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Asthma and COPD: Confounders, Mimics and New Developments

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Asthma and COPD: Confounders, Mimics and New Developments: Learning Objectives

In a Clinical Case-Based Approach:

- **Discuss Asthma and COPD, and Selected Confounders and Mimics of Them**
- **Discuss Selected New Developments in These Diseases**

Sybil: Simple COPD or *COPD Plus?*

Red Flags of Concern

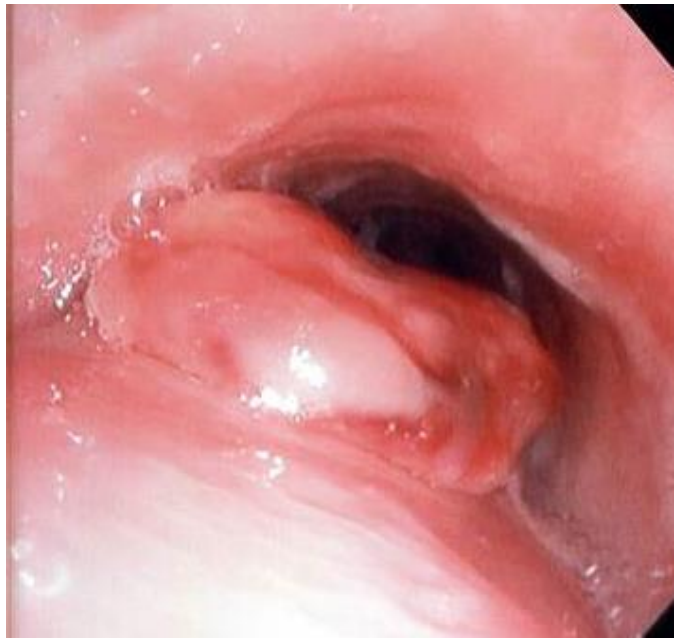
- **Frequent Urgent Care Visits**
  - **“. . . requiring several urgent care visits. . .”**
  - **“. . . several more urgent care visits this year . . .“**
- **Troubling Increased Symptoms Including Nocturnal**
  - **“. . . simple things . . . cause her to develop shortness of breath. . . .”**
  - **“. . . us(ing) her albuterol 2 to 3 times/day almost daily . . .“**
- **Relatively Unresponsive to Standard Therapies**
  - **Albuterol, Low Dose ICS/LABA, High Dose ICS/LABA, Prednisone, Antibiotic**

Case 1

- 43 yr old man, cough, sputum, wheeze, progressive DOE, weight gain over 6 months
- Albuterol, ICS, Oral Steroids, 2 Hospitalizations

Presumptive Diagnosis of Uncontrolled Asthma

- Presents to ED near-respiratory failure, stridor, CO_2 retention
- Admitted to MICU

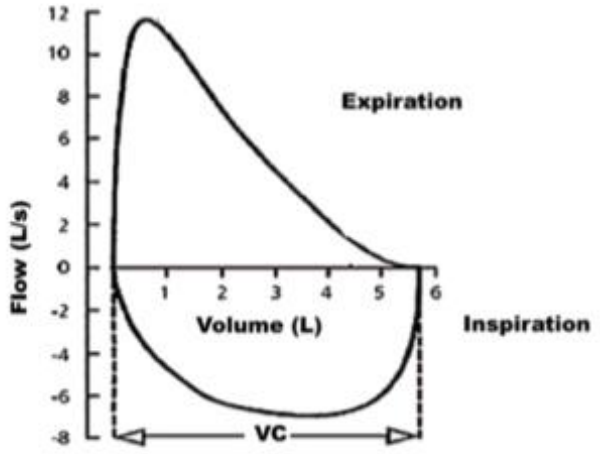


Clinical Pearls in Tracheal Obstruction

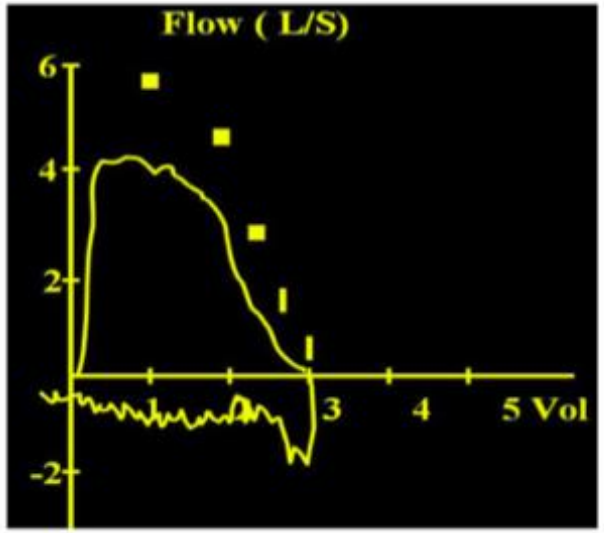
- Tracheal obstruction often mistaken for asthma / COPD
  - CLASSIC – No response to bronchodilator and steroids
  - Progression from DOE to SOB at rest despite tx
- Impaired mucus clearance and difficult to expectorate sputum common
- Patients most commonly are diagnosed with “late” disease
- Stridor is inconsistent finding

Usefulness of Flow Volume Loops

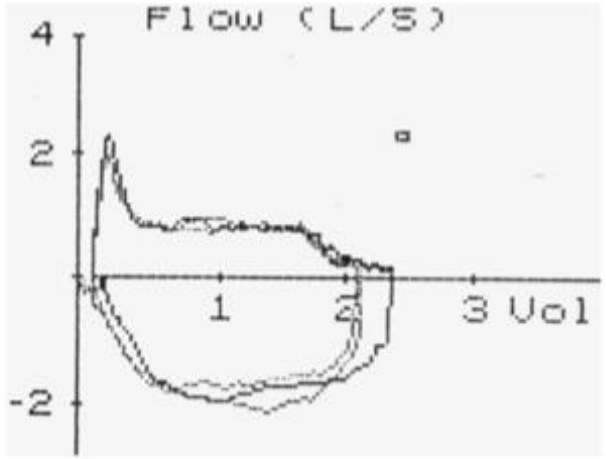
A. Normal



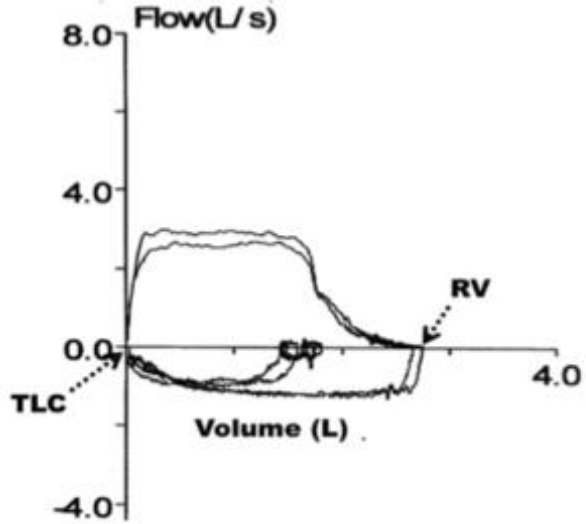
B. Variable Extra-Thoracic Obstruction



C. Lower Airway Obstruction



D. Fixed Extra-Thoracic Obstruction



Al-Quadi, 2013. Respiratory Medicine, 107:1301

Sybil: Lung Function Testing

SPIROMETRY:	BASELINE	POSTBRONCHODILATOR
FVC:	83% Predicted	INCREASED 5%
FEV 1:	69% Predicted	INCREASED 10%
FEV1/FVC	0.66	0.69

Flow Volume Loops Could Have Been Informative

Complete PFTs (Done)

Key Point

You can't get the correct answer if you ask the wrong question.

- **The question maybe should not be "Why is my patient's asthma (COPD) not responding to treatment?"**

BUT

- **"Why is my patient Short of Breath?"**

Make the Correct Diagnosis!

Case 2 – Presentation

Wechsler. JAMA 1998; 279:455-457

Healthy Woman, Sinusitis and Asthma at 40 yr

- **ICS, theo, β-Ag, frequent OCS**
- **Zafirlukast – Improved over 2 mo; D/C OCS**
- **2 wk – Rash, Fever, Diarrhea, Dyspnea**
- **Tachycardia, Wheezes**
- **Unilateral Foot Drop**

- **WBC 26K, 37% Eos**
- **CXR – Patchy Infiltrates**
- **ECHO – Global Hypokinesis, EF 35-40%**
- **Skin Bx – lymphocytic and eos perivascular infiltrates**
- **Lung Bx – Necrotizing, granulomatous vasculitis**
- **Treatment – Corticosteroids and Cyclophosphamide**

Churg-Strauss: LTRA and Systemic Steroid Discontinuation

Asthma Plus[1]

- Churg Strauss Syndrome – Vasculitis, GI involvement, ?Medications
- Allergic Bronchopulmonary Aspergillosis – Infiltrates, Obstruction and Restriction, IgE
- Occupational Asthma (vs RAD –Reactive Airways Dysfunction) – History, PFTs
- Anaphylaxis – Multisystem, Serum Tryptase

[1] Every Patient with Severe Airways Disease test for α1-AT Deficiency

Case 3 - Presentation

56 year old Woman in NC

- **Chronic dyspnea, and DOE**
- **Cough, occasionally productive sputum**
- **History of pneumonia in past**
- **30 pk-yr Smoking**
- **Wheeze on examination**
- **Symptom improvement with bronchodilators, occasional antibiotics**

Spirometry

- **FEV1/FVC = 67% (Obstructed)**
- **FEV1 78% predicted (Abnormal)**
- **FVC 98% predicted (Normal)**
- **8% FEV1 Increase After Albuterol (Incomplete Reversibility)**

Diffusing Capacity

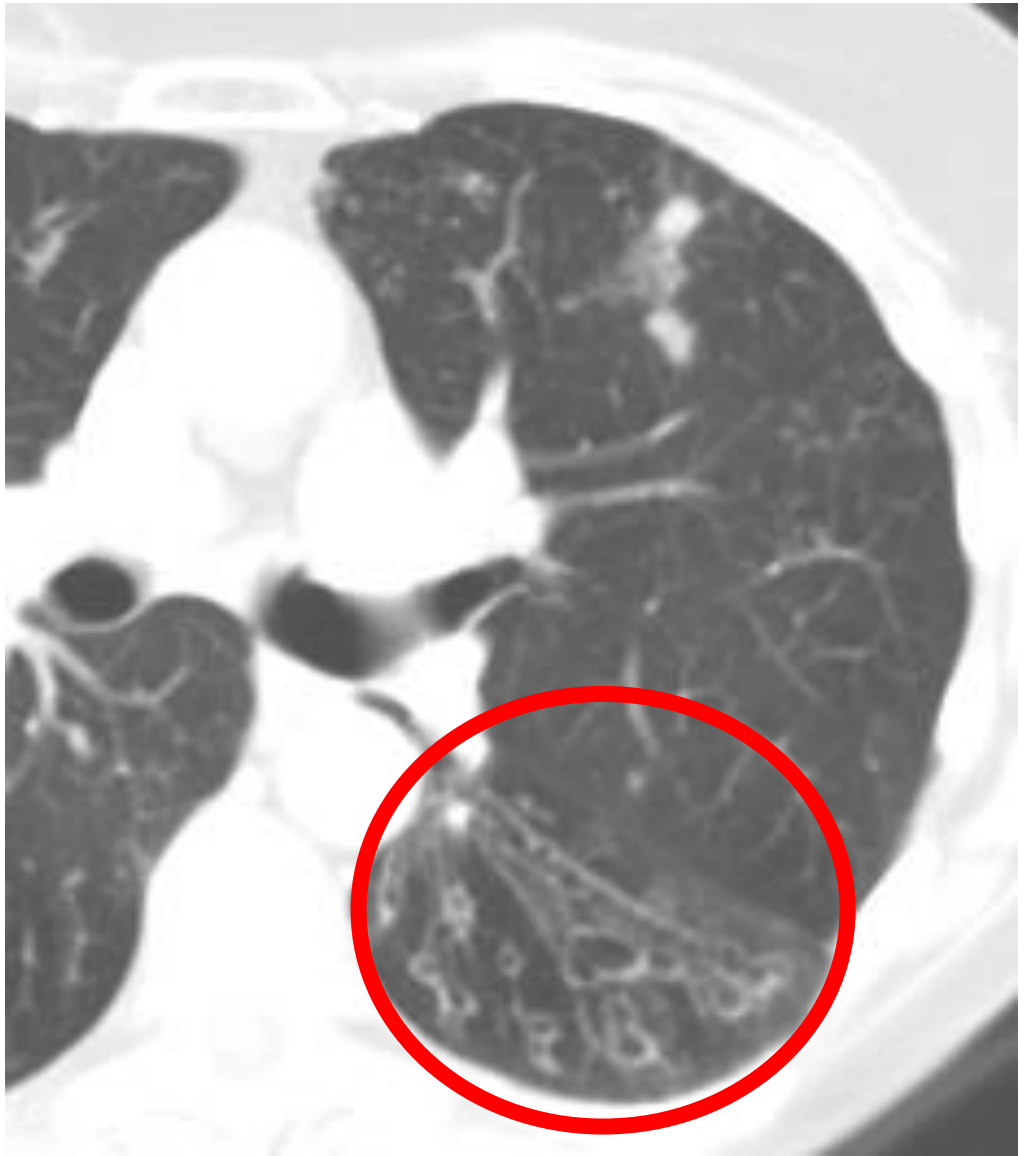
- **73% predicted (Reduced)**

What is this Patient's Obstructive Airways Disease?

Other Obstructive Lung Diseases

- COPD
  - FEV1/FVC < 70% after Bronchodilators
  - Emphysema (Decreased D_LCO)
  - Chronic Bronchitis (History - Cough & Spit)
- Alpha-1 Antitrypsin Deficiency (Younger Onset, CXR, Blood Test)
- Bronchiectasis (History, CXR, CT Scan)
- Bronchiolitis (Exam, FEV_{25-75}, CT Scan)
- Cystic Fibrosis (CXR, CT Scan, CF features, Sweat Cl^-, Genetics)
- Endobronchial Diseases (Systemic Features, Decreased TLC [Restrictive Lung Disease], Bronchoscoscopy with Biopsy)
  - Sarcoidosis
  - Amyloidosis

Other Obstructive Lung Diseases - Bronchiectasis



Bronchiectasis or other pulmonary disease (infective, neoplastic, or granulomatous)

Sybil: Does She Have *COPD Plus?*

- **Anatomic/Structural Issues**
  - Flow Volume Loops
  - Airway Exam?
- **A Secondary Cardio- Pulmonary Issue**
  - Lung Imaging - HCT Scan [Done], CT Scan with Contrast
  - Specialized Testing - α1-AT, Cystic Fibrosis, etc.
  - Cardiac Echo - Heart Failure, Pulmonary Hypertension
- **Issues Associated with Obesity (Ht. 5 ft. 6 in. Wt. 190 lb. BMI: 30.7)**
  - Sleep Disorder - OSA, OHS
  - Diabetes, PreDiabetes – HbA1c Elevated?
    - Candidate for GLP-1 agonist: Semaglutide (Weight Loss!)

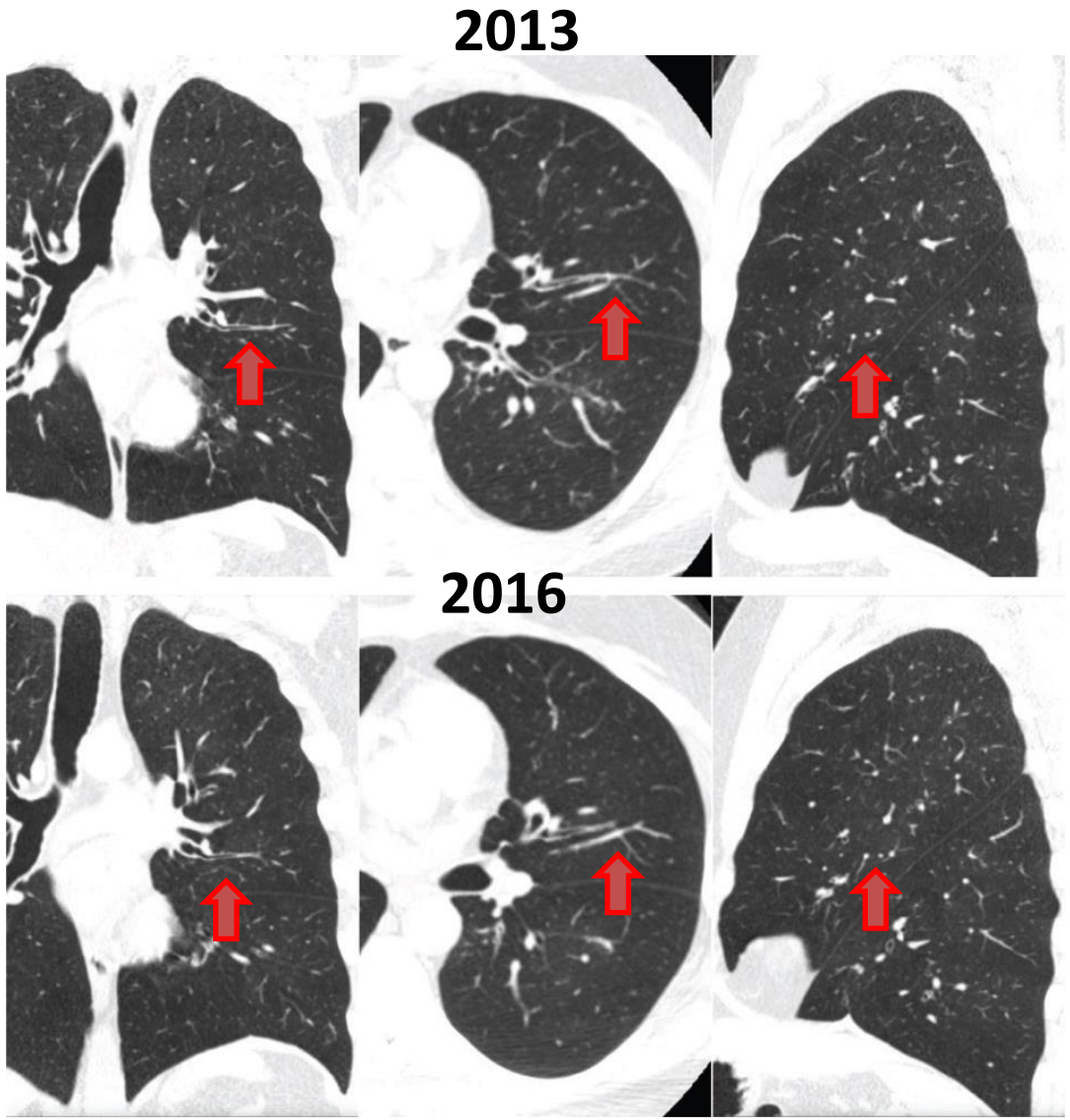
Emerging Concepts in Asthma and COPD Insights from Imaging

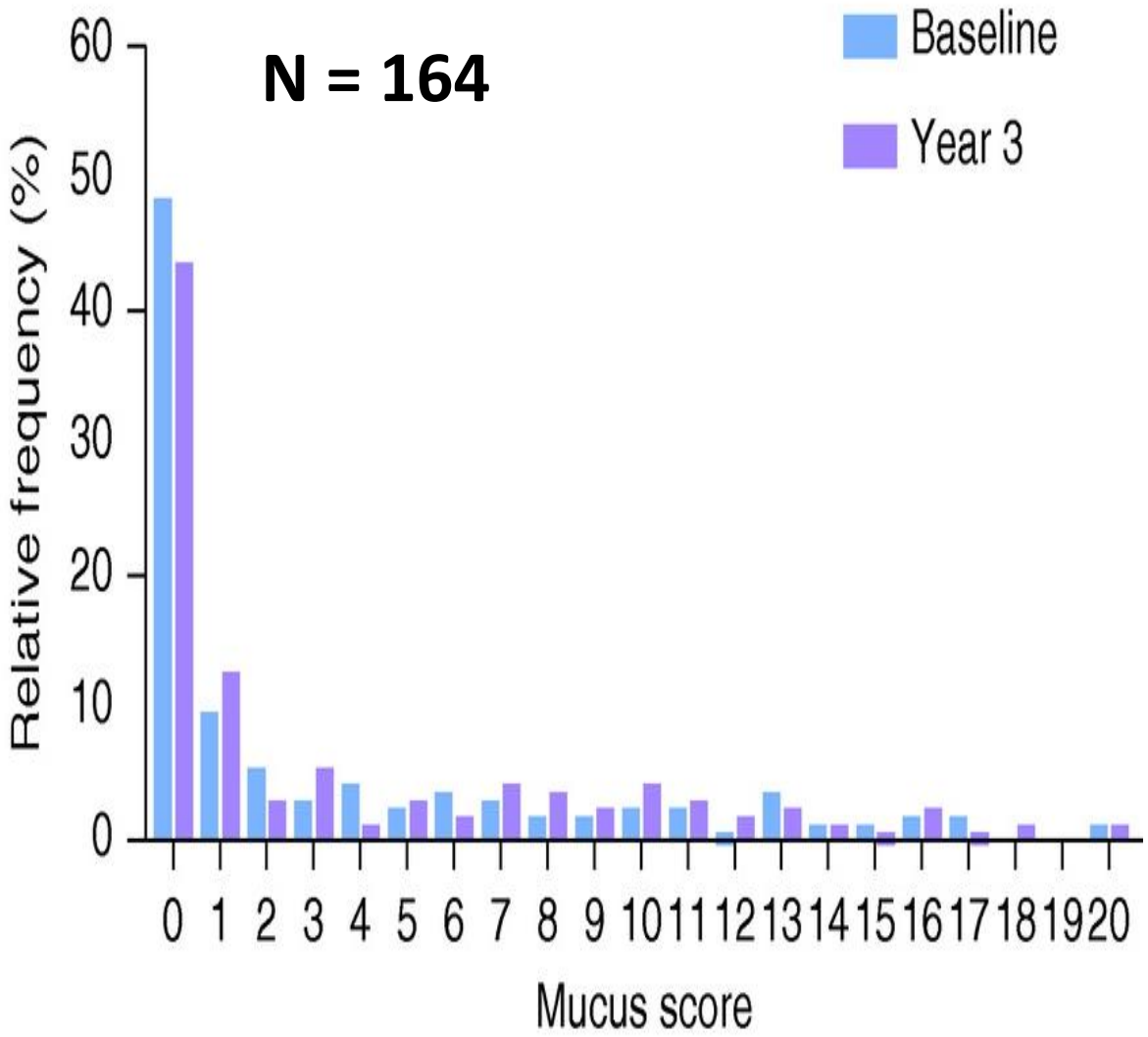
- **Mucus: Important in the Pathogenesis of Aiways Disease in Many Patients**
  - **Hard to Quantitate**
  - **Difficult to Treat**

- **Importance of Mucus Plugging**
  - **Asthma**
  - **COPD**

Persistent Mucus Plugging in Asthma

Tang, et al. Am J Respir Crit Care Med 2022; 205:1036-1045





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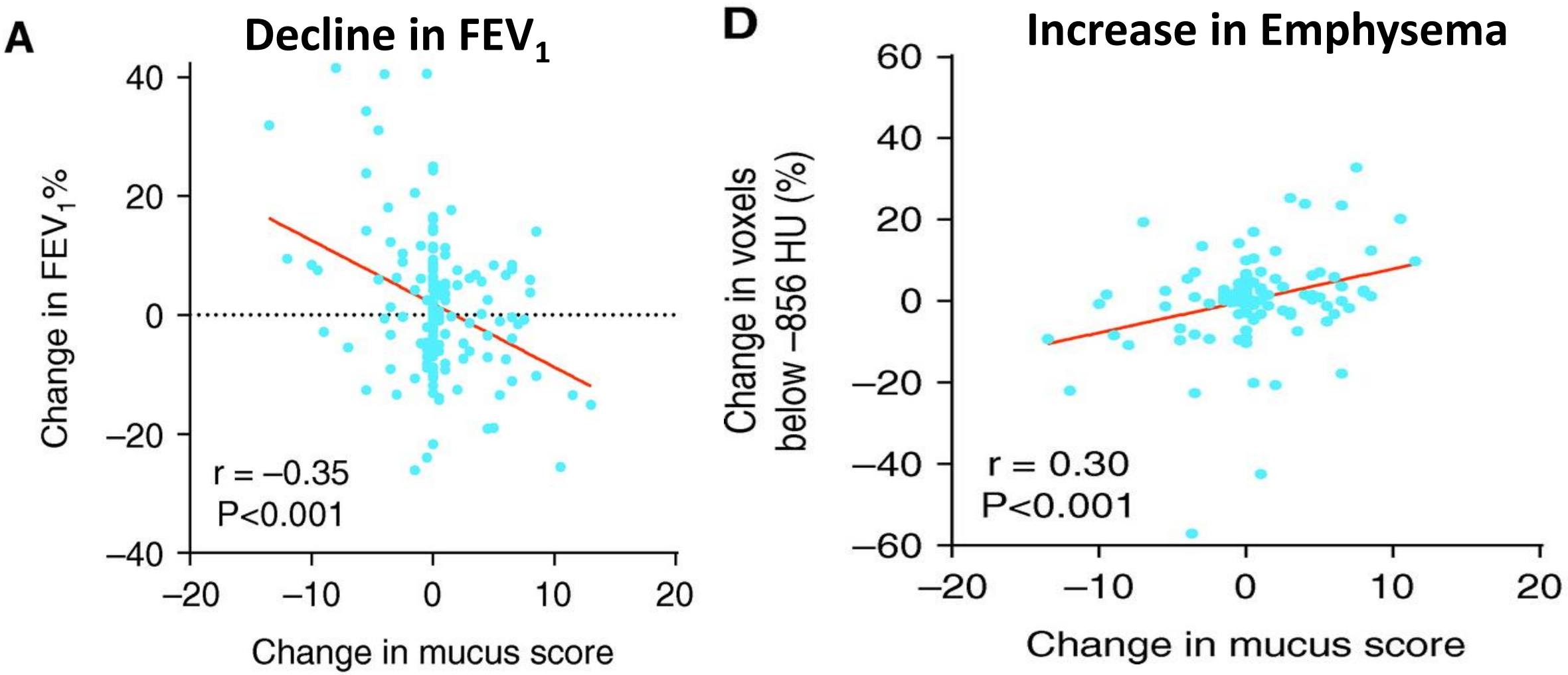
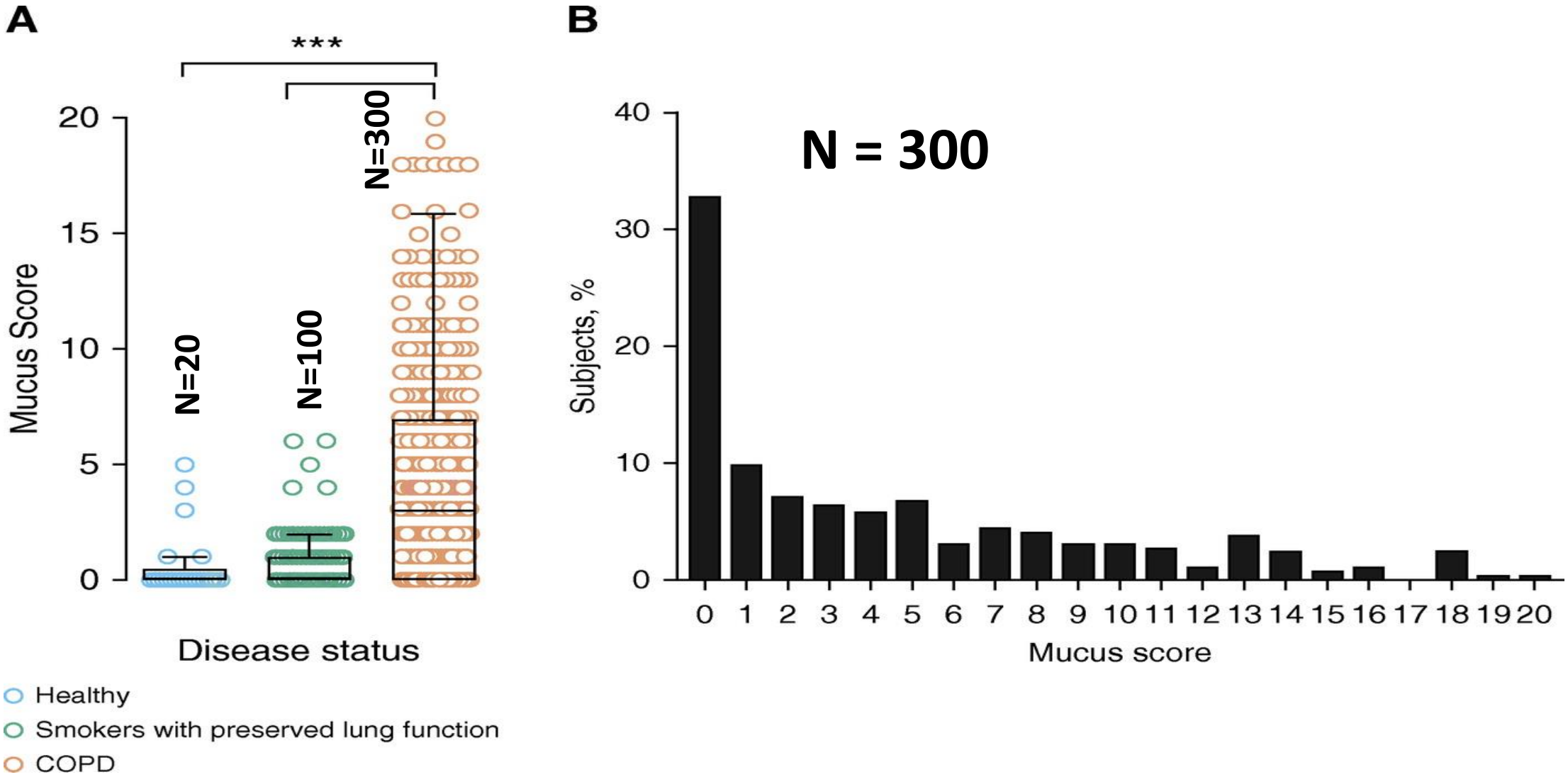
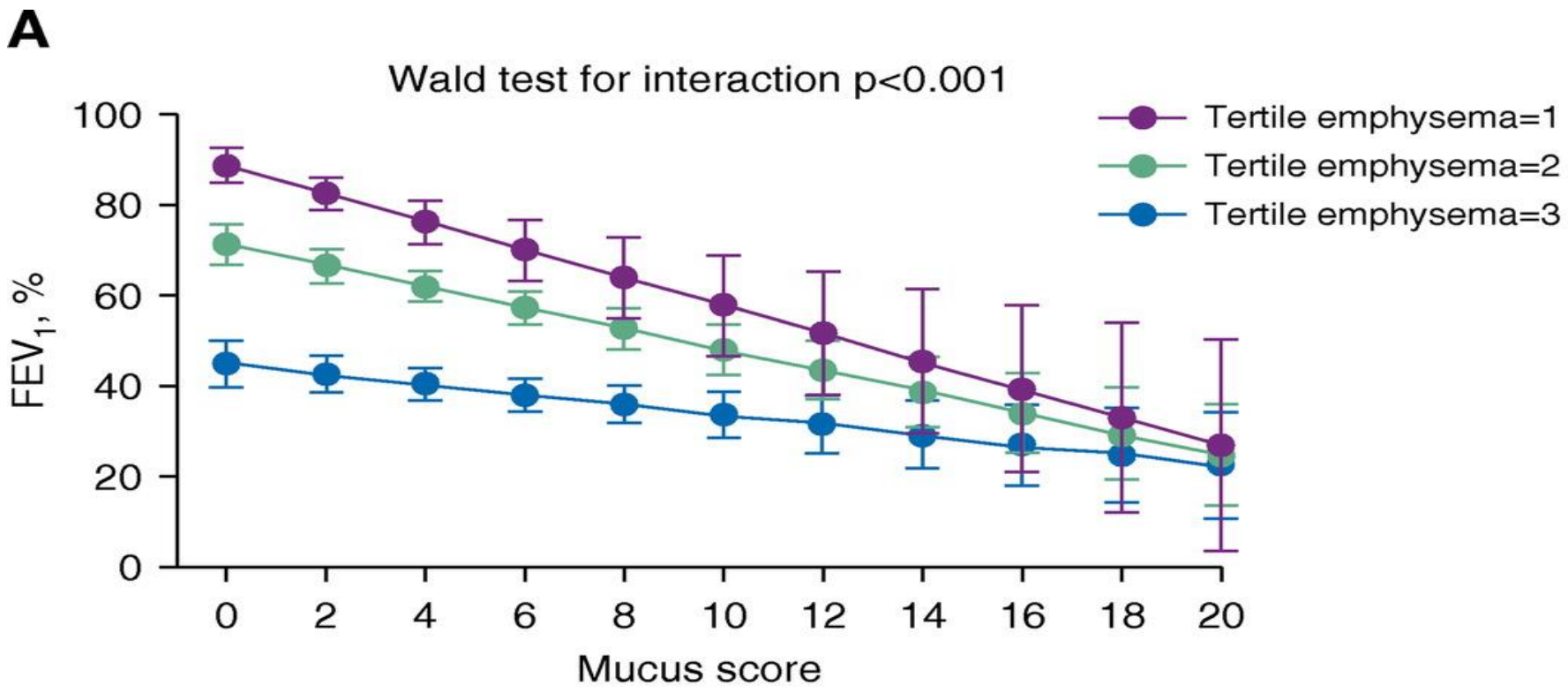


Mucus Plugs in COPD – A Common Finding

Dunican, et al., Am J Respir Crit Care Med 2021; 203:957-968



Mucus Plugs in COPD – ⇩ FEV1 Unrelated to Emphysema Dunican, et al., Am J Respir Crit Care Med 2021; 203:957-968



Percent Emphysema Tertile	N (%)	dy/dx	95% CI	P value
1 (0.04 – 2.4)	134 (33.6)	–3.1	–4.3, –1.9	<0.001
2 (2.5 – 13.0)	132 (33.1)	–2.3	–3.0, –1.7	<0.001
3 (13.1 – 48.8)	133 (33.3)	–1.1	–1.9, –0.4	0.004

Case 4 - Presentation

- **45 yr old Man: Cough and Progressive Dyspnea Over Past Year**
- **25 Pk-Yr Smokings history (1 ppd)**
- **CAT: 15**
- **Exam Unremarkable**
- **CXR: few increased markings**
- **FEV_1/FVC 75%, FVC 85% Predicted (Post BD, 5% BD Response)**

Emerging Concepts in Asthma and COPD

The Conundrum of Symptomatic Smokers[1]
with Preserved Spirometry

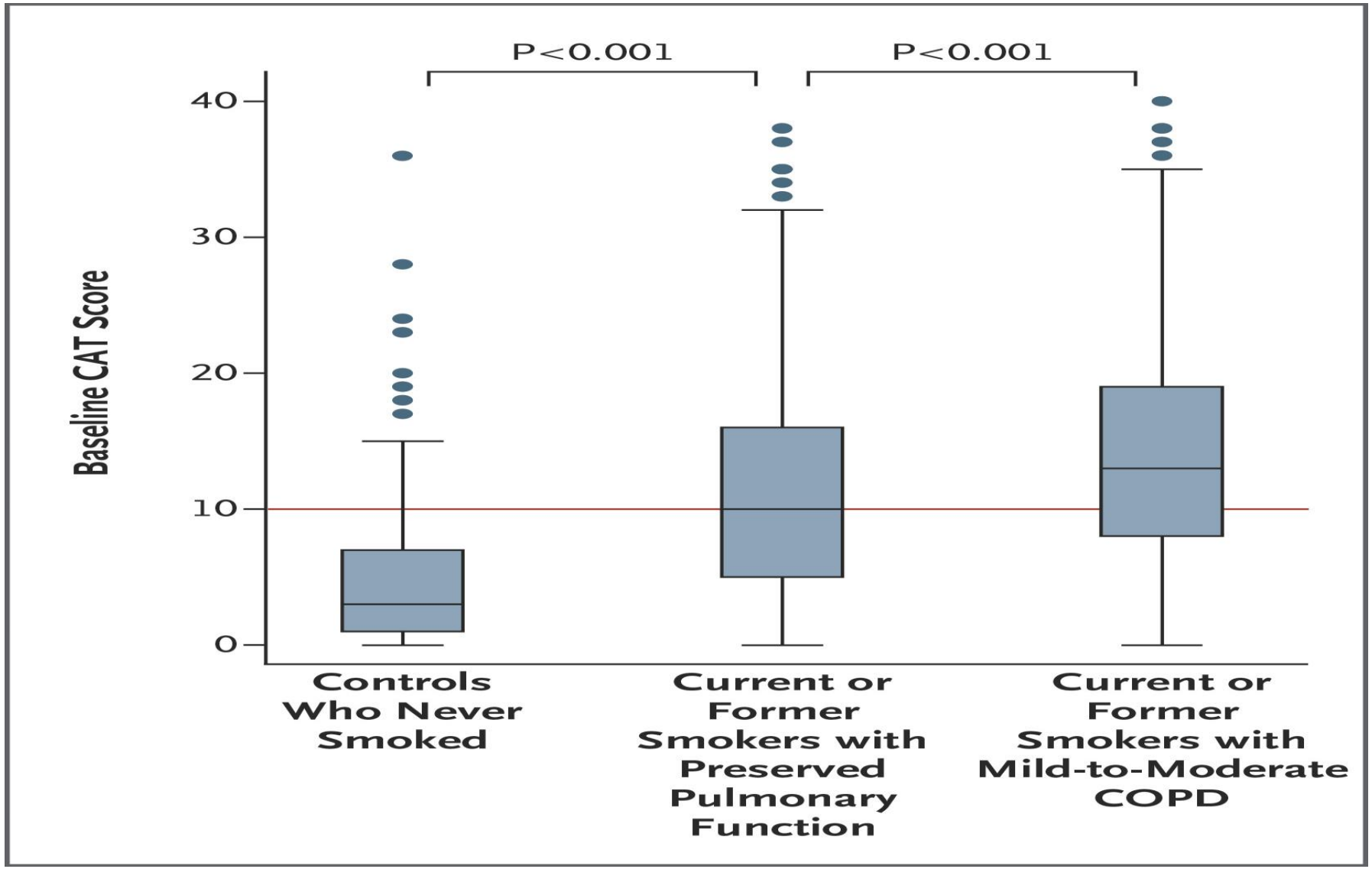
Symptomatic Tobacco-Exposed Persons[1]
with Preserved Spirometry (sTEPPS)

Non-Obstructive Chronic Airways Disease (NCAD)

[1]From Politically Correct Police

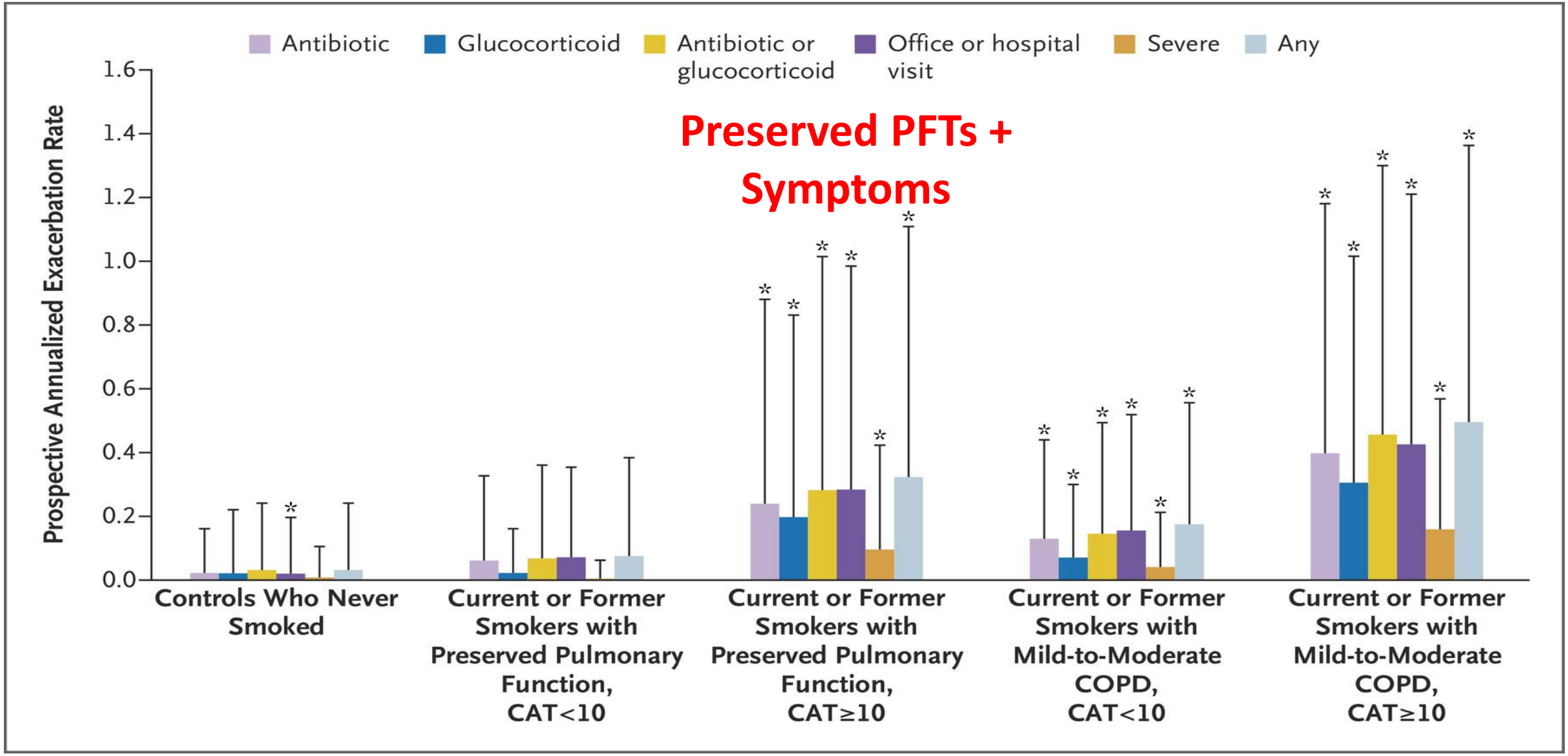
Smokers with Preserved Lung Function - Symptoms

Woodruff, et al. N Engl J Med 2016; 374:1811-1821

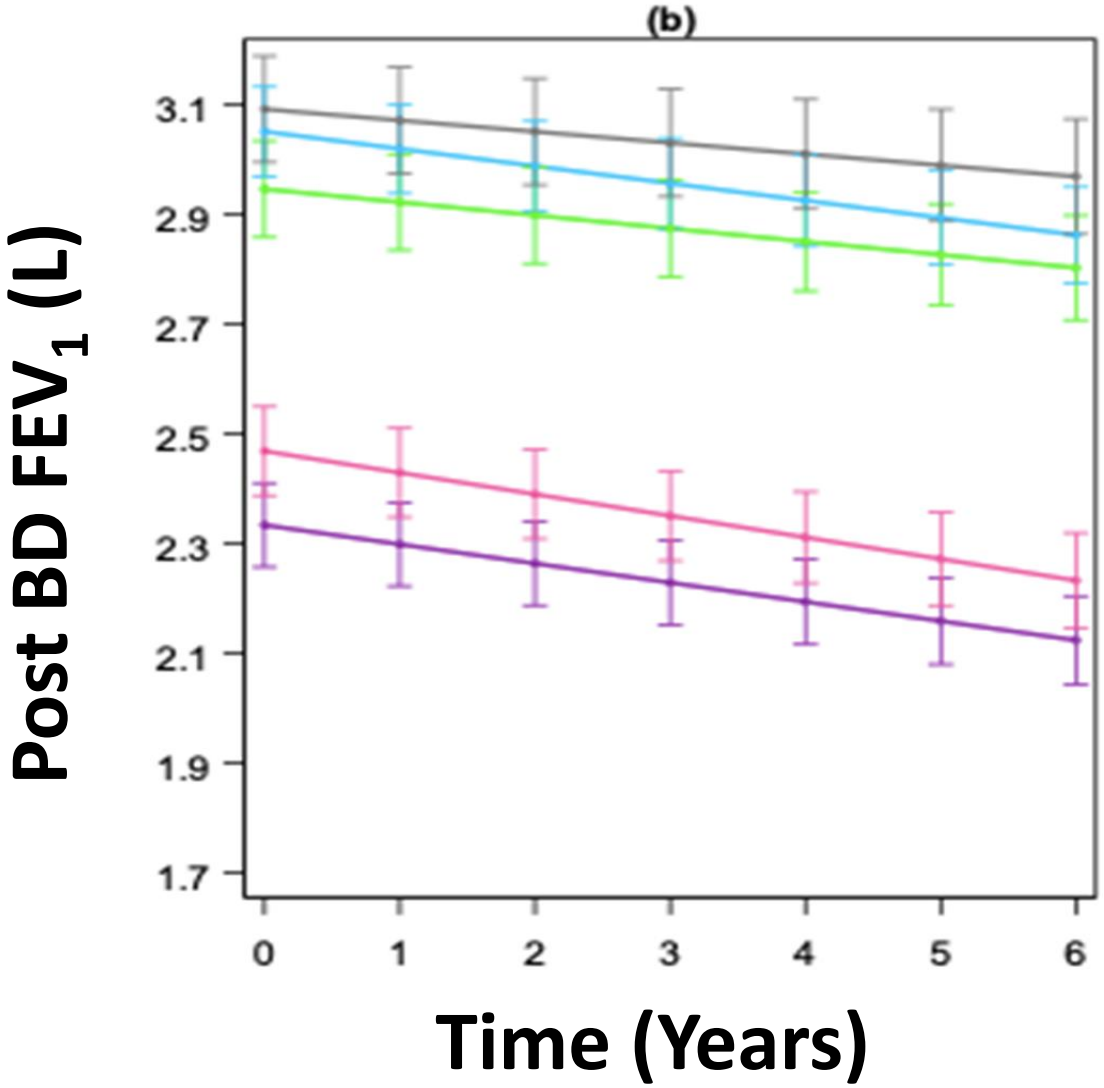


Smokers with Preserved Lung Function - Exacerbations

Woodruff, et al. N Engl J Med 2016; 374:1811-1821



Annual FEV_1 Decline: Never, nTEPPS, sTEPPS, nGOLD 1/2, sGOLD 1/2 McKleroy, et al. JAMA 2023;330:442-453.



Never Smoked

nTEPPS
sTEPPS

10 ml/yr > Never Smoked

nGOLD 1/2

sGOLD 1/2

Does Treating sTEPPS Help Them? (RETHINC) - NO

Han, et al., N Engl J Med 2022; 387:1173-1184.

- N = 535. $FEV_1/FVC \geq 70\%$. FVC $\geq$ 70%. CAT $\geq$ 10 (0-40)
- 12 Wk: Indacaterol (27.5 μg)/Glycopyrrolate (15.6 μg) vs Pbo bid
- Primary End Point: % Patients ≥4 Improvement SGRQ (0-100)

Results	Ind/Gly	Pbo	OR (95% CI)
≥4 SGRQ	56.4 %	59.0 %	0.91 (0.60 – 1.37)
FEV_1	2.4 %	-0.09 %	
IC	0.12 L	0.02 L	

The Conundrum of Symptomatic Tobacco-Exposed Persons with Preserved Spirometry (sTEPPS)

and

Non-Obstructive Chronic Airways Disease (NCAD)

An Emerging Story

. . . . . To be Continued!

Thank You!