Updates for COPD

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Dr. Strange is a grant recipient from the Alpha-1 Foundation, BTG, CSL Behring, Grifols, Inhibrx, MatRx, Novartis, Pulmonx, Shire, and Vertex. He is a consultant to AstraZeneca, BTG, CSA Medical, CSL Behring, Glaxo Smith Kline, Grifols, Shire and Uptake Medical

Learning Objectives

1. Improve the care of persons with asthma and COPD
2. Identify the use of spirometry for COPD diagnosis
3. Improve use of long acting bronchodilators for COPD
4. Review and understand new options of devices for COPD

COPD in 2019

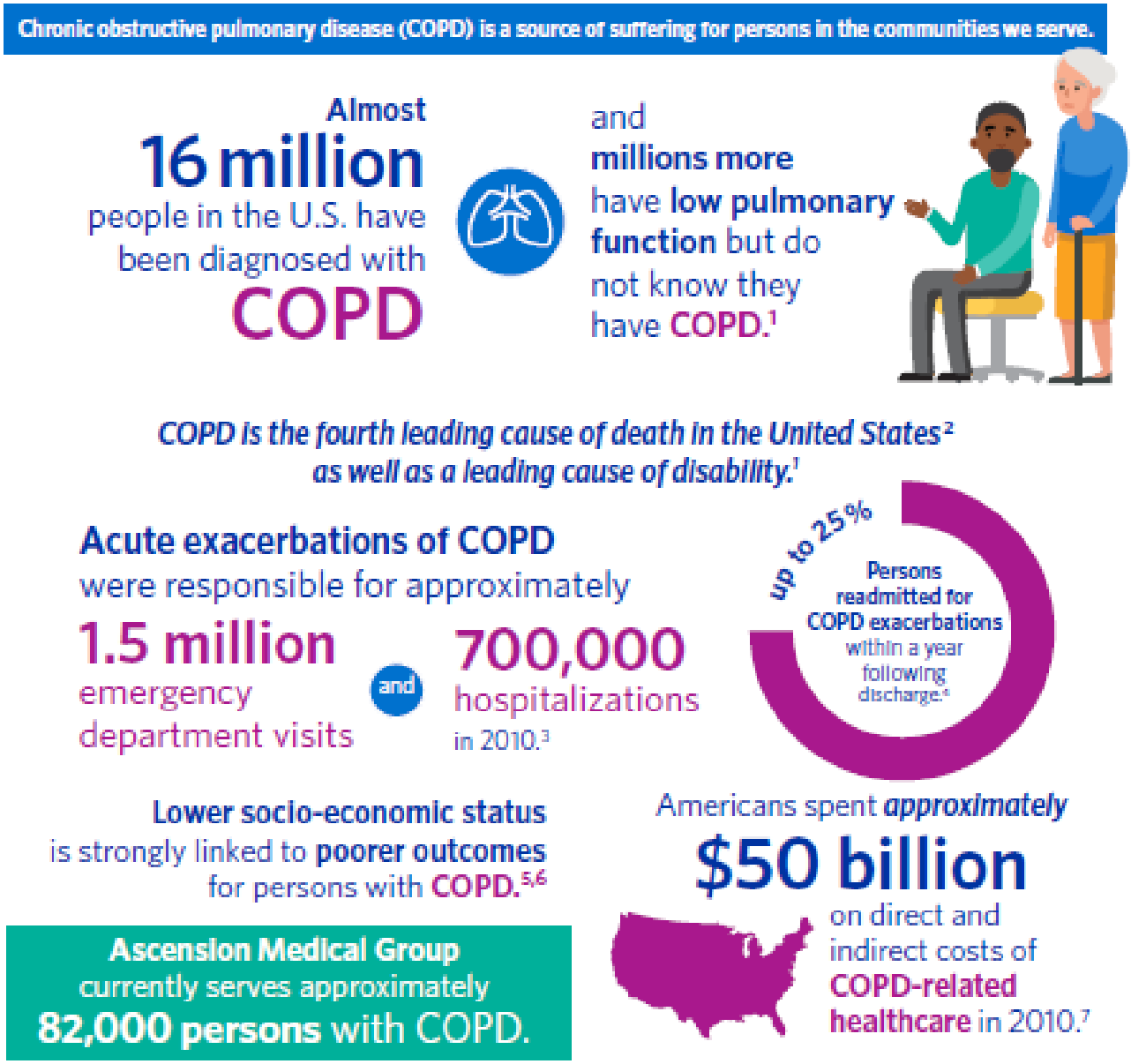
- 15 million Americans diagnosed
- Estimates suggest 12 million more undiagnosed
- 70% of COPD sufferers are in workforce
- COPD is now 2nd leading cause of disability in US
- COPD is now 4rd leading cause of death in US
- Cost of care now over 50 billion dollars a year

What did the BRFSS tell us?

- Prevalence in 18 and up age group: 6.1%
- Prevalence in 45 and up age group 9.0%
- Women reported higher COPD rates: 6.5% vs 5.3%
- 24.9% of those with COPD never smoked
- 43.2% saw physician for COPD in last year
- 17.7% ER visit or hospitalization in last year

2011-2013 BRFSS Data

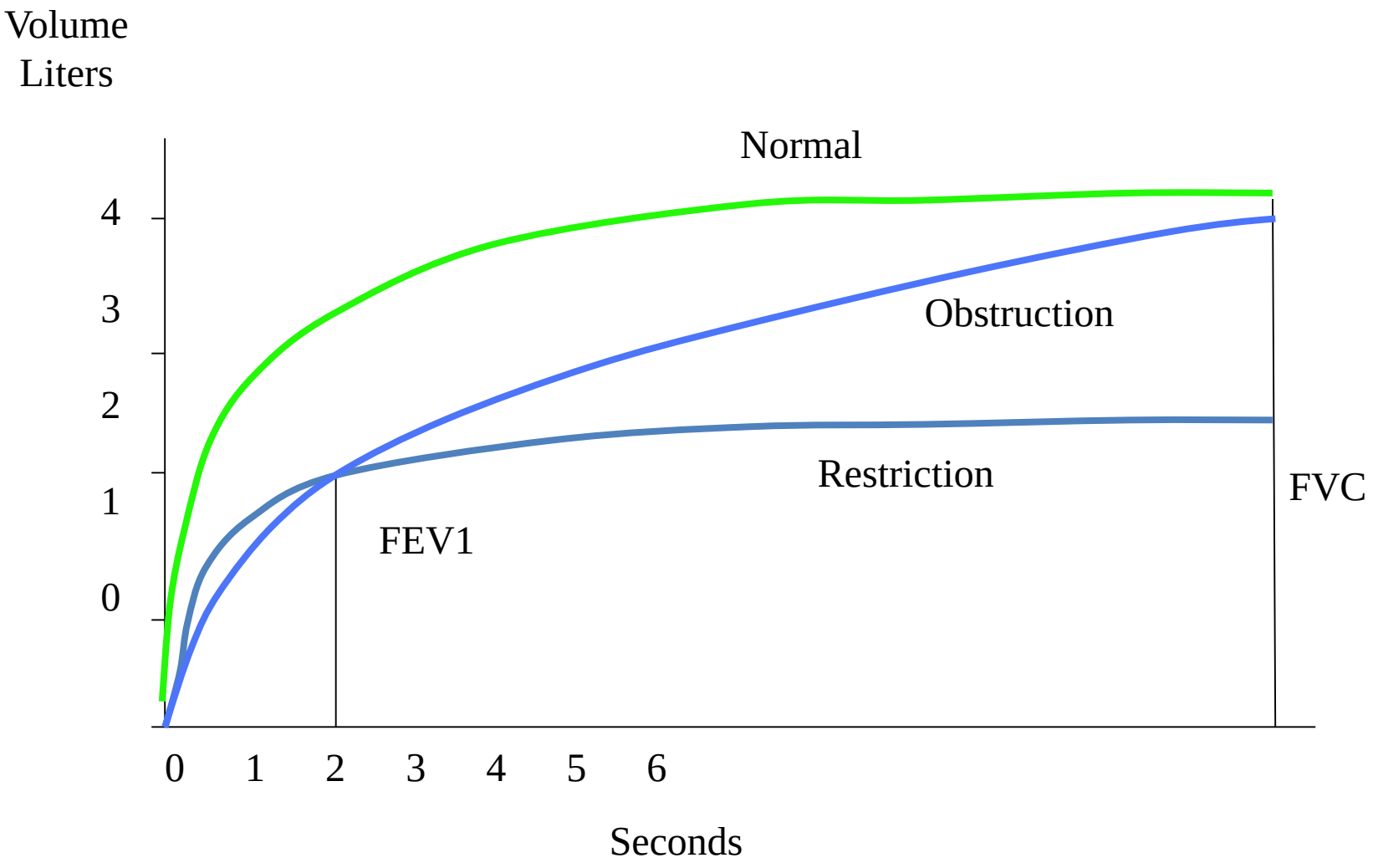
Chronic obstructive pulmonary disease (COPD) is a source of suffering for persons in the communities we serve.



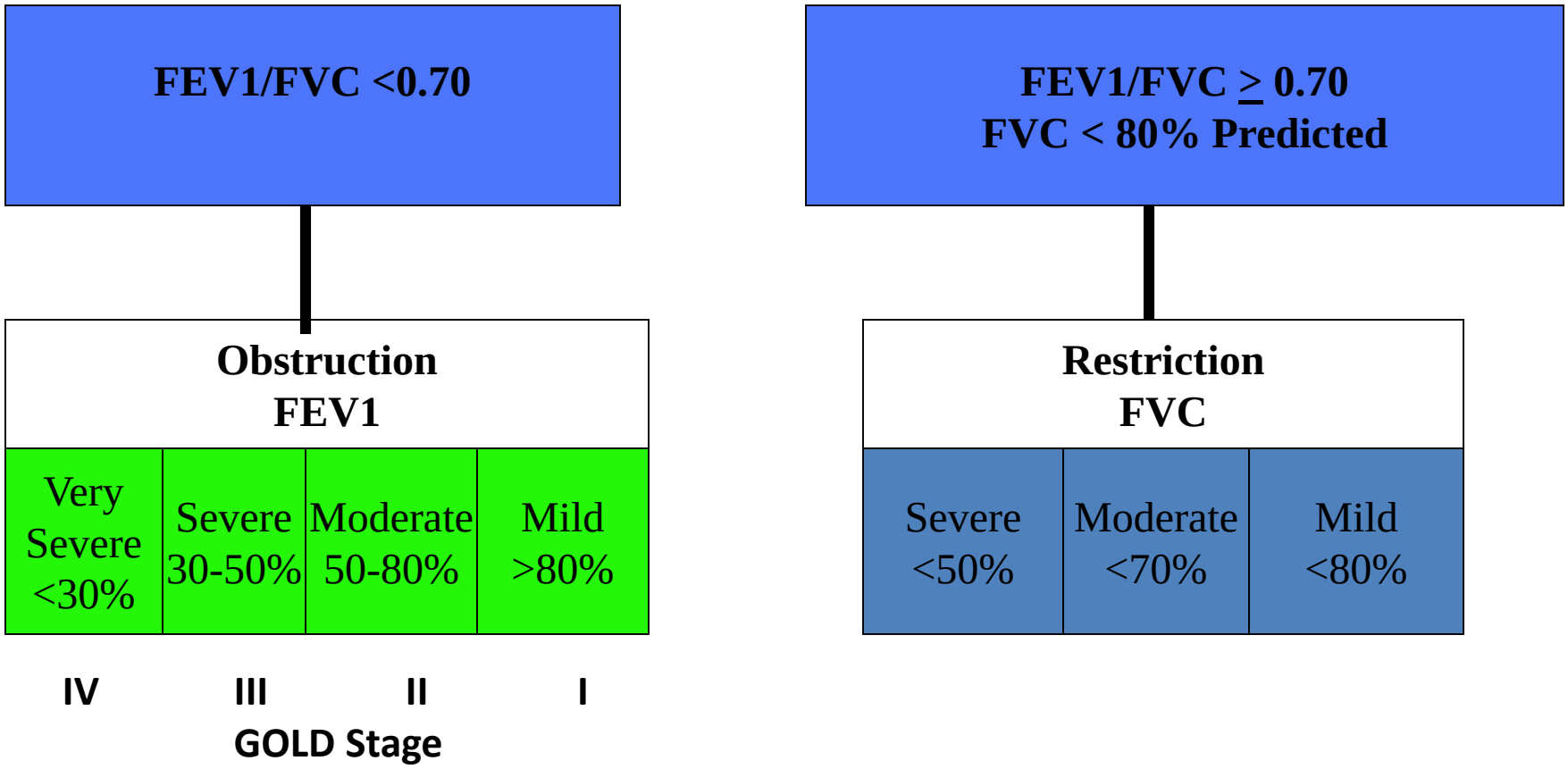
What is the Ascension FY20 asthma and COPD priority goal?

- Improve the care of persons with asthma and COPD:
  - Ascension will achieve a **6% reduction in hospital admissions** for Ascension Medical Group (AMG) patients with a diagnosis of asthma or COPD.
- Denominator criteria
  - Patients 18 years of age or greater with a diagnosis of asthma or COPD during an ambulatory or acute care inpatient/outpatient encounter. Patients 2-17 years of age must only have an asthma diagnosis.
- Numerator criteria
  - Discharge from an acute inpatient encounter with an asthma or COPD diagnosis.
- Exclusion criteria and COPD admissions rate
  - Deceased any time prior to the measurement end date.
  - Evidence of hospice care exists during the measurement period.
  - Patients with end-stage renal disease (ESRD).
- Evaluation period
  - Eligibility period: patient encounters during FY2019.
  - Follow-up period: asthma in FY2020 for patient encounters in the eligibility period.

Spirometry


Volume
Liters
Normal
Obstruction
Restriction
FEV1
FVC
4
3
2
1
0
0
1
2
3
4
5
6
Seconds

Spirometry Interpretation



Chronic Obstructive Pulmonary Disease (COPD)

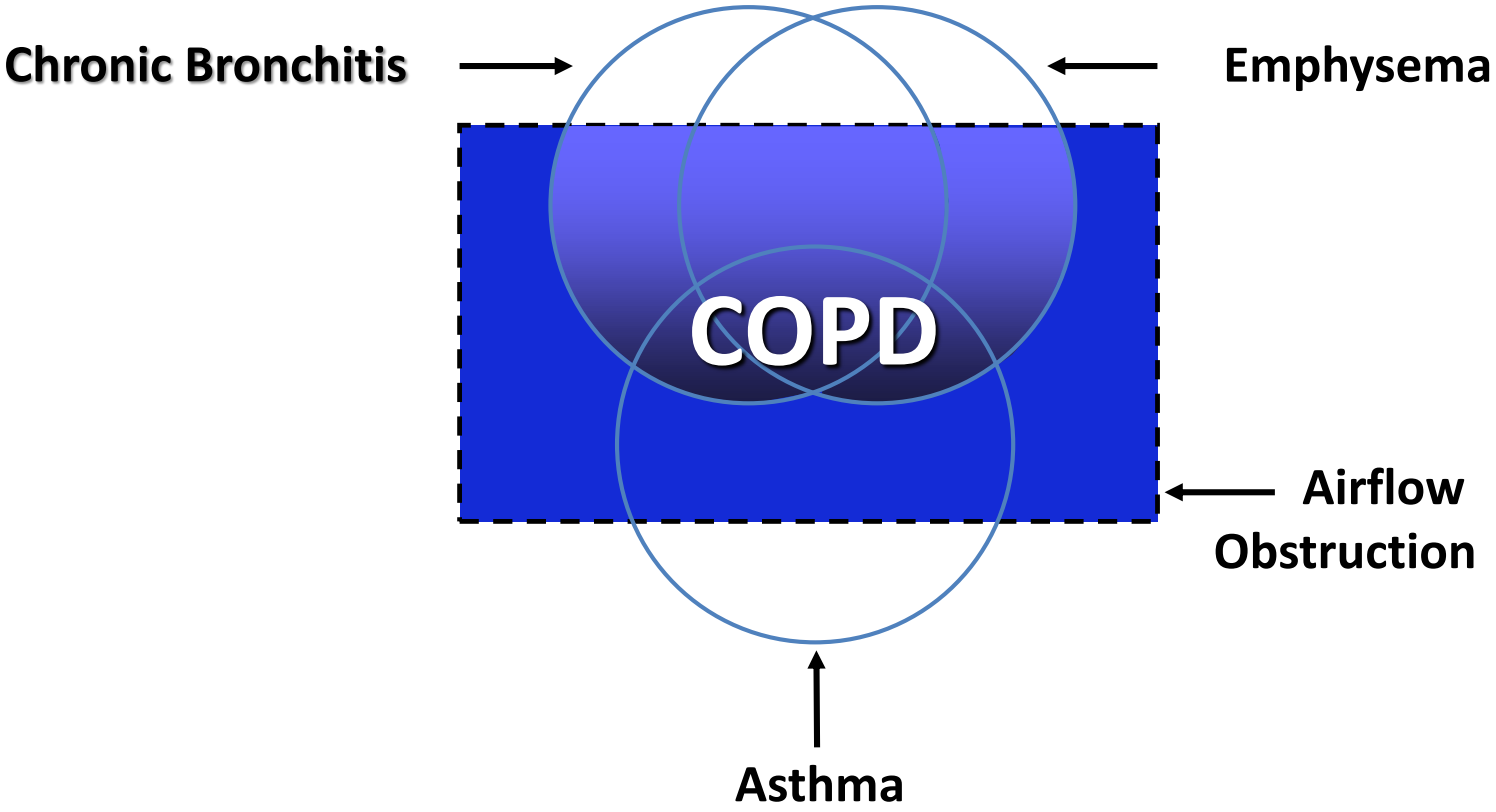
Definition:

- A common, preventable, and treatable disease
- Characterized by persistent respiratory symptoms and airflow limitation
- Airflow limitation is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases

Dyspnea and exacerbations (two treatable traits) are common features of COPD.

Reference: Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2019 report.

Current Definition of COPD



Vestbo, J et al. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease: GOLD Executive Summary. Am J Respir Crit Care Med 2013, 187(4):347-365.

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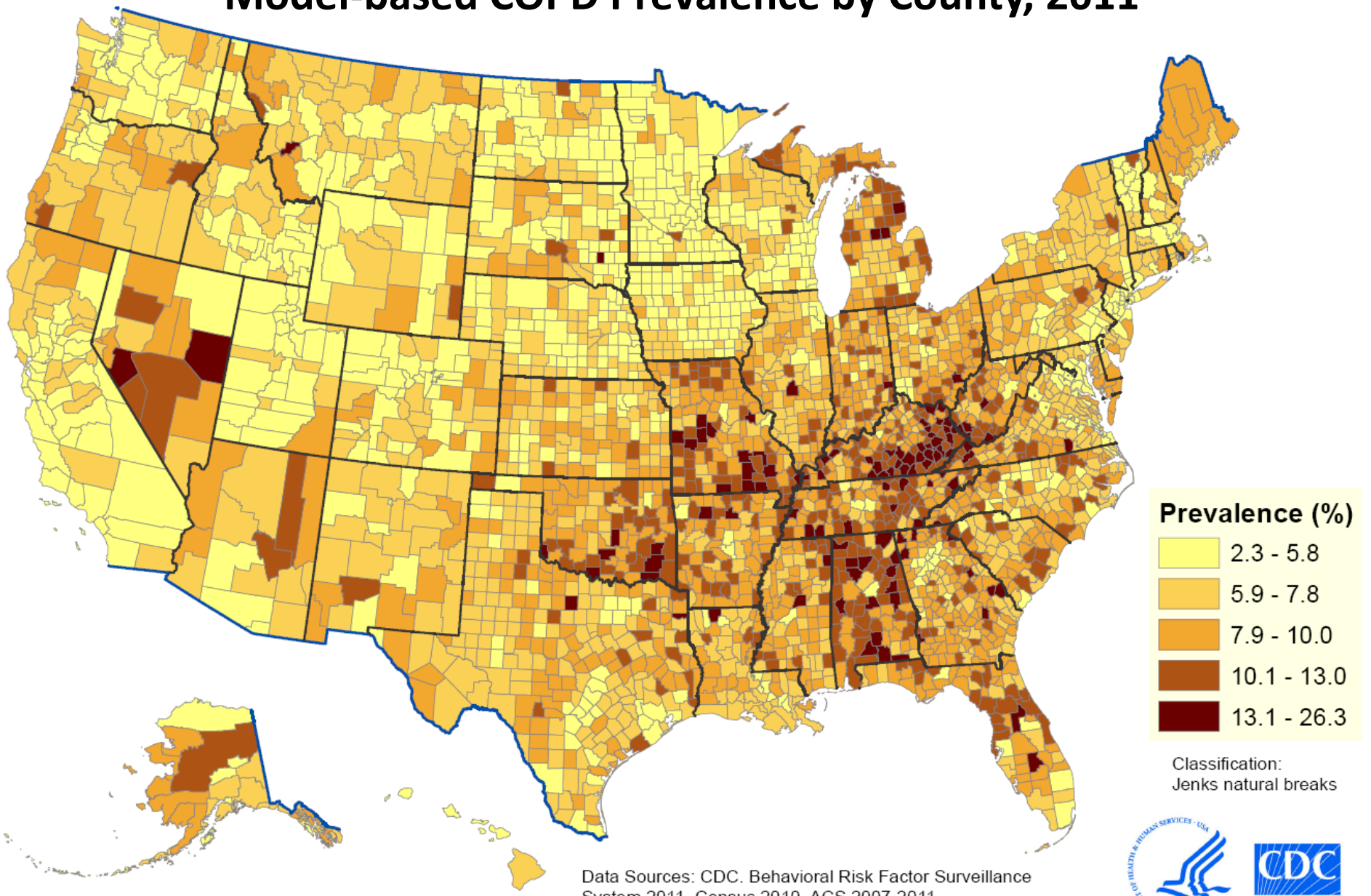
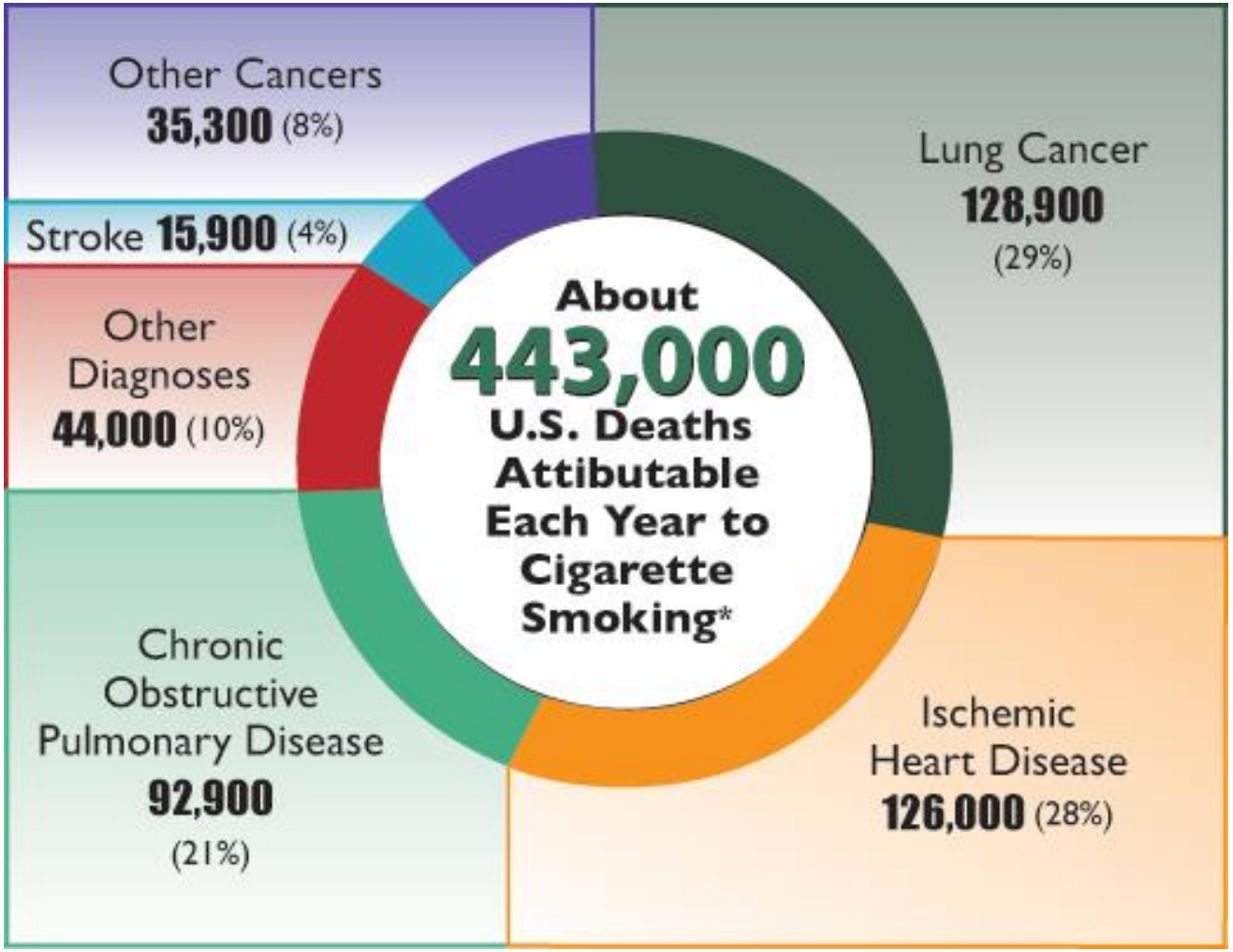
Model-based COPD Prevalence by County, 2011



Adapted from Zhang X et al. Am J Epidemiol 2014;179 (8):1025-1033

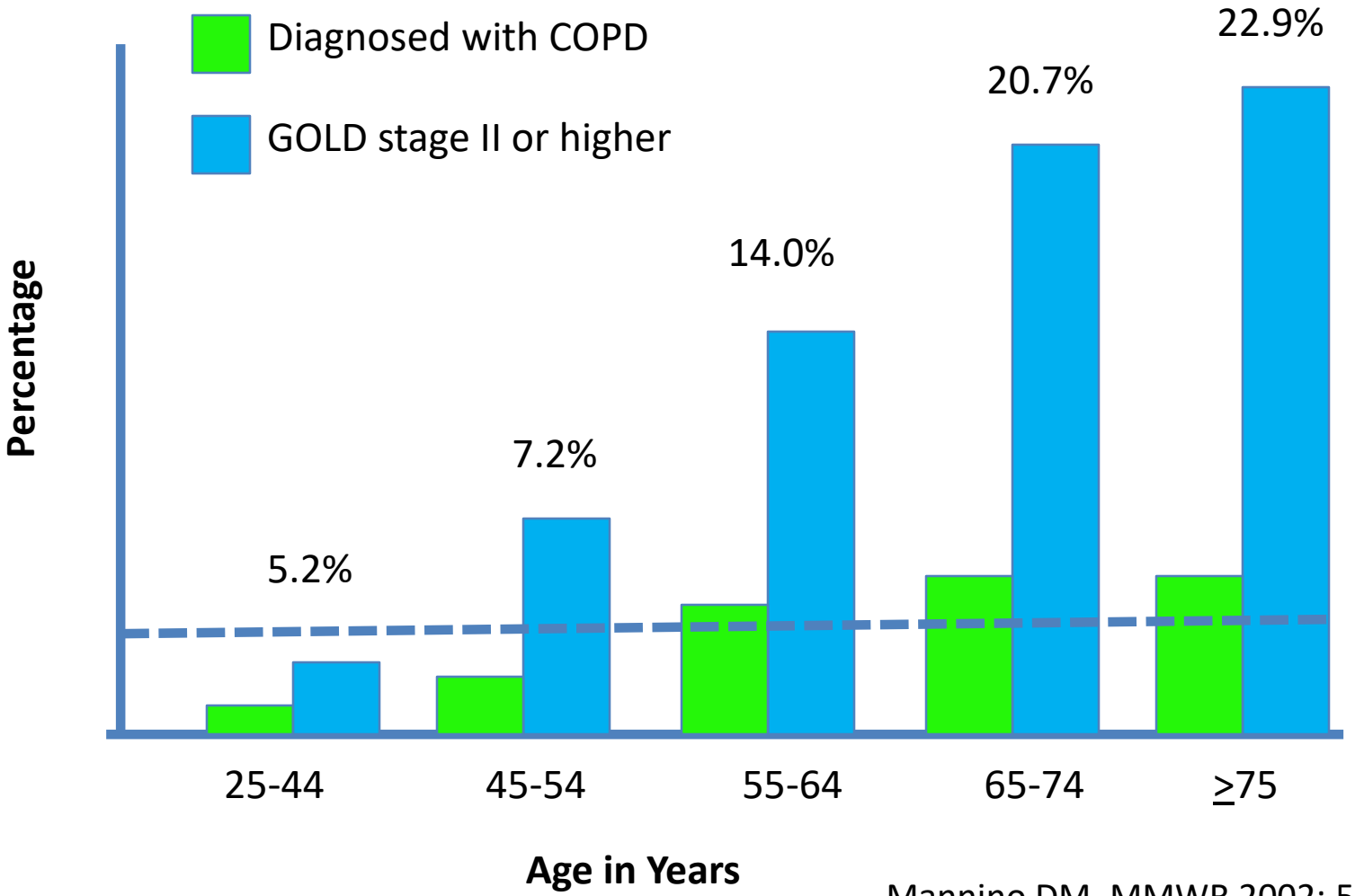
Date: 4/16/2014

Cigarette smoking—a leading cause of preventable death



Source: MMWR 2008;57(45):1226–1228.

Underdiagnosis of COPD in the United States



Mannino DM, MMWR 2002; 51:1-16

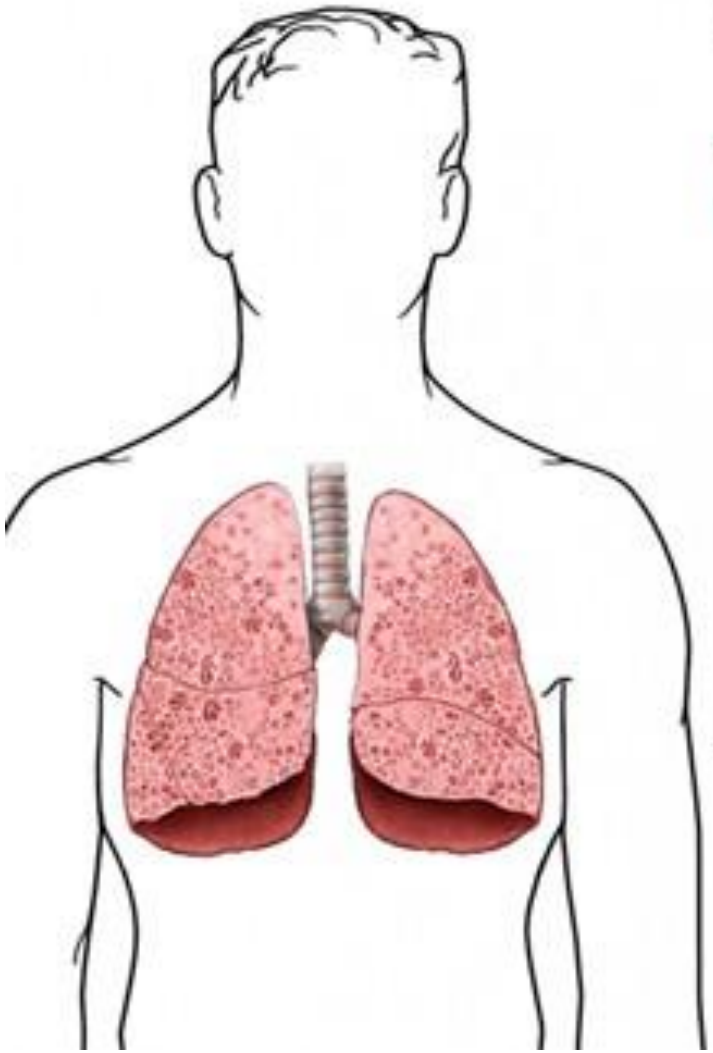
CAPTURE*TM©

For each question, place an X in the box with the answer that is best for you.
There are no right or wrong answers, only answers which are right for you.

Please answer each question	No	Yes	
1. Have you ever lived or worked in a place with dirty or polluted air, smoke, second-hand smoke, or dust?	☐	☐	
2. Does your breathing change with seasons, weather, or air quality?	☐	☐	
3. Does your breathing make it difficult to do things such as carry heavy loads, shovel dirt or snow, jog, play tennis, or swim?	☐	☐	
4. Compared to others your age, do you tire easily?	☐	☐	
	0	**1**	**2 or more**
5. In the past 12 months, how many times did you miss work, school, or other activities due to a cold, bronchitis, or pneumonia?	☐	☐	☐

*COPD Assessment in Primary Care to Identify
Undiagnosed Respiratory Disease & Exacerbation Risk

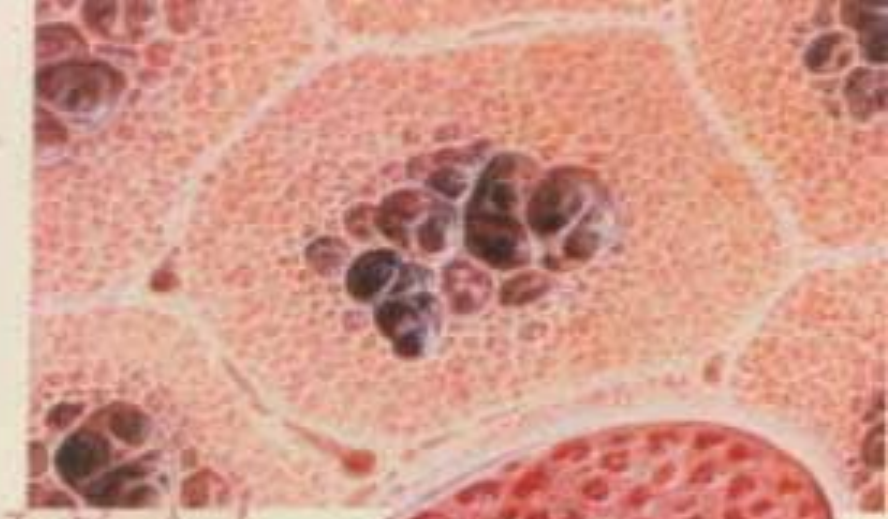
Emphysema

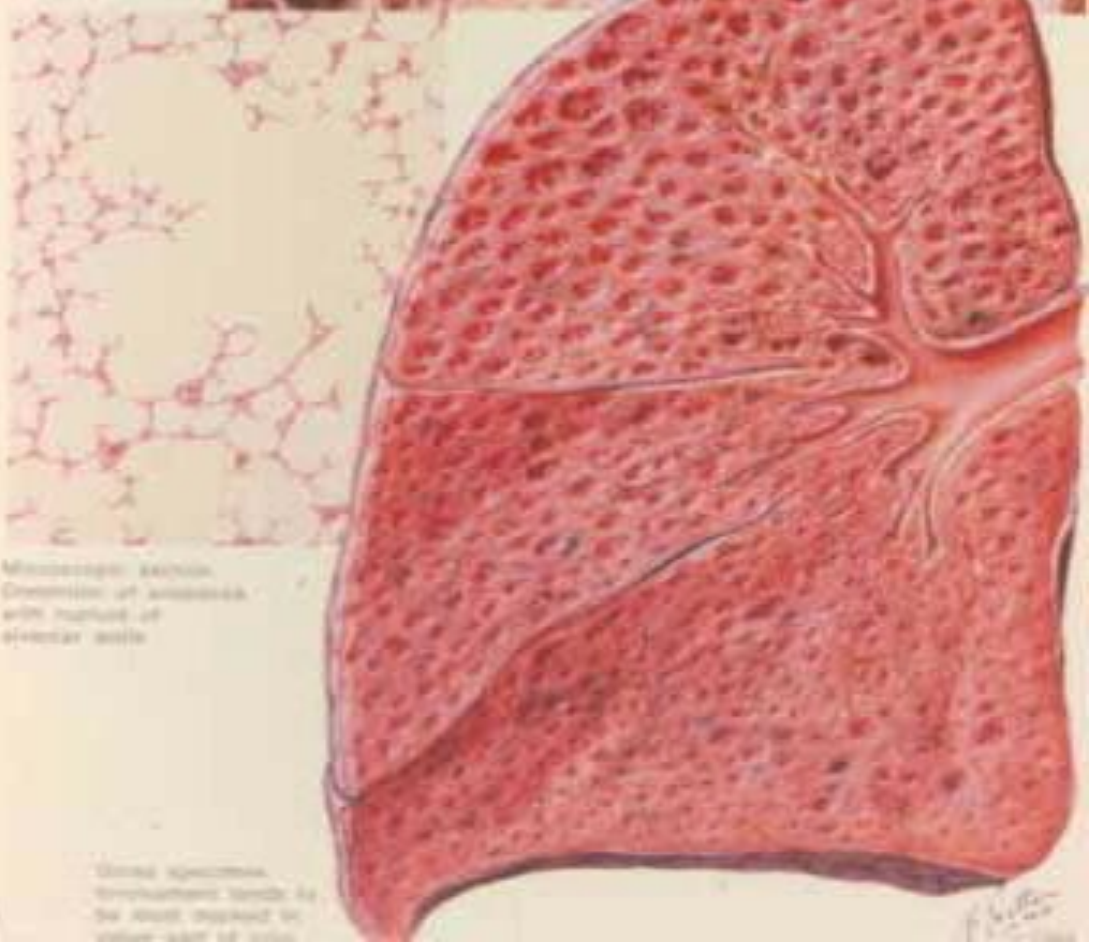


Normal bronchiole and alveoli

Emphysema

(Centrilobular)
Emphysema

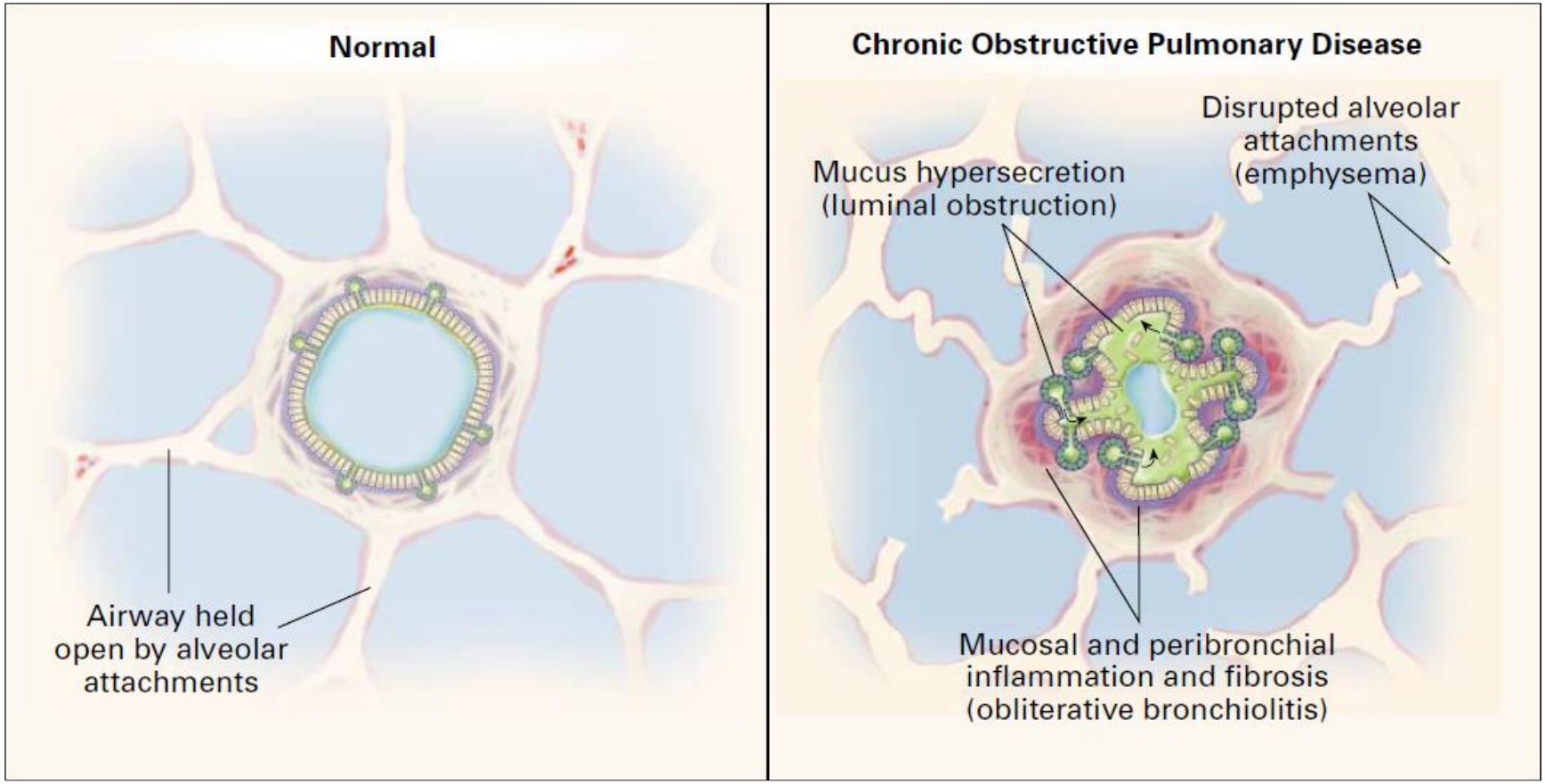




Chronic Bronchitis

The presence of a chronic productive cough in 3 months of 2 successive years in patients with other causes of chronic cough excluded.

Mechanisms of Airflow Limitation in COPD



Barnes PJ. *N Engl J Med.* 2000;343:269-280.

Risk Factors for COPD

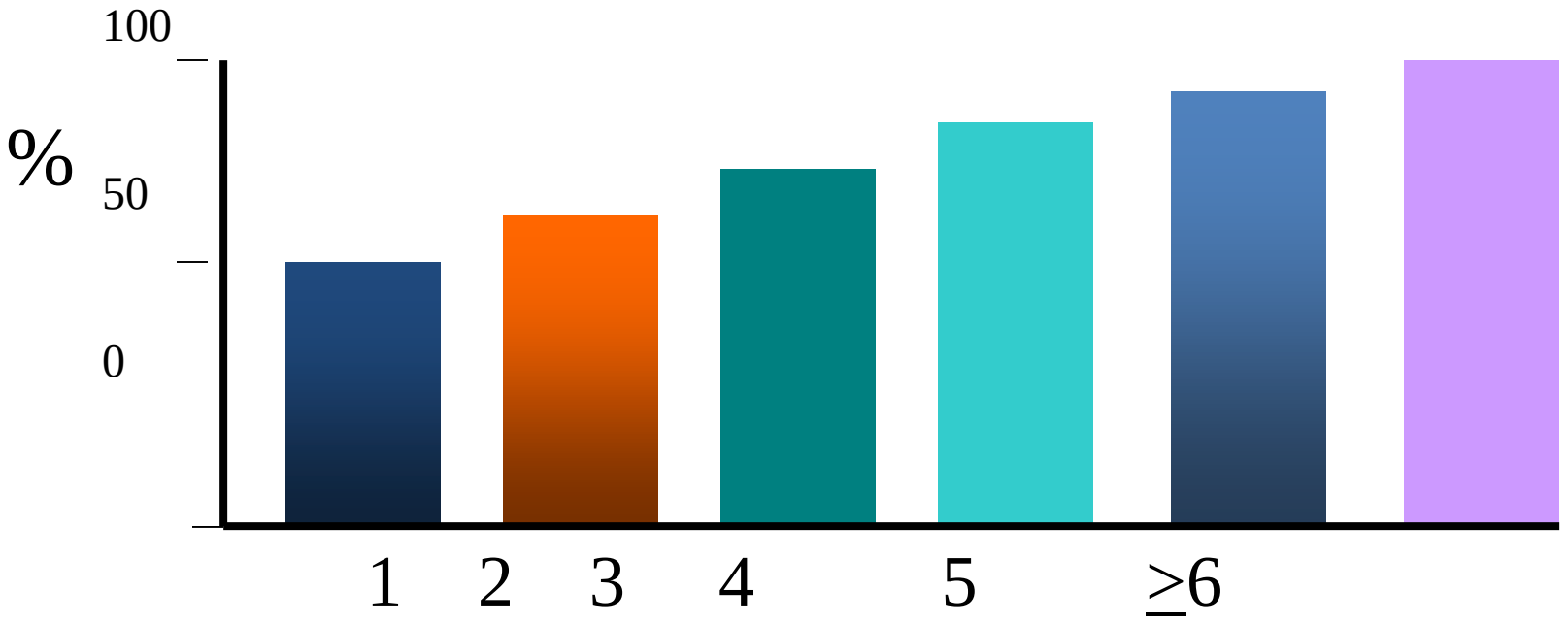
Smoking — Tobacco in any form
Marijuana
Passive smoking

Ambient air pollution (eg. uranium)
Hyperresponsive airways
Alpha-1 antitrypsin deficiency
HIV
Marfan Syndrome, Ehler's Danlos
Cutis laxa
Hypocomplementemic urticarial vasculitis
Crack cocaine, IV Ritalin

Alpha-1 Antitrypsin Deficiency
Clinical Presentation

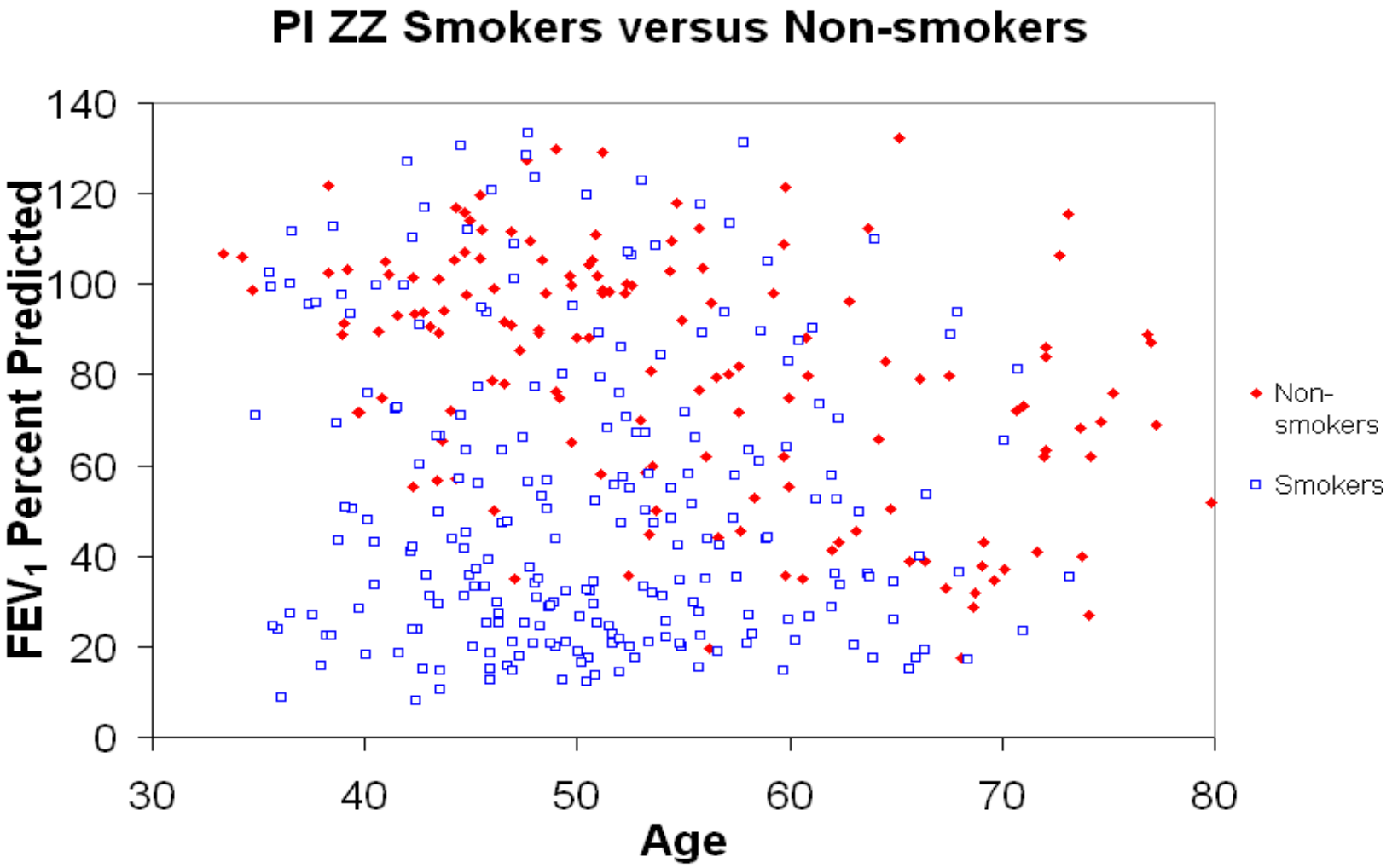
Mean Age at first symptoms 35 years

Mean Age at diagnosis 41 years



Stoller, Clev Clinic J Med 1994; 61:461

Impact of Smoking in AATD



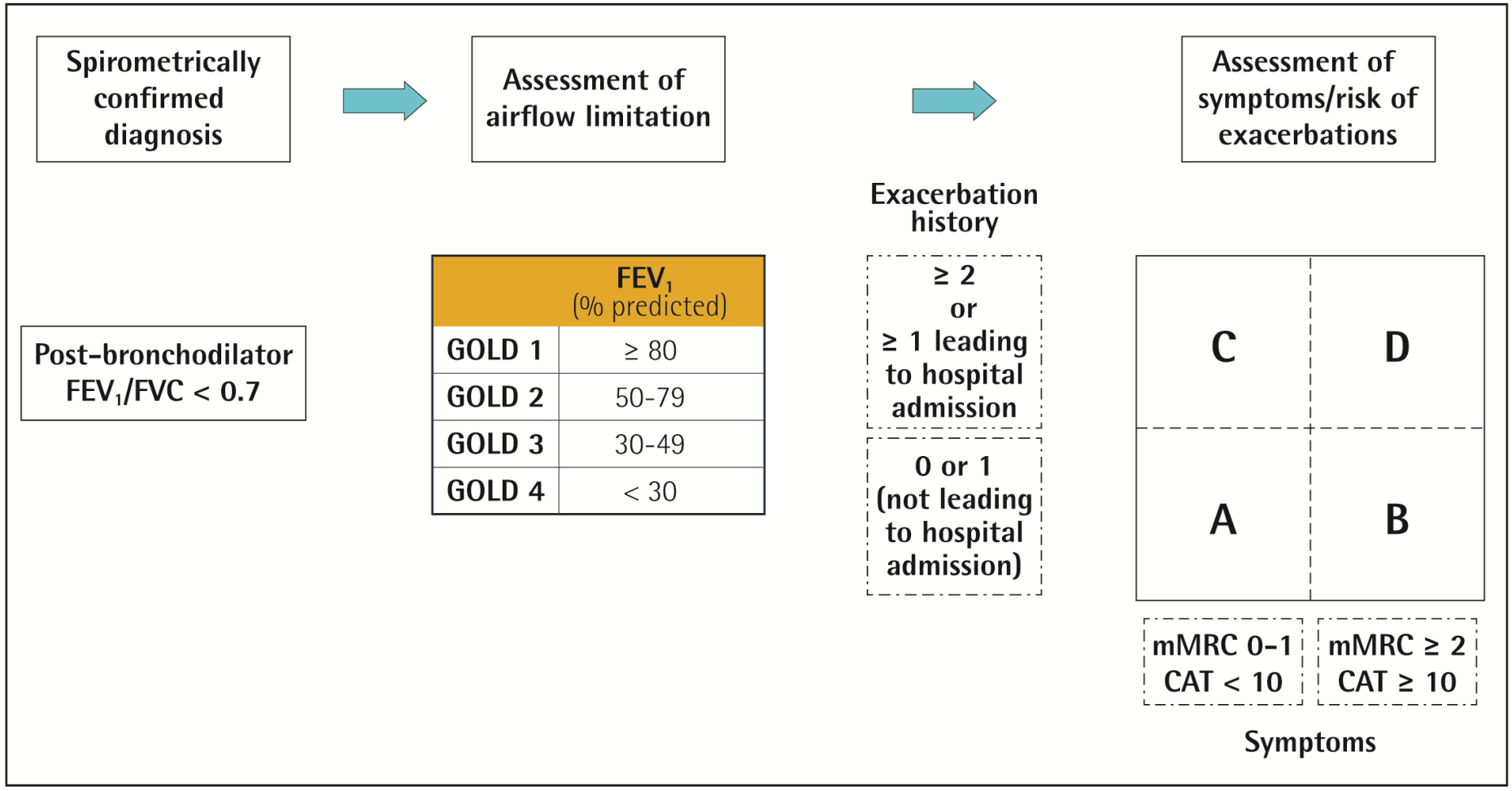
Demeo, DL, et al. Thorax 2007; 62:806

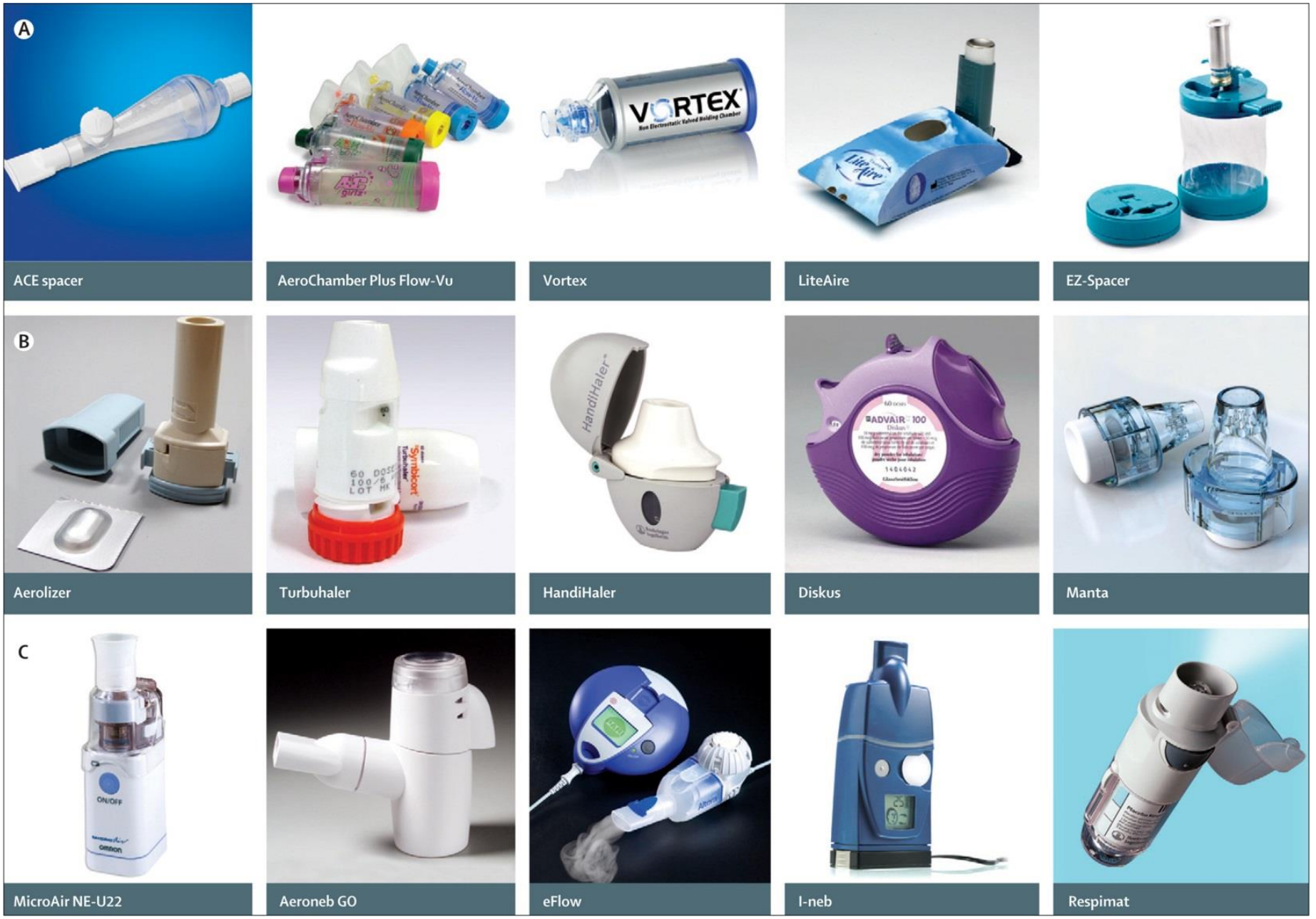
Blood Tests for COPD

- Alpha-1 antitrypsin level
- CBC with differential (Eosinophil >2%)
- IgE

GOLD COPD

Figure 2.4. The refined ABCD assessment tool





Dolovich M, Dhand R. *Lancet.* 2011;377:1032-1045.

Currently Available Single Agent Bronchodilators

	Drug	MDI 2 Puffs	DPI / Mist	Nebulizer Dose	MDI to Equal Neb
SABA/SAMA	Albuterol (Ventolin, Proventil, Proair)	0.18 mg		2.5 mg	28
	Levoalbuterol (Xopenex)	0.09 mg		0.63-1.25 mg	14-28
	Ipratroprium (Atrovent)	0.36 mg		0.5 mg	28
LABA	Salmeterol (Serevent)	0.42 mg	0.50mg BID		
	Oladaterol (Striverdi)		2. 5mcg QD		
	Indacaterol (Arcapta)		75 mcg QD		
	Formoterol (Foradil, Perforomist)		12 mcg BID	20 mcg BID	
	Aformoterol (Brovana)			15 mcg BID	
LAMA	Tiotroprium (Spiriva)		0.18 mg QD		
	Aclidinium (Tudorza)		0.4 mg BID		
	Umeclidinium (Incruze)		62.5 mcg QD		
	Revefenacin (Yupelri)			175 mcg QD	

ICS /LABA

Fluticasone propionate/ Salmeterol	**GlaxoSmithKline, Teva, Mylan**	**Advair® (Diskus & HFA) AirDuo®, Generics**
Budesonide/Formoterol	**AstraZeneca**	**Symbicort®**
Mometasone/Formoterol	**Merck**	**Dulera®**
Fluticasone furoate/ Vilanterol	**GlaxoSmithKline**	**Breo Ellipta®**

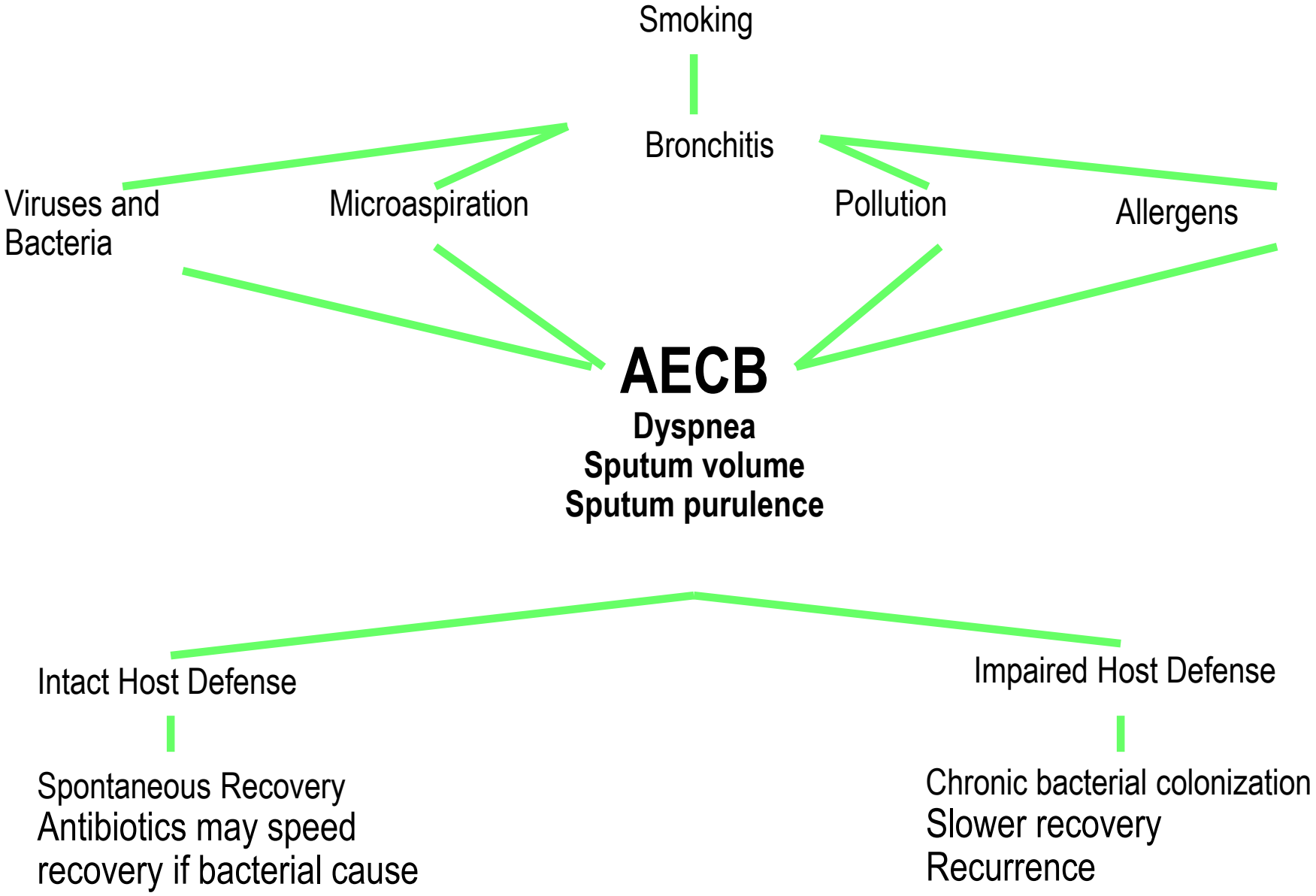
LAMA/LABA

Tiotropium/Olodaterol	**Boeringher Ingeheim**	**Stiolto®**
Vilanterol/Umeclidinium bromide	**GlaxoSmithKline**	**Anoro Ellipta®**
Indacaterol/Glycopyronium	**Novartis**	**Ultibro Breezhaler ®**
Formoterol fumarate/Glycopyrolate	**Astra Zeneca**	**Bevespi Aerosphere®**

Fluticasone propionate/ Salmeterol

	Brand Name	Inhaler	BID Dose (mcg)	Indication
GlaxoSmithKline	Advair	Diskus	500/50 250/50 100/50	Asthma Asthma/COPD Asthma
GlaxoSmithKline	Advair	HFA	2 puffs of: 230/21 115/21 45/21	Asthma Asthma/COPD Asthma
Teva	AirDuo	RespiClick	113/14	Asthma
Mylan	Wixela	Inhub	500/50 250/50 100/50	Asthma Asthma/COPD Asthma

Acute Exacerbation of Chronic Bronchitis

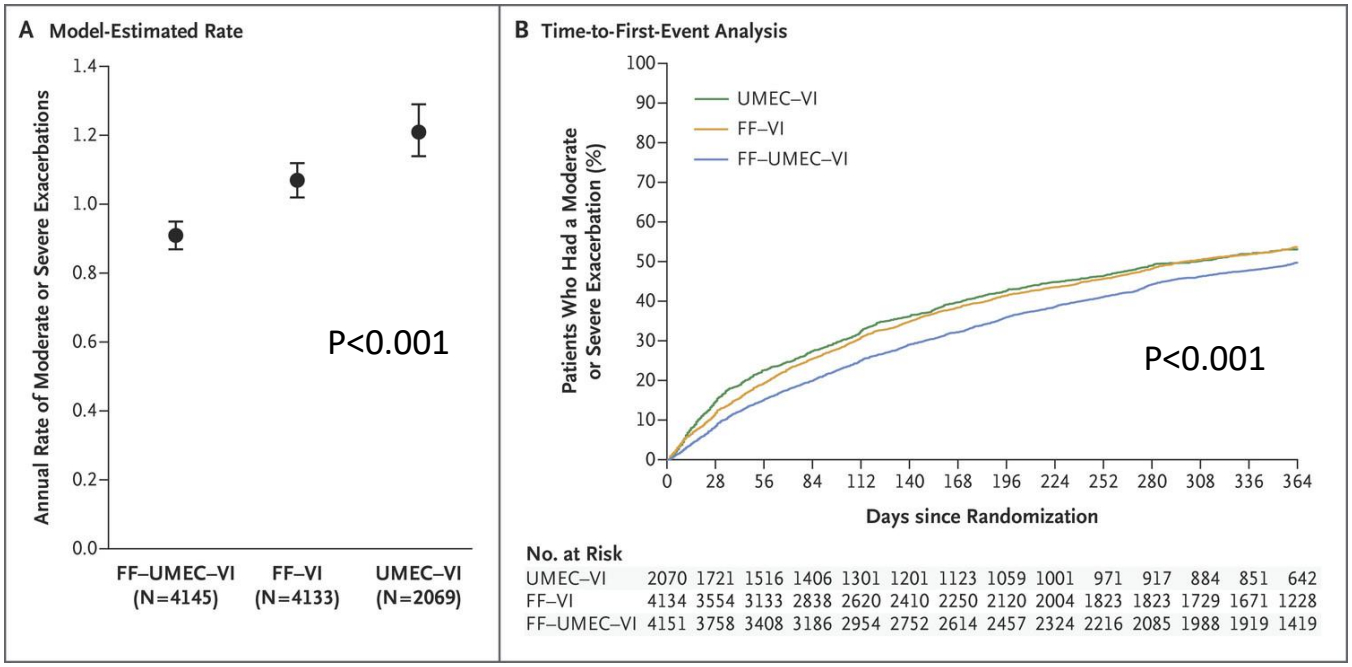


LABA/LAMA/ICS

IMPACT Study

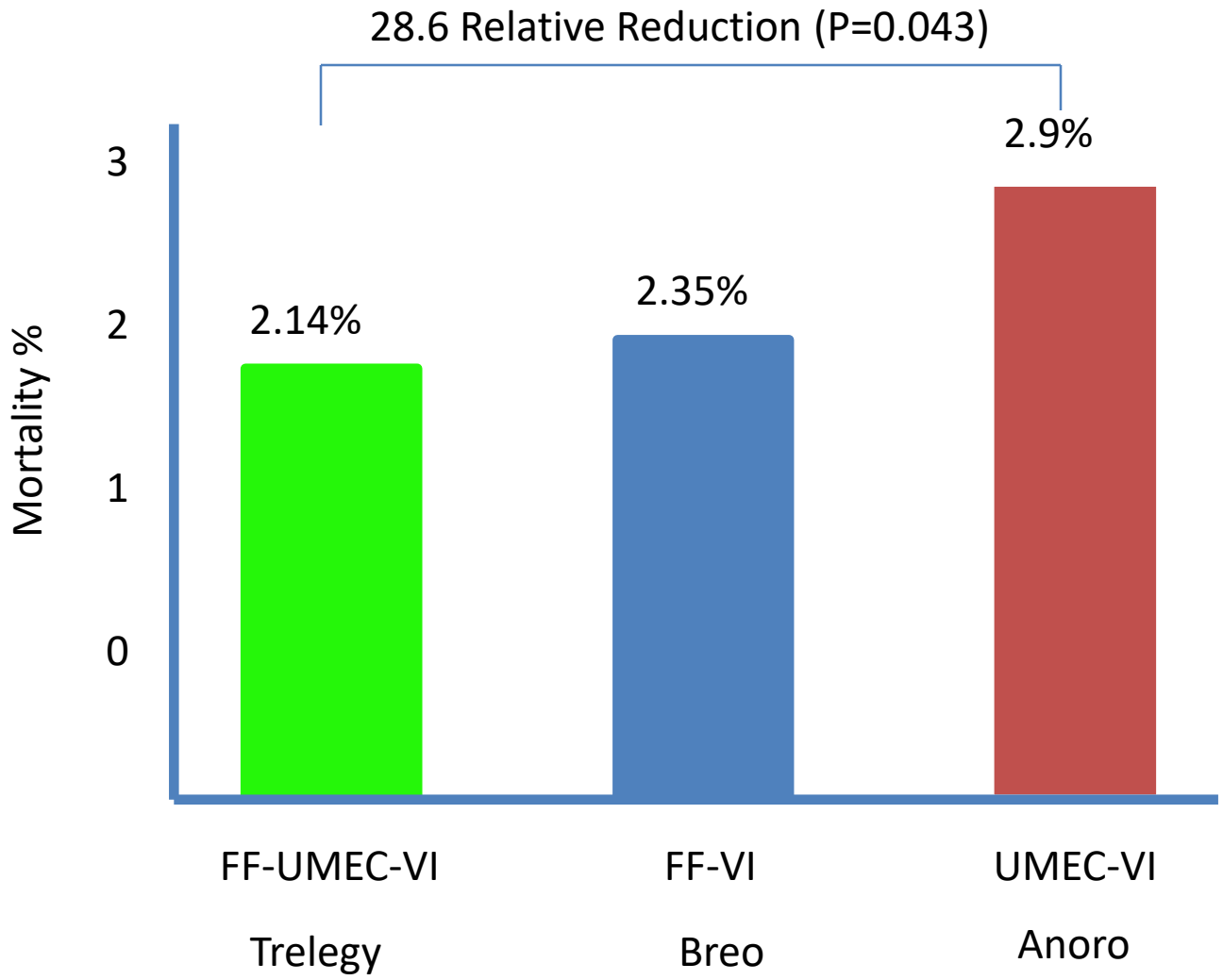
10,355 Patients– 1 °Exacerbation Rate

LAMA/LABA	UMEC-VI	(Anoro)
ICS/LABA	FF-VI	(Breo)
ICS/LAMA/LABA	FF-UMEC-VI	(Trelegy)



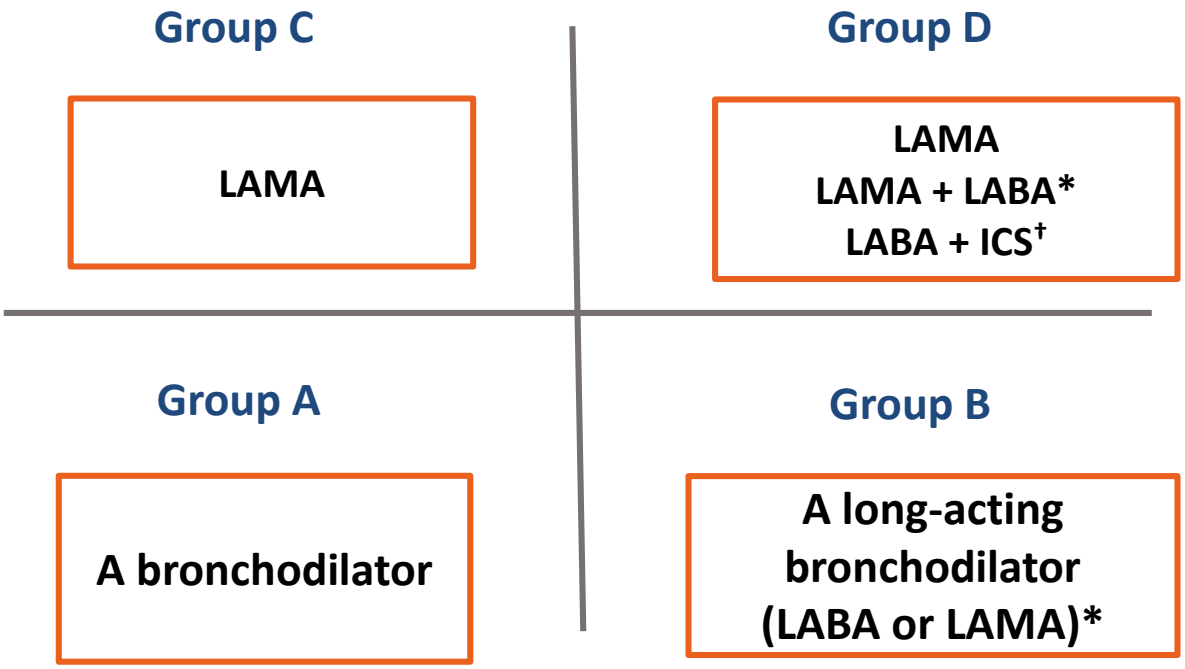
Lipson DA, et al., N Engl J Med 2018; 378:1671-1680

Triple Therapy FF-UMEC-VI improves All Cause Mortality over UMEC-VI



Lipson DA, et al., N Engl J Med 2018; 378:1671-1680

Initial Pharmacologic Treatment by ABCD Group



LABA=long-acting $beta_2$ agonists
LAMA=long-acting antimuscarinic antagonists
ICS=inhaled corticosteroids

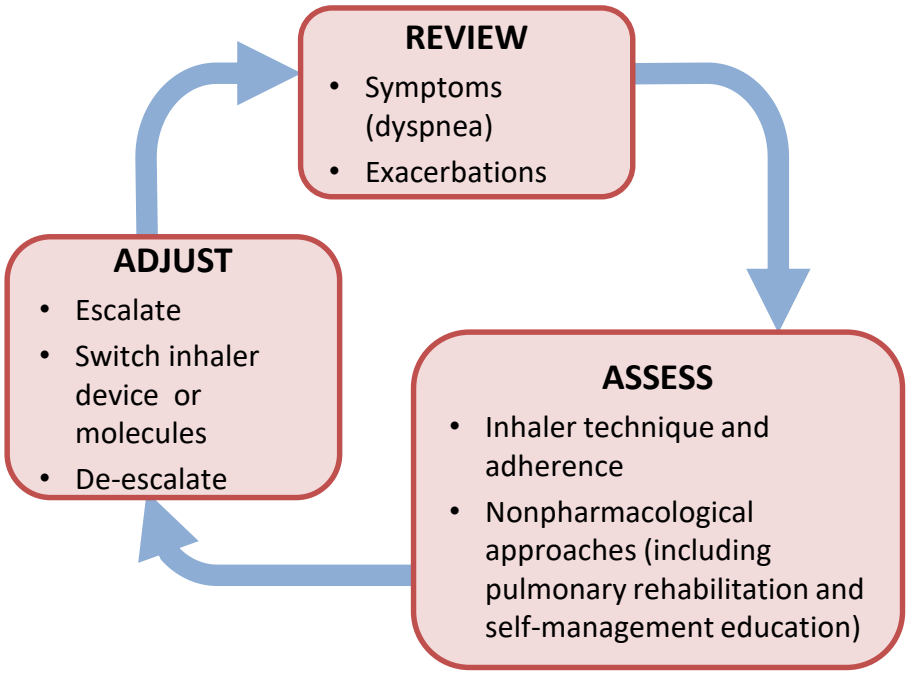
***For patients with severe breathlessness, initial Rx with two bronchodilators may be considered**
†Consider if there are concerns regarding asthma overlap or if eosinophils ≥ 300 cells/µl

2019 GOLD Guidelines

Initial Pharmacological Treatment

- Recommendations are based on symptoms and exacerbation risk at diagnosis
- Based on the ABCD assessment scheme

Management Cycle



Follow-Up

- Recommendations are based on continued dyspnea and exacerbation risk
- The predominant treatable trait is used to guide treatment choice
- ABCD assessment scheme is not used to guide follow-up treatment

Treatment Overview of COPD

Nonpharmacological Approaches

- Smoking cessation
- Pulmonary rehabilitation
- Exercise
- Diet

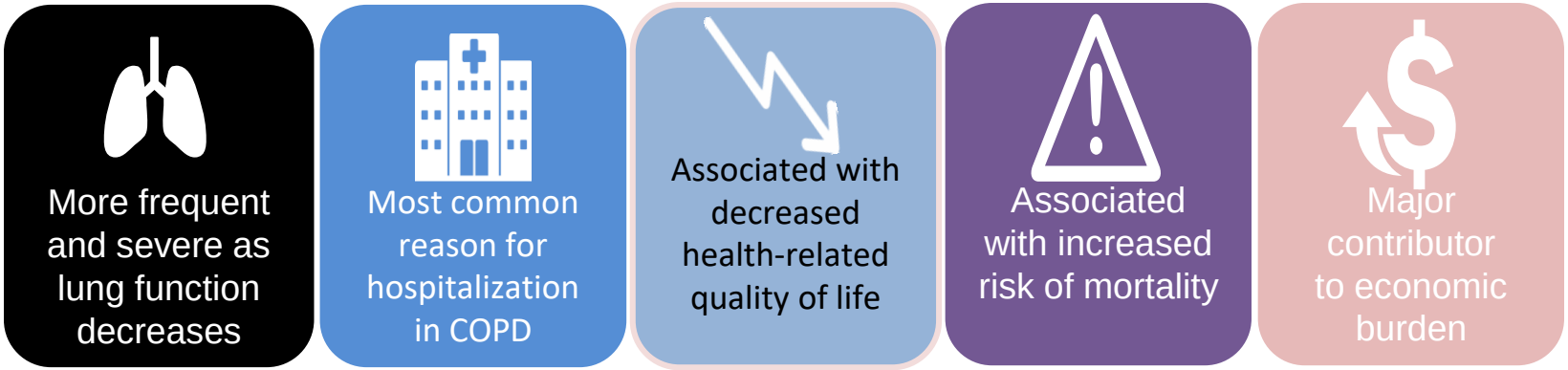
Pharmacological Approaches

- Pharmacotherapy for smoking cessation
- Vaccinations (eg, influenza, pneumococcal)
- Inhaled and other treatments

Assessments and Education

- Inhaler techniques
- Patient adherence to therapy
- Understanding of multiple medication regimens
- Early recognition of exacerbations and symptom changes
- Regular HCP contact

Exacerbations of COPD are important



An acute worsening of respiratory symptoms that results in additional therapy is defined as a COPD exacerbation

COPD Exacerbations Requiring Hospitalization Are Associated With Increased Mortality

11%

of patients with COPD died within 90 days of hospitalized exacerbation in a retrospective study of COPD exacerbation admissions (N=16,016)

3.6 Years

Median Survival after first hospitalized exacerbation in a cohort of patients identified using healthcare databases and followed until death or end of study (N=73,106)

Hartl S et al. *Eur Respir J*. 2016;47(1):113-121.
Suissa S et al. *Thorax*. 2012;67(11):957-963.

Management of Exacerbations

	Objective	Strategy
Acute	Relieve dyspnea	SABA +/- SAMA
	Reduce airway inflammation	Systemic corticosteroids
	Improve lung function	Systemic corticosteroids
	Eradicate infections	Antibiotics
Maintenance	Reduce risk of new exacerbation	Smoking cessation
		Pharmacotherapy •LAMA, LABA, LABA/ICS, LABA/LAMA, LABA/LAMA/ICS
		Immunizations •Influenza •Pneumonia
		Pulmonary rehab
		Self-management support

Non-Drug Treatment of COPD

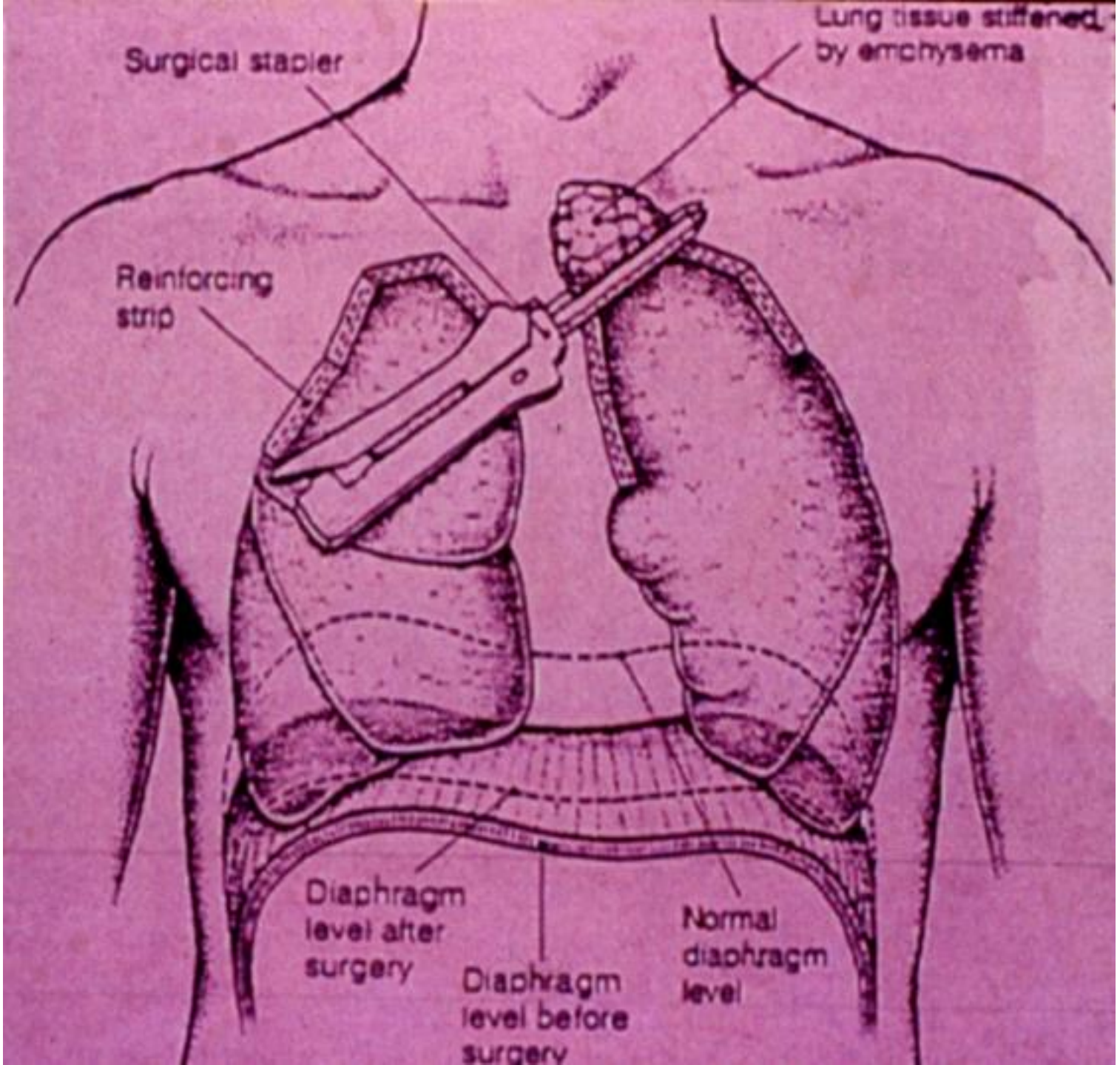
Chronic Non-invasive Ventilation

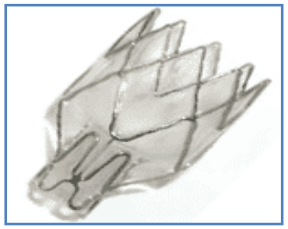
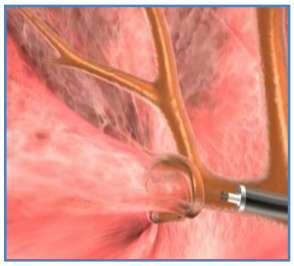
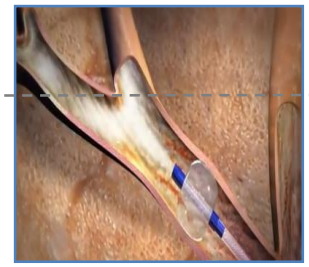
Pulmonary Rehabilitation

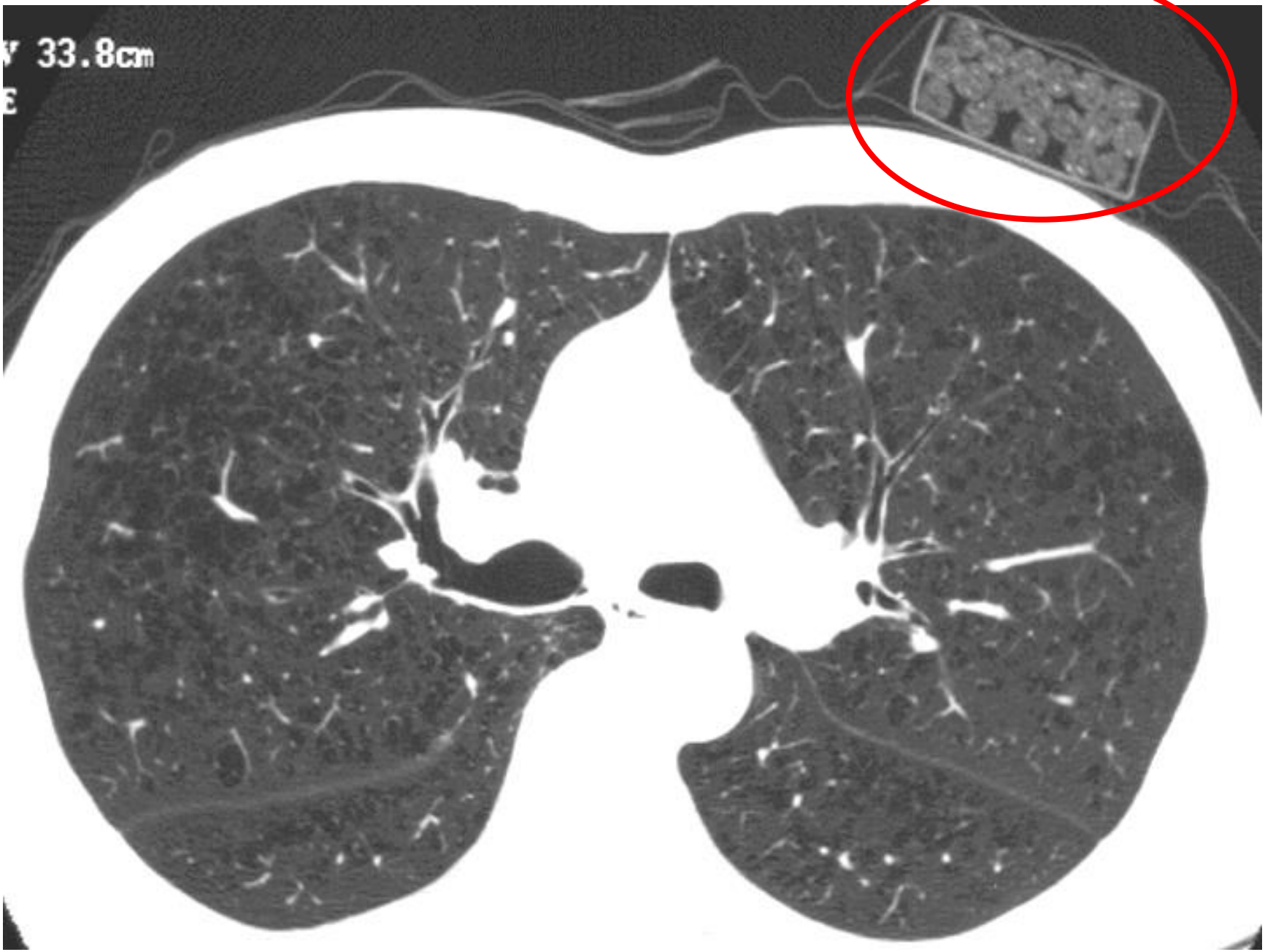
Devices

- **Coils**
- **Endobronchial Valves**
- **Vapor**

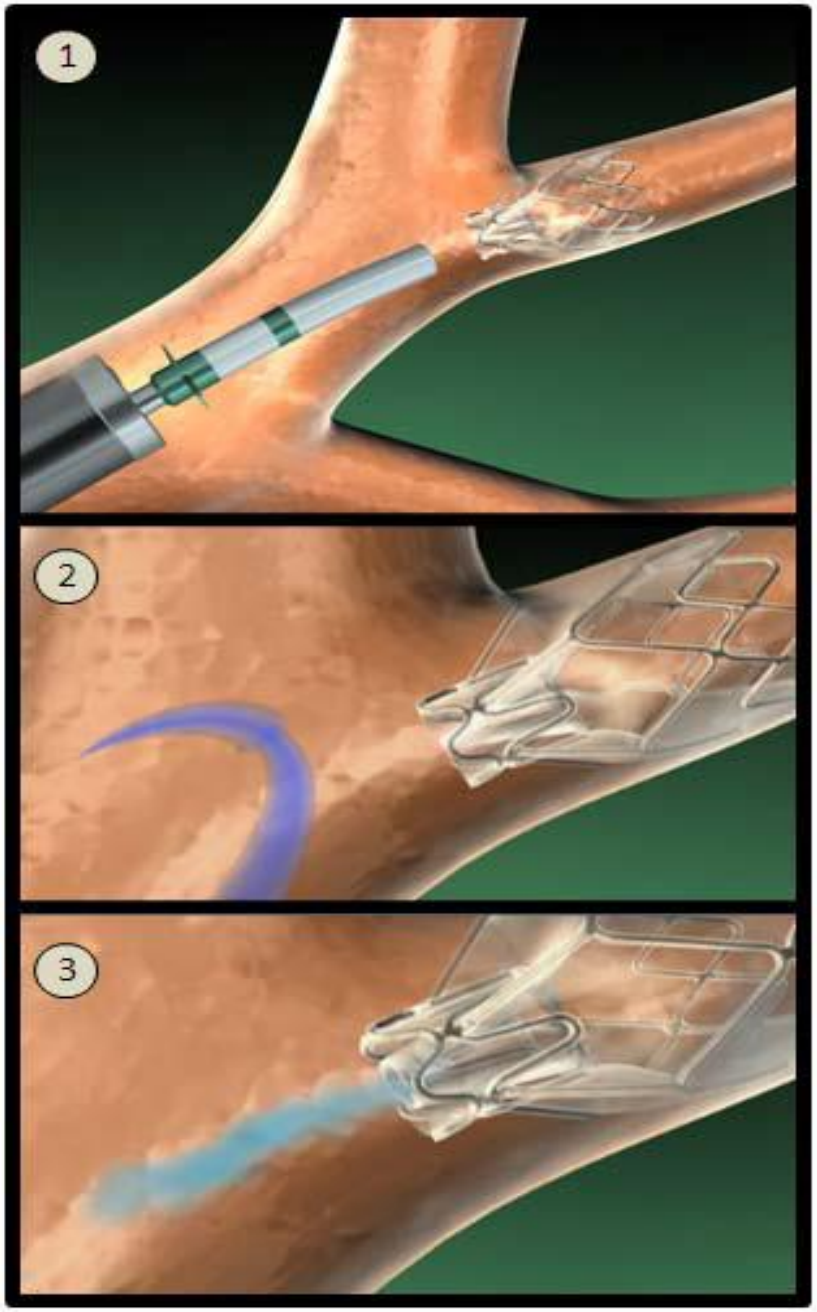
Lung Transplantation


Surgical stapler
Lung tissue stiffened by emphysema
Reinforcing strip
Diaphragm level after surgery
Diaphragm level before surgery
Normal diaphragm level

	Product	Image	Mechanism of Action
Flow regulation	Zephyr-Endobronchial Valves (EBV) **PulmonX**		One-way valves prevent air from entering the blocked emphysematous segment, while allowing the venting of expired gas and bronchial secretions, leading to atelectasis of the isolated segments with subsequent reduction in lung volume.
	Intrabronchial Valves (IBV) **Spiration**		
Tissue compression	PneumRx® Elevair™ Endobronchial Coil **PneumRx**		Coils are delivered to the lung in a straight configuration through a bronchoscope. Once deployed, LVRC reduces the diseased lung volume by coiling up thereby compressing the diseased tissue and allowing expansion of the healthier areas
	InterVapor - Bronchoscopic Thermal Vapor Ablation (BTVA) **Uptake**		BTVA uses heated water vapor to produce a thermal reaction leading to an initial localized inflammatory response followed by permanent fibrosis and atelectasis with subsequent reduction in lung volume.


33.8cm

Pulmonx Zephyr® Valve



Emphysema Targeting

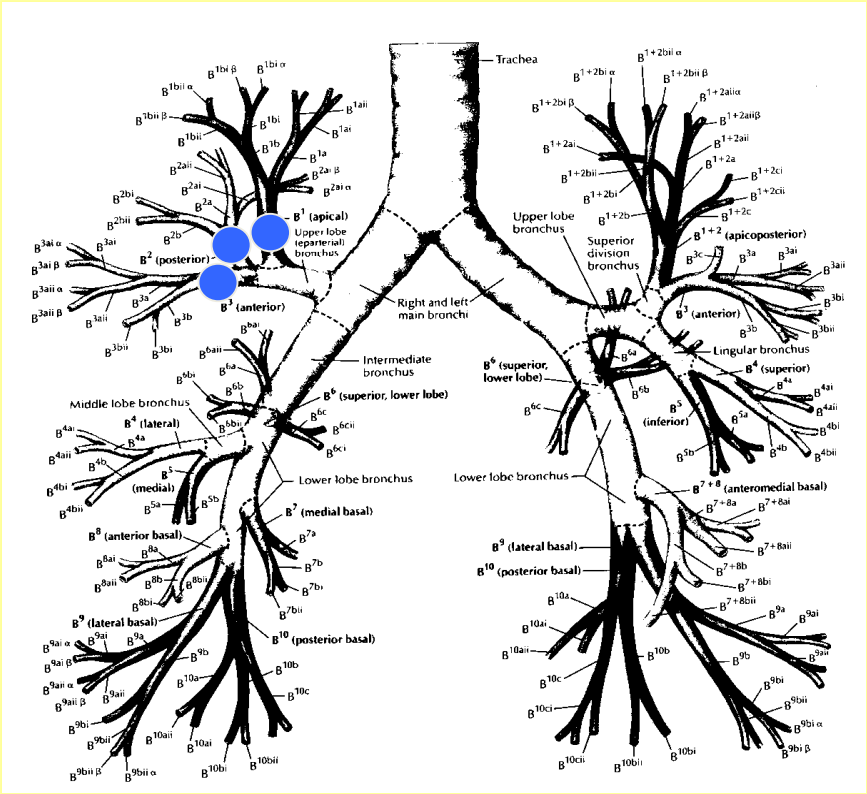


Figure 2

- Lobar Exclusion
  Occlude all airways supplying lobe

Strange C, et al. for the VENT Study Group. BMC Pulmonary Medicine 2007, 7:10.

Key Inclusion/Exclusion Criteria

Inclusion criteria

- **Age ≥ 35 years**
- **Bilateral emphysema (CT)**
- **Post BD FEV_1 ≤45 % predicted**
- **TLC > 100 % predicted**
- **RV ≥ 175 % predicted**
- **Dyspnea : ≥2 (mMRC)**
- **Stopped cigarette smoking (min> 8 wks prior to study)**
- **Completed pulmonary rehab w/in 6 months and/or regularly performing maintenance**

Exclusion criteria

- **Post BD FEV1 < 20%**
- **DLCO <20% predicted**
- **6MWT < 140 m**
- **Recurrent RTI**
- **PH >50 mmHG systolic**
- **Bullae > 1/3 lung**
- **Prior LVR Surgery, Lung Transplant, Lobectomy, or other LVR devices in either lung**
- **>20 mg prednisone daily**

It Takes a Village

Pulmonologist

Asthma specialist

Advanced practice provider

Clinic nurse

Clinic core team

Emergency department provider

Senior leader

Pediatrician

Social worker

Care management

Behavioral and mental health provider

Dietitian

Palliative care coordinator

Person and family engagement leader

Hospitalist

Acute care nurse

Clinical pharmacist

Respiratory therapist

Conclusions

- COPD medication management using the ABCD classification system is not going to change and should be embraced by the medical community.
- We finally have generic medications for COPD!
- Exacerbation prevention with daily long acting medications saves money and probably improves mortality