vs. OSAS Airway: Sagittal View

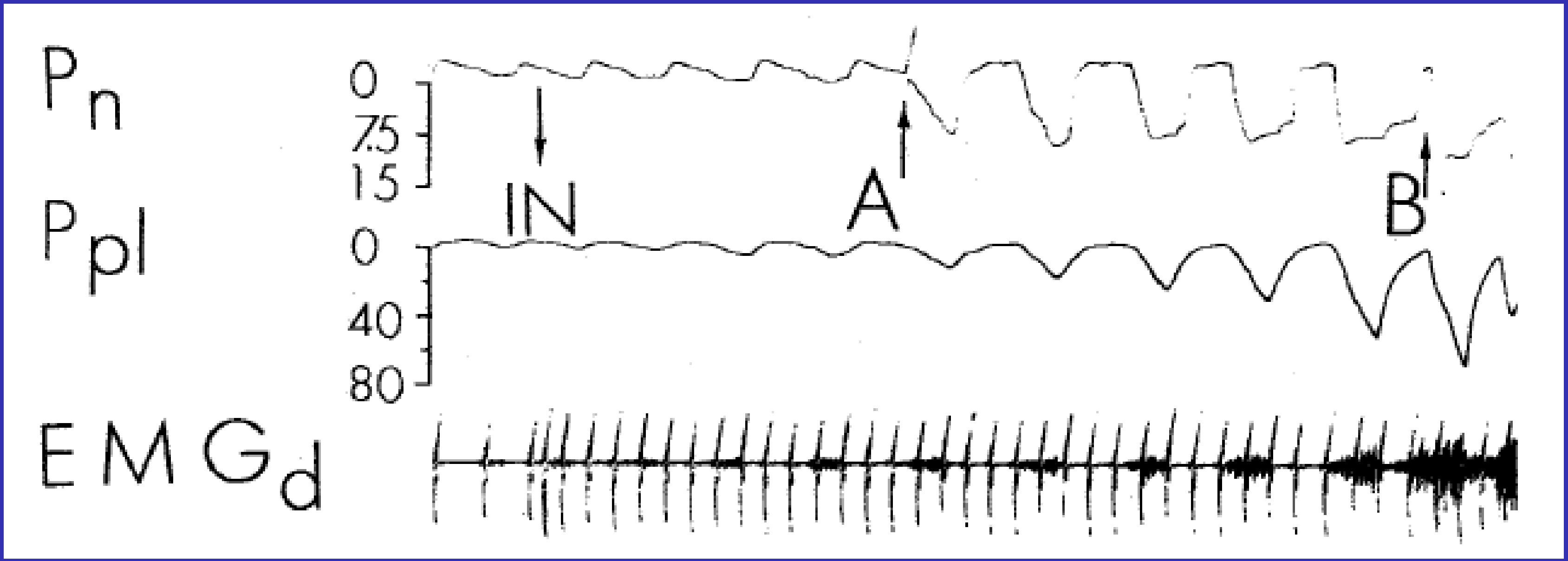


Normal vs. OSAS Airway: Transverse View



Airway size and orientation both correlate with OSA

OSA Pathophysiology



Nasal airway occlusion test during sleep in OSA patient

Issa et al., J Appl Physiology, 57(2):520-527, 1984

OSA Prevalence

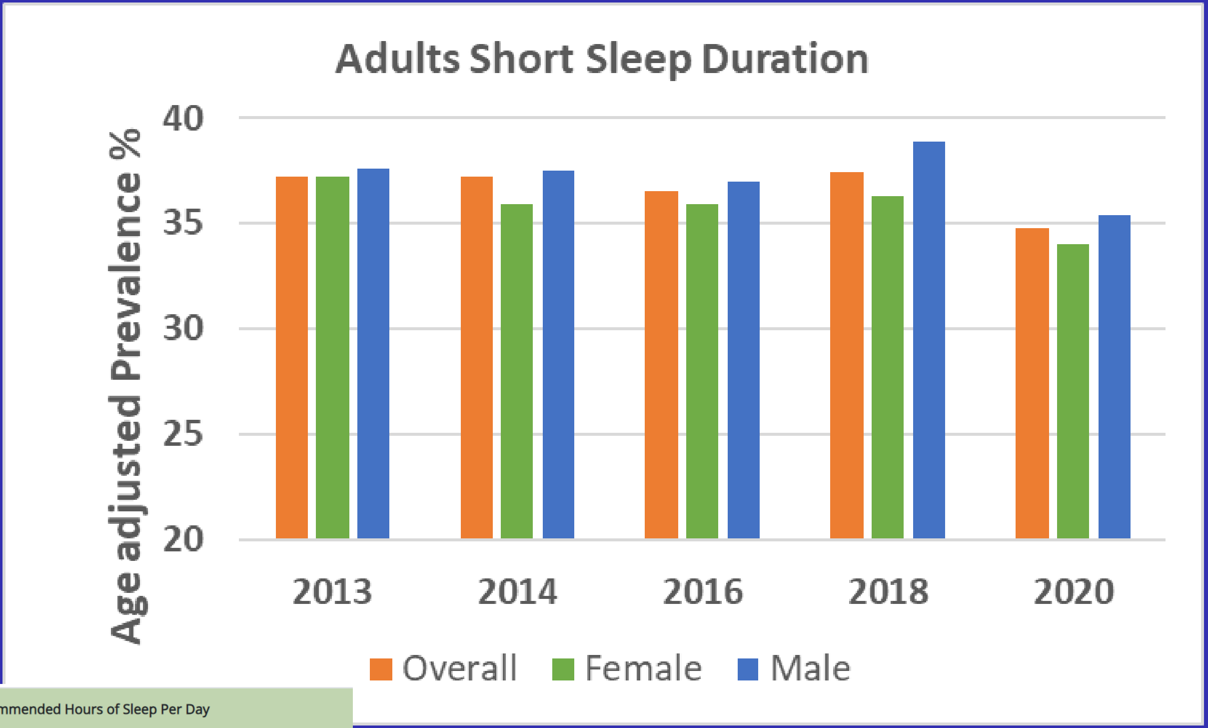
- 14% - 26% of population has OSA

Benjafield AV, et al. Lancet Respir. Med. 2019; 7: 687–98;
American Academy of Sleep Medicine, 2014

- OSA is still grossly underdiagnosed
  - Large French population-based cohort (n=20,151)
  - 1 in 5 has high likelihood of OSA (20%)
  - Only 3.5% are diagnosed for OSA

Balagny P, et al. ERJ Open Res 2023; 9: 00053-2023

Sleep Deficit Prevalence



Age Group		Recommended Hours of Sleep Per Day
Newborn	0–3 months	14–17 hours (National Sleep Foundation)[1] No recommendation (American Academy of Sleep Medicine)[2]
Infant	4–12 months	12–16 hours per 24 hours (including naps)[2]
Toddler	1–2 years	11–14 hours per 24 hours (including naps)[2]
Preschool	3–5 years	10–13 hours per 24 hours (including naps)[2]
School Age	6–12 years	9–12 hours per 24 hours[2]
Teen	13–18 years	8–10 hours per 24 hours[2]
Adult	18–60 years	7 or more hours per night[3]
	61–64 years	7–9 hours[1]
	65 years and older	7–8 hours[1]

CDC Behavioral Risk Factor Surveillance System (BRFSS), 2013, 2014, 2016, 2018, 2020

Obstructive Lung Disease (OLD)

- OLD includes distinct sub-phenotypes:
  - Chronic bronchitis
  - Emphysema

  } COPD

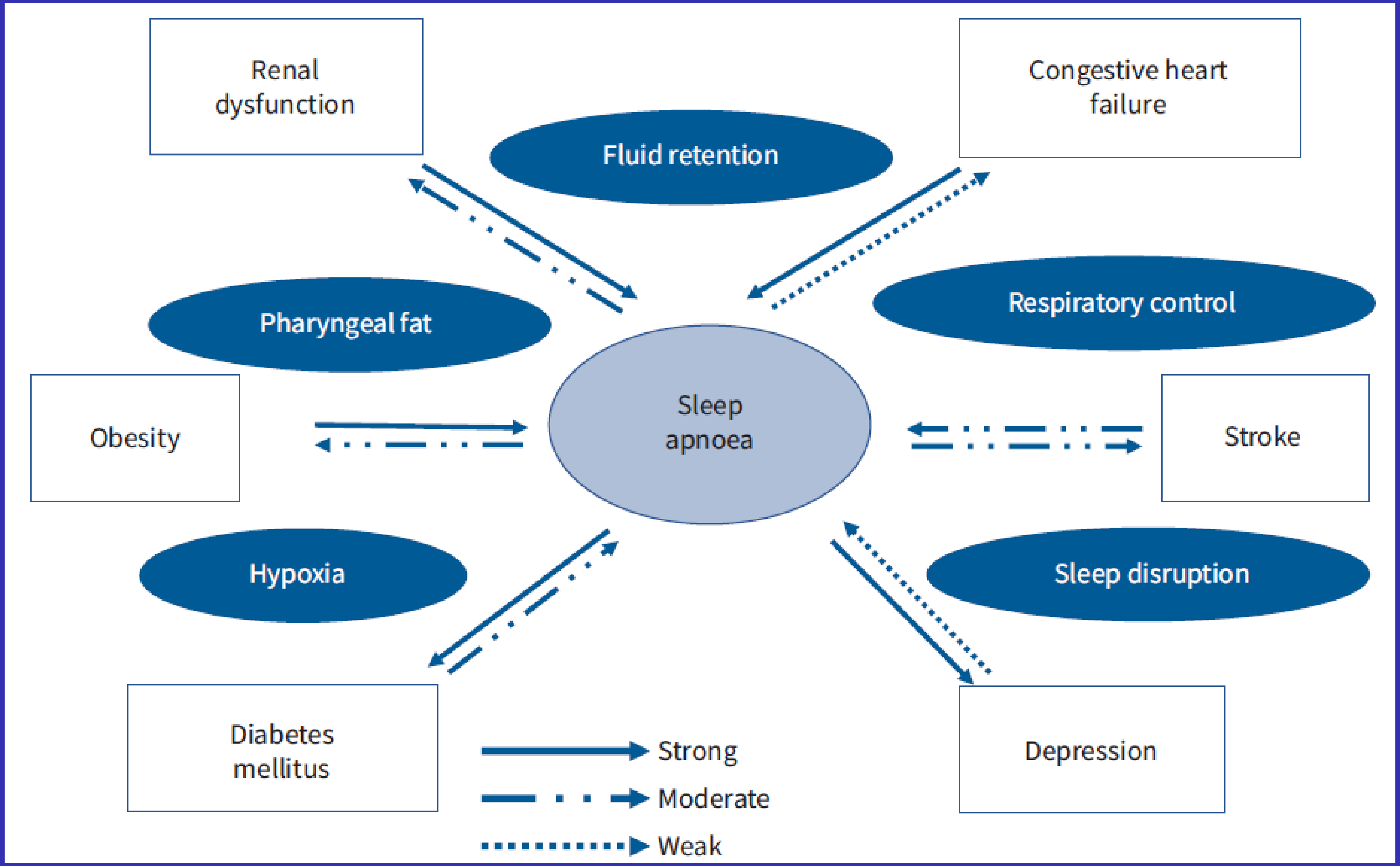
  - Asthma with airway hyperreactivity
  - Asthma with remodeling and no airflow reversibility

  } ASTHMA

  - Small airway disease

  - Disease phenotypes often overlaps

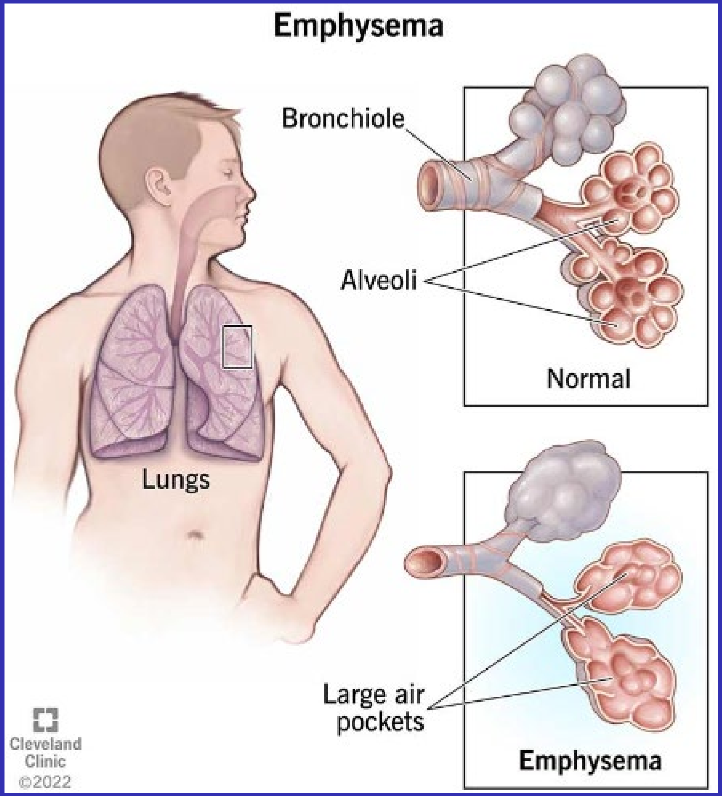
OSA & Comorbidities
Bidirectional Relationships



Gleeson et al, Eur Respir Rev 2022; 31: 210256

COPD

- Definition: A group of diseases that cause airflow blockage and breathing-related problems. It includes emphysema and chronic bronchitis.

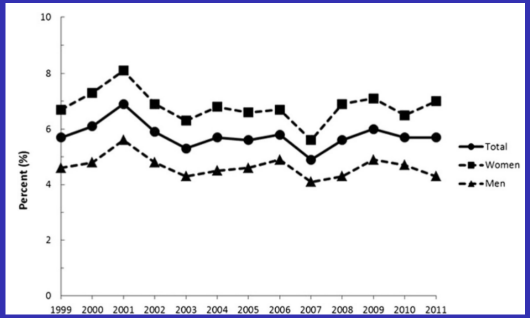


Cleaveland Clinic

- Chronic Bronchitis: cough & sputum production for >3 months; ≥ 2 consecutive years
- Emphysema: Permanent enlargement and destruction of walls in distal air spaces

COPD Prevalence

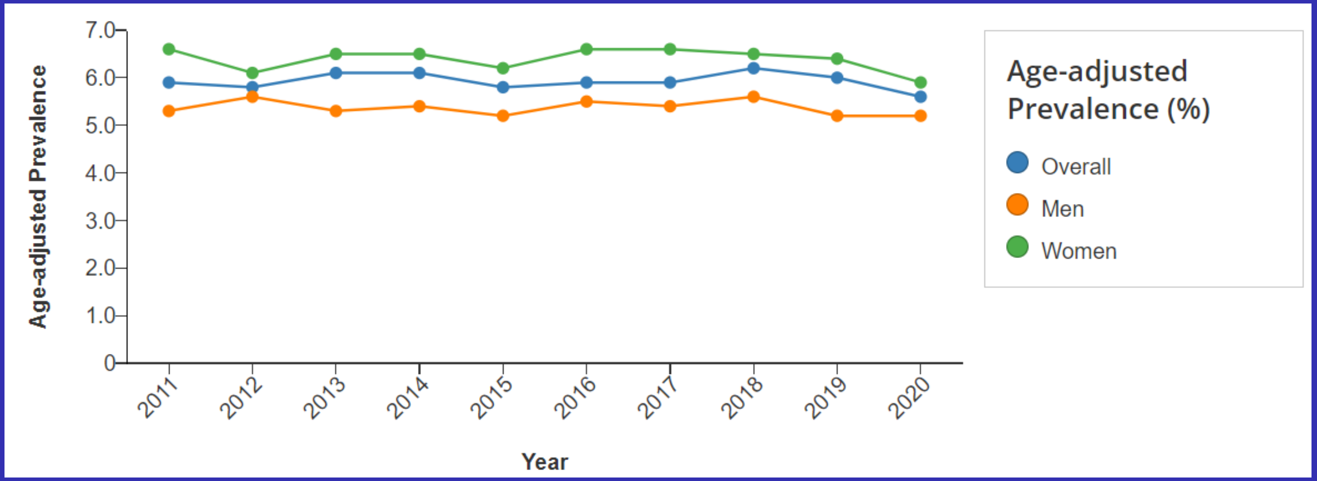
- About 16 million people in the United States has COPD and trend is unchanged during 2011-2022.



CDC Behavioral Risk Factor Surveillance System (BRFSS), 1999-2011

Ford et al, CHEST 2013; 144(1):284 –305

7%



CDC Behavioral Risk Factor Surveillance System (BRFSS), 2011-2020

Asthma

- Definition: A condition in which a person's airways become inflamed, narrow and swell, and produce extra mucus, which makes it difficult to breathe.

- Causes variable and recurrent episodes of wheezing, breathlessness, chest tightness, cough – especially at night or early morning

- Prevalence:
  - About 1 in 13 people in the United States has asthma, according to the Centers for Disease Control and Prevention.

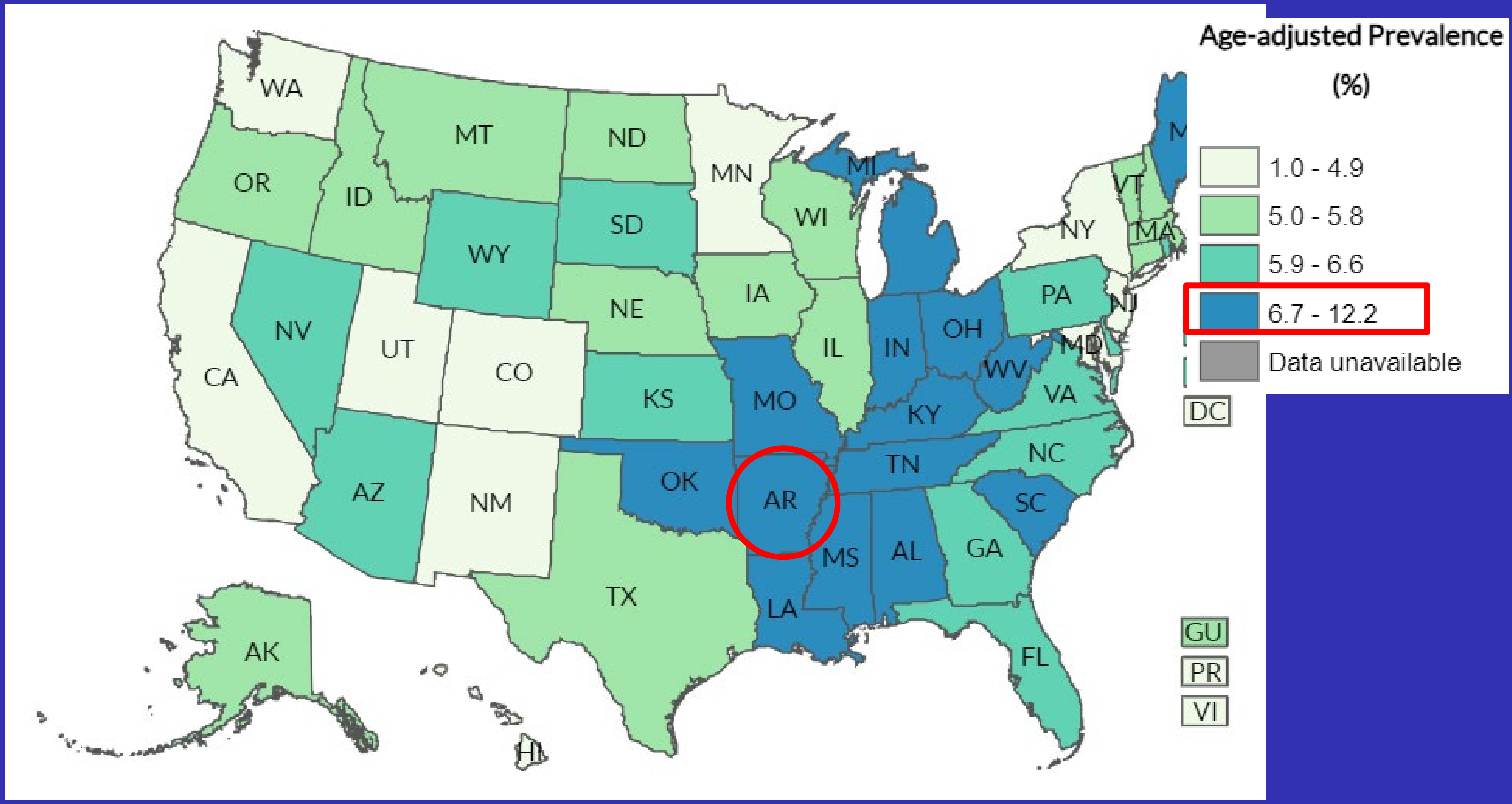
    8%

    NHIS, 2021

  - 26 million people in United States has physician-diagnosed asthma, costs US economy about $82 billion in 2013 alone

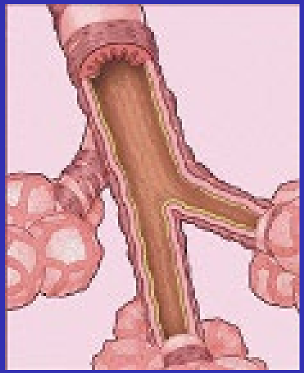
    Yoghoubi, AJRCCM 2019 (200-9)

Asthma Prevalence

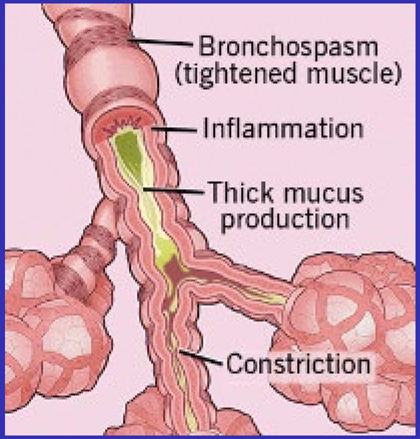


CDC BRFSS Prevalence & Trends Data 2022

Bronchospasm constricts the airway

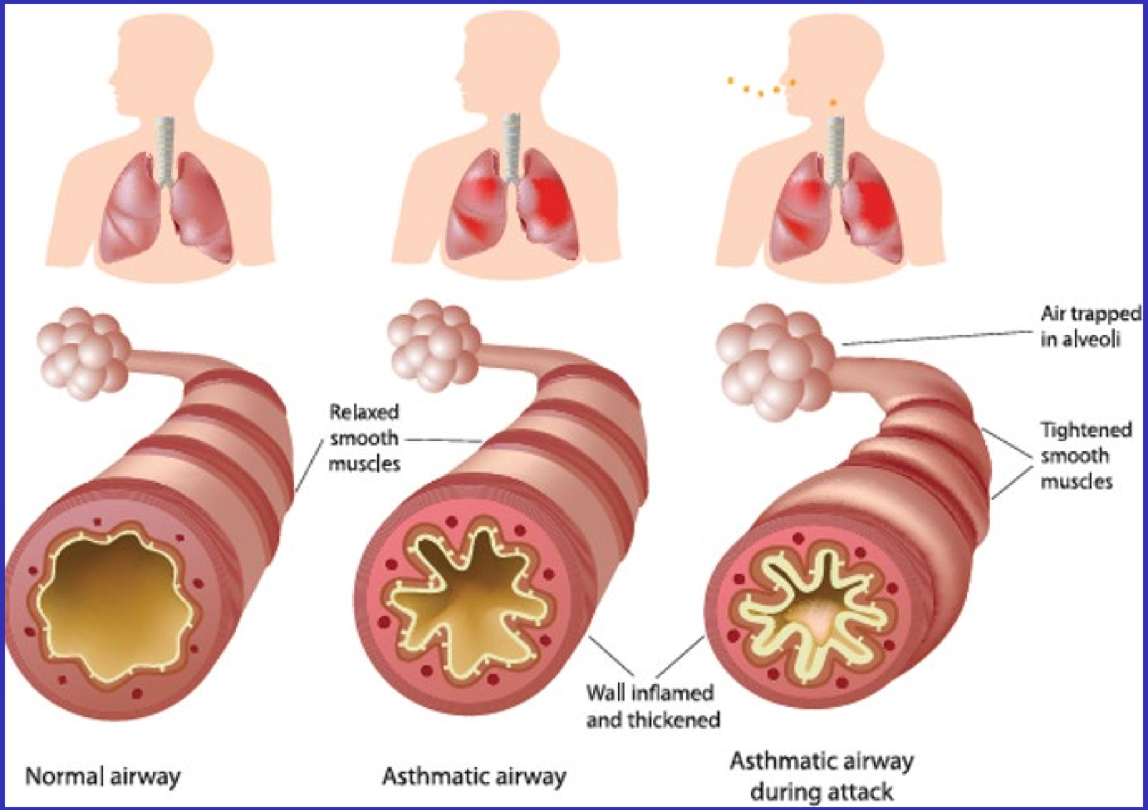


Normal Airway



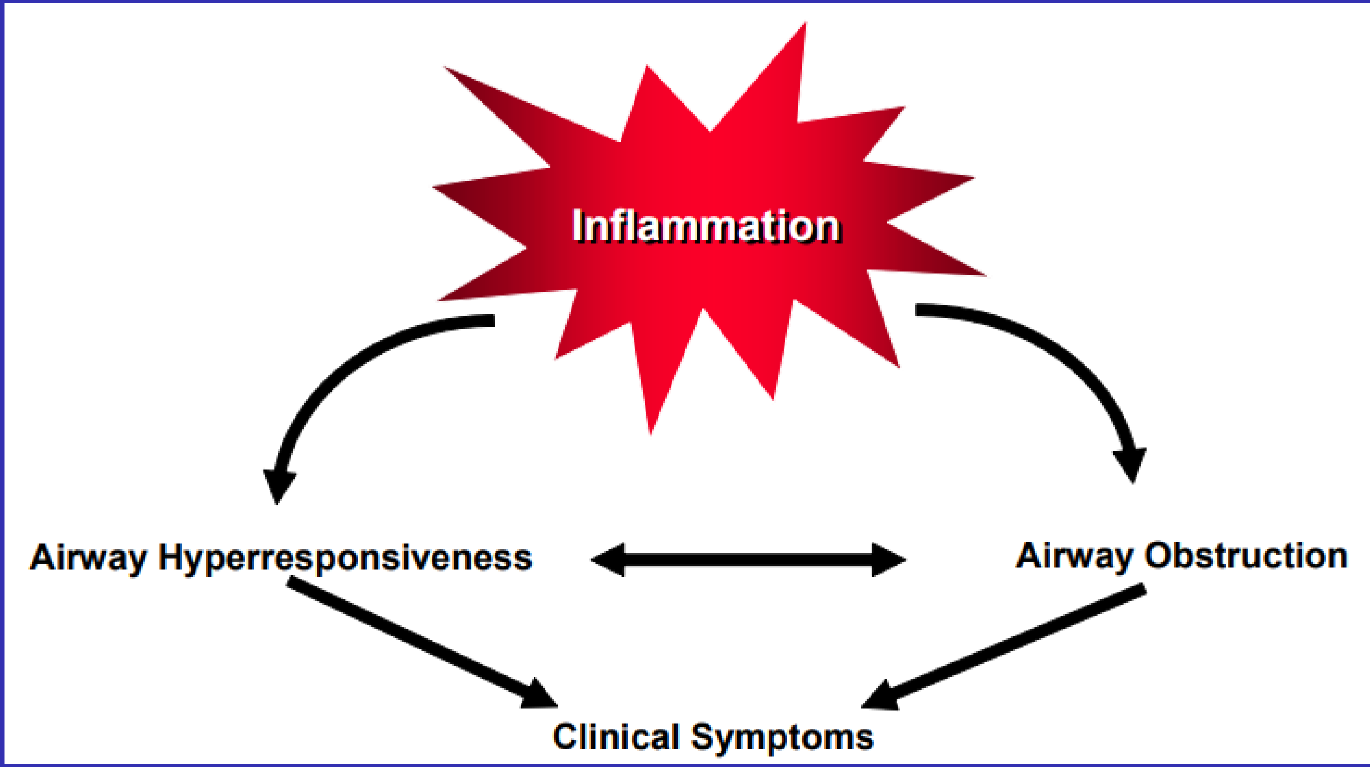
Asthmatic Airway

Cleaveland Clinic



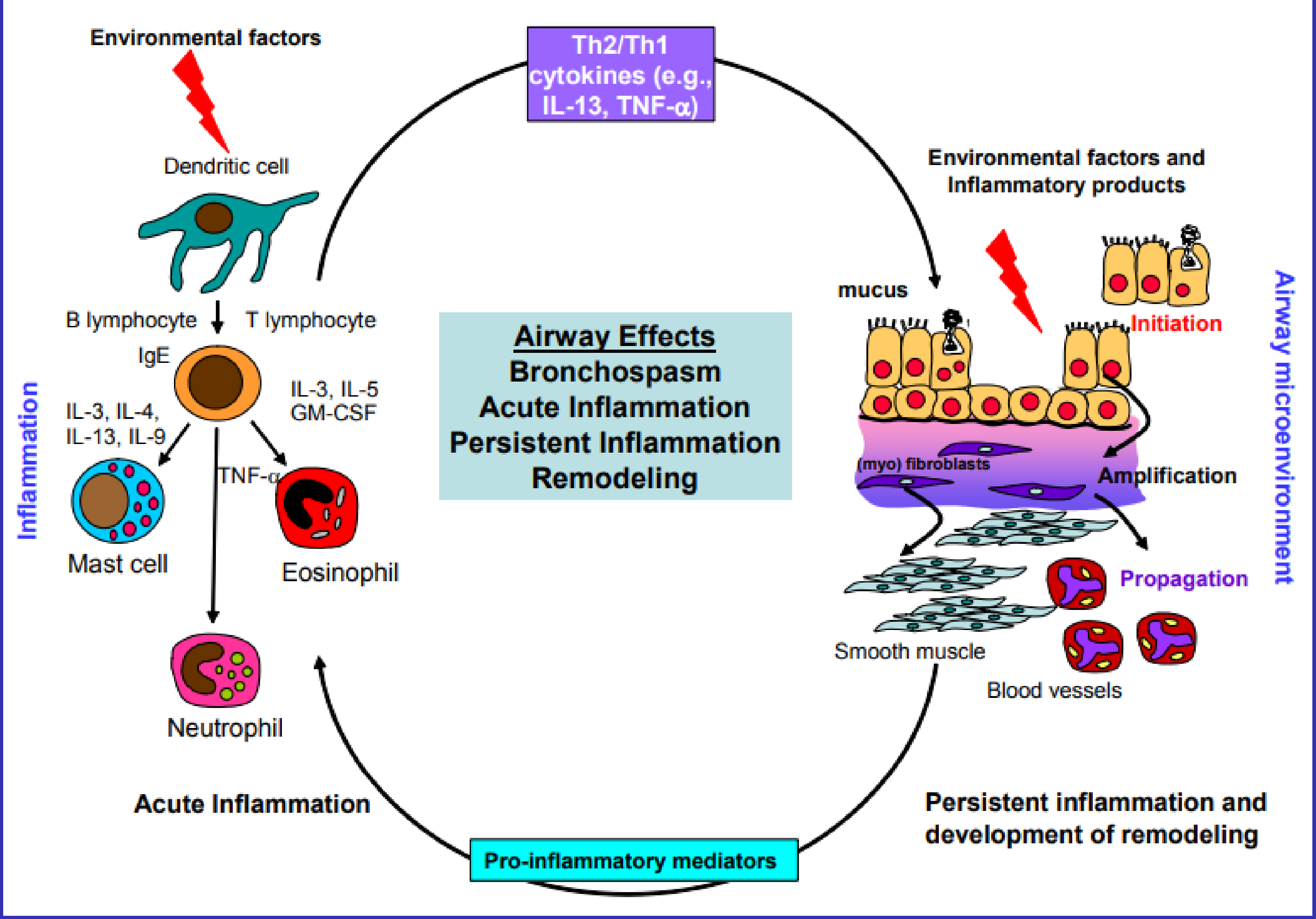
Ophea Asthma Friendly website (CA)

Interplay and Interaction between Airway Inflammation and Clinical Symptoms and Pathophysiology of Asthma



NHLBI Asthma Guidelines, EPR-3, Aug 2007

Asthma - Pathophysiology



Holgate ST, Polosa R. The mechanisms, diagnosis, and management of severe asthma in adults, The Lancet, 2006 Aug 26;368(9537):780-93

Asthma - Pathophysiology

Airflow limitation in asthma is recurrent and caused by a variety of changes in the airway:

- Bronchoconstriction: airway narrowing interfering with airflow. Bronchoconstriction narrows the airways in response to exposure to a variety of stimuli
- Airway edema: further limits airflow
- Airway hyperresponsiveness: an exaggerated bronchoconstrictor response to a wide variety of stimuli
- Airway remodeling: Permanent structural changes can occur in the airway; Associated with a progressive loss of lung function that is not prevented by current therapy

Asthma is not COPD

- They have different:
  - etiology;
  - symptoms;
  - type of airway inflammation;
  - inflammatory cells;
  - mediators;
  - consequences of inflammation;
  - response to therapy;
  - course.

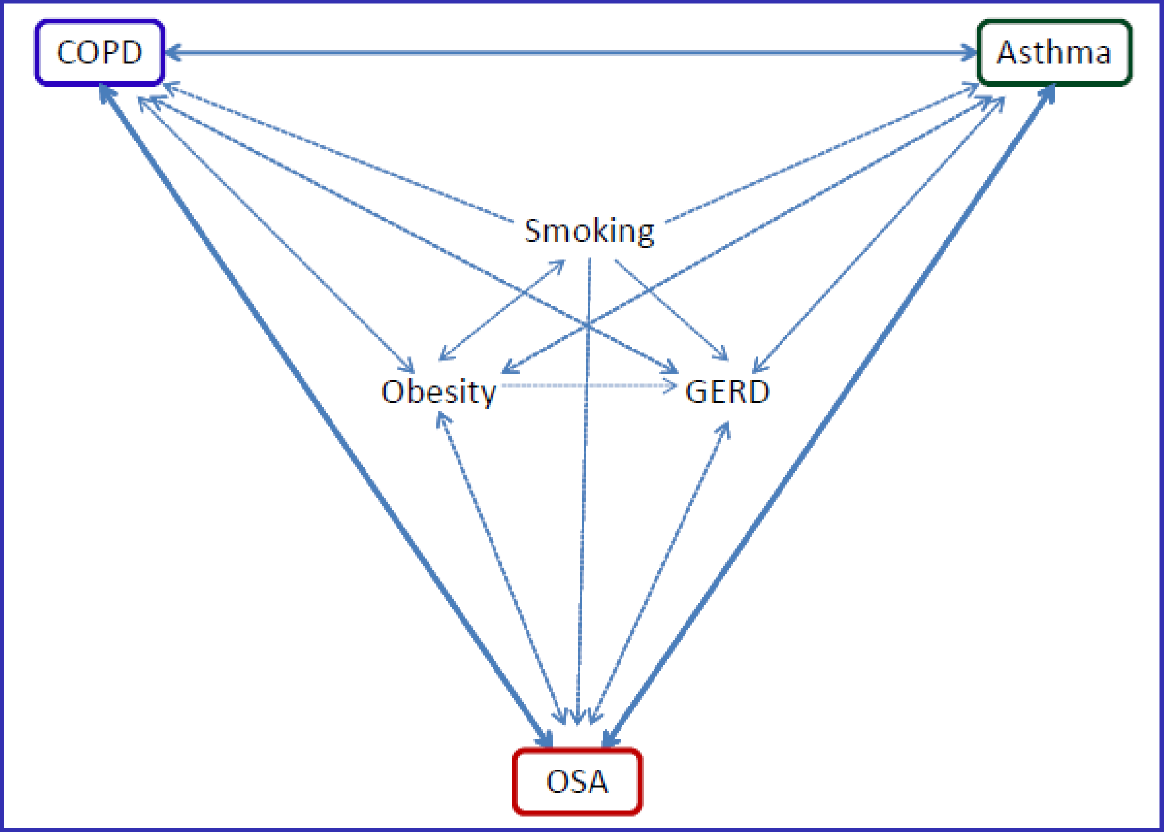
ASTHMA and COPD

	ASTHMA		COPD
Cause:	sensitive agent		noxious agent (mainly cigarette smoking)
	Asthmatic airway inflammation (CD4+T-lymphocytes and Eosinophils)		**COPD airway inflammation** (CD8+T-lymphocytes, Macrophages and Neutrophils)
	Reversible	**AIRFLOW LIMITATION**	Not fully reversible

Cukic et al, Mat Soc Med. 2012 Jun; 24(2): 100-105

OLD Overlap with OSA

- OSA features bi-directional interaction with OLD
  - Complex interaction between COPD, Asthma, OSA
  - Contribution of Smoking, Obesity, GERD



Ioachimescu et al, Respirology (2013) 18, 421-431

OLD ⟷ OSA

- Clinic population study:
  - N=67 OLD patients (57% COPD, 43% Asthma), Mean FEV_1 = 71%
  - N=75 Control group
  - OSA risk was higher for COPD group (50% vs 7.5% for control)
  - OSA risk higher for Asthma group (62% vs 7.5% for control)
  - PSG (n=26 high risk OSA)
    - 24 diagnosed with OSA (92% predicitivity using BQ)
    - Mean AHI 17.1/h; Predominantly REM related AHI in 61.5%
- Urban outpatients in pulmonary clinic with OLD are very frequently at high risk for OSA

Sharma et al, Lung. 2011; 189(1): 37–41

OLD ⟷ OSA

- Patients with overlap syndrome has ↑ risk of morbidity and mortality (compared to COPD or OSA alone)
- Nocturnal hypoxaemia ↑ as COPD patients do not return to normal O_2 saturation levels
  - Leads to pulmonary HTN and cor pulmonale
  - Prevalence of cor pulmonale in overlap syndrome patients is 80% with 30% 5-year survival
- Overlap syndrome patients had $4,155 more in Medicaid claims than COPD alone
- CPAP+O_2 → 5-year survival of 71% (versus 26% with O_2 alone)

Rasche et al, IInternist (Berl) 2007; 48: 276–82

Shaya et al, Sleep Breath. 2009; 13: 317–23

Machado et al, Eur. Respir. J. 2009; 35: 132–7

OLD ⟷ OSA Pathophysiology

- COPD and OSA may exacerbate each other due to commonalities:
  - Aging, Smoking, vagal tone ↑, GERD, Hypoxia, pulmonary HTN, Endothelial dysfunction, inflammatory state

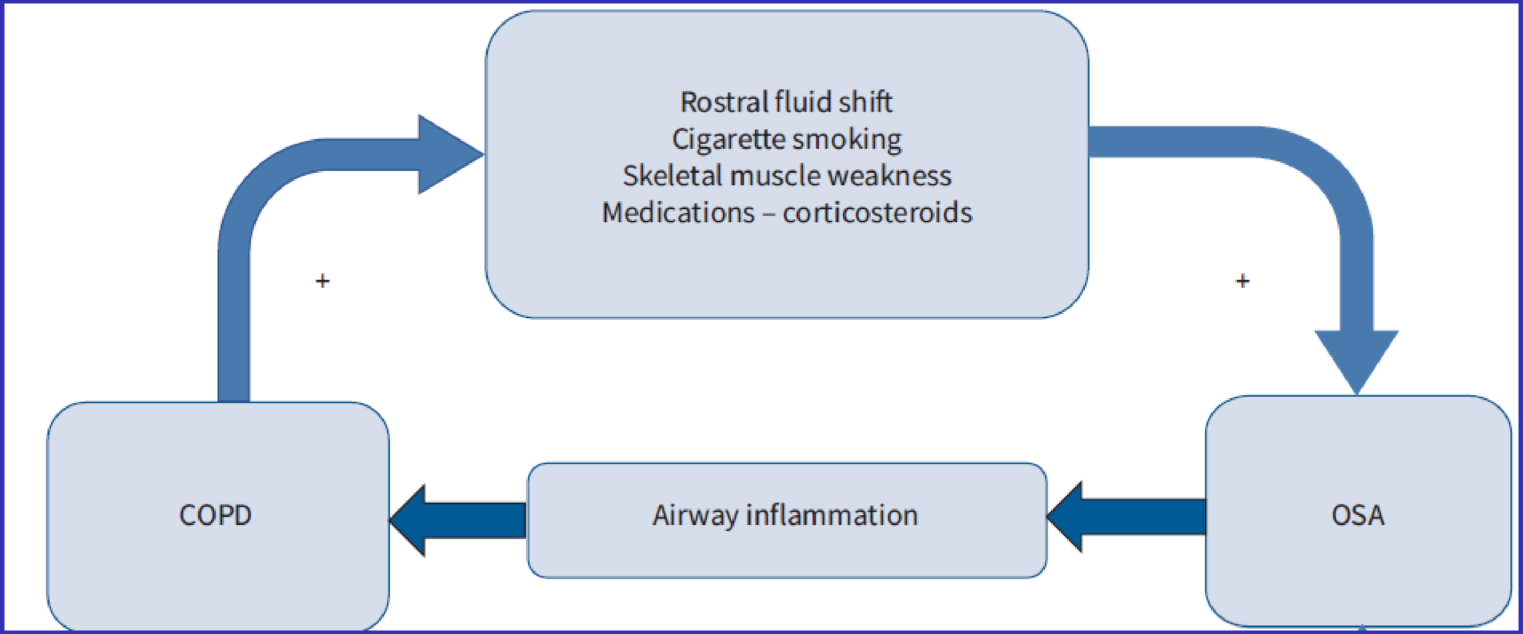
  - Smoking
    - → Sleep Q ↓
    - → expiratory flow limitation ↑
    - → upper airway collapse ↑ & Obesity ↑

OLD → OSA Pathophysiology

- COPD → Corticosteroid ↑
- → Fat deposition in neck ↑
- → abdominal fat effect on diaphragm ↑
- → Upper airway closure ↑

Ioachimescu et al, Respirology (2013) 18, 421-431

OSA ⟷ OLD
Bi-directional Relationship



Gleeson et al, Eur Respir Rev 2022; 31: 210256

COPD: Comorbidity of Asthma

- 12,743 asthmatics, study at 187 centers in Hungary

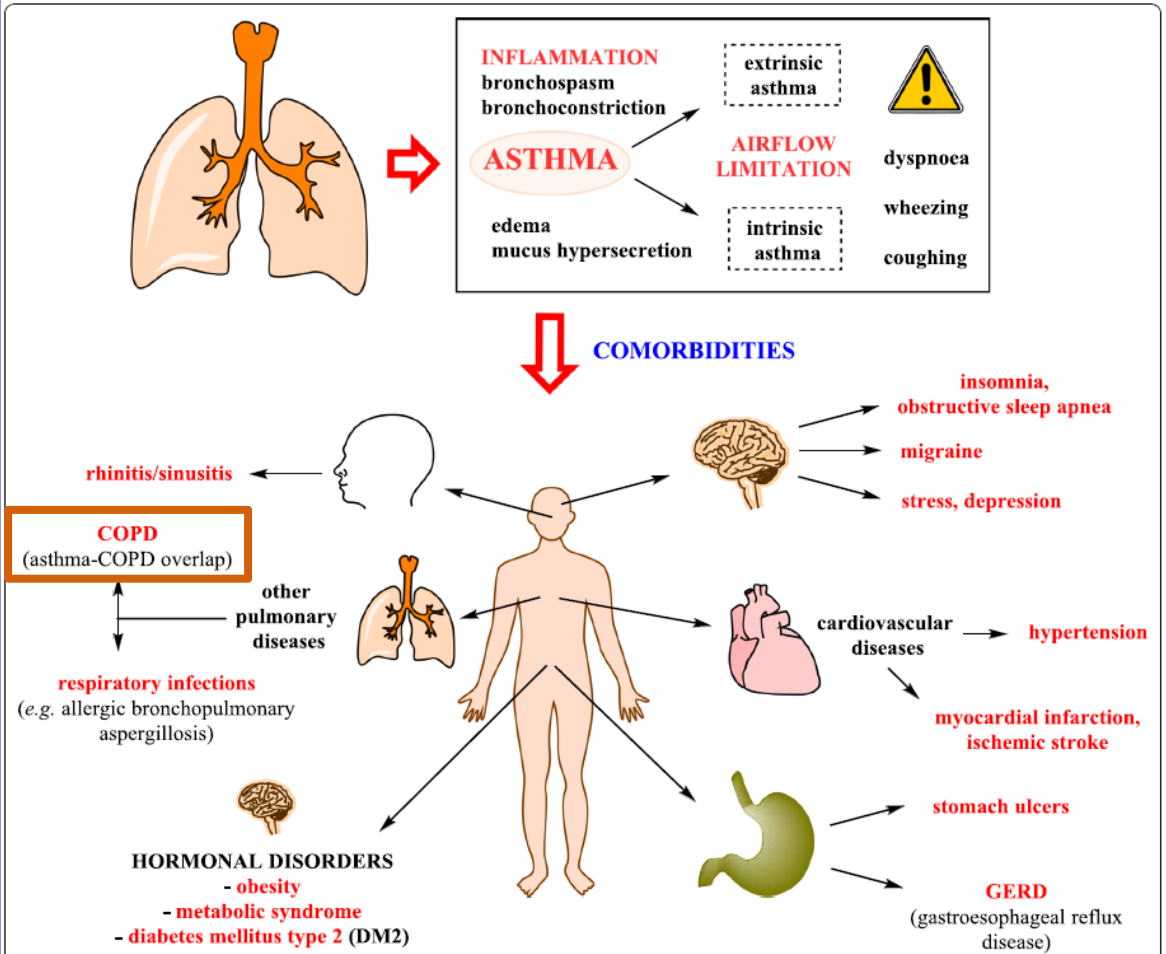
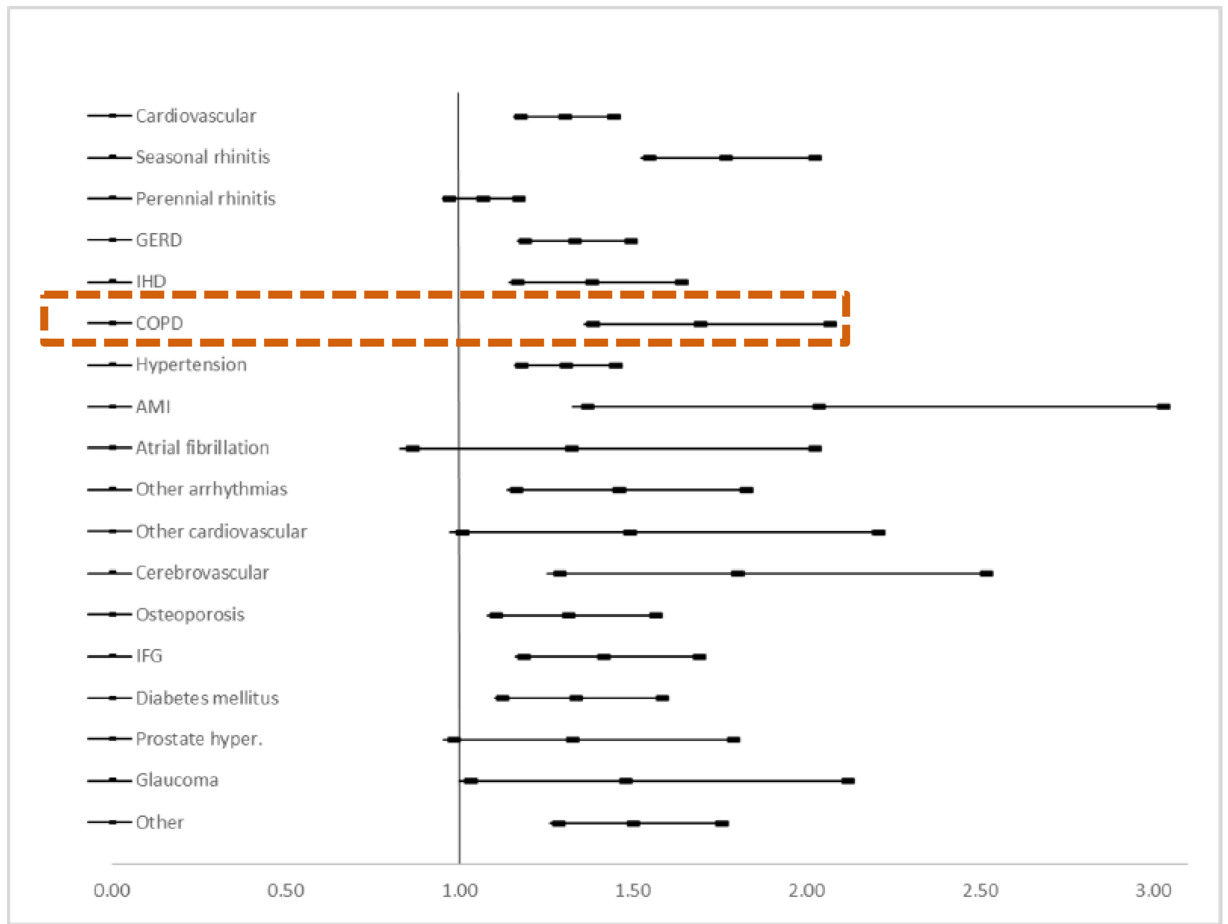


Fig. 1 The inflammatory cells and mediators in the pathogenesis of asthma (above) [3, 35], and the most frequently reported comorbid conditions (below) [11–13]. COPD = chronic obstructive pulmonary disease

Tomisa et al, Allergy Asthma Clin Immunol (2021)17-95

COPD: Comorbidity of Asthma

- COPD presence: high for partially controlled asthma

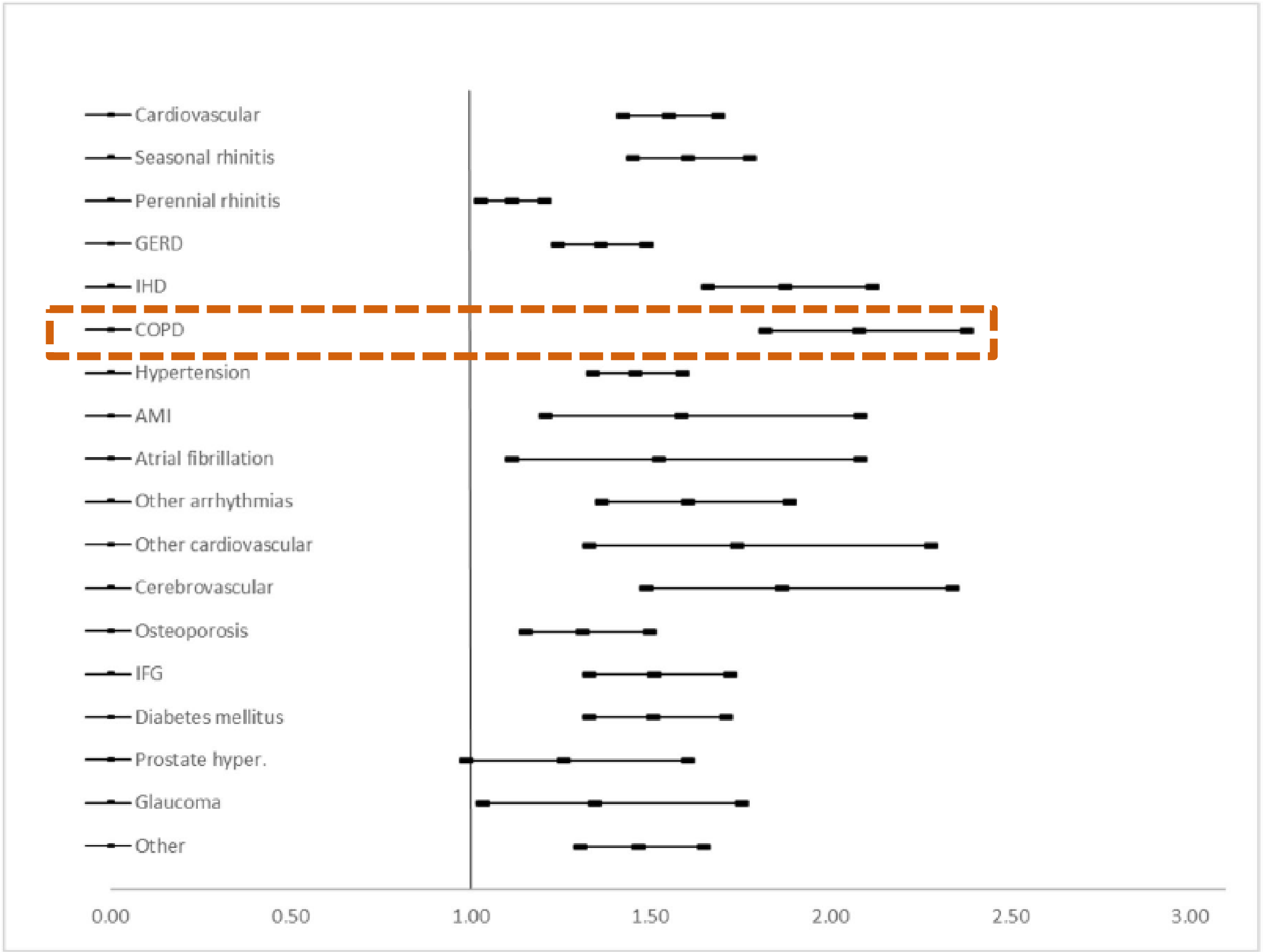


Risk of having partially controlled asthma if the given comorbidity is present

Tomisa et al, Allergy Asthma Clin Immunol (2021)17-95

COPD: Comorbidity of Asthma

- COPD presence: <u>higher</u> for uncontrolled asthma



Risk of having uncontrolled asthma if the given comorbidity is present

Tomisa et al, Allergy Asthma Clin Immunol (2021)17-95

Asthma & OSA
Alternative Overlap Syndrome

- 35% prevalence of OSA in asthmatics

- Both OSA & Asthma are highly prevalent disease
  - Coexists in some patients

Kong et al, Scientific Report 2017; 7-4088

- Have overlapping comorbidities
  - GERD, rhino sinitis, obesity

Kasabef et al, Sleep Med Rev 2007; 11)1):47-58

Asthma ⟶ OSA Pathophysiology

- GERD (commonly encountered with Asthma)
  - Proximal migration of gastric acid & prolonged acid clearance during sleep → Pharyngeal spasm & mucosal exudative neurogenic inflammation → upper airway dysfunction and prone to collapse during sleep

Harding et al, Immunol. Allergy Clin. North Am. 2005; 25: 131–48; Orr WC et al, Am. J. Gastroenterol. 2000; 95: 37–42

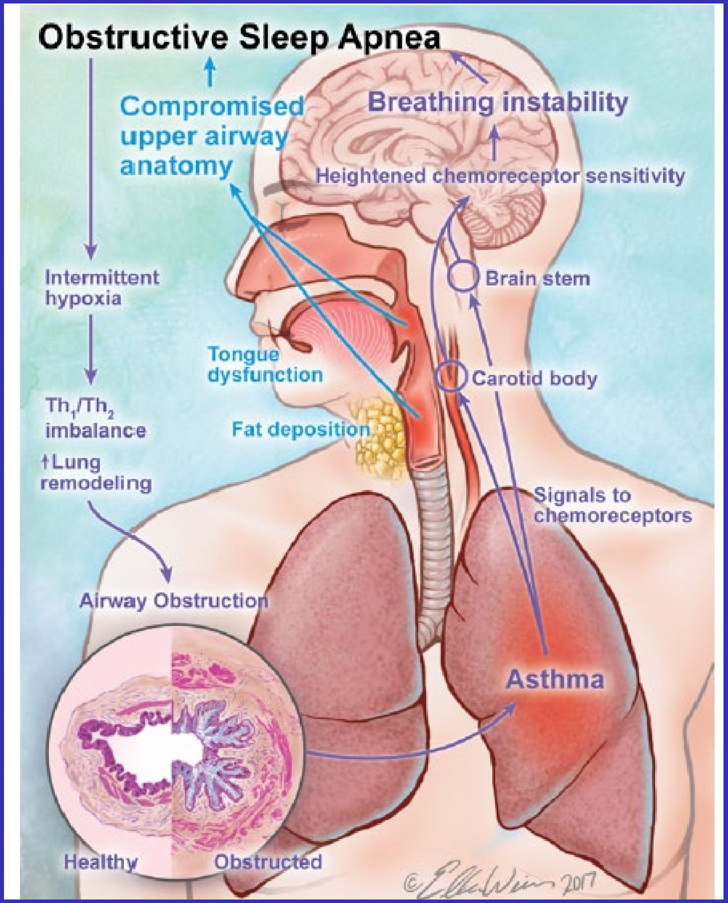
- Corticosteroids → upper airway patency
  - Local myopathy of its dilators (muscle fiber atrophy)
  - Regional fat accumulation around upper airway due to systemic absorption

Shipley et al, Sleep 1992; 15: 514–8; Donnelly et al, Am. J. Respir. Crit. Care Med. 1997; 156: 1746–51;
Martin RJ et al, Am. J.Respir. Crit. Care Med. 2002; 165: 1377–83

Asthma ⟶ OSA Pathophysiology

- Asthma's pathognomonic features, notably airway and systemic inflammation, could destabilize peripheral and central breathing and upper-airway control mechanisms.

- In conjunction with anatomical effects of long-term inhaled corticosteroid (ICS) therapy on the pharyngeal airway, it sets the stage for upper-airway collapse during sleep and OSA.



Prasad et al, Am J Respir Crit Care Med Vol 201, Iss 11, pp 1345–1357, Jun 1, 2020

Asthma → OSA

- Correlation of Asthma causing OSA is not well established.
- Evidence is based on observational studies.
- However, the evidence is quite overwhelming.

Asthma ⟶ OSA Impact

- Wang et al Meta-analysis
  - 34 studies with 27,912 subjects were included.
  - OSA was associated with more severe or difficult-to-control asthma with decreased %FEV1 in children.
  - Asthma increased daytime sleepiness in OSA patients.
  - %FEV1 tended to decrease in adult asthma patients complicated with OSA.
  - More severe asthma or difficult-to-control asthma was independently associated with OSA
  - It is strongly recommended that people with moderate-to severe or difficult-to-control asthma screen for OSA and get the appropriate treatment.

Wang et al, Eur. Journal of Medical Research 2023; 28: 139

Asthma ⟶ OSA Impact

- Teodorescu et al

  Teodorescu et al, JAMA 2015(313)2:157

  - Wisconsin Sleep Cohort Study (1988 onwards)
    - Adults to attend PSG (through 2013) at 4-year intervals
    - 1105 4-year follow-ups by 547 patients (52% women)
    - 466 = non-asthmatic; 81 = asthmatic
    - OSA = AHI >5 in 2 baseline PSGs
  - Incident OSA in 27% asthmatics versus 16% non-asthmatic
  - Asthma also associated with new onset OSA w/ habitual sleepiness

  - Asthma associated with increased risk of new-onset OSA.

Asthma ⟶ OSA
Impact

Table 1. Obstructive Sleep Apnea Burden in Asthma: Epidemiologic and Clinical Studies

Reference	Sample	Assessment and Exclusion of Treated Patients with OSA	Results
Cross-sectional studies			
Community cohorts			
Larsson *et al.*, 2001 (4)	$n = 4{,}648$	OSA*: questionnaire; OSA treatment not specified Asthma: physician diagnosis	• ↑ Prevalence of snoring (OR, 1.6†) and apnea (OR, 2.3†) in asthma
Clinical populations			
Yigla *et al.*, 2003 (5)	$n = 22$ Pulmonary clinic	OSA*: PSG; OSA treatment not specified Asthma: PFT diagnosis on long-term oral steroids	• 95% (21/22) prevalence of OSA • ↑ RDI in continuous OCS vs. intermittent OCS group (21.4 ± 3.4 vs. 11.1 ± 1.6)
Karachaliou *et al.*, 2007 (89)	$n = 1{,}501$ Primary care	OSA*: self-reported symptoms Asthma: physician diagnosis + spirometry	• Asthma diagnosis not associated with OSA symptoms
Auckley *et al.*, 2008 (90)	$n = 177$, asthma clinic $n = 328$, internal medicine clinic	OSA*: Berlin questionnaire Asthma: physician diagnosis + spirometry	• ↑ OSA risk in asthma (39% vs. 27%) • No association between asthma severity and OSA risk
Julien *et al.*, 2009 (3)	$n = 52$, asthma clinic $n = 26$, community control group	OSA*: PSG; treated OSA excluded Asthma: physician diagnosis. Severity by spirometry, ACQ, and steroid use	• ↑ OSA prevalence: severe asthma 88%, moderate asthma 58%, control 31% ($P < 0.001$) • ↑ AHI in asthma
Teodorescu *et al.*, 2009 (27)	$n = 244$ Pulmonary and asthma clinic	OSA: OSA risk (SA-SDQ); treated OSA excluded Asthma: NAEPP classification severity	• Use of ICS ↑ risk of habitual snoring; OR, 1.6† • OSA risk positively associated with asthma severity and ICS use
Teodorescu *et al.*, 2010 (61)	$n = 472$ Pulmonary and allergy clinic	OSA: OSA risk (SA-SDQ); treated OSA excluded Asthma: physician diagnosis and ACQ	• ↑ OSA risk in uncontrolled asthma; OR, 2.9†
Williams *et al.*, 2011 (91)	Asthma, $n = 200$ No asthma, $n = 1{,}135$ Prenatal clinic	OSA*: habitual snoring Asthma: self-report of physician diagnosis	• ↑ Habitual snoring before (OR, 2.1†) and during (OR, 1.8†) pregnancy in asthma

Prasad et al, Am J Respir Crit Care Med Vol 201, Iss 11, pp 1345–1357, Jun 1, 2020

Asthma → OSA
Impact

Teodorescu *et al.*, 2012 (62)	$n = 752$ Pulmonary and allergy clinic	OSA: SA-SDQ and medical records (diagnosis with PSG); treated OSA excluded Asthma: physician diagnosis	• ↑ OSA risk in asthma with persistent day and night symptoms; OR, 1.9† • ↑ Risk of PSG-diagnosed OSA in asthma with day symptoms; OR, 2.1†
Braido *et al.*, 2014 (92)	Asthma, $n = 740$ Asthma and allergic rhinitis, $n = 1,201$ Primary care	OSA*: STOP-BANG questionnaire Asthma: physician diagnosis and allergic rhinitis questionnaire	• ↑ OSA risk in asthma with rhinitis vs. asthma without rhinitis; OR, 1.4†
Teodorescu *et al.*, 2015 (6)	Nonsevere asthma, $n = 161$ Severe asthma, $n = 94$ Control, $n = 146$ Multicenter study	OSA: OSA risk (SA-SDQ); treated OSA excluded Asthma: physician diagnosis, severity by spirometry and inflammatory markers	• ↑ SA-SDQ scores in poorly controlled asthma • ↑ Sputum neutrophils associated with higher SA-SDQ

Prasad et al, Am J Respir Crit Care Med Vol 201, Iss 11, pp 1345–1357, Jun 1, 2020

Asthma ⟶ OSA
Impact

Table 1. (*Continued*)

Reference	Sample	Assessment and Exclusion of Treated Patients with OSA	Results
Longitudinal studies, population-based cohorts			
Knuiman *et al.*, 2006 (16)	*n* = 967 Prospective	Incident OSA*: self-reported habitual snoring Asthma: questionnaire	• ↑ Risk of habitual snoring in new-onset asthma; OR, 2.8†
Teodorescu *et al.*, 2015 (17)	No asthma, *n* = 547 Asthma, *n* = 81 Prospective	No OSA or PAP use at baseline Incident OSA: PSG AHI > 5 or starting CPAP treatment for OSA Asthma: physician diagnosis	• Adjusted RR of incident OSA, 1.4† in asthma vs. nonasthma • ↑ Asthma duration (> 10 yr) related to increased risk for incident OSA (RR, 1.71†) and for clinically significant OSA (OSA + excessive sleepiness; RR, 2.94†)
Shen *et al.*, 2015 (12)	*n* = 38,840 Retrospective, insurance database	Incident OSA*: ICD-9 Asthma: ICD-9	• ↑ OSA incidence in asthma vs. nonasthma HR 12.1 vs. 4.8 per 1,000 person-years • ↑ Incidence of OSA with > 1 ER visit/yr (HR, 23.8†) and with ICS use (HR, 1.3†)

Definition of abbreviations: ↑ = increased; ACQ = Asthma Control Questionnaire; AHI = apnea–hypopnea index; CPAP = continuous positive airway pressure; ER = emergency room; HR = hazard ratio; ICD = International Classification of Diseases; ICS = inhaled corticosteroid; NAEPP = National Asthma Education and Prevention Program; OCS = oral corticosteroid; OR = odds ratio; OSA = obstructive sleep apnea; PFT = pulmonary function test; PSG = polysomnography; RDI = respiratory disturbance index; RR = relative risk; SA-SDQ = sleep apnea scale of the Sleep Disorders Questionnaire; STOP-BANG = snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck circumference, and gender.

*History of OSA or treatment not specified.

†Statistically significant OR, HR, or RR.

Prasad et al, Am J Respir Crit Care Med Vol 201, Iss 11, pp 1345–1357, Jun 1, 2020

OSA ⟶ Asthma Pathophysiology

- OSA → GERD (Asthma trigger)

Demeter et al, J. Gastroenterol.n2004; 39: 815–20

- Hypoxia impairs important defenses during sleep
  - Arousal threshold to resistive loading
  - Cough & asthma symptom perception

Hlavac et al, Sleep 2006; 29: 624–31; Eckert et al, Am. J.Respir. Crit. Care Med. 2006; 173: 506–11;
Eckert et al, Am. J. Respir. Crit. Care Med. 2004; 169: 1224–30

- OSA → Persistent upper airway inflammation → CV morbidity & systemic inflammation of Asthma

Li et al, Thorax 2007; 62: 75–9; Ryan et al, Arch. Physiol.Biochem. 2008; 114: 261–6;
Lampinen et al, Allergy 2004; 59: 793–805

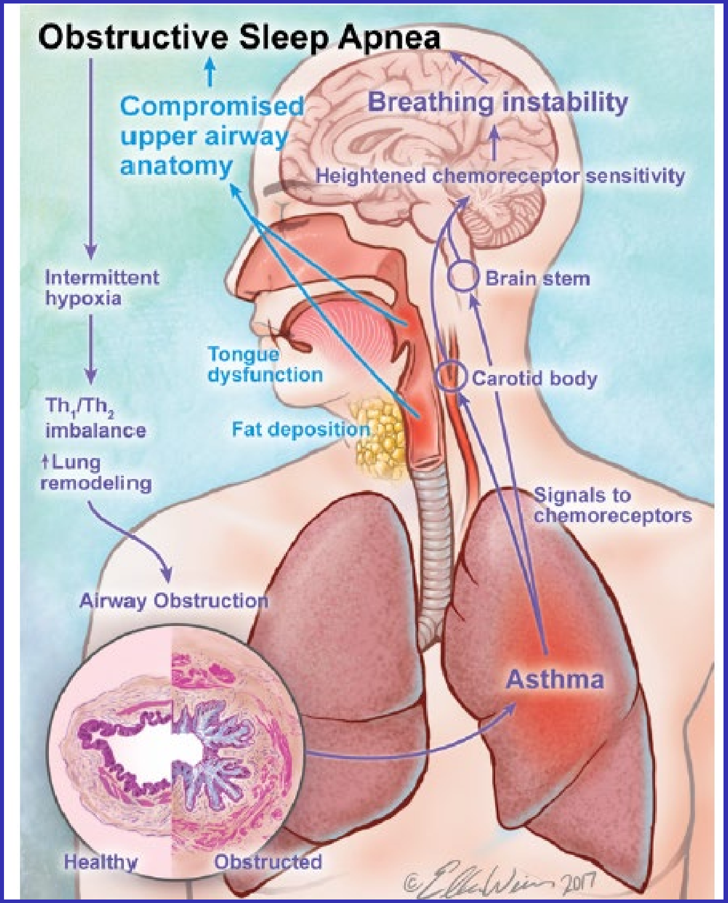
OSA ⟶ Asthma Pathophysiology

- Stimulation of upper airway during obstructive events vagally mediated bronchoconstriction in asthmatics
  - Worsens BHR through alterations of chemical arousal threshold or thorough resistive loading

Guilleminault et al, Eur. Respir. J. 1988; 1: 902–7; Morrison et al, Respir. Med. 1991; 85: 285–9

OSA ⟶ Asthma Pathophysiology

- OSA, through its features, notably chronic intermittent hypoxia, has been shown to shift the airway inflammatory profile away from T-helper cell type 2 (Th2) pathways, which leads to lung remodeling and airway dysfunction, in a pattern that is less responsive to ICS therapy.
- Asthma control would likely require a step-up in ICS dose and repeated steroid bursts, further raising the risk for or the severity of OSA.



Prasad et al, Am J Respir Crit Care Med Vol 201, Iss 11, pp 1345–1357, Jun 1, 2020

OSA ⟶ Asthma
Impact

Table 3. Impact of OSA on asthma severity and control.

Author	Year	Sample	Definition of OSA	Findings
Cross sectional				
ten Brinke [62]	2005	*n* = 136 difficult-to-treat asthma	PSG or history of snoring and daytime sleepiness with frequent apnea periods of >10 s	↑ frequent exacerbation OR 3.4 (1.2–10.4) adjusted for age and asthma duration. ↔ frequent exacerbation after accounting for covariates
Teodorescu [59]	2010	*n* = 472 outpatient clinic	Sleep Apnea Scale of the Sleep Disorders Questionnaire (high OSA risk vs. without high risk)	↑ uncontrolled asthma in high OSA risk. OR 2.87 (95% CI 1.54–5.32) accounting for covariates
Kim [60]	2013	*n* = 217 outpatient clinic	Berlin questionnaire (high risk vs. low risk)	↓ asthma specific quality of life score in high OSA risk (vs. low OSA risk) ↔ asthma control
Teodorescu [61]	2013	*n* = 813 outpatient clinic	PSG	↑ worse asthma severity step (OR 2.91, 95% CI 1.15–7.36) ↑ severe asthma (OR 6.67, 95% CI 1.74–25.56) in older subjects (age 60–75) vs. OR 2.61, 95% CI 1.28–5.33) in younger subjects (age 18–59).
Tay [63]	2016	*n* = 90 difficult asthma clinic	Berlin questionnaire (high OSA risk vs. low risk)	↔ frequent exacerbation, ACT score, and asthma-specific quality of life accounting for increasing BMI and other comorbid conditions
Ozden Mat [58]	2021	*n* = 137 outpatient clinic	Berlin questionnaire (high OSA risk vs. low risk)	↑ 7.9 times increased odds of uncontrolled asthma Odds ratio 7.896, 95% CI 2.902–21.487.

Saxena et al, J Clin Med 2023; 12, 6552

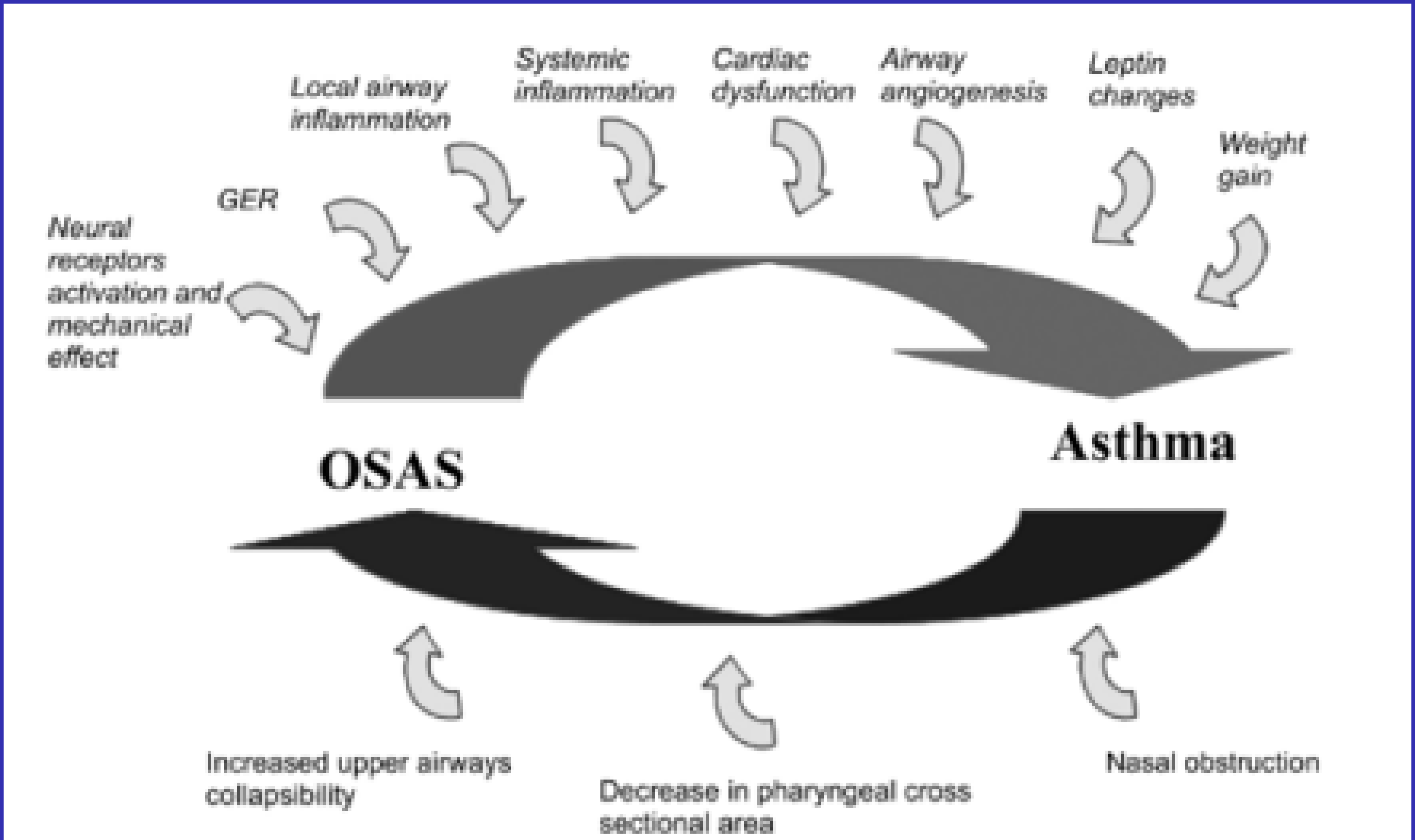
OSA ⟶ Asthma
Impact

Author	Year	Sample	Definition of OSA	Findings
Longitudinal				
Jordan [64]	2015	n = 2445 World Trade Center Health Registry, 10–11 years follow up	Physician-diagnosed OSA	↑ 1.39 and 1.48 times increased risk of poorly controlled asthma and very poorly controlled asthma, respectively, adjusting for covariates
Wang [65]	2016	n = 146 asthma n = 157 no asthma 1 year follow up	PSG	↑ AHI increased risk of severe asthma exacerbations (OR 1.322, 95% CI 1.148–1.523)
Yii [66]	2017	n = 177 Step 4 of GINA treatment ladder 5 years follow up	PSG	↔ severe asthma exacerbation

AHI, apnea hypopnea index; BMI, body mass index; CI, confidence interval; OR, odds ratio; OSA, obstructive sleep apnea; PSG, polysomnography; ↑: increased, ↓: decreased, ↔: unchanged.

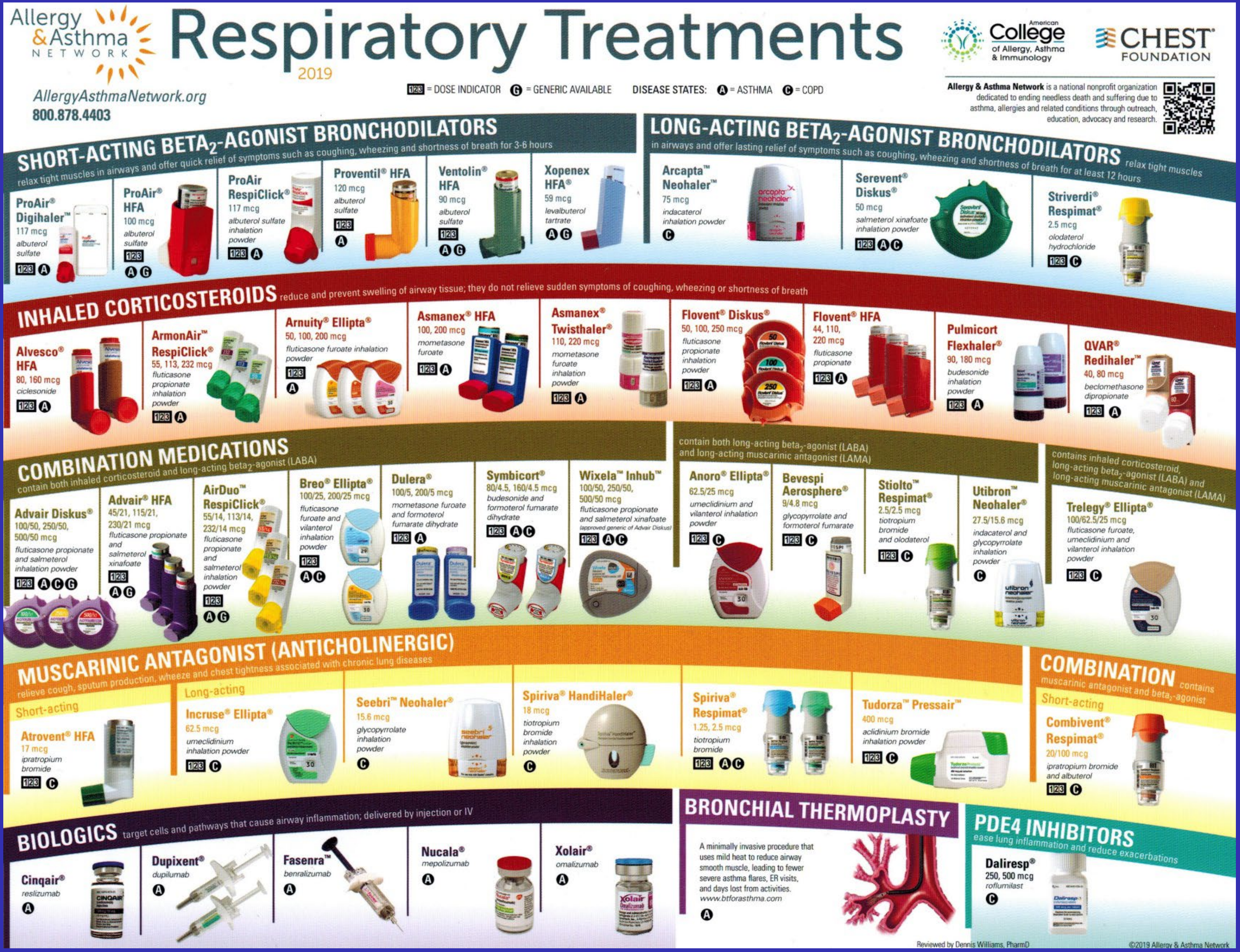
Saxena et al, J Clin Med 2023; 12, 6552

Asthma ⟷ OSA
Bi-directional Relationship



Alkhalil et al, J Clin Sleep Med 2009;5(1):71-78

Treatment of Asthma/COPD



Most Effective Treatment of OSA

Abundance of literature available showing CPAP benefits to treat OSA

CPAP ⟶ Asthma

Table 4. Impact of CPAP therapy on asthma severity and control.

Author	Year	Sample	Study Design	Findings
Lafond [69]	2007	*n* = 20 OSA and asthma	Prospective, 6 weeks after CPAP therapy	CPAP use 6.7 h/d ↔ airway responsiveness, %FEV1, FEV1/FVC ratio ↑ asthma-specific quality of life
Teodorescu [16]	2012	*n* = 75 CPAP therapy, OSA and asthma	Cross-sectional	↓ persistent daytime asthma symptoms ↔ persistent nighttime asthma symptoms
Shaarawy [73]	2013	*n* = 15 uncontrolled asthma and OSA	Prospective, 6 weeks after CPAP therapy	↓ Epworth sleepiness scale ↓ arousal index ↔ % FEV1, %FVC, FEV1/FVC ratio ↔ ACT score
Kauppi [68]	2016	*n* = 152 CPAP started after asthma treatment	Cross-sectional, survey questionnaire	CPAP use 6.3 h/d, mean 5.7 years. ↓ self-reported asthma severity and ↑ACT score without significant changes in BMI ↓ daily rescue medication use
Serrano-Pariente [71]	2017	*n* = 99 OSA and asthma	Prospective, before and after 6 months of CPAP	↓ asthma control questionnaire score ↓ % of uncontrolled asthma ↓ % of asthma attacks ↓ GERD symptoms ↓ positive bronchodilation test ↓ FeNO ↑ Asthma control and ↑ quality of life among patients compliant with CPAP (≥4 h/night) vs. noncompliant subjects.

Saxena et al, J Clin Med 2023; 12, 6552

CPAP ⟶ Asthma

Shaker [74]	2017	n = 12 OSA and asthma	Prospective, 3 months after CPAP therapy	↓ daytime and nighttime asthma symptoms ↓ GERD symptoms ↓ difficult to control asthma ↓ Epworth sleepiness scale ↑ %FEV1 ↑ FEV1/FVC ratio ↑ sleep efficiency ↓ total sleep time
Ng [72]	2018	n = 17 CPAP group n = 20 control group Nocturnal asthma symptoms and OSA	Randomized controlled trial	CPAP use, 5.0 h/d at 1 month and 5.2 h/d at 3 months ↓ Epworth sleepiness score ↑ asthma specific quality of life ↑ vital domain of quality of life ↔ ACT score ↔ asthma exacerbation rate, spirometry, and airway responsiveness
Cisneros [70]	2023	n = 100 OSA and asthma	Retrospective, before and ≥3 months after CPAP	↑ clinical asthma control ↑ ACT score

ACT, asthma control test; CPAP, continuous positive airway pressure; FeNO, fractional exhaled nitric oxide; FEV1, forced expiratory volume in 1 s; FVC, forced vital capacity; GERD, gastroesophageal reflux disease; OSA, obstructive sleep apnea; PSG, polysomnography; ↑: increased, ↓: decreased, ↔: unchanged.

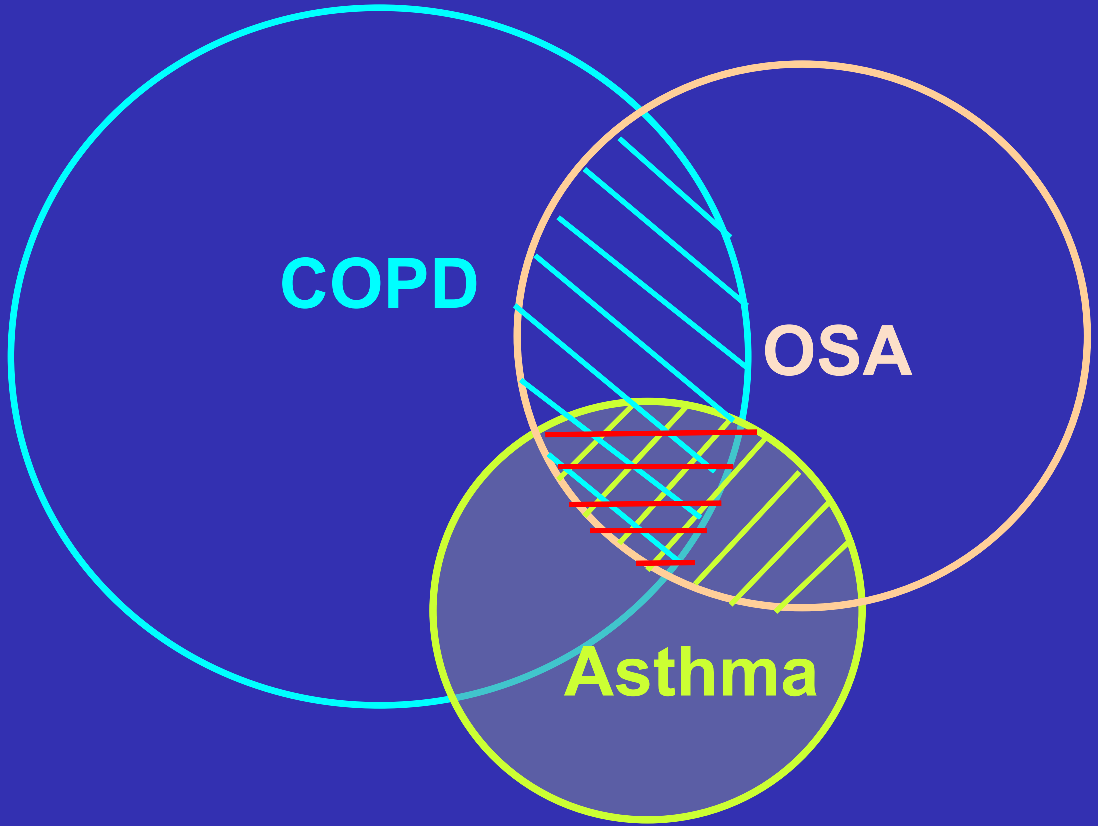
Saxena et al, J Clin Med 2023; 12, 6552

CPAP ⟶ Asthma

- Evidence mainly derived from observational studies
- More RCTs are needed to understand the impact of PAP therapy on Asthma control
- Impact of alternative OSA treatment (HNS, dental appliance etc.) on Asthma – only few studies; most with significant limitations

Integrated (OLDOSA) Overlap Syndrome

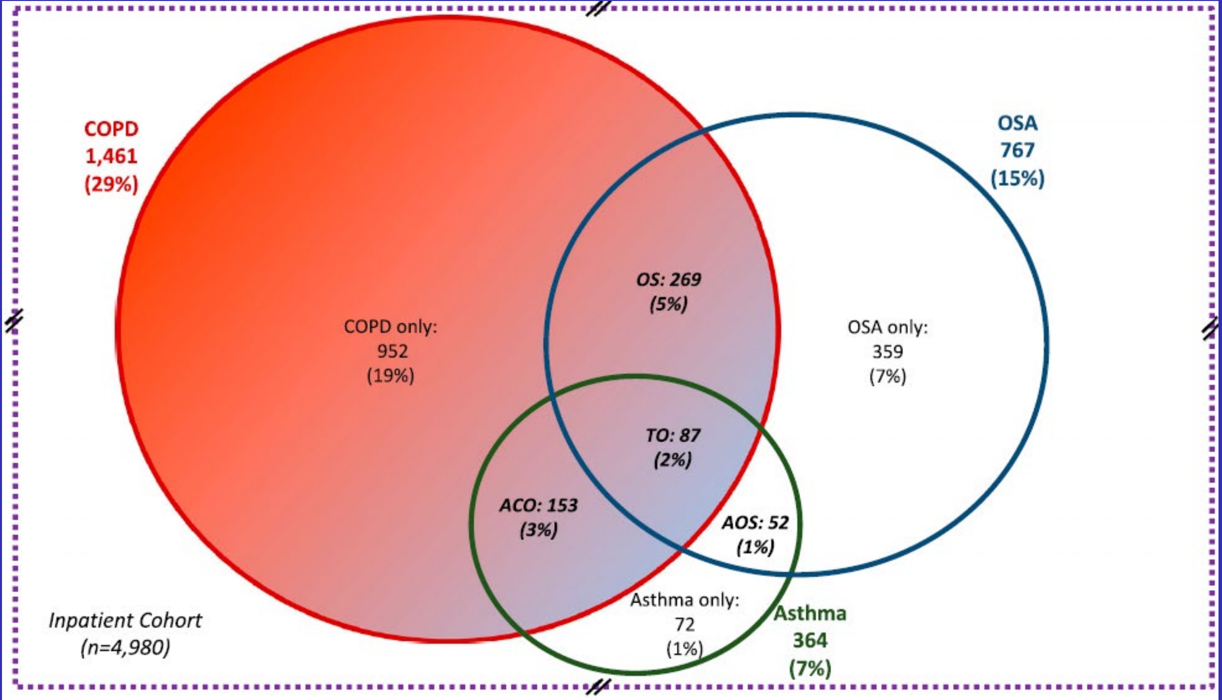
- COPD ←→ OSA
- Asthma ←→ OSA
- OLD (COPD + Asthma) ←→ OSA = OLDOSA



Ioachimescu et al, Respirology (2013) 18, 421-431

(OLDOSA) cohort study: 10-year assessment

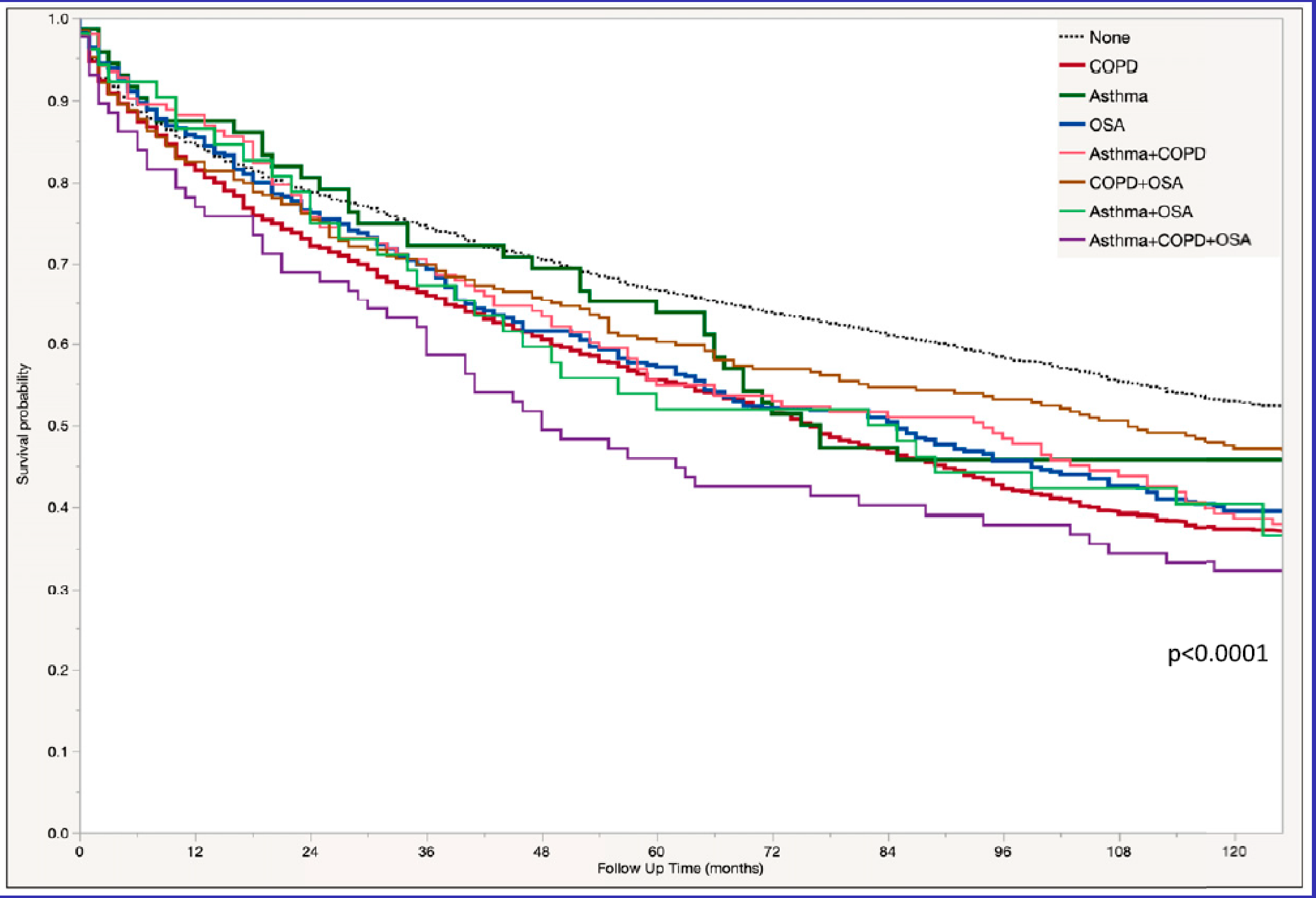
- 4,980 veterans with an acute hospitalization (Atlanta VA)
  - Asthma, COPD, OSA, overlapping conditions (40%), OR none of these had been diagnosed (60%)



Proportional Venn diagram of the OLDOSA Cohort (n = 4,980). Patient population outside the circles and inside the rectangle is represented by patients with no OSA, COPD, or asthma. Asthma, COPD, and OSA "only" = nonintersecting or nonoverlapping disorders. ACO = asthma and COPD (no sleep apnea), AOS = asthma and OSA (no COPD), COPD = chronic obstructive pulmonary disease, OSA = obstructive sleep apnea, OS = COPD and OSA (no asthma), TO = triple overlap of asthma, COPD and OSA.

Ioachimescu et al, J Clin Sleep Med. 2020;16(2):267–277

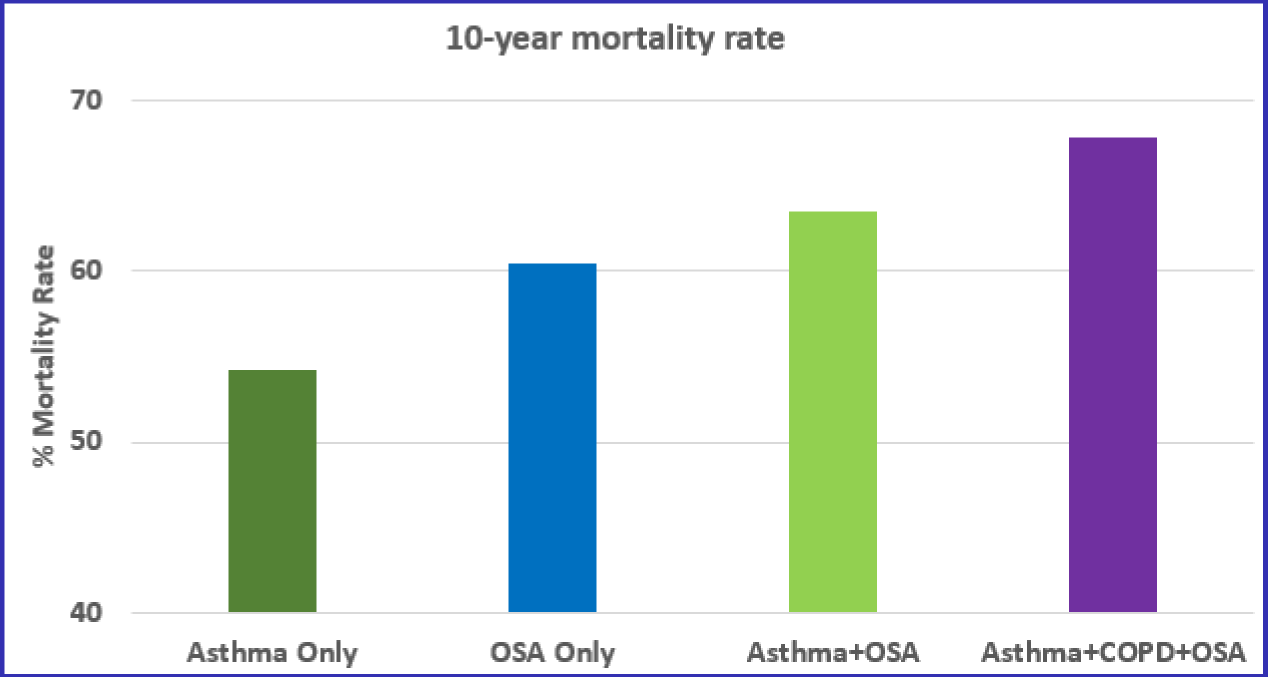
(OLDOSA) cohort study: 10-year assessment



Ioachimescu et al, J Clin Sleep Med. 2020;16(2):267–277

(OLDOSA) cohort study: 10-year assessment

- Asthma, COPD, OSA and their overlap syndromes had very high long-term mortality.

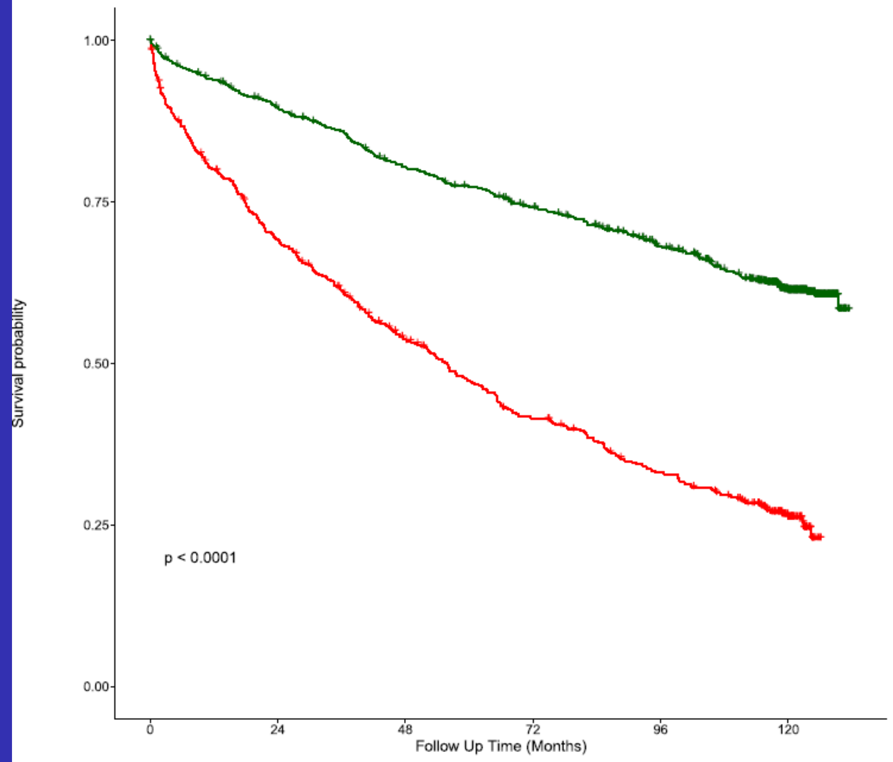


Ioachimescu et al, J Clin Sleep Med. 2020;16(2):267–277

(OLDOSA) cohort study: 10-year assessment

- OSA patients not on PAP therapy had 1.34 times higher risk of death

Figure 3—Survival plots by PAP therapy.



Number at risk (number censored)

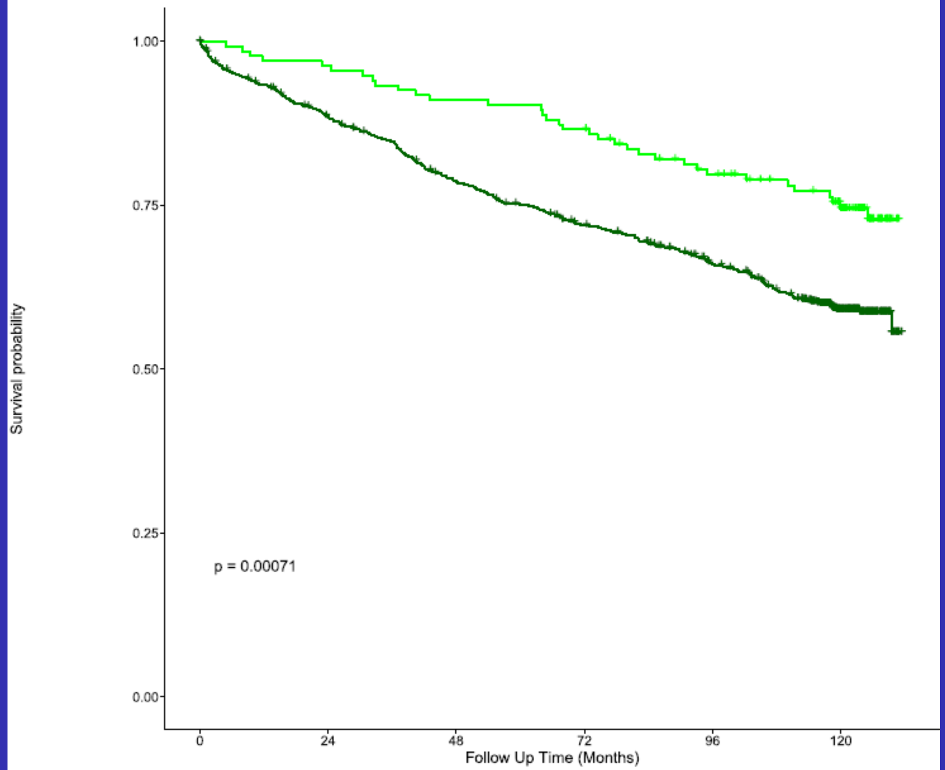
	0	24	48	72	96	120
OSA not on PAP	506 (0)	341 (11)	253 (24)	190 (30)	147 (36)	59 (96)
OSA on PAP	925 (1)	815 (15)	725 (22)	657 (33)	580 (57)	354 (230)

Ioachimescu et al, J Clin Sleep Med. 2020;16(2):267–277

(OLDOSA) cohort study: 10-year assessment

- OSA patients nonadherent to PAP therapy had 1.78 times higher risk of death

Figure 4—Survival plots by PAP adherence.



Number at risk (number censored)

	0	24	48	72	96	120
OSA: PAP Adherent	134 (0)	129 (0)	122 (0)	116 (0)	101 (6)	79 (23)
OSA: PAP Non−Adherent	791 (1)	686 (15)	603 (22)	541 (33)	479 (51)	275 (207)

Ioachimescu et al, J Clin Sleep Med. 2020;16(2):267–277

Summary

- Asthma & OSA both are highly prevalent diseases
- OSA ↔ Asthma : Bi-directional relationship
- Moderate-to-Severe or Difficult to control Asthma → OSA workup
- Higher mortality rate for OSA Asthmatics than OSA only or Asthma only
- CPAP therapy reduces mortality in asthmatics OSA patients
  - Adherence to CPAP further helps reducing mortality
- COPD+Asthma+OSA may present an independent clinical category that needs to be studied further
  - Integrated OLDOSA Overlap Syndrome

Recommendations

- Closely look at screening Asthma patients for OSA
  - Especially in patients with higher BMI and more severe form of Asthma
- Clinicians should keep a low threshold to rule out OSA
  - Particularly in elderly/overweight male asthmatics with difficult to control asthma
  - Use STOP-Bang Questionnaire
- Look out for development of Asthma in OSA patients
  - Especially in younger patients, and in patients with co-existing COPD
- Manage both OSA and Asthma simultaneously
  - Coordination of care among providers

Thank You !

Questions?