

VIRTUAL AHN PULMONARY, CRITICAL CARE, ALLERGY AND SLEEP MEDICINE SYMPOSIUM

Saturday, March 27, 2021



Thank you to the following for their Virtual Exhibitor Support

- AstraZeneca
- Boehringer-Igelheim Interstitial Lung Disease
- Boehringer-Ingelheim Pharmaceuticals
- Breathe Pennsylvana
- Electromed, Inc.,-Smart Vest Airway Clearance System
- Gilead
- Glaxo Smith Kline
- Grifols
- Insmed
- Janssen
- Lifeline Physical Therapy Pulmonary Rehab
- Sanofi Genzyme-Regeneron
- Theravance Biopharma

Faculty Disclosures

The following speakers have nothing to disclose:

Ahmad Alhajhusain, MD, Tiffany DuMont, DO, Amit Kaura, MD, Jeffrey McGovern, MD,

Kevin Nauer, RN, BS, Christine Rauscher, MD, Daniel Shade, MD

Amy Schmetzer, DNP-FNP-C, Anil Singh, MD

The following speakers disclosed:

Tariq Cheema, MD Speaker's Bureau: AstraZeneca, Boehringer-Ingelheim Pharmaceutical and Glaxo Smith Kline

Sohini Ghosh, MD- Consultant: Intuitiv, Speaker's Bureau: AstraZeneca

Timothy Mickus, MD-Speaker's Bureau: Boehringer-Ingelheim Pharmaceuticals

Benny Weksler, MD- Consultant: Intuitive, Speaker's Bureau:Astra Zeneca

Meilin Young, MD- Speaker's Bureau: Glaxo Smith Kline

***All relevant financial conflicts have been mitigated.**

Interstitial Lung Diseases

Tariq Cheema M.D, FCCP,MMM

Associate Professor of Medicine

Temple University School of Medicine

Objectives

- Overview and Classification of Interstitial Lung disease.
- Diagnosis and management of Idiopathic Pulmonary fibrosis.

Introduction

- Diverse group of 150 disorders.
- Similar symptoms, physiology and radiology
- Successful treatment depends on the accurate diagnosis

Allows specific treatment for individual disease

Allows for physician to provide appropriate prognostic **information**

Interstitial Lung Disease

Characterized clinically by:

1. ***Radiologically*** diffuse infiltrates.

2. ***Histologically*** by distortion of the gas exchanging units.

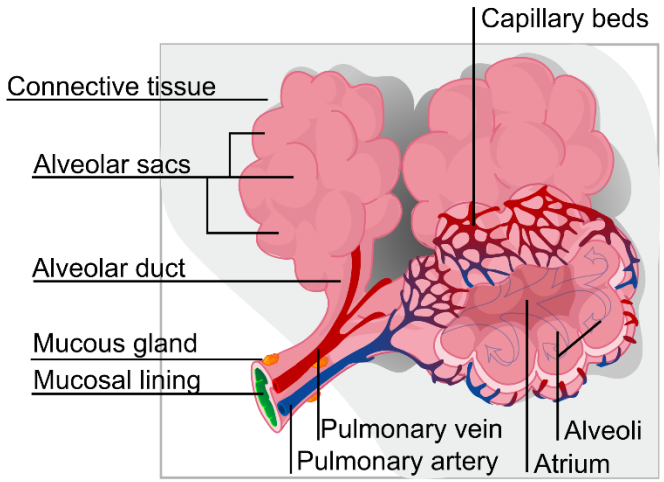
3. ***Physiologically*** by restriction of lung volumes and impaired oxygenation

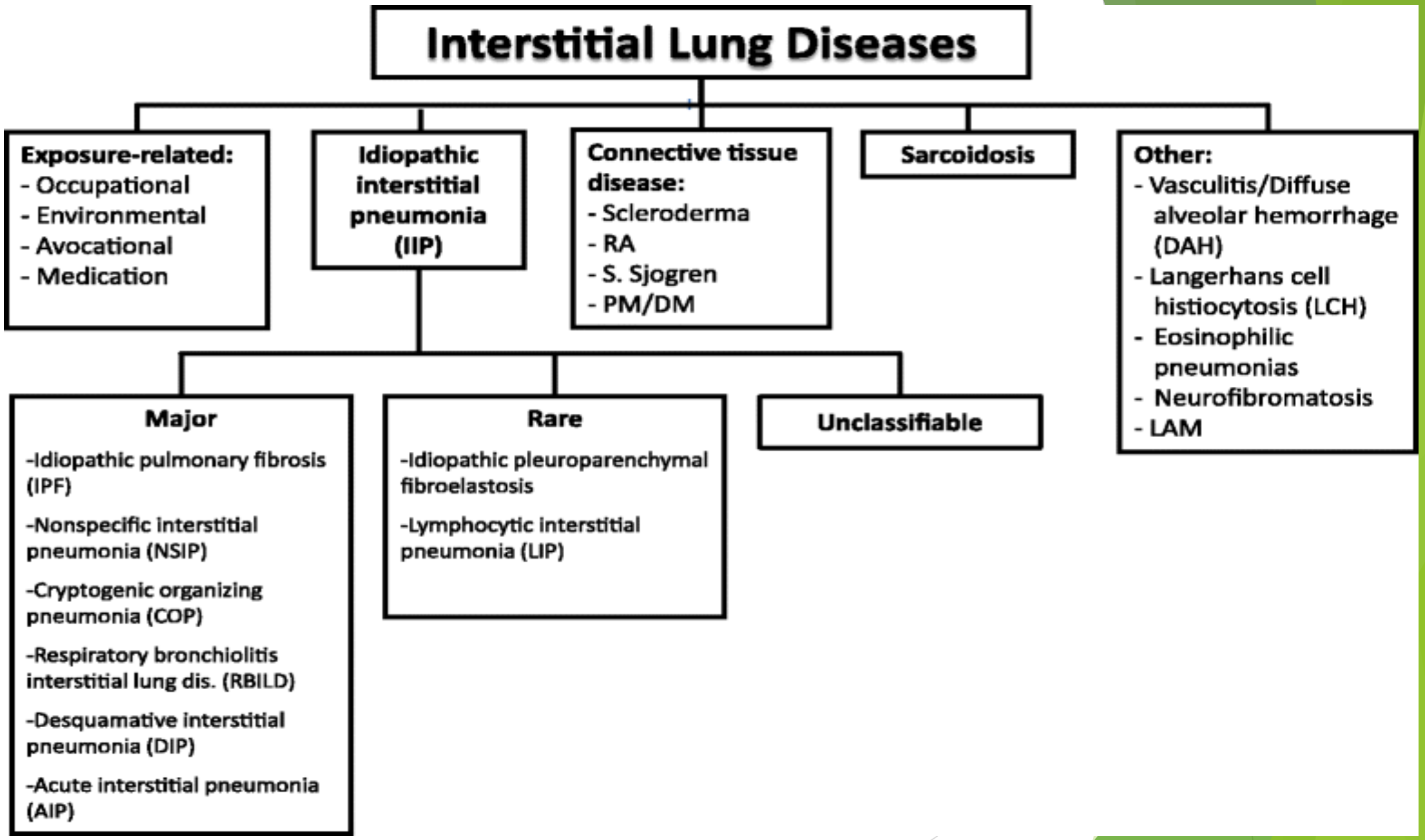
What does “Interstitial” mean

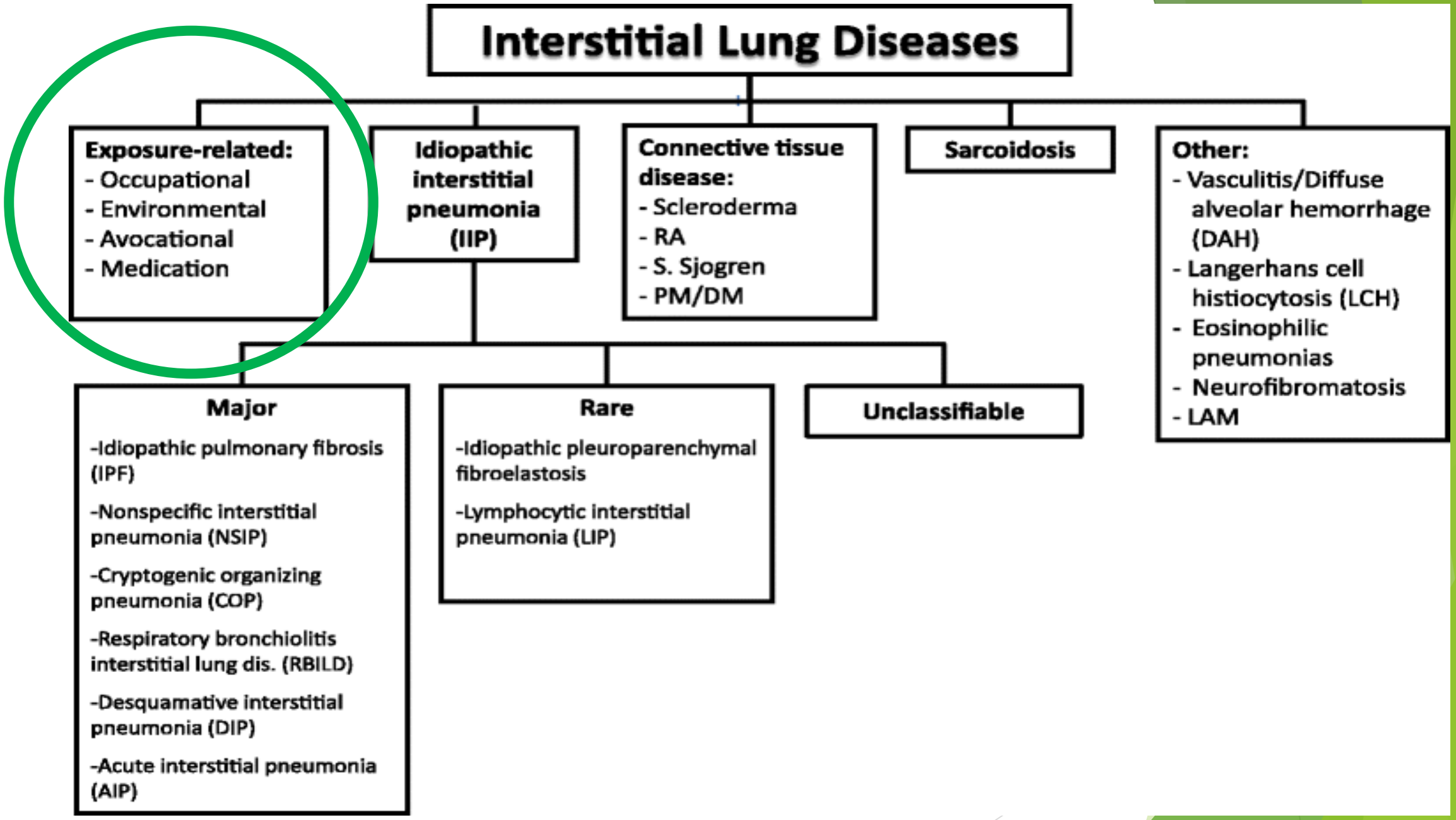
This term is actually a ***misnomer***. It implies that the inflammatory process is limited specifically to the area between the alveolar epithelial and capillary endothelial basement membranes.

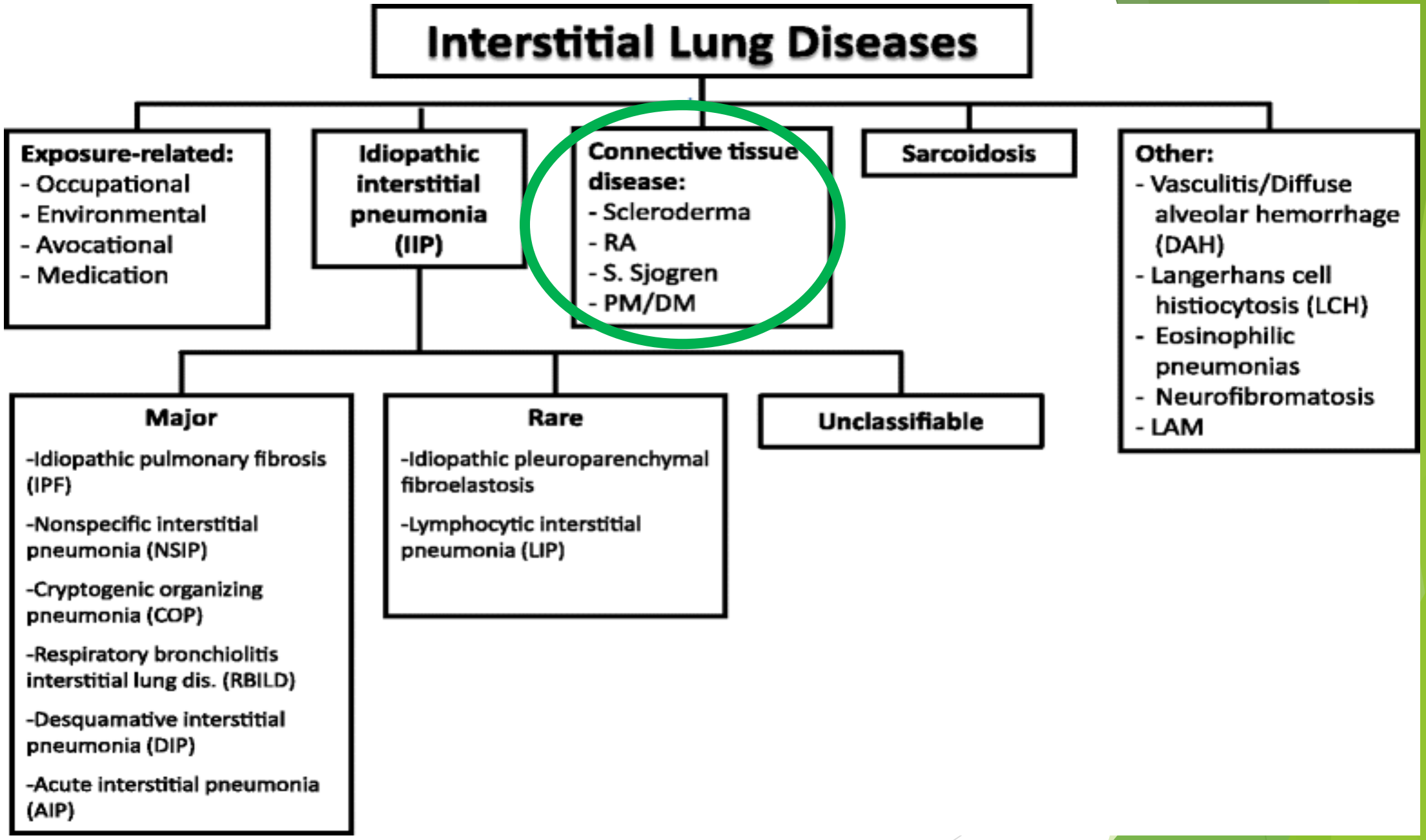
This group of pulmonary disorders frequently involves:

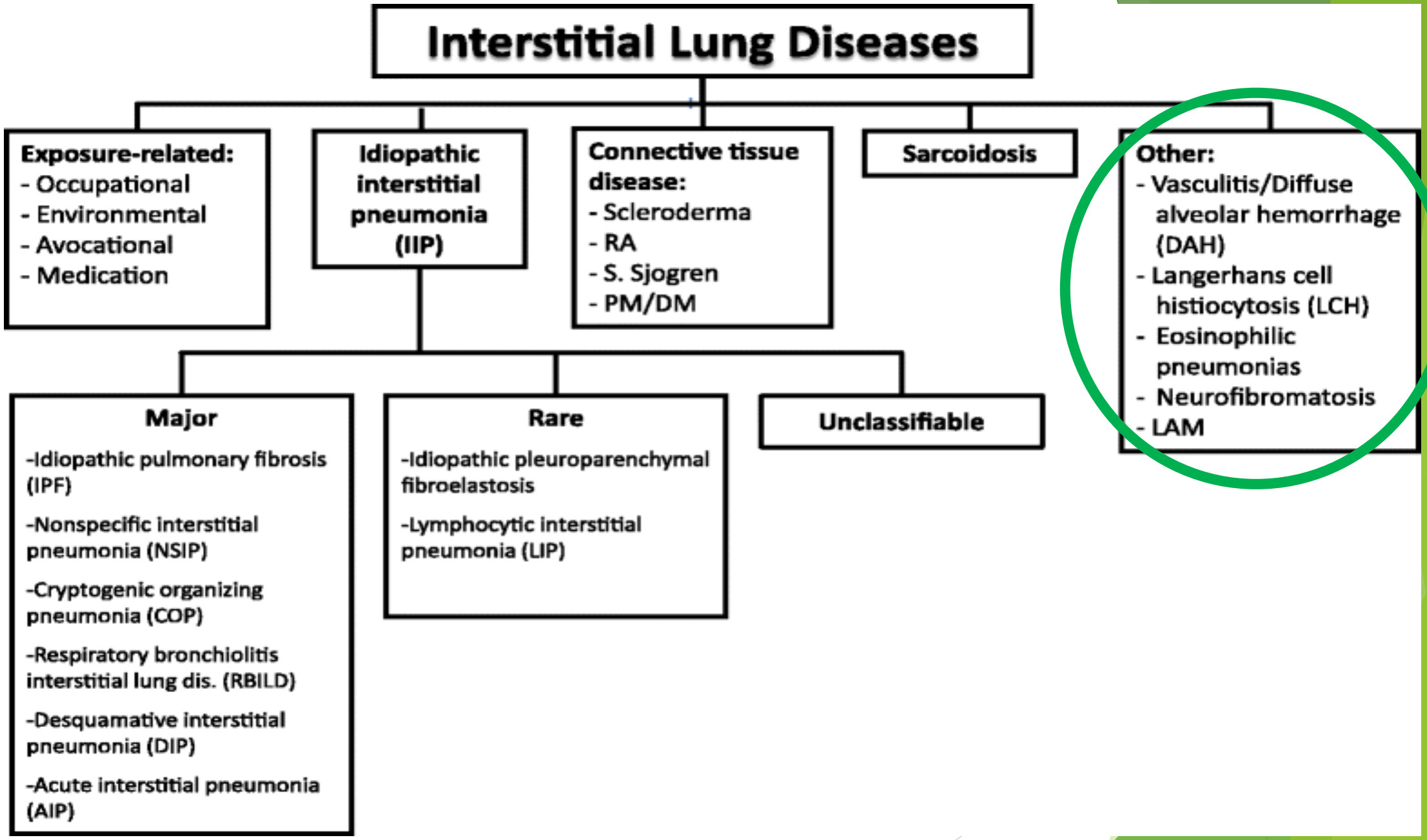
1. **Alveolar epithelium**
2. **Alveolar space**
3. **Pulmonary microvasculature**
4. **Respiratory bronchioles**
5. **Larger airways**
6. **Pleura**

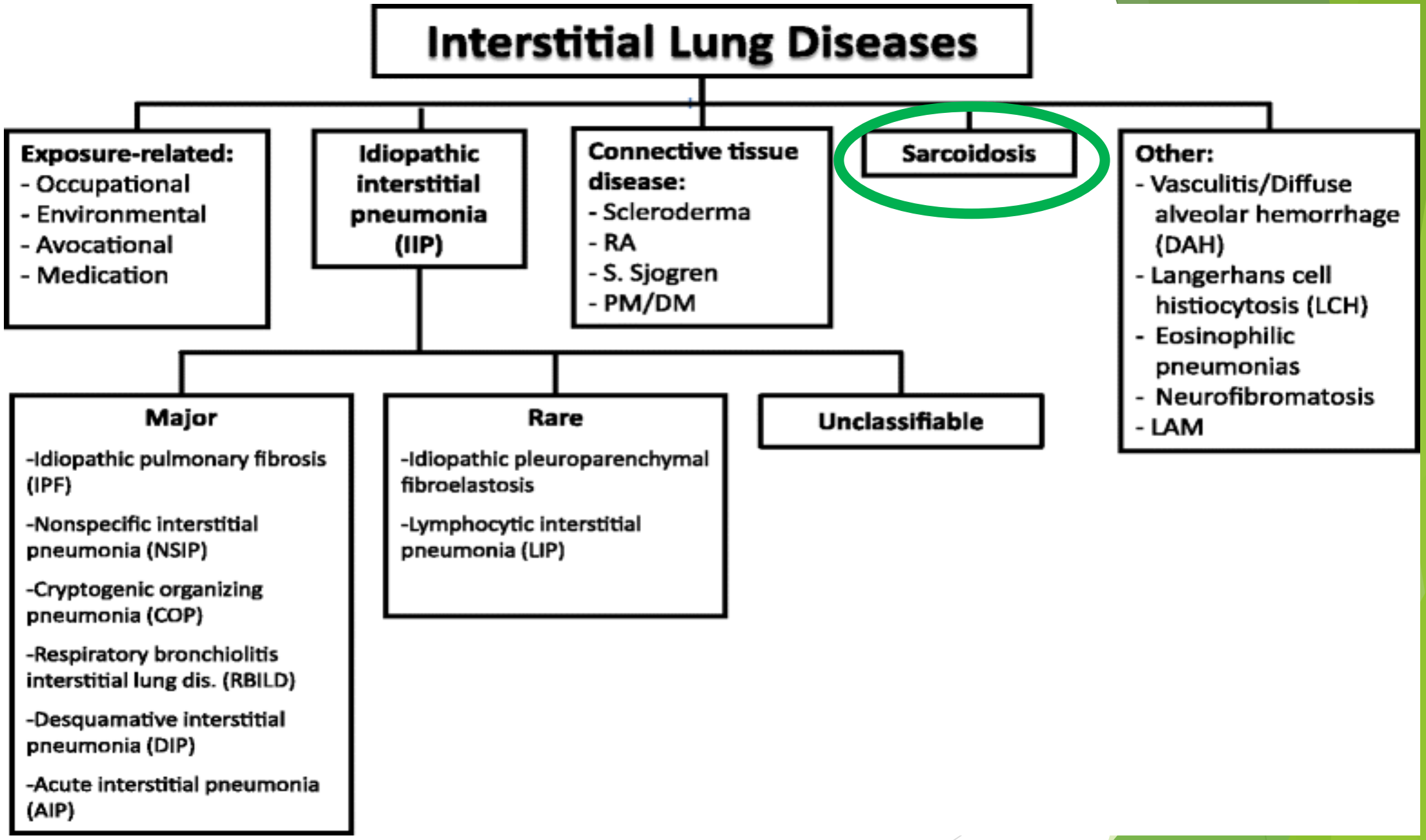


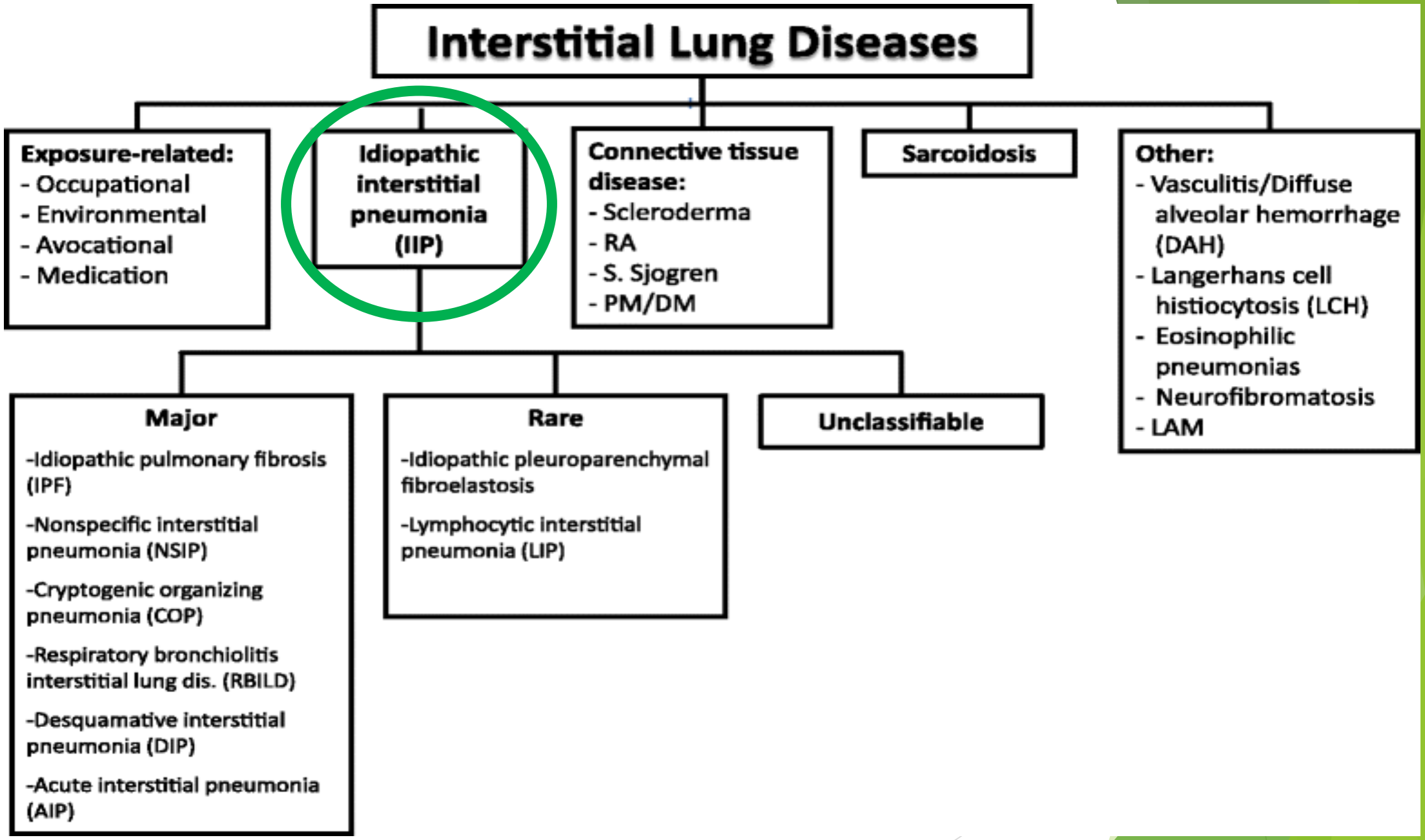

Interstitial Lung Diseases
Exposure-related:
- Occupational
- Environmental
- Avocational
- Medication
Idiopathic interstitial pneumonia (IIP)
Connective tissue disease:
- Scleroderma
- RA
- S. Sjogren
- PM/DM
Sarcoidosis
Other:
- Vasculitis/Diffuse alveolar hemorrhage (DAH)
- Langerhans cell histiocytosis (LCH)
- Eosinophilic pneumonias
- Neurofibromatosis
- LAM
Major
-Idiopathic pulmonary fibrosis (IPF)
-Nonspecific interstitial pneumonia (NSIP)
-Cryptogenic organizing pneumonia (COP)
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-Acute interstitial pneumonia (AIP)
Rare
-Idiopathic pleuroparenchymal fibroelastosis
-Lymphocytic interstitial pneumonia (LIP)
Unclassifiable

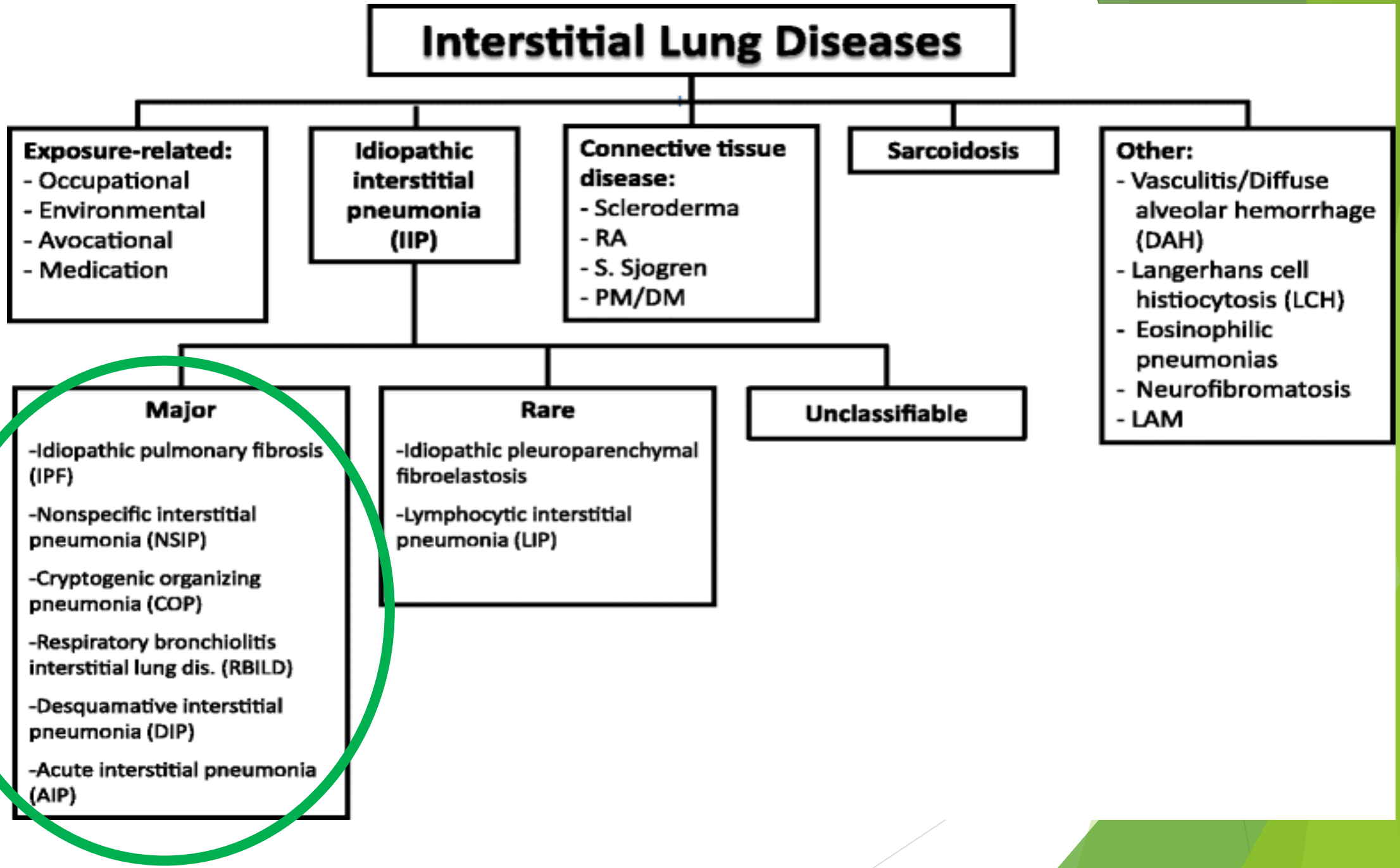

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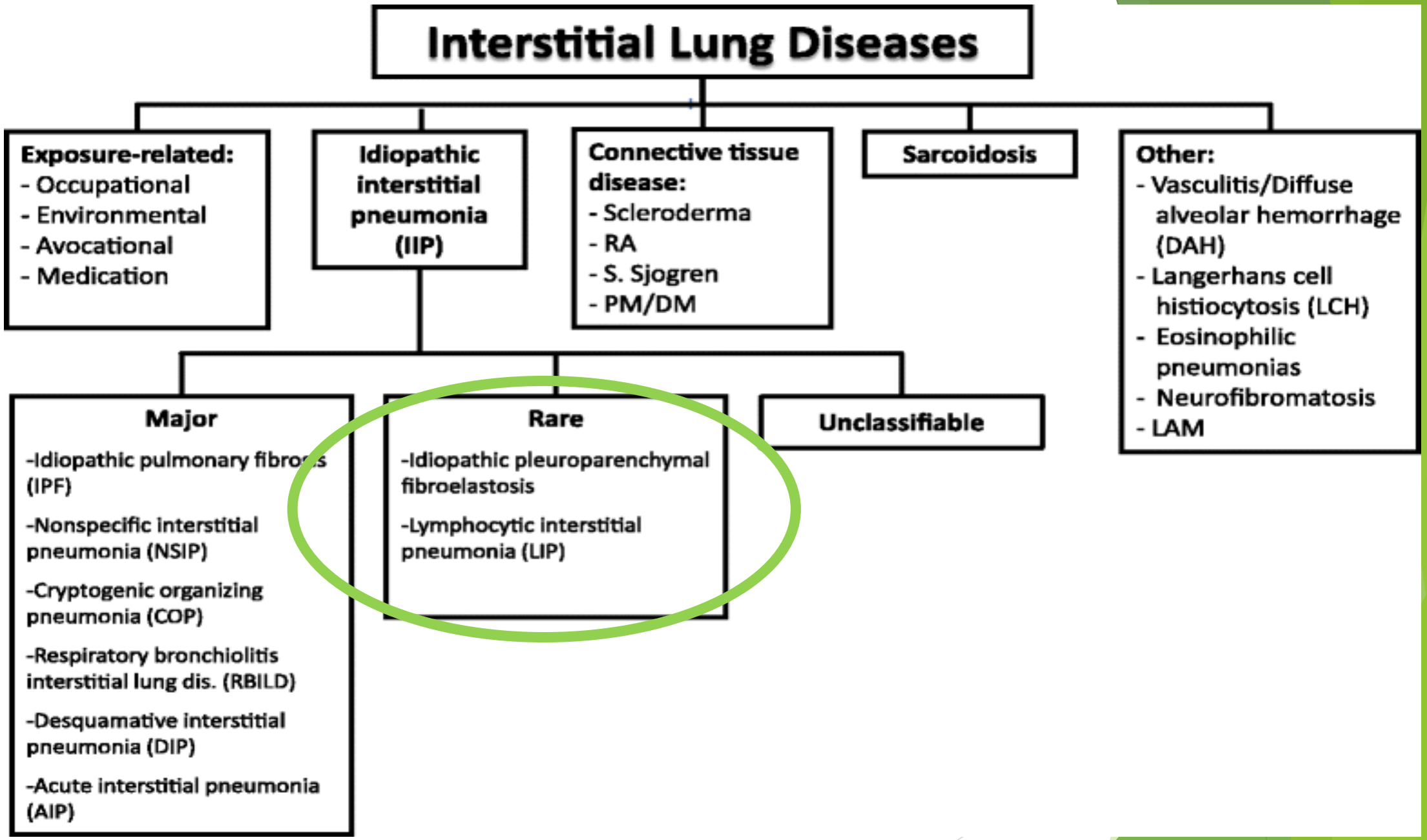

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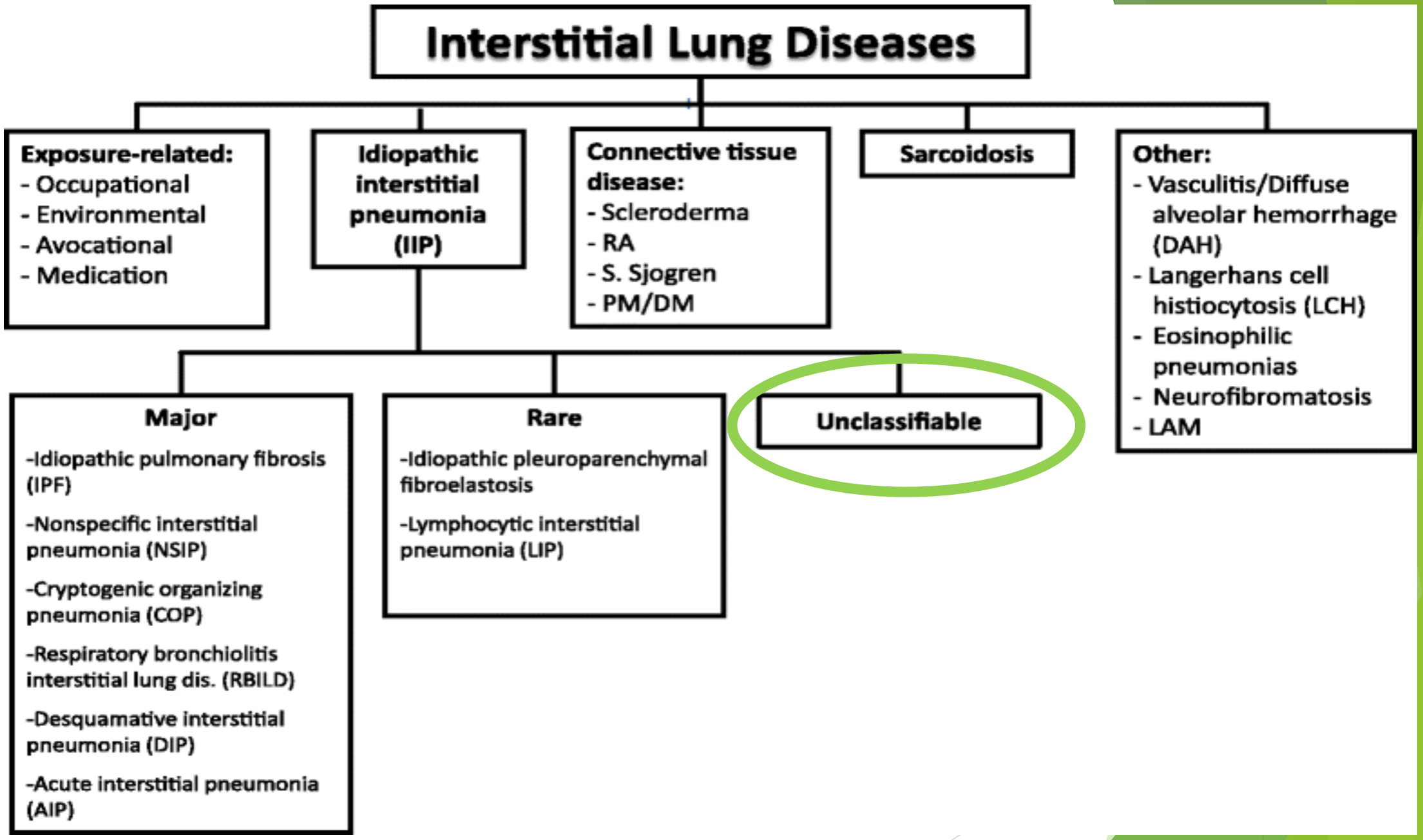

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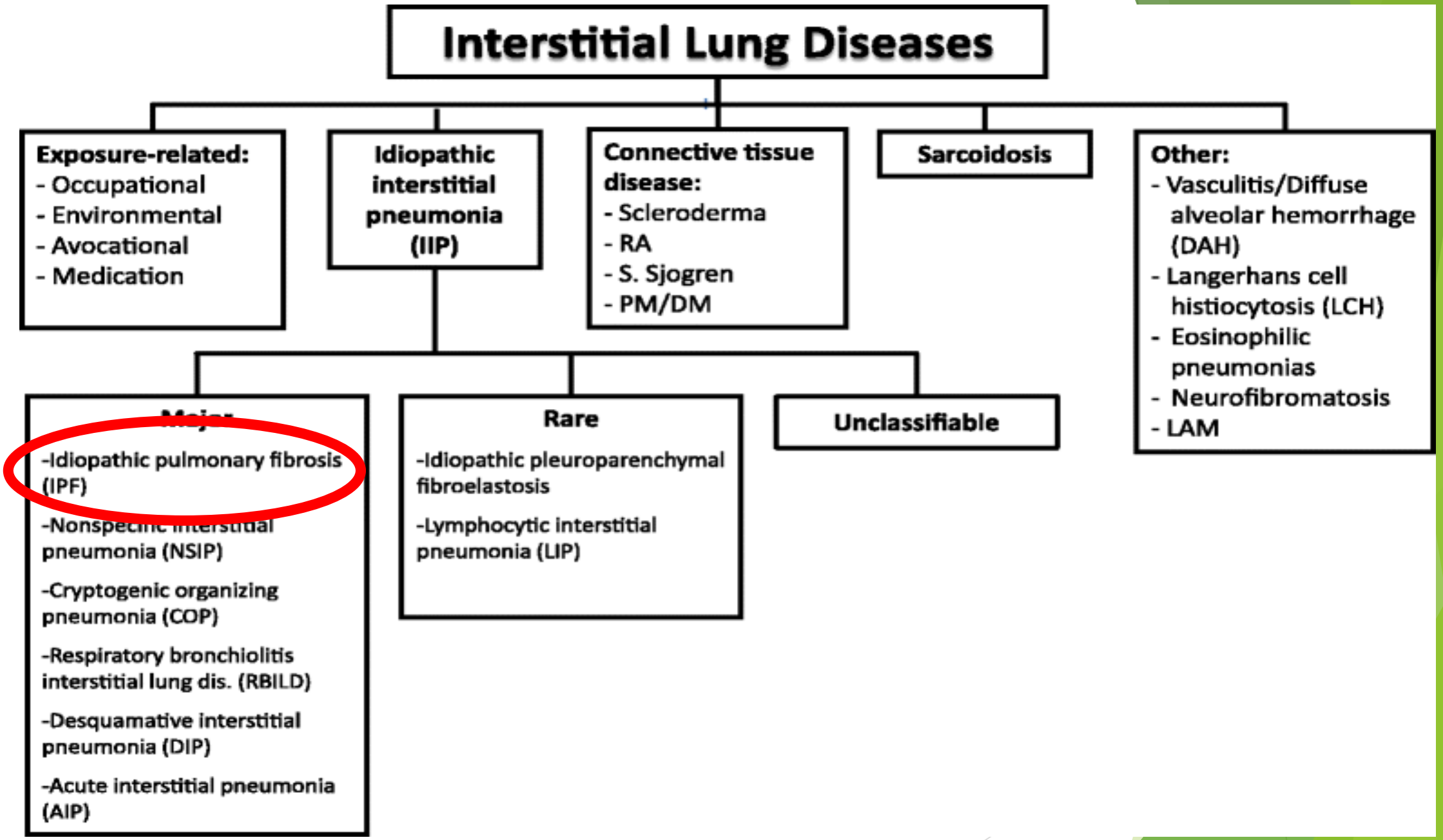

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Diagnosis of Interstitial Lung Disease

The diagnosis of a specific ILD is based on:

1. History- occupation, social, family, medications
2. Imaging-X ray and CT chest (HRCT)
3. Bronchoscopy(BAL, Biopsy)
5. Open lung biopsy
6. Biopsy of extra thoracic tissues



Clinical Presentation

- ILD present in certain age groups more commonly

- **Age 20-40 years**
  - Sarcoidosis
  - Connective tissue disease related ILD
  - Lymphangioleiomyomatosis(LAM)
  - Eosinophilic granuloma

- **> 50years**
  - Idiopathic pulmonary fibrosis

Clinical Presentation

Women predominant

LAM (lymphangioleiomatosis)

ILD associated with CTD.

Male predominant:

ILD associated with RA

Pneumoconiosis

Clinical Presentation

Duration

- **Insidious over months or years (e.g., IPF)**

- **Acute (less than 3 weeks)** (e.g. drug reaction, acute hypersensitivity pneumonitis, chemical exposure)

- **Subacute: (3-12 weeks)** Cryptogenic organizing pneumonia(COP)

Clinical Presentation

Smoking related :

- - Eosinophilic granuloma
- - Desquamative interstitial pneumonitis(DIP)
- - Respiratory bronchiolitis(RB-ILD)



Diseases less likely to be seen in smokers :

- Hypersensitivity pneumonitis
- Sarcoidosis

Pulmonary Hemorrhage is far more frequent in current smokers and Good Pasture's syndrome

https://www.pneumotox.com

Table 2. Drug-Induced Interstitial Lung Disease

Antibiotics
- Nitrofurantoin, acute and chronic
- Sulfasalazine

Anti-inflammatory agents
- Aspirin
- Gold
- Penicillamine

Chemotherapeutic agents
- Antibiotics
  - Bleomycin sulfate
  - Mitomycin C
- Alkylating agents
  - Busulfan
  - Cyclophosphamide
  - Chlorambucil
  - Melphalan
- Antimetabolites
  - Azathioprine
  - Cytosine arabinoside
  - Methotrexate

Miscellaneous
- O2
- Drugs inducing pulmonary infiltrates eosinophilia
- Radiation
- L-tryptophan

Drug-induced systemic lupus erythematosus
- Procainamide hydrochloride
- Isoniazid
- Hydralazine hydrochloride
- The hydantoins
- Penicillamine

Illicit drugs
- Heroin
- Methadone hydrochloride
- Propoxyphene hydrochloride (Darvon)
- Talc



Redrawn from Rosenow, EC, III, Martin WJ, II. Drug-induced interstitial lung disease. In: Interstitial Lung Disease, Schwarz, MI, King, TE, Jr, (Eds), Mosby Year Book, St. Louis, 1993, p. 255-270.

Table 2. Drug-Induced Interstitial Lung Disease

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- **Nitrofurantoin**, acute and chronic
- Sulfasalazine

Anti-inflammatory agents
- **Aspirin**
- Gold
- Penicillamine

Chemotherapeutic agents
- Antibiotics
  - Bleomycin sulfate
  - Mitomycin C
- Alkylating agents
  - Busulfan
  - Cyclophosphamide
  - Chlorambucil
  - Melphalan
- Antimetabolites
  - Azathioprine
  - Cytosine arabinoside
  - **Methotrexate**

Miscellaneous
- O2
- Drugs inducing pulmonary infiltrates eosinophilia
- Radiation
- L-tryptophan

Drug-induced systemic lupus erythematosus
- Procainamide hydrochloride
- Isoniazid
- Hydralazine hydrochloride
- The hydantoins
- Penicillamine



Illicit drugs
- **Heroin**
- **Methadone hydrochloride**
- Propoxyphene hydrochloride (Darvon)
- Talc

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INORGANIC DUSTS ASSOCIATED WITH DIFFUSE PULMONARY INFILTRATES (PNEUMOCONIOSIS)

Inorganic Dust	**Occupations Associated with Exposure**
Coal	Mining: cutting, loading
Silica (silicosis)	Mining, tunneling, foundry work, sandblasting, boiler-scaling. , ceramics, paints, varnishes, grinders
Asbestos	Pipefitting, boiler work, ship manufacturing and repair, insulation work, Spouses of asbestos workers

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Symptoms of Interstitial Lung Disease

- Exertional dyspnea
- Non productive cough
- Wheezing is uncommon
- Hemoptysis is seen in vasculitis **(e.g. Granulomatosis with polyangiitis -- *Wegener's granulomatosis*)**
- Dysphagia (Systemic sclerosis)
- Neurological, manifestations**(Eosinophilic granulomatosis with polyangiitis- *Churgh Strauss)***
- Upper airway obstruction
- Skin rashes **(Vasculitis)**



Physical Examination

“Velcro rales” are common in most forms of ILD. Mainly present when there is fibrosis

Clubbing: most commonly seen in IPF but non-specific.

Extra thoracic findings: suggestive but not diagnostic.(Connective tissue disorders)

Cyanosis in late stage of ILD.



Recommended Autoantibody Screening

Signs and Symptoms	Laboratory Test	Disease
Pleurisy/effusions Morning stiffness Arthritis Rash	ANA[1,2a] RF[1,2] Anti-CCP[1,2]	Rheumatoid arthritis Multiple others
Dry mouth (Sicca syndrome) Dry eyes	ANA[1,2] Anti-dsDNA[2] Sm/RNP (ENAs)[2] SS-A (Anti-Ro)[1,2] SS-B (Anti-La)[1,2]	Lupus Sjögren's syndrome
Skin thickening Esophageal symptoms Raynaud's phenomenon Sclerodactyly	Anti-Scl-70[1,2] Nucleolar pattern ANA[2] Anti-U1 RNP[2]	Systemic sclerosis/ scleroderma
Proximal muscle pain or weakness Heliotrope rash	Anti-Jo1[1-3] CK[1] Aldolase[1]	Dermatomyositis Polymyositis
Mechanic's hands Raynaud's phenomenon Muscle pain	Anti-Jo-1 (antisynthetase)[1,3b] CK[1] Aldolase[1]	Antisynthetase syndrome

ANA, antinuclear antibody; CCP, cyclic citrullinated peptide antibody; CK, creatine kinase; CP, citrullinated peptide; dsDNA, double stranded DNA; ENA, extractable nuclear antigen; RF, rheumatoid factor; RNP, ribonucleoprotein; Sm, Smith antigen.

[a]New multiplex (direct, immunobead) ANA assays are limited in the type of antigens assayed and frequently miss systemic lupus erythematosus, scleroderma, and myositis antibodies.[4,5]
[b]Anti-Jo1 is the most commonly identified antibody for antisynthetase syndrome.[3]

1. Bagby G et al. *Am J Respir Crit Care Med*. 2011;183:788-824. 2. Satoh M et al. *Med Rheumatol*. 2009;19(3):210-228. 3. Solomon J et al. *J Bras Pneumol*. 2011;37(1):100-109. 4. Shanmugam V

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ANA, antinuclear antibody; CCP, cyclic citrullinated peptide antibody; CK, creatine kinase; CP, citrullinated peptide; dsDNA, double stranded DNA; ENA, extractable nuclear antigen; RF, rheumatoid factor; RNP, ribonucleoprotein; Sm, Smith antigen.

[a]New multiplex (direct, immunobead) ANA assays are limited in the type of antigens assayed and frequently miss systemic lupus erythematosus, scleroderma, and myositis antibodies.[4,5]
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Recommended Autoantibody Screening

Signs and Symptoms	Laboratory Test	Disease
Pleurisy/effusions Morning stiffness Arthritis Rash	ANA[1,2a] RF[1,2] Anti-CCP[1,2]	Rheumatoid arthritis Multiple others
Dry mouth (Sicca syndrome) Dry eyes	ANA[1,2] Anti-dsDNA[2] Sm/RNP (ENAs)[2] SS-A (Anti-Ro)[1,2] SS-B (Anti-La)[1,2]	Lupus Sjögren's syndrome
Skin thickening Esophageal symptoms Raynaud's phenomenon Sclerodactyly	Anti-Scl-70[1,2] Nucleolar pattern ANA[2] Anti-U1 RNP[2]	Systemic sclerosis/ scleroderma
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Pulmonary Function Testing

*Most of the ILD have a **restrictive defect**.*

Mixed pattern(both obstructive and restrictive)

- - Eosinophilic granulomatosis
- - Lymphangioleiomyomatosis (LAM)
- - Granulomatosis with polyangiitis (Wegener's granulomatosis)
- - Cryptogenic organizing pneumonia
- - Hypersensitivity Pneumonitis (HP)
- - Sarcoidosis



Pulmonary Function Testing

Moderate - severe reduction in DLCO but normal lung volumes in a patient with ILD suggest:

- Combined COPD and Pulmonary fibrosis(CPFE)
- Pulmonary Vascular Disease



Imaging

- Chest X-ray can raise suspicion
- ***Always look for old x-rays***
- HRCT (High Resolution CT Chest)is almost always needed



Bronchoscopy

It is often the initial procedure of choice.

Transbronchial bx can be diagnostic in the following

-Lymphangitic carcinomatosis

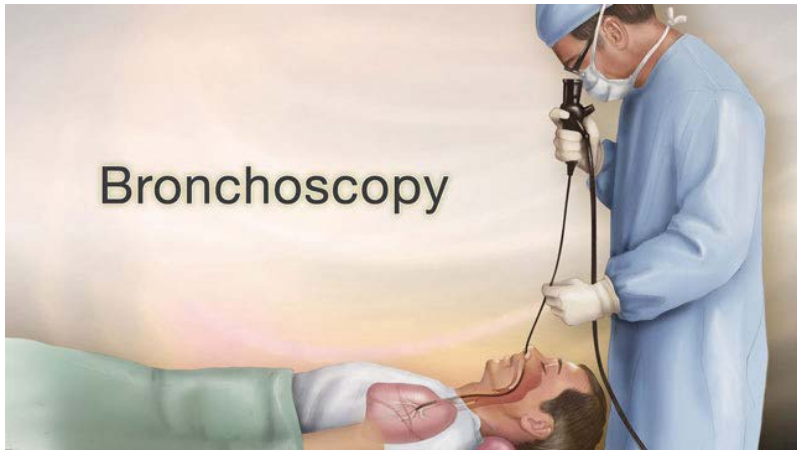
-Eosinophilic pneumonia

-Pulmonary alveolar proteinosis

-Eosinophilic granulomatosis

-Good pasture’s syndrome

-Sarcoidosis (80%)

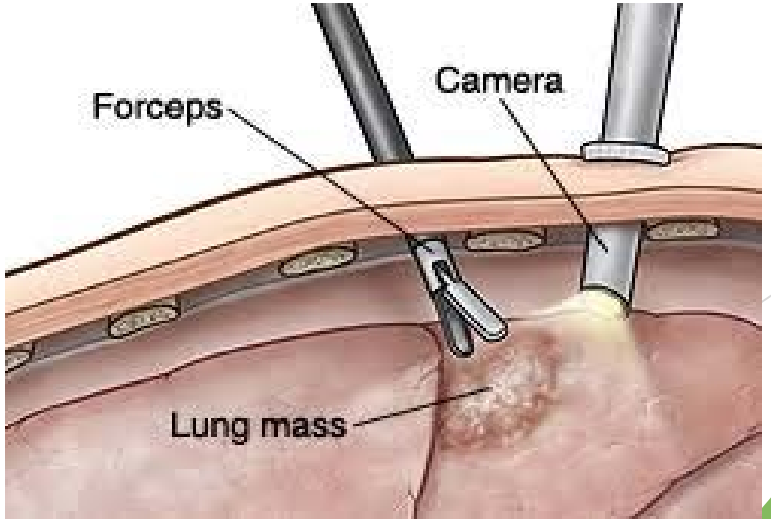


Indications for Lung Biopsy

- Exclude neoplasm or infection

- Identification of a more treatable condition

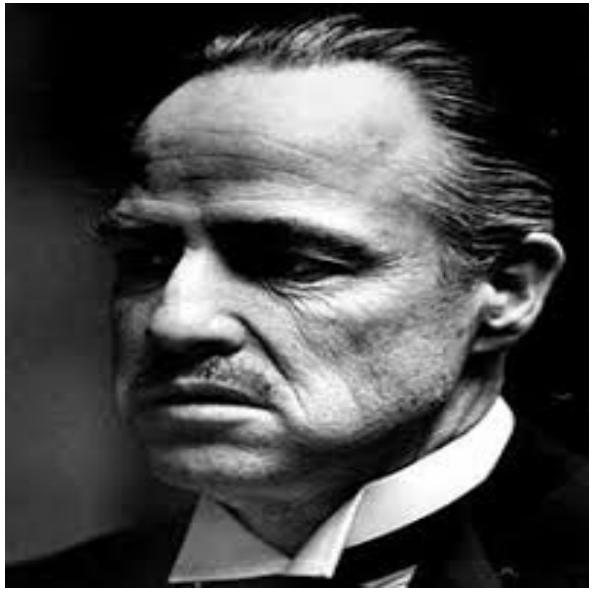
- For a definitive diagnosis before starting treatment, for patients with atypical or progressive pattern



Idiopathic Pulmonary Fibrosis




CM
1 2 3 4 5

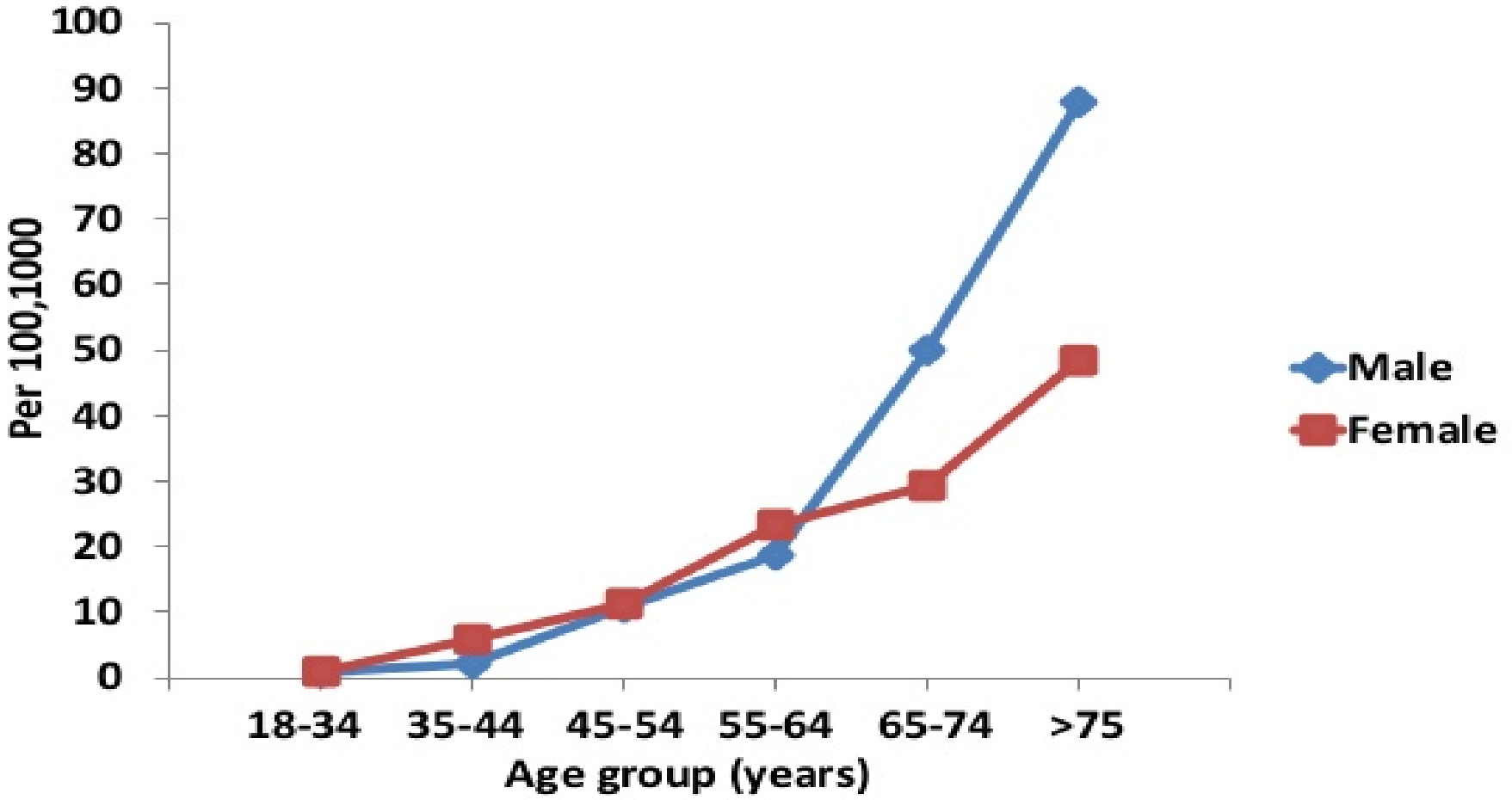



HISTORY
WEEK

Overview of Idiopathic pulmonary Fibrosis(IPF)

- IPF is a progressive, fatal lung disease of unknown etiology
- Fibrosis is limited to the lung alveoli and interstitium
- According to the National Institutes of Health, about **100,000 people** in the United States have IPF, and approximately **30,000** to **40,000** new cases are found each year.
- Accurate diagnosis requires
  1. Exclusion of other known causes of ILD
  2. Presence of a usual interstitial pneumonia(UIP)pattern on high resolution CT chest
  3. If necessary ,Surgical Lung Biopsies

Incidence of IPF



Am J Respir Crit Care Med 2006;175: 810-816

Risk Factors for IPF

- Etiology is unknown but certain environmental and genetic risk factors have been described
- Metal dust, Coal, agricultural chemicals

- Genetic factors have been linked to the Familial form of IPF

5% of all cases of IPF are familial

Family history increases the odd of IPF to 6 fold

- Familial and sporadic forms of IPF are radiologically ,clinically and pathologically identical.

When to suspect IPF

- Patients who present with **exertional dyspnea**
- Patients who present with **subacute or chronic cough**
- Patient who have a **family history** of Pulmonary Fibrosis
- **Incidental** finding of fibrosis on X ray or HRCT
- Spirometry with low FVC (restriction) or low Diffusion capacity

Look ,Listen, walk approach



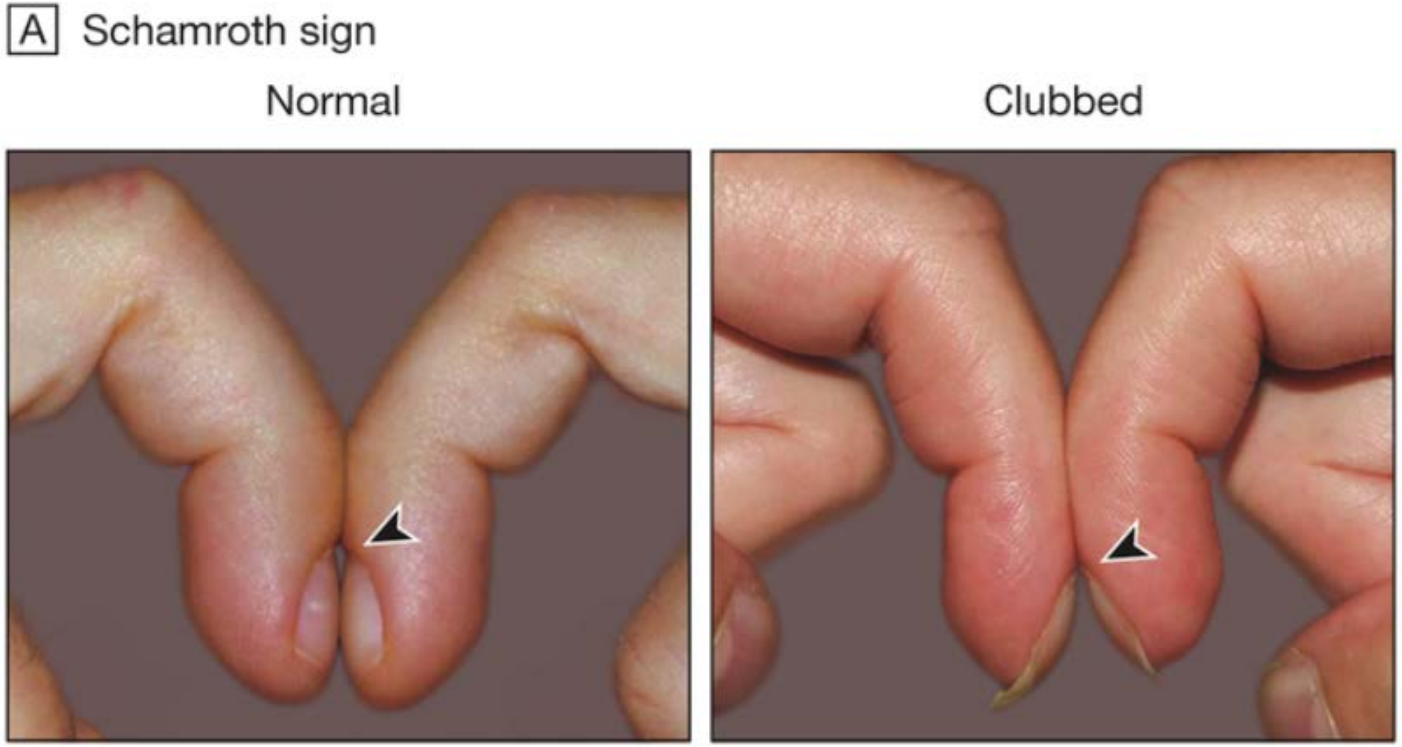
- **Look** at the skin and fingers
- **Listen** carefully for crackles
- both lung bases
- Laterally in mid axillary line
- Anteriorly



- **Walk** the patient in the hallway(or staircase)
- Try to elicit exertional dyspnea if possible
- Measure Spo2 before and after walking
- A 3% drop in Spo2 indicates exertional desaturation



Schamroth's sign



Clinical presentation

- Insidious onset of chronic exertional dyspnea and a dry cough
- Shortness of breath at rest suggest an alternate diagnosis such as heart failure
- Wheezing is not common in IPF and suggests airway disease rather than interstitial disease
- **“Velcro-like ”** crackles on auscultation of the lungs
- Fever is uncommon in IPF and a alternative diagnosis should be sought
- Clubbing is present

Diagnosis

Comprehensive history :

Social history ,environmental exposures(birds and pets), occupational history, drug exposures and family history

Pulmonary Function Test

FVC, Diffusion capacity, 6 MWT

Radiological Assessment

Chest X-ray

HRCT

Surgical Assessment

Open lung biopsy if necessary

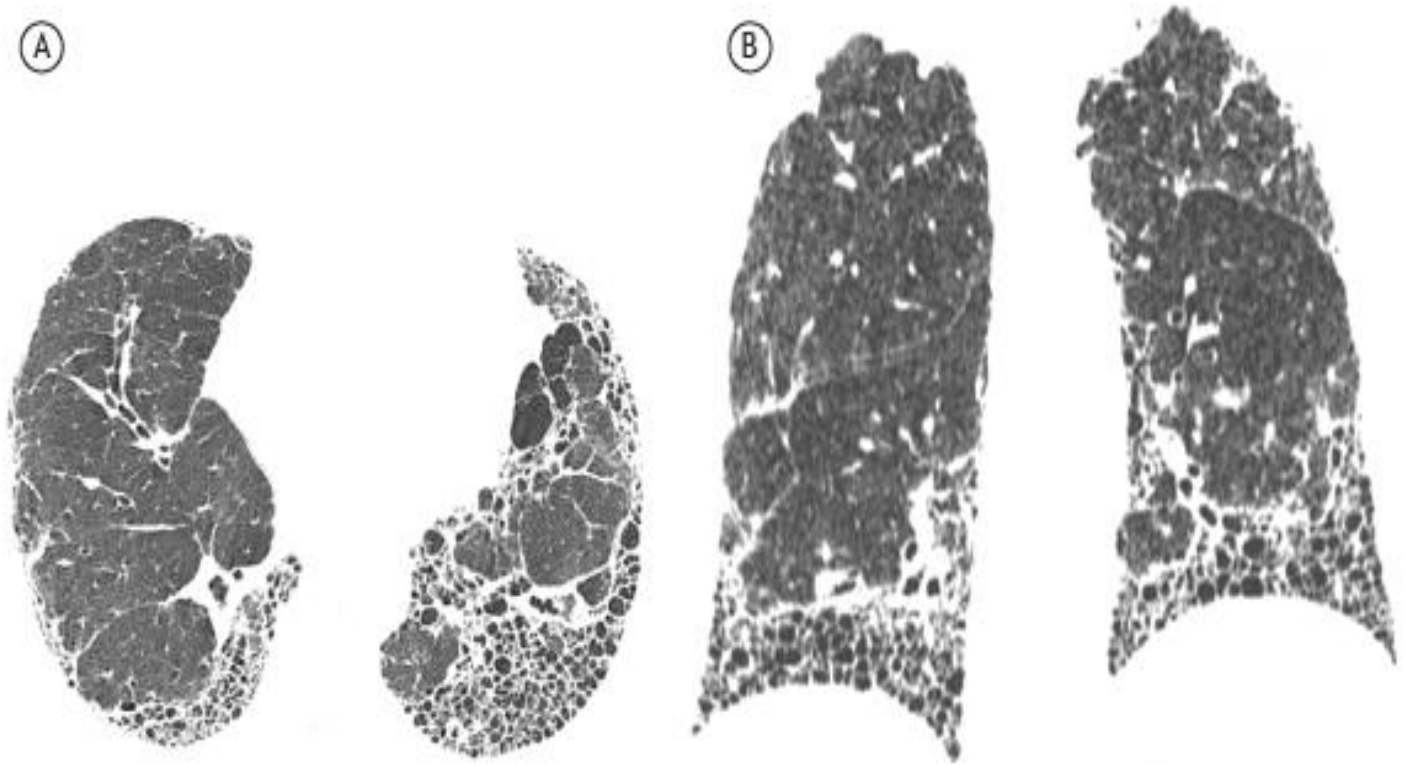
2018 ATS guidelines for CT interpretation

- UIP pattern
- Probable UIP
- Indeterminate pattern
- Alternate diagnosis

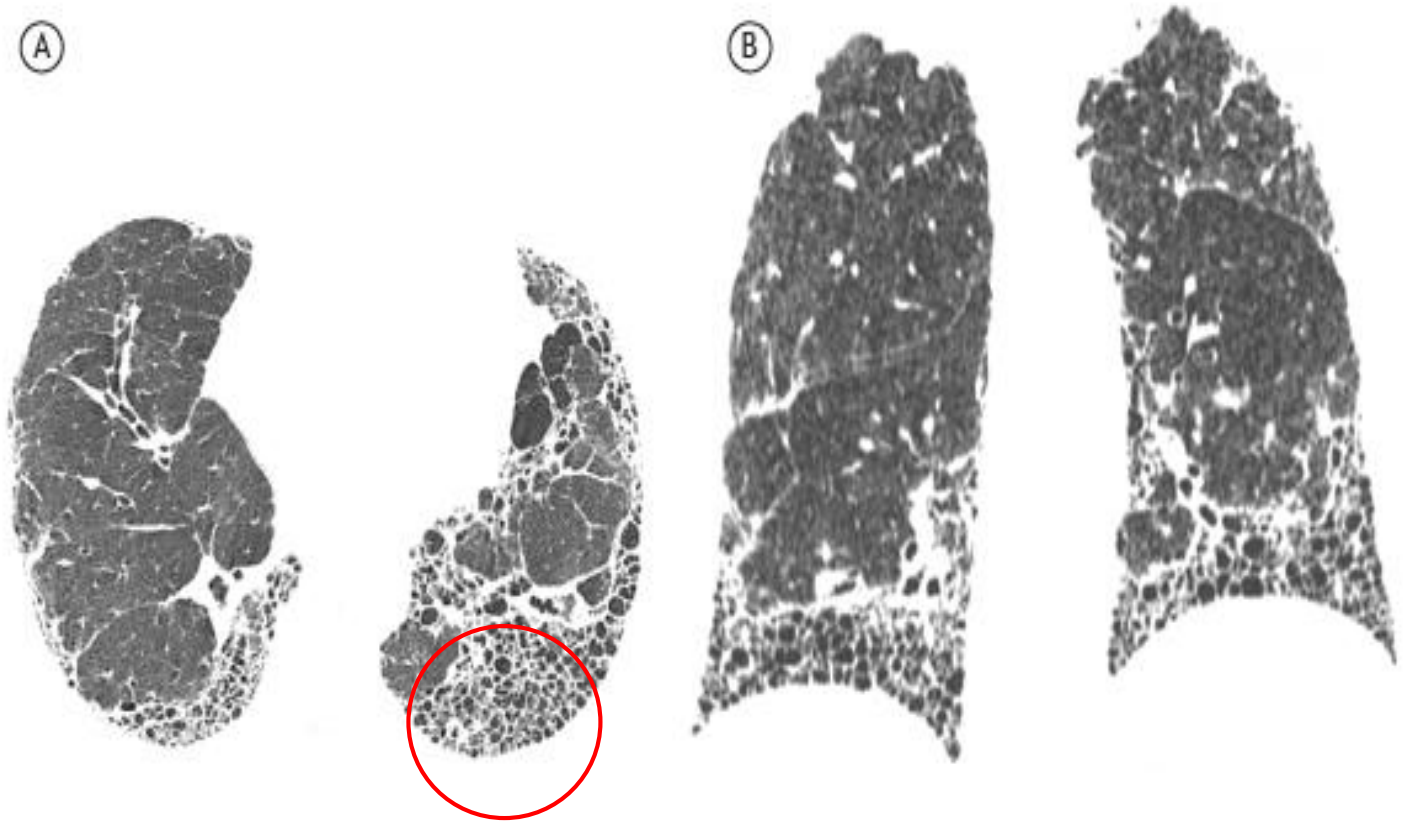
UIP Pattern

- **Honeycombing**
- **Reticular opacities**: often associated with honeycombing and traction bronchiectasis, with peripheral and lower lobe predominance
- **Lung architectural distortion**: which reflects lung fibrosis and is often prominent
- **Lobar volume loss** (predominantly lower lobes) is seen in cases of more advanced fibrosis

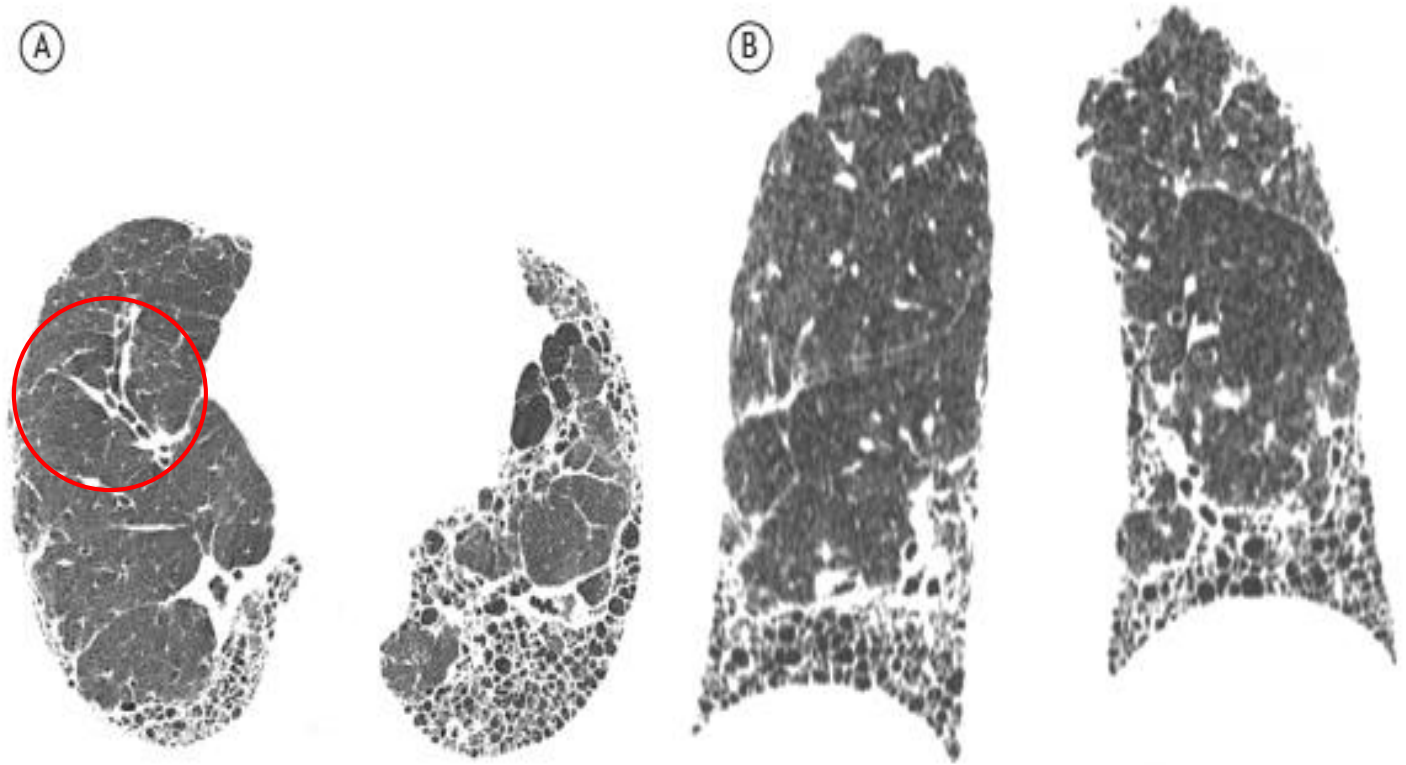
UIP Pattern



UIP Pattern - Honeycombing



UIP Pattern -Traction Bronchiectasis

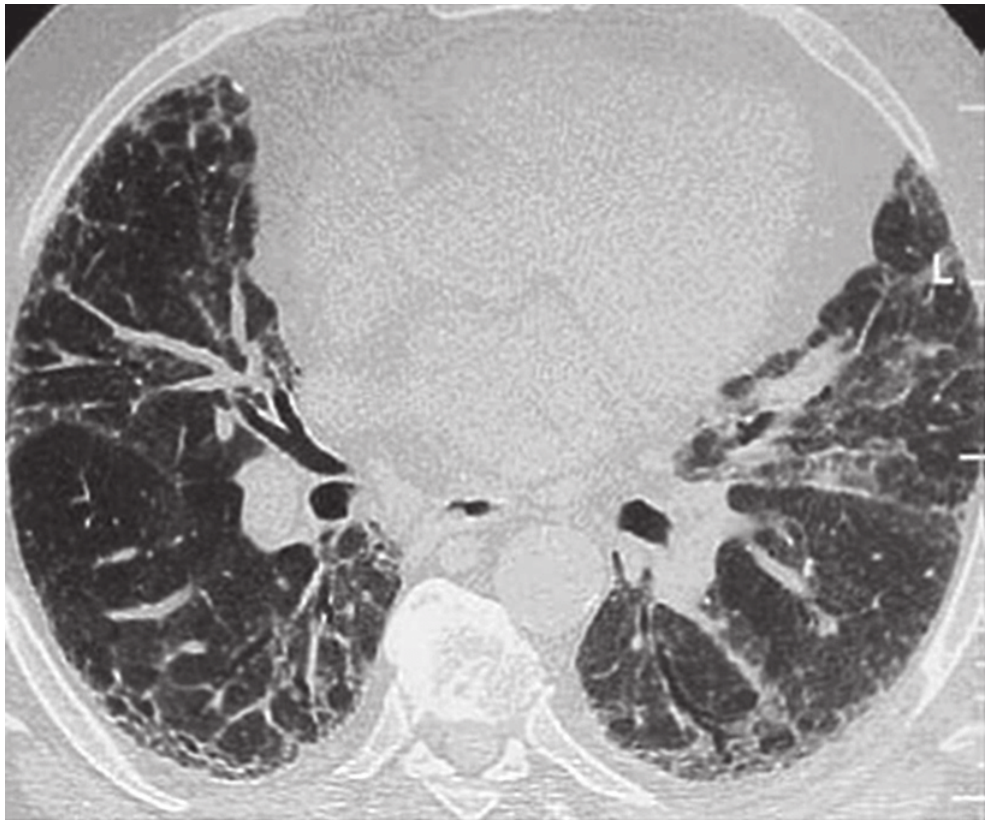


Probable UIP pattern

- **Reticular opacities**: often associated with honeycombing and traction bronchiectasis, with peripheral and lower lobe predominance
- **Lung architectural distortion**: which reflects lung fibrosis and is often prominent
- **Lobar volume loss** (predominantly lower lobes) is seen in cases of more advanced fibrosis

- **No honeycombing present**

Probable UIP Pattern -Traction Bronchiectasis



Indeterminate pattern

- Subpleural and basal predominate
- May have subtle reticulation
- Features and fibrosis that are not consistent with any etiology

Indeterminate pattern



Alternate diagnosis



Alternate diagnosis

- Features not consistent with IPF
- Ground glass opacities predominate
- Nodules
- Consolidations

Histopathology

- UIP pattern
- Probable UIP
- Indeterminate pattern
- Alternate diagnosis

Histopathology

- Basilar and peripheral fibrosis (Figure 4-2)
- Microscopic subpleural and paraseptal fibrosis
- Subpleural microscopic honeycombing
- Fibroblastic foci (Figure 4-3)
- Interspersed normal areas of lung (temporal heterogeneity)

Key Fact

Temporal heterogeneity is the cardinal feature distinguishing UIP from other idiopathic interstitial pneumonias.

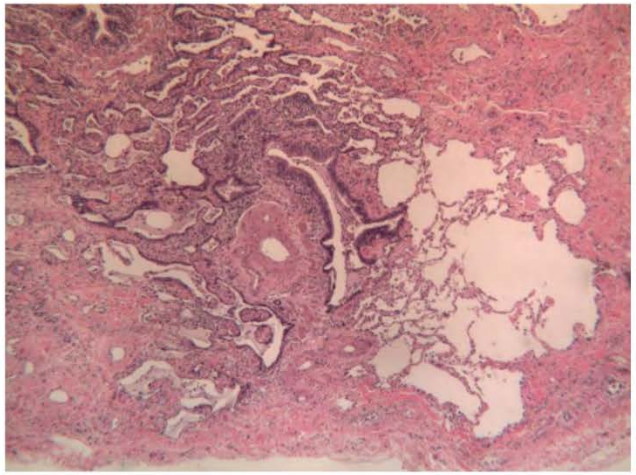


Figure 4-2. Usual interstitial pneumonia showing low-magnification patchy interstitial fibrosis with juxtaposition of normal areas of lung with fibrotic and honeycombing changes.
(Image courtesy of Joseph F. Tomashefski, Jr., MD, Department of Pathology, MetroHealth Medical Center, Case Western Reserve University, Cleveland, Ohio.)

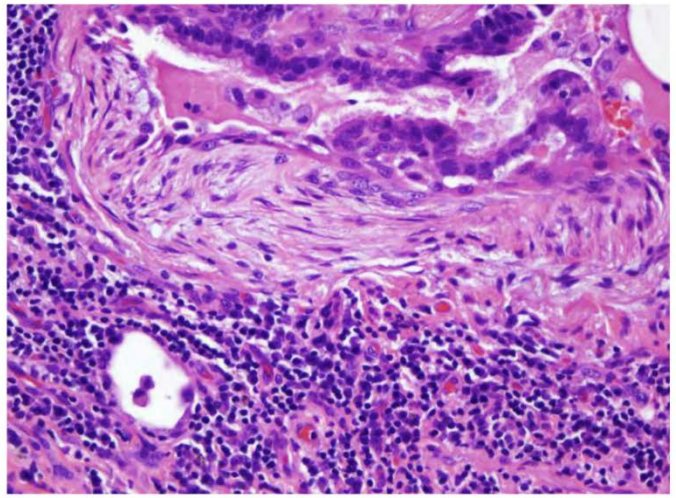
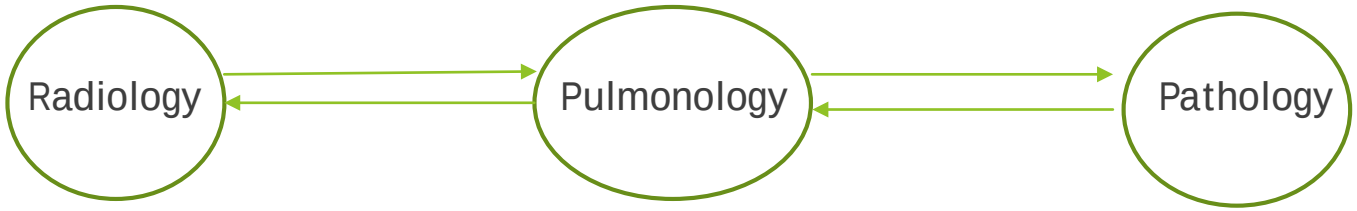


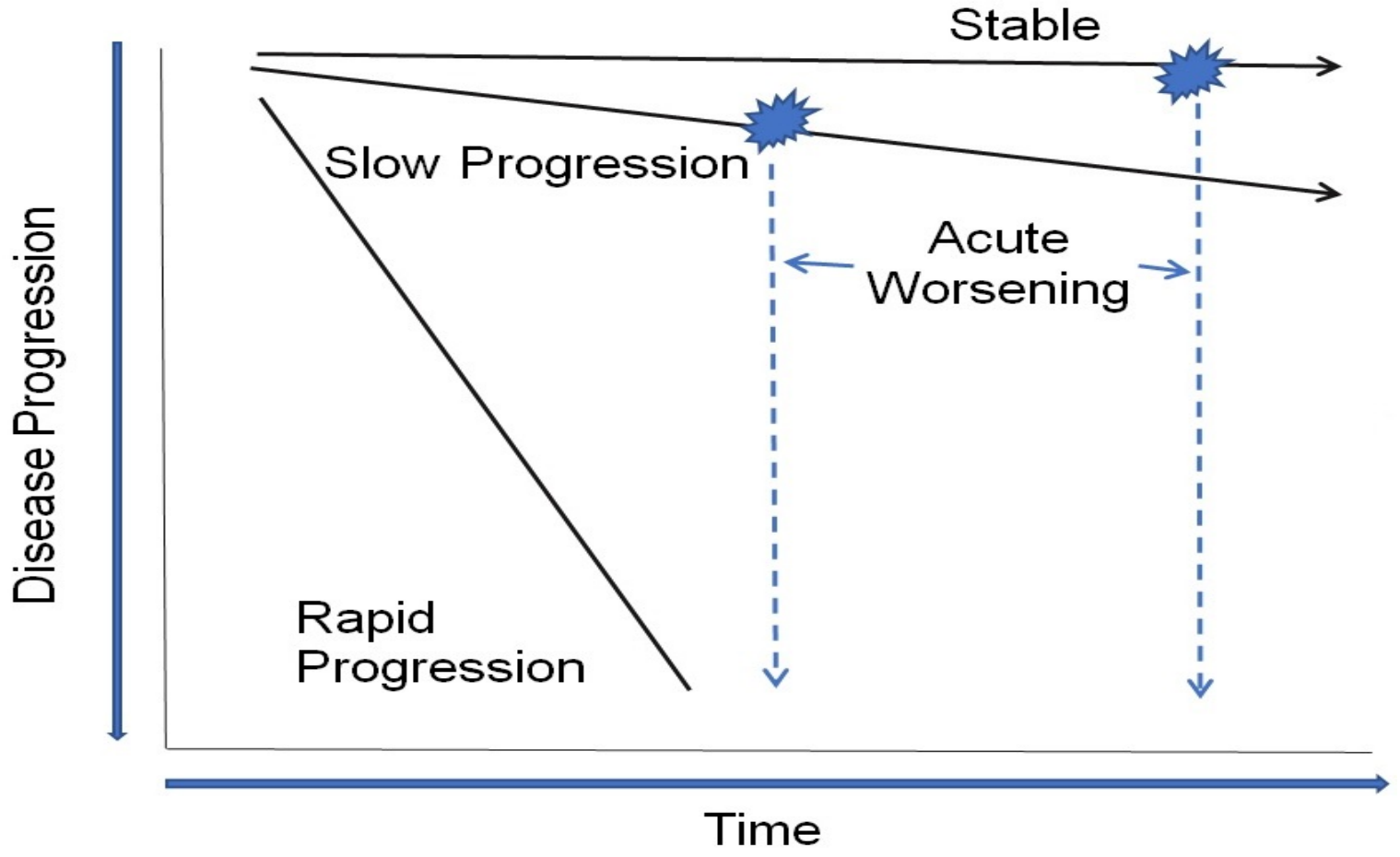
Figure 4-3. Usual interstitial pneumonia fibroblastic foci characterized by dome-shaped fibroblastic tissue over collagen fibrosis.
(Image courtesy of Joseph F. Tomashefski, Jr., MD, Department of Pathology, MetroHealth Medical Center, Case Western Reserve University, Cleveland, Ohio.)

Multidisciplinary approach to diagnosis



- A multidisciplinary approach is recommended when approaching cases of suspected interstitial lung disease
- Accuracy of diagnosis is increased
- If there is no multidisciplinary approach available, then refer to a ILD center is advised.

Disease Progression



Acute Exacerbations are associated with poor prognosis

- Unexplained worsening or development of dyspnea
- New pulmonary infiltrates on a x-ray or HRCT without pleural effusion or Pneumothorax
- Exclusion of other causes (Heart failure, Pulmonary Embolism and infection .

- **Median survival after an exacerbation is 2.2 months**
- Frequency and timing is variable

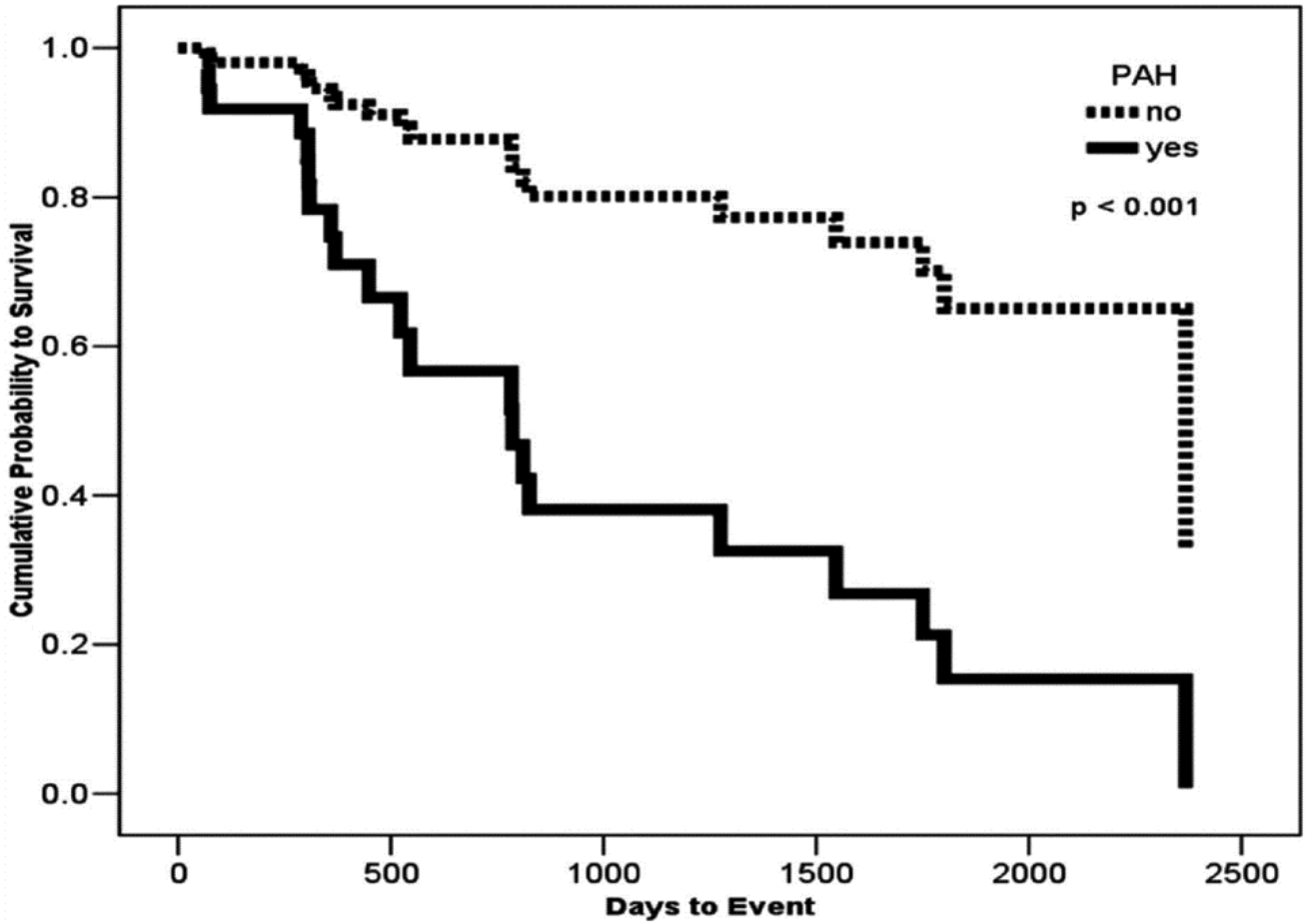
Recommendations for management of IPF

- All patients should be referred to **Pulmonary Rehab**
- Patients with hypoxia should be started on **long term oxygen therapy**
- Consider evaluation of **Lung transplant**
- Patients should be evaluated for **anti fibrotic agents**
- Yearly influenza vaccination

Diseases associated with IPF

- Pulmonary Hypertension
- Emphysema
- Lung cancer
- GERD
- OSA
- CAD

IPF and Pulmonary Hypertension



Adapted from Lettieri, et al. 2006.

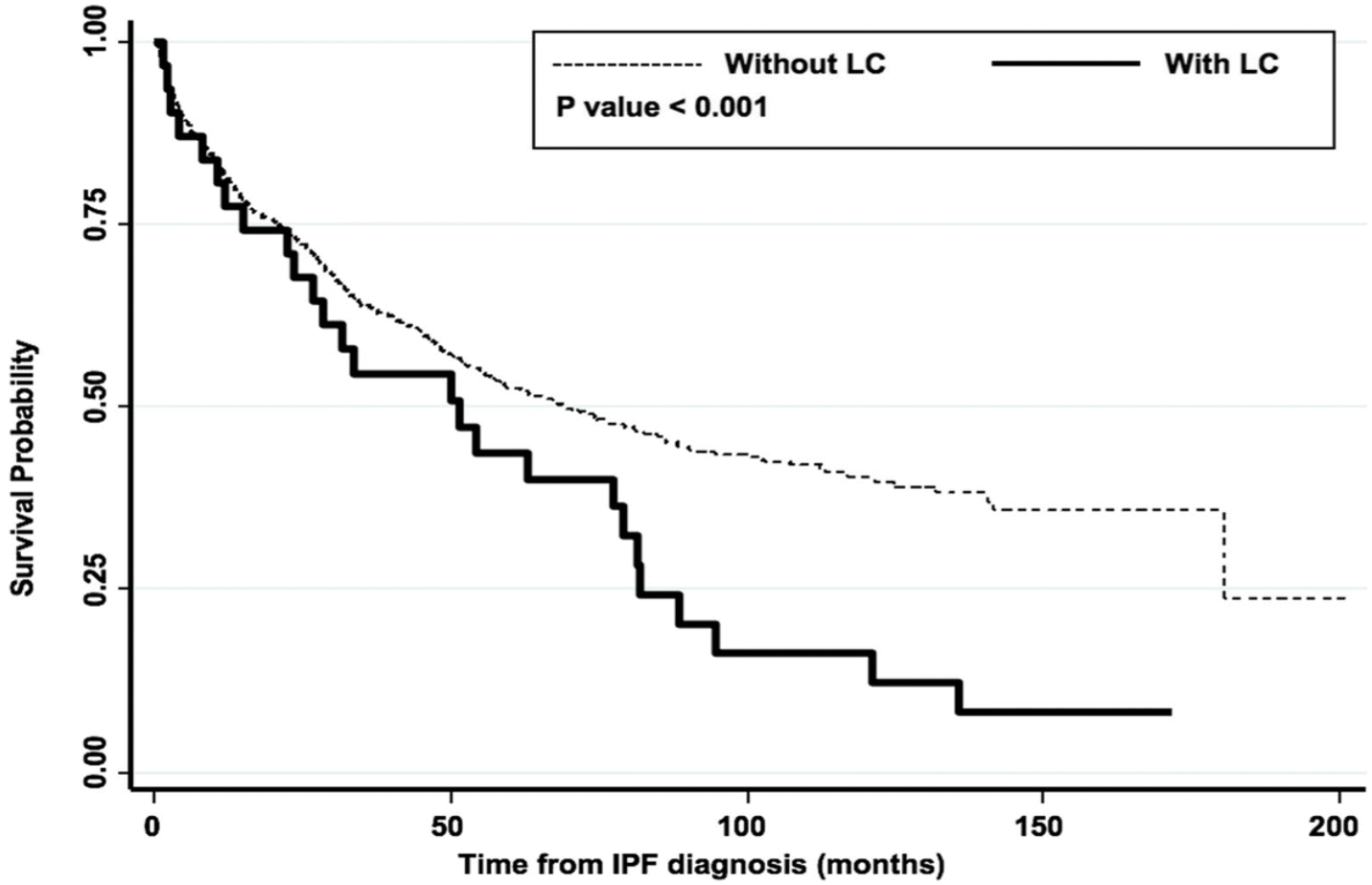
Emphysema and IPF (CPFE)

- Incidence of emphysema and IPF is 30-40%
- Out of these cases 98% are smokers.
- Typical patient is a 65 year old with a > 40 pack year smoking history
- Difficult to diagnose as FVC and TLC may be normal because of the counter balancing effects of both diseases
- Symptoms are non specific
- Disproportionately decreased diffusion capacity may be a clue.
- Radiologically upper lobe emphysema and lower lobe fibrosis



Reproduced with permission from *Histopathology*.
Awano N et al.[2]

Lung cancer and IPF



Tomassetti S et al. *Chest.* 2015;147:157-164.

GERD and IPF

- 95 % of patients with IPF have GERD
- 50% are asymptomatic



- Micro aspiration may play a role in disease progression
- Treatment of GERD is a conditional recommendation by ATS guidelines

Obstructive Sleep Apnea and IPF

- Sleep disturbance may be from coughing and nocturnal hypoxia
- No evidence based recommendations to treat sleep disordered breathing in IPF



Treatment

- No role for steroids
- Pirfenidone and Nintedanib (conditional recommendation for use from ATS guidelines)
- Lung Transplant

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MAY 29, 2014 VOL. 370 NO. 22

Efficacy and Safety of Nintedanib in Idiopathic Pulmonary Fibrosis

Luca Richeldi, M.D., Ph.D., Roland M. du Bois, M.D., Ganesh Raghu, M.D., Arata Azuma, M.D., Ph.D., Kevin K. Brown, M.D., Ulrich Costabel, M.D., Vincent Cottin, M.D., Ph.D., Kevin R. Flaherty, M.D., David M. Hansell, M.D., Yoshikazu Inoue, M.D., Ph.D., Dong Soon Kim, M.D., Martin Kolb, M.D., Ph.D., Andrew G. Nicholson, D.M., Paul W. Noble, M.D., Moisés Selman, M.D., Hiroyuki Taniguchi, M.D., Ph.D., Michèle Brun, M.Sc., Florence Le Maulf, M.Sc., Mannaïg Girard, M.Sc., Susanne Stowasser, M.D., Rozsa Schlenker-Herceg, M.D., Bernd Disse, M.D., Ph.D., and Harold R. Collard, M.D., for the INPULSIS Trial Investigators*

ABSTRACT

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

A Phase 3 Trial of Pirfenidone in Patients with Idiopathic Pulmonary Fibrosis

Talmadge E. King, Jr., M.D., Williamson Z. Bradford, M.D., Ph.D., Socorro Castro-Bernardini, M.D., Elizabeth A. Fagan, M.D., Ian Glaspole, M.B., B.S., Ph.D., Marilyn K. Glassberg, M.D., Eduard Gorina, M.D., Peter M. Hopkins, M.D., David Kardatzke, Ph.D., Lisa Lancaster, M.D., David J. Lederer, M.D., Steven D. Nathan, M.D., Carlos A. Pereira, M.D., Steven A. Sahn, M.D., Robert Sussman, M.D., Jeffrey J. Swigris, D.O., and Paul W. Noble, M.D., for the ASCEND Study Group*

ABSTRACT

The NEW ENGLAND JOURNAL of MEDICINE

PERSPECTIVE

Conquering Atherosclerotic Cardiovascular Disease — 50 Years of Progress

ORIGINAL ARTICLE

Nintedanib in Progressive Fibrosing Interstitial Lung Diseases

Kevin R. Flaherty, M.D., Athol U. Wells, M.D., Vincent Cottin, M.D., Anand Devaraj, M.D., Simon L.F. Walsh, M.D., Yoshikazu Inoue, M.D., Luca Richeldi, M.D., Martin Kolb, M.D., Kay Tetzlaff, M.D., Susanne Stowasser, M.D., Carl Coeck, M.D., Emmanuelle Clerisme-Beaty, M.D., et al., for the INBUILD Trial Investigators*

CONCLUSIONS

In patients with progressive fibrosing interstitial lung diseases, the annual rate of decline in the FVC was significantly lower among patients who received nintedanib than among those who received placebo. Diarrhea was a common adverse event. (Funded by Boehringer Ingelheim; INBUILD ClinicalTrials.gov number, NCT02999178.)

Format: Abstract Send to

Respirology. 2018 Mar;23(3):311-317. doi: 10.1111/resp.13230. Epub 2017 Dec 5.

Unfavourable outcome of glucocorticoid treatment in suspected idiopathic pulmonary fibrosis.

Wiertz IA[1], Wuyts WA[2], van Moorsel CHM[1,3], Vorselaars ADM[1], van Es HW[4], van Oosterhout MFM[5], Grutters JC[1,3].

Author information

Abstract

BACKGROUND AND OBJECTIVE: The diagnostic classification of 'possible idiopathic pulmonary fibrosis (posIPF)' is characterized by a radiological pattern of inconsistent usual interstitial pneumonia (UIP) on high-resolution computed tomography (HRCT) scan and a UIP pattern in surgical lung biopsy (SLB). The evidence base to guide treatment for patients with posIPF is lacking; the clinician must choose between observation, treatment with immunomodulatory agents or anti-fibrotic agents.

METHODS: To evaluate outcomes of immunomodulatory treatment, a multicentre cohort of 59 posIPF patients treated with prednisone was analysed retrospectively. Prednisone starting dose was 0.5 mg/kg/day and tapered to 0.15 mg/day/kg over 6 months. Outcome measures were forced vital capacity (FVC) and serious adverse events (SAE), defined as death or hospital admissions.

RESULTS: The majority of prednisone-treated posIPF patients were non-responders (68%) with a decrease in FVC >5% or death within 6 months from baseline; 90% of patients with radiographical presence of honeycombing were non-responders. In contrast, six out of seven patients with focal desquamative interstitial pneumonia-like reaction in the SLB who had stopped smoking for <5 years ago were responders to prednisone, demonstrating <5% FVC decline. The mean decline of FVC was 8.7% (95% CI: 3.1-14.3%) before treatment and 20% (95% CI: 9.4-31.1%) after treatment (P = 0.018) in the 32 patients with available FVC data. Twelve SAE occurred within the first 3 months on prednisone (at dosage >0.3 mg/kg/day), including five deaths.

CONCLUSION: Patients with posIPF demonstrated an accelerated FVC decline and a substantial number of SAE on steroid therapy.

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Lung Transplant

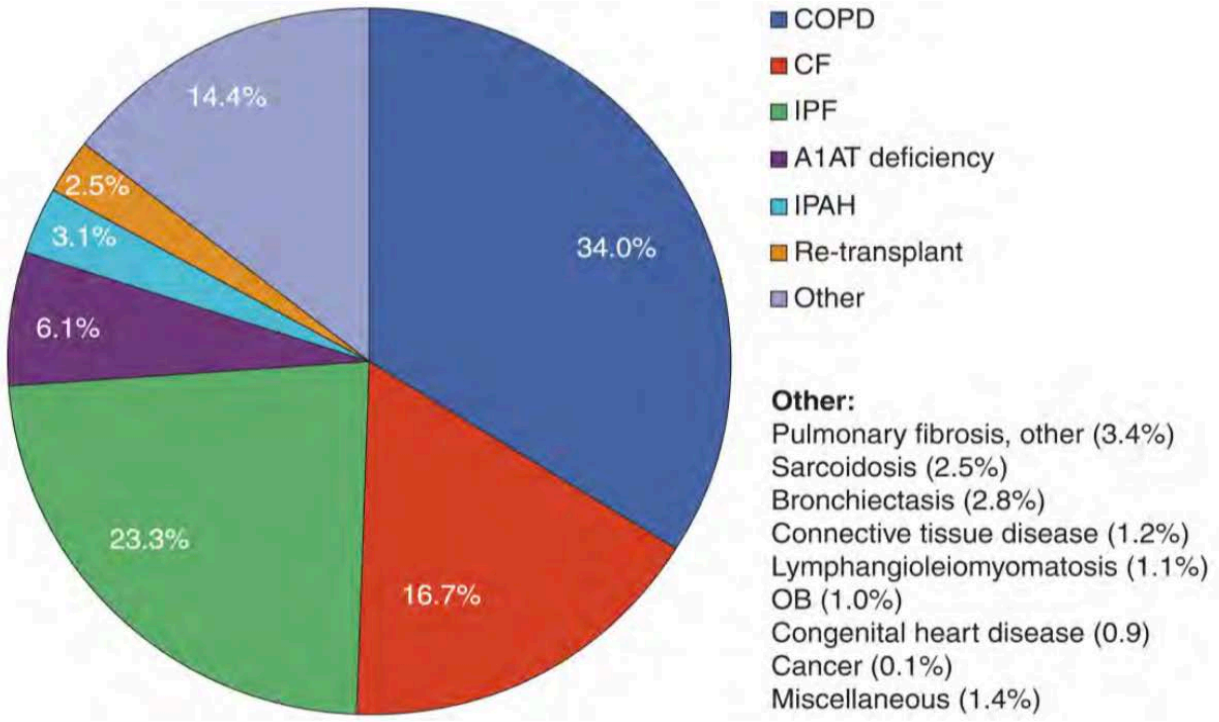


Figure 9-1. Indications for adult lung transplantation.
COPD, chronic obstructive pulmonary disease; CF, cystic fibrosis; IPAH, idiopathic pulmonary arterial hypertension; IPF, idiopathic pulmonary fibrosis; LAM, lipoarabinomannan; OB, obliterative bronchiolitis.

Table 9-1. Disease-Specific Indications

Disease	Indication
COPD and A1AT	BODE Index score of at least 7–10 (**BODE** Index derived from **b**ody mass index, degree of airflow **o**bstruction, **d**yspnea, and **e**xercise capacity measured by 6MWT) or at least one of the following: • Hospitalization for exacerbation with acute $Paco_2$ > 50 mm Hg • Pulmonary hypertension and/or cor pulmonale despite oxygen therapy • FEV_1 < 20% AND either DLCO < 20% or homogenous distribution of emphysema
Cystic fibrosis	FEV_1 < 30% or rapid decline, especially in young women Exacerbation requiring ICU stay Increased frequency of exacerbations requiring antibiotics Refractory or recurrent pneumothorax Recurrent hemoptysis not controlled with embolization Oxygen-dependent respiratory failure or PaO_2 < 55 mm Hg on room air Hypercapnia with $Paco_2$ > 50 mm Hg Pulmonary hypertension
Idiopathic pulmonary fibrosis	UIP pattern on CT scan or biopsy with any of the following: • 6MWT desaturation (SpO2 < 89%) • Long-term oxygen therapy • > 10% decline in FVC over 6 months • DLCO < 39% • Honeycombing on high-resolution computed tomography scan (fibrosis score > 2)
Pulmonary arterial hypertension (including congenital heart disease and Eisenmenger syndrome)	Functional class III or IV despite maximal medical therapy (IV epoprostenol or equivalent) Cardiac index < 2 L/min/m^2 Mean RAP > 15 mm Hg Low (< 350 m) or declining 6MWT

A1AT, alpha-1 antitrypsin deficiency; 6MWT, 6-minute walk test; COPD, chronic obstructive pulmonary disease; CT, computer tomography; DLCO, diffusion lung capacity for carbon monoxide; FVC, forced vital capacity; IV, intravenous; FEV_1,1-second forced expiratory volume; $Paco_2$, partial pressure of carbon dioxide; Pao_2, partial pressure of oxygen, arterial; RAP, right atrial pressure; Spo_2, oxygen saturation; UIP, usual interstitial pneumonia.

	Recurrent hemoptysis not controlled with embolization Oxygen-dependent respiratory failure or PaO_2 < 55 mm Hg on room air Hypercapnia with $PaCO_2$ > 50 mm Hg Pulmonary hypertension
Idiopathic pulmonary fibrosis	UIP pattern on CT scan or biopsy with any of the following: • 6MWT desaturation (SpO2 < 89%) • Long-term oxygen therapy • > 10% decline in FVC over 6 months • DLCO < 39% • Honeycombing on high-resolution computed tomography scan (fibrosis score > 2)
Pulmonary arterial hypertension (including congenital heart disease and Eisenmenger syndrome)	Functional class III or IV despite maximal medical therapy (IV epoprostenol or equivalent) Cardiac index < 2 L/min/m^2 Mean RAP > 15 mm Hg Low (< 350 m) or declining 6MWT


TAKE PREDNISONE THEY SAID.
YOU'LL FEEL BETTER THEY SAID.



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COPD Care Transformation & Inpatient Care

Meilin Young, MD
Director – COPD Care Transformation Program

Conflicts of interests

- Member of GlaxoSmithKline Speakers Bureau

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Outline

- Why is COPD important
- What is the burden of COPD
- How to manage an acute exacerbation
- Discharge preparation
- Preventing a re-admission
- Introduction to COPD Care Transformation

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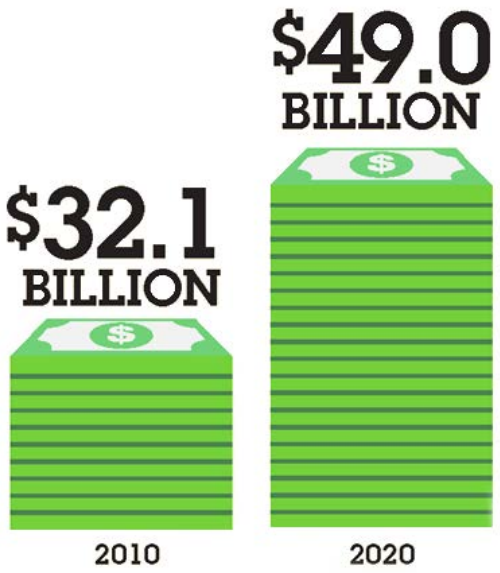
The Numbers

- 3rd leading cause of death by disease in the United States
- Death resulting from COPD in women are higher than in men
- 16.4 million people have been diagnosed with disease with millions more undiagnosed

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The Finances

- Costs attributed to COPD estimated around $49 billion in 2020
  - 2010:
    - 51% (Medicare)
    - 25% (Medicaid)
    - 18% (private insurance)



- 2010:
  - Total absenteeism costs were $3.9 billion
  - Estimated 164 million days of work lost

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The Burden of COPD



A COPD readmission costs the Hospital an average of **$10,900 per readmission**[3]



Roughly **2 out of 10** people who are hospitalized for COPD are **readmitted within 30 days**[1]



It can **take weeks**, to schedule and receive results for a pulmonary function test



COPD is expected to cost the US **$49 billion annually**[2]



Almost **31%** of COPD patients that also have CHF are **readmitted within 30 days**[3]

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How to prevent an Exacerbation

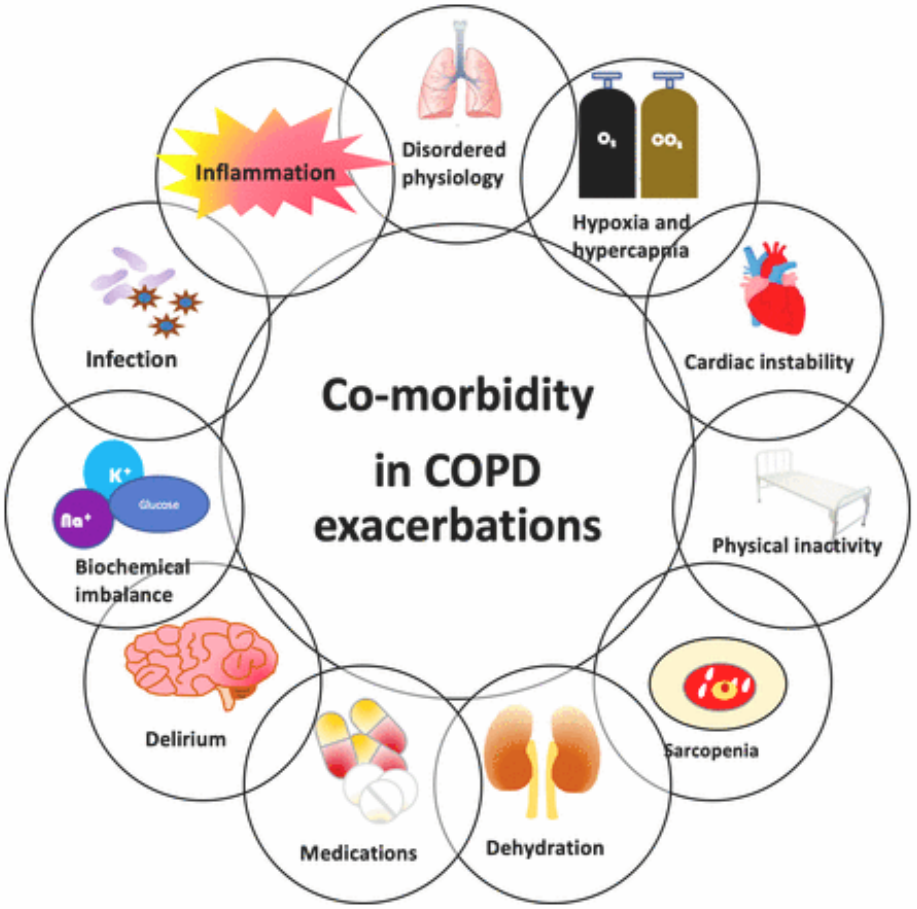
- ***Management*** *
  - Smoking cessation and reducing exposure to occupational dusts, fumes, gases, and pollutants
  - Vaccination – *Influenzae*, *Pneumococcal*, etc.
  - Physical and respiratory exercise
  - Education
  - Early identification and diagnosis
  - Proper pharmacotherapy



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Treating an exacerbation

- Bronchodilator therapy
- Antibiotics
- Oral or IV glucocorticosteroids
- Non-invasive mechanical ventilation
- Hemolung-RAS*
- Invasive mechanical ventilation



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What to use

- Steroids: 40mg Prednisone for 5 days*
  - IV or PO
  - Dose – higher doses associated with worse clinical outcomes
  - Duration – shorter is just as effective as longer courses

- Bronchodilators – Nebulizers vs. Inhalers

- Non-invasive positive pressure ventilation – BiPAP
  - Hypercarbia
  - Hypoxemia

HemoLung RAS (ALung)

- Extracorporeal carbon dioxide removal ($ECCO_2R$) with fully-integrated Respiratory Dialysis ® system
- VENT-AVOID Trial
  - U.S.-based clinical trial to validate the safety and efficacy of the Hemolung RAS for the treatment of adults with severe acute exacerbation of chronic obstructive pulmonary disease (COPD).
  - First pivotal trial of ECCO2R for treating patients with COPD exacerbations.
  - Forty-five hospitals will enroll up to 180 patients in the trial, which was launched in 2017.





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Discharge planning and preparation

- ? Pharmacotherapy
- ? Extra equipment
  - Supplemental Oxygen
  - NIPPV
- ? Provider follow-up
- ? Rehab
- ? PFT's



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How do we prevent another exacerbation or re-admission?

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Predictors of another exacerbation:

- Age
- Degree of lung function impairment
- Frequency of exacerbations during the previous year
- Duration of symptoms
- Health status
  - Comorbidities –
    - Cardiovascular disease
    - Cerebrovascular disease
    - Metabolic disease (Diabetes)
  - Dementia

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COPD exacerbation resulting in a hospitalization is an independent predictor of mortality

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Patient Centered Care



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Basics of COPD Care Transformation



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Current Locations:

- Allegheny General
- West Penn
- Forbes Regional
- Jefferson Regional
- Grove City

To come:

- St. Vincent
- Allegheny Valley

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The Team



Amy Schmetzer, DNP, FNP-C
Program Manager



Joseph Gordon, RRT
Navigator – AGH & WPH



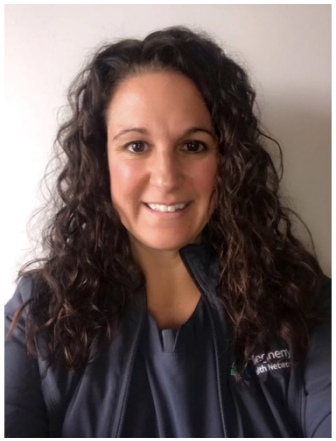
Lindsay Kuniak, RN, BSN
Navigator – CGH, FRH



Kristin DeRenzo, RRT
Navigator – JRH



Kevin Nauer, RN,MS
AHN Lung Transplant coordinator
AHN Pulmonary Rehab Manager
Navigator - Wexford



Stephanie Hamila, RRT
Navigator – GCH

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PRESENTED BY Kevin Nauer

March 27, 2021

Pulmonary Rehabilitation

AHN

Pulmonary Rehabilitation

Pulmonary rehabilitation is the cornerstone of the Pulmonary patient's treatment plan. In current times we must adapt to meet the patient needs and use a variety of delivery options (not in competition) but in cooperation, to achieve successful outcomes for the patient and bottom line.

Objectives:

- ✓ Referral and Evaluation
- ✓ Design and Delivery of the pulmonary rehab program/programs
- ✓ Results by creating the ability to continue
- ✓ Using the Trickle Learning



Benefits of Pulmonary Rehabilitation

Pulmonary Rehabilitation can:

Reduce “Shortness of Breath” allowing increased functioning of ADL’s
Decrease symptoms which lead to exacerbations and re-admission
Decrease anxiety, isolation and depression through socialization and education
Change unhealthy behaviors like smoking and maximize healthy behaviors like daily exercise
Breathing exercises, proper inhaler and oxygen use, provide nutrition and disease education for family

Pulmonary Rehabilitation is designated for patients with the Diagnosis:

- Chronic Obstructive Pulmonary Disease COPD
- Emphysema
- Chronic Bronchitis
- Bronchiectasis
- Sarcoidosis
- Pulmonary Hypertension
- Pulmonary Fibrosis, Cystic Fibrosis, Muscular Dystrophy
- Interstitial Lung Disease
- Lung Cancer and Post Lung Cancer surgery
- Lung Transplant Pre and Post surgery
- Asthma

Program Components

No matter the delivery method-Pulmonary Rehabilitation should offer:

1. **Individually designed program/goals**:
   Design-by gathering information in the evaluation, structure program on ability and to meet patient needs.
   Encourage-the best delivery method: virtual, telephonic, PR-guide, in-home, in facility or hybrid.

2. **Guided exercise program**:
   Importance of daily exercise: cardio/pulmonary (consider the concept/goal to train-like pulmonary athlete)
   Stretching with purpose relaxation and breathing control
   Strength training with what is available but with purpose

3. **Psychosocial support:**
   Talking with social worker: assessment for Depression screening (Pandemic)
   Identifying social needs in the home and with family see what resources are available in your area

4, **Educational programs (Trickle Learning)**
   By-understanding the disease process and how to manage or change - i.e. using nutrition or smoking cessation
   Plan outcome for reaching goals-celebrate-“Write your own story” (Power of Story and Who Moved my Cheese)
   Value of daily **habit-**leads to **routine**-leads to **lifestyle**-become a Human-Being what **you** want to be.
   Lung Transplant, Bronchial Valves, other opportunities with internal/external partners, create goal for patient.

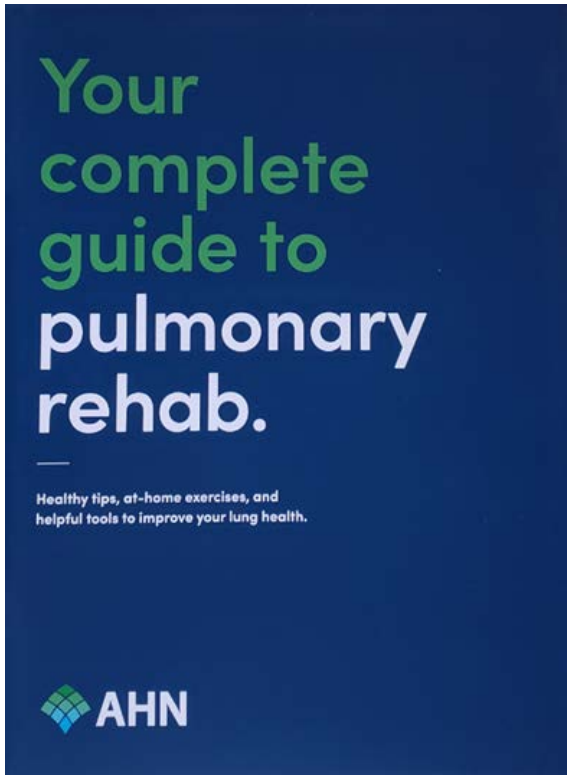
AHN Locations

Keep your lungs healthy and your pulmonary disease under control with pulmonary rehabilitation. Our team of experts will guide you through an individualized program, so you can return to a more active lifestyle.

Locations:

Allegheny Valley Hospital	724-226-7120
Canonsburg Hospital	724-271-2159
Forbes Hospital	724- 325-6051
Grove City Hospital	724-450-7000
Jefferson Hospital	412-469-5045
Saint Vincent Hospital	814-452-7843
West Penn Hospital	412-578-1956

Learn more at AHN.org/pulmonaryrehab



Types of Pulmonary Rehabilitation

Virtual
Defined by a patient seeing/speaking with a rehab professional via i-pad, personal computer or smartphone. (virtual visit) Uses patient equipment at home and materials sent to patient.

Telephonic
Defined by the patient speaking with a rehab professional via cell phone or home phone. No visual interaction with this option. Also uses equipment in the home and mailed materials.

In-Home
Defined by a rehab professional going into the patient's home to work with the patient in their space. Can be done by through Home Care or Out-patient rehab provider.

In-Patient Hospital
Defined by patient being seen by rehab professional while admitted to the hospital.

Onsite Facility
Defined by patient traveling to a facility, hospital based or free-standing facility. Patient can participate in a group or individually, use onsite equipment and lead by rehab professionals.

Referral Process

The traditional referral process:
One in which a provider speaks to the patient about pulmonary rehab in the hospital or office, then places an order in the EMR which is electronically sent or printed and faxed. Rehab facility will contact the patient.

WHAT COULD GO WRONG?
What if the referral is not placed. What if it goes to the wrong facility
What if the facility is too busy and can not take the patient for 2-3 weeks
What if facility is shut down due to COVID-19-What if patient is scared or not vaccinated
What if patient does not have the right diagnosis, insurance, transportation, problems with support or wants to stay home.

Change the process- Change the Outcome:
It is vital for the program-manager, case manager, or social worker to evaluate the patient's ability to participate
I would suggest it is the most important part of successful participation and the desired outcome.
Have a designated professional in the organization who will evaluate the referral and direct patient to the correct type of service.
This will:

- Reduce patient waiting days/weeks for a call,
- Reinforce the value of Pulmonary Rehab, correct referral placed-based on patient's ability, needs, and input.
- Increase participation through enrollment into the right program, and drive patients back to ongoing-program
- Allow for follow-up, track the barriers, create cooperation which leads to valued outcomes.

Pulmonary Rehabilitation Stats

Reviews of national patient outcomes done from 2015-2018 have shown that less then 15% of all patients who received a formal referral to pulmonary rehab were evaluated and participated in a program.
Less than 11% completed pulmonary rehab; completion was defined as participating in 70 % of approved sessions and achieving at least 2 educational goals.

Looking at our own statistics over the past 3 years 2018-2020 we discovered in our health care system for all patients we averaged 1,500 referrals to pulmonary rehab each year for the last 3 years.

In 2019 AHN had 1,280 COPD patients referred to pulmonary rehab, an increase of 36% from the year prior. Of those referrals, 45% were formally evaluated which is a 10% increase from the prior year of 2018 and a 20% increase from 2 years prior in 2017.
In 2019 the completion rate for pulmonary rehab was 34%.

Year	Total Referrals (COPD)	Care Path Program (CCP)
2015	103	pre-COPD CCP
2016	399	Start of COPD CCP
2017	686	Developing COPD CCP
2018	939	NN/Manager of PR added
2019	1,280	Dedicated COPD CCP team
2020	1,177	COPD CCP/COVID19*

***2020-1177 COPD Care Path-COVID-19 with 62% of referrals going to Virtual, Telephonic, and In-Home options*.**

Breakdown-Referrals Outside Vendor

	Referrals	In-clinic Assessments	In-home Assessments	Virtual/tele Assessments	% Enrolled
1/1/20-3/31/20	56	35	0	0	62%
4/1/20-12/31/	207	63	28	51	69%
Total 2020	263	98	28	51	67%

Barriers and Options

The COVID-19 Pandemic has shown us how using a variety of delivery models in-conjunction with communication between programs can overcome barriers to participation.

Barriers:

Fear of COVID-19-facility size and no vaccine
Transportation concerns
Co-pay-insurance
Co-morbidity
Lack of follow-up and education

Options:

The right delivery model can increase patient engagement and drive long term participation
Eliminating barriers can reduce gaps in care which may cause exacerbations and re-admissions
Continued support of CDC guidelines can reduce transmission of COVID19
Create new programs and opportunities for growth and reimbursement

Evaluation

Phone Call:

- Reinforcement of referral from the provider
- Simple questions about the desire to participate and what barriers exist
- Present options by asking “What if”
- Listening to answers and send information, within 72 hours schedule evaluation.



Design



Here is the opportunity to discover what type of program (by patient design) will engage participation and give best chance for completion and continuation.

- Engage with the patient on what is most important to them (#1 goal). What would they like to learn (#2 goal).
- Educate ”Trickle Learning” using written virtual, written, telephonic tools, **not to compete** but to reinforce the message of lifestyle change.

Tomorrow stand in front of your mirror and say: “Behold an Athlete”

Results



Pulmonary Athlete

Help your patient write the story they want to follow and live!

Playbook for success.

- Eliminate barriers to participation (What if…?)
- Trickle-learning - slowly increase options/goals
- Eliminate gaps with timely and correct interventions (i.e. inhalers, nutrition, support)
- Collaborate with team internally and externally
- Transition to ongoing program

Smoking Cessation

PR+AA model:

If you are currently running a successful smoking cessation program please stand up, take a bow, and please share your secret with all of us.

All the programs I have taught or worked-in, the one that I have found that makes the most difference is being in pulmonary rehab.

Create your model similar to AA - provide mentors, meet one on one or meet in a group weekly.

- Have time to tell your story
- You can’t exercise and smoke
- When you fail, you can start over



Home Care Pulmonary Therapy

Pilot Program developed by AHN Pulmonary and AHN HC/DME
Program developed to close the gaps in care and offer care to COPD CPP patients creating a new model using RN, PT and RT to work with patients in their homes, for rehab goals, respiratory care, oxygen needs, etc.

Program Criteria:

- On CPP — **Care Path COPD -** confirmed diagnosis by PFT, CAT-measure outcome, staging
- Insurance Type — **Medicare**
- Location — **North Pod of PA.**
- Home Care Need — **Dx. example -** Post discharge, Shortness of breath, Oxygen, In-home need

Outcomes/Program Goals:

- Increase referrals to Home Health Provider (COPD patient)
- Education for Home Care Staff and engage RT into patient care under reimbursement
- Alternative option to a create new method of rehab (bridge the gap)
- Increase communication and referrals between staff/programs in cooperation not competition
- Ongoing program for patient, always communicating with patient
- Reduce re-admission rate at 30, 60, and 90 days

Milestones

Important milestones for your PR-program:

- MD-encourage providers to refer- all COPD diagnosed
- Funnel referral information to point person
- Follow-up call within 72 hrs. of referral or discharge
- Use all available options to meet patient needs
- Partner with all programs in your system and area
- Use all available materials, PR Guide-but ask the patient
- Patients will return if they see success
- Requirement for Lung Transplant Pre and Post



Resources

Breathe Pennsylvania – breathepa.org

American Association of Cardiovascular and Pulmonary Rehabilitation (AACVPR) – www.aacvpr.org

PA 2-1-1 powered by United Way – Dial 211, Visit pa211sw.org or Text your zip to 898-211

AHN – Kevin Nauer at 412-616-1462 or kevin.nauer@ahn.org



Questions?



Thank you!

Kevin Nauer: kevin.nauer@ahn.org
412-616-1462

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COPD Care Model

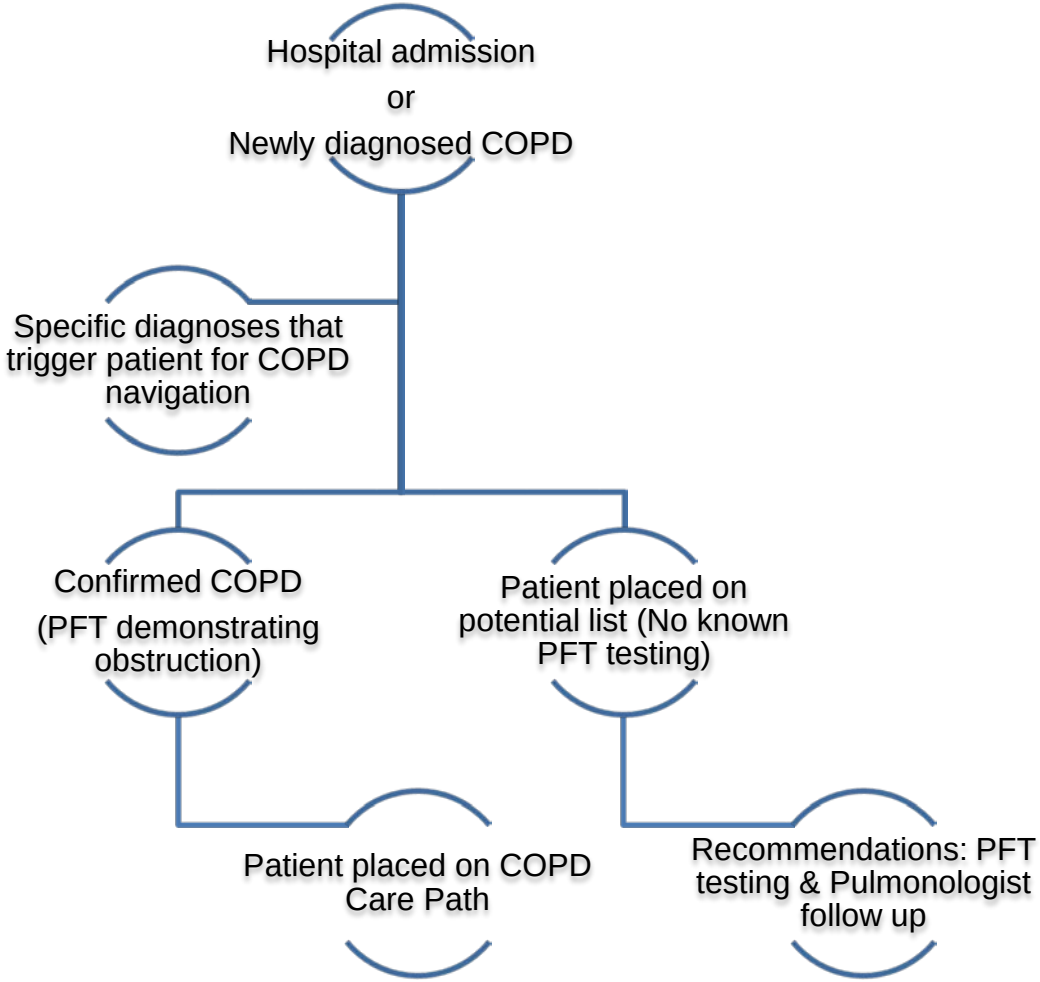
Amy Schmetzer, DNP, FNP-C
Program Manager of COPD Transformation
Division of Pulmonary & Critical Care Medicine

Objectives

- Enrollment process for the COPD Care Pathway
- Integration of virtual navigation through the COVID Pandemic
- Inpatient and outpatient COPD management
- Multidisciplinary care approach and collaboration with the AHN Chronic Care Specialty Centers (CCSC)
- AHN COPD readmission data 2020
- Navigation team and designated locations
- Review of patient resources

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Review of COPD Pathway: Enrollment Process



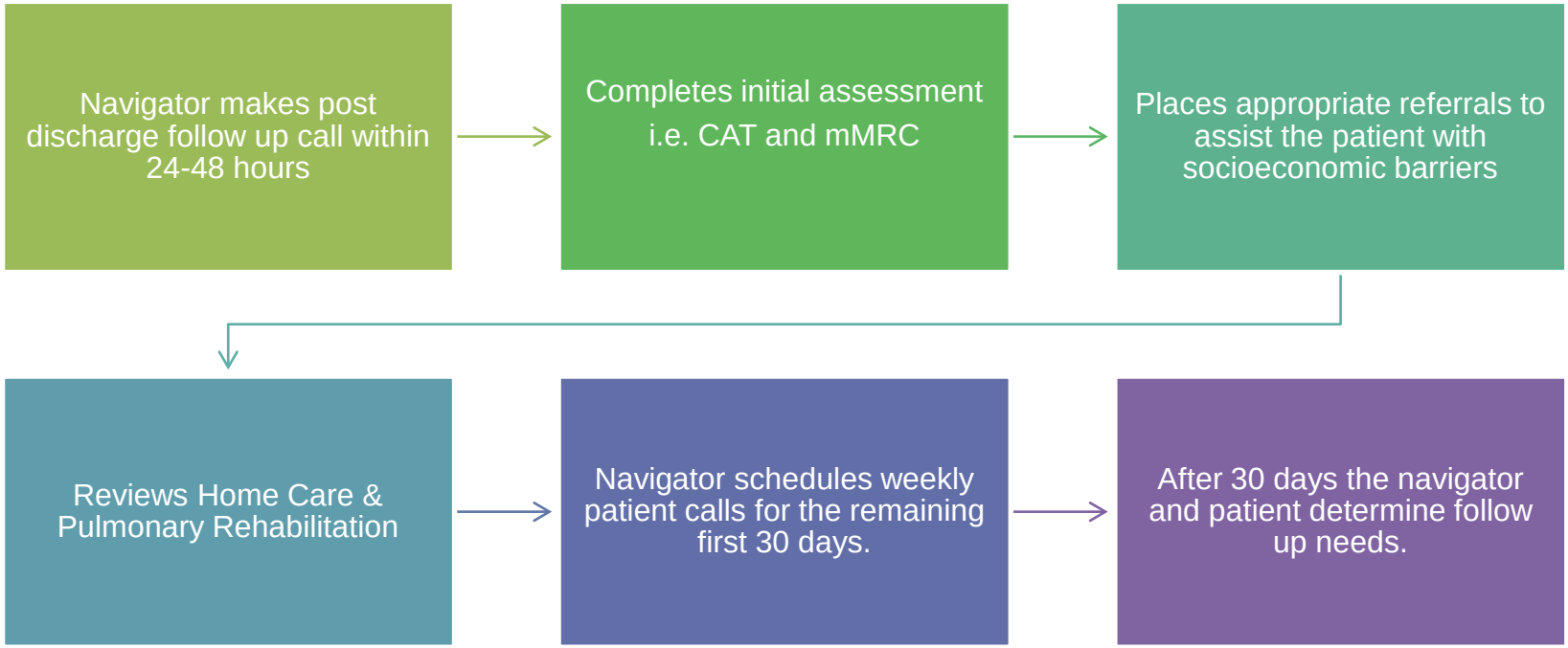
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Pathway Through Virtual Inpatient COPD Navigation

- Navigator assigns themselves to the care team & establishes communication with admitting team
- Reviews inpatient treatment course; i.e. antibiotics, steroids, inhalers, oxygen, and NIVM
- Reviews social determinants of health
- Reviews testing prior to discharge
- Meds to Beds consult
- Reviews orders; i.e. home nebulizer and inhalers
- Personalized education identified for outpatient following
- Reviews discharge plan; i.e. home care/pulmonary rehab
- Schedules follow up visit with pulmonologist (goal 72 hours)
- Schedules 24-48 hour post discharge telephone call with Navigator

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Transition of COPD Care in the Outpatient Setting



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Patient Centered Care: COPD and the Chronic Care Specialty Center (CCSC)

- Virtual and in-person holistic, team-based care for people with significant chronic medical conditions (CHF, DM, COPD, Supportive and Palliative Care) and/or psychosocial issues

- Targeted as “time limited”, goal to teach self-management and graduate back to referring team

- Team works with the specialists and the patients PCP, and includes:
  - Nurse Navigator
  - Pharmacist
  - Social Worker
  - Nutritionist (RD)
  - Behavioral Health Clinician



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CCSC: Locations and Referral Process

Virtual Visits

- Available for patients with CHF, COPD, DM, and Supportive at clinical sites



Patients Referred CCSC via:

- EPIC Referral
- Phone intake/triage to CCSC – **(878) 332-4131**

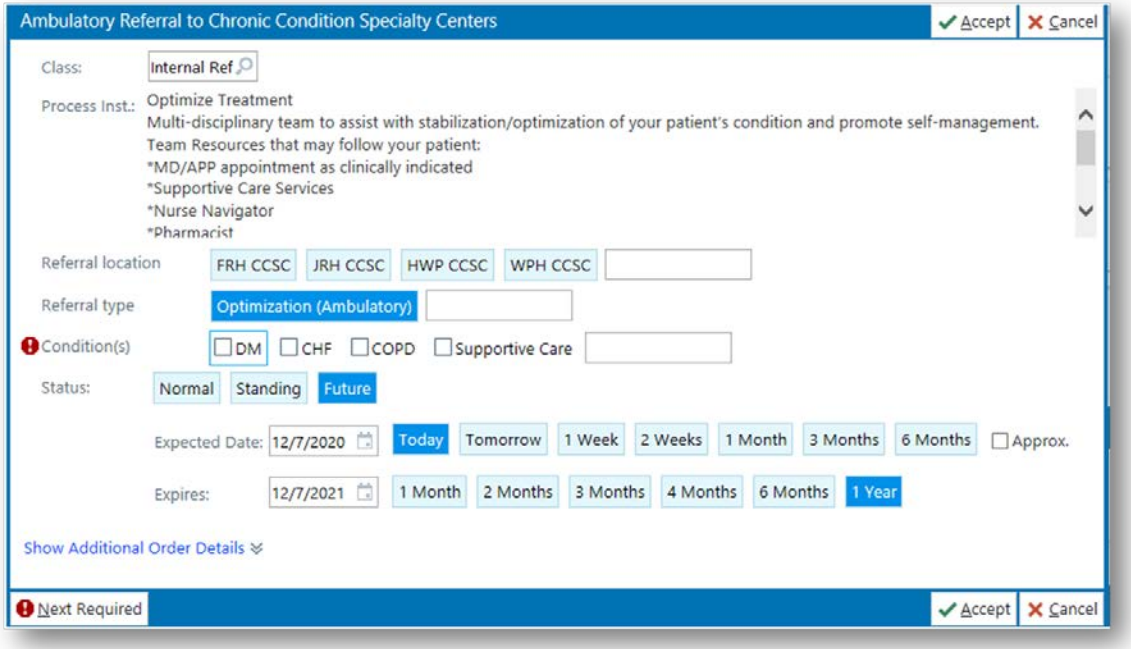
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EPIC Referral Steps

1.) Search the CCSC or Chronic Care

2.) Complete Referral

3.) Referral is routed to CCSC Access Coordinators who will reach out to schedule the patient



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COPD Navigation and the Future in Innovation

- Development of digital platforms that complement the integrative and multidisciplinary care
  - Med Respond
  - Virtual Pulmonary Rehab
  - Virtual Video Navigation

- Current research and development for monitoring COPD
  - Research study predicting COPD exacerbations
  - Collaboration in research with pulmonary rehabilitation and COPD
  - Future in device advancements and pharmacological research in COPD



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COPD Care Path: Readmission Data

Patients hospitalized for COPD have a 30-day readmission rate of **22.6%** *(per the National Institute of Health)*

Operational COPD Care Path Patient Readmissions

Year of Discharge Date	Patient Count	Readmit Count	Total Admits	Readmission Rate
2019	333	159	901	17.6%
2020	192	85	527	16.1%

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Patient Resources

- Breathe PA
  - https://breathepa.org/
- 1-800-QUIT-NOW
- Care Partners (EPIC referral)
- 2-1-1
  - http://pa211sw.org/
- American Lung Association
  - https://www.lung.org/
- Various pharmacologic programs



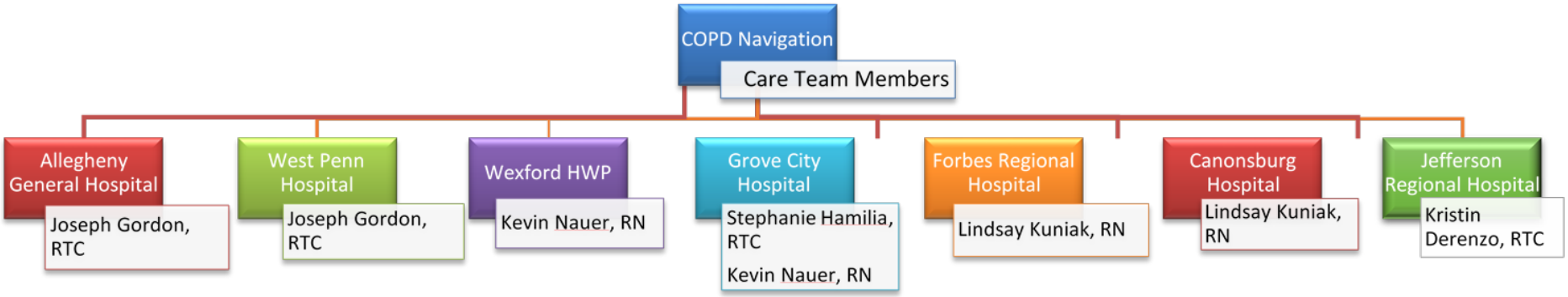






COPD Care Model: Care Team Members

Division Director: Tariq Cheema, MD
Program Director: Meilin Young, MD
Program Manager: Amy Schmetzer, DNP, FNPC



Location	COPD Navigator	Phone Number
West Penn Hospital	Joe Gordon	412-660-5030
Allegheny General Hospital	Joe Gordon	412-660-5030
Wexford Health and Wellness Pavilion	Kevin Nauer	412-616-1462
Grove City Hospital	Stephanie Hamilla	412-804-1428
Grove City Hospital	Kevin Nauer	412-616-1462
Canonsburg General Hospital	Lindsay Kuniak	412-737-0606
Jefferson Regional Hospital	Kristin Derenzo	412-327-3347
Forbes Regional Hospital	Lindsay Kuniak	412-737-0606

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THANK YOU!

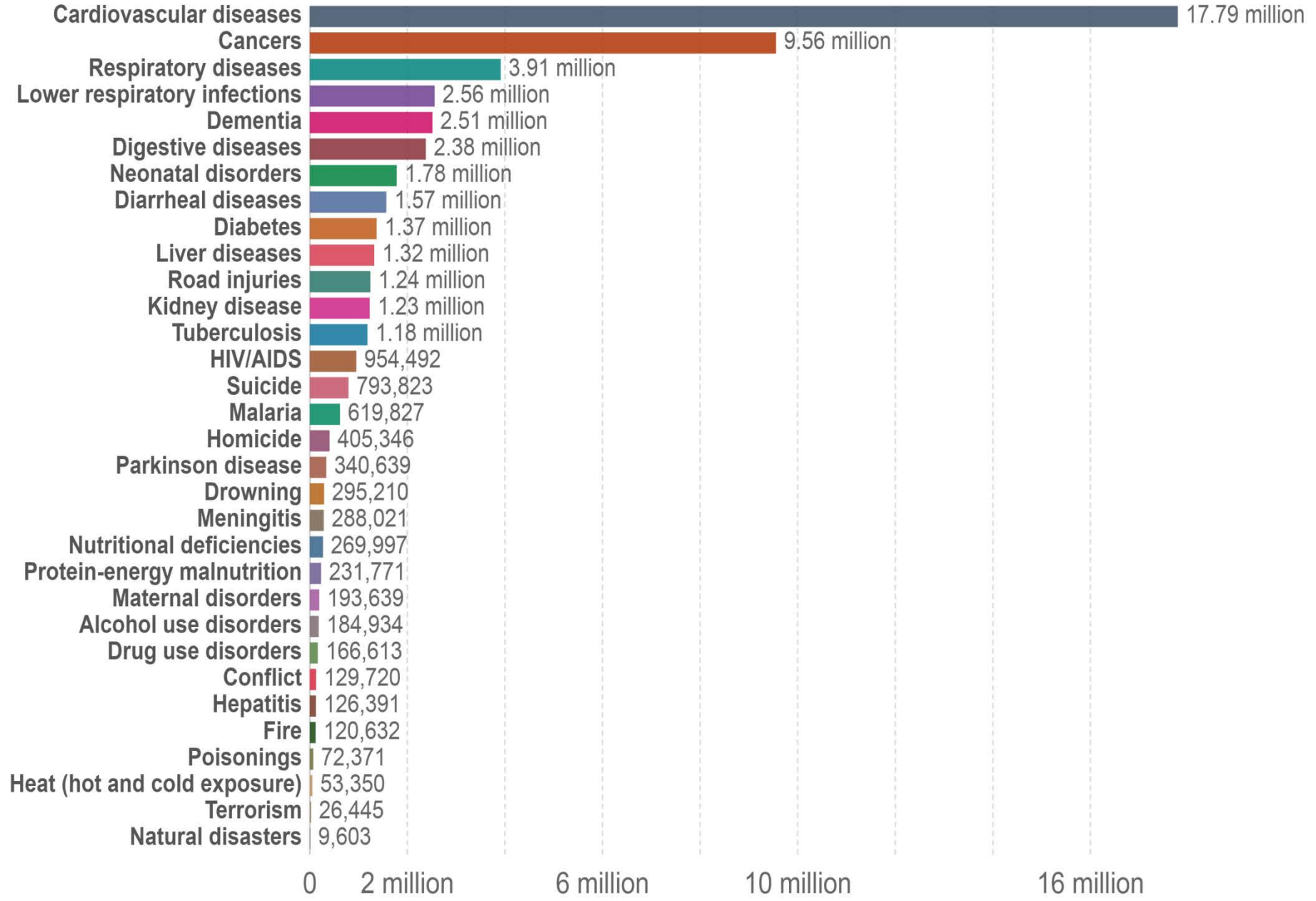
QUESTIONS?



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COPD

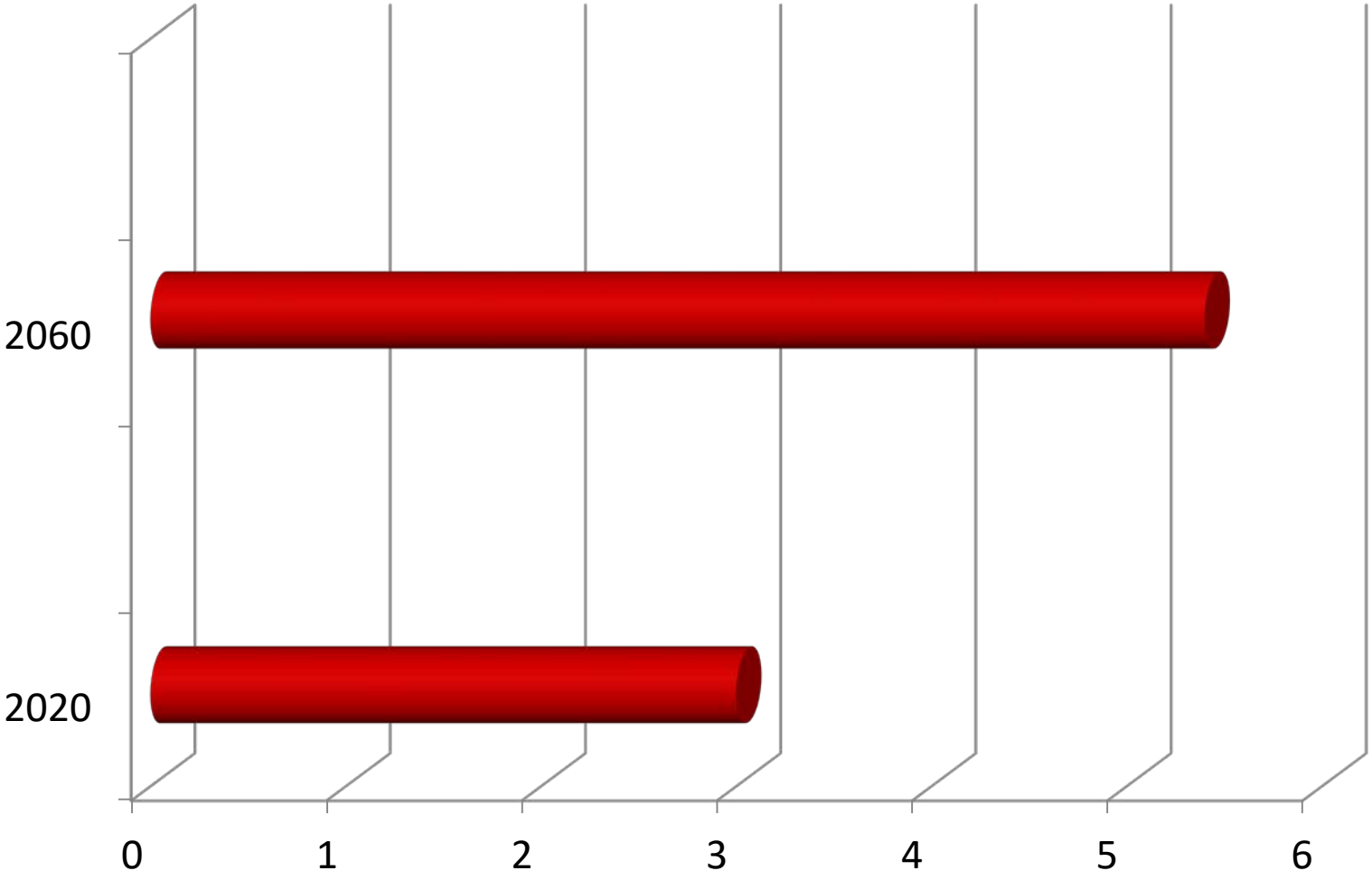
Tiffany DuMont, D.O.



Source: IHME. Global Burden of Disease

OurWorldInData.org/causes-of-death • CC BY

COPD Deaths



What Percentage of people who smoke develop COPD?

A) 90%

B) 75%

C)50%

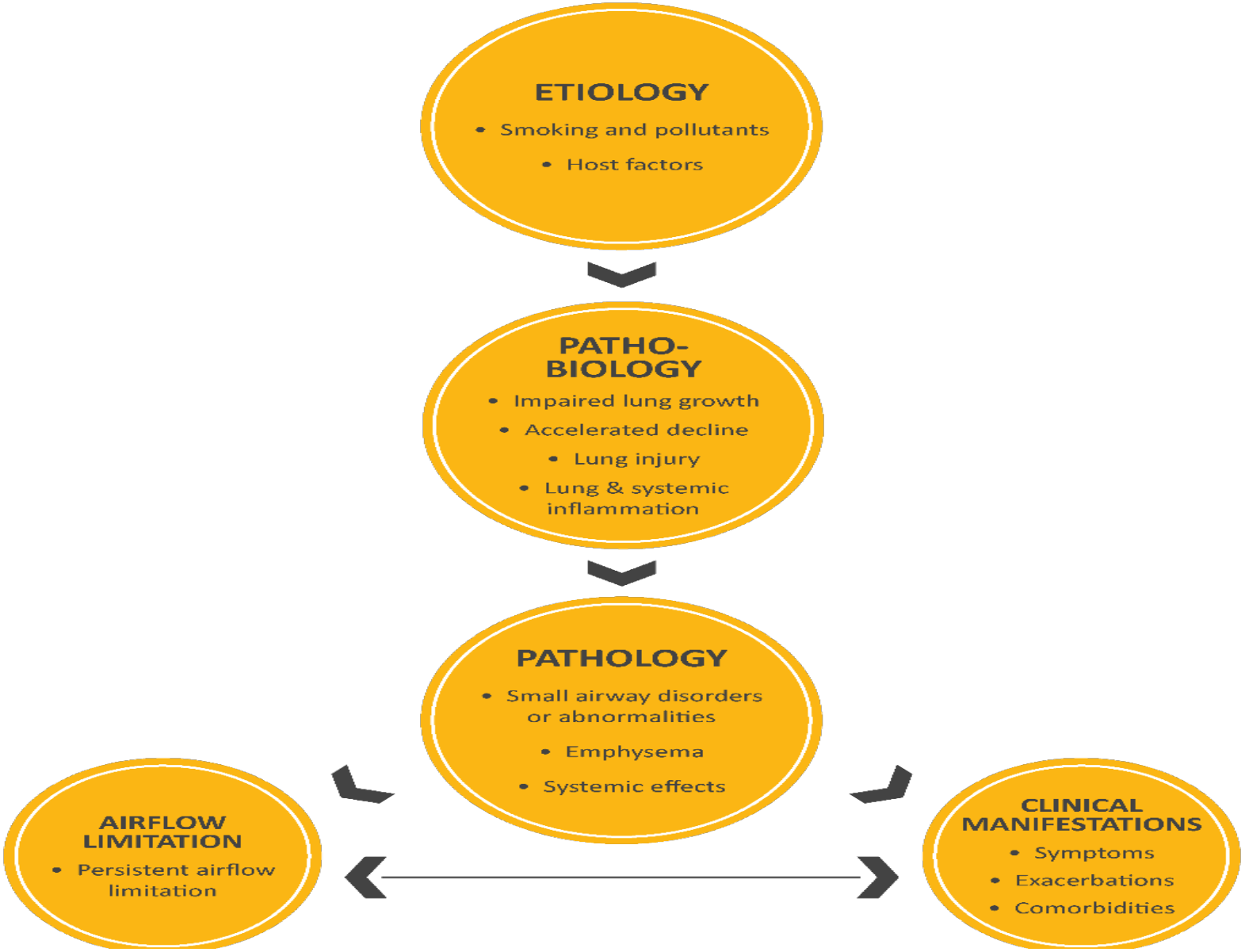
D)25%

E)10%

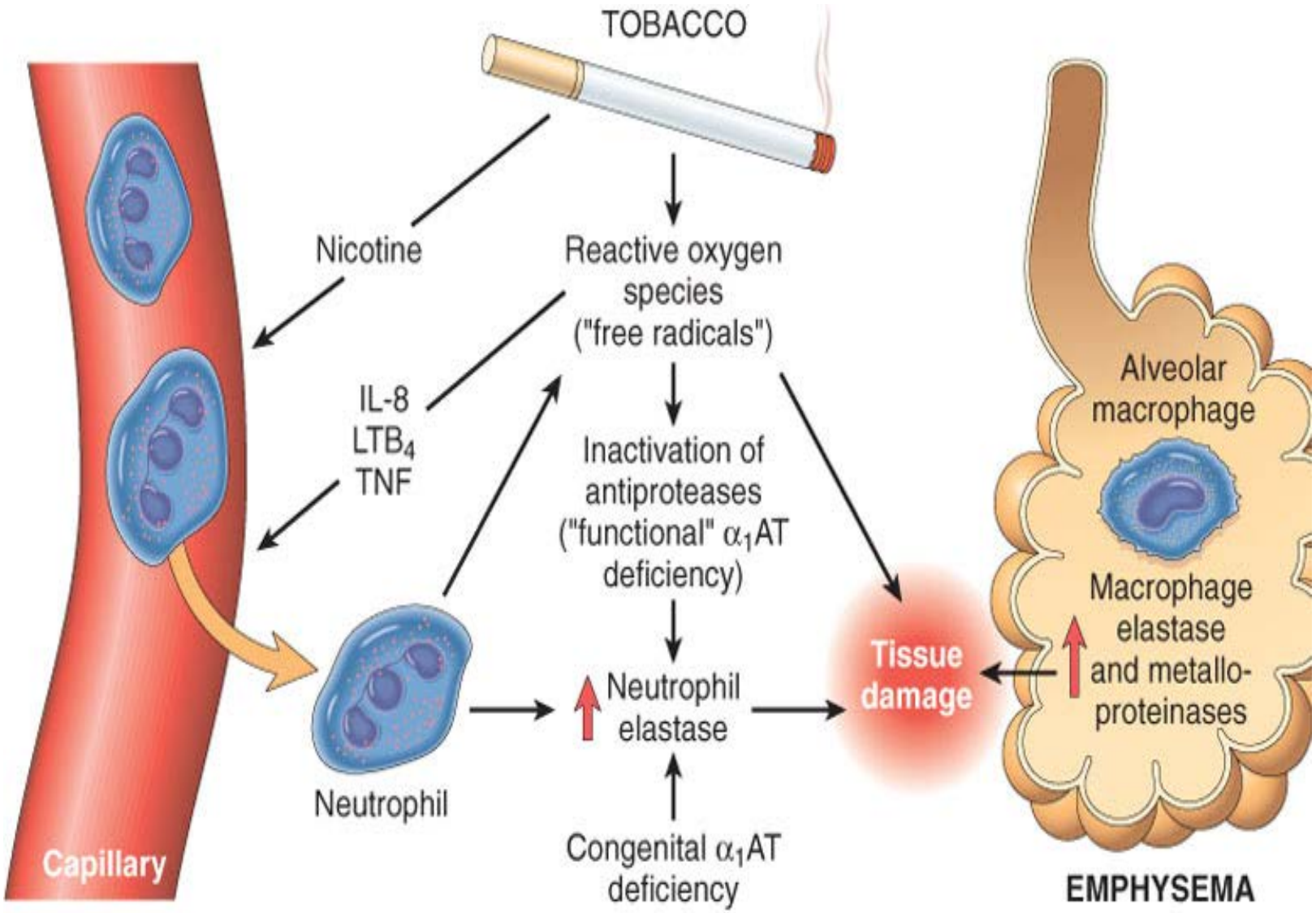




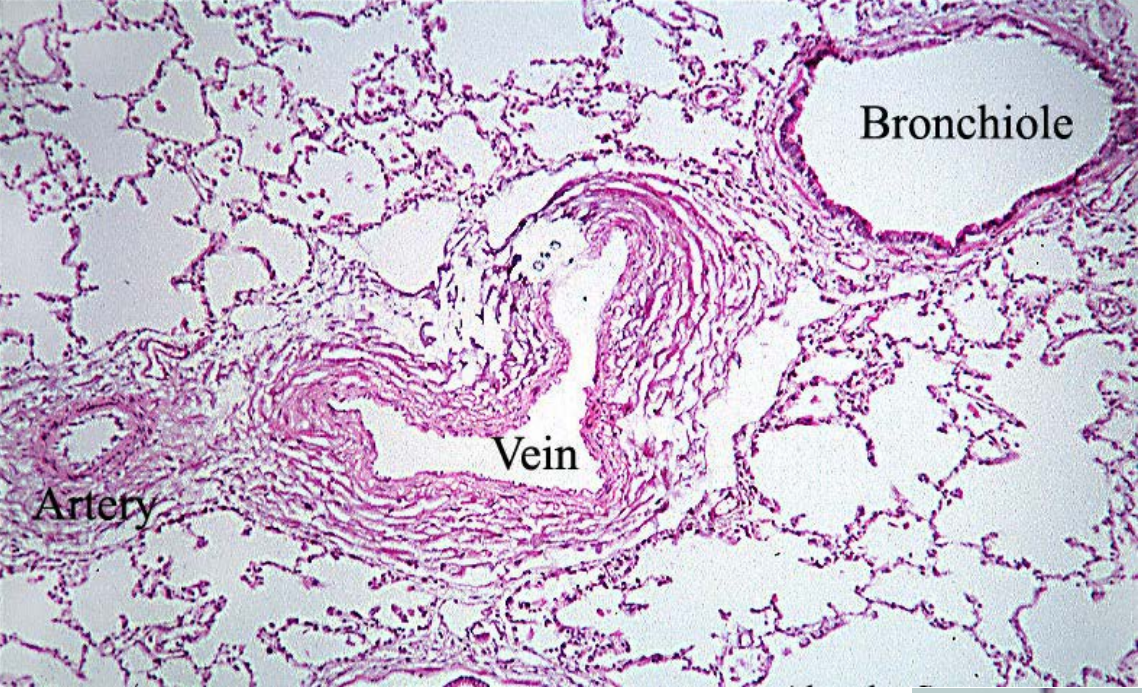


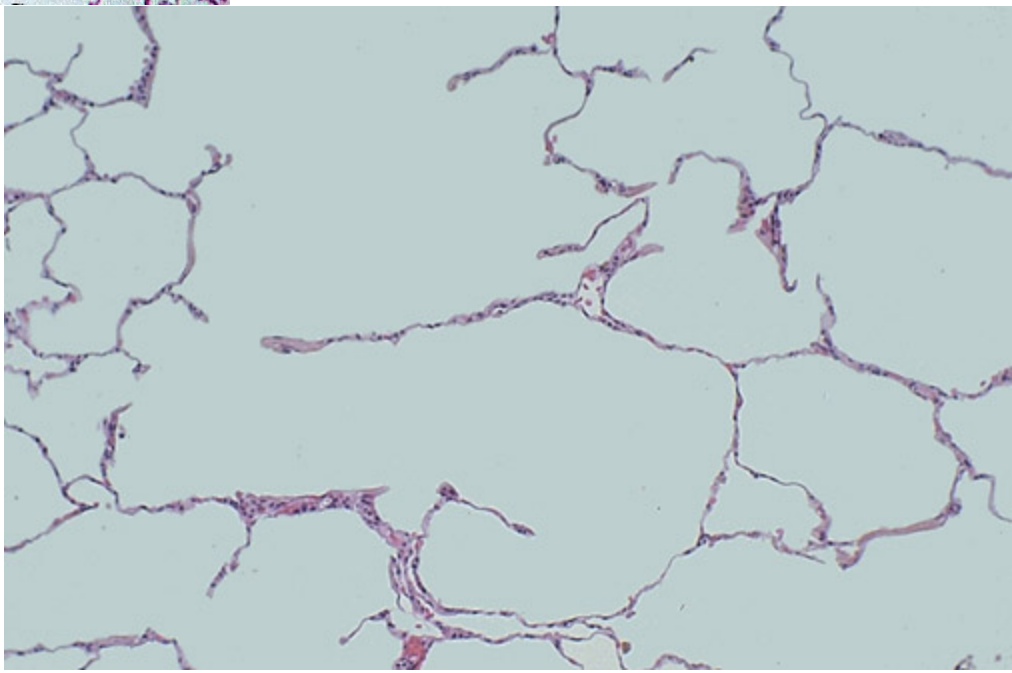


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© Elsevier. Kumar et al: Robbins Basic Pathology 8e - www.studentconsult.com





http://www.columbia.edu/cu/biology/courses/w2501/histology.html

PATHWAYS TO THE DIAGNOSIS OF COPD

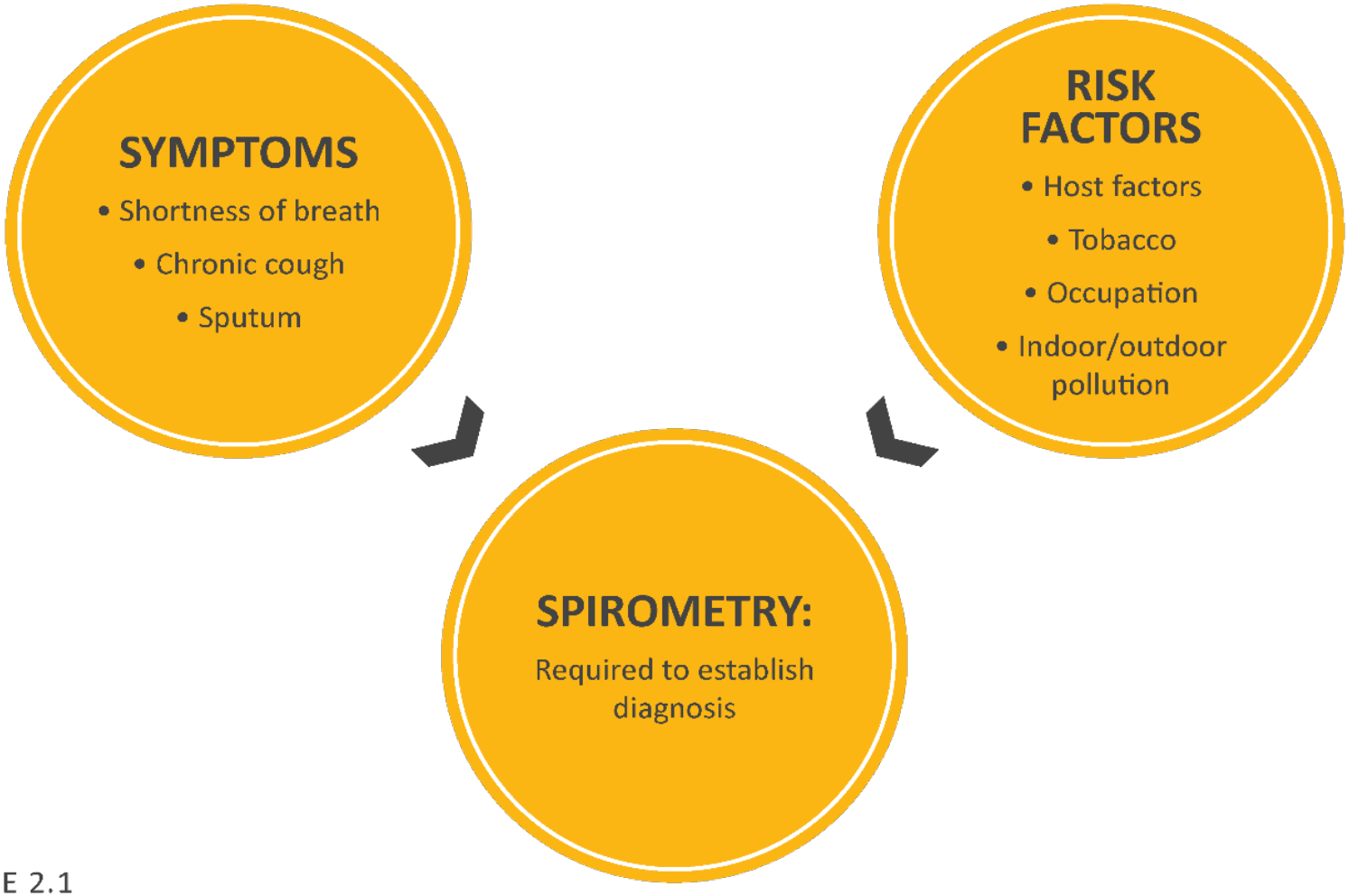


FIGURE 2.1

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SPIROMETRY - NORMAL TRACE

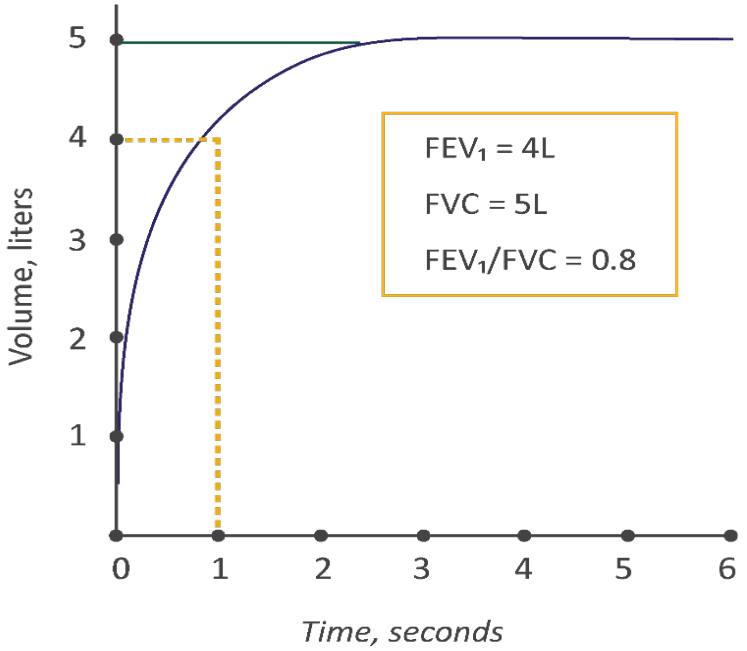


FIGURE 2.2A

SPIROMETRY - OBSTRUCTIVE DISEASE

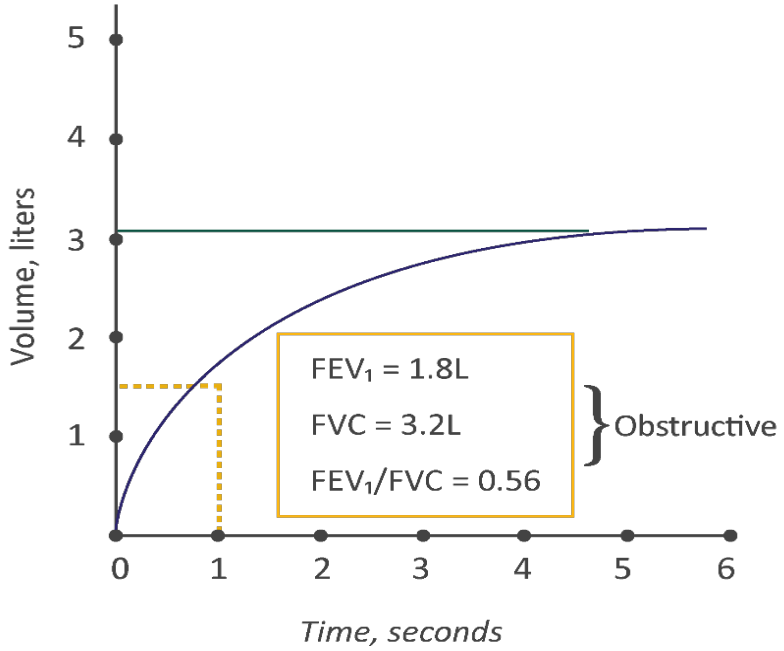


FIGURE 2.2B

FVC =

FEV_1 =

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CLASSIFICATION OF AIRFLOW LIMITATION SEVERITY IN COPD (BASED ON POST-BRONCHODILATOR FEV_1)

In patients with FEV1/FVC < 0.70:

GOLD 1:	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2:	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3:	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4:	Very Severe	$FEV_1 < 30\%$ predicted

TABLE 2.4

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MODIFIED MRC DYSPNEA SCALE[a]

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0.	I only get breathless with strenuous exercise.	☐
mMRC Grade 1.	I get short of breath when hurrying on the level or walking up a slight hill.	☐
mMRC Grade 2.	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level.	☐
mMRC Grade 3.	I stop for breath after walking about 100 meters or after a few minutes on the level.	☐
mMRC Grade 4.	I am too breathless to leave the house or I am breathless when dressing or undressing.	☐

[a] Fletcher CM. BMJ 1960; 2: 1662.

TABLE 2.5

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CAT™ ASSESSMENT

For each item below, place a mark (x) in the box that best describes you currently.
Be sure to only select one response for each question.

			SCORE
EXAMPLE: I am very happy	0 (X) 2 3 4 5	**I am very sad**	
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

TOTAL SCORE: ◯

Reference: Jones et al. ERJ 2009; 34 (3); 648-54.

FIGURE 2.3

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THE REFINED ABCD ASSESSMENT TOOL

Spirometrically Confirmed Diagnosis

Post-bronchodilator $FEV_1/FVC < 0.7$

Assessment of airflow limitation

Grade	FEV_1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

Assessment of symptoms/risk of exacerbations

Moderate or Severe Exacerbation History

≥2 or ≥ 1 leading to hospital admission

0 or 1 (not leading to hospital admission)

C	D
A	B

mMRC 0-1 CAT < 10	mMRC ≥ 2 CAT ≥ 10

Symptoms

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Exacerbation

- Classified as:
  - Mild
  - Moderate
  - Severe



- 62 year old female with a 35 pack year history has PFTs which reveal FEV1/FVC of 62% and an FEV1 of 45% she had one hospitalization and her CAT score is 12. Please Classify her COPD

A. GOLD 3, Stage D
B. GOLD 4, Stage D
C. GOLD 3, Stage C
D. GOLD 2, Stage B

- No existing medications for COPD modify the long-term decline in lung function.



INITIAL PHARMACOLOGICAL TREATMENT

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	**Group C** LAMA	**Group D** LAMA or LAMA + LABA* or ICS + LABA** *Consider if highly symptomatic (e.g. CAT > 20) **Consider if eos ≥ 300
0 or 1 moderate exacerbations (not leading to hospital admission)	**Group A** A Bronchodilator	**Group B** A Long Acting Bronchodilator (LABA or LAMA)
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10

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FACTORS TO CONSIDER WHEN INITIATING ICS TREATMENT

Factors to consider when initiating ICS treatment in combination with one or two long-acting bronchodilators (note the scenario is different when considering ICS withdrawal):

· STRONG SUPPORT ·	· CONSIDER USE ·	· AGAINST USE ·
• History of hospitalization(s) for exacerbations of COPD#	• 1 moderate exacerbation of COPD per year#	• Repeated pneumonia events
• ≥ 2 moderate exacerbations of COPD per year#	• Blood eosinophils 100-300 cells/μL	• Blood eosinophils <100 cells/μL
• Blood eosinophils >300 cells/μL		• History of mycobacterial infection
• History of, or concomitant, asthma		

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NON-PHARMACOLOGIC MANAGEMENT OF COPD*

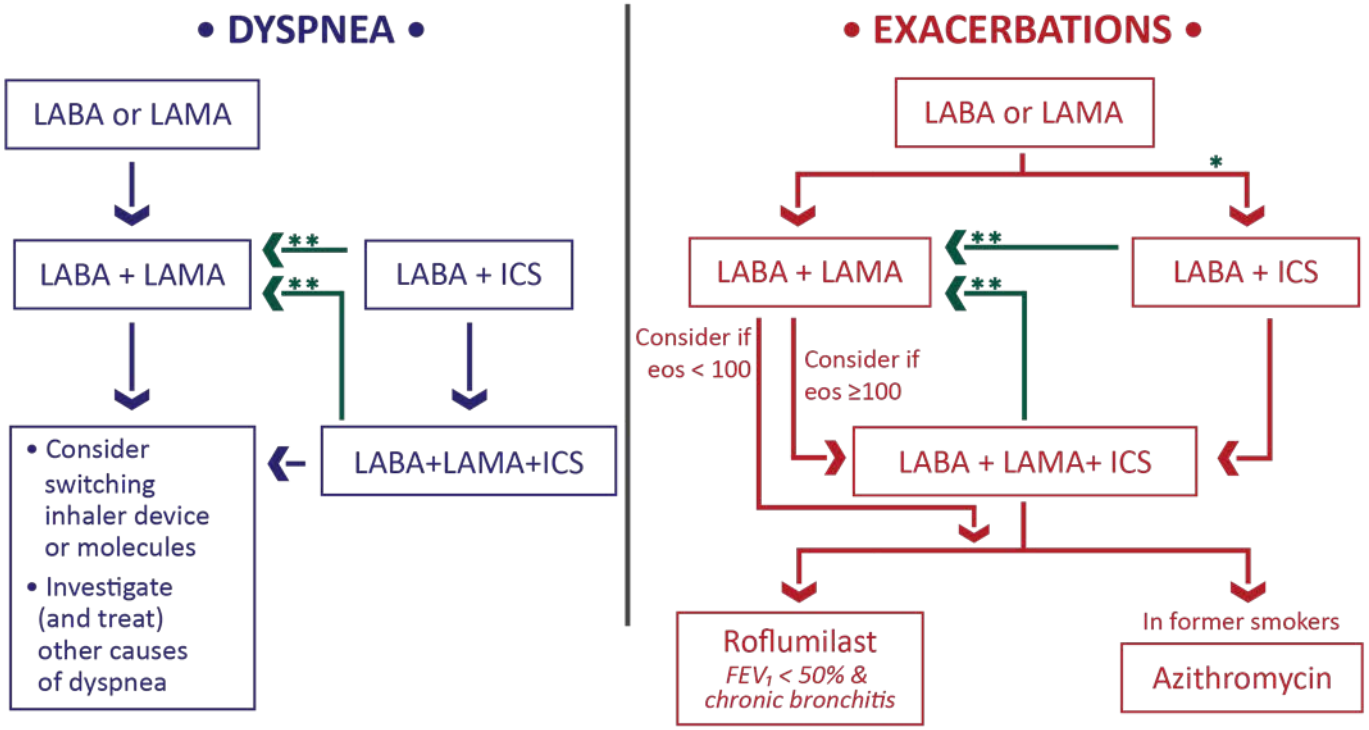
PATIENT GROUP	ESSENTIAL	RECOMMENDED	DEPENDING ON LOCAL GUIDELINES
A	Smoking Cessation (can include pharmacologic treatment)	Physical Activity	Flu Vaccination Pneumococcal Vaccination Pertussis Vaccination
B, C and D	Smoking Cessation (can include pharmacologic treatment) Pulmonary Rehabilitation	Physical Activity	Flu Vaccination Pneumococcal Vaccination Pertussis Vaccination

*Can include pharmacologic treatment.

TABLE 4.8

FOLLOW-UP PHARMACOLOGICAL TREATMENT

1. **IF RESPONSE TO INITIAL TREATMENT IS APPROPRIATE, MAINTAIN IT.**
2. **IF NOT:**
   - ✓ Consider the predominant treatable trait to target (dyspnea or exacerbations)
     - Use exacerbation pathway if both exacerbations and dyspnea need to be targeted
   - ✓ Place patient in box corresponding to current treatment & follow indications
   - ✓ Assess response, adjust and review
   - ✓ These recommendations do not depend on the ABCD assessment at diagnosis



eos = blood eosinophil count (cells/µL)
** Consider if eos ≥ 300 or eos ≥ 100 AND ≥2 moderate exacerbations / 1 hospitalization*
*** Consider de-escalation of ICS or switch if pneumonia, inappropriate original indication or lack of response to ICS*

FIGURE 4.4

CT Imaging for ILD:

A Review of the Fleischner Society White Paper

Timothy Mickus MD

Disclosure

- I am a medical educational consultant for Boehringer Ingelheim


RETICULATION
EMPHYSEMA
PLCH
INTERSTITIAL
RBILD
CPFE
INTERSTITIAL
BOOP
ILD
GGO
ILD
ILD
BRONCHIECTASIS
NSIP
UIP
PNEUMONIA
DIP
ILD
CEP
INTERSTITIAL
INTERSTITIAL
PNEUMONIA
INTERSTITIAL
PNEUMONIA
GLILD
INTERSTITIAL
ILD
PNEUMONIA
LUNG
ILD
INTERSTITIAL
PNEUMONIA
INTERSTITIAL
INTERSTITIAL
PNEUMONIA
ORGANIZING
PNEUMONIA
PNEUMONIA
ILD
PNEUMONIA
INTERSTITIAL
DISEASE
PCOP
LIP
ILD
PNEUMONIA

Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper

David A Lynch, Nicola Sverzellati, William D Travis, Kevin K Brown, Thomas V Colby, Jeffrey R Galvin, Jonathan G Goldin, David M Hansell, Yoshikazu Inoue, Takeshi Johkoh, Andrew G Nicholson, Shandra L Knight, Suhail Raoof, Luca Richeldi, Christopher J Ryerson, Jay H Ryu, Athol U Wells

Lancet Respir Med 2018; 6: 138–53

Published Online November 15, 2017 http://dx.doi.org/10.1016/S2213-2600(17)30433-2

See Comment page 82

Department of Radiology (Prof D A Lynch MB), **Department of Medicine** (Prof K K Brown MD), **and Library and Knowledge Services** (S L Knight MS), **National Jewish Health, Denver, CO, USA; Department of Medicine and Surgery, University of Parma, Parma, Italy** (N Sverzellati MD); **Department of Pathology, Memorial Sloan Kettering Cancer Center, New York, NY, USA** (Prof W D Travis MD); **Department of Pathology, Mayo Clinic Scottsdale, Scottsdale, AZ, USA** (Prof T V Colby MD); **Department of Radiology, University of Maryland, Baltimore, MD, USA** (Prof J R Galvin MD); **Department of Radiology, David Geffen School of Medicine at UCLA, Santa Monica, CA, USA** (Prof J G Goldin MD); **Department of Radiology** (Prof D M Hansell MD), **Department of Histopathology** (Prof A G Nicholson DM), **and Department of Respiratory Medicine** (Prof A U Wells MD), **Royal Brompton and Hospital NHS Foundation Trust and National Heart and Lung Institute, Imperial College, London, UK; Clinical Research Center, National Hospital Organization Kinki-Chuo Chest Medical Center, Osaka, Japan** (Prof Y Inoue MD); **Department of Radiology, Kinki Central Hospital of Mutual Aid Association of Public School Teachers, Itami, Japan** (Prof T Johkoh MD); **Division of Pulmonary Medicine, Lenox Hill Hospital, New York, NY, USA** (Prof S Raoof MD); **Unità Operativa Complessa di Pneumologia, Agostino Gemelli University Hospital of the Catholic University of the Sacred Heart, Rome, Italy**

This Review provides an updated approach to the diagnosis of idiopathic pulmonary fibrosis (IPF), based on a systematic search of the medical literature and the expert opinion of members of the Fleischner Society. A checklist is provided for the clinical evaluation of patients with suspected usual interstitial pneumonia (UIP). The role of CT is expanded to permit diagnosis of IPF without surgical lung biopsy in select cases when CT shows a probable UIP pattern. Additional investigations, including surgical lung biopsy, should be considered in patients with either clinical or CT findings that are indeterminate for IPF. A multidisciplinary approach is particularly important when deciding to perform additional diagnostic assessments, integrating biopsy results with clinical and CT features, and establishing a working diagnosis of IPF if lung tissue is not available. A working diagnosis of IPF should be reviewed at regular intervals since the diagnosis might change. Criteria are presented to establish confident and working diagnoses of IPF.

Introduction

The approval of medical treatments for idiopathic pulmonary fibrosis (IPF) marks a new era in approaching this deadly disease: offering hope to patients and their physicians, a clearer path forward for companies interested in the development of new treatments, and the potential for new biological insights. This new era also offers clinicians the opportunity to review approaches to diagnosis. The diagnostic criteria for IPF published by the American Thoracic Society (ATS), European Respiratory Society (ERS), Japanese Respiratory Society (JRS), and Latin American Thoracic Association (ALAT) in 2011[1] have been crucial for defining entry criteria and ensuring appropriate recruitment for prospective clinical trials.[2–7] In turn, these trials, with large cohorts of well characterised patients, have provided considerable new clinically relevant information about disease presentation and its longitudinal behaviour.[8,9] The specific inclusion and exclusion criteria used in these studies have also highlighted the limitations of current diagnostic guidelines, and indicated opportunities for improvement.[9,10]

The diagnosis of IPF requires the collaboration of multiple specialists, the ability to interpret and communicate complex clinical data patterns, and to integrate uncertain or sometimes conflicting information. The clinician interprets the history and physical examination of the patient to develop a clinical context, the thoracic radiologist interprets the pattern present on high-resolution CT images of the chest and, if needed, the pathologist interprets the histopathological pattern seen on lung biopsy samples. All the information gained must then be shared in a common language to enable clinical decision making. Since so-called classic clinical stories and patterns are uncommon, some degree of clinical uncertainty is often present, and acknowledgment of this limitation and a clear plan to address it are essential.

For this Review, we identified specific questions pertaining to the diagnosis of IPF (panel 1), and did a search of the medical literature to identify evidence related to the topics identified and that had been published after the 2011 ATS/ERS/JRS/ALAT guidelines.[1] Using this research and the expert opinion of members of the Fleischner Society, we provide IPF diagnostic criteria that we believe will be useful for clinicians, clinical trialists, trial sponsors, and other interested groups.

Systematic review

An international multidisciplinary committee, including 17 members of the Fleischner Society with expertise in interstitial lung disease (ILD) and evidence-based medicine (eight pulmonologists, six radiologists, and three pathologists), and a medical librarian expert (SLK), developed the key questions believed to be important for the diagnosis of IPF (panel 1). Several face-to-face meetings were held, in addition to monthly conference calls. We did a literature search with the assistance of a medical librarian (search strategy and selection criteria and appendix). The committee was divided into subgroups assigned to specific

Key messages

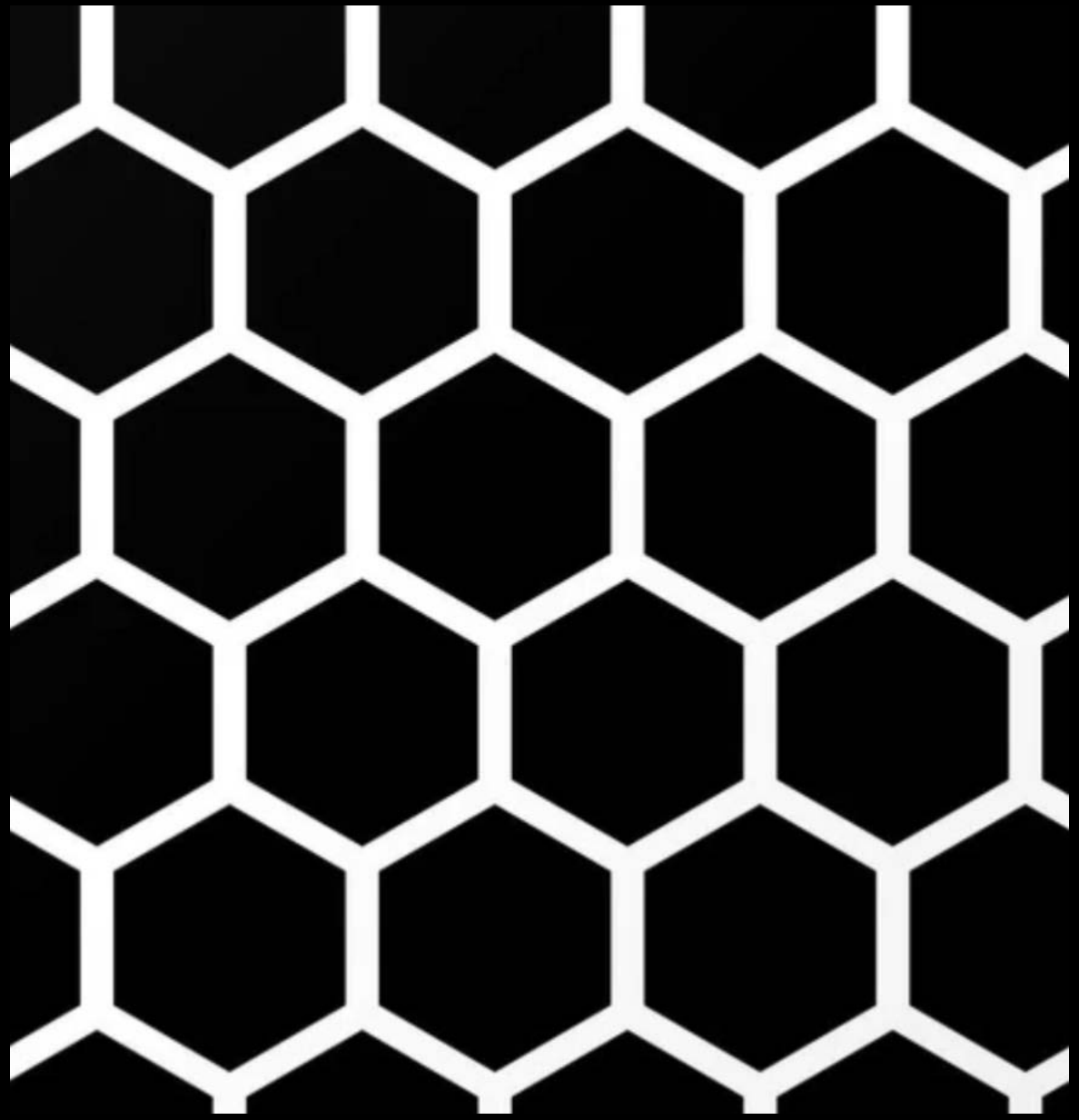
- A confident diagnosis of IPF (idiopathic pulmonary fibrosis) can be made in the correct clinical context when CT imaging shows a pattern of typical or probable UIP (usual interstitial pneumonia)
- If the clinical context is indeterminate for IPF, or the CT pattern is not indicative of typical or probable UIP, biopsy should be considered to confirm the presence of a UIP histological pattern, and a confident diagnosis of IPF could then be made on the basis of a multidisciplinary evaluation
- If diagnostic tissue is not available, a working diagnosis of IPF could be made after a careful multidisciplinary evaluation
- All patients with an IPF diagnosis, particularly those with a working diagnosis, should have this diagnosis reviewed at regular intervals

Talk outline

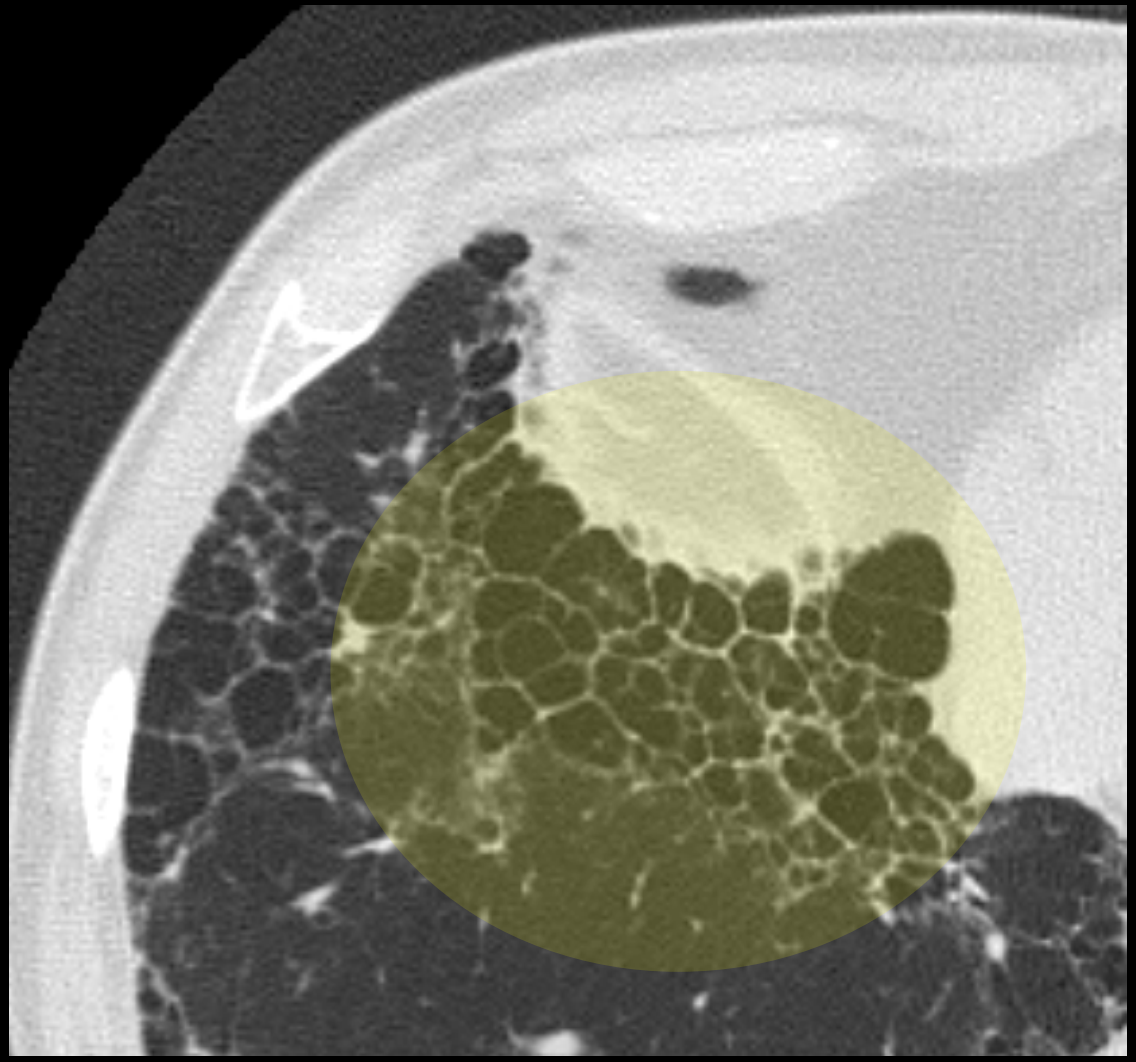
- Descriptive imaging terminology
- CT patterns in usual interstitial pneumonia
- Case examples

Honeycombing

- Clustered, thick-walled, cystic spaces of similar diameters, generally measuring between 3–25 mm
- Can be stacks or single layers
- Difficult to always determine in setting of bronchiectasis and emphysema



Honeycombing

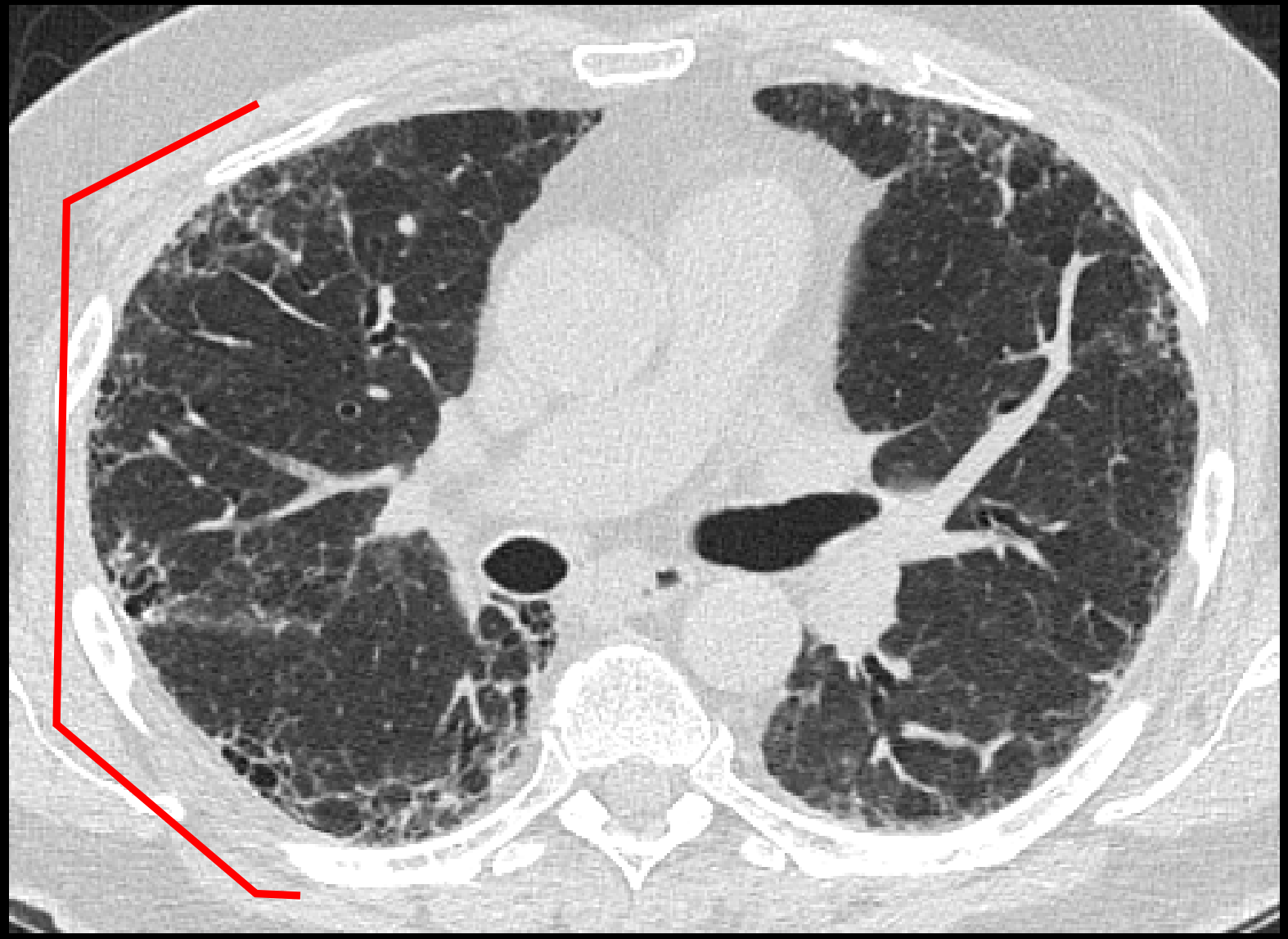


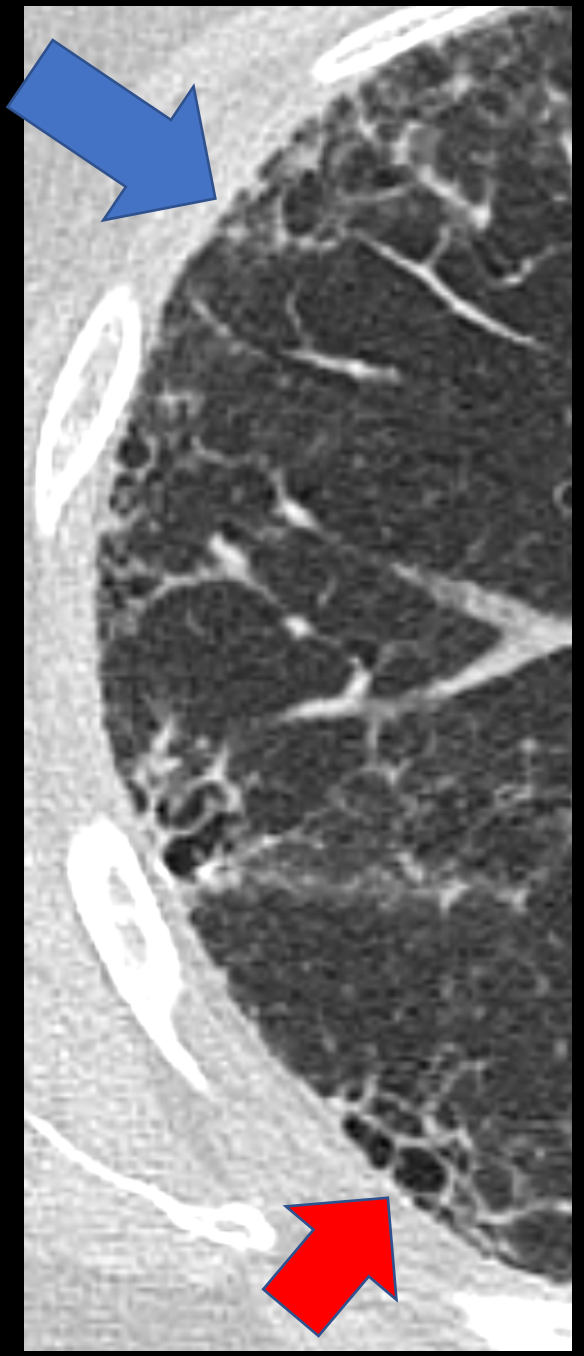
Reticulation

- Fine linear densities seen in the lungs
- Mesh-like/net-like appearance
- In UIP, the lines are more irregular in thickness and in spacing
- In NSIP, the lines tend to be more uniform in spacing and thickness



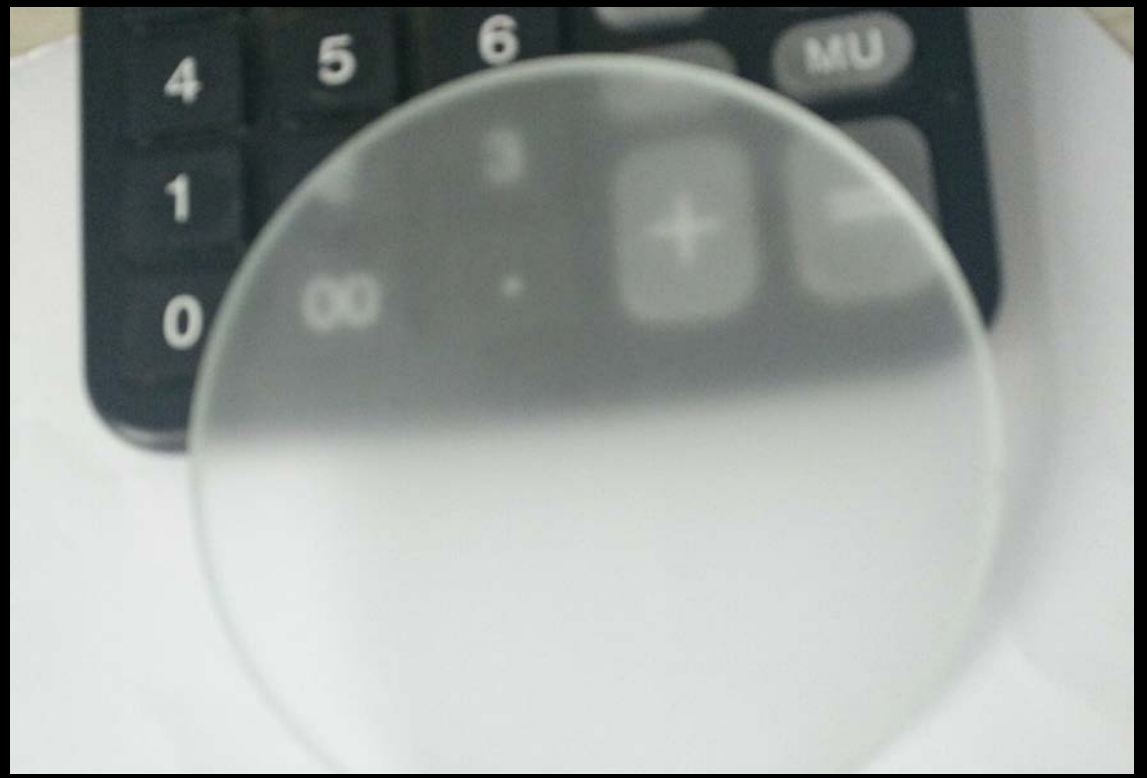
Reticulation





Ground glass opacity

- Increased attenuation in the lung parenchyma
- “Translucent”
- A completely non-specific but common imaging finding
- Should not predominate in UIP



Ground-glass opacity



Traction bronchiectasis

- Irreversible airway dilatation
- Caused by surrounding fibrosis in the lung parenchyma
- Peripheral in location
- Can resemble honeycombing at the bases, and often co-exists with honeycombing
  - Possibility that honeycombing is ”end-stage” bronchiectasis



CT patterns in UIP

- Typical UIP
- Probable UIP
- CT-pattern indeterminate for UIP
- Alternative/Non-IPF Diagnosis

	Typical UIP CT pattern	Probable UIP CT pattern	CT pattern indeterminate for UIP	CT features most consistent with non-IPF diagnosis
Distribution	Basal predominant (occasionally diffuse), and subpleural predominant; distribution is often heterogeneous	Basal and subpleural predominant; distribution is often heterogeneous	Variable or diffuse	Upper-lung or mid-lung predominant fibrosis; peribronchovascular predominance with subpleural sparing
Features	Honeycombing; reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; absence of features to suggest an alternative diagnosis	Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis*; honeycombing is absent; absence of features to suggest an alternative diagnosis	Evidence of fibrosis with some inconspicuous features suggestive of non-UIP pattern	Any of the following: predominant consolidation, extensive pure ground glass opacity (without acute exacerbation), extensive mosaic attenuation with extensive sharply defined lobular air trapping on expiration, diffuse nodules or cysts

UIP=usual interstitial pneumonia. IPF=idiopathic pulmonary fibrosis. *Reticular pattern is superimposed on ground glass opacity, and in these cases it is usually fibrotic. Pure ground glass opacity, however, would be against the diagnosis of UIP or IPF and would suggest acute exacerbation, hypersensitivity pneumonitis, or other conditions.

Table 1: **Diagnostic categories of UIP based on CT patterns**

Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper
***Lancet Respir Med* 2018; 6: 138–53**
Published **Online** November 15, 2017 http://dx.doi.org/10.1016/ S2213-2600(17)30433-2

Typical UIP

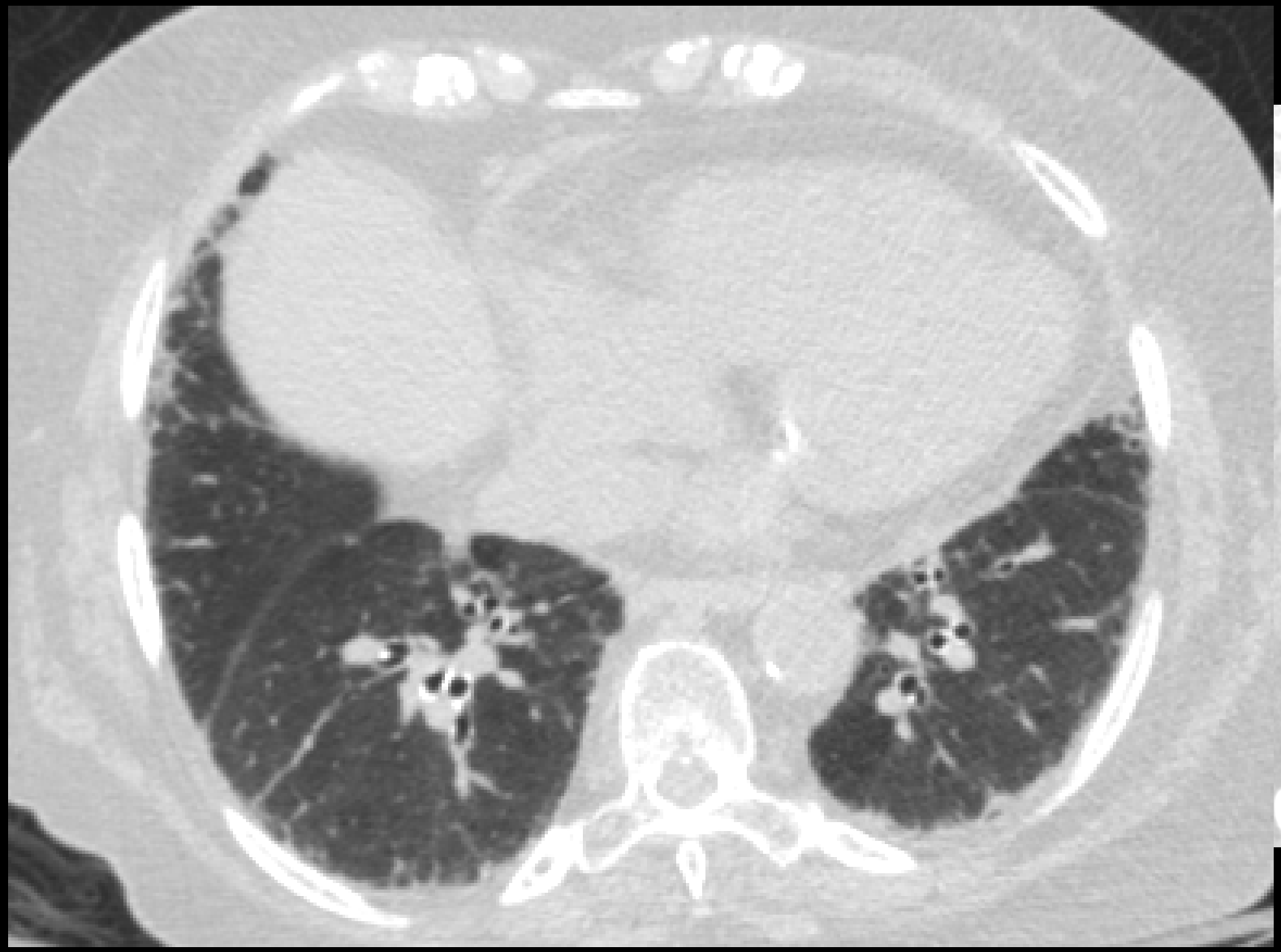
- Distribution:
  - Basal, peripheral, heterogeneous
- Honeycombing
- Reticulation
- Traction bronchiectasis

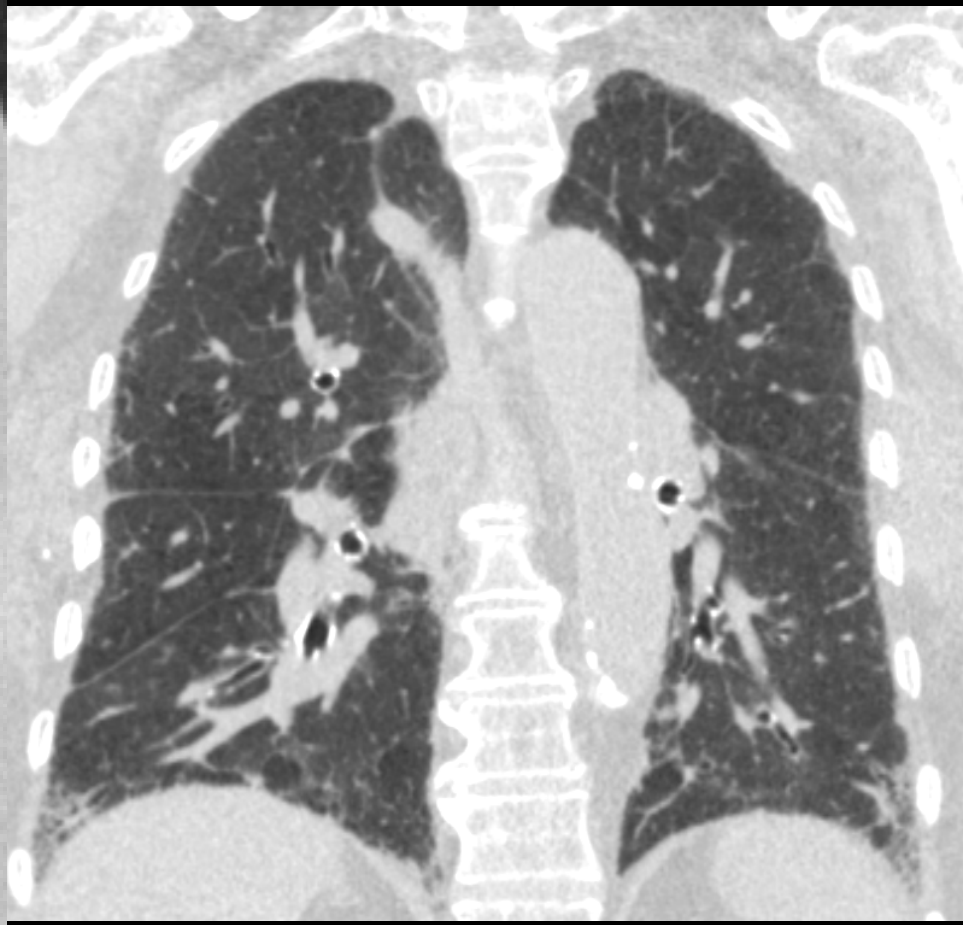




Probable UIP

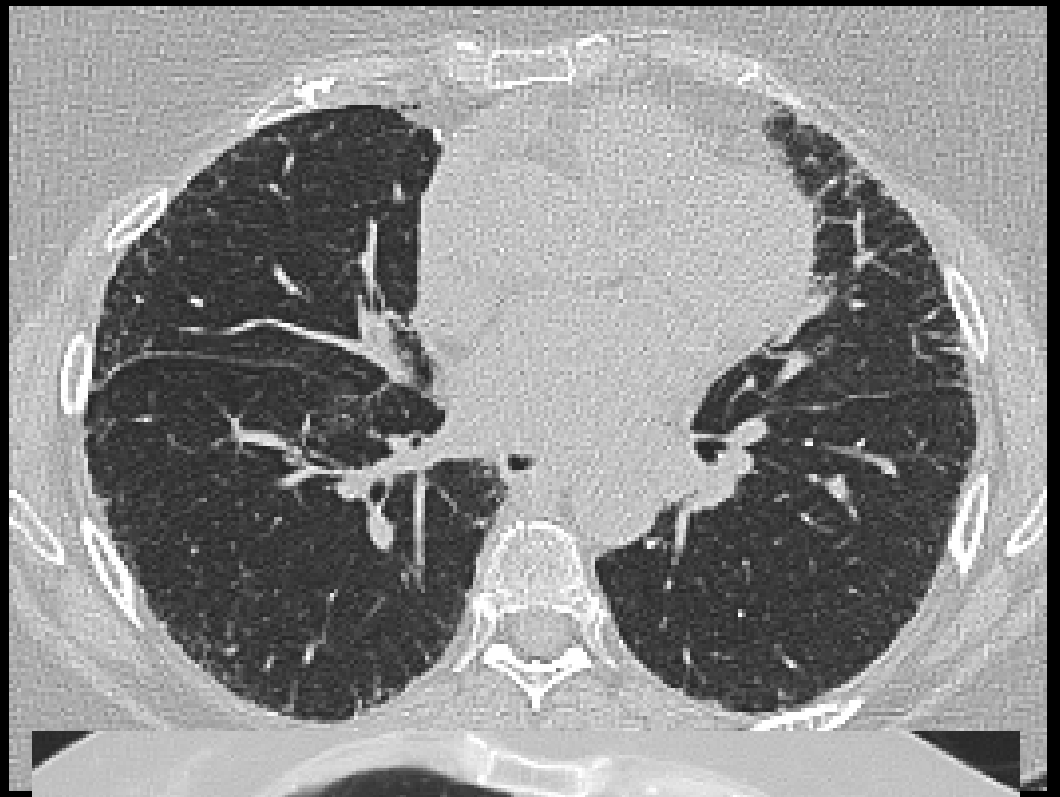
- Distribution:
  - Basal, peripheral, heterogeneous
- Honeycombing ABSENT
- Reticulation
- Traction bronchiectasis

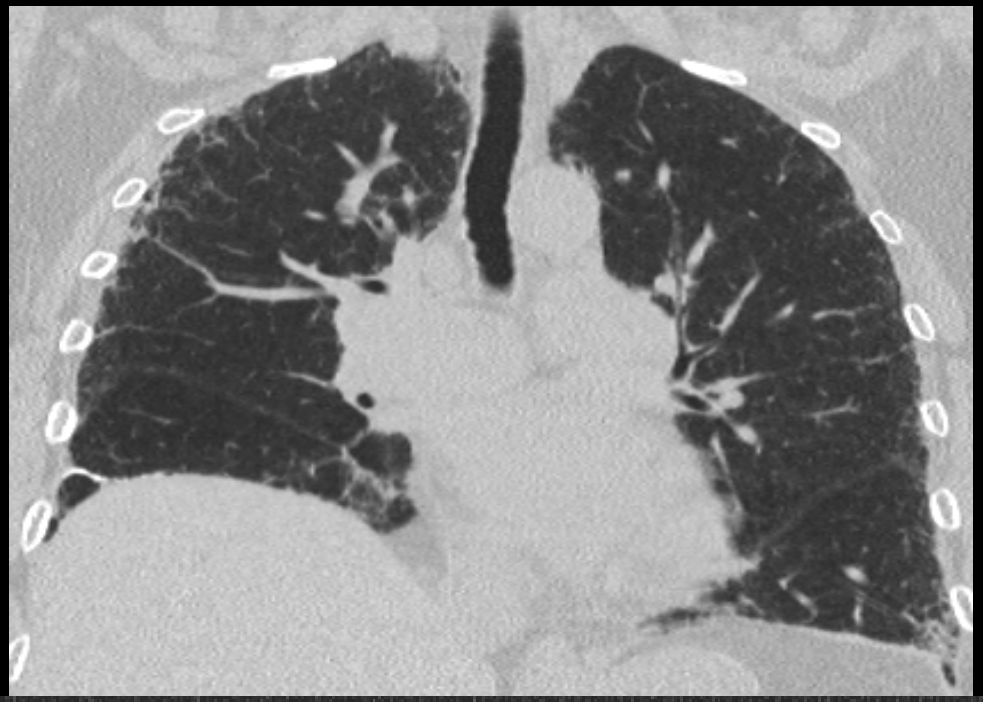




CT-pattern indeterminate for UIP

- Variable or diffuse distribution
- CT findings suggesting fibrosis



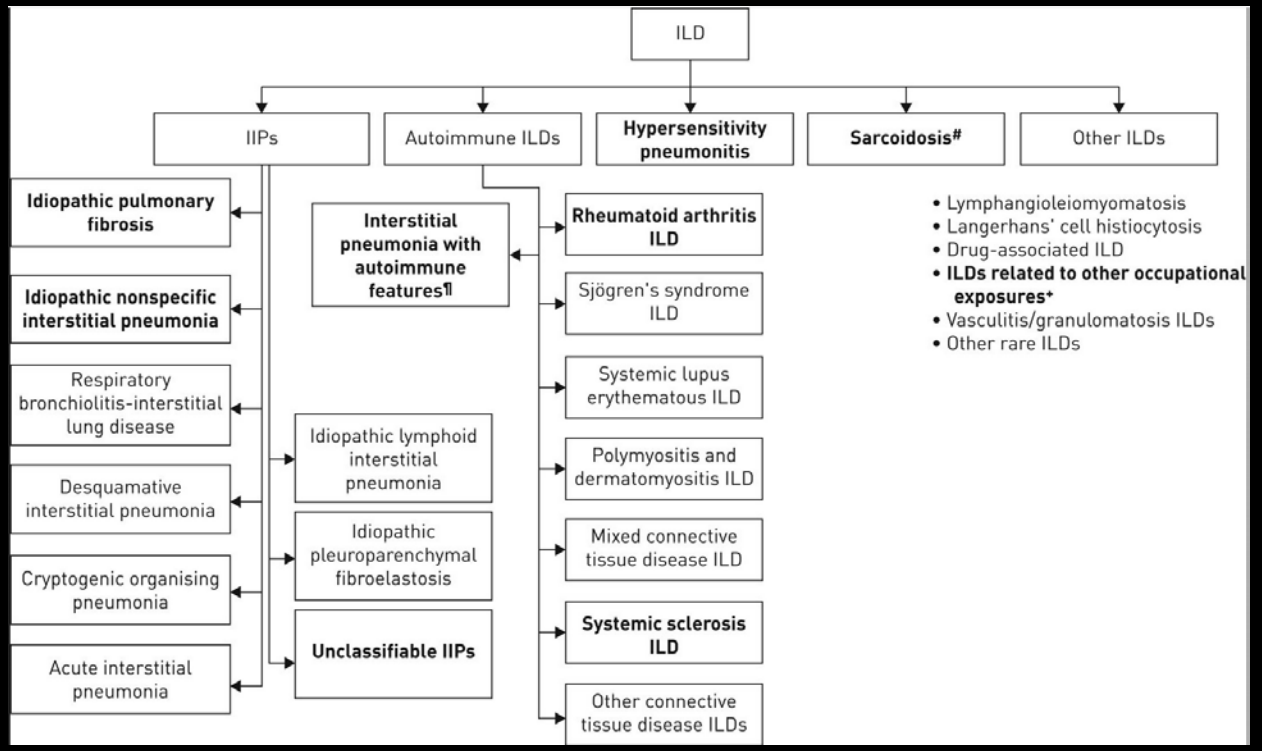






Alternative/Non-IPF Diagnosis

- Distubution:
  - Upper/mid lung
  - Peribronchovascular
  - Subpleural sparing
- Consolidation
- Ground glass
- Mosaic attenuation/air-trapping
- Nodules
- Cysts



Summary

- Terminology
- Four CT patterns for UIP
  - Typical UIP pattern
  - Probable UIP pattern
  - CT pattern indeterminate for UIP
  - CT features most consistent with a non-IPF diagnosis

Thank you

- Timothy.Mickus@ahn.org

Overview of Asthma

Ahmad AlhajHusain, MD
Associate Professor
Pulmonary and Critical Care
2021

Objectives

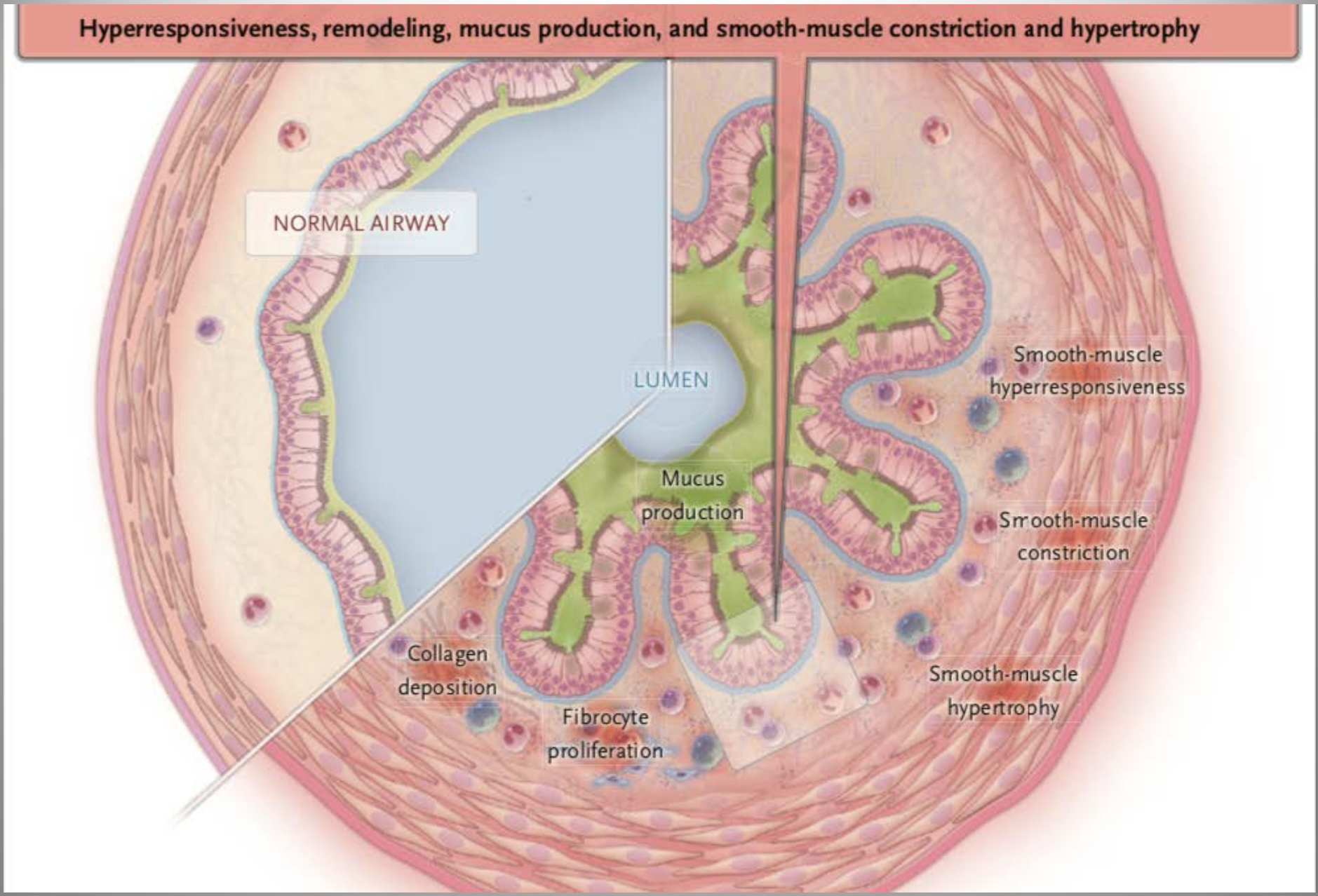
- Definition and Prevalence
- Diagnosis
- Treatment update
- Severe uncontrolled asthma

What is Asthma?

- Heterogeneous disease, usually characterized by chronic airway inflammation.

What is Asthma?

- Heterogeneous disease, usually characterized by chronic airway inflammation.
- Defined by the history of wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.
- Airway limitation may become persistent

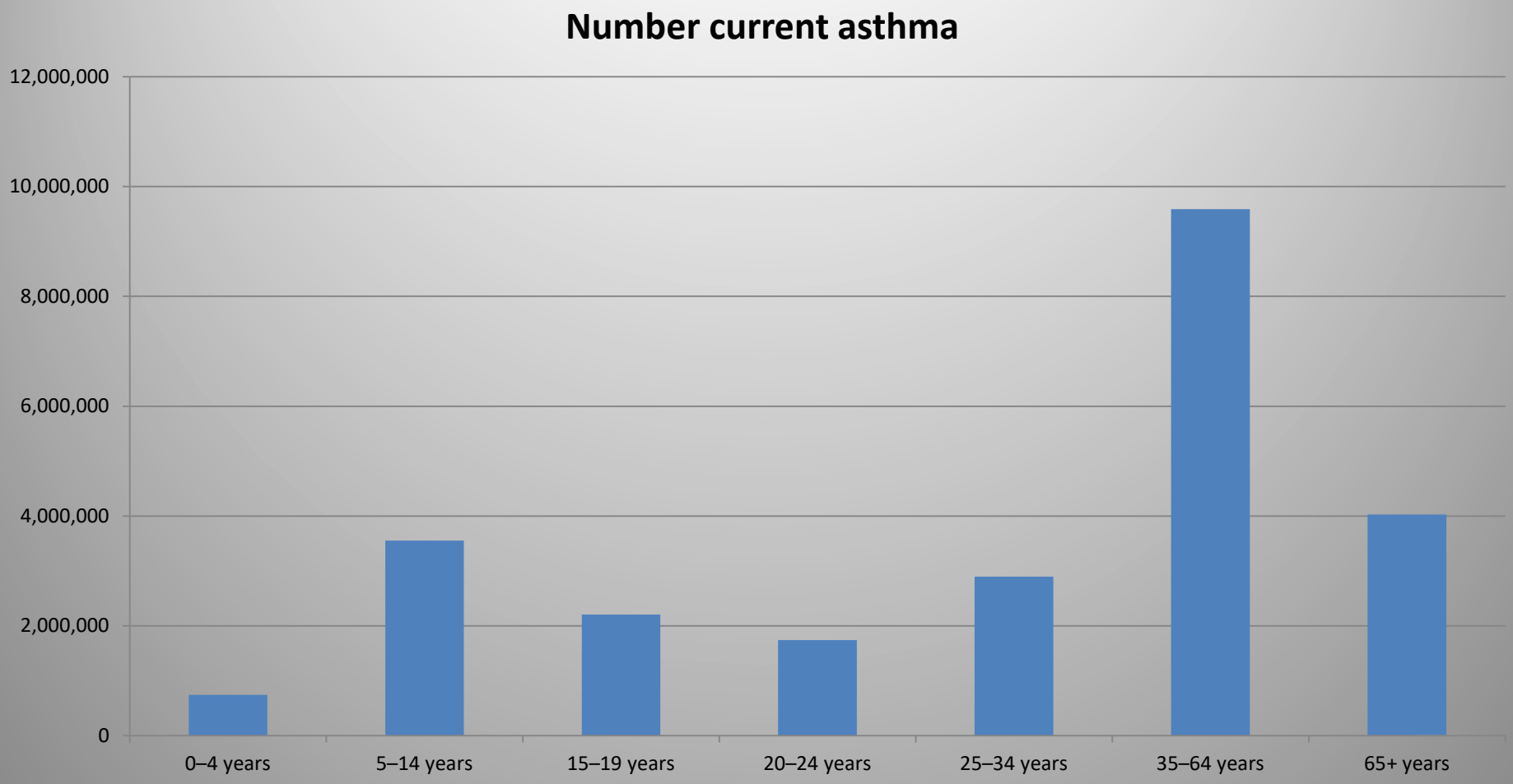


Israel, N Engl J Med 2017;377:965-76

National
Current Asthma[1] Prevalence (2018)

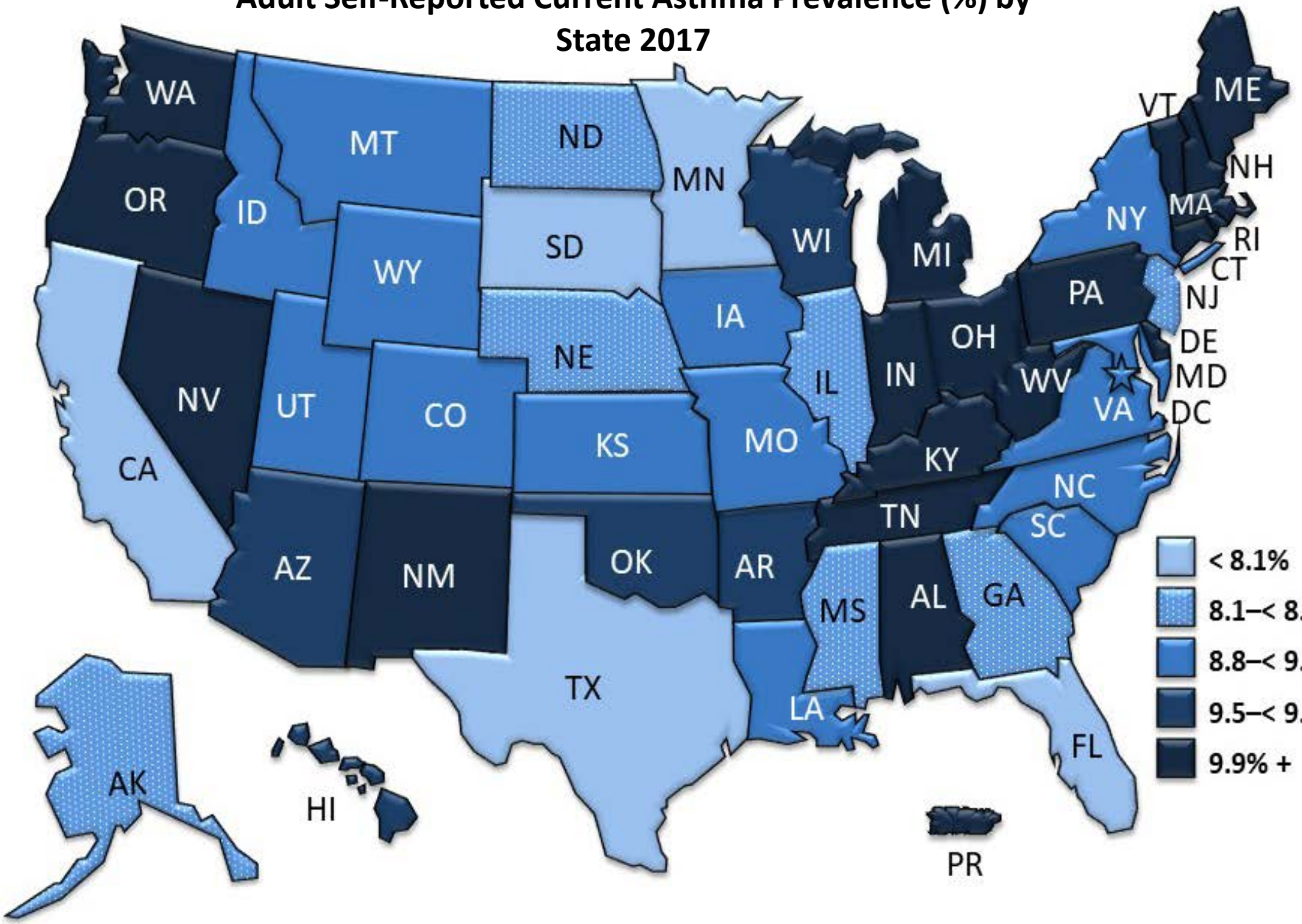
Characteristic[2]	Weighted Number with Current Asthma[1]	Percent (SE)
Total	24,753,379	7.7 (0.20)
Child (Age <18 years)	5,530,131	7.5 (0.37)
Adult (Age 18+ years)	19,223,248	7.7 (0.22)

www.cdc.gov


Number current asthma
12,000,000
10,000,000
8,000,000
6,000,000
4,000,000
2,000,000
0
0–4 years
5–14 years
15–19 years
20–24 years
25–34 years
35–64 years
65+ years

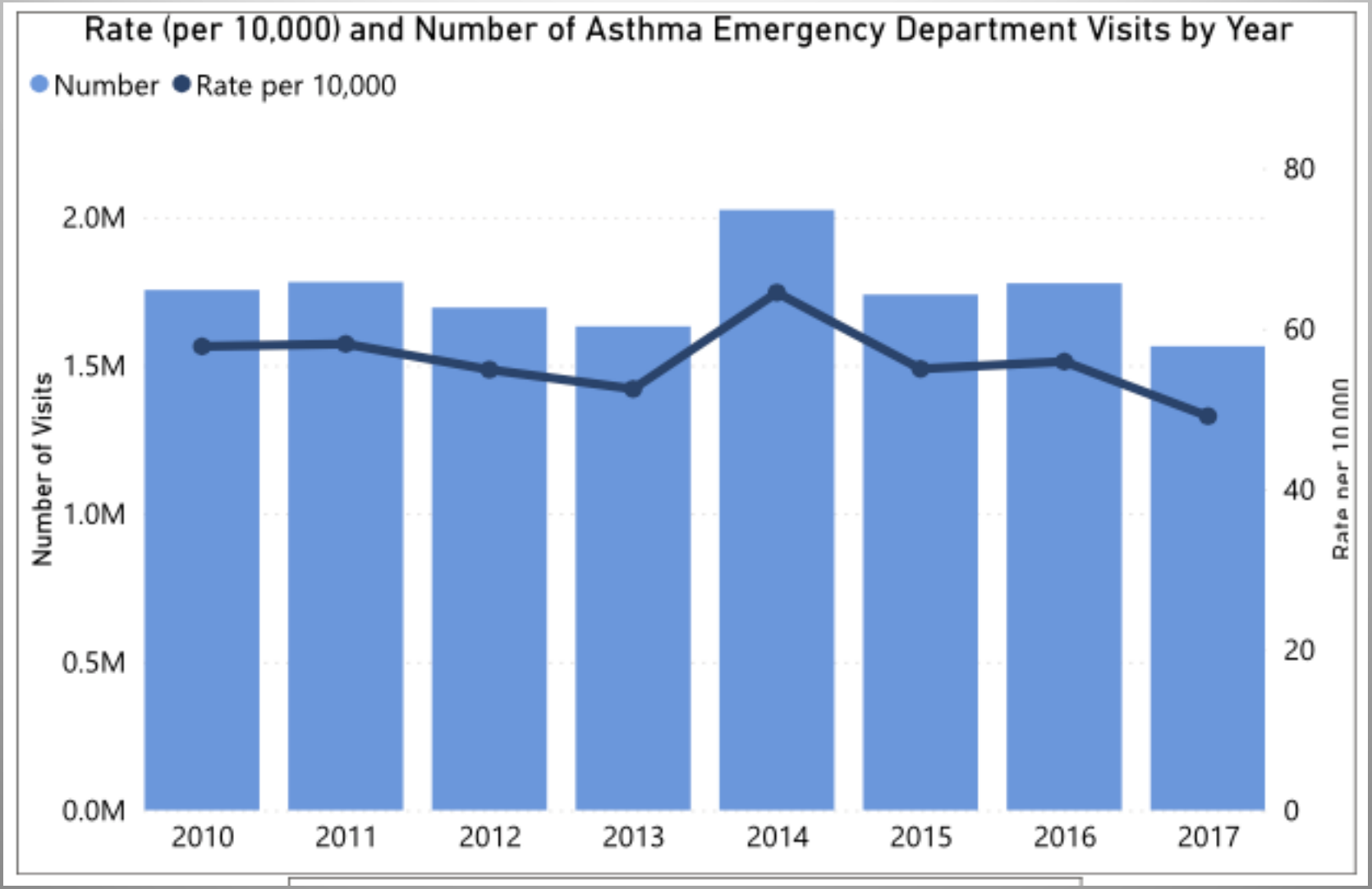
www.cdc.gov

Adult Self-Reported Current Asthma Prevalence (%) by State 2017



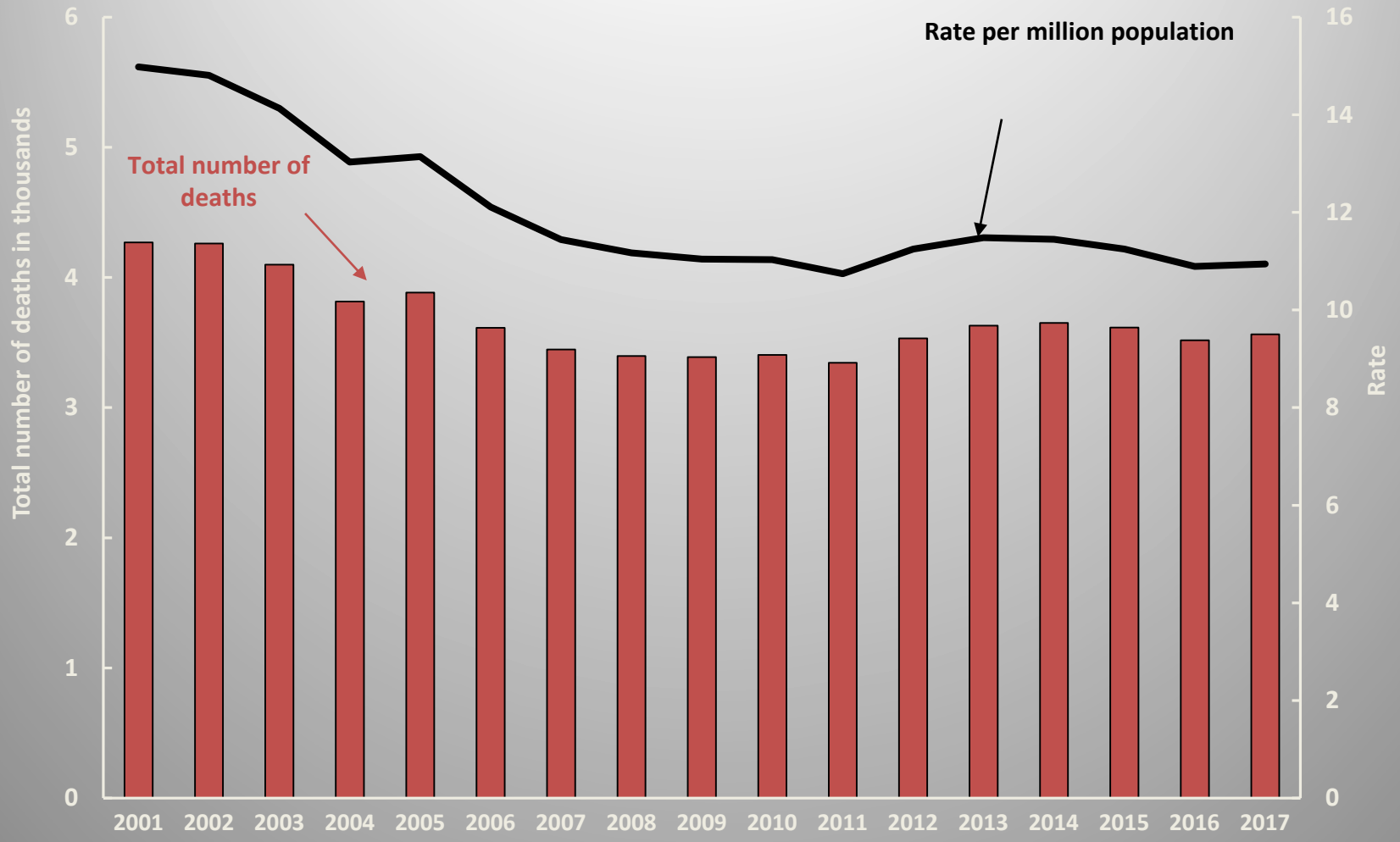
www.cdc.gov

Emergency department visit per year



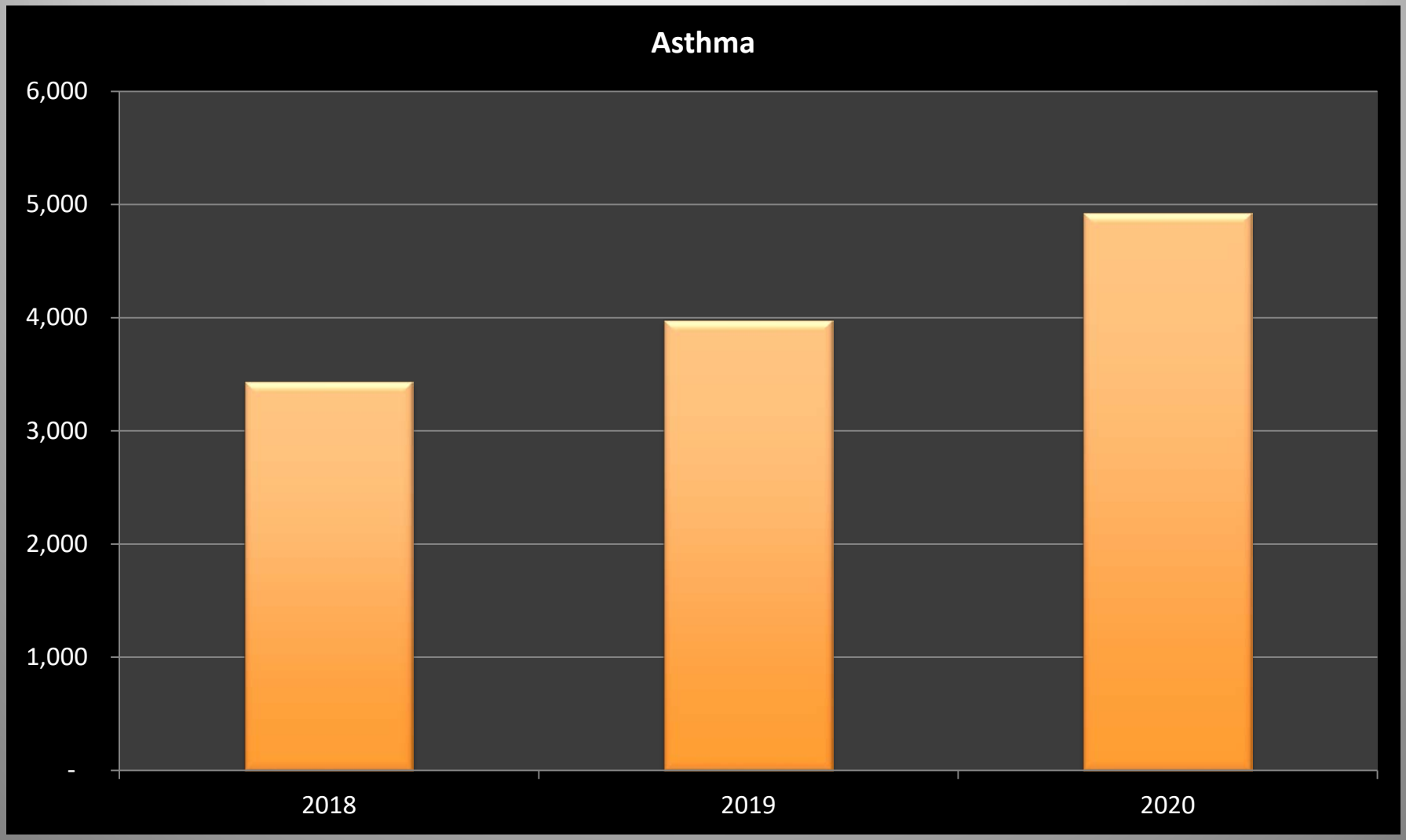
www.cdc.gov

Asthma Deaths:
United States, 2001–2017

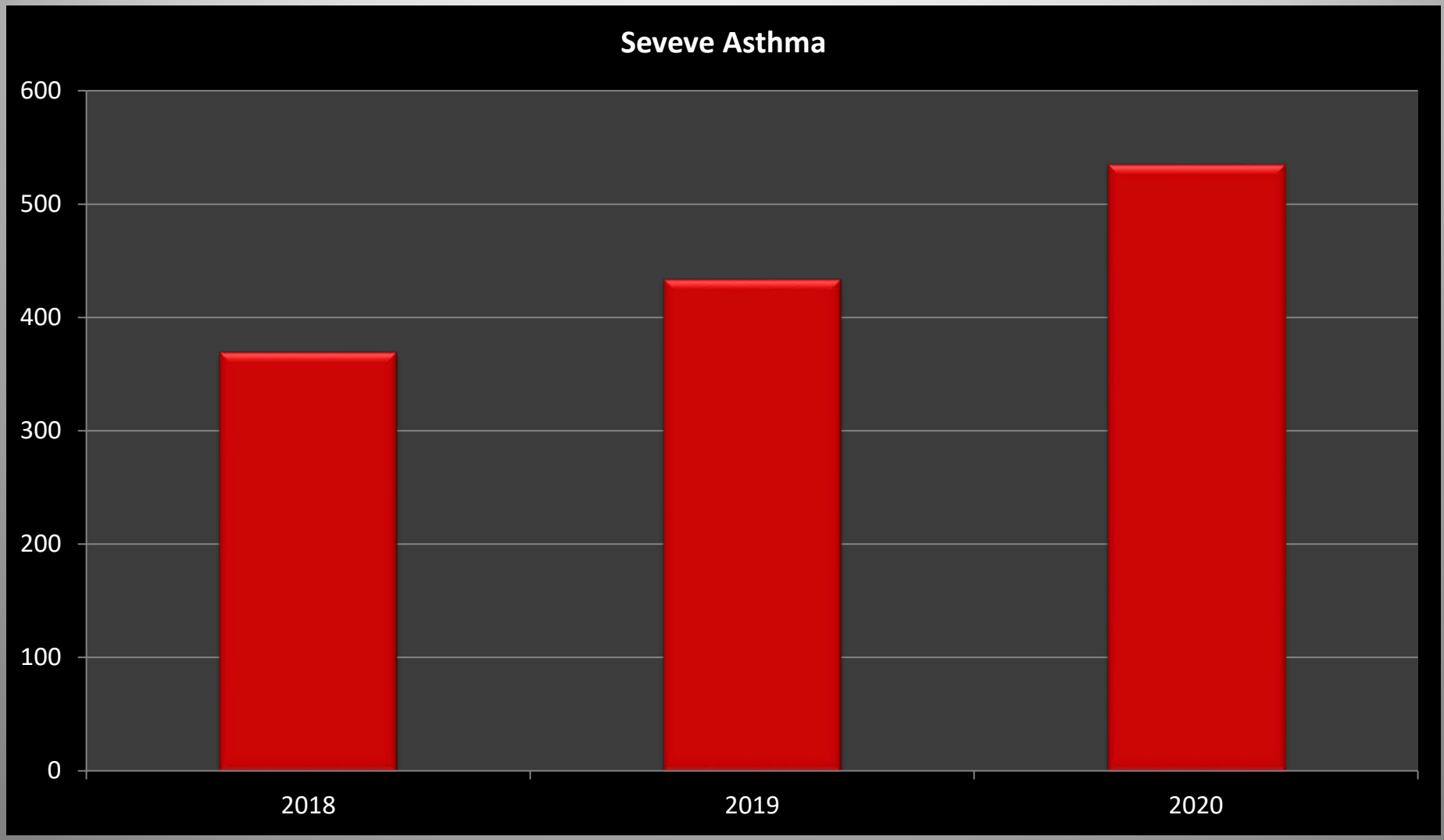


www.cdc.gov

Out patient visits by year, our pulmonary office



Out patient visits for Severe Asthma by year, pulmonary office



Criteria for making diagnosis

A. History of variable respiratory symptoms

A. Evidence of variable expiratory airflow limitation

Criteria for making diagnosis

A. History of variable respiratory symptoms

- Wheeze, shortness of breath, chest tightness, and cough
- Symptoms occur variably over time and vary in intensity
- Worse at night and early morning
- Triggered by exercise, laughter, allergens, cold air, irritants or viral infections

Global Initiative for asthma 2020

Evidence of variable expiratory airflow limitation

Positive bronchodilator reversibility test	FEV1>12%, and 200 ml post bronchodilator
Excessive variability in twice daily PEF over 2 weeks	> 10%
Significant increase in lung function after 4 weeks on anti-inflammatory treatment	FEV1>12%, and 200 ml or PEF >20%
Positive exercise challenge test	Fall in FEV1 > 10%
Positive bronchial challenge test	
Excessive variation in lung function between visits	FEV1 > 12% and 200 ml between visits outside respiratory infection

Asthma phenotypes

- *Allergic asthma*:
  - Starts in childhood
  - Past and/or family history of allergic disease such as eczema, allergic rhinitis, or food or drug allergy.
  - Induced sputum before treatment often reveals eosinophilic airway inflammation.
  - Respond well to ICS treatment.

Asthma phenotypes

- *Non-allergic asthma*:
  - Adults
  - Not associated with allergy.
  - The cellular profile of the sputum of these patients may be neutrophilic, eosinophilic or contain only a few inflammatory cells (paucigranulocytic).
  - Responds less well to ICS.

Asthma phenotypes

- *Late-onset asthma*:
  - Adults, particularly women, present with asthma for the first time in adult life.
  - tend to be non-allergic, and often require higher doses of ICS
  - Relatively refractory to corticosteroid treatment.

Asthma phenotypes

- *Asthma with fixed airflow limitation*: long-standing asthma develop fixed airflow limitation that is thought to be due to airway wall remodeling.

- *Asthma with obesity*: little eosinophilic airway inflammation.

Asthma assessment

A. Asthma symptom control		Level of asthma symptom control		
In the past 4 weeks, has the patient had:		**Well controlled**	**Partly controlled**	**Uncontrolled**
• Daytime asthma symptoms more than twice/week?	Yes☐ No☐	None of these	1–2 of these	3–4 of these
• Any night waking due to asthma?	Yes☐ No☐			
• SABA reliever for symptoms more than twice/week?*	Yes☐ No☐			
• Any activity limitation due to asthma?	Yes☐ No☐			

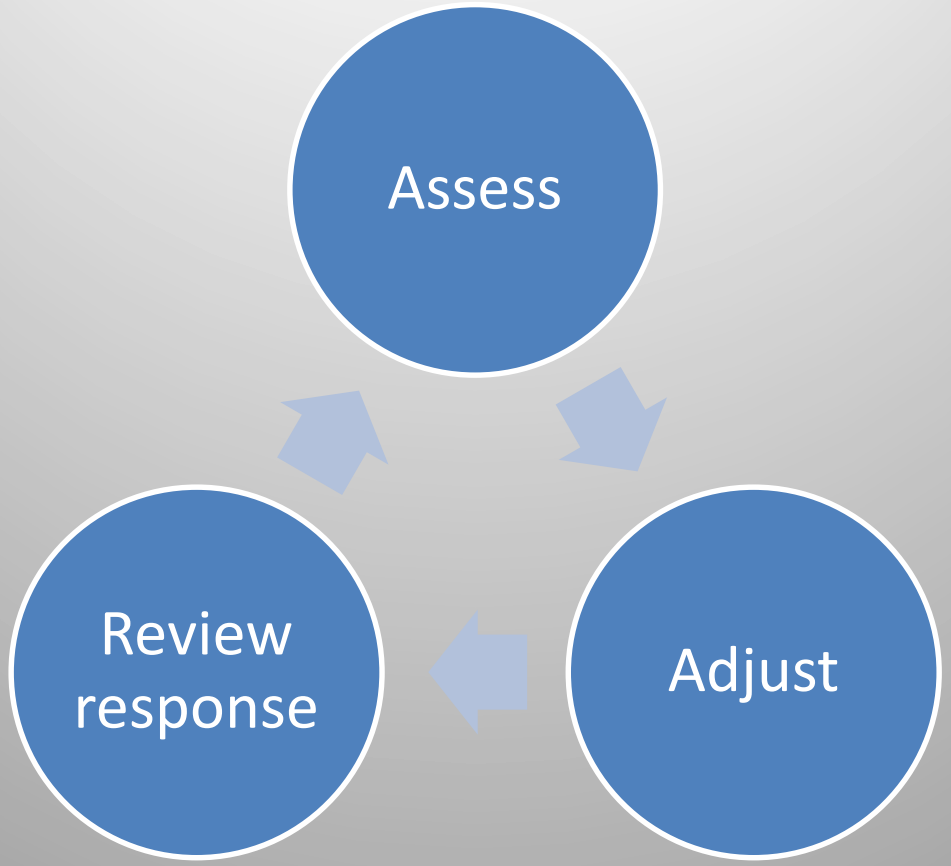
Numerical tools:

- Asthma Control Questionnaire (ACQ)
- Asthma Control Test (ACT)

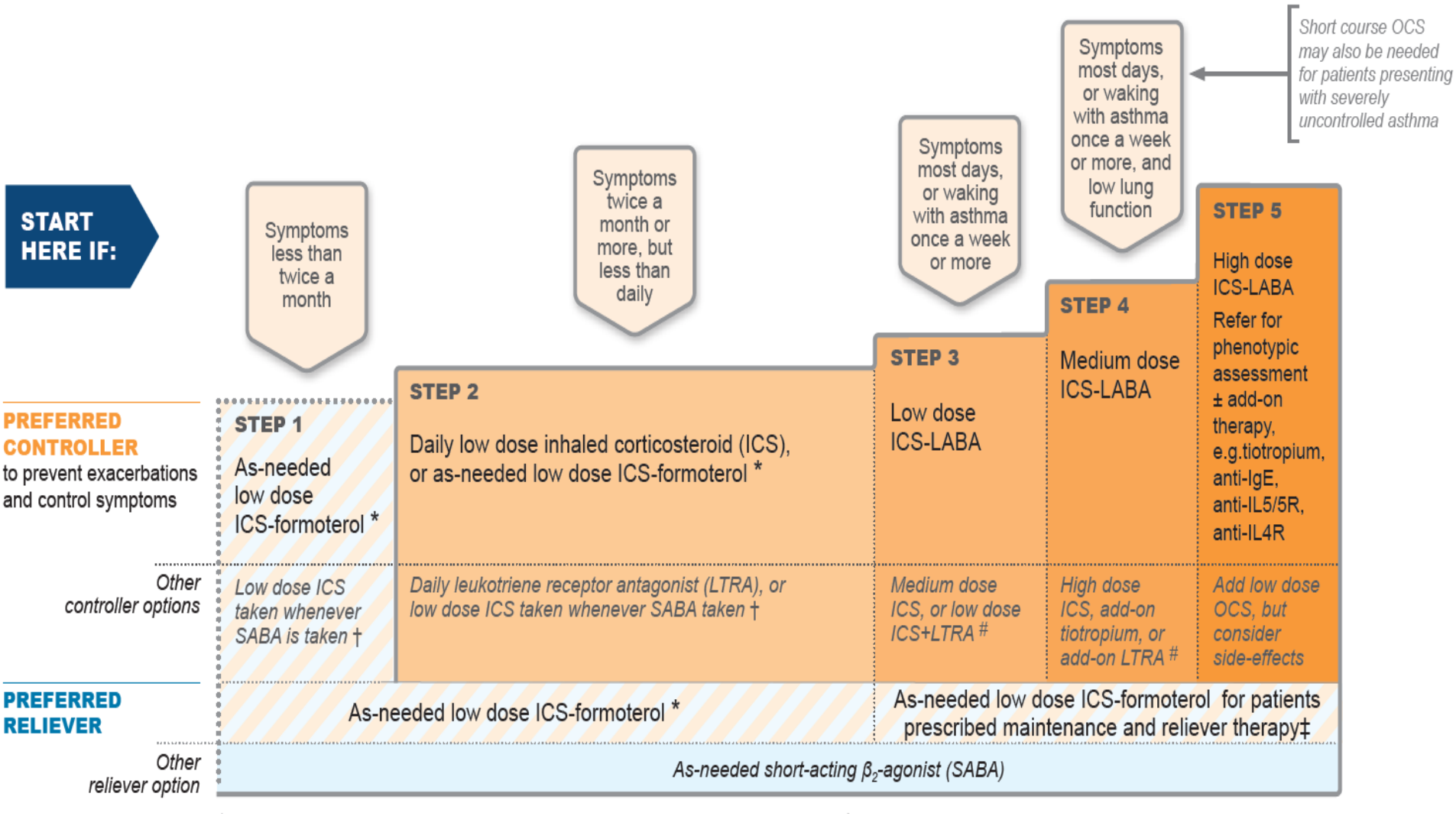
Asthma severity

- Mild Asthma: Asthma that is well controlled with Step 1 or Step 2
- Moderate Asthma: Asthma that is well controlled with Step 3
- Severe Asthma: Asthma that is controlled with Step 4 and 5

Asthma management



SUGGESTED INITIAL CONTROLLER TREATMENT IN ADULTS AND ADOLESCENTS WITH A DIAGNOSIS OF ASTHMA



© Global Initiative for Asthma, www.ginasthma.org

Background to changes in 2019 - the risks of SABA-only treatment

- Regular or frequent use of SABA is associated with:
  - β-receptor downregulation, decreased bronchoprotection, rebound hyperresponsiveness, decreased bronchodilator response
  - Increased allergic response, and increased eosinophilic airway inflammation

(Aldridge, AJRCCM 2000)

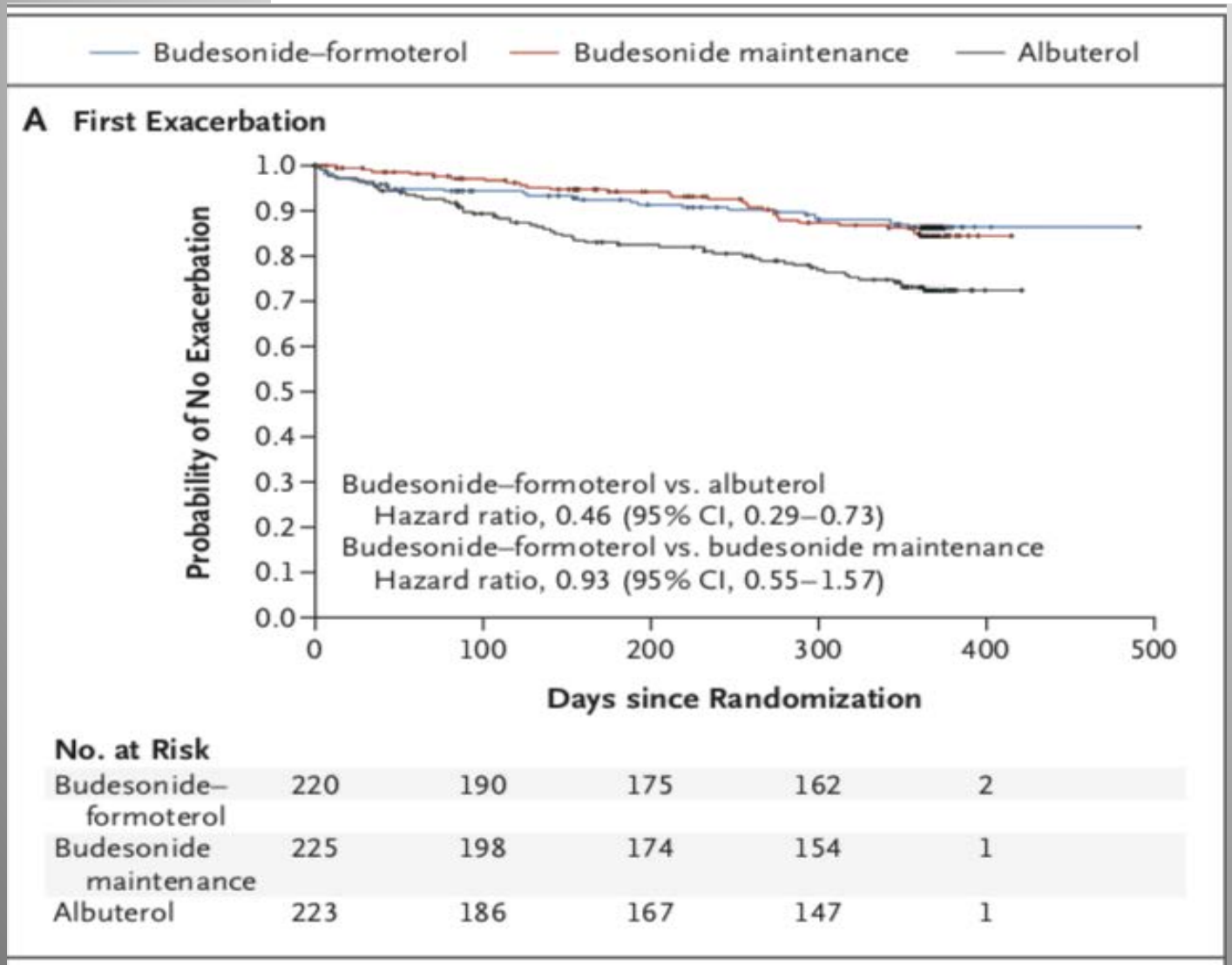
Background to changes in 2019 - the risks of SABA-only treatment

- Higher use of SABA is associated with adverse clinical outcomes:
  - Dispensing of ≥3 canisters per year is associated with higher risk of emergency department presentations *(Stanford, AAAI 2012)*
  - Dispensing of ≥12 canisters per year is associated with higher risk of death *(Suissa, AJRCCM 1994)*

(Hancox, Respir Med 2000)

ORIGINAL ARTICLE

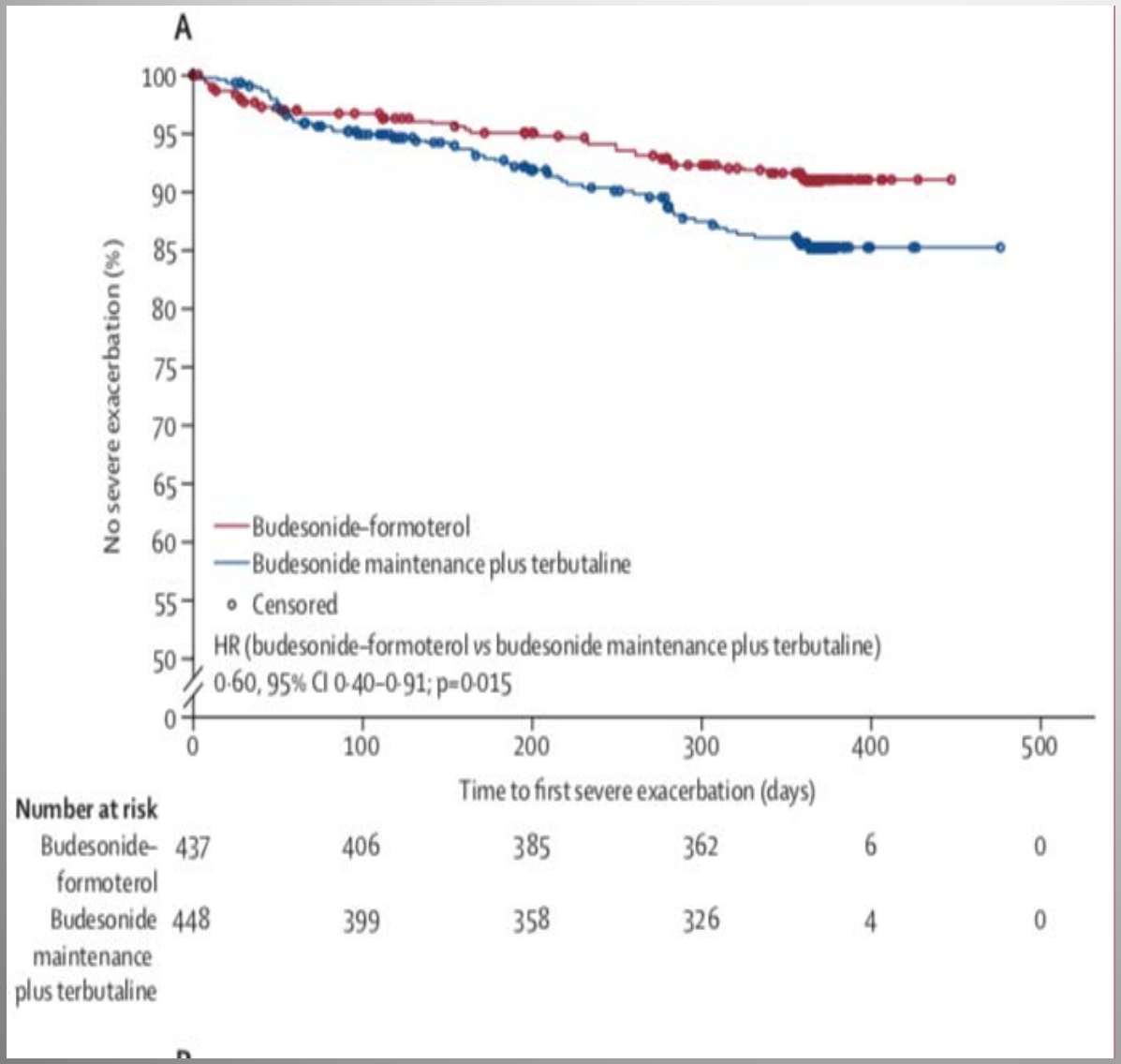
Controlled Trial of Budesonide–Formoterol as Needed for Mild Asthma



No. at Risk

Budesonide–formoterol	220	190	175	162	2
Budesonide maintenance	225	198	174	154	1
Albuterol	223	186	167	147	1

Beasley, NEJM 2019



Budesonide-formoterol reliever therapy vs maintenance budesonide plus terbutaline reliever therapy in adults with mild to moderate asthma

Hardy Lancet 2019

GINA 2019 – landmark changes in asthma management

- GINA no longer recommends SABA-only treatment for Step 1

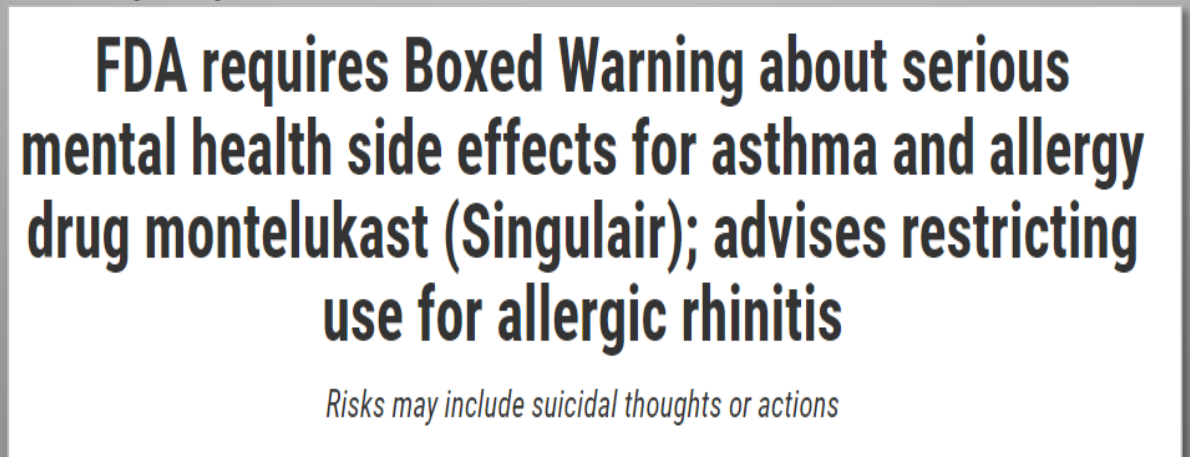
- GINA now recommends that all adults and adolescents with asthma should receive ICS-containing controller treatment, to reduce the risk of serious exacerbations

Montelukast

- Daily dose, 10 mg
- Add to step 2, 3, 4 and 5
- Helps in patient with allergic rhinitis

Adverse effects with montelukast

- FDA boxed warning in March 2020 about risk of serious neuropsychiatric events
  - Includes suicidality in adults and adolescents
  - Nightmares and behavioral problems in children
- Patients should be counselled about the risk of neuropsychiatric events



FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis

Risks may include suicidal thoughts or actions

Severe Asthma

Definition of severe asthma

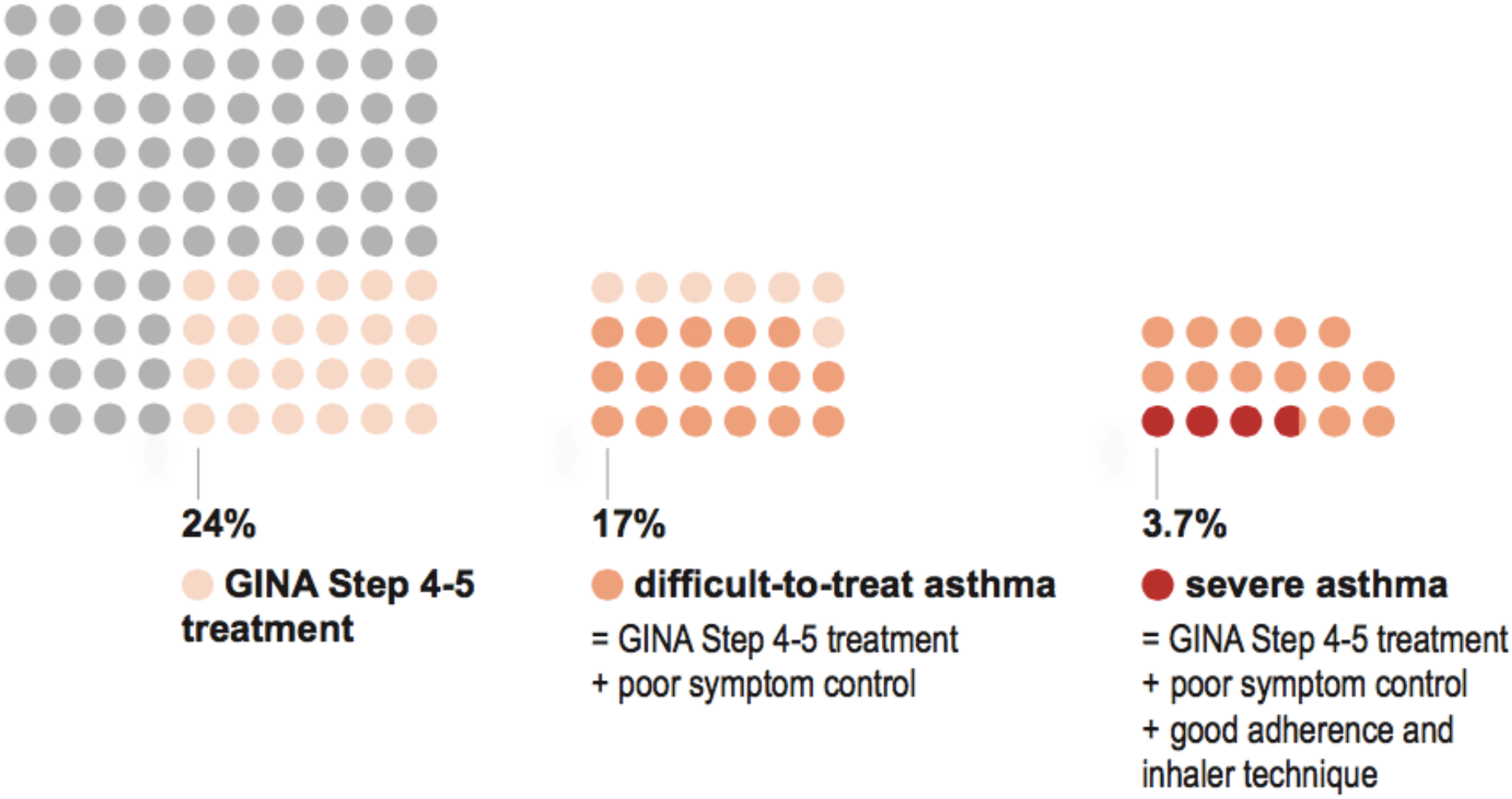
- Asthma which requires treatment with high dose ICSs plus a second controller (and/or systemic corticosteroids) to prevent it from becoming uncontrolled or which remains uncontrolled despite this therapy.

Uncontrolled asthma

Defined as at least one of the following:

- Asthma control questionnaires > 1.5, Asthma control test < 20
- Frequent exacerbations: two or more exacerbations in the previous year
- History of serious exacerbation in previous year (hospitalization)
- Airflow limitation, FEV1 <80% (FEV1/FVC < LLN)

Prevalence of severe Asthma



Severe Asthma endotypes

- Type 2 inflammation (T2 High):
  - Increased epithelial expression of Th2-type cytokines, such as IL-4, IL-5 and IL-13
  - Atopy, and/or eosinophilia airway inflammation

- Non type 2 (T2 Low):
  - absence of markers of Th2-mediated inflammation.
  - Neutrophilic or paucigranulocytic airway infiltration.
  - Airway remodeling

Severe Asthma endotypes

- Type 2 inflammation (T2 High):

  at least 2 criteria:

  – IgE ⩾100 IU·mL
  – Blood eosinophil count ⩾300 µL (or >150*)
  – FENO ⩾30 ppb (or > 20*)

* while on high dose ICS

Severe Asthma treatment

Clinical treatment approach in treating severe asthma

- Re-evaluate the diagnosis.

Clinical treatment approach in treating severe asthma

- Re-evaluate patients'
  - comorbidities (GERD, sinusitis, OSA)
  - exposure to allergens or other noxious agents (smoking)
  - adherence and **proper use of current treatment**.
  - Medications side effects (high dose beta blockers and NSAIDs)
- Switch to a different inhaler device (MDI to dry powder inhaler or vice versa) or to a different ICS/LABA strategy
- **Re-evaluate in 3 months**

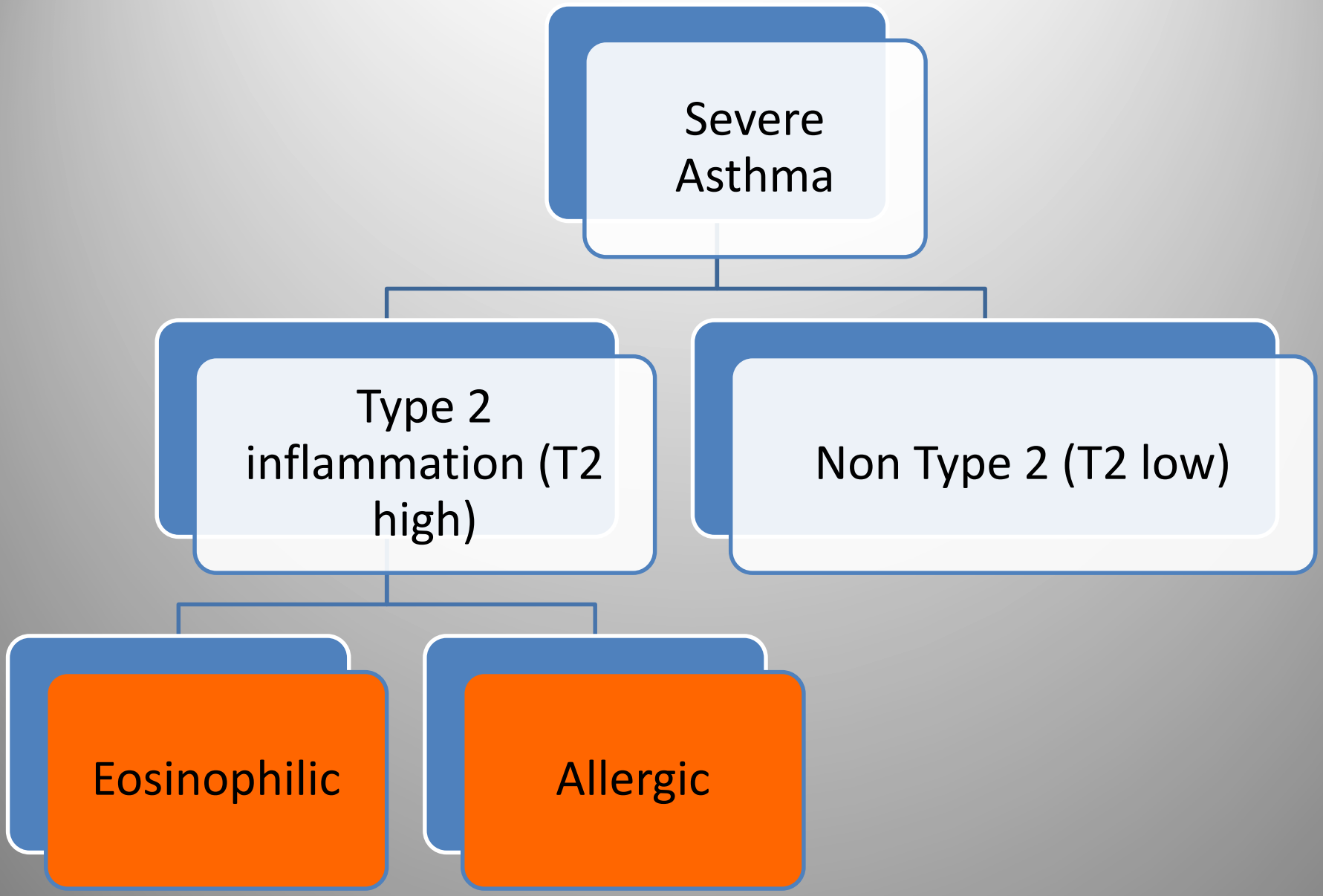
Severe Asthma endotypes

- Type 2 inflammation (T2 High):
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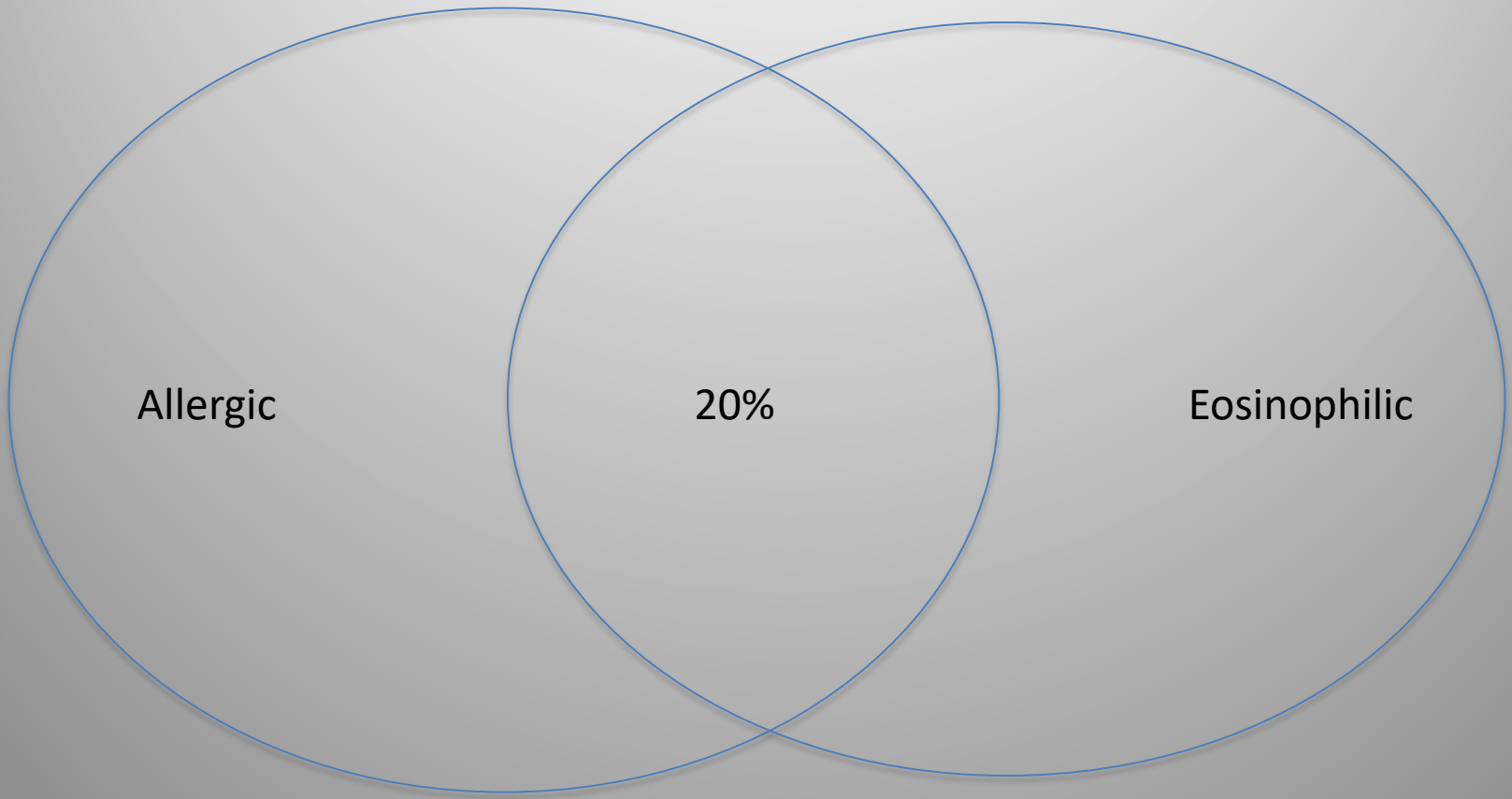


Consider adding biologics

* while on high dose ICS


Severe Asthma
Type 2 inflammation (T2 high)
Non Type 2 (T2 low)
Eosinophilic
Allergic

Type 2 (T2-high endotype)



T2-high endotype
Allergic vs eosinophilic

	A: allergic-predominant asthma	B: eosinophilic-predominant asthma
1	Early onset	Late onset
2	SPT/RAST+ with clinically significant allergies[#]	SPT/RAST– or + with no clinically significant allergies
3	IgE >100 IU·mL^{-1}	IgE <100 IU·mL^{-1}
4	Allergic rhinitis	Nasal polyps
5	High *F*ENO (30–50 ppb)	Very high *F*ENO (>50 ppb)
6	Blood eosinophils <300 cells·μL^{-1}	Blood eosinophils >300 cells·μL^{-1}[#]

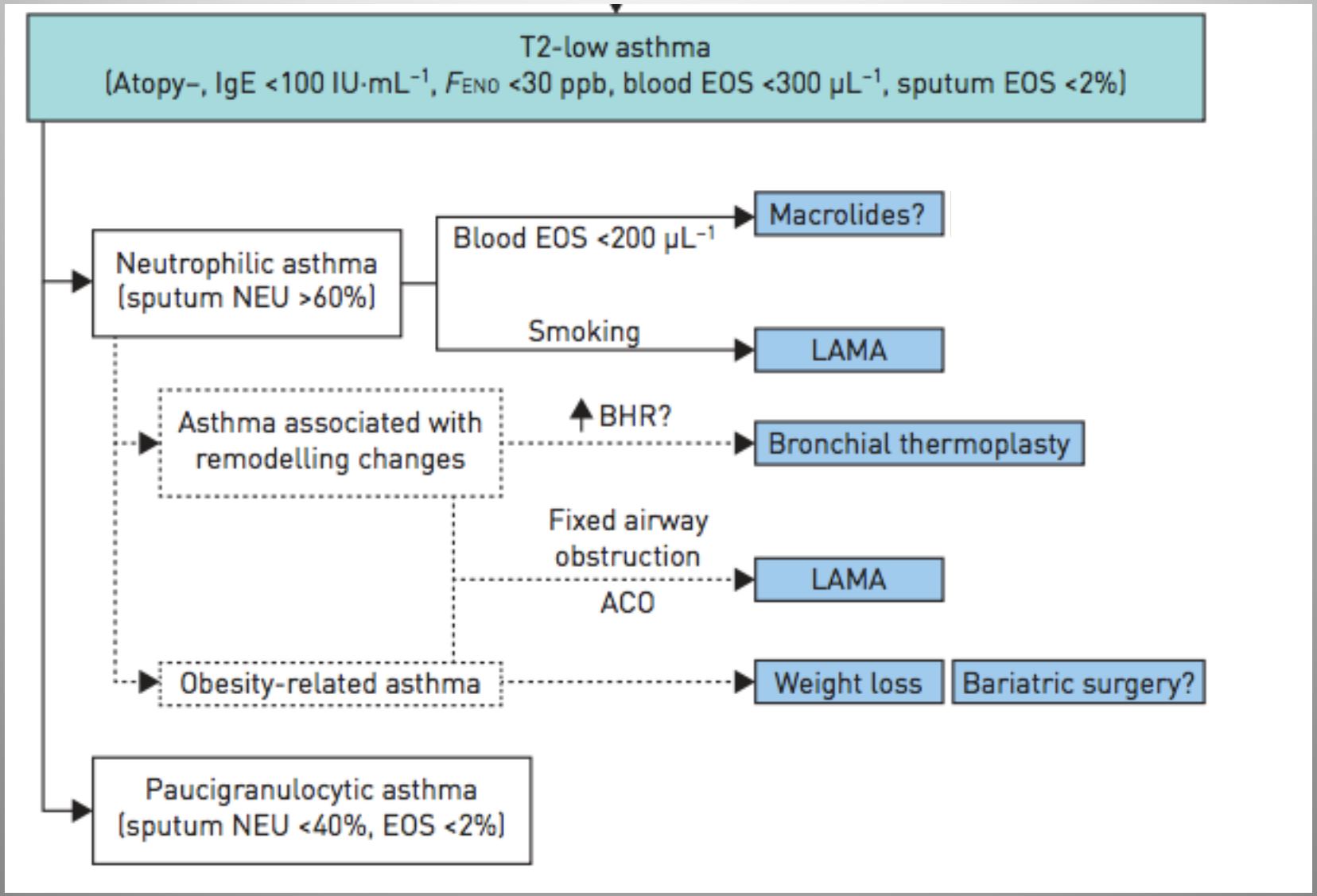
T2-high endotype

- Allergic predominant asthma:
  - Anti IgE treatment (omalizumab)
- Eosinophilia predominant asthma:
  - Anti-IL-5 treatment (mepolizumab, Benralizumab, reslizumab)
  - Anti IL 4 (Dupilumab)
- Allergic/Eosinophlic overlap:
  - Start with Anti IgE then Anti IL5
  - Start with Anti IL5 in steroid dependent patients
  - Anti IL4

Clinical treatment approach in treating severe asthma

- Assess response to treatment in 3 months and in 6 months
- If no response switch to another agent

T2-low endotype



Questions



Allegheny
Health Network

Hypereosinophilic syndrome

Virtual AHN Inaugural Critical Care, Allergy and Sleep Medicine Symposium

Christine Rauscher, MD 3/27/21

About Me

Review > Allergy Asthma Proc. 2018 May 1;39(3):252-256. doi: 10.2500/aap.2018.39.4120.

Drug-induced eosinophilia

Christine Rauscher [1], Allison Freeman [2]

Affiliations + expand

PMID: 29669671 DOI: 10.2500/aap.2018.39.4120

> Allergy Asthma Proc. 2020 Sep 1;41(5):386-388. doi: 10.2500/aap.2020.41.200039.

Clinical implications of C6 complement component deficiency

Christine K Rauscher [1], Merritt L Fajt [1], Jodie Bryk [2], Andrej A Petrov [1]

Affiliations + expand

PMID: 32867893 DOI: 10.2500/aap.2020.41.200039



> Curr Drug Saf. 2020 Oct 2. doi: 10.2174/1574886315666201002153354. Online ahead of print.

Factors Associated with Self-Reported Drug Allergies in a Large Chronic Spontaneous Urticaria Cohort

Christine Rauscher [1], Andrej A Petrov [1], Merritt L Fajt [1]

Affiliations + expand

PMID: 33006537 DOI: 10.2174/1574886315666201002153354

Unexpected Oral Lesions in a Patient with a Novel Cytotoxic T-lymphocyte Antigen-4 (CTLA-4) Variant - A Case Report

Christine Rauscher, MD[1], Miguel Reyes-Mugica, MD[2], Elaine Cassidy, MD[3], Raymond Shupak, DMD, MD, MBE[4], Xiaoyi Zhang, MD, PhD[5], Hey Chong, MD, PhD[6]

Disclosures

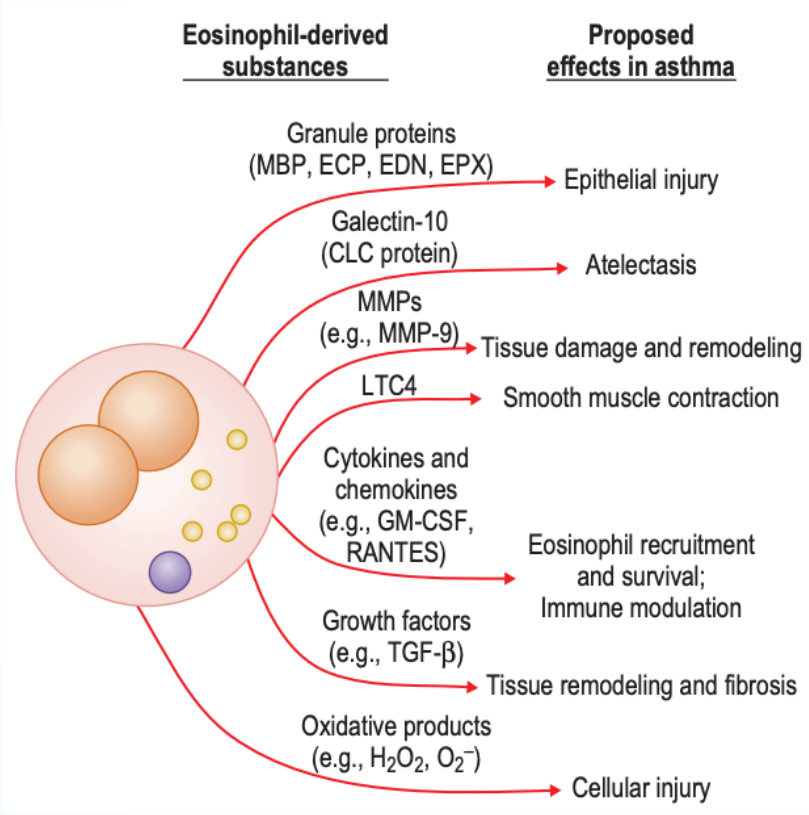
- None

Hypereosinophilic syndrome (HES)

- Affects approx 0.36-6.3 per 100,000 people
- Most patients diagnosed between 20-50 yo
- Majority of HES affects men and women equally
  - However, with *FIPL1-PDGFRA* fusion gene, men predominantly affected
- The goal of workup is to **identify a cause** and **assess for end organ involvement**

Eosinophil basics

- Eosinophilopoiesis can be elicited in the bone marrow by three cytokines:
  - GM-CSF
  - IL-3
  - **IL-5**
- Majority of eosinophils are found in the tissues and not blood
- Levels vary throughout day
  - Diurnal pattern


Eosinophil-derived substances
Proposed effects in asthma
Granule proteins (MBP, ECP, EDN, EPX)
Epithelial injury
Galectin-10 (CLC protein)
Atelectasis
MMPs (e.g., MMP-9)
Tissue damage and remodeling
LTC4
Smooth muscle contraction
Cytokines and chemokines (e.g., GM-CSF, RANTES)
Eosinophil recruitment and survival; Immune modulation
Growth factors (e.g., TGF-β)
Tissue remodeling and fibrosis
Oxidative products (e.g., H_2O_2, O_2^-)
Cellular injury

Question

What is the the absolute eosinophil count (AEC) that correlates with hypereosinophilia?

A. 500
B. 1,000
C. 1,500
D. 3,000

Answer

Differential diagnosis of hypereosinophilia

- Infectious disease
  - Strongyloides, trichinellosis, toxocariasis, filariasis, coccidiomycosis
- Organ-specific diseases
  - Lungs: ABPA, idiopathic eosinophilic pneumonia
  - Vascular: EGPA
  - Rheumatologic: SLE
  - Endocrine: adrenal insufficiency
- Allergic disorders
  - Drug hypersensitivity reaction
  - Atopy and related conditions
- Hematologic and neoplastic disorders
  - Systemic mastocytosis with eosinophilia
- Immunologic disorders

Question

You see this while you perform a complete physical exam for your patient with eosinophilia. What is the likely diagnosis?

A. HES
B. Strongyloides
C. Larva migrans
D. Scabies



Answer

Larva currens “running larva”

- Pathognomonic for Strongyloides
- Frequently in buttock area
- Other cutaneous findings include: nonpalpable purpura, angioedema, and erythroderma that can mimic a drug reaction



Strongyloides

- Tropical, subtropical
  - Rural, south-eastern parts of US
  - Appalachia
- Can be asymptomatic
- Send IgG
- Risk of strongyloides hyperinfection with systemic CS which has high case fatality rate
  - Ivermectin, in a single dose, 200 µg/kg orally for 1- 2 days

Contemporary consensus of HES

- Eosinophilia:
  - > 0.5 Eosinophils × 10^9/L blood
- Hypereosinophilia:
  - >1.5 Eosinophils × 10^9/L blood on 2 examinations (interval ≥1 month) and/or tissue HE
- Hypereosinophilic syndrome
  - 1. Criteria for peripheral blood HE fulfilled **AND**
  - 2. Organ damage and/or dysfunction attributable to tissue HE **AND**
  - 3. Exclusion of other disorders or conditions as major reason for organ damage

Valent et al. JACI. 2012.

HES is a spectrum of disease

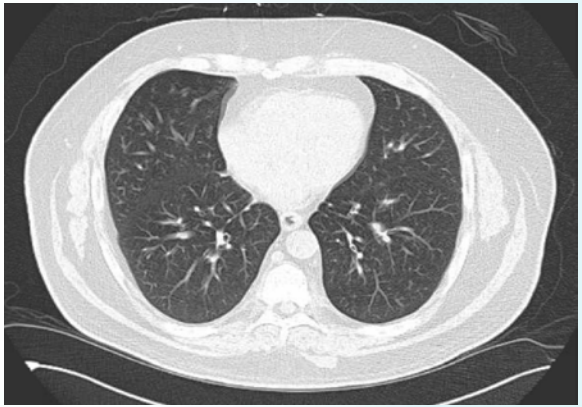
Organ System Involvement	Frequency at presentation	Eventual Frequency
Dermatologic	37	70
Pulmonary	25	45
Gastrointestinal	14	38
Rheumatologic	7	NA
Constitutional	5	NA
Cardiac	5	20
Neurologic	5	21

Ogbogu et al. JACI. 2009.

Idiopathic HES







Inayat. BMJ Case Rep. 2018.

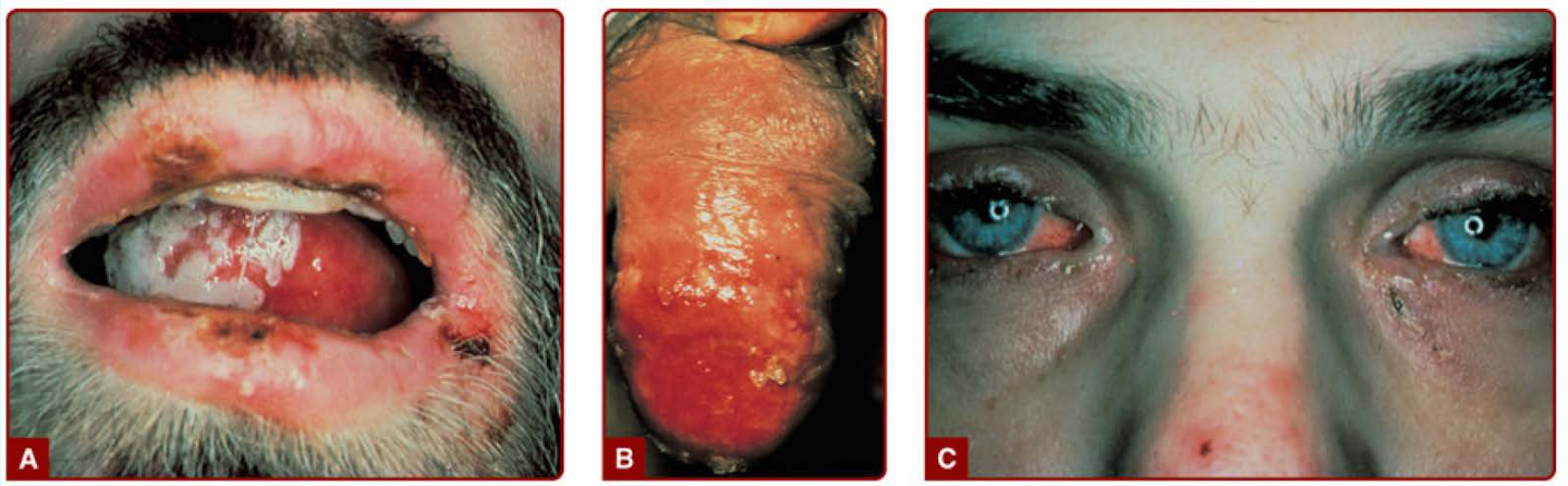
Subject	AEC/mm^3 at presentation to the National Institutes of Health	End-organ manifestations	HES therapy* (chronological order)	Years of eosinophilia before treatment
1	2,999	Pruritic skin rash	Prednisone	0.7
2	4,884	Urticaria, pruritus, fatigue, night sweats	Prednisone	0.5
3	4,136	Myalgias, fatigue, weight loss	Prednisone	0.5
4	6,878	Cough, pulmonary infiltrates/fibrosis	Unknown†	0.5
5	45,990	Sinusitis, testicular pain, lymphadenopathy, fatigue, malaise	Prednisone	0.1
6	5,111	Necrotic skin ulcers, lymphadenopathy	Prednisone, IFN-α	0.1
7	2,062	Asthma, sinusitis, urticaria, facial rash, paresthesias, Raynaud's phenomenon, fatigue, malaise	Prednisone, hydroxyurea, mepolizumab	10
8	3,510	Urticaria, fatigue, dyspnea, pulmonary infiltrate, malabsorption	Prednisone	1.75
9	6,420	Fever, fatigue, splenomegaly, polycythemia	Prednisone, imatinib, IFN-α, mepolizumab, hydroxyurea	0.4
10	10,080	Arthralgias, myalgias, angioedema, pruritic skin rash, abdominal pain, fatigue	Prednisone, hydroxyurea, IFN-α, imatinib, reslizumab, cyclosporine, IVIG, mycophenolate mofetil, mepolizumab, lenalidomide, cytoxan, bone marrow transplant	0.5
11	4,160	Cough, fever, diarrhea, night sweats, eosinophilic hepatitis	Prednisone	3
12	2,901	Myalgias, arthritis, flushing, splenomegaly, fatigue	Prednisone, hydroxyurea, imatinib, IFN, mepolizumab, methotrexate, cyclophosphamide, dasatinib, mycophenolate mofetil, alemtuzumab	2
13	1,669	Gastroesophageal reflux, dysphagia	None	NA†
14	3,016	Asthma	Imatinib, prednisone, mepolizumab	1.5

Chen et al. JACI. 2014.

Subject	AEC/mm^3 at presentation to the National Institutes of Health	End-organ manifestations	HES therapy* (chronological order)	Years of eosinophilia before treatment
15	2,310	Pruritic rash, bullous skin lesions, lymphadenopathy, episcleritis	Unknown‡	NA
16	2,334	Myalgia, nausea, vomiting, fever, eosinophilic hepatitis	Prednisone	4
17	1,654	Diarrhea, abdominal pain	Prednisone	1
18	1,640	Asthma, sinusitis, pulmonary infiltrates, myocarditis	Prednisone	4
19	2,208	Myalgias, arthralgias, fatigue, weight loss, pulmonary infiltrates	Prednisone	12
20	3,550	Myalgias, arthralgias, night sweats, fatigue, pruritic skin rash, angioedema	Unknown‡	NA
21	7,080	Asthma, sinusitis, urticaria, skin rash, alopecia	Prednisone, hydroxyurea, IFN-α, omalizumab, IVIG	0.2
22	13,357	Cough, pulmonary fibrosis, pruritic rash	Prednisone, imatinib	3
23	3,674	Sinusitis, asthma, chronic cough, pulmonary infiltrates	Prednisone, mepolizumab	On steroids at the time of presentation
24	7,797	Nausea, right upper-quadrant pain, myalgias, arthralgias, fevers, headache, malaise, fatigue, pruritic rash, eosinophilic hepatitis	Prednisone, imatinib, mepolizumab	0.1
25	6,070	Asthma, eosinophilic enteritis with protein-losing enteropathy	Prednisone, mepolizumab	0.1
26	2,177	Abdominal pain, diarrhea, pulmonary infiltrates	Prednisone, imatinib	4
27	3,780	Angioedema, pulmonary infiltrates, neuropathy	Prednisone, mepolizumab	2
28	1,530	Asthma, pulmonary infiltrates, sinusitis, paresthesias	Prednisone	0.2

Chen et al. JACI. 2014.

M-HES



M-HES

- Myeloid malignancy or myeloproliferative disease
  - I.e. may or may not have clonality
  - HSM, anemia, thrombocytopenia, dysplastic eos
  - May see ↑ B12 & tryptase
  - May see elevated mast cells and c-kit mutations
- FIPL1/PDGFRA gene fusion
  - Test for prevalence of F/P every 3-6 months while on stable Imatinib
- *PDGFRB*
- *FGFR1*
- *JAK2*
- *BCR-ABL*

Imatinib

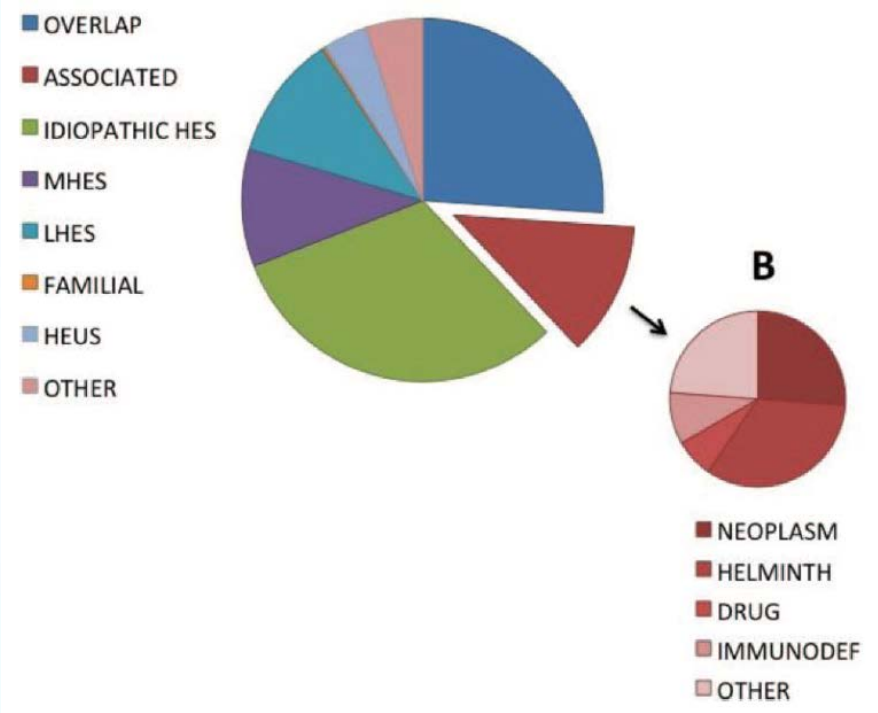
Klion. Blood. 2015.

L-HES

- Two types:
  - Clonal T cells or TCR
    - Most common T cell phenotypes: CD3-/CD4+ or CD3+ CD4-CD8-
  - Non-clonal, but activated T cells
- Prevalent skin manifestations
- Risk of peripheral T cell lymphoma



Simon et al. JACI. 2010. Kuang et al. NEJM. 2019.



Klion AD. Blood. 2015.

Systemic CS

- Indications for prompt CS:
  - Concern for hypereosinophilia-induced organ damage
    - Clinical evidence or laboratory markers that indicate eosinophilic cardiomyopathy
    - Thromboemboli that affect the CNS
  - Exceedingly high level of eosinophils (ie AEC >100k)
  - Clinical evidence suggestive of leukostasis
- Dosing
  - 1 gm methylprednisolone or 1 mg/kg depending on severity of symptoms
- Important to consider **potential strongyloides**
  - Ivermectin 200 mcg/kg/d x 2 days
    - Given prior to strongyloides results returning back

Mepolizumab

- Approved for pts 12 yo and older with HES ≥ 6 months without an identifiable non-hematologic secondary cause
  - Approved as 3 separate 100-mg injections subcutaneously administered once every 4 wks



FDA NEWS RELEASE

FDA Approves First Drug to Treat Group of Rare Blood Disorders in Nearly 14 Years

Approval is for hypereosinophilic syndrome, which occurs when there is a high number of a type of white blood cells

Share Tweet Linkedin Email Print

ements **For Immediate Release:** September 25, 2020

Kuang et al. .JACI. 2018.

Benralizumab

- Not yet approved
- Three doses of 30 mg monthly subcutaneous injections

Kuang et al. NEJM. 2019.

Other therapies investigated

- Reslizumab- limited effect in small trial
- JAK-inhibitors
  - Ruxolitinib
  - Tofacitinib
- Alemtuzumab

Dispenza & Bochner. Curr Hematol Malig Rep. 2019.

	HES	Chronic Eosinophilic Pneumonia
Similarities with EGPA	•Persistent eosinophilia •Cardiac & pulmonary manifestations	•Asthma •Persistent eosinophilia •Pulmonary infiltrates & BAL with eosinophils •Constitutional symptoms
Differences from EGPA	•Rarely asthma & nasal polyps •Vasculitic complications are rare though thrombotic complications exist •ANCA negative	•Does not exhibit other organ involvement •ANCA negative

Questions?

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Allegheny Health Network

COVID-19 Overview & What we have learned

Meilin Young, MD

Conflicts of interests

- Member of GlaxoSmithKline Speakers Bureau

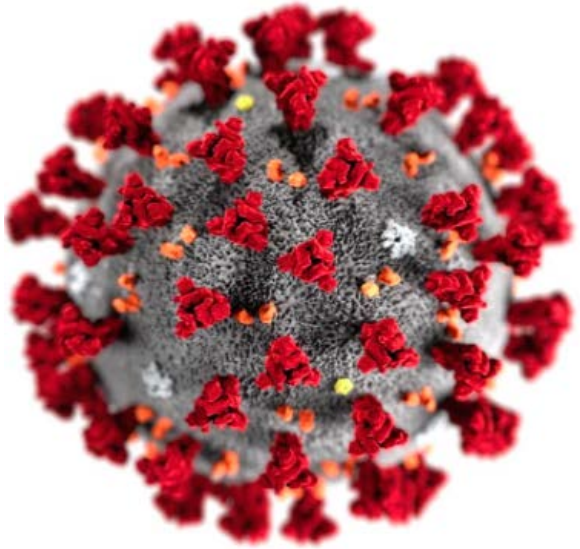
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Outline

- What we know
- Treatment - Outpatient vs. Inpatient
- Discharge Planning
-
- The Recovery Period
- Post-Acute COVID Syndrome Clinic
- Vaccination

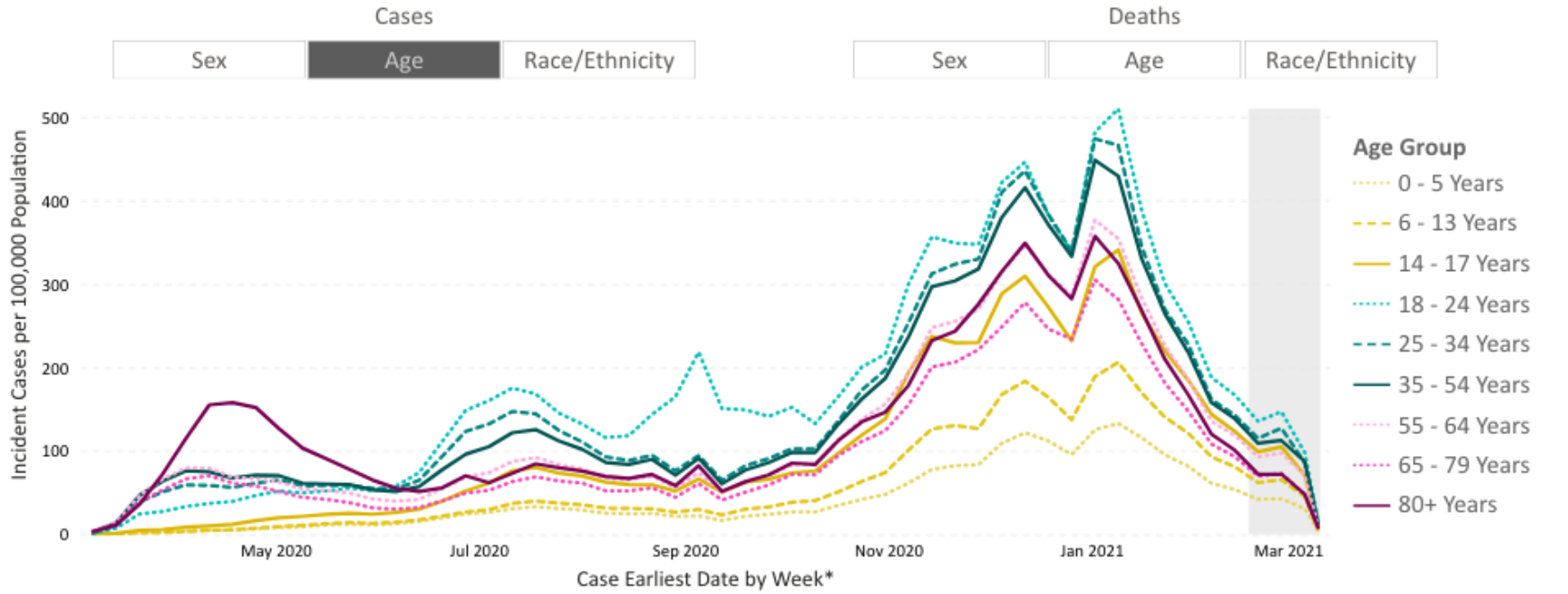
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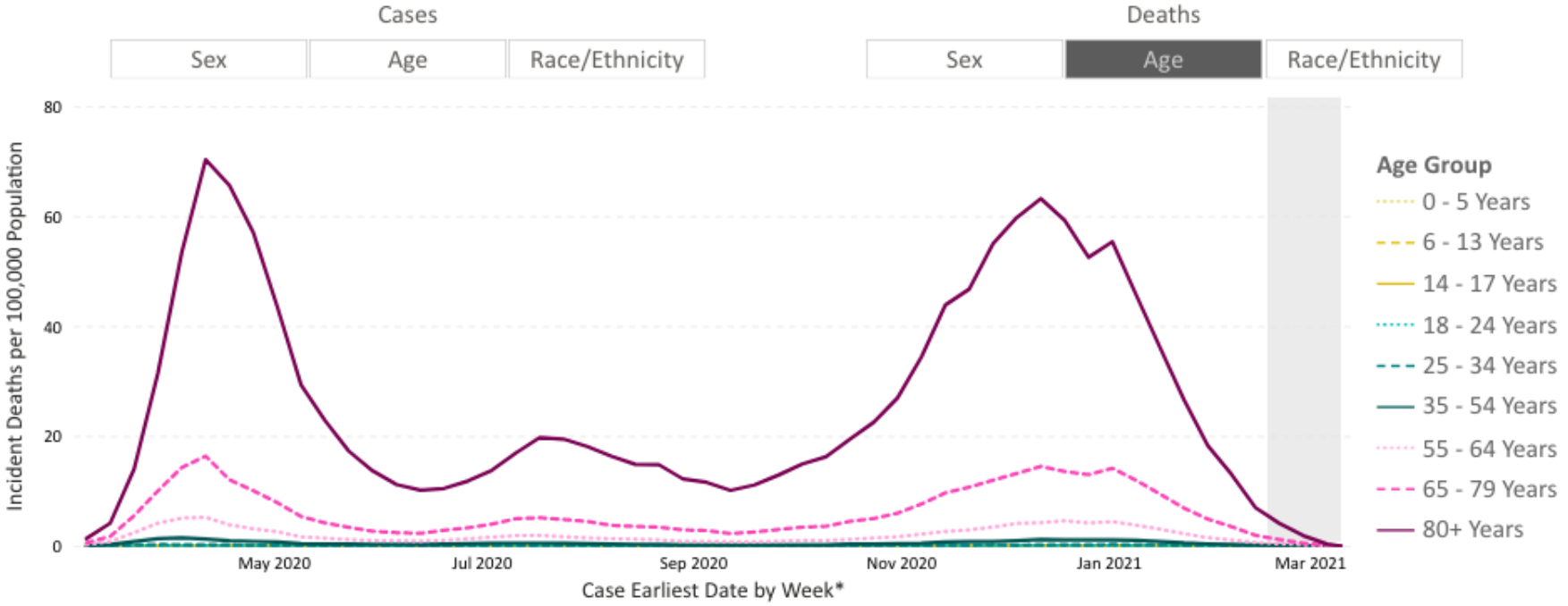
COVID-19



- Total Cases in the US: 29,552,459
- Total Deaths in the US: 538, 261
- New variants
  - **B.1.1.7**: the United Kingdom (UK)
  - **B.1.351**: South Africa
  - **P.1**: Brazil
  - Mutation D614G is shared by these three variants, giving the variants the ability to spread more quickly than the predominant viruses
- Total Vaccines Administered: 121 million

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Cases
Sex
Age
Race/Ethnicity
Deaths
Sex
Age
Race/Ethnicity
Incident Cases per 100,000 Population
500
400
300
200
100
0
May 2020
Jul 2020
Sep 2020
Nov 2020
Jan 2021
Mar 2021
Case Earliest Date by Week*
Age Group
0 - 5 Years
6 - 13 Years
14 - 17 Years
18 - 24 Years
25 - 34 Years
35 - 54 Years
55 - 64 Years
65 - 79 Years
80+ Years


Cases
Sex
Age
Race/Ethnicity
Deaths
Sex
Age
Race/Ethnicity
Incident Deaths per 100,000 Population
80
60
40
20
0
May 2020
Jul 2020
Sep 2020
Nov 2020
Jan 2021
Mar 2021
Case Earliest Date by Week*
Age Group
0 - 5 Years
6 - 13 Years
14 - 17 Years
18 - 24 Years
25 - 34 Years
35 - 54 Years
55 - 64 Years
65 - 79 Years
80+ Years

Symptoms

Common	Less Common	Rare
Fever	Myalgia/arthralgia	Palpitations
Cough	Headaches	Chest tightness
Anosmia	Sore throat	Hemoptysis
Ageusia	Chills	Confusion
Fatigue	Pleuritic pain	Seizures
Sputum production	Diarrhea	Paresthesia
Shortness of breath		Stroke
GI upset		Conjunctivitis
		Rash

Treatment –

Outpatient

- Supportive
  - Decongestants
  - Antitussives
  - Antipyretics
- Bamlanivimab + etsevimab *
- Baricitinib + Remdesivir + Corticosteroids *

Inpatient

- Corticosteroids
- Tocilizumab
- Remdesivir
- Convalescent Plasma
- Baricitinib + Remdesivir *

Treatment	Indication	Administration
Corticosteroids	• P/F > 200 • P/F ≤ 200	• 6mg daily x 10 days • 20mg daily x 5 days + 10mg daily x 5 days
Tocilizumab	Respiratory + Inflammatory component • BiPAP/CPAP P/F ≤ 150 • Optiflow > 30LPM, FiO_2 > 80%, P/F ≤ 150 • Mechanical ventilation • CRP ≥ 7.5	Single dose: • > 90kg = 800mg • 65kg < x ≤ 90kg = 600mg • 40kg < x ≤ 65 kg = 400mg • ≤ 40kg = 8mg/kg
Remdesivir	SpO2 ≤ 94% x 2 on room air SpO2 < 90% on room air ≥ 2L to maintain 92-95 > 2L above home O_2 Mechanical ventilation < 7 days	200mg x1 + 100mg daily x 4 days
Convalescent Plasma	Requiring > 3L O2 to maintain O_2 92-95% within 3 days of diagnosis	1 unit
Baricitinib + Remdesivir		if corticosteroids are contraindicated Baricitinib – 4mg daily x 14 days

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Anticoagulation

- Prophylactic dosing
  - LMWH or Unfractionated Heparin (UFH)
- Intermediate dosing
  - Low bleeding risk + > 6L NC
  - CrCl > 30 – Enoxaparin 1mg/kg/day or 0.5mg/kg BID
  - CrCl < 30 – UFH gtt
    - low intensity anti-Xa normogram
- Therapeutic dosing
  - New proven VTE or on prior anticoagulation
  - CrCl > 30 – LMWH 1.5mg/kg daily or 1mg/kg BID
  - CrCl < 30 –UFH gtt
    - Acute thrombus anti-Xa normogram

Oxygen support and Mechanical Ventilation

Supplemental Oxygen and non-invasive support

- Nasal Cannula
- Face mask
- Non-rebreather
- Optiflow
- CPAP/BiPAP

Mechanical Ventilation +

- Proning
- Sedatives and Paralytics
- ECMO
- HemoLung

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Discharge Planning

- Ambulatory Pulse Oximeter Testing
- Anticoagulation
  - VTE – 3 months of therapeutic anticoagulation
  - PPX – Rivaroxaban 10mg daily – IMPROVE VTE score > 4 or 2-3 + D-dimer 2x ULN

Modified VTE Score	
Previous VTE	3
Known thrombophilia	2
Currently lower limb paralysis or paresis	2
History of cancer	2
Complete immobilization > 1 day	1
ICU/CCU stay	1
Age > 60 yo	1

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The Recovery Period

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Post Acute COVID Syndrome

- Persistent respiratory symptoms
  - Chest tightness
  - Wheezing
  - Coughing
  - Shortness of breath
- Brain fog
  - Concentration difficulty
- Cardiomyopathy
- Anxiety & Depression
- Fatigue & Myalgias

Post-Acute COVID Syndrome Clinic

- COVID Navigators
  - Tracking of patients admitted on inpatient set to arrange for a virtual outpatient follow-up 2-4 weeks after discharge
- Team of specialists
  - Pulmonology*
  - Cardiology
  - Neurology
  - Psychiatry
- AHN Home Care – HME/DME
- Pulmonary Rehab

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Vaccination

- 3 main types authorized and recommended or undergoing large-scale clinical trials in the US
  - mRNA vaccine
    - Pfizer-BioNTech
    - Moderna
  - Protein subunit vaccines
  - Vector vaccines
    - Johnson & Johnson's Janssen



Timing of vaccination

- Pfizer BioNTech
  - 2 doses
  - 21 days apart
- Moderna
  - 2 doses
  - 28 days apart
- Johnson & John's Janssen
  - 1 dose

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Vaccination post-COVID infection

- After testing COVID (+)…
  - Asymptomatic and out of isolation, did not receive monoclonal antibody therapy or convalescent plasma
  - 90 days after having received monoclonal antibody therapy or convalescent plasma

References

- IDSA.org
- CDC.gov

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Critical Care Overview 2020: More Than COVID

Amit Kaura, MD, FACP, FCCP
Division of Pulmonary, Critical Care and Sleep Medicine
Allegheny Health Network

Financial Disclosures

None

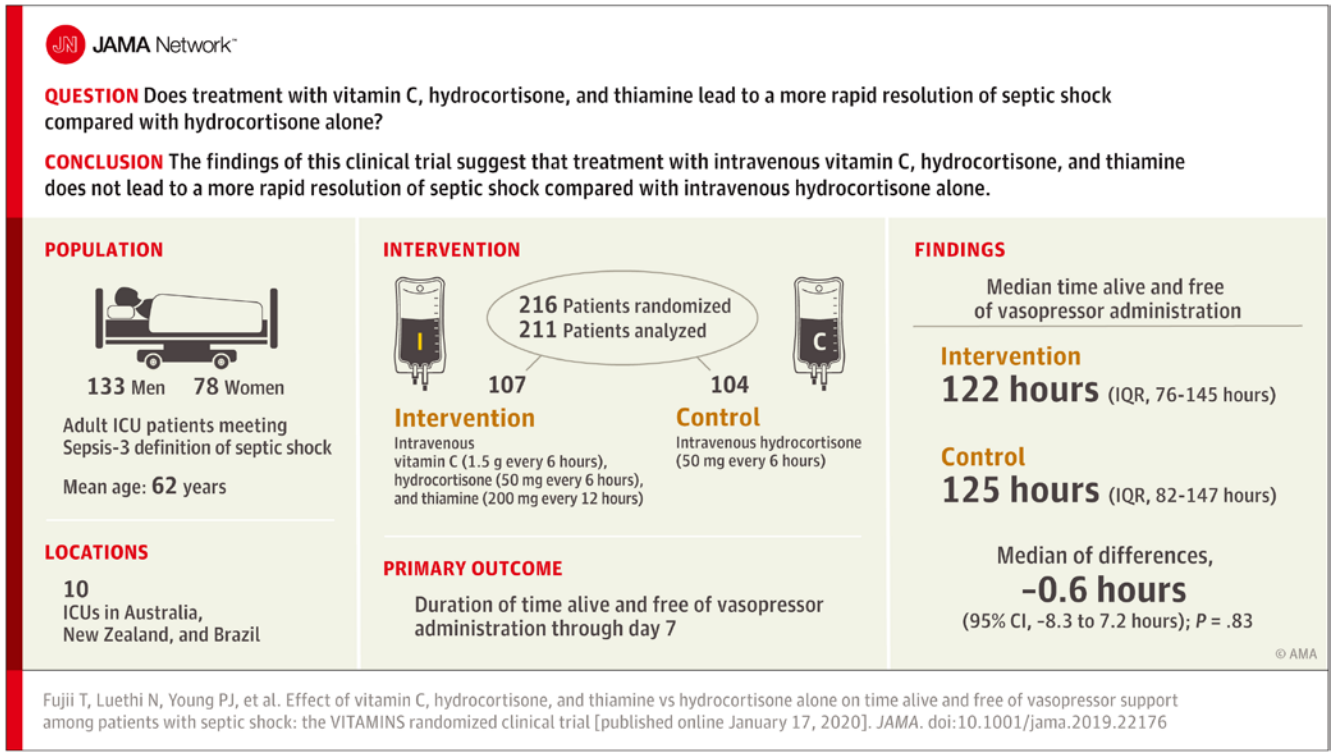
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There is No Magic “HAT” for Sepsis

- 4 studies looking at the treatment of severe sepsis with septic shock using hydrocortisone, ascorbic acid, and thiamine (HAT)
- VI-TAMINS, HYVCTTSSS, ORANGES RCT, and ACTS RCT
- All studies showed no mortality benefit with the use of hydrocortisone, ascorbic acid and thiamine in sepsis with or without septic shock



VI-TAMINS



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Table 2. Primary and Secondary Outcomes

Outcomes	Intervention (n = 107)	Control (n = 104)	Difference (95% CI)	*P* Value
Primary Outcome				
Time alive and free of vasopressors, median (IQR), h	122.1 (76.3 to 145.4)	124.6 (82.1 to 147.0)	-0.6 (-8.3 to 7.2)[a]	.83
Secondary Outcomes				
28-d Mortality, No. (%)	24 (22.6) [n = 106]	21 (20.4) [n = 103]	2.3 (-8.9 to 13.4)	.69
90-d Mortality, No. (%)	30 (28.6) [n = 105]	25 (24.5) [n = 102]	4.1 (-8.0 to 16.1)	.51
ICU mortality, No. (%)	21 (19.6)	19 (18.3)	1.4 (-9.2 to 11.9)	.80
Hospital mortality, No. (%)	25 (23.4)	21 (20.4) [n = 103]	3.0 (-8.2 to 14.1)	.60
28-d Cumulative vasopressor-free days, median (IQR)	25.6 (17.8 to 26.8) [n = 106]	25.8 (19.6 to 26.8) [n = 103]	-0.2 (-1.7 to 1.2)	.66
28-d Cumulative mechanical ventilation-free days, median (IQR)	25.3 (5.2 to 28.0) [n = 106]	24.8 (9.5 to 28.0) [n = 103]	0.4 (-2.6 to 3.4)	.73
28-d Renal replacement therapy-free days, median (IQR)	28.0 (23.5 to 28.0) [n = 105]	28.0 (21.0 to 28.0) [n = 103]	0.0 (-0.6 to 0.6)	.71
Change in SOFA score at day 3, median (IQR)[b]	-2 (-4 to 0) [n = 82]	-1 (-3 to 0) [n = 75]	-1.0 (-1.9 to -0.1)	.02
28-d ICU-free days, median (IQR)	21.9 (0 to 25.8) [n = 106]	22.1 (3.9 to 25.8) [n = 103]	-0.2 (-4.1 to 3.7)	.66
Hospital length of stay, median (IQR), d	12.3 (6.2 to 26.0)	12.3 (6.2 to 26.1) [n = 103]	0.0 (-4.9 to 4.9)	.75
Prespecified Exploratory Outcome				
Acute kidney injury, No. (%)				
Stage 1	18 (16.8)	14 (13.5)	3.4 (-6.3 to 13.0)	.80
Stage 2	18 (16.8)	22 (21.2)	-4.3 (-14.9 to 6.2)	
Stage 3	39 (36.4)	39 (37.5)	-1.1 (-14.1 to 12.0)	

Abbreviations: ICU, intensive care unit; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

[a] Hodges-Lehmann estimate, the median of all paired differences between observations in the intervention group minus the control group.

[b] Change in SOFA score: score at day 3 minus score at baseline.

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HYVCTTSSS

Table 2 Primary and Secondary Outcomes

Variable	Treatment Group (n = 40)	Control Group (n = 40)	Relative Risk or Difference (95% CI)	*P* Value
28-d mortality	11 (27.5)	14 (35)	0.79 (0.41-1.52)	.47
ICU LOS, d	7.5 (4-12.8)	7.5 (4-11.8)	…	.98
Duration of vasopressors,[a] h	46 (23.8-102.5)	58.5 (28-104)	…	.70
New AKI after entering ICU	1 (2.5)	2 (5)	0.50 (0.05-5.30)	> .99
△SOFA score, 72 h	3.5 ± 3.3	1.8 ± 3.0	…	.02
Procalcitonin clearance, 72 h	75.8 (62.2-86.4)	68.2 (25.9-82.5)	…	.07
Duration mechanical ventilation,[b] h	126.5 (63.5-239.3)	94.5 (39.8-211)	…	.36
Lactate clearance, 72 h, %	21.3 (−49.7 to 44.2)	0 (−35.1 to 47.7)	…	.98

Values are No. (%), median (interquartile range), mean ± SD, or as otherwise indicated. Missing data for indicators were estimated using the last observation carried forward scheme. AKI = acute kidney injury; LOS = length of stay. See Table 1 legend for expansion of other abbreviation.

a Excluding patients without vasopressor support (18 patients in the treatment group vs 16 patients in the control group).
b Excluding patients without mechanical ventilation (10 patients in the treatment group vs eight patients in the control group).

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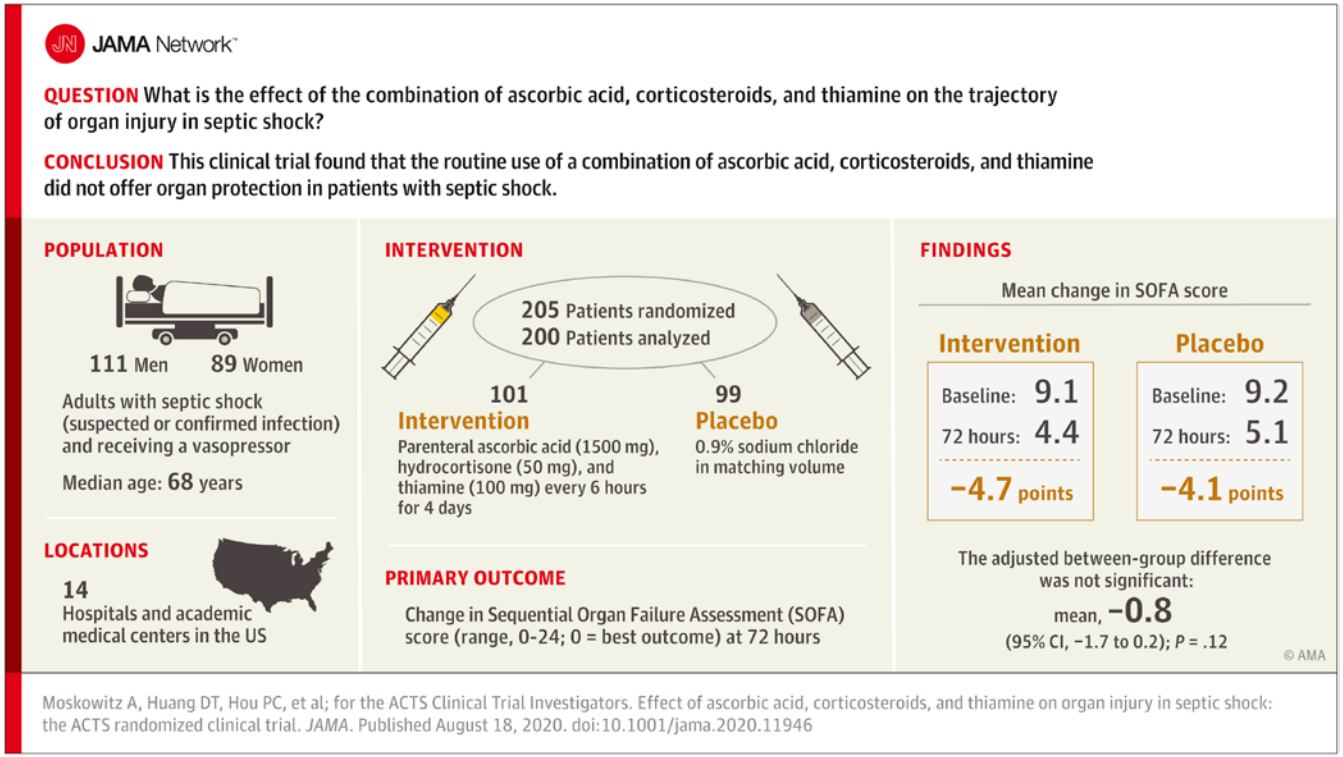
ORANGES

Table 3 Treatment and Clinical Outcome

Treatments	HAT Treatment (n = 68)	Comparator (n = 69)	*P*	OR	95% CI
Days of HAT therapy or placebo	3.3 ± 0.8	3.25 ± 1	.94		
Fluid balance at 24 hours (mL/kg)	53 ± 26	46 ± 24.1	.09		
Fluid balance at 72 hours (mL/kg)	83 ± 97	80 ± 75	.82		
Vasopressors at time of enrollment	56 (82%)	47 (68%)	.05	0.45	0.2-1.02
Vasopressor initiated after study enrollment	4 (6%)	10 (14.5%)	.16	2.7	0.8-9.1
Renal replacement therapy for AKI	2 (3%)	8 (11.5%)	.1	4.1	0.84-20.3
Primary outcome					
Δ SOFA score at 72 hours	2.9 ± 3.3	1.93 ± 3.5	.1		
Duration of vasopressors, h	27 ± 22	53 ± 38	<.001		
Secondary outcomes					
Hospital mortality (%)	11 (16%)	13 (19.4)	.6	1.2	0.50-2.97
ICU mortality (%)	6 (9%)	10 (14%)	.3	1.7	0.59-2.63
Hospital LOS, d	11.5 ± 6.8	11 ± 6.2	.75		
ICU LOS, d	4.76 ± 4.3	4.66 ± 3.45	.88		
Procalcitonin clearance, %	63 ± 170	58 ± 66	.44		
Ventilator-free days	22 ± 6.2	22.4 ± 4.3	.63		
AKI	54 (79%)	52 (75%)	.57	0.76	0.35-1.77

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ACTS



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Table 2. Primary and Secondary Outcomes

Outcomes	Intervention (n = 101)	Placebo (n = 99)	Effect estimate (95% CI)	*P* value
SOFA score over time (primary outcome measure), mean (SD)				
At enrollment	9.1 (3.5)	9.2 (3.2)		
At 72 h	4.4 (4.1) [n = 90]	5.1 (4.3) [n = 88]	Adjusted mean difference: −0.8 (−1.7 to 0.2)[a]	.12
Secondary outcomes[b]				
All-cause mortality over 30 d, No. (%)	35 (34.7)	29 (29.3)	Hazard ratio: 1.3 (0.8 to 2.2)	.26
Kidney failure, No. (%)	32 (31.7)	27 (27.3)	Adjusted risk difference: 3% (−10% to 20%)	.58
Ventilator-free days, median (IQR)[c]	6 (2-7)	6 (0-7)	Median difference: 0.0 (−1.9 to 1.9)[d]	>.99
Shock-free days, median (IQR)	5 (3-5)	4 (1-5)	Median difference: 1.0 (0.2 to 1.8)[d]	.02
Incidence of delirium, No./total (%)	31/83 (37.4)	35/76 (46.1)	Adjusted risk difference: −12% (−25% to 4%)	.16
ICU-free days, median (IQR)[e]	22 (3-25)	21 (4-25)	Median difference: 1.0 (−3.0 to 6.0)[d]	.69
All-cause mortality to ICU discharge, No. (%)	23 (22.7)	20 (20.2)	Adjusted risk difference: 2% (−10% to 10%)	.80
All-cause mortality to hospital discharge, No. (%)	28 (27.7)	23 (23.2)	Adjusted risk difference: 3% (−10% to 20%)	.55
Survivors discharged home, No./total (%)	34/73 (46.6)	35/76 (46.1)	Adjusted risk difference: −1.8% (−18% to 14%)	.82

Abbreviations: ICU, intensive care unit; IQR, interquartile range; SOFA, Sequential Organ Failure Assessment.

[a] Adjusted mean difference of the difference in SOFA score change between enrollment and 72 hours. *P* value is for the interaction term.

[b] Individual SOFA score outcomes over 72 hours can be found in eTable 8 in Supplement 2.

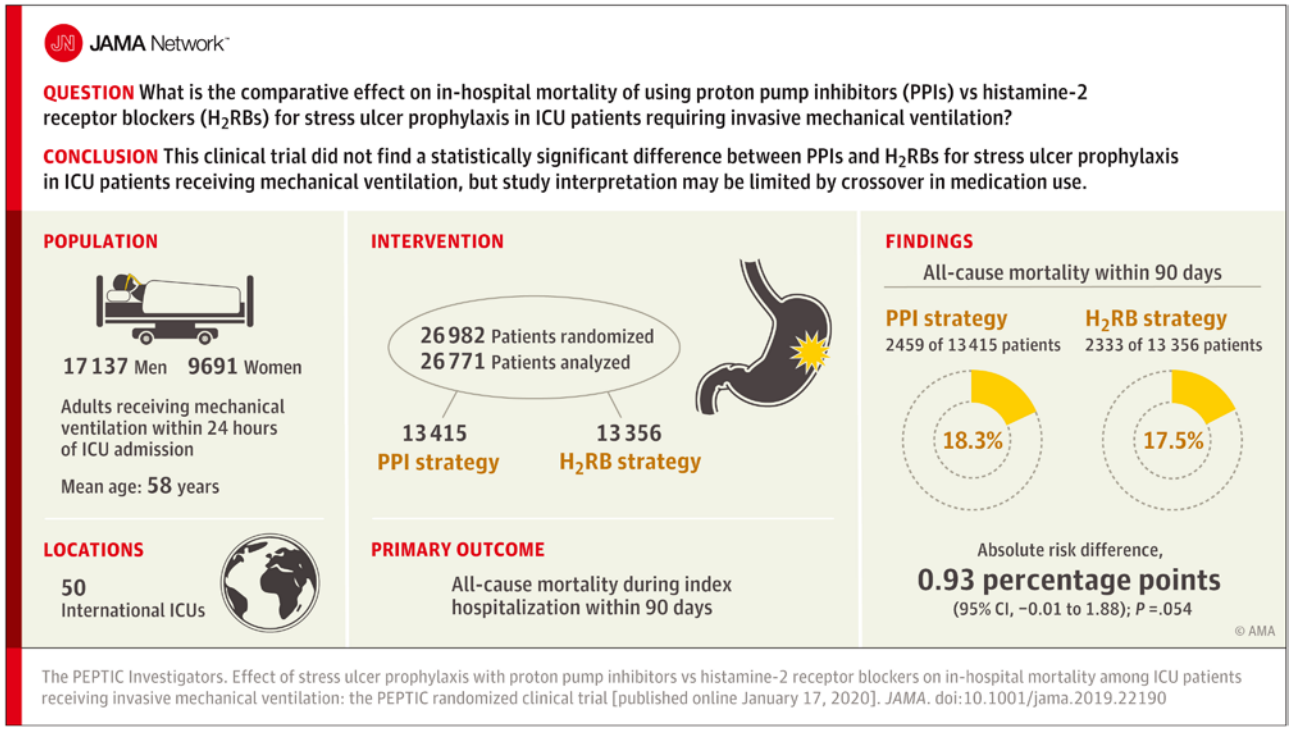
[c] During the first 7 days after enrollment.

[d] Median difference using quantile regression.

[e] During the first 28 days after enrollment.

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PEPTIC



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PEPTIC

- **Secondary outcomes**: comparing PPI vs. H2RB groups

Clinically important upper GI bleeding – significantly lower in the PPI group

1.3% vs. 1.8%

Relative risk 0.73 (95% CI 0.57 – 0.92)

Clostridium difficile infection – no significant difference

0.3% vs. 0.43%

Relative risk 0.74 (95% C.I. 0.51-1.09)

90 day in-hospital mortality in patients who had cardiac surgery – significantly increased in PPI group

Relative Risk 1.27 (95% CI, 1.04-1.57)

- **Tertiary outcomes**:

Median hours until removed alive from mechanical ventilation – no significant difference

48 vs. 48

Ventilator associated conditions – no significant difference

6.5% vs. 5.8%

Relative risk 1.18 (95% C.I. 0.87-1.59)

- **Post-Hoc Analysis**:

Difference in mortality was mostly found in the group of patients with high illness severity, comparing primary outcome for PPI vs. H2RB according to patients' APACHE II scores:

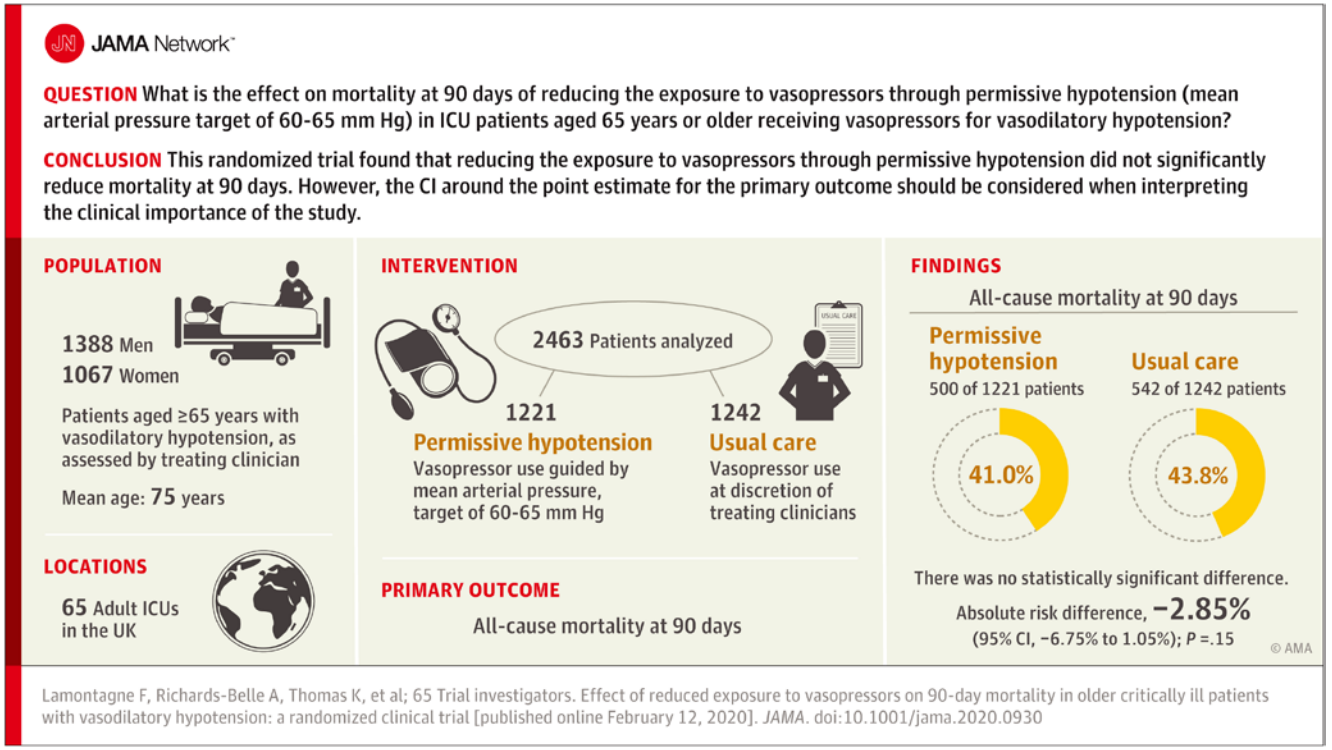
APACHE II score 0-13: 3.7% vs. 4.0%, RR 0.92 (95% C.I. 0.77-1.11)

APACHE II score 14-17: 7.1% vs. 7.5%, RR 0.96 (95% C.I. 0.86-1.08)

APACHE II score 18-23: 17.5% vs. 14.7%, RR 1.15 (95% C.I. 1.05-1.25)

APACHE II score 24-61: 45.3% vs. 43.5%, RR 1.05 (95% C.I. 1.00-1.11)

65 TRIAL



Lamontagne F, Richards-Belle A, Thomas K, et al; 65 Trial investigators. Effect of reduced exposure to vasopressors on 90-day mortality in older critically ill patients with vasodilatory hypotension: a randomized clinical trial [published online February 12, 2020]. *JAMA*. doi:10.1001/jama.2020.0930

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65 TRIAL

	Permissive Hypotension n/N (%)	Usual Care n/N (%)	95% CI (p value)	OR (95% CI)
90 Day Mortality	500/1221 (41%)	542/1242 (43.8%)	-6.75 to 1.05 (p= 0.15)	0.89 (0.76 -1.04)
Adjusted 90-day mortality				0.82 (0.68 -0.98)
Chronic hypertension subgroup	214/560 (38.2%)	253/571 (44.3%)		0.67 (0.51-0.88)

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HALT-IT

Primary Outcome		
	TXA	Placebo
Death due to bleeding within 5 days	222/5956 (3.7%)	226/5981 (3.8%)
RRR 0.99 (95% CI 0.82 - 1.18). ARR 0.05 (95% CI -0.63 - 0.73)		
Secondary Outcomes		
	TXA	Placebo
Death due to bleeding within 24 hours	124/5956 (2.1%)	120/5981 (2.0%)
RRR 1.04 (95% CI 0.81 - 1.33). ARI 0.08 (95% CI -0.43 - 0.58)		
Venous events (DVT, PE)	48/5952 (0.8%)	26/5977 (0.4%)
RRR 1.85 (95% CI 1.15 - 2.98), ARI 0.37 (95% CI 0.09 - 0.65). NNH 270 (95% CI 153 - 1117)		
Any surgical, endoscopic or radiological intervention	5216/5956 (87.6%)	5236/5981 (87.5%)
RRR 1.00 (95% CI 0.99 - 1.01). ARI 0.03 (95% CI -1.15 - 1.22)		
Any transfusion of blood products	4076/5951 (68.5%)	4129/5978 (69.1%)
RRR 0.99 (95% CI 0.97 - 1.02). ARR 0.58 (95% CI -1.09 - 2.24)		

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STARRT-AKI

Table 2. Primary and Secondary Outcomes.*

	Accelerated Strategy (N=1465)	Standard Strategy (N=1462)	Relative Risk or Difference (95% CI)
Primary outcome			
Death from any cause at 90 days — no. (%)†	643 (43.9)	639 (43.7)	1.00 (0.93 to 1.09)‡
Secondary outcomes			
RRT dependence among survivors at 90 days — no./total no. (%)	85/814 (10.4)	49/815 (6.0)	1.74 (1.24 to 2.43)‡
Death or RRT dependence at 90 days — no./total no. (%)	728/1457 (50.0)	688/1454 (47.3)	1.06 (0.98 to 1.14)‡
Major adverse kidney events at 90 days — no./total no. (%)	867/1131 (76.7)	860/1115 (77.1)	0.99 (0.95 to 1.04)‡
Serum creatinine at 90 days — mg/dl§	1.20±1.00	1.23±1.00	−0.03 (−0.11 to 0.06)¶
Estimated glomerular filtration rate‖			
At 90 days — ml/min/1.73 m^2	65±30	64±31	0.31 (−3.88 to 4.49)¶
Reduction of >25% from baseline at 90 days — no./total no. (%)	139/403 (34.5)	172/427 (40.3)	0.86 (0.72 to 1.02)‡
Death from any cause — no./total no. (%)			
At any time in the ICU	461/1464 (31.5)	468/1462 (32.0)	0.98 (0.88 to 1.09)‡
At 28 days	538/1465 (36.7)	523/1462 (35.8)	1.03 (0.93 to 1.13)‡
During hospitalization	552/1458 (37.9)	546/1459 (37.4)	1.01 (0.92 to 1.11)‡
Use of health services			
Median no. of days of use (IQR)			
RRT-free days at 90 days**	50 (0 to 87)	64 (0 to 90)	−2.62 (−5.66 to 0.42)¶
RRT††	4 (2 to 8)	5 (3 to 9)	−0.48 (−0.82 to −0.14)¶
Continuous RRT††	4 (3 to 8)	5 (3 to 8)	−0.40 (−0.78 to −0.02)¶
Sustained low-efficiency dialysis††	2 (1 to 4)	2 (1 to 4)	0.15 (−0.65 to 0.96)¶
Intermittent hemodialysis††	2 (1 to 4)	3 (2 to 5)	−0.45 (−0.80 to −0.09)¶
Median length of stay in ICU (IQR) — days			
Survivors	9 (5 to 16)	10 (5 to 19)	−1.58 (−2.90 to −0.26)¶
Nonsurvivors	7 (3 to 13)	7 (4 to 15)	−1.33 (−2.56 to −0.09)¶
Median length of hospital stay (IQR) – days			
Survivors	28 (16 to 50)	29 (17 to 54)	−1.23 (−3.87 to 1.41)¶
Nonsurvivors	8 (3 to 18)	9 (4 to 19)	−0.99 (−2.66 to 0.67)¶
Median no. of ventilator-free days at 28 days (IQR)	13 (0 to 24)	12 (0 to 24)	0.50 (−0.34 to 1.35)¶
Median no. of days free of vasoactive agents at 28 days (IQR)	21 (0 to 26)	20 (0 to 26)	0.31 (−0.57 to 1.18)¶
Median no. of days out of ICU at 28 days (IQR)	8 (0 to 21)	4 (0 to 20)	0.69 (−0.06 to 1.43)¶
Median no. of days out of hospital at 90 days (IQR)	10 (0 to 65)	9 (0 to 64)	0.55 (−1.82 to 2.91)¶
Rehospitalization at 90 days — no./total no. (%)	191/913 (20.9)	156/916 (17.0)	1.23 (1.02 to 1.49)‡
Health-related quality of life			
Median score on EQ-5D-5L at 90 days (IQR)			
Descriptive system‡‡			
Mobility	2 (1 to 3)	2 (1 to 3)	−0.07 (−0.23 to 0.08)¶
Self care	1 (1 to 3)	1 (1 to 3)	−0.10 (−0.25 to 0.05)¶
Usual activities	2 (1 to 3)	2 (1 to 4)	−0.15 (−0.31 to 0.01)¶
Pain or discomfort	2 (1 to 3)	2 (1 to 3)	−0.04 (−0.17 to 0.08)¶
Anxiety or depression	1 (1 to 3)	2 (1 to 3)	−0.06 (−0.19 to 0.07)¶
EQ-VAS§§	70 (50 to 80)	70 (50 to 80)	0.11 (−2.55 to 2.76)¶
Score of >4 on Clinical Frailty Scale at 90 days — no. (%)¶¶	213/655 (32.5)	227/647 (35.1)	0.93 (0.80 to 1.08)‡

* Plus–minus values are means ±SD. ICU denotes intensive care unit, and RRT renal-replacement therapy.
† P=0.92 for the primary outcome. P values were not calculated for the secondary outcomes because comparisons were not adjusted for multiple comparisons.
‡ This value is expressed as a relative risk.
§ Data regarding serum creatinine levels are for survivors at 90 days who were not dependent on kidney-replacement therapy. Of these 1511 patients, data were available for 830 (54.9%): 403 patients in the accelerated-strategy group and 427 patients in the standard-strategy group.
¶ This value is expressed as a mean difference.
‖ The estimated glomerular filtration rate was calculated with the Chronic Kidney Disease Epidemiology Collaboration equation.
** Data regarding RRT-free days are provided for 2900 of 2927 (99.0%) patients: 1448 in the accelerated-strategy group and 1452 in the standard-strategy group.
†† Included in this category are patients who received renal-replacement therapy.
‡‡ On the European Quality of Life–5-Dimensions 5-Level questionnaire (EQ-5D-5L), scores for each of the five domains of the descriptive system range from 1 to 5, with higher scores representing greater impairment or worse function. Scores at 90 days were available for 1164 of 1645 patients (70.8%) for the mobility domain (581 patients in the accelerated-strategy group and 583 patients in the standard-strategy group); 1165 of 1645 (70.8%) for the self-care domain (582 patients and 583 patients, respectively); 1163 of 1645 (70.7%) for the usual activities domain (581 patients and 582 patients, respectively); 1162 of 1645 (70.6%) for the pain or discomfort domain (580 patients and 582 patients, respectively); and 1153 of 1645 (70.1%) for the anxiety or depression domain (576 patients and 577 patients, respectively).
§§ Scores on the Visual Analogue Scale of the EQ-5D-5L questionnaire (EQ-VAS) range from 0 to 100, with higher scores indicating better health. EQ-VAS scores were available for 1103 of 1645 survivors (67.0%) at 90 days: 555 patients in the accelerated-strategy group and 548 in the standard-strategy group.
¶¶ Scores on the Clinical Frailty Scale range from 1 to 9, with higher scores indicating a higher degree of frailty. A score of more than 4 is the threshold for the definition of frailty. Scores on this scale at 90 days were available for 1302 of 1645 survivors (79.1%).

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Conservative vs interventional treatment of spontaneous pneumothorax

- **Primary outcome**:

Complete radiological resolution at 8 weeks after randomization

129 of 131 (98.5%) in the intervention arm vs 118 of 125 (94.4%) in the conservative management arm

Risk difference of -4.1% (95% CI -8.5 to 0.5) p=0.02

This falls within the 9% non inferiority margin

If the missing follow up data is imputed as failure, then conservative management did not show statistically significant non inferiority

93.5% resolution in the intervention group vs 82.5% in the conservative management group

Risk difference, −11.0 percentage points; 95% CI, −18.4 to −3.5)

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Conservative vs interventional treatment of spontaneous pneumothorax

Table 2. Secondary Outcomes.*

Outcome	Interventional Management (N=154)	Conservative Management (N=162)	Relative Risk (95% CI)	Risk Difference (95% CI)†
One or more procedures — no. (%)	145 (94.2)	25 (15.4)	6.10 (4.24–8.77)	78.1 (72.0–85.4)
Chest drainage for ≥72 hr — no./total no. (%)	78/153 (51.0)	15/162 (9.3)	5.51 (3.32–9.14)	41.7 (32.6–50.8)
Suction — no. (%)	52 (33.8)	12 (7.4)	4.56 (2.53–8.20)	26.4 (17.9–34.9)
At least one CT scan — no./total no. (%)	28/146 (19.2)	12/154 (7.8)	2.46 (1.31–4.66)	11.4 (3.7–19.1)
Hospital revisit — no. (%)	41 (26.6)	28 (17.3)	1.54 (1.01–2.36)	9.3 (0.3–18.4)
Any adverse event — no. (%)	41 (26.6)	13 (8.0)	3.32 (1.85–5.95)	18.6 (10.5–26.7)
Any serious adverse event — no. (%)	19 (12.3)	6 (3.7)	3.30 (1.37–8.10)	8.6 (2.7–14.6)
Pneumothorax recurrence within 12 mo — no./total no. (%)	25/149 (16.8)	14/159 (8.8)	1.90 (1.03–3.52)	8.0 (0.5–15.4)
No. of chest radiographs per patient	10.9±7.1	6.4±3.9	1.7 (1.6–1.8)‡	4.5 (3.2–5.8)§
No. of surgical procedures per patient¶	0.3±0.5	0.1±0.2	4.21 (2.10–8.41)‡	
Length of hospital stay in first 8 wk — days				
Mean	6.1±7.6	1.6±3.5	2.8 (1.8–3.6)‖	
Median (IQR)	3.8 (0.8–9.3)	0.2 (0.2–0.8)		
Days off from work				
Mean	10.9±12.7	6.0±7.3	2.0 (1.0–3.0)‖	
Median (IQR)	6.0 (2.0–14.0)	3.0 (1.0–8.0)		

* Plus–minus values are means ±SD. CT denotes computed tomographic, and IQR interquartile range.
† Shown is the risk difference between the intervention group and the conservative-management group, as measured in percentage points, unless otherwise indicated.
‡ Shown is the relative rate.
§ Shown is the mean difference in the number of chest radiographs.
¶ In the intervention group, 34 video-assisted thoracic surgeries were performed in 33 patients and 6 thoracotomies were performed in 6 patients. In the conservative-management group, 10 video-assisted thoracic surgeries were performed in 10 patients.
‖ Shown is the Hodges–Lehmann location shift for the intervention group minus the conservative-management group.

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MIDAS

- **Primary outcome**:

Median time from study drug initiation until discontinuation of IV vasopressors – no significant difference

23.5 hours (IQR 10 – 54 hours) in midodrine group vs. 22.5 hours (IQR 10.4 – 40 hours) in placebo

Difference 1 hour (95% C.I. -10.4 to 12.3, p=0.62)

Discontinuation defined as a vasopressor free period of 24 hours

- **Secondary outcomes**:

No statistical difference in time to readiness for ICU discharge, ICU length of stay (LOS), hospital LOS and ICU readmission

- **Post-Hoc Subgroup Analyses for primary outcome – time to vasopressor discontinuation**

In patients with epidural analgesia – significantly reduced in midodrine vs. placebo group

Difference -18.4 hours (95% C.I. -33.5 to -3.3, p=0.045)

In patients without epidural analgesia – no significant difference

Difference 9.7 hours (95% C.I. -6.3 to 25.7, p=0.1)

No differences found based on the following subgroups: ICU admission reason or opioid usage

Opioid usage analyzed to address possibility of impaired GI absorption

Adverse Events:

Bradycardia significantly more common in midodrine group

8% vs. 0%, p=0.02

Bradycardia defined as HR < 40, or decrease in HR > 20% from specified goal

DEXA-ARDS

	Dexamethasone group (n=139)	Control group (n=138)	Between-group difference (95% CI)	p value
Ventilator-free days at 28 days	12·3 (9·9)	7·5 (9·0)	4·8 (2·57 to 7·03)	<0·0001
All-cause mortality at day 60	29 (21%)	50 (36%)	−15·3% (−25·9 to −4·9)	0·0047
ICU mortality	26 (19%)	43 (31%)	−12·5% (−22·4 to −2·3)	0·0166
Hospital mortality	33 (24%)	50 (36%)	−12·5% (−22·9 to −1·7)	0·0235
Actual duration of mechanical ventilation in ICU survivors, days	14·2 (13·2)	19·5 (13·2)	−5·3 (−8·4 to −2·2)	0·0009
Actual duration of mechanical ventilation in survivors at day 60, days	14·3 (13·3)	20·2 (14·0)	−5·9 (−9·1 to −2·7)	0·0004
Adverse events and complications*				
Hyperglycaemia in ICU	105 (76%)	97 (70%)	5·2% (−5·2 to 15·6)	0·33
New infections in ICU	33 (24%)	35 (25%)	1·6% (−8·5 to 11·7)	0·75
Barotrauma	14 (10%)	10 (7%)	2·8% (−4·0 to 9·8)	0·41

Data are n (%) or mean (SD). ICU=intensive care unit. *Data included the period from randomisation to day 10 (for hyperglycaemia) and from randomisation to ICU discharge (for new infections and barotrauma).

Table 2: **Outcomes, adverse events, and complications**

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Thank you

Allegheny Health Network

Update on Tele ICU

Anil Singh, MD, MPH, MMM, FCCP
Executive Medical Director
Clinical Solutions, Design and Implementation
Highmark Health

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HIGHMARK.

ICU - Background

- Resource intensive and demands meticulous process control
- Complexity has increased
- Improved outcomes predicated by the following:
  - Early recognition of illness
  - Defined care processes
  - Patient/physician/nurse ratios
  - Timing of admissions
  - Staffing models

Insufficient supply of intensivists

Methodist Debakey Cardiovasc J. 2018 Apr-Jun; 14(2): 126–133.
doi: 10.14797/mdcj-14-2-126

ICU Models

More favorable outcomes with “high intensity models”

- Closed units
- Mandatory intensivist consultation.

- Problem with 24/7 coverage
  - No mortality benefit
  - No ICU length of stay (LOS)
    - However, sepsis, renal failure, blood product use, and hospital LOS were reduced
  - Increased cost
  - Lack of availability of intensivists
- ICU telemedicine has been proposed to increase access to critical care expertise.

Crit Care Med. 2000 Dec; 28(12):3925-31.

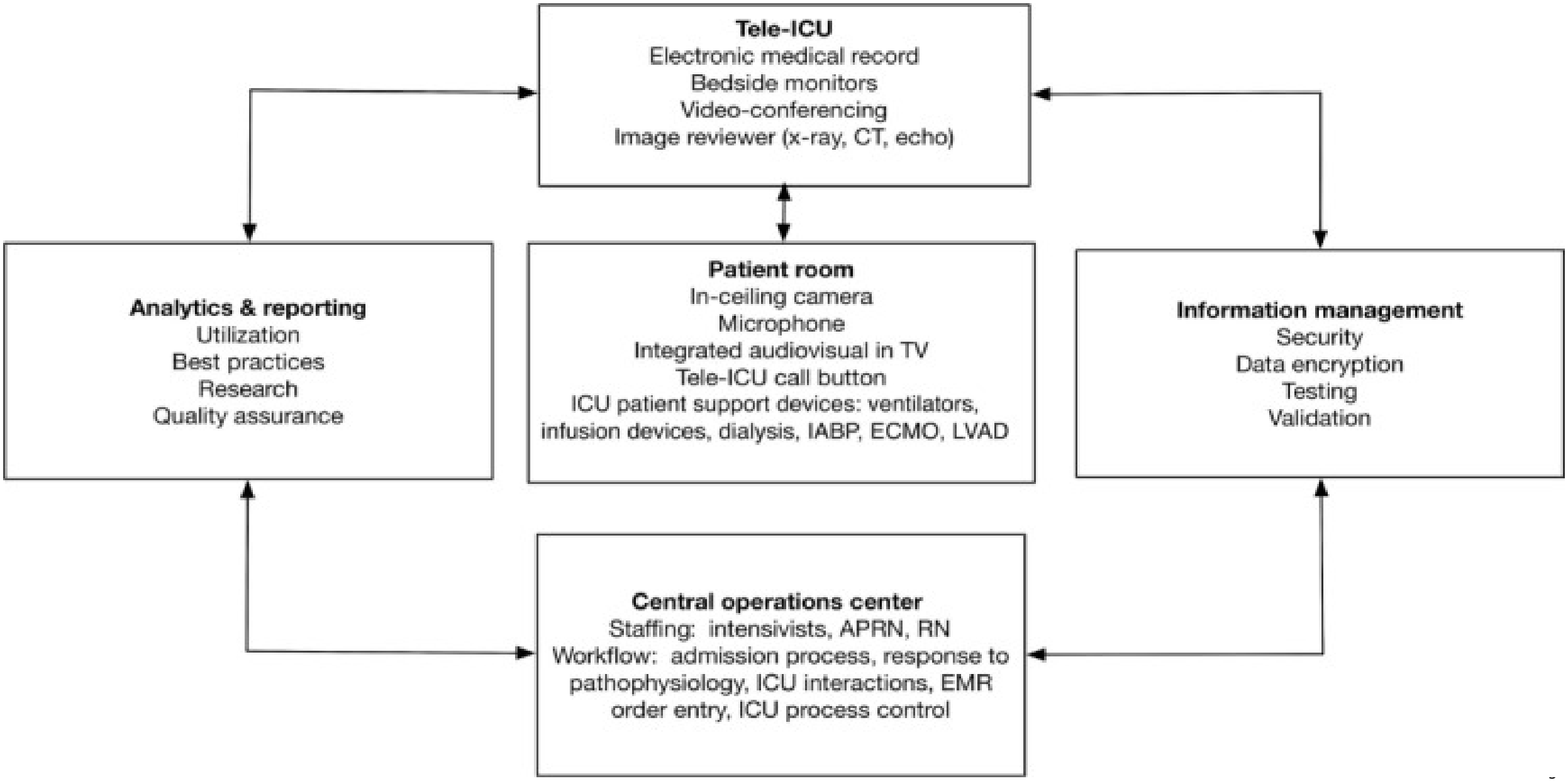
JAMA. 2002 Nov 6; 288(17):2151-62

J Thorac Cardiovasc Surg. 2014 Jul; 148(1):290-297.e6.

The case of Tele ICU

- Remote video visualization of patients
- Biomedical devices and access to EHRs
- Platforms leverage algorithms to scrutinize patient data
- Prediction of deterioration
  - Combination of physiological parameters
  - Clinical risk factors
- Decision support
- Augmentation of conventional coverage in multiple ICUs

.


Tele-ICU
Electronic medical record
Bedside monitors
Video-conferencing
Image reviewer (x-ray, CT, echo)
Analytics & reporting
Utilization
Best practices
Research
Quality assurance
Patient room
In-ceiling camera
Microphone
Integrated audiovisual in TV
Tele-ICU call button
ICU patient support devices: ventilators, infusion devices, dialysis, IABP, ECMO, LVAD
Information management
Security
Data encryption
Testing
Validation
Central operations center
Staffing: intensivists, APRN, RN
Workflow: admission process, response to pathophysiology, ICU interactions, EMR order entry, ICU process control

Pros/Cons

BENEFITS OF TELE-ICU
Promotes evidence-based best practices through checklists and prompting[19]
Enhanced monitoring, early identification, and treatment of critical illness pathophysiology[20]
Improved coordination of care[21]
Increased night-time vigilance[22]
POTENTIAL CONCERNS OF TELE-ICU
Disruption of traditional ICU practice
Diffusion of responsibility[23]
Underutilization of tele-ICU (e.g., insufficient authority)
Insufficient contact between tele-ICU hub and ICU
Skepticism of ICU staff re: tele-ICU technology[24]
Differences between postulated and proven benefits[25]
Increased fixed and variable costs

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Meta analysis and systemic reviews

FIRST AUTHOR	YEAR	STUDIES # (YEARS)	ICU # (HOSPITAL #)	PATIENT # (PRE/POST)	ICU MORTALITY
Chen[31]	2017	19 (2004-2014)	110 (72)	192,265: (156,413/35,952)	Significantly reduced (RR 0.83; CI 0.72 to 0.96; I^2 = 78%) in 15 studies
Mackintosh[32]	2016	2 (2011-2014)	Study 1: 7 (2) Study 2: 38 (56)	6,290 (1,529/4,761)	Study 1: Significantly reduced (OR 0.37; CI 0.28 to 0.49) Study 2: Significantly reduced (HR 0.74; CI 0.68 to 0.79)
Wilcox[7]	2012	9 (2000-2012)	37 (20)	49,457 (15,587/33,870)	Significantly reduced (RR 0.79; CI 0.65 to 0.96; I^2 = 70%) in 9 studies
Young[33]	2011	13 (2004-2009)	35 (27)	41,374 (15,677/25,707)	Significantly reduced (OR 0.80; CI 0.66 to 0.97; I^2 = 77.1%) in 12 studies

Meta-analysis and systemic reviews continued

HOSPITAL MORTALITY	ICU LOS	HOSPITAL LOS	COMMENTS
Significantly reduced (RR 0.74; CI 0.58 to 0.96; I^2 = 97%) in 13 studies	Signficantly reduced (MD -0.63; CI -0.28 to 0.17; I^2 = 93%) in 9 studies	No significant change (MD -0.27; CI -1.14 to 0.59; I^2 = 92%) in 8 studies	Multiple sensitivity analyses were included: year of publication, sample size, age, tele-ICU duration were not significant
Study 1: Significantly reduced (OR 0.40; CI 0.31 to 0.52) Study 2: Significantly reduced (HR 0.84; CI 0.78 to 0.89)	Study 1: Significantly reduced (HR of discharge 1.26, CI 1.17-1.36) Study 2: Significantly reduced (20% shorter; CI 14-17%; P <0.001)	Study 1: Significantly reduced (HR of discharge: 1.44, CI 1.33 to 1.56) Study 2: Significantly reduced (15% shorter; CI 14% to 17%; P < 0.001)	No aggregation of data; both studies assessed with high risk of bias
Significantly reduced (RR 0.83; CI 0.73 to 0.94; I^2 = 72%) in 9 studies with 33,183 patients	Significantly reduced (MD -0.62; CI -1.21 to -0.04; I^2 > 90%) in 7 studies with 29,837 patients	Significantly reduced (MD -1.26; CI -2.49 to -0.03; I^2 > 90%) in 6 studies	All studies used before and after design
No significant change (OR 0.82; CI 0.65 to 1.03; I^2 = 84.9%) in 10 studies	Significantly reduced (MD −1.26 days; CI −2.21 to −0.30; I^2 = 99.8%) in 7 studies	No significant change (MD -0.64; CI -1.52 to 0.25; I^2 = 99.8%) in 6 studies	All studies used before and after design

Pilot program at AHN

- Problem
  - Not a high intensity system
- Staffing
  - Not enough physicians for coverage
- Solution
  - Transition to a high intensity model
  - Emphasis on creating single standard of critical care access across AHN
  - Keep care in the community/originating hospital

  - Goals/Outcomes
    - Improve quality and safety standards
    - Reduce transfers/leakage
    - Lower cost
    - Generate capacity

Mercy Virtual Partnership/AHN/Highmark Health

vICU Solution: 24/7/365 Intensivist Coverage w/ Proactive Monitoring - 64 medical ICU beds:
- Jefferson (20 beds) / Canonsburg (8 beds) / AVH (16 beds) / SVH (20 beds)

vICU Tablets: 12/7 Intensivist Coverage (7pm–7am) - 82 vICU Tablet beds:
- SVH (40 beds) / Jefferson (20 beds) / Grove City (12 beds) / AVH (10 beds)

Licensed/Credentialed Mercy Virtual Providers:
- Intensivists (52) / Nurses & Navigators (90) / 142 Total MV Providers

AHN Care Teams (~400 AHN Staff):
- AVH – Medical ICU & PACU / SVH – Medical ICU, CNICU, Step Down, 7N and 9N
- Jefferson – Medical ICU, CVU and 3 South / Canonsburg – Medical ICU
- Grove City – Medical ICU and Acute Care Unit

In Scope for ‘21: vICU – Grove City ICU (March ‘21 – 7 beds) / Westfield Med/Surg (July ‘21 – 4 beds) / Wexford ICU (September ‘21 – 20 beds)

Our internal outcomes

Discharges

- decreased by 3.6% (pandemic effect)

Transfers out

- decreased by 16.6%

Transfers in

- increased by 7.9%

CMI

- increased by 10%

Net patient revenues

- increased by 6.9%

Quality data

- Pending

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Thank you
Questions?

Allegheny Health Network

A Pulmonary Approach to Lung Cancer

Sohini Ghosh, MD
Director, Interventional Pulmonology
3/27/2021

Disclosures

Consulting fees from Intuitiv
Speaker Bureau for AstraZeneca

Objectives:

- Lung cancer epidemiology
- How to sample the lung nodule
- Palliative bronchoscopy in advanced stage cancer

- Early 1900s: Lung cancer was 1% of all cancers
- 1950s: first study showing a link between lung cancer and smoking
- 1964: The seminal US Public Health Service report by the Surgeon General
  "cigarette smoking is an important health hazard in the US and action is required"
- 1980-1985: 5 year survival 12%
- 1995: 10% improvement in 1 year survival in those treated with chemotherapy
- Late 1990s and early 2000s: advances in chemotherapy and multi-modal therapy, imaging modalities, biopsy modalities, staging guidelines, SBRT
- 2003: discovery of EGFR
- 2007: discovery of ALK
- 2006: Discovery of checkpoint blockade in cancer
- 2011: NLST trial leading to implementation of lung cancer screening
- Present day
  - 5 year survival ~20%
  - ongoing studies of personalized therapy, immunotherapy, molecular markers.

M. Patricia Rivera, R. Matthay, Clin Chest Med 2020

Estimated New Cases

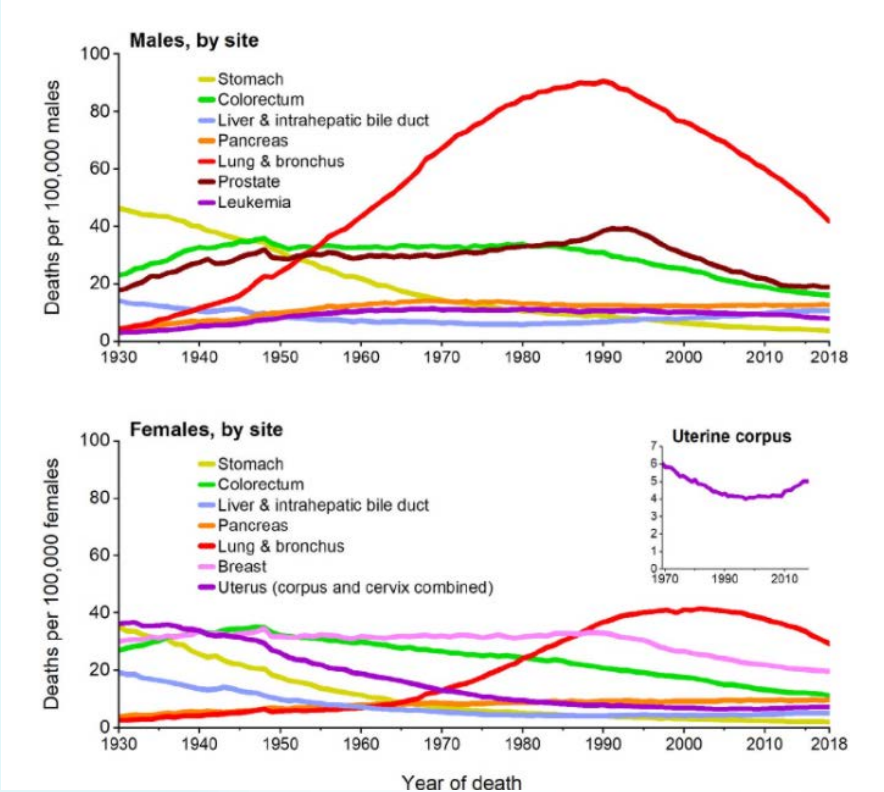
	Males			Females	
Prostate	248,530	26%		Breast	281,550	30%
Lung & bronchus	119,100	12%		Lung & bronchus	116,660	13%
Colon & rectum	79,520	8%		Colon & rectum	69,980	8%
Urinary bladder	64,280	7%		Uterine corpus	66,570	7%
Melanoma of the skin	62,260	6%		Melanoma of the skin	43,850	5%
Kidney & renal pelvis	48,780	5%		Non-Hodgkin lymphoma	35,930	4%
Non-Hodgkin lymphoma	45,630	5%		Thyroid	32,130	3%
Oral cavity & pharynx	38,800	4%		Pancreas	28,480	3%
Leukemia	35,530	4%		Kidney & renal pelvis	27,300	3%
Pancreas	31,950	3%		Leukemia	25,560	3%
All Sites	**970,250**	**100%**		**All Sites**	**927,910**	**100%**

Estimated Deaths

	Males			Females	
Lung & bronchus	69,410	22%		Lung & bronchus	62,470	22%
Prostate	34,130	11%		Breast	43,600	15%
Colon & rectum	28,520	9%		Colon & rectum	24,460	8%
Pancreas	25,270	8%		Pancreas	22,950	8%
Liver & intrahepatic bile duct	20,300	6%		Ovary	22,950	5%
Leukemia	13,900	4%		Uterine corpus	12,940	4%
Esophagus	12,410	4%		Liver & intrahepatic bile duct	9,930	3%
Urinary bladder	12,260	4%		Leukemia	9,760	3%
Non-Hodgkin lymphoma	12,170	4%		Non-Hodgkin lymphoma	8,550	3%
Brain & other nervous system	10,500	3%		Brain & other nervous system	8,100	3%
All Sites	**319,420**	**100%**		**All Sites**	**289,150**	**100%**

- Lung cancer causes more deaths than breast, prostate and colon cancer and **combined**
- Pennsylvania estimated to have 11,170 new diagnosis of lung cancer (surpassed only by FL, CA, TX, NY)
- Estimated number of deaths in PA in 2021 expected to be 6140

Siegal et al, Cancer statistics 2021 , A cancer journal for clinicians



- From its peak death rate has dropped by 51% in males and 26% in females
  - Improvements seen 20-30 years after smoking prevalence began to fall

- 5 year survival 2011: 15.6%
- 5 year survival in 2019: 19.4%

- Huge disparities in lung cancer death rates along socioeconomic and geographic variables

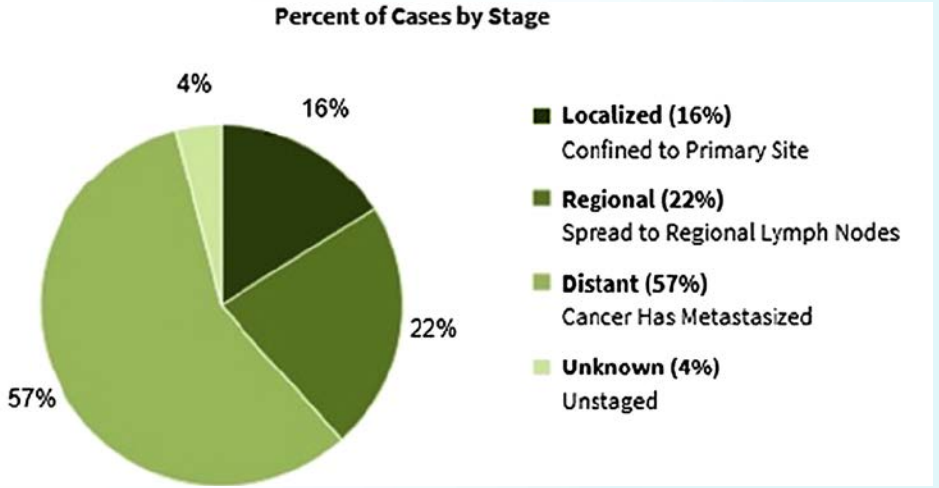
Bade et al, Lung Cancer 2020 Epidemiology, Etiology , and Prevention
Clin Chest Med
Siegal et al, Cancer statistics 2021 , A cancer journal for clinicians

Causes of slight improvement?

- Improvement in tobacco cessation
- Increased minimally invasive treatment options
  - VATS
  - SBRT
- Targeted therapy and immunotherapy
- Lung cancer screening?
  - Slow uptake….

- Unfortunately most are still diagnosed at an advanced stage

A



Bade et al, Lung Cancer 2020 Epidemiology, Etiology , and Prevention, Clin Chest Med

80-90 % of lung cancers develops in current or former smokers

- What about the 10-20% who are non smokers?
  - Globally: 15% of lung cancers in men and 53% of women are not attributable to smoking
  - US: 9% in men and 19% in women
    - Proportion of never smokers with adenoCA increased from 8.0% to 14.9%
  - Other RFs: biomass burning, air pollution, Radon (uranium mining), occupational exposures (arsenic, asbestos, beryllium, silica), genetic predisposition, HIV, chronic lung disease

Bade et al, Lung Cancer 2020 Epidemiology, Etiology , and Prevention, Clin Chest Med

Updated lung Cancer Screening Guidelines

- Aged 50-80 with ≥20 pack year history who has not quit within 15 years
- “Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the **ability or willingness to have curative lung surgery**. ”

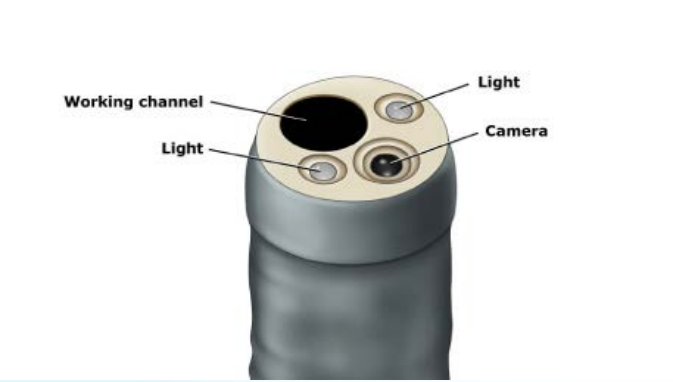
USPSTF, March 2021

How to biopsy a lung nodule

Flexible Bronchoscopy

- Good for central disease: sensitivity 88%
- Performs poorly in peripheral nodules
  - <2cm: sensitivity 34%
  - >2cm: sensitivity 63%



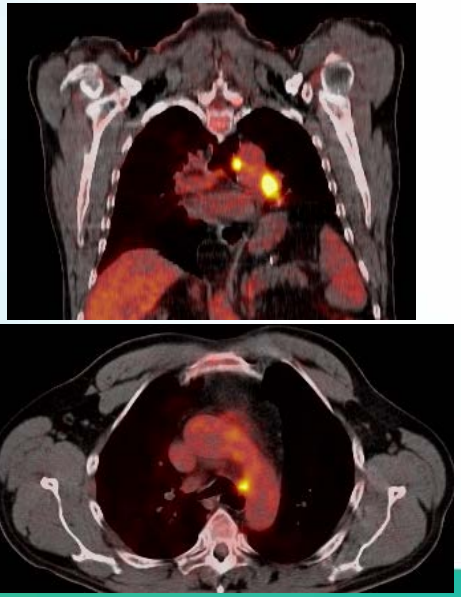




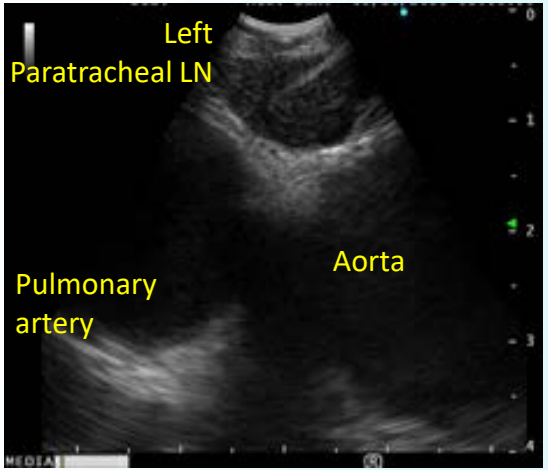
Burks & Akulian, *Clin Chest Med* 2020
Rivera MP, Mehta AC, Wahidi NM. Establishing the diagnosis of lung cancer, ACCP guidelines 2013
Image courtesy of Olympus Medical
Image courtesy of www.uptodate.com

Convex (linear) probe Endobronchial US

- Available since 2004
- Real-time US images of central, mediastinal and hilar lesions and lymph nodes
- Improved yield of TTNA. Higher sensitivity than mediastinoscopy
- First line in diagnosing and staging lung cancer







Silvestri et al. CHEST 2013; 143 suppl
Burks & Akulian, *Clin Chest Med* 2020
Anantham, Koh & Ernsst, *Endobronchial Ultrasound* Resp Med, 2009

Sampling Peripheral Lung nodules

Radial Probe Endobronchial Ultrasound

- Introduced 1990s
- 360^{0} imaging of lung parenchyma
- Diagnostic yield ranging from 58 – 85%
  - Higher when combined with ENB
  - Higher in larger (>2cm) nodules
- AQuIRE registry yield: 38.5%
- Many limitations to use

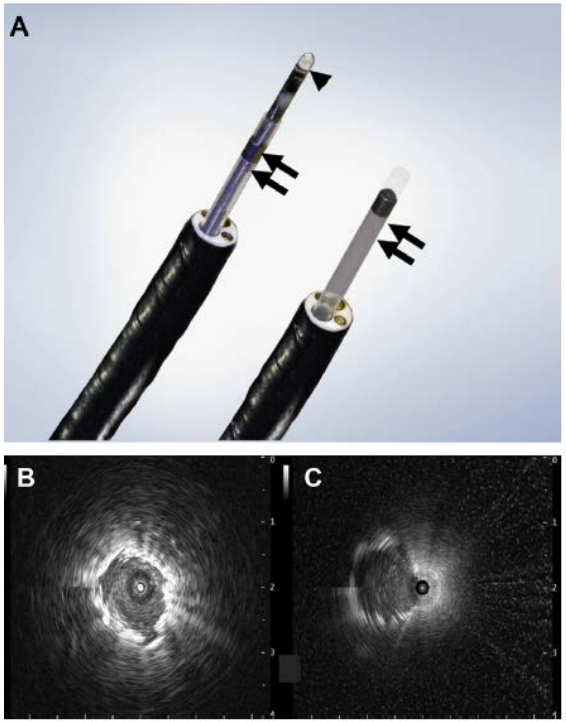
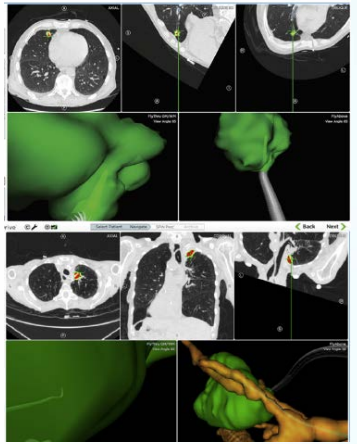


Fig. 4. (*A*) Radial probe EBUS (*arrowhead*) within guide sheath (*double arrows*). (*B*) Radial EBUS image within nodule, concentric view. (*C*) Radial EBUS image adjacent to nodule, eccentric view. (*Courtesy of* Olympus Medical, Tokyo, Japan.)

Burks & Akulian, *Clin Chest Med* 2020
Ost et al, *AQuIRE registry*, AJRCCM, 2016

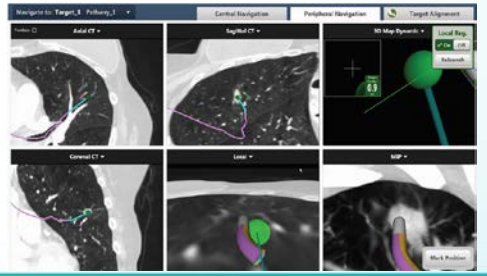
Electromagnetic Navigation Bronchoscopy

- Pre-procedural thin cut CT scan to create a virtual tracheobronchial tree
- Creation of a magnetic field around the patient
- Detects tracked devices within the patient – matching the CT scan and creating a map



VeranSPiN-Drive, Veran Medical Technologies

- No multicenter prospective trials
  - Yields reported from 39-94% in poorly done meta-analyses
  - Yield likely closer to 60-70% range

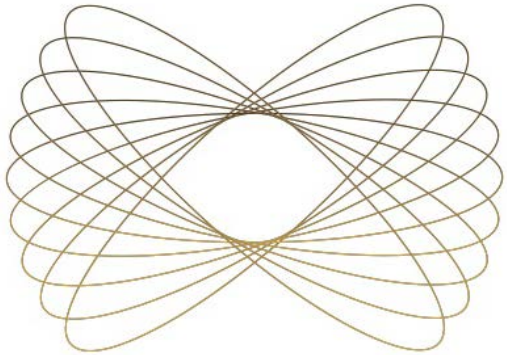


Super Dimension, Medtronic

Burks & Akulian, *Clin Chest Med* 2020
Katsis et al, *J Thorac Dis* 2020

Robotic bronchoscopy

- Two commercially available platforms: Ion and Monarch
- Robotic bronchoscope + navigation software platform
- Combine radial EBUS +/- fluoroscopy

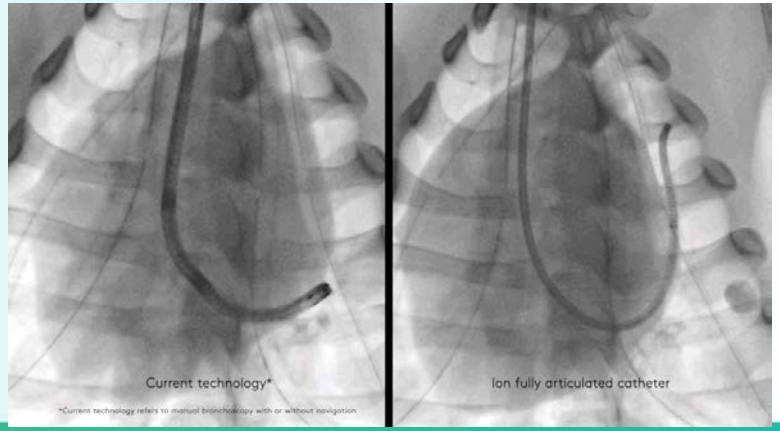


AURIS

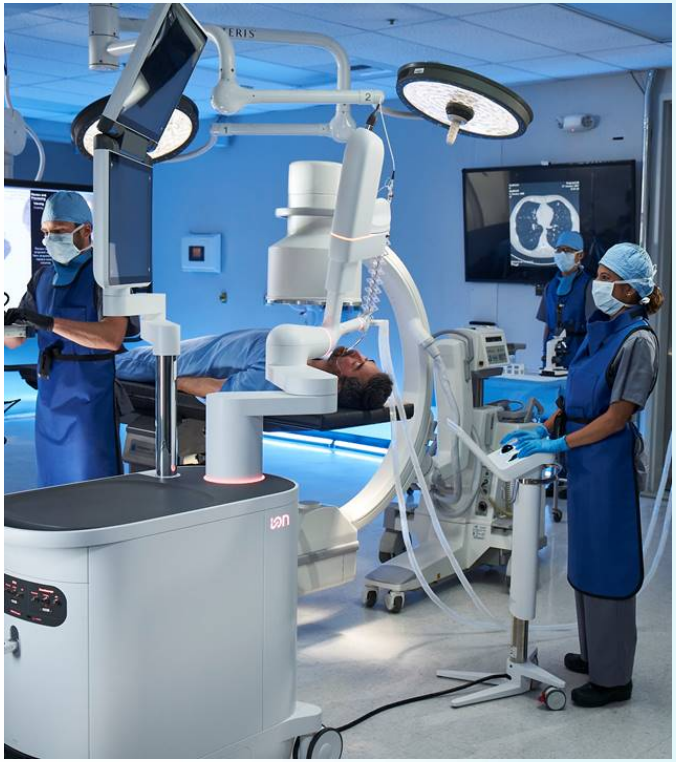
INTUITIVE™

Ion Platform

- Available at AGH
- Navigation by shape sensing technology
- FHU study: 29 patients
  - Mean lesion size 1.3 cm
  - 96.6% lesion localization
  - Diagnostic yield of 79.3%
  - Diagnostic yield of malignancy of 88%



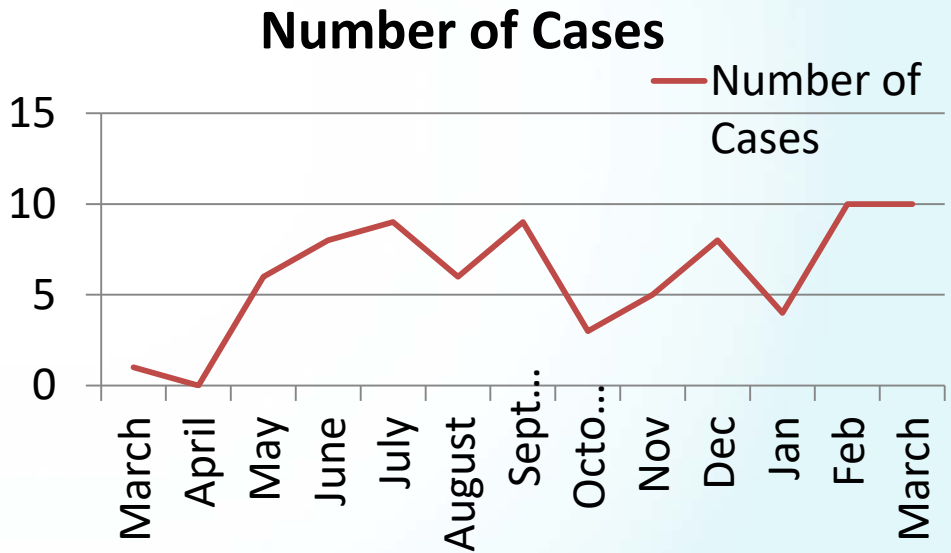




Images courtesy of Intuitive Medical, Sunnyvale, CA
Fielding et al, *FHU,* Respiration, 2019

Ion at AHN

- 93 total nodules
- Past 6 months:
  - 48 cases
  - 95% diagnostic yield for those which we have follow up data on
  - Mean nodule size 19.7mm



Trans-thoracic biopsy

Location: peripheral, away from fissure
More biopsies with a co-axial system
Higher complications rates in core biopsies and large FNA needles

- Pneumothorax rates >25%
  - Requiring intervention ~7%
- Hemorrhage 18%

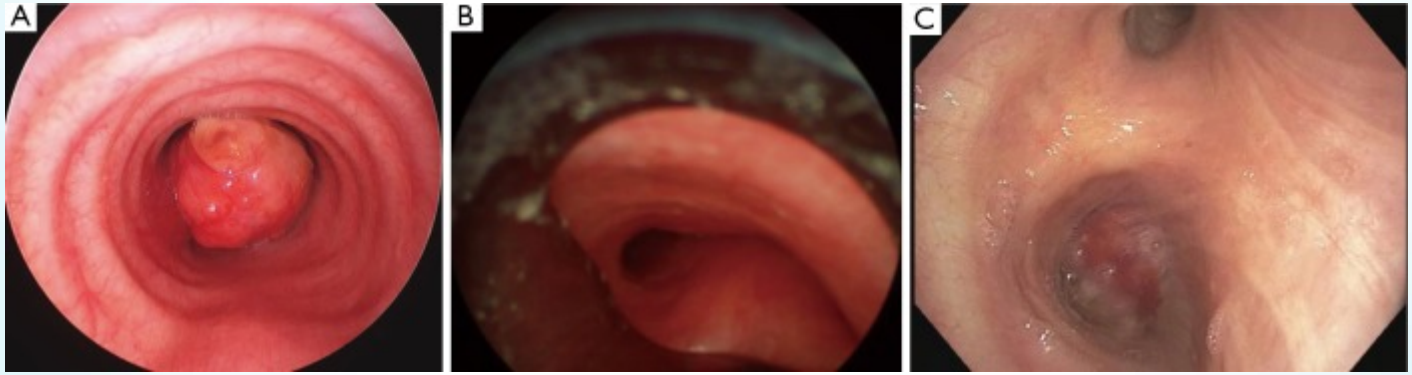


- **CT guided**
- Electromagnetic navigation
  - Benefit of staging lymph nodes at the same time
- Cone Beam
  - Real time multi-planar images
  - Beneficial in both TTNA and TBNA

Heerink et al, Eur Radiol 2016
Kalnejeri et al, Clin Chest Med 2018

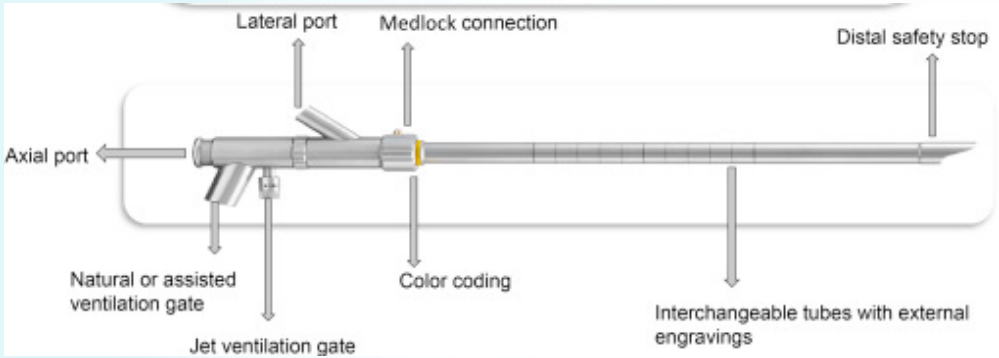
Therapeutic bronchoscopy

- 20-30% of patients with lung cancer will develop central airway obstruction (CAO) → cough, dyspnea, hemoptysis and recurrent pneumonia
  - Majority not amenable to surgery and require palliative interventions

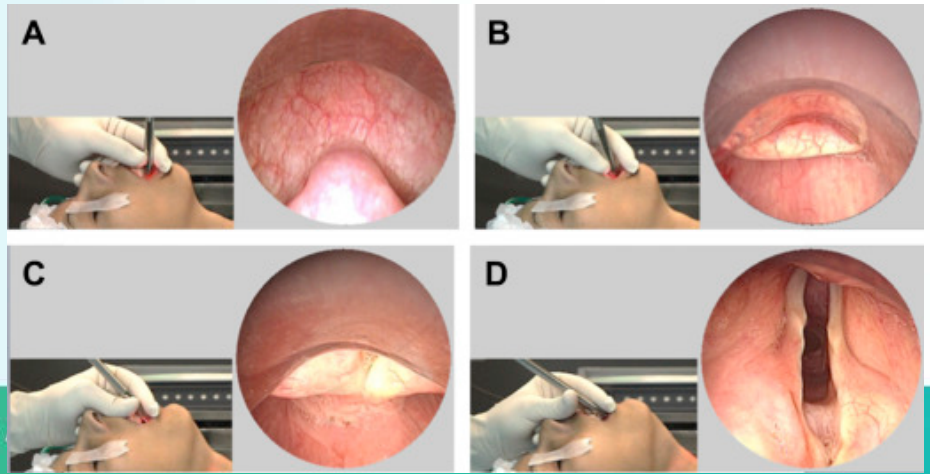


Ali & Sorathia, Clin Chest Med 2018
Seeman & Yarmus, J Thorac Dis 2015

Rigid bronchoscopy









Flannery, Clin Chest Med, 2018
Diaz-Medoza, Semin in Respir and CCM 2018

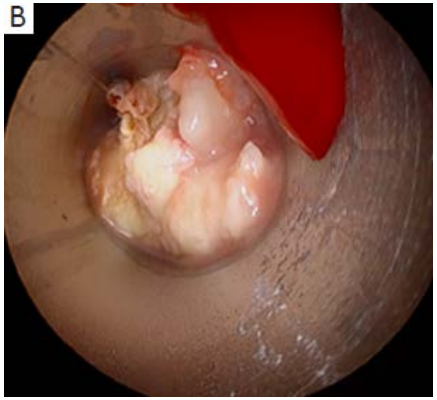
Relief of CAO

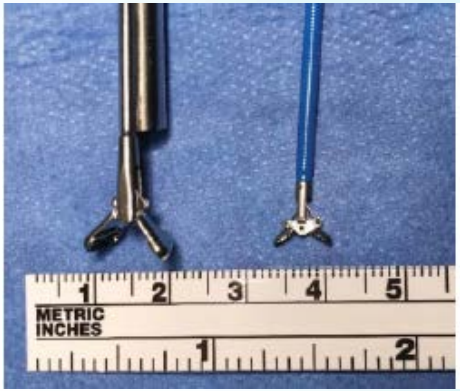
- Goals
  - Improve performance status
  - Improve complications related to CAO
  - Palliation
- 40% of patients had significant improvement in dyspnea and quality of life
- No difference in survival
- Most benefit in larger airways
- Require radiation for longer term relief

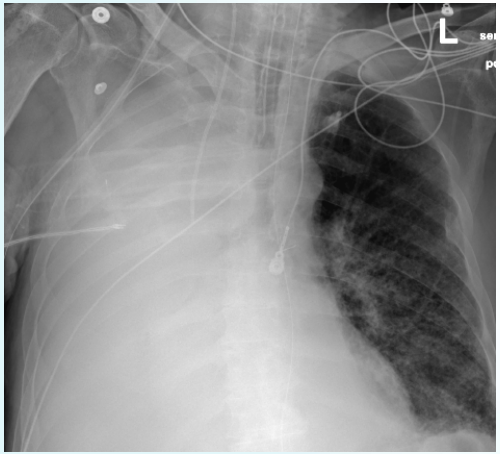
Flannery, Clin Chest Med, 2018
Diaz-Medoza, Semin in Respir and CCM 2018
Ost, ACQuIRE Registry, AJRCCM

Relief of CAO

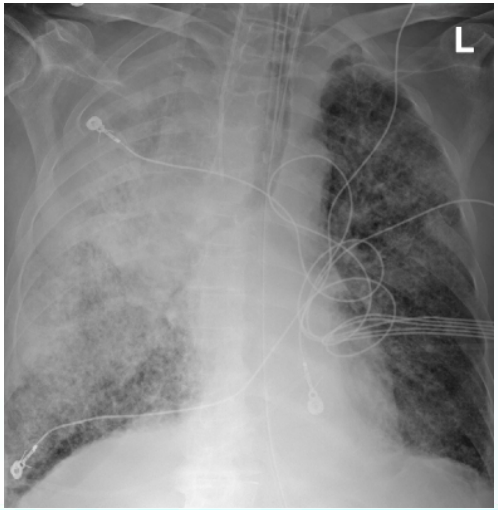
- Mechanical debulking

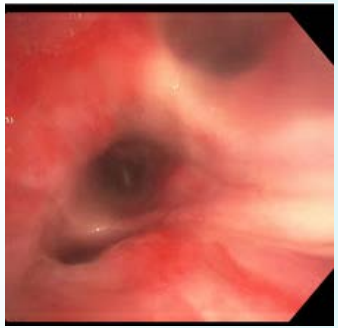










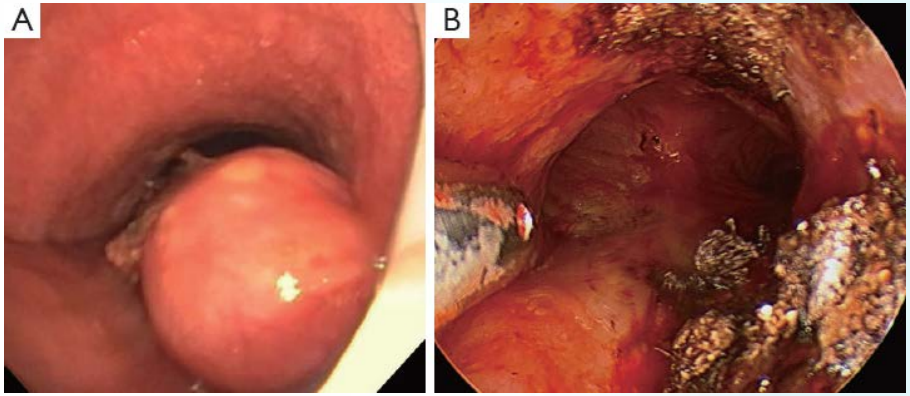


Shepherd, Ann Transl Med, 2019
Diaz-Medoza, Semin in Respir and CCM 2018

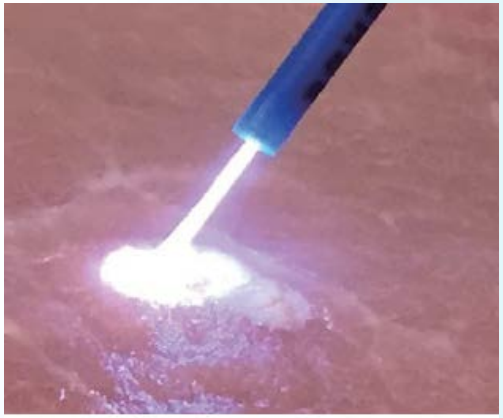
Relief of CAO

Ablative Therapies

- LASER (light amplification by simulated emission of radiation)
- Electrocautery
  - Probe, Knife, Forceps, Snare
- Argon Plasma Coagulation (APC)





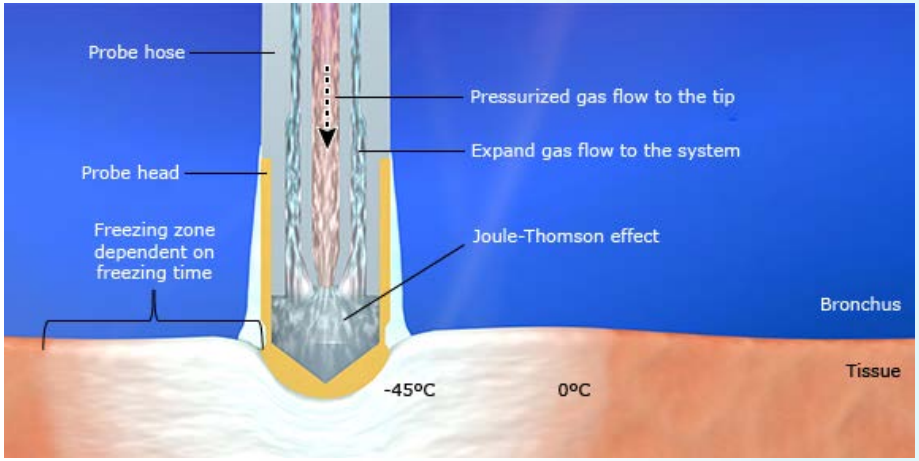


Images: Sachdeva et al, J Thorac Dis 2015

Relief of CAO

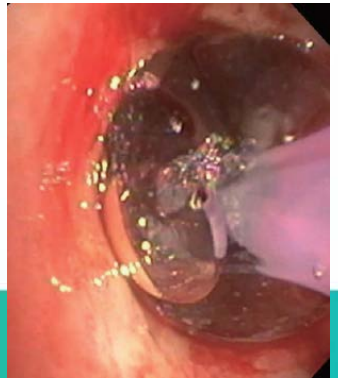
Ablative Therapies

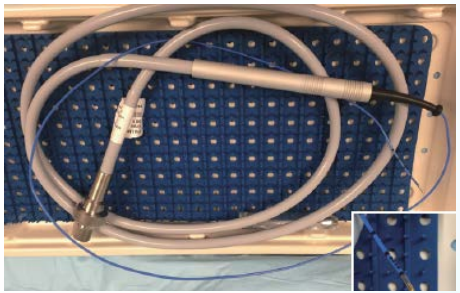
- Cryotherapy
  - Cryoablation
  - Cryorecanalization
- Photodynamic therapy (PDT)



Balloon Dilation





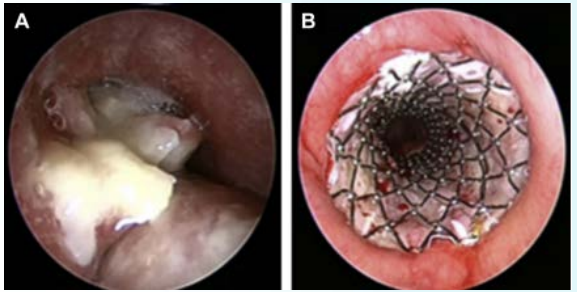




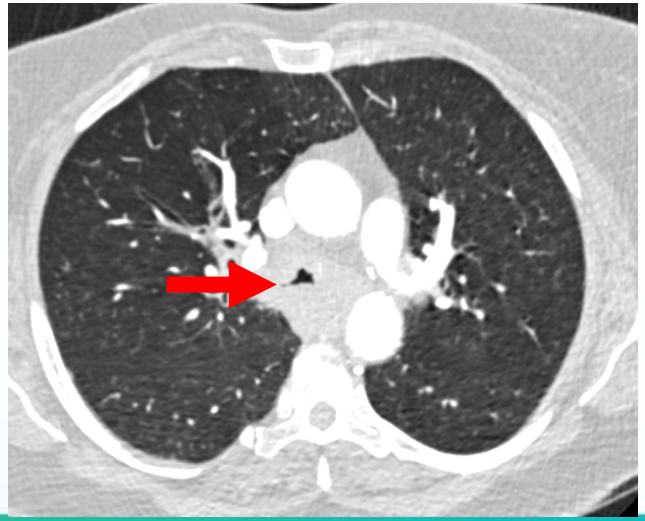
Relief of CAO

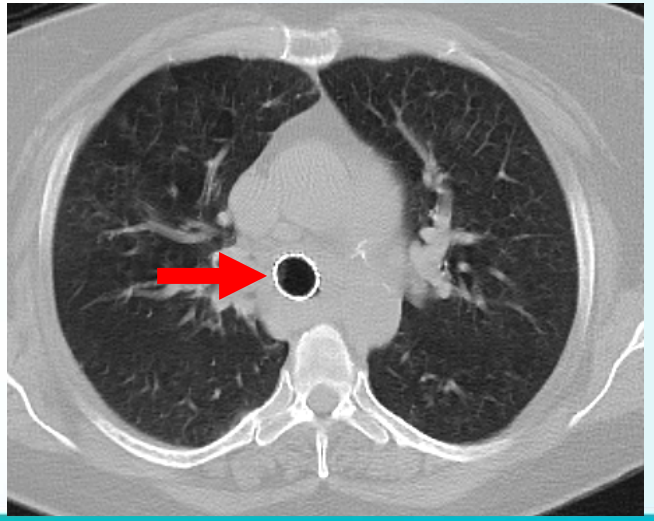
Airway stenting





- Silicone
- SEMS (Self-expanding metal stents)
  - Covered
  - Uncovered
    - Black-Box warning in benign disease





Flannery, Clin Chest Med, 2018

Conclusions

- Lung cancer causes more deaths than breast, prostate and colon cancer and combined
- Lung cancer screening has led to more nodules being found requiring sampling
- A multi-disciplinary approach is required
- Many modalities available for sampling, each with their own risks and benefits
- Rigid bronchoscopy is a key procedure to palliate symptoms related to CAO

Thank you!



Surgical Treatment of Lung Cancer

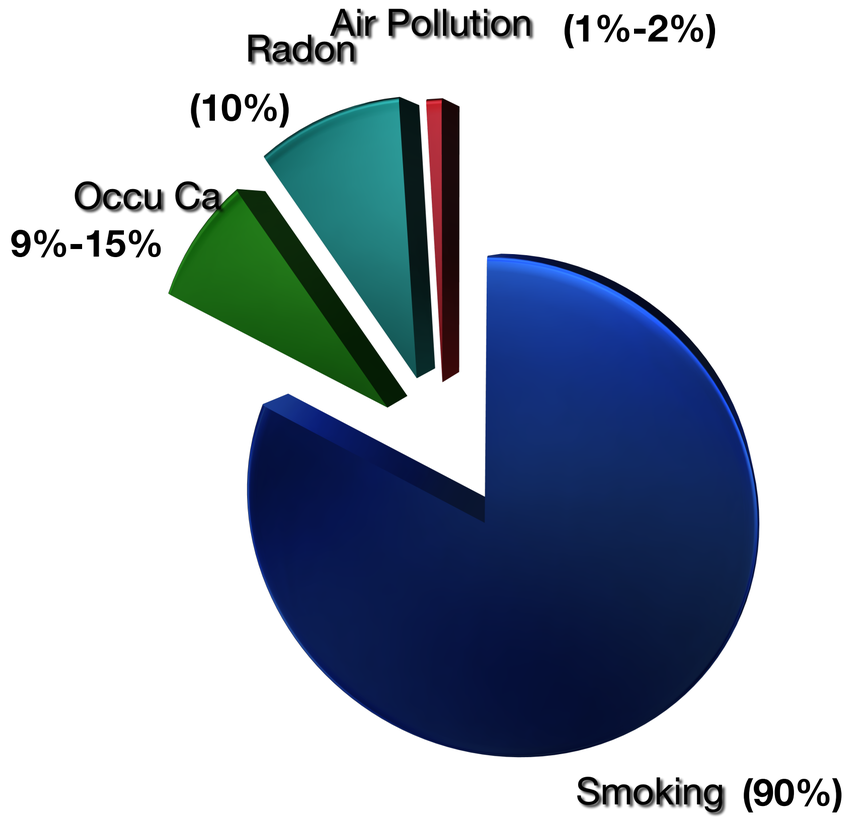
Benny Weksler, MBA, MD
Professor of Surgery
Drexel College of Medicine
Edward Kent Professor of Thoracic Surgery
Allegheny General Hospital
System Chief of Thoracic Surgery
Allegheny Health Network

Financial disclosures:
Proctor Intuitive Surgery
Speaker Astrazeneca

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Lung Cancer-Etiology



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Cancer Mortality in the US

Cancer facts and figures 2018

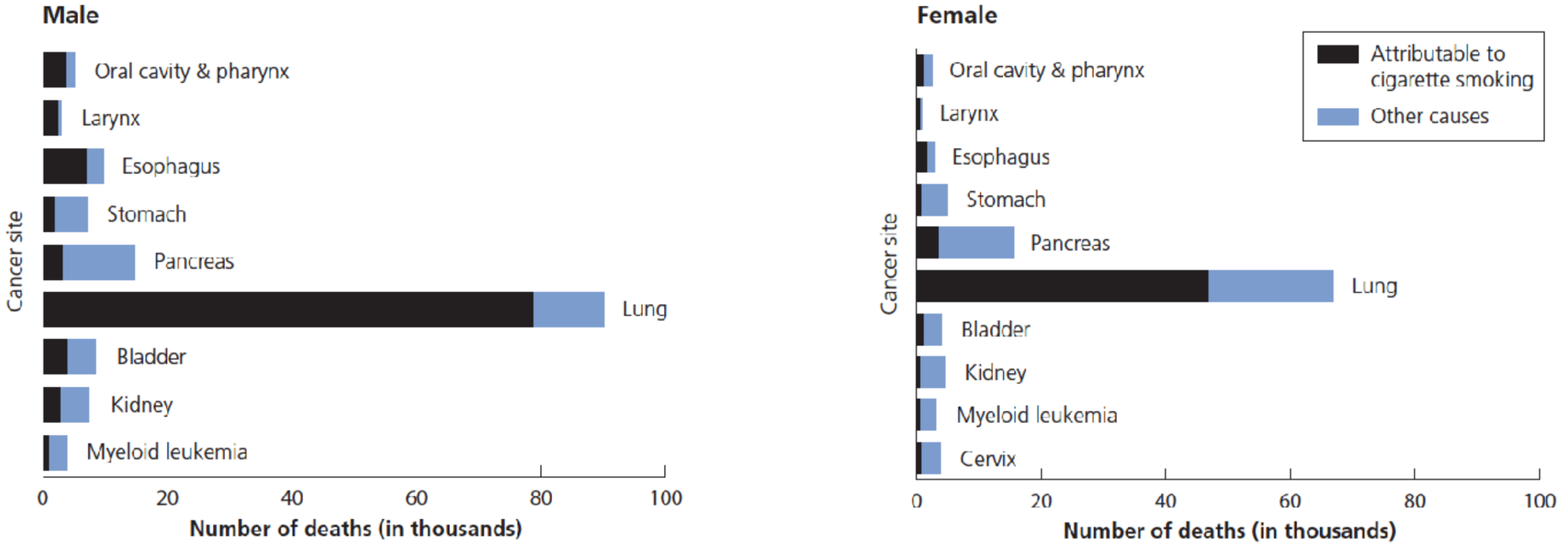
Site	Deaths
1. Lung	154,050
2. Colon/Rectum	50,630
3. Breast	41,400
4. Pancreas	44,330
5. Esophagus	15,850

} 152,210

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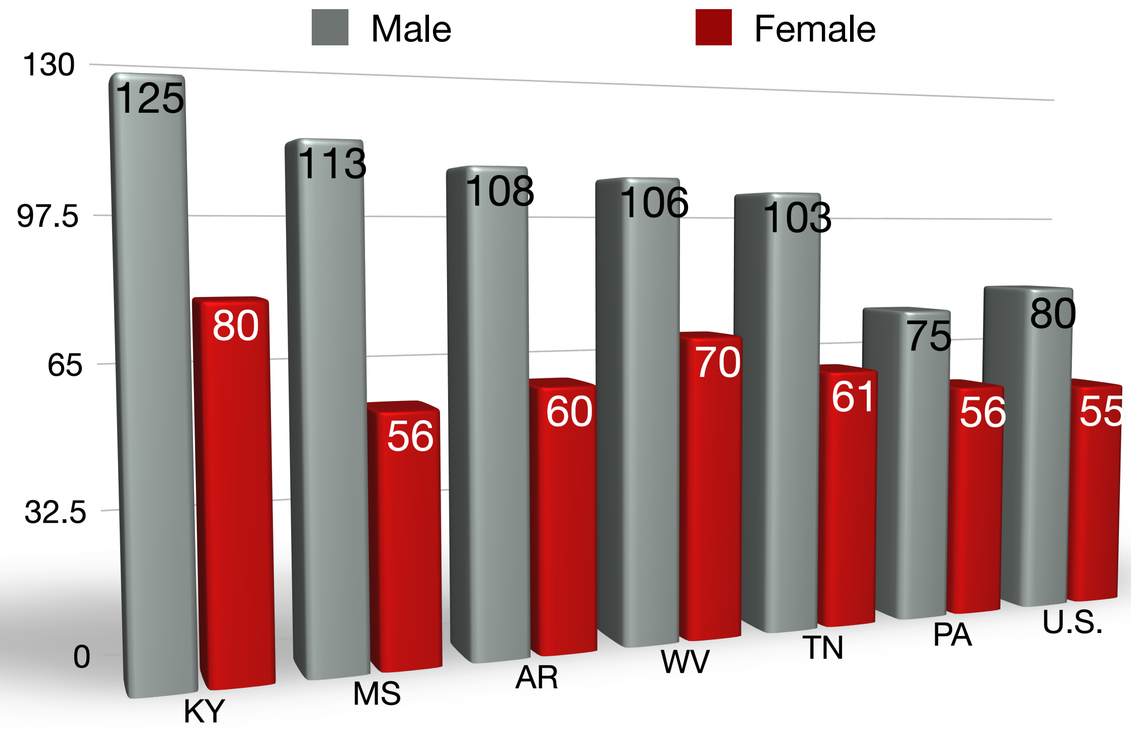
Annual Number of Cancer Deaths Attributable to Smoking by Sex and Site, US, 2000-2004



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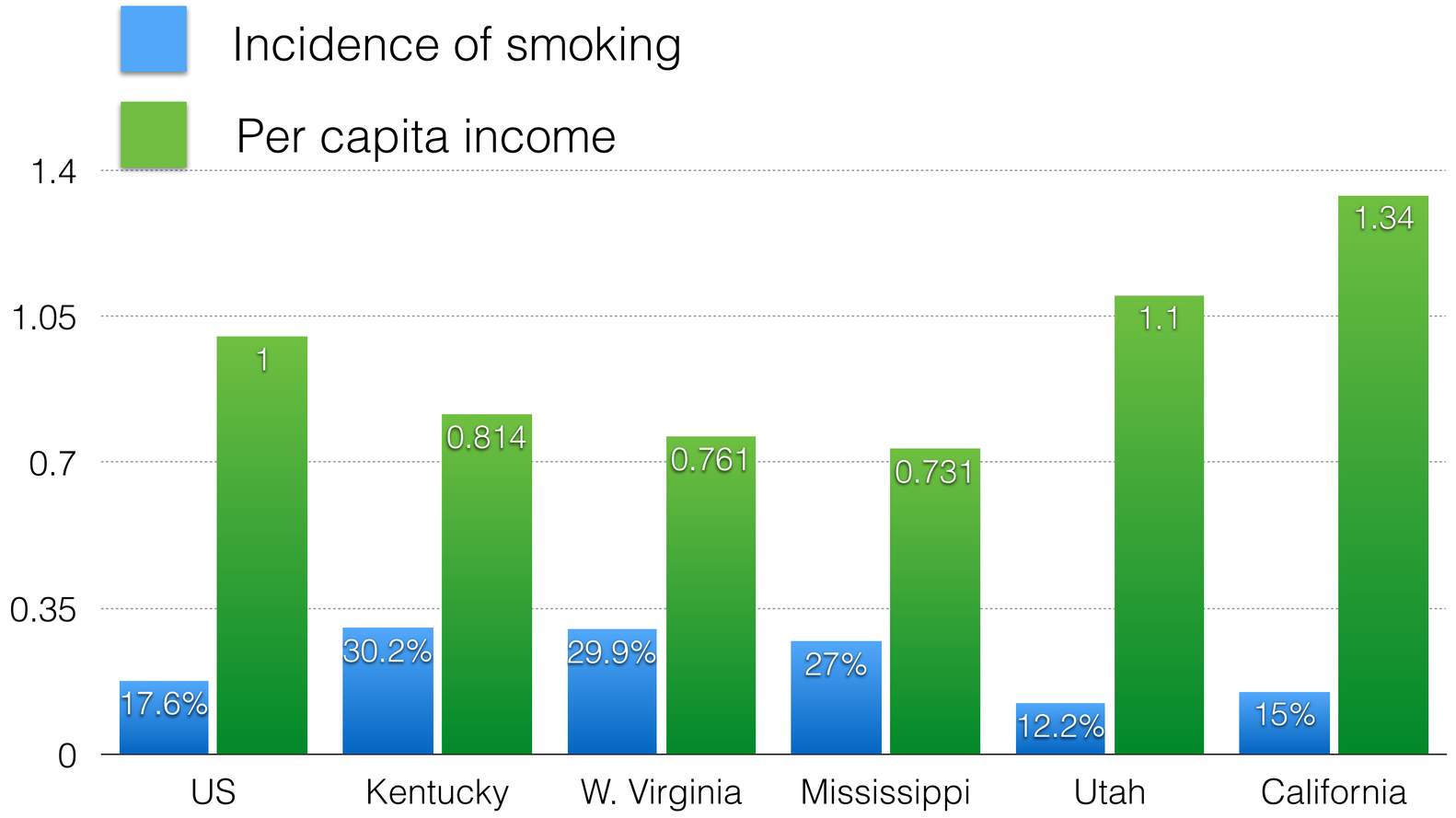
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Lung Cancer Incidence per 100,00



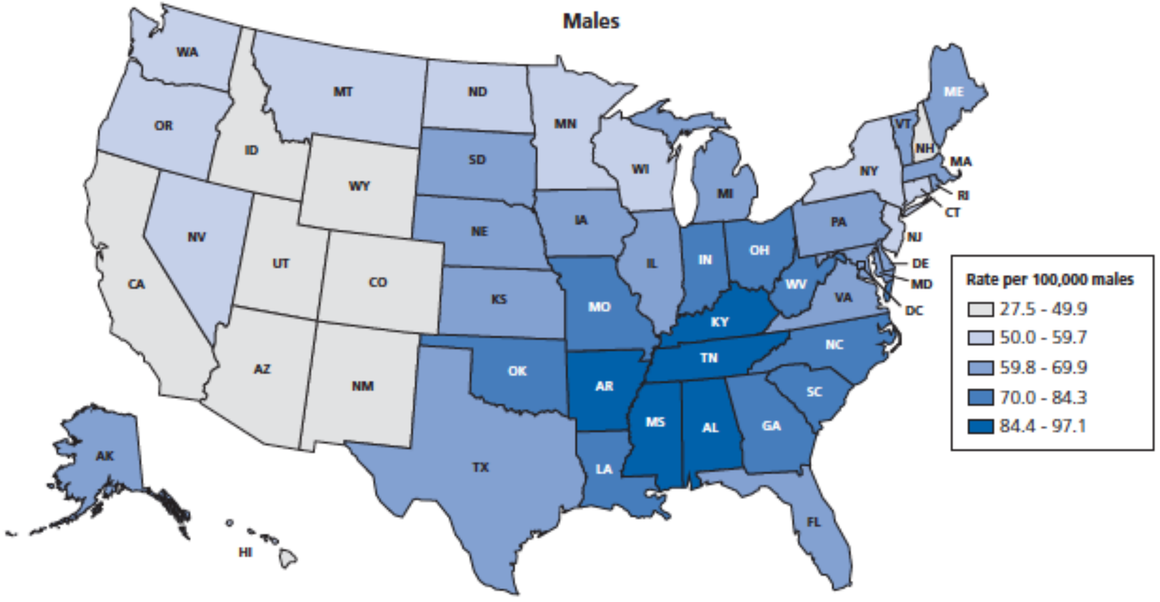
Allegheny Health Network
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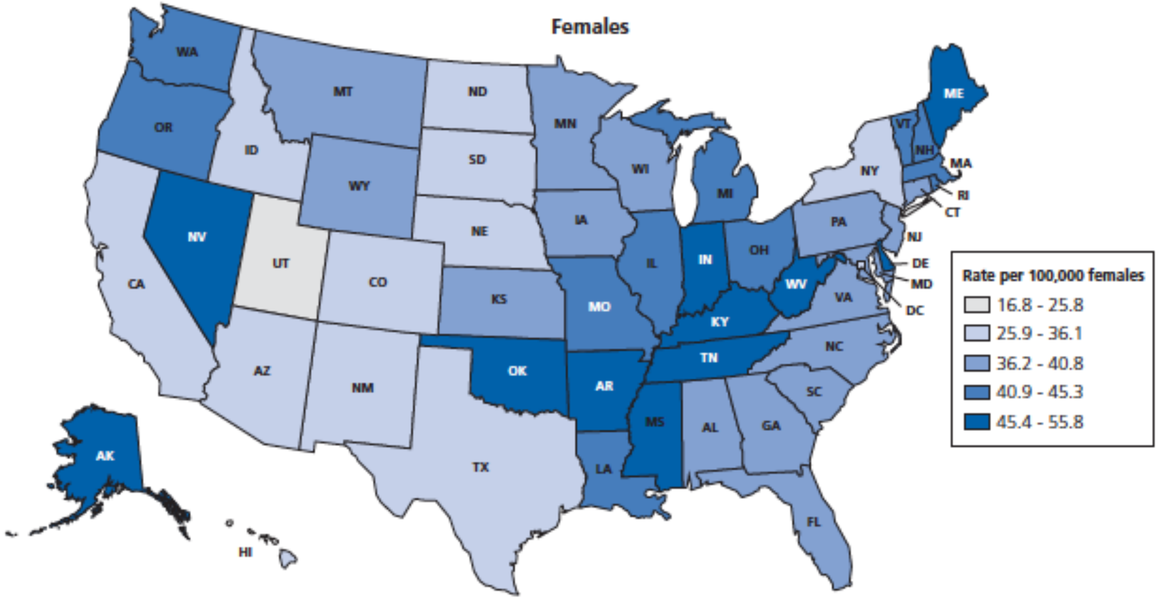
Incidence of Smoking vs Income



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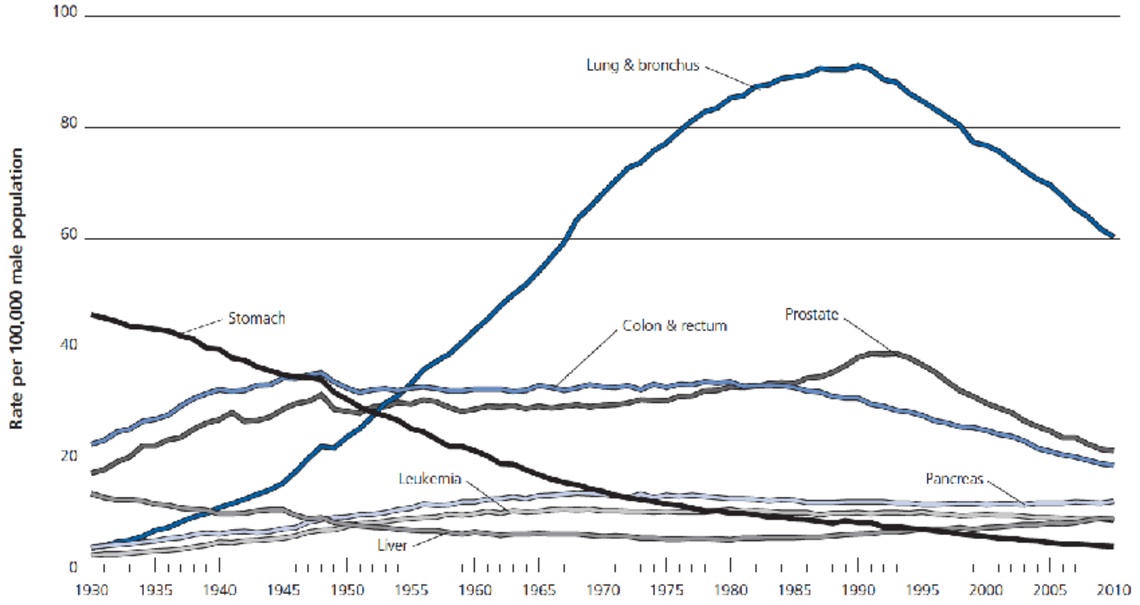
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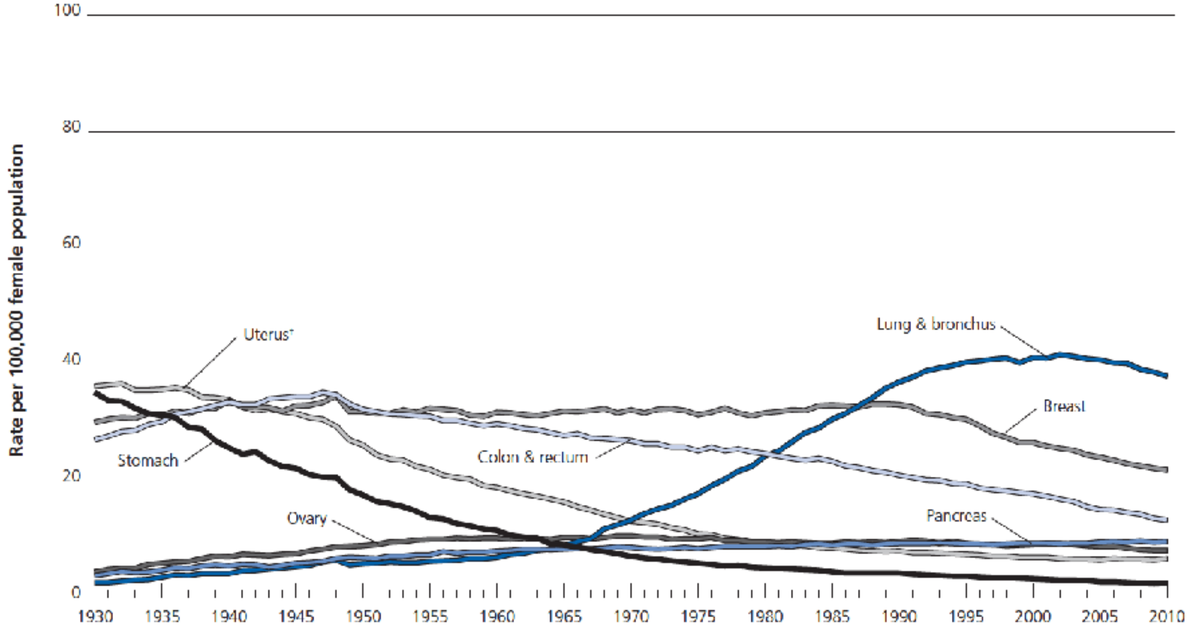


"Why is it you never ask me to stop smoking?"

Age-adjusted Cancer Death Rates*, Males by Site, US, 1930-2010



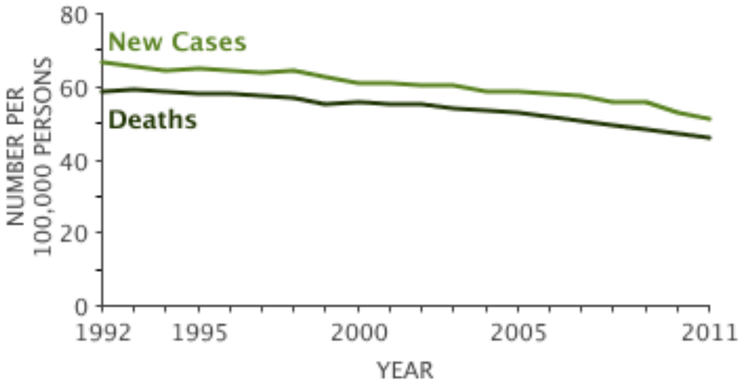
Age-adjusted Cancer Death Rates*, Females by Site, US, 1930-2010



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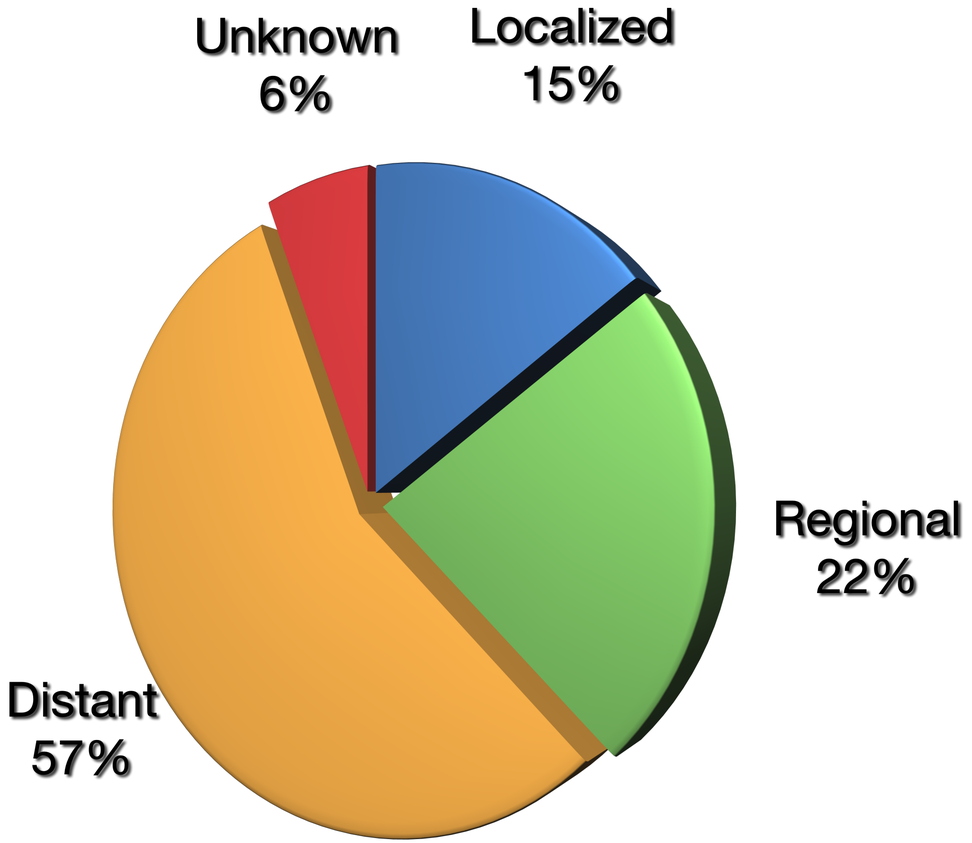
Estimated New Cases in 2014	224,210
% of All New Cancer Cases	13.5%
Estimated Deaths in 2014	159,260
% of All Cancer Deaths	27.2%



Percent Surviving 5 Years
16.8%
2004–2010

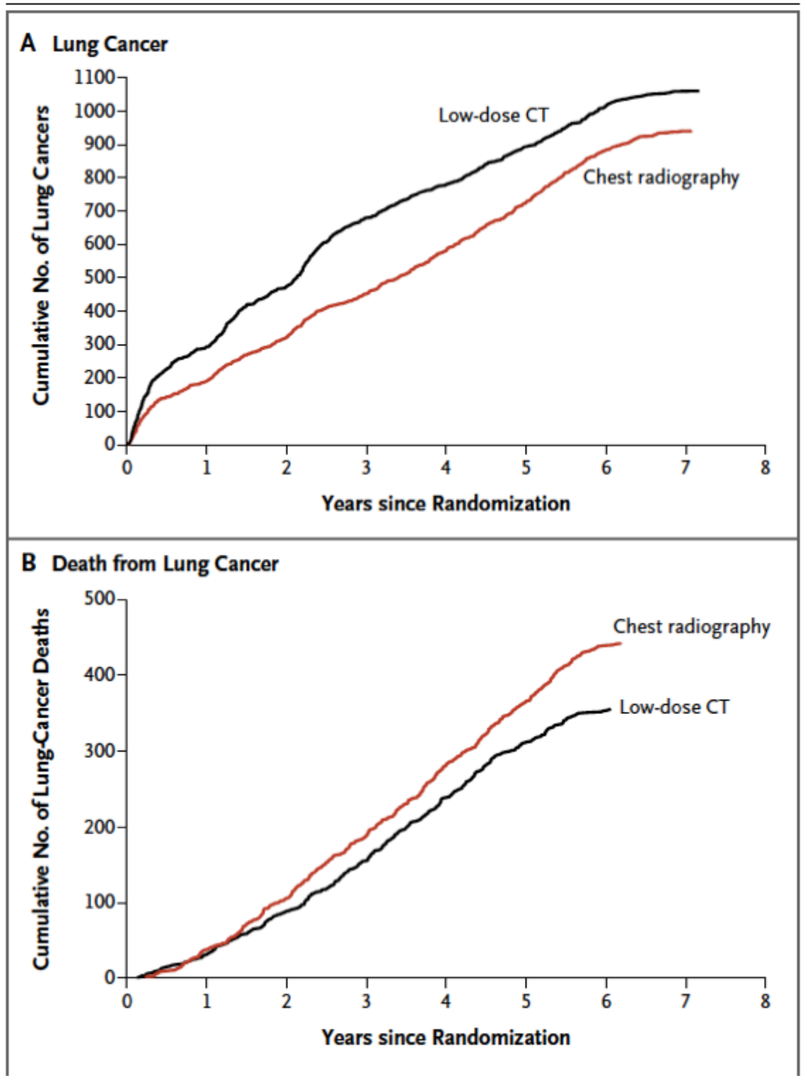
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A Lung Cancer
Cumulative No. of Lung Cancers
1100
1000
900
800
700
600
500
400
300
200
100
0
0 1 2 3 4 5 6 7 8
Years since Randomization
Low-dose CT
Chest radiography
B Death from Lung Cancer
Cumulative No. of Lung-Cancer Deaths
500
400
300
200
100
0
0 1 2 3 4 5 6 7 8
Years since Randomization
Chest radiography
Low-dose CT

AJCC 7th Edition Lung Cancer Staging

T Component		N0	N1	N2	N3	M1a[a] Any N	M1b[b] Any N
T1	T1a ≤2 cm	IA	IIA	IIIA	IIIB	IV	IV
	T1b >2 but ≤3 cm	IA	IIA	IIIA	IIIB	IV	IV
T2	T2a >3 but ≤5 cm	IB	IIA	IIIA	IIIB	IV	IV
	T2b >5 but ≤7 cm	IIA	IIB	IIIA	IIIB	IV	IV
T3	T3 >7 cm	IIB	IIIA	IIIA	IIIB	IV	IV
	T3 *Invasion*	IIB	IIIA	IIIA	IIIB	IV	IV
	T3 *Satellite*	IIB	IIIA	IIIA	IIIB	IV	IV
T4	T4 *Ipsilateral Nodule*	IIIA	IIIA	IIIB	IIIB	IV	IV
	T4 *Invasion*	IIIA	IIIA	IIIB	IIIB	IV	IV

AJCC 8th Edition Lung Cancer Staging

T Component[a]		N0	N1	N2	N3	M1a[b] Any N	M1b[c] Any N	M1c[d] Any N
T1	T1a ≤1 cm	IA1	IIB	IIIA	IIIB	IVA	IVA	IVB
	T1b >1-2 cm	IA2	IIB	IIIA	IIIB	IVA	IVA	IVB
	T1c >2-3 cm	IA3	IIB	IIIA	IIIB	IVA	IVA	IVB
T2	T2a *Central, Visceral Pleura*	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
	T2a >3-4 cm	IB	IIB	IIIA	IIIB	IVA	IVA	IVB
	T2b >4-5 cm	IIA	IIB	IIIA	IIIB	IVA	IVA	IVB
T3	T3 >5-7 cm	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
	T3 *Invasion*	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
	T3 *Satellite*	IIB	IIIA	IIIB	IIIC	IVA	IVA	IVB
T4	T4 >7 cm	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB
	T4 *Ipsilateral Nodule*	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB
	T4 Invasion	IIIA	IIIA	IIIB	IIIC	IVA	IVA	IVB

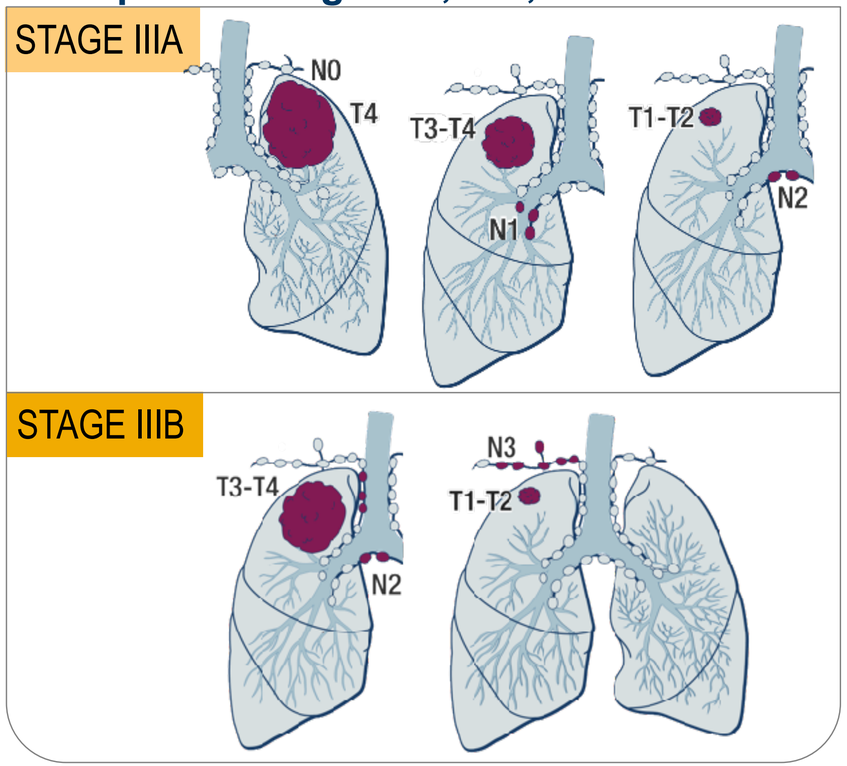
- T2b (>5 but ≤ 7 cm) and T3 (>7 cm) were reclassified as T3 and T4 respectively
- T3 N2 was upstaged from IIIA to IIIB
- T3-4 N3 was upstaged from IIIB to newly created IIIC

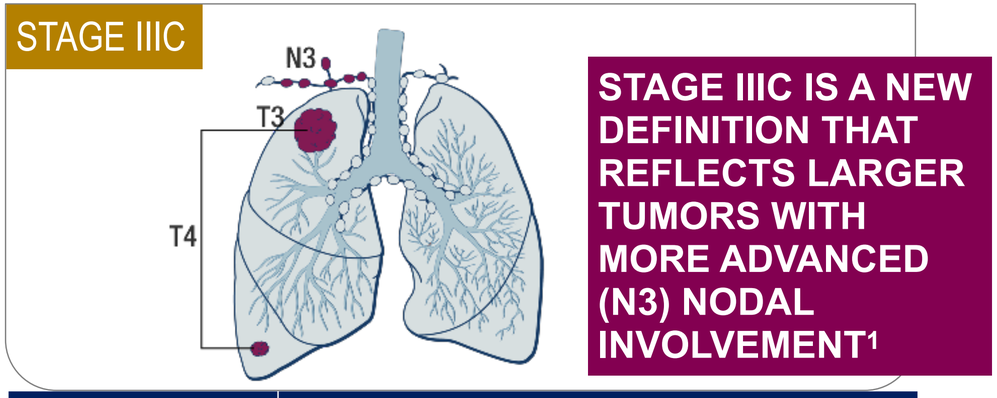
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Stage III Captures a Heterogeneous Range of Tumor Size and Nodal Involvement[1]

Examples of Stage IIIA, IIIB, and IIIC NSCLC[1]





STAGE IIIC IS A NEW DEFINITION THAT REFLECTS LARGER TUMORS WITH MORE ADVANCED (N3) NODAL INVOLVEMENT[1]

Extent of Primary Tumor	Involvement of Lymph Nodes[2,3,a,b]			
	N0	N1	N2	N3
T1	–	–	IIIA	IIIB
T2	–	–	IIIA	IIIB
T3	–	IIIA	IIIB	IIIC
T4	IIIA	IIIA	IIIB	IIIC
All positive nodes contralateral to the primary tumor are staged as N3				

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Overall Sensitivity/Specificity of Select Staging Methods

Staging Method	Sensitivity	Specificity
CT	50%-70%[a]	63%-86%[a]
PET-CT	50%-85%[a]	74%-93%[a]
Mediastinoscopy	≈78%	100%
Video mediastinoscopy	≈89%	100%
EBUS	≈89%	100%
EUS	≈89%	100%
Combination EUS/ EBUS	≈91%-100%[a]	100%

[a]**Approximate ranges based on published studies.**

Recent studies have shown that understaging of the mediastinal lymph nodes by CT and/or PET occurs in up to 20% of patients[8,9]

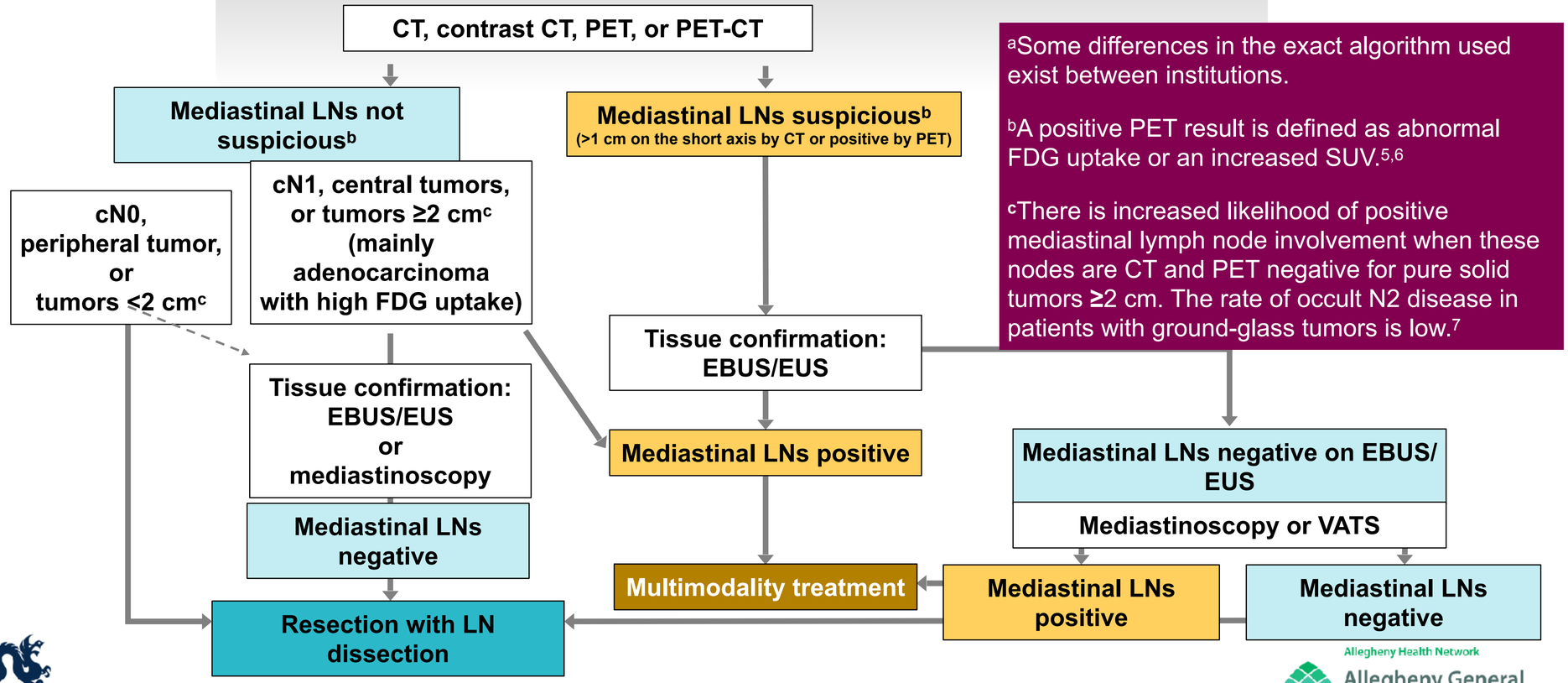
The use of invasive staging methods in patients with NSCLC is crucial for accurate staging, proper prognosis, and appropriate therapy selection[4]

The accuracy agreement between clinical and invasive staging is only 50%-60%, emphasizing the importance of complete staging using both

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Suggested Algorithm for Locoregional Lymph



[a]Some differences in the exact algorithm used exist between institutions.

[b]A positive PET result is defined as abnormal FDG uptake or an increased SUV.[5,6]

[c]There is increased likelihood of positive mediastinal lymph node involvement when these nodes are CT and PET negative for pure solid tumors ≥2 cm. The rate of occult N2 disease in patients with ground-glass tumors is low.[7]

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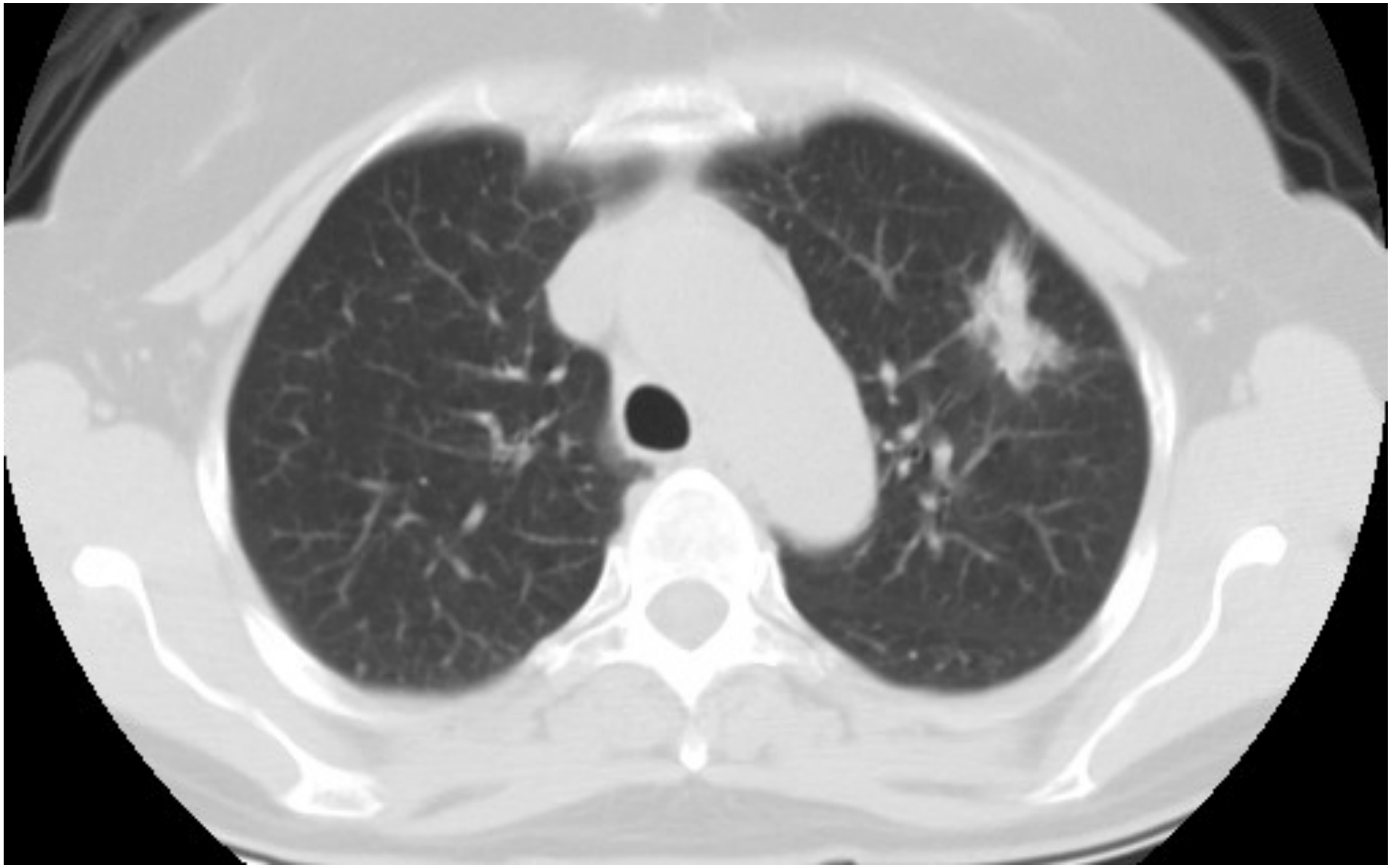
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Clinical Stage I by CT and PET

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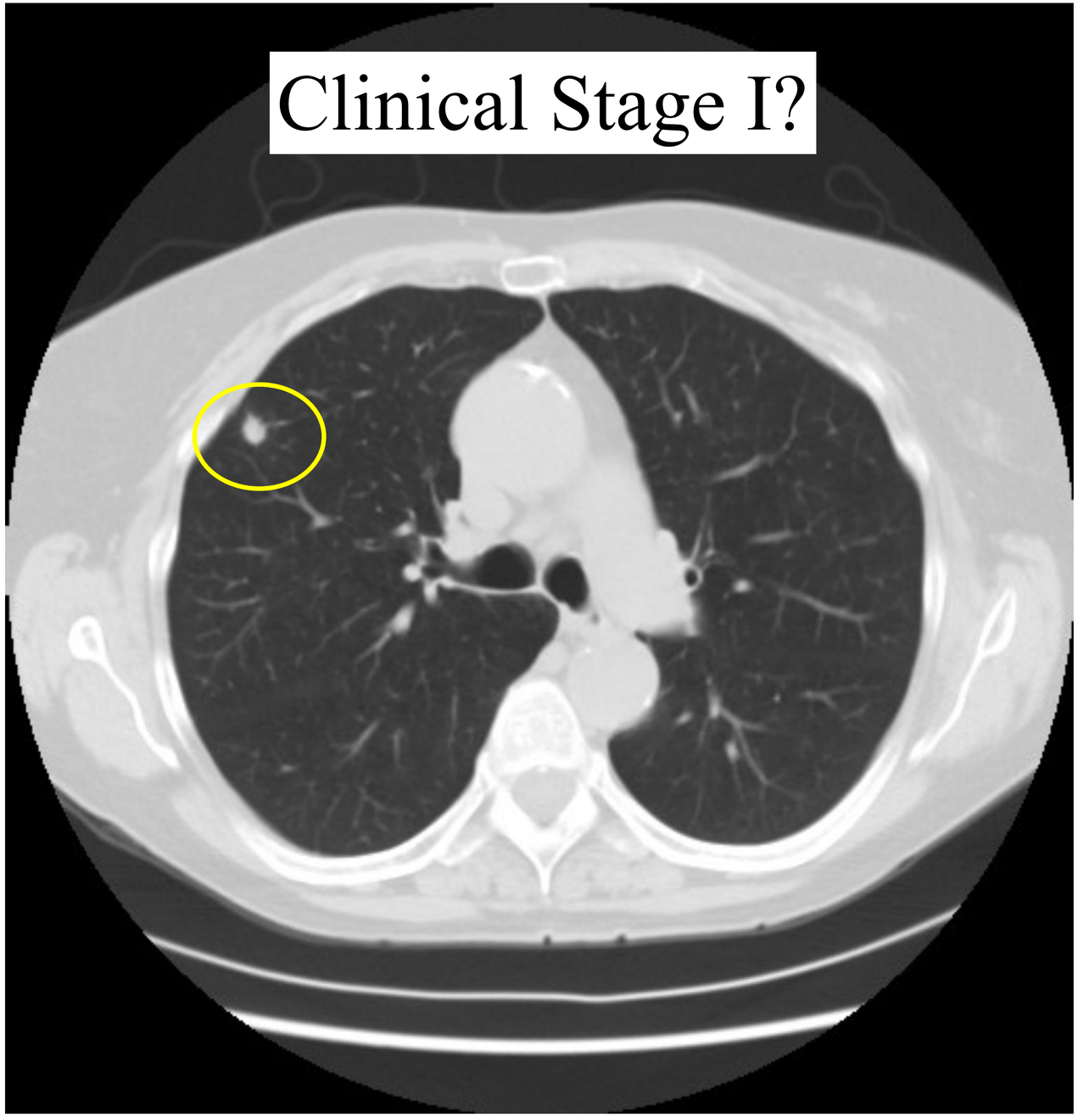
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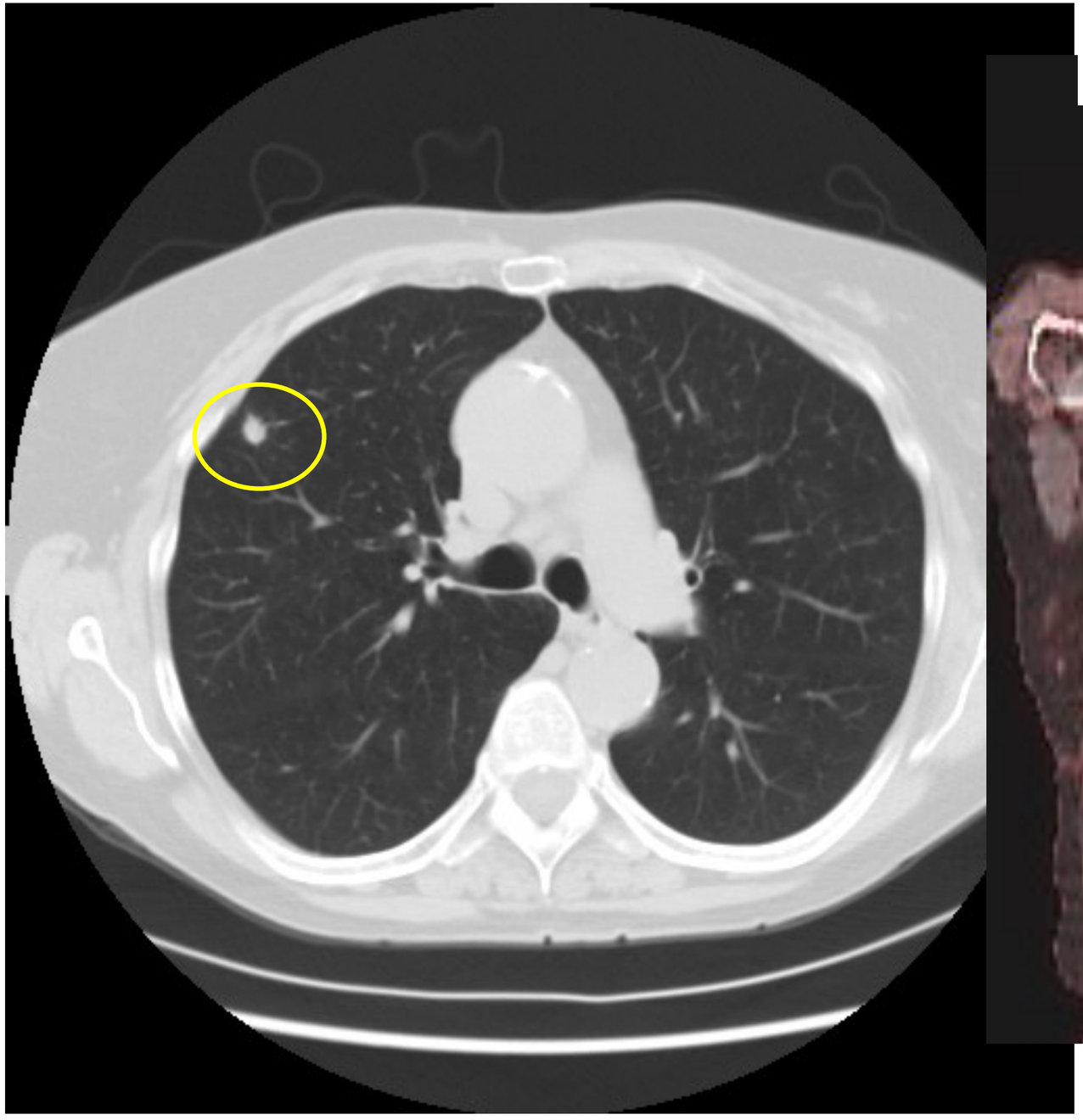
Stage IIIB (N3) at Mediastinoscopy

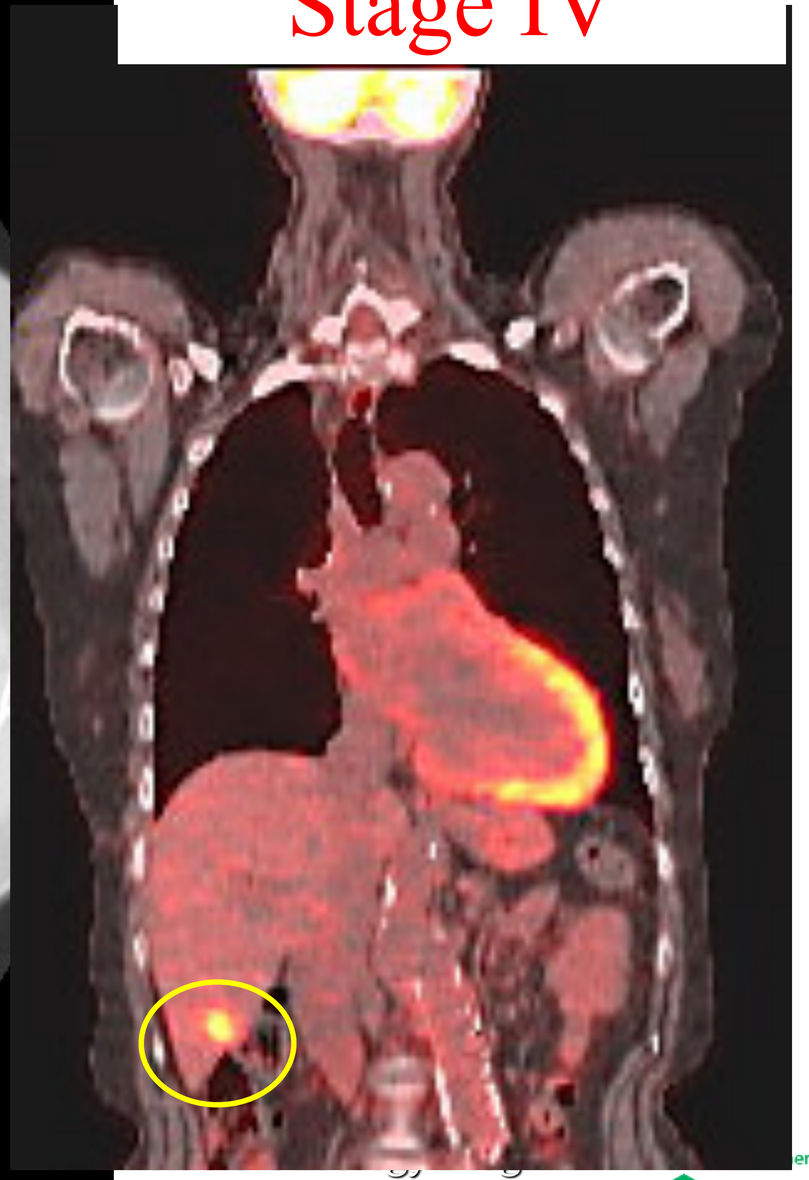
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Clinical Stage I?

Stage IV





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Results of Aggressive Lung Cancer Staging

- Reduction in inappropriate / incomplete resections of advanced lung cancer
- Identification of patients who require primary systemic therapy

  Reduction in unnecessary surgery for benign disease

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Lung Resection

1933 – 1st Pneumonectomy for NSCLC

The patients was a gynecologist from Pittsburgh practicing at AGH.
He outlived Dr. Graham by 30 years.

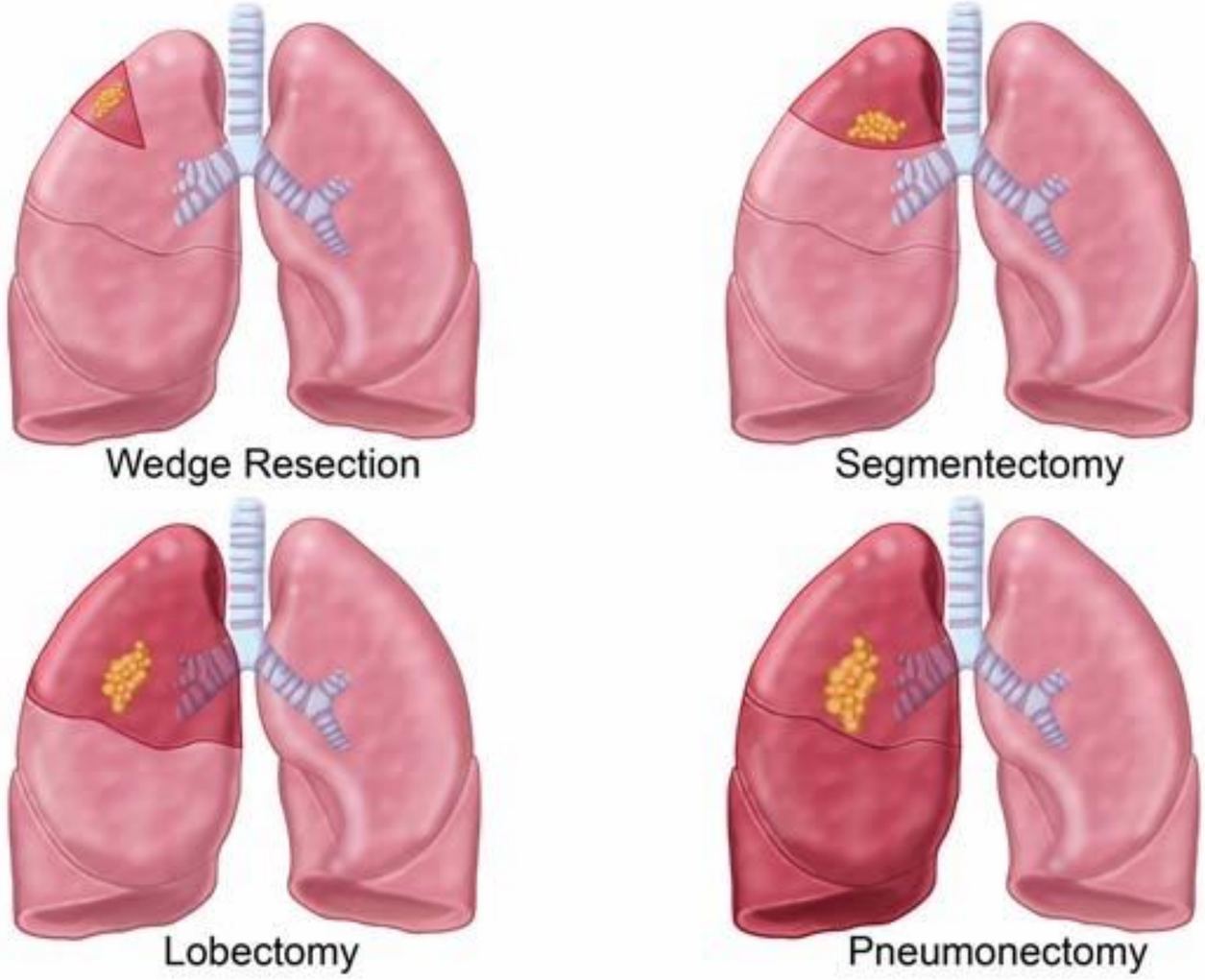


Evarts A. Graham

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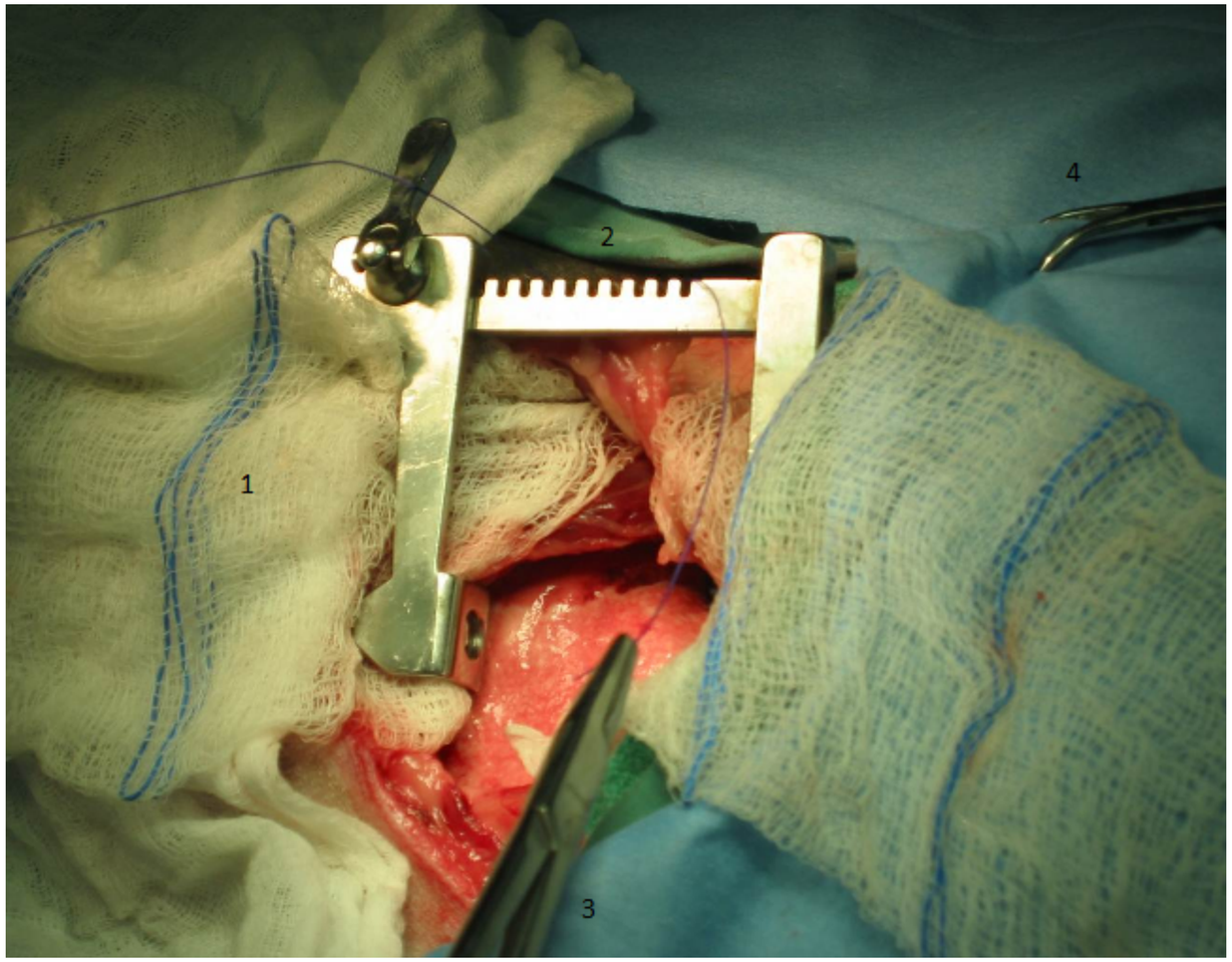
Lung Resections for Lung Cancer



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CleanOp with MOLNLYCKE



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Open Lobectomy Morbidity

Author	Year	n	Morbidity- Major (%)	Morbidity-Minor (%)	Mortality (%)
Nagasaki	1982	961	8	9	2
Keagy	1985	369	41	-	2.2
Deslauriers	1989	1076	19	9.8	3.2
LCSG	1994	783	21	27	3.8

Open Lobectomy Mortality

Study	Year	Study Type	n	Mortality (%)
Ginsberg et al. (LCSG)	1983	Retrospective	1058	2.9
Ginsberg et al (LCSG)	1995	Prospective, Randomized	125	1.6
Duque et al.	1997	Retrospective	294	4.4
Wada et al..	1998	Retrospective	5609	1.2
Thomas et al.	2002	Retrospective	390	2.3
Stoelben et al.	2003	Retrospective	699	2.7
Birkmeyer et al.	2003	Retrospective, National Database	75,563	4.2 (High Volume) 6.4 (Low Volume)
Deslauriers et al.	2004	Retrospective	184	1.6

Schuchert MJ et al. Surgery: Basic Science and Clinical Evidence, 2005

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Initial Experience With Video-Assisted Thoracoscopic Lobectomy

Thomas J. Kirby, MD, Michael J. Mack, MD, Rodney J. Landreneau, MD, and Thomas W. Rice, MD

Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio; Humana Hospital, Dallas, Texas; and Section of Thoracic Surgery, University of Pittsburgh, Pittsburgh, Pennsylvania

(Ann Thorac Surg 1993;56:1248–53)

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Video-Assisted Thoracic Surgery Lobectomy: Experience With 1,100 Cases

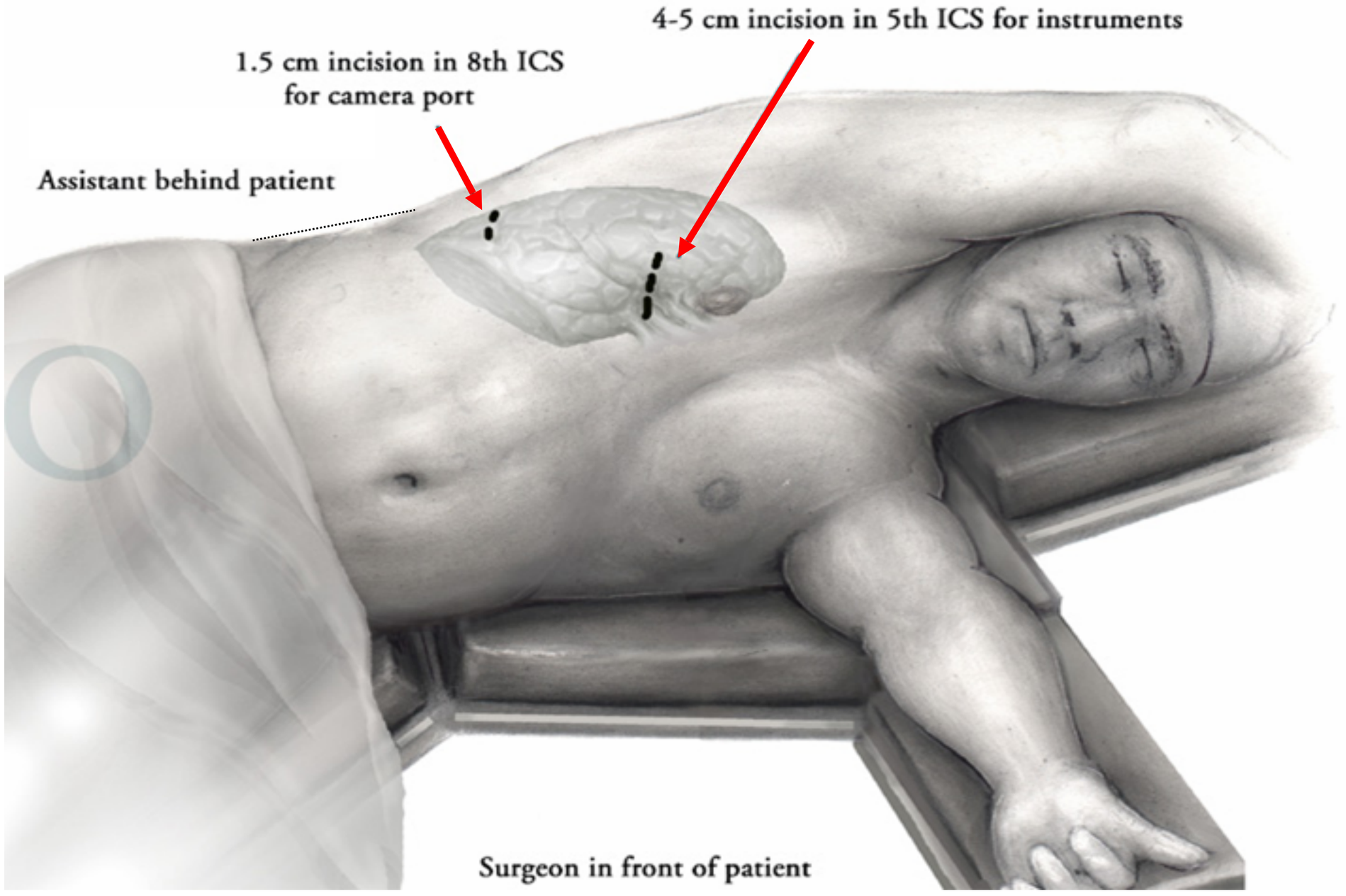
Robert J. McKenna, Jr, MD, Ward Houck, MD, and Clark Beeman Fuller, MD

Cedars Sinai Medical Center, Los Angeles, California

(Ann Thorac Surg 2006;81:421–6)

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4-5 cm incision in 5th ICS for instruments
1.5 cm incision in 8th ICS
for camera port
Assistant behind patient
Surgeon in front of patient

VATS Lobe Definition

- Anatomic resection of an entire lobe of a lung using a video camera
- No use of retractors
- Resection of lung and lymph node dissection as with thoracotomy (open procedure)
- Same oncologic principles
  - Individual vessel ligation
  - Complete node dissection

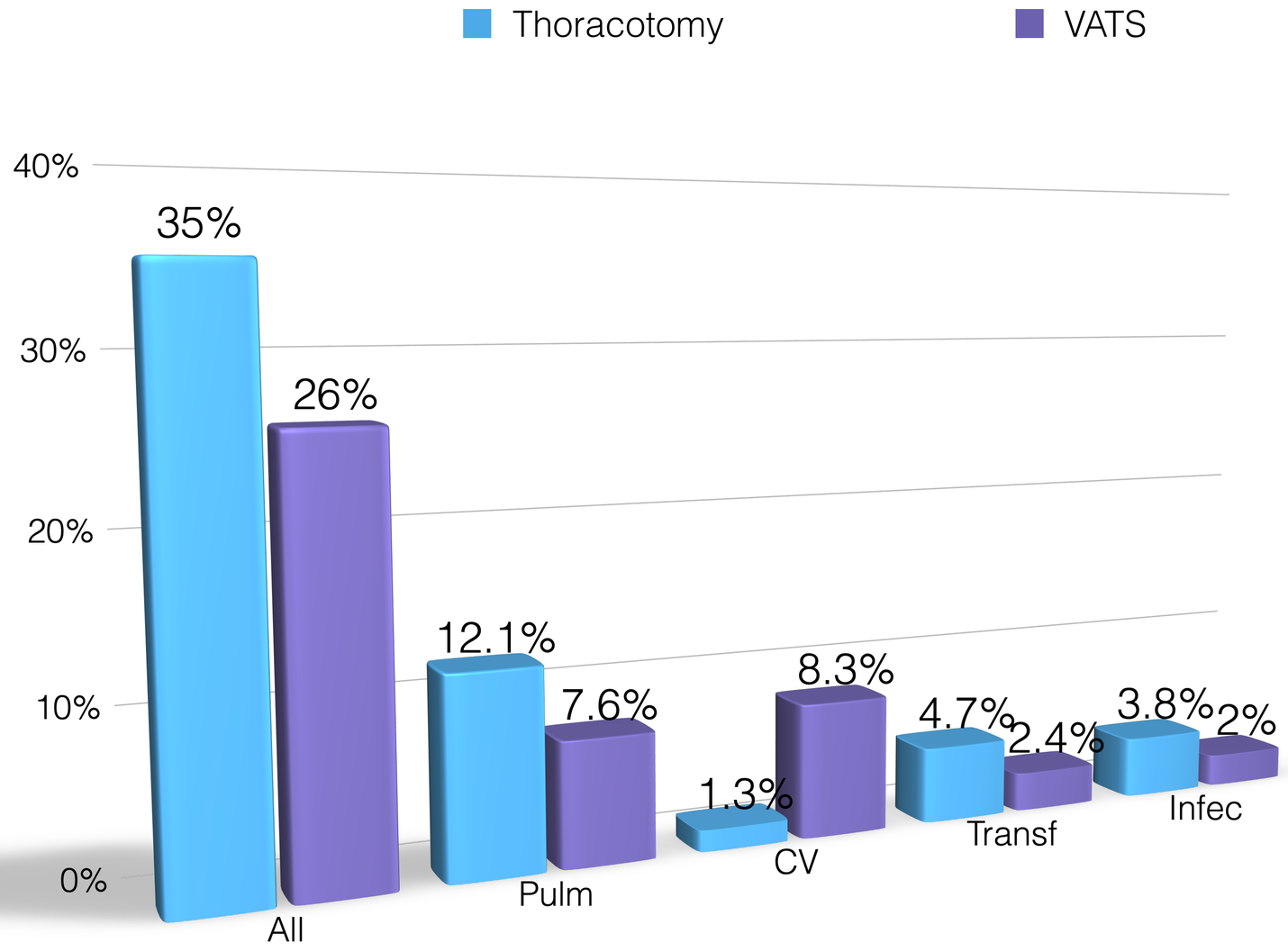
Thoracoscopic lobectomy is associated with lower morbidity than open lobectomy: A propensity-matched analysis from the STS database

Subroto Paul, MD,[a] Nasser K. Altorki, MD,[a] Shubin Sheng, PhD,[b] Paul C. Lee, MD,[a] David H. Harpole, MD,[c] Mark W. Onaitis, MD,[c] Brendon M. Stiles, MD,[a] Jeffrey L. Port, MD,[a] and Thomas A. D'Amico, MD[c]

JTCVS 2010; 139:366-378

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Petersen 2007

Compliance	VATS = 57	Open = 43	p
Time to chemo (days)	***58***	***54***	***ns***
Pts with delay doses	10 (18%)	25 (58%)	0.001
Pts with reduced doses	***15 (26%)***	***26 (49%)***	***0.02***
> 75% planned regimen	35 (61%)	17 (40%)	0.03

Thoracoscopic Lobectomy Has Increasing Benefit in Patients With Poor Pulmonary Function

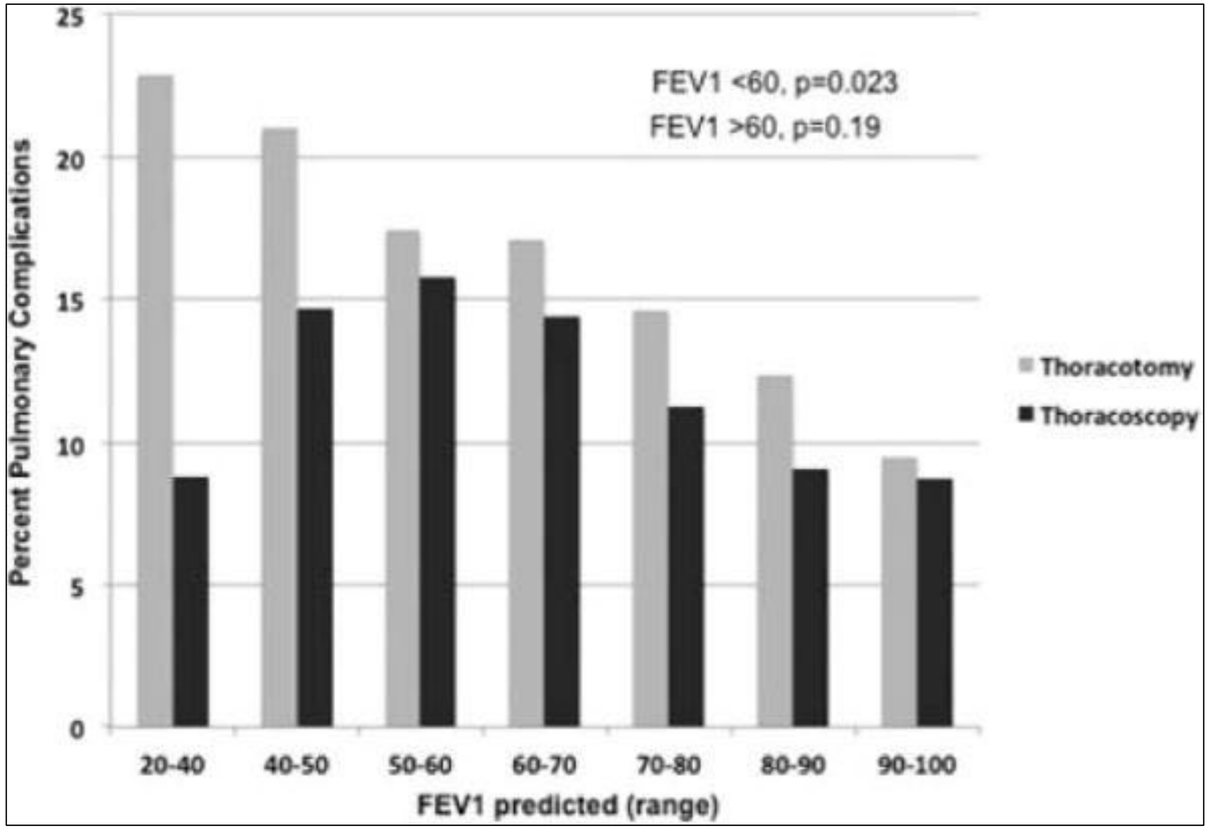
A Society of Thoracic Surgeons Database Analysis

DuyKhanh P. Ceppa, MD, Andrzej S. Kosinski, PhD,† Mark F. Berry, MD,* Betty C. Tong, MD,* David H. Harpole, MD,* John D. Mitchell, MD,‡ Thomas A. D'Amico, MD,* and Mark W. Onaitis, MD**

(*Ann Surg* 2012;256: 487–493)

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25
20
15
10
5
0
Percent Pulmonary Complications
FEV1 <60, p=0.023
FEV1 >60, p=0.19
Thoracotomy
Thoracoscopy
20-40
40-50
50-60
60-70
70-80
80-90
90-100
FEV1 predicted (range)

Available online at www.sciencedirect.com

ScienceDirect

EJSO 39 (2013) 957–963

EJSO
the Journal of Cancer Surgery

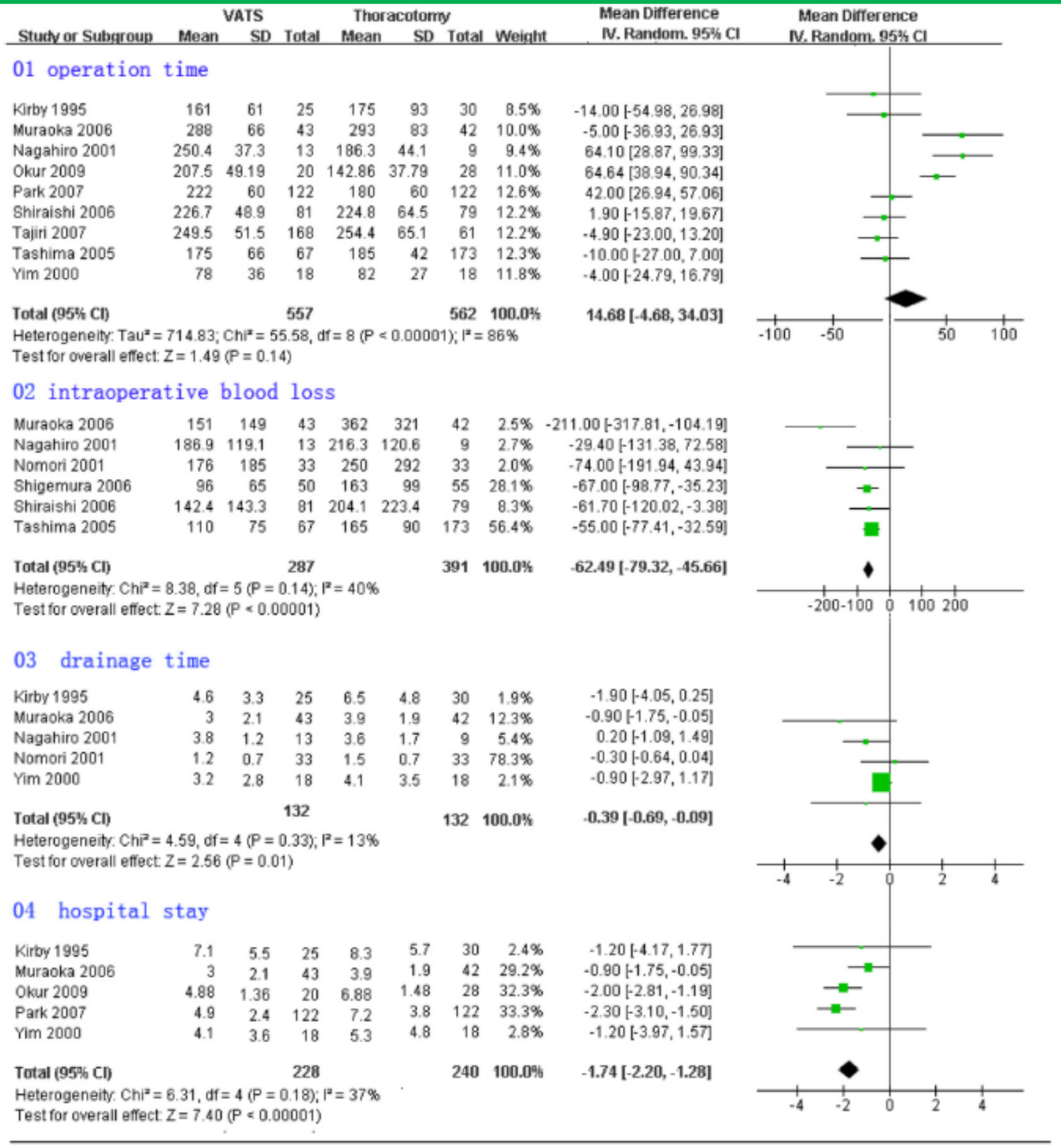
www.ejso.com

Video-assisted thoracoscopic surgery lobectomy versus open lobectomy in patients with clinical stage I non-small cell lung cancer: A meta-analysis

F.F. Chen, D. Zhang, Y.L. Wang, B. Xiong*

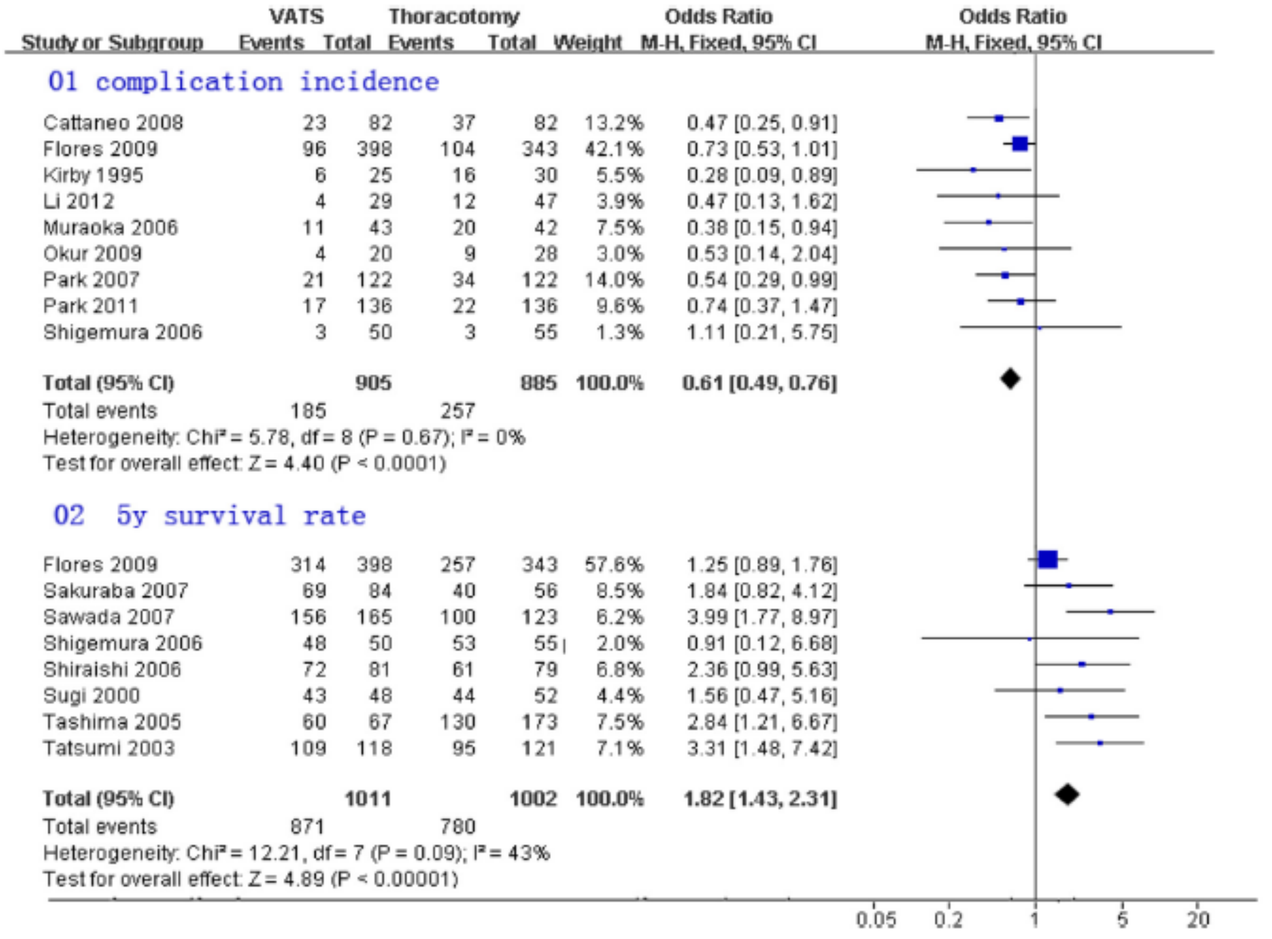
Department of Oncology, Zhongnan Hospital of Wuhan University, Hubei Cancer Clinical Study Center, Hubei Key Laboratory of Tumor Biological Behaviors, 430071 Wuhan, China

Accepted 17 June 2013
Available online 8 July 2013



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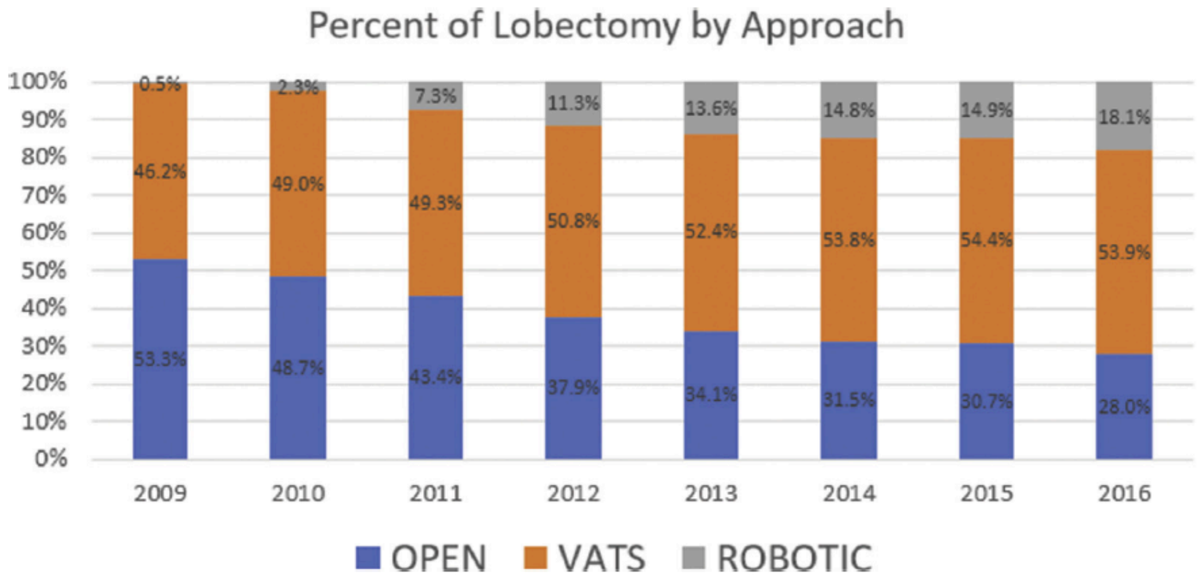
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Background

- The DaVinci robot may offers several advantages over VATS:
  - Superior optics
  - 3 dimensional imaging
  - Endowrists with 7 degrees of freedom
  - Scaled motion and tremor control
  - Ambidexterity

Background

- Other possible advantages:
  - Less pain?
  - Ability to do more advanced cases?
- Clinical outcome not improved compared to VATS
  - Higher costs



Ann Thorac Surg 2019, 109:1013-20

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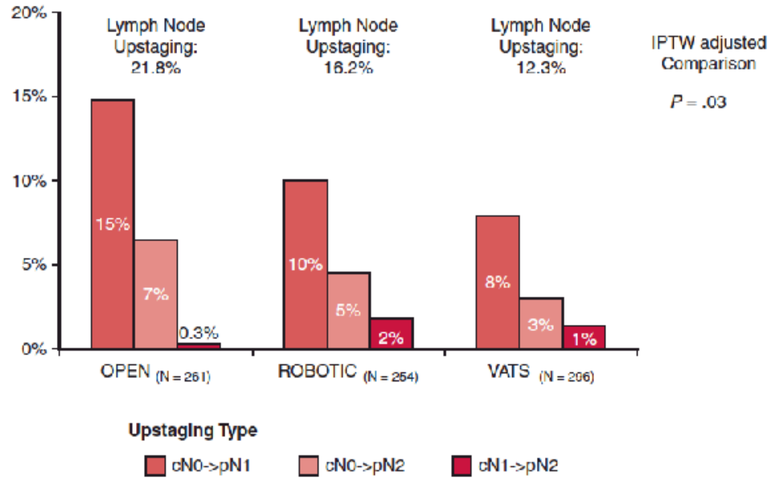
Advantages of Sublobar Resection

- Better residual pulmonary function
- Improved quality of life
- Less pulmonary complications

Propensity-score adjusted comparison of pathologic nodal upstaging by robotic, video-assisted thoracoscopic, and open lobectomy for non–small cell lung cancer

Check for updates

Peter J. Kneuertz, MD,[a] Danjouma H. Cheufou, MD,[b] Desmond M. D'Souza, MD,[a]
Khaled Mardanzai, MD,[b] Mahmoud Abdel-Rasoul, MS, MPH,[c] Dirk Theegarten, MD,[d]
Susan D. Moffatt-Bruce, MD, PhD, MBA,[a] Clemens Aigner, MD, MBA,[b] and Robert E. Merritt, MD[a]



J Thorac Cardiovasc Surg 2019; 158:1457-66

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Table 3. Postoperative Morbidity

Variable	Overall N = 13,598	Robotic N = 1,220	VATS N = 12,378	*p* Value
Air leak >5 days	1,334 (9.8%)	122 (10.0%)	1,212 (9.8%)	0.8135
Atelectasis requiring bronchoscopy	391 (2.9%)	31 (2.5%)	360 (2.9%)	0.4625
Pneumonia	442 (3.3%)	33 (2.7%)	409 (3.3%)	0.2596
Adult respiratory distress syndrome	61 (0.4%)	2 (0.2%)	59 (0.5%)	0.1187
Respiratory failure	119 (1.9%)	16 (1.9%)	103 (1.9%)	0.9971
Bronchopleural fistula	42 (0.3%)	7 (0.6%)	35 (0.3%)	0.0808
Pulmonary embolus	62 (0.5%)	4 (0.3%)	58 (0.5%)	0.4858
Pneumothorax requiring CT reinsertion	474 (3.5%)	51 (4.2%)	423 (3.4%)	0.1697
Initial ventilatory support >48 hours	50 (0.4%)	6 (0.5%)	44 (0.4%)	0.4535
Reintubation	308 (2.3%)	25 (2.0%)	283 (2.3%)	0.5928
Tracheostomy	99 (0.7%)	9 (0.7%)	90 (0.7%)	0.9688
Atrial arrhythmia requiring treatment	1,346 (9.9%)	125 (10.2%)	1,221 (9.9%)	0.6840
Deep venous thrombosis	52 (0.4%)	5 (0.4%)	47 (0.4%)	0.8722
Empyema requiring treatment	50 (0.4%)	6 (0.5%)	44 (0.4%)	0.4546
Chylothorax requiring medical intervention	64 (0.5%)	4 (0.3%)	60 (0.5%)	0.4435
Unexpected admission to intensive care unit	452 (3.3%)	36 (3.0%)	416 (3.4%)	0.4547
Myocardial infarction	42 (0.3%)	5 (0.4%)	37 (0.3%)	0.5069
Recurrent laryngeal nerve Paresis/paralysis	26 (0.2%)	2 (0.2%)	24 (0.2%)	0.8177
Required reoperation for bleeding	65 (0.9%)	3 (0.8%)	62 (0.9%)	0.8449

CT = chest tube; VATS = video-assisted thoracoscopic surgery.

Ann Thorac Surg 2016; 102:917-24

Long-term Survival Based on the Surgical Approach to Lobectomy For Clinical Stage I Nonsmall Cell Lung Cancer

Comparison of Robotic, Video-assisted Thoracic Surgery, and Thoracotomy Lobectomy

Hao-Xian Yang, MD,† Kaitlin M. Woo, MS,‡ Camelia S. Sima, MD, MS,‡ Manjit S. Bains, MD,*§ Prasad S. Adusumilli, MD,*§ James Huang, MD, MS,*§ David J. Finley, MD,*§ Nabil P. Rizk, MD, MS,*§ Valerie W. Rusch, MD,*§ David R. Jones, MD,*§ and Bernard J. Park, MD*§*

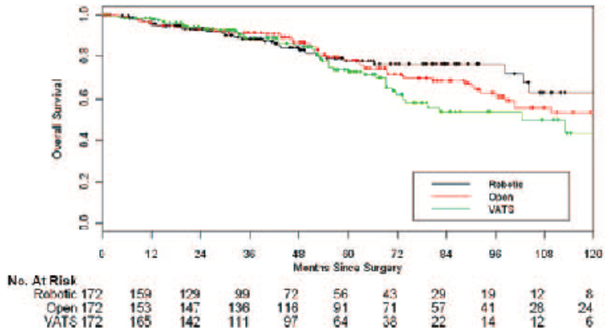


FIGURE 1. Overall survival in the matched cohort (N = 516), by surgical approach (VATS vs robotic, $P = 0.10$; open vs robotic, $P = 0.53$).

Ann Thorac Surg 2017; 265:431-437

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TABLE 4. Surgery-related and Postoperative Outcomes of the Propensity Score-matched Groups (N = 470)

Characteristics	Approach			*P*
	Robotic (n = 172)	VATS (n = 141)	Open (n = 157)	
Mortality	0	1 (1)	0	0.30
LOS, d, median (range)	4 (1–32)	4 (2–50)	5 (2–29)	<0.001
Conversion to open	16 (9)	8 (6)	—	0.32
Conversion for bleeding	3	0	—	
Conversion for other reasons	13*	8†	—	
Sampled LN stations, median (range)	5 (0–8)	3 (0–7)	4 (1–8)	<0.001
Cases with complications	51 (29.7)	35 (24.8)	47 (29.9)	0.55
Resection completeness				0.99
R0	170 (99)	141 (100)	157 (100)	
R1	2 (1)	0	0	
Pathologic type				0.82
Adenocarcinoma	19 (11)	23 (16)	22 (14)	
Squamous cell carcinoma	91 (53)	69 (49)	73 (46)	
Carcinoid	39 (23)	30 (21)	40 (25)	
Other	23 (13)	19 (13)	22 (14)	
Pathologic N category				0.64
N0	145 (84)	121 (86)	137 (87)	
N1	20 (12)	14 (10)	11 (7)	
N2	7 (4)	6 (4)	9 (6)	
Pathologic stage				0.13
0-I‡	133 (77)	114 (81)	135 (86)	
II	29 (17)	21 (15)	12 (8)	
III/IV§	10 (6)	6 (4)	10 (6)	

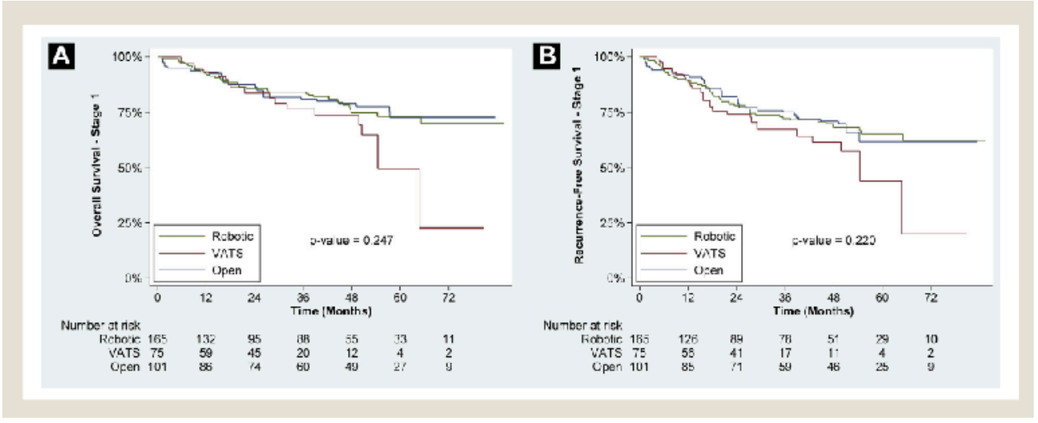
Ann Thorac Surg 2017; 265:431-437

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Long-Term Oncologic Outcomes After Robotic Lobectomy for Early-stage Non–Small-cell Lung Cancer Versus Video-assisted Thoracoscopic and Open Thoracotomy Approach

Peter J. Kneuertz,[1] Desmond M. D'Souza,[1] Morgan Richardson,[1] Mahmoud Abdel-Rasoul,[2] Susan D. Moffatt-Bruce,[1] Robert E. Merritt[1]



Clinical Lung Cancer, Vol. 21, No. 3, 214-24 © 2019

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“The Americans have need of the telephone, but we do not. We have plenty of messenger boys.”
William Preece, British Postal Office 1876

“The horse is here to stay but the automobile is only a novelty — a fad.”
1903 George Peck, president of the Michigan Saving Bank

“Remote shopping, while entirely feasible, will flop.”
1966 Time Magazine

Robotic pulmonary lobectomy The future and probably should remain so
Scott J. Swanson
J Thorac Cardiovasc Surg 2010;140:954-
DOI: 10.1016/j.jtcvs.2010.07.025

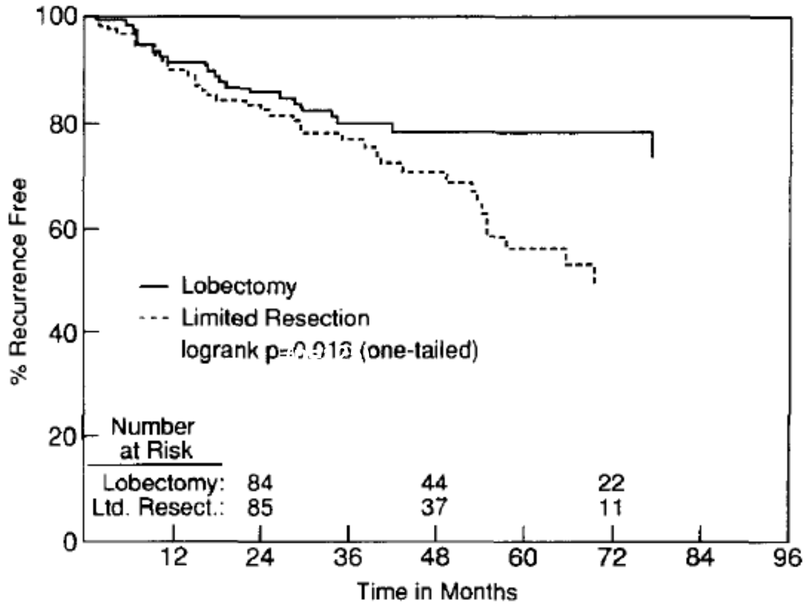
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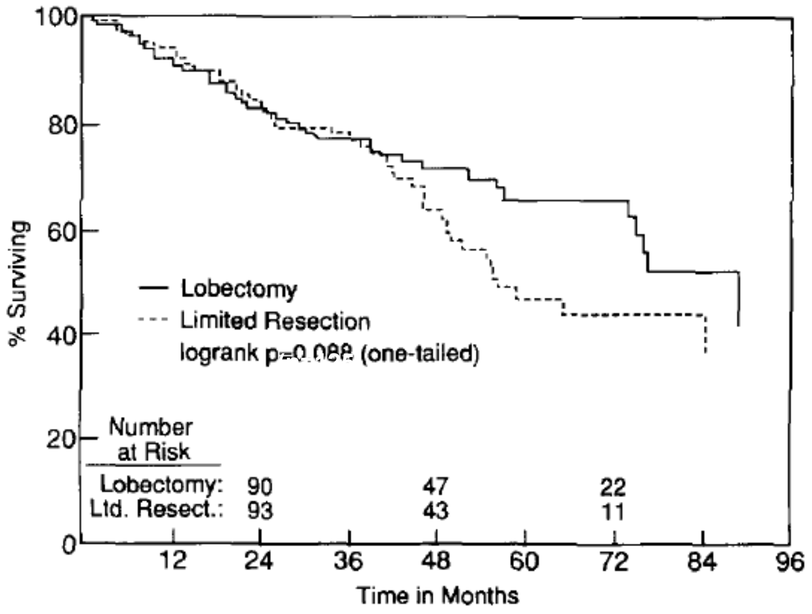
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Randomized Trial of Lobectomy Versus Limited Resection for T1 N0 Non–Small Cell Lung Cancer

Lung Cancer Study Group (Prepared by Robert J. Ginsberg, MD, and Lawrence V. Rubinstein, PhD)

(Ann Thorac Surg 1995;60:615–23)





- **Increased risk of locoregional recurrence (17.2% vs. 6.4%)**
- **Equivalent survival compared with lobectomy**

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Effect of tumor size on prognosis in patients with non–small cell lung cancer: The role of segmentectomy as a type of lesser resection

Morihito Okada, MD, PhD
Wataru Nishio, MD, PhD
Toshihiko Sakamoto, MD, PhD
Kazuya Uchino, MD
Tsuyoshi Yuki, MD
Akio Nakagawa, MD
Noriaki Tsubota, MD, PhD

J Thorac Cardiovasc Surg 2005;129:87-93

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Lobectomy vs. Sublobar Resection

5 Year Cancer Specific Survival “Stage I”

TUMOR SIZE	Segmental Resection	Lobectomy	Wedge Resection
20 mm or less	96.7	92.4	85.7
20-30 mm	84.6	87.4	39.4
More than 30 mm	62.9	81.3	0

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Lobectomy vs. Segmental Resection

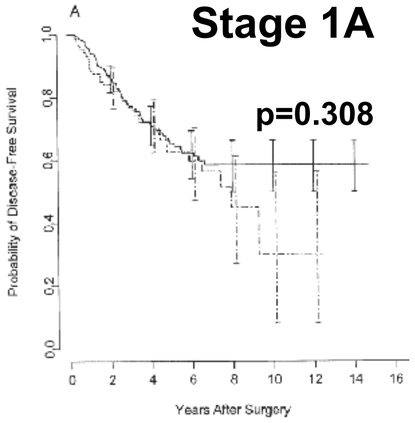
Tumor size is an important prognostic factor affecting planning of surgical treatment

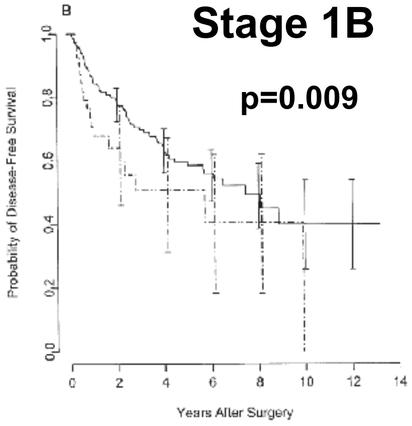
Sublobar resection appears to be an acceptable treatment for patients with a tumor of 20 mm or less in diameter.

Complete intra-operative lymph node staging is important to accurately classify stage and predict results

Outcomes of Sublobar Resection Versus Lobectomy for Stage I Non–Small Cell Lung Cancer: A 13-Year Analysis

Amgad El-Sherif, MD, William E. Gooding, MS, Ricardo Santos, MD, Brian Pettiford, MD, Peter F. Ferson, MD, Hiran C. Fernando, MD, Susan J. Urda, BS, James D. Luketich, MD, and Rodney J. Landreneau, MD (Ann Thorac Surg 2006;82:408–16)







- n=784 (1990-2003)
- Median follow-up = 31 mos

* No significant difference in recurrence or survival for Stage 1A disease

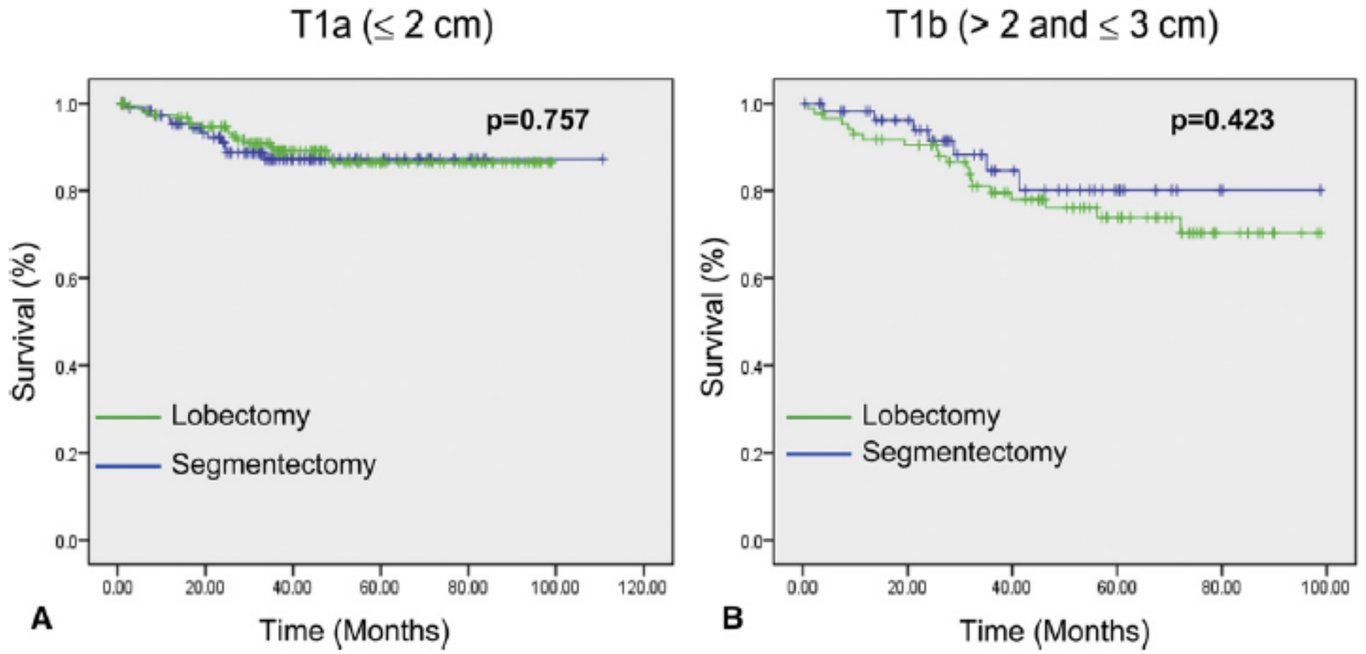
Table 3. Disease Recurrences

Recurrence	Lobar Resection	Sublobar Resection
Disease-free	415 (71.9%)[a]	147 (71.0%)
Local	24 (4.2%)	15 (7.2%)
Regional	22 (3.8%)	14 (6.8%)
Distant	116 (20.0%)	31 (15.0%)
Total	577	207

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Recurrence Free Survival



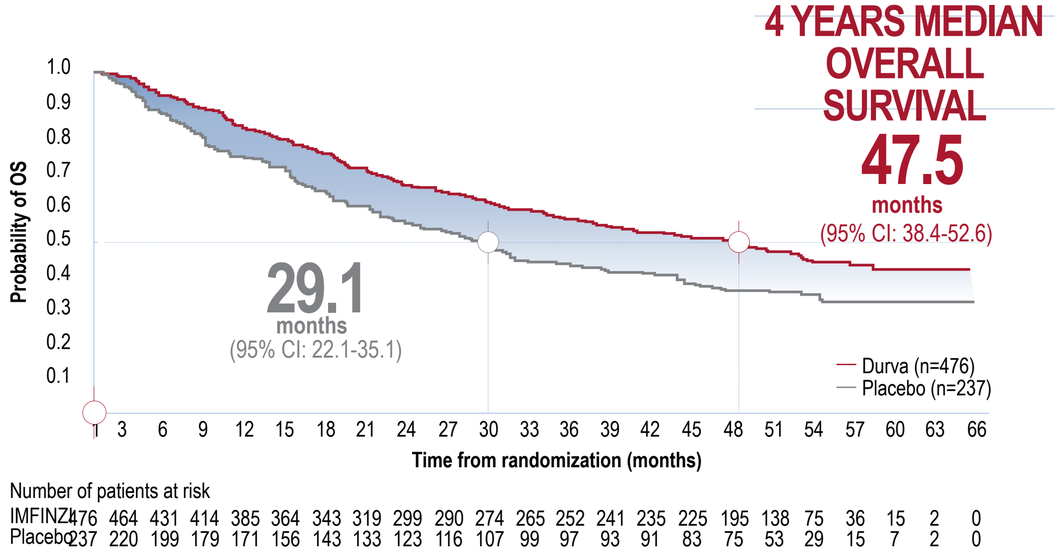
Carr et al, JTCVS 2012; 143:390-7

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- Small Tumors: < 2 cm in diameter
- Confined to a discrete segmental boundary
- Peripheral location (outer 1/3)
- Pathologic Margin > 1 cm (Margin/Tumor ratio>1)
- Elderly (Age >80)
- Marginal pulmonary function (FEV1/DLCO < 60%)
- Ground glass opacities – Adenocarcinoma in situ
- Prior lung resection
- Metastases

4-YEAR OVERALL SURVIVAL UPDATE



4-Year OS Update	Median OS, months (95% CI)
DURVA (n=476)	47.5 (38.4-52.6)
Placebo (n=237)	29.1 (22.1-35.1)

- Updated post-hoc OS analysis at ≈4 years after randomization
- **29%** reduction in risk of death vs placebo (HR=0.71; 95% CI: 0.57-0.88)
- 4 years OS rate was 50% with IMFINZI vs 36%
  with placebo

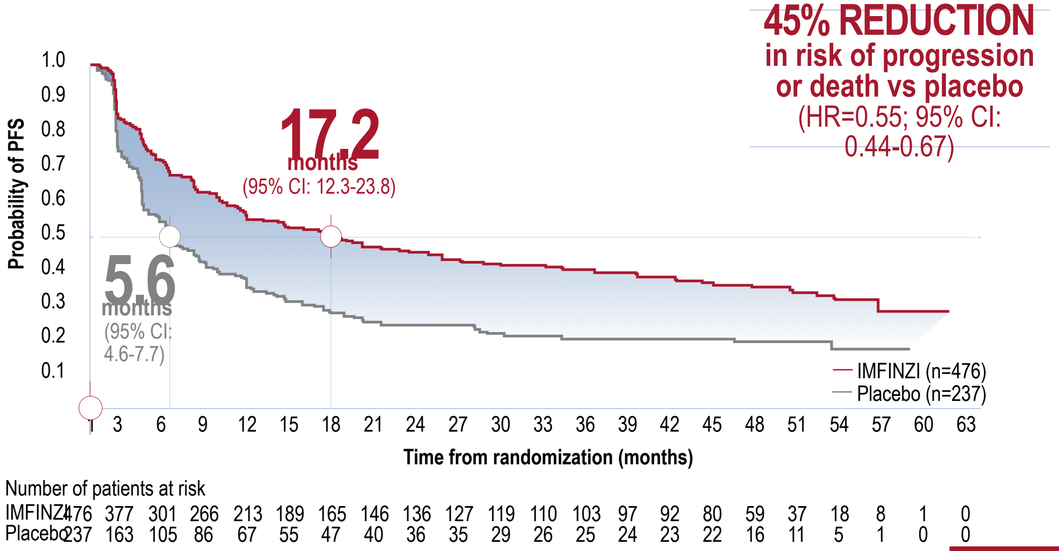
Primary 2-Year OS Analysis[2,3]
(25.2 months median follow-up)[b]

- **32% reduction in the risk of death vs placebo (HR=0.68; *P*=0.0025)[c]**
- **Median OS not reached with IMFINZI vs 28.7 months with placebo[d]**

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Allegheny General Hospital

4-YEAR PROGRESSION-FREE SURVIVAL UPDATE



4-Year PFS Update	Median PFS, months (95% CI)
Durva (n=476)	17.2 (12.3-23.8)
Placebo (n=237)	5.6 (4.6-7.7)

- Updated post-hoc PFS analysis at ≈4 years after randomization
- **45%** reduction in the risk of progression or death vs placebo (HR=0.55; 95% CI: 0.44-0.67)
- 4-year PFS rate was 35% with IMFINZI vs 20% with placebo

Primary PFS Analysis[2,3]
(14.5 months median follow-up)

- **48% reduction in the risk of progression or death vs placebo (HR=0.52; *P*<0.0001)[b]**
- **Median PFS: 16.8 months with IMFINZI vs 5.6 months with placebo[c]**

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Key inclusion criteria:

- Confirmed primary nonsquamous Stage IB, II, IIIA NSCLC (AJCC 7th edition)
- Complete tumor resection, with or without prior adjuvant chemotherapy
- EGFR exon 19 deletions or exon 21 L858R mutation-positive NSCLC
- MRI or CT scan of the brain prior to surgery or randomization
- Maximum interval between surgery and randomization:

Stratification by:
- Stage (IB vs II vs IIIA)
- EGFR mutation (exon 19 deletion vs L858R mutation)
- Race (Asian vs non-Asian)

TAGRISSO
80 mg, once daily
(n=339)

Randomization
1:1
(N=682)

Placebo, once daily
(n=343)

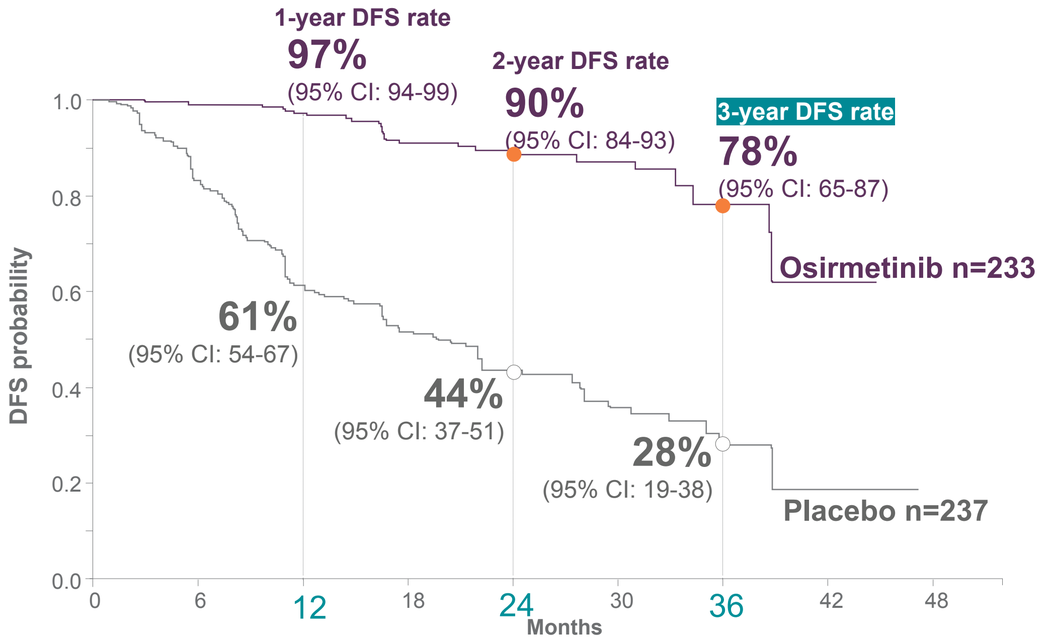
Treatment duration: **3 years**

Treatment continues until:
- Disease recurrence
- Treatment completed
- Discontinuation criterion met

Follow-up:
- Until recurrence: Weeks 12 and 24, then every 24 weeks to 5 years, then yearly
- After recurrence: Every 24 weeks for 5 years, then yearly

Endpoints
- **Primary**: DFS by investigator assessment in Stages II-IIIA
- **Secondary**: DFS in the overall population (Stages IB-IIIA), OS, HRQoL, safety

Primary Endpoint: DFS in Patients With Stage II/IIIA Disease[1-3]



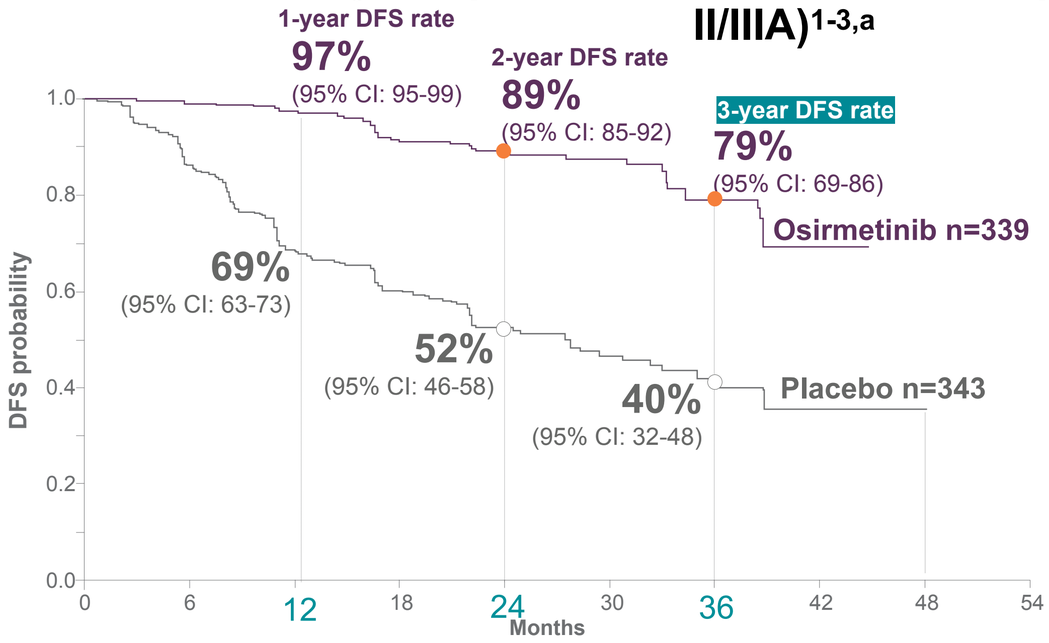
Median DFS, months (95% CI)	
Osirmetinib	NR (38.8-NE)
Placebo	19.6 (16.6-24.5)
HR (95% CI)	**0.17 (0.12-0.23); *P*<0.0001**

- Patients in the ADAURA trial are treated with oral Osirmetinib for 3 years or until disease recurrence or unacceptable toxicity[1]

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Secondary Endpoint: DFS in the Overall Population (Stage IB/II/IIIA)[1-3,a]



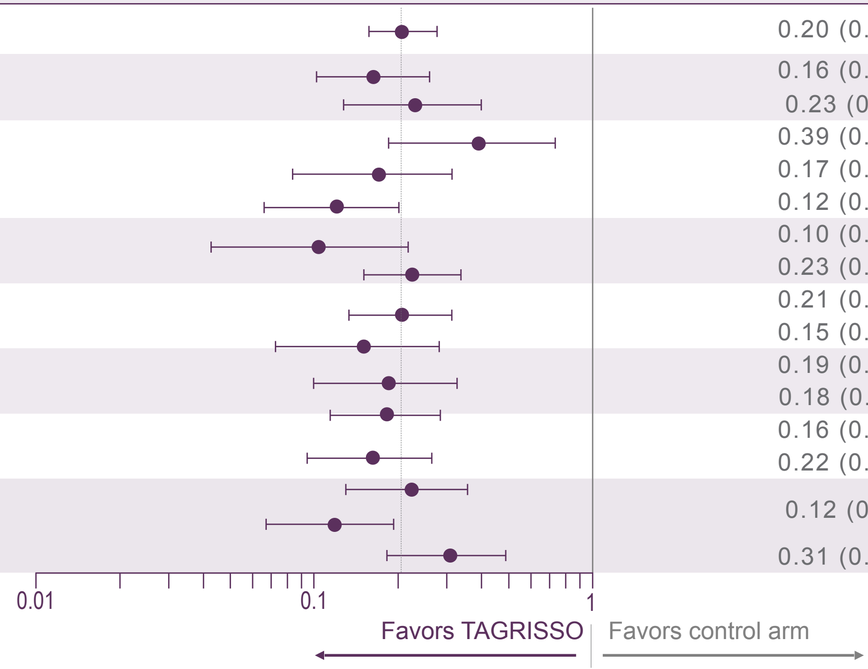
Median DFS, months (95% CI)	
Osirmetinib	NR (NE-NE)
Placebo	27.5 (22.0-35.0)
HR (95% CI)	**0.20 (0.15-0.27); *P*<0.0001**

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Consistent DFS Results Were Observed Across All Predefined Patient Subgroups in the ADAURA Study

Subgroup	Hazard Ratio for Disease Recurrence or Death (95% CI)
Overall (N=682)	Stratified log-rank: 0.20 (0.15-0.27)
Adjuvant chemotherapy	Yes (n=410): 0.16 (0.10-0.26)
	No (n=272): 0.23 (0.13-0.4)
Stage	Stage IB (n=212): 0.39 (0.18-0.76)
	Stage II (n=236): 0.17 (0.08-0.31)
	Stage IIIA (n=234): 0.12 (0.07-0.20)
Smoking status	Smoker (n=194): 0.10 (0.04-0.22)
	Nonsmoker (n=488): 0.23 (0.15-0.34)
Race	Asian (n=434): 0.21 (0.13-0.31)
	Non-Asian (n=248): 0.15 (0.07-0.28)
Sex	Male (n=204): 0.19 (0.10-0.33)
	Female (n=478): 0.18 (0.11-0.28)
Age	<65 (n=380): 0.16 (0.09-0.26)
	≥65 (n=302): 0.22 (0.13-0.36)
EGFRm	Exon 19 deletion (n=378): 0.12 (0.07-0.2)
	L858R mutation (n=304): 0.31 (0.18-0.49)



Regardless of patient type or stage of resectable disease, test patients for EGFR mutations and treat with TAGRISSO.

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Conclusions

- Early stage lung cancer can be cured by surgery
- Agressive staging improves results and properly selects patients for appropriate therapy
- Sublobar resection is equivalent to lobectomy in selected cases and may allow for more residual lung function. Even wedge resection offers advantages over non-operative procedures

Conclusions

- VATS/robotic lobectomy should be the standard of care in the treatment of patients with lung cancer, carrying less morbidity and mortality and improving quality of life

Drexel UNIVERSITY

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Allegheny General Hospital

Thank You!

Drexel UNIVERSITY

Allegheny Health Network
Allegheny General Hospital

OSA OVERVIEW
27 MARCH 2021

Daniel Shade, Jr., MD, FCCP, FAASM
Medical Director, AHN Center for Sleep Medicine

Sleep disordered breathing

- Obstructive Sleep Apnea (OSA)
- Overlap syndrome
- Central Sleep Apnea (CSA)
  - Periodic breathing
  - Cheyne-Stokes Respiration
- Mixed Apneas
- “Complex” Sleep Apnea
- Disordered breathing secondary to other primary processes

OSA



Prevalence

- Young et al. *NEJM* 1993
  - Middle aged cohort (30-60years)
  - Diagnosed by PSG, in laboratory
  - AHI ≥ 5 Women 9% Men 24%
  - AHI ≥ 5 Women 2% Men 4%
    - w/ sleepiness

UP TO 25%

Definitions (and therefore prevalence vary).

Population is aging, (and growing), w/ more comorbidities

UP TO 60% IN CERTAIN POPULATIONS!!


Steelers
towel
A PITTSBURGH ORIGINAL
SUPER BOWL XL • FEBRUARY 5, 2006
DETROIT, MICHIGAN

Undiagnosed OSA

Sleep, 20(9):705–706
© 1997 American Sleep Disorders Association and Sleep Research Society

Fast Track Publication

Estimation of the Clinically Diagnosed Proportion of Sleep Apnea Syndrome in Middle-aged Men and Women

Terry Young, Linda Evans, Laurel Finn and Mari Palta

Sleep and Respiration Research Group, Department of Preventive Medicine, University of Wisconsin–Madison, Madison, Wisconsin, U.S.A.

Summary: The proportion of sleep apnea syndrome (SAS) in the general adult population that goes undiagnosed was estimated from a sample of 4,925 employed adults. Questionnaire data on doctor-diagnosed sleep apnea were followed up to ascertain the prevalence of diagnosed sleep apnea. In-laboratory polysomnography on a subset of 1,090 participants was used to estimate screen-detected sleep apnea. In this population, without obvious barriers to health care for sleep disorders, we estimate that 93% of women and 82% of men with moderate to severe SAS have not been clinically diagnosed. These findings provide a baseline for assessing health care resource needs for sleep apnea. **Key Words:** Sleep apnea—Epidemiology—Sleep disorders—Prevalence.

Medical Staff Recognition of Risk for OSA in Hospitalized Medical Patients Without Dedicated Screening Tool

Andrew Hameroff; Tiffany Dumont; Tejpreet Lamba; Daniel Shade

Author and Funding Information Allegheny General Hospital, Department of Pulmonology and Critical Care, Pittsburgh, PA

Chest 2014;146:A963

Only 4% medicine admissions identified as ‘at risk’
Only 57% patients *with history of OSA* were identified

Risk factors

- Obesity (70%), also neck circumference >17in
- *Age* (40-70 years)
  - ? Anatomic primarily if younger
- Male
- Postmenopausal
- Family history (2-4X)
- Medications/alcohol/smoking
- Anatomic abnormalities
- Thyroid disease, acromegaly, PCOS

OSA: Symptoms

- Loud snoring
- Witnessed apneas
- AM headaches
- Enuresis
- Nocturnal choking
- EDS
- Fatigue
- Depression
- Depressed libido
- Cognitive impairment
- Restless sleep

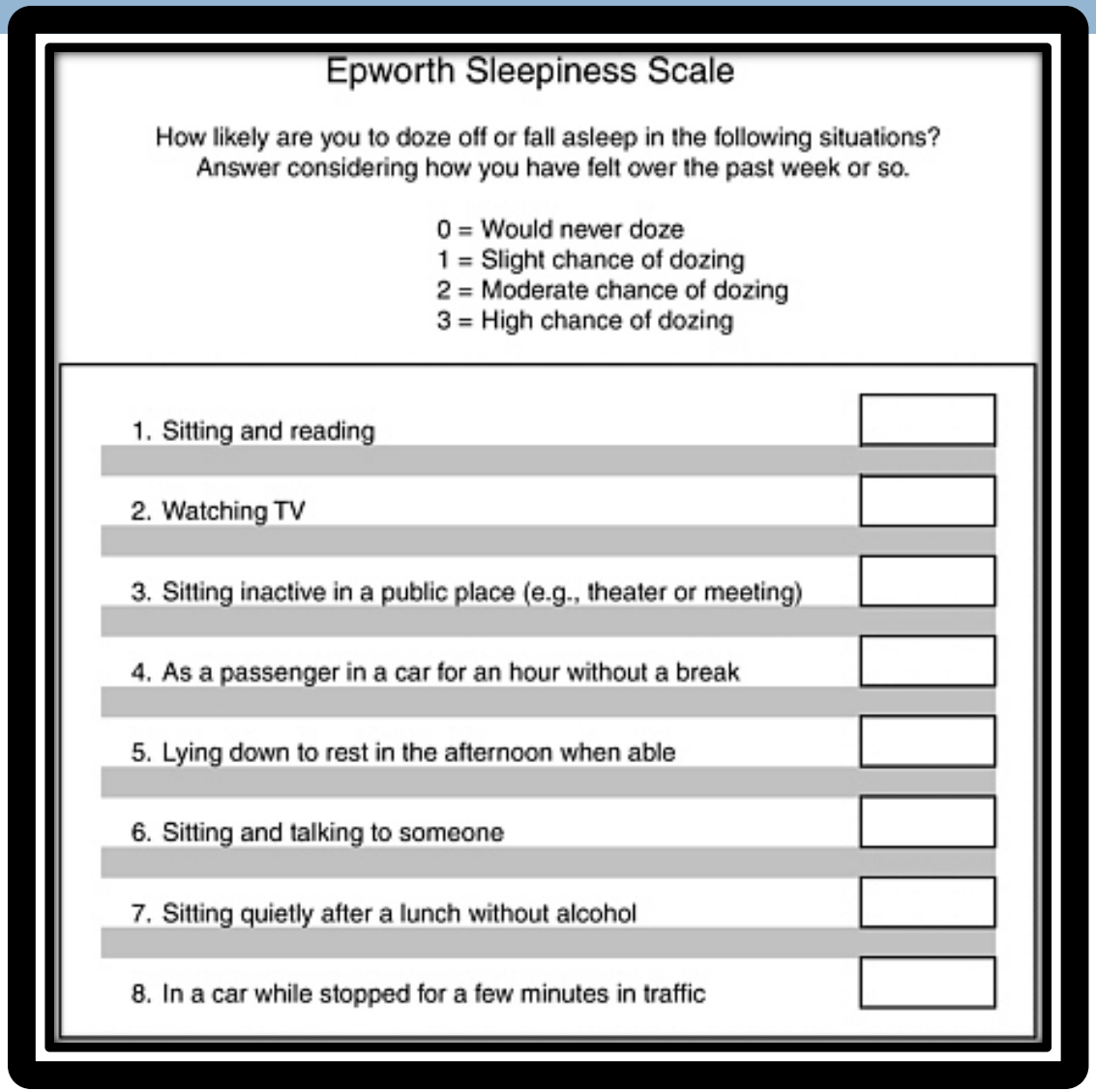
Questionnaires

**These do not establish or r/o SDB*



From mayleelim blogspot

Epworth scale



Epworth Sleepiness Scale

How likely are you to doze off or fall asleep in the following situations?
Answer considering how you have felt over the past week or so.

0 = Would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

1. Sitting and reading	
2. Watching TV	
3. Sitting inactive in a public place (e.g., theater or meeting)	
4. As a passenger in a car for an hour without a break	
5. Lying down to rest in the afternoon when able	
6. Sitting and talking to someone	
7. Sitting quietly after a lunch without alcohol	
8. In a car while stopped for a few minutes in traffic	

STOP *(simple yes/no)*

- Snoring
- Tired
- Observed (apneas)
- Pressure (Have or being treated for BP)

High risk OSA: 'yes' to 2 or more questions

Low risk OSA: 'yes' to fewer than 2

Anesthesiology 2008;108:812

STOP-BANG

- STOP questions, plus:

- BMI (>35)
- Age (over 50)
- Neck circumference (>40cm) (15.7 in)
- Gender (?male)

High risk OSA: yes to 3 or more

Low risk OSA: yes to fewer than 3

Modified STOP-BANG score

For general population

Low risk of OSA: Yes to 0-2 questions

Intermediate risk of OSA: Yes to 3-4 questions

High risk of OSA: Yes to 5-8 questions

or Yes to 2 or more of 4 STOP questions + male gender

or Yes to 2 or more of 4 STOP questions + BMI > 35 kg/m^2

or Yes to 2 or more of 4 STOP questions + neck circumference

(17”/43cm in male, 16”/41cm in female)

Proprietary to University Health Network. www.stopbang.ca

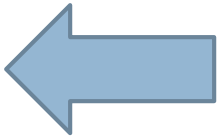
Modified from: Chung F et al. Anesthesiology 2008; 108:812-21; Chung F et al. Br J Anaesth 2012, 108:768–75; Chung F et al. J Clin Sleep Med 2014;10:951-8.

Screening questionnaires

Table 2
Screening questionnaires for OSA

Berlin Questionnaire	ASA Checklist	STOP Questionnaire	STOP-Bang Questionnaire
Netzer et al 2003[31]	Gross et al 2006[33]	Chung et al 2008[30]	Chung et al 2008[30]
Clinician-administered	Clinician-administered	Self-administered	Clinician-administered
Validated in primary care setting and perioperative setting	Validated in perioperative setting	Validated in perioperative setting	Validated in perioperative setting
10-item	14-item	4-item	8-item
3 categories: snoring, daytime sleepiness, driving	3 categories: predisposing characteristics, symptoms of OSA, complaints	No categories	No categories
High risk if 2 or more categories score positive	High risk if 2 or more categories score positive	High risk if 2 or more items score positive	High risk if 3 or more items score positive
For AHI >30 Sensitivity 87% Specificity 46% PPV 32% NPV 93%	For AHI >30 Sensitivity 87% Specificity 36% PPV 28% NPV 91%	For AHI >30 Sensitivity 80% Specificity 49% PPV 30% NPV 90%	For AHI >30 Sensitivity 100% Specificity 37% PPV 31% NPV 100%
For AHI >15 Sensitivity 79% Specificity 51% PPV 51% NPV 78%	For AHI >15 Sensitivity 79% Specificity 37% PPV 45% NPV 73%	For AHI >15 Sensitivity 74% Specificity 53% PPV 51% NPV 76%	For AHI >15 Sensitivity 93% Specificity 43% PPV 52% NPV 90%
Complicated scoring procedure	Clinician required to complete checklist	Concise, easy to use	Improve sensitivity compared with the STOP questionnaire

Abbreviations: NPV, negative predictive value; PPV positive predictive value.



Exam---50/50





Diagnosis

- Underestimation of patient's risk for OSA, underdiagnosis is still very common
- Most patient's understanding of risks/complications of OSA is minimal

Oximetry?

- ? Screen for OSA
  - Obese, FRC reduced/*reserve*?
  - Apneas, what type?
  - -or is it hypoventilation?
  - ODI
    - >4%, >10sec duration ODI>10/hour



Laryngoscope 2021; Feb 131(2):440

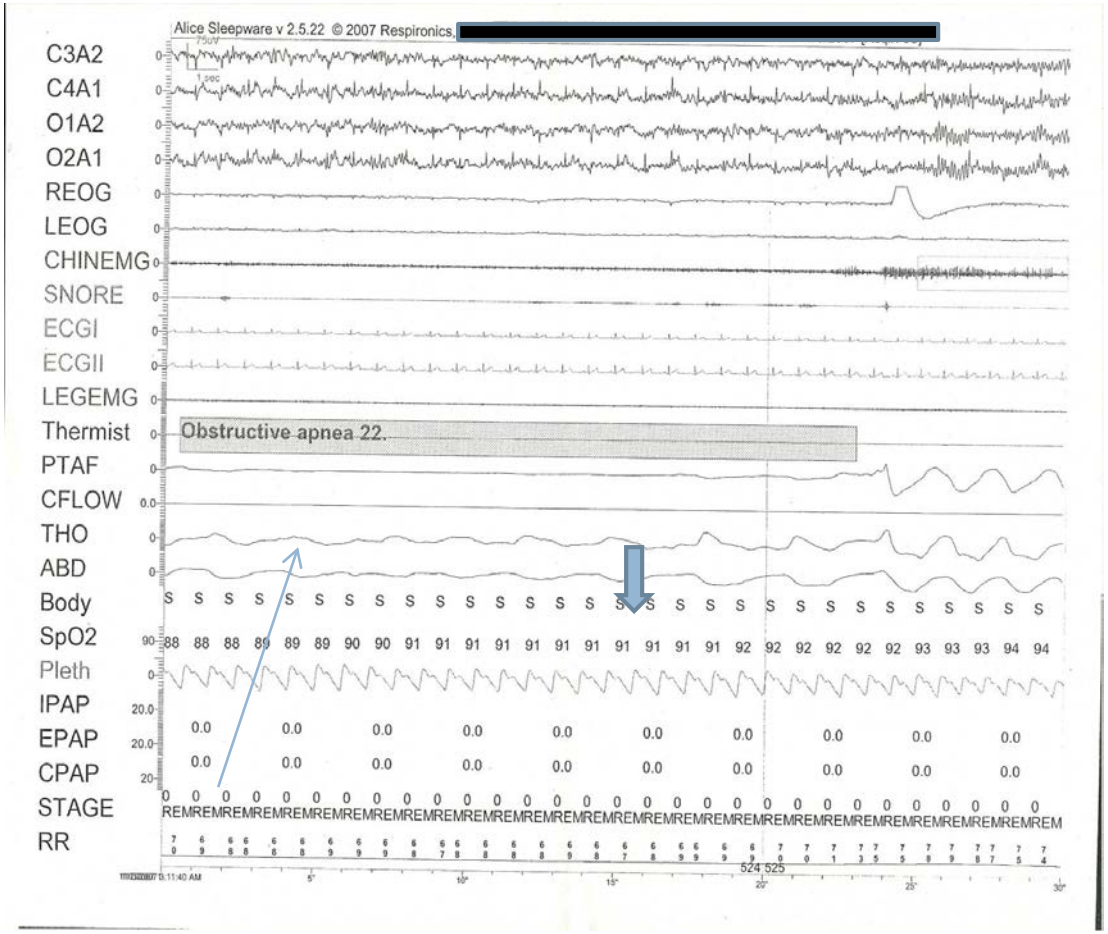
HSAT or in-lab PSG?

- What are you looking for?
- Sleep Disordered Breathing (SDB)
  - HSAT if no significant comorbidity
  - Or- the comorbidity is well controlled

HSAT may underestimate true AHI.

A borderline or negative study w/ a high suspicion should prompt further investigation (in-lab PSG)

Obstructive apnea



Upper Airway

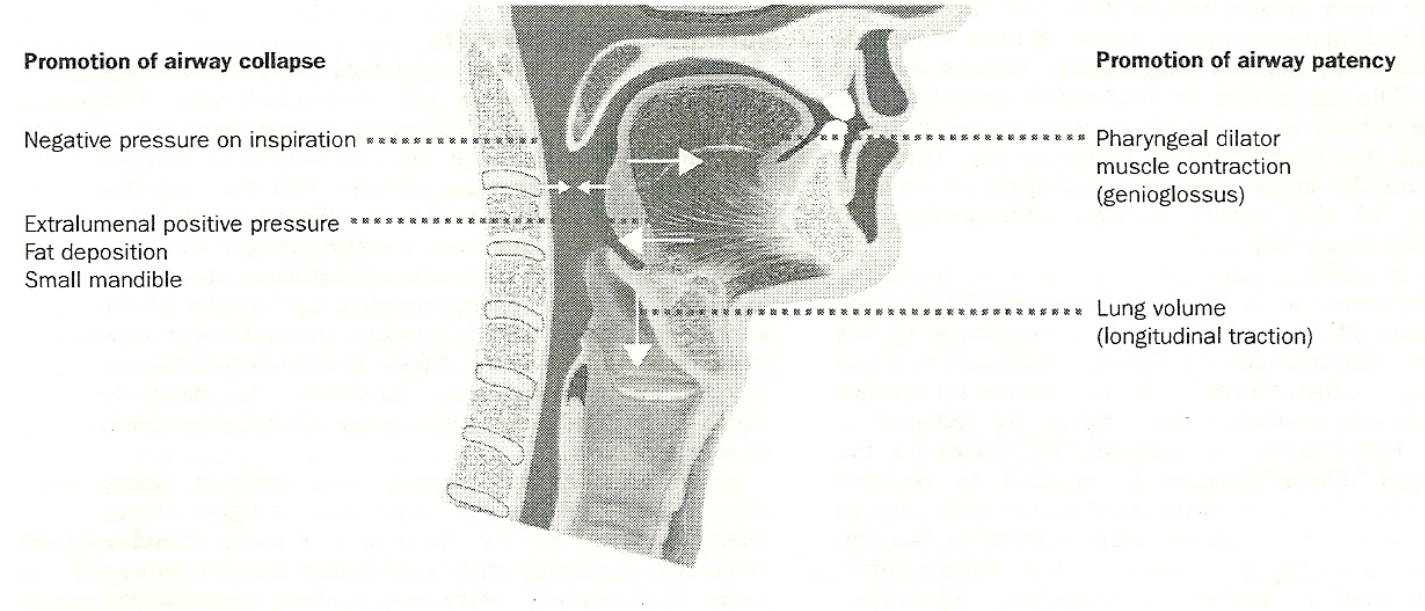


Figure 1: **The balance of forces**[35]
Inspiratory negative pressure and extraluminal positive pressure tend to promote pharyngeal collapse. Upper airway dilator muscles and increased lung volume tend to maintain pharyngeal patency.

Pathophysiology

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Pathophysiology: over time…

- Pharyngeal occlusion and hypoxia:
  - Free radical generation
  - Muscle and neuronal fiber injury, endothelial damage
  - Release proinflammatory/prothrombotic mediators
  - Surges in sympathetic system/BP
  - Changes in preload/afterload
    - CBF

REMEMBER (!):

- ETOH, sedatives, pain medication
- Anesthesia



Complications/Overview

Complication	Odds ratio
HTN	1.4-2.9
CAD	1.3-23
CVA	1.6-6
CHF	2.4
MVA	7

Malhotra, *Lancet* 2002

Complications

From *Lancet* 2002;360:237-245

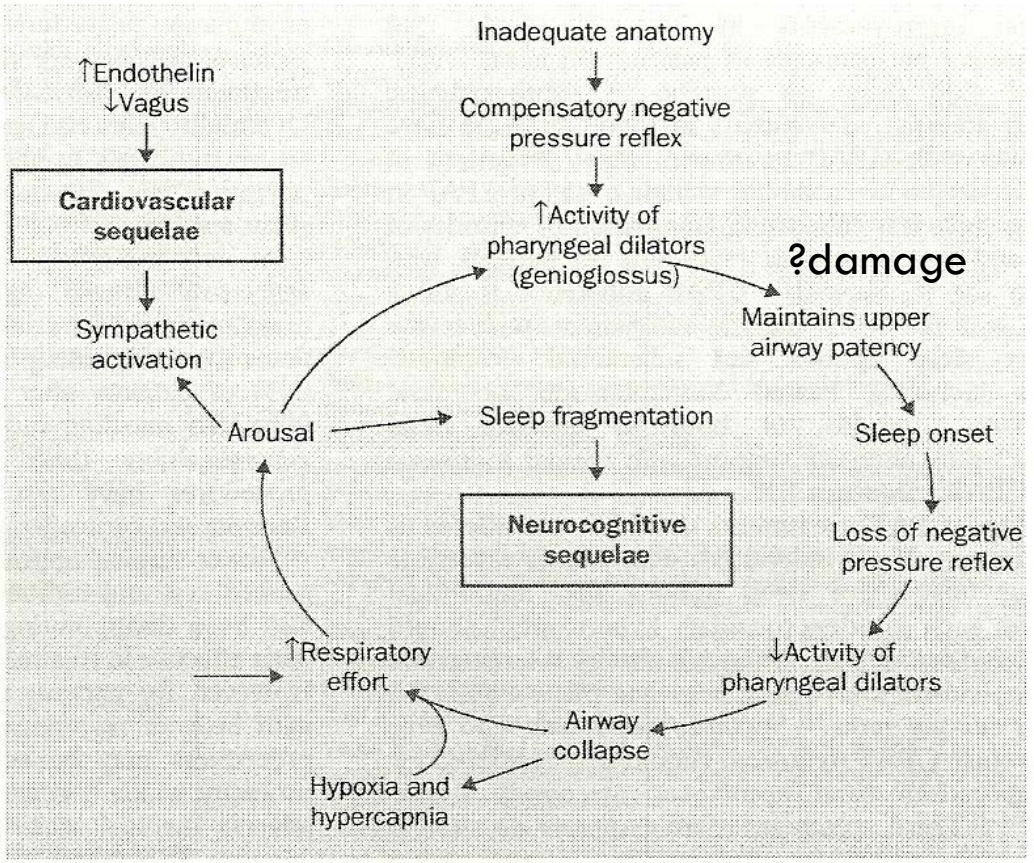


Figure 2: **Processes leading to neurocognitive and cardiovascular sequelae**

Complications

Bradley, *Lancet* 2009

- Obstruction leads to cycles of hypoxia, exaggerated negative intrathoracic pressure, and arousals>
- Depress myocardial contractility
- Activate sympathetic nervous system
- Raise BP, HR (myocardial wall stress)
- Depress parasympathetic activity
- Provide oxidative stress, systemic inflammation
- Activate platelets and impair vascular endothelial function



JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Obstructive Sleep Apnea is an Independent Risk Factor for Hospital Readmission

Nicholas J. Scalzitti, MD[1,2]; Peter D. O'Connor, MD[1,2]; Skyler W. Nielsen, DO[2]; James K. Aden, PhD[3]; Matthew S. Brock, MD[1,4]; David M. Taylor, DO[2]; Vincent Mysliwiec, MD[1]; Gregory R. Dion, MD[2]

[1]Department of Sleep Medicine, San Antonio Military Medical Center, Fort Sam Houston, Texas; [2]Department of Otolaryngology-Head and Neck Surgery, San Antonio Military Medical Center, Fort Sam Houston, Texas; [3]Biostatistician, San Antonio Military Medical Center, Fort Sam Houston, Texas; [4]Department of Neurology, San Antonio Military Medical Center, Fort Sam Houston, Texas

BRIEF SUMMARY

Current Knowledge/Study Rationale: Obstructive sleep apnea is commonly associated with comorbidities that are known to affect hospital readmission rates. Our study sought to explore whether obstructive sleep apnea itself is a modifiable risk factor for hospital readmission.

Study Impact: This study identifies obstructive sleep apnea as an independent risk factor for hospital readmission. There appears to be inadequate use of positive airway pressure both during hospitalization and after discharge in patients with obstructive sleep apnea.

J Clin Sleep Med 2018;14(5):753

Arrhythmogenesis

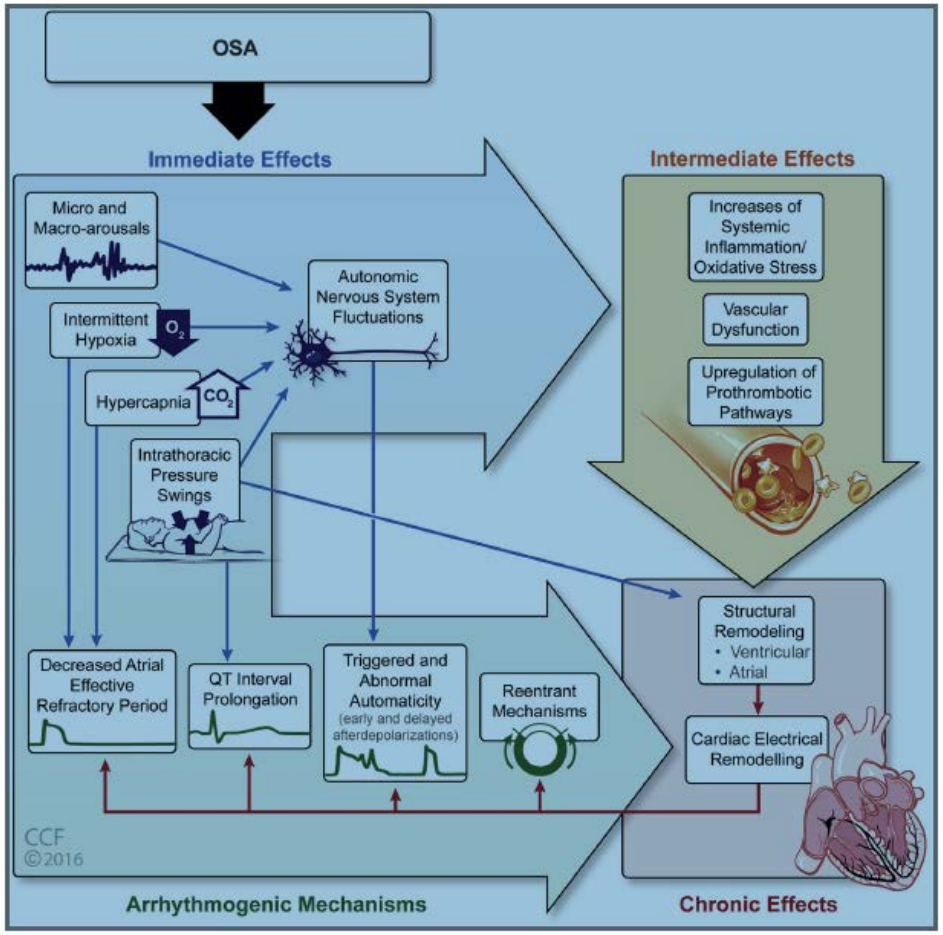
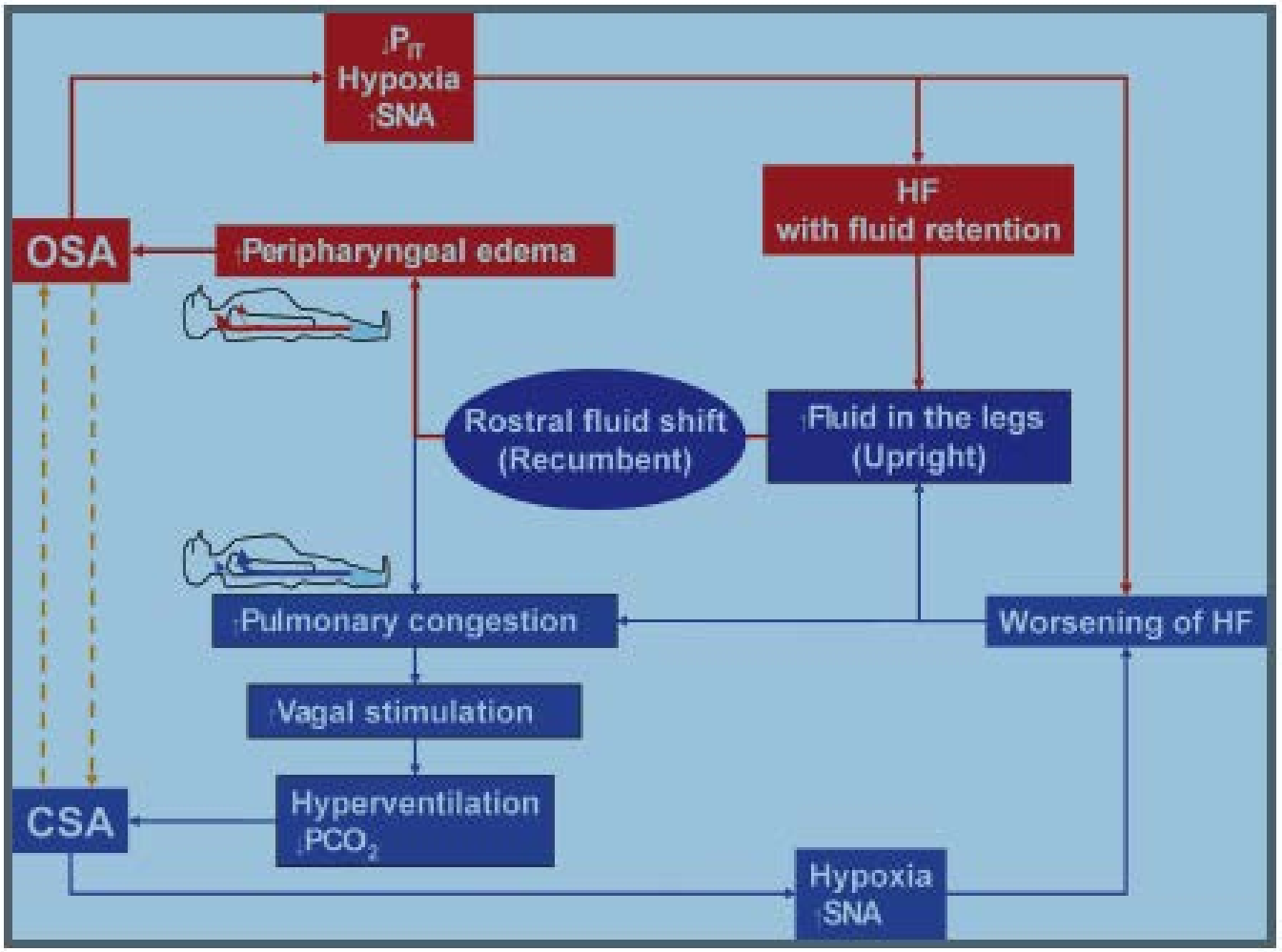


Figure 1 – *Overview of putative sleep apnea pathophysiologic pathways with varying levels of evidence potentially predisposing to cardiac arrhythmogenesis. O_2 = oxygen. Reprinted with permission, Cleveland Clinic Center for Medical Art & Photography © 2016. All Rights Reserved.*

Chest 2017;151(1):225

- Higher prevalence AF, NSVT, and~
- Lower recurrence AF after cardioversion if CPAP used (82% vs. 42%)
  - *Circulation* 2003;107:2589

CHF?



Circulation 2012;126:1495-1510

Bidirectional relationship between OSA and Cardiovascular disease (CHF)

NEW RESEARCH

JCSM
Journal of Clinical Sleep Medicine
pii: jc-00265-13
http://dx.doi.org/10.5664/jcsm.4096

Diagnosis and Treatment of Sleep Disordered Breathing in Hospitalized Cardiac Patients: A Reduction in 30-Day Hospital Readmission Rates

Shilpa R. Kauta, M.D.[1]; Brendan T. Keenan, M.S.[1]; Lee Goldberg, M.D.[2]; Richard J. Schwab, M.D.[1]
[1]*Center for Sleep and Circadian Neurobiology, University of Pennsylvania, Philadelphia, PA;*
[2]*Department of Cardiology, University of Pennsylvania, Philadelphia, PA*

50% readmitted within 6 months!

J Clin Sleep Med 2014;10(10):1051

SAVE Trial / ISAACC Trial

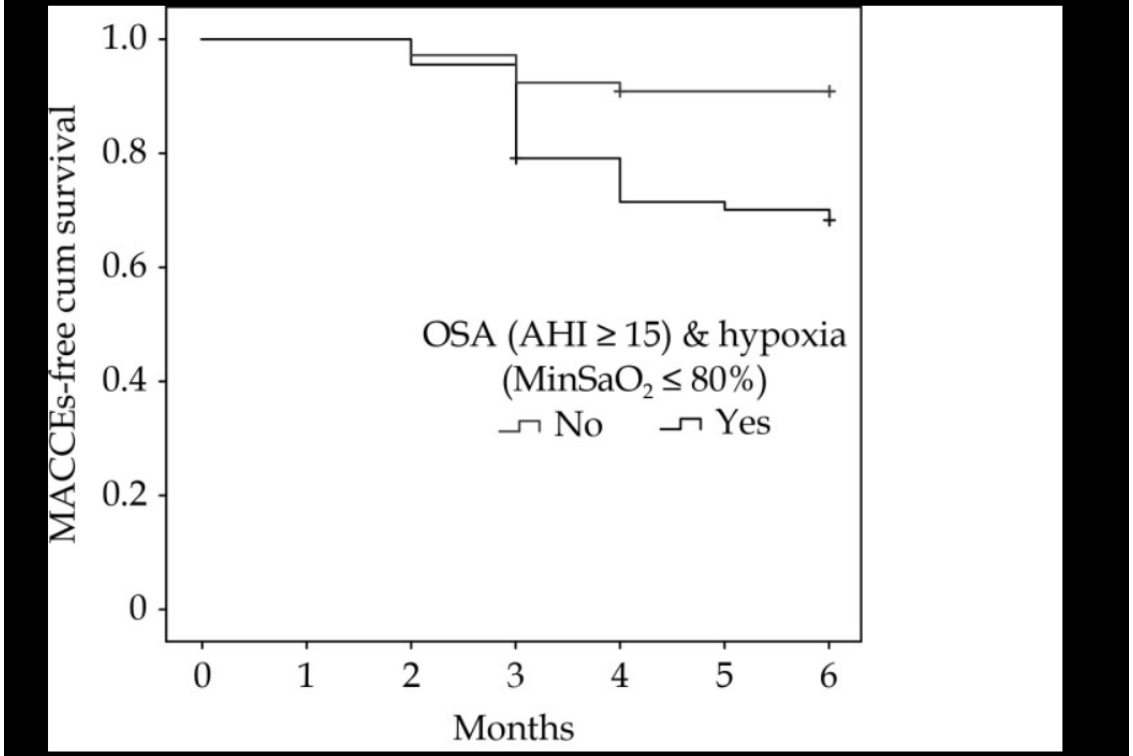
- SAVE
  - CAD/CVD
  - Low adherence
  - No effect on CV
- ISAACC
  - ACS
  - Low adherence
  - No effect on CV
  - F/U 1 year

Low adherence (<4 hours/night)
Excluded hypersomnolence/severe hypoxic patients
Established disease (heart already damaged)

Improvement EDS/HTN/sleep parameters

OSA and CAD

Is OSA ‘protective’ in CAD?

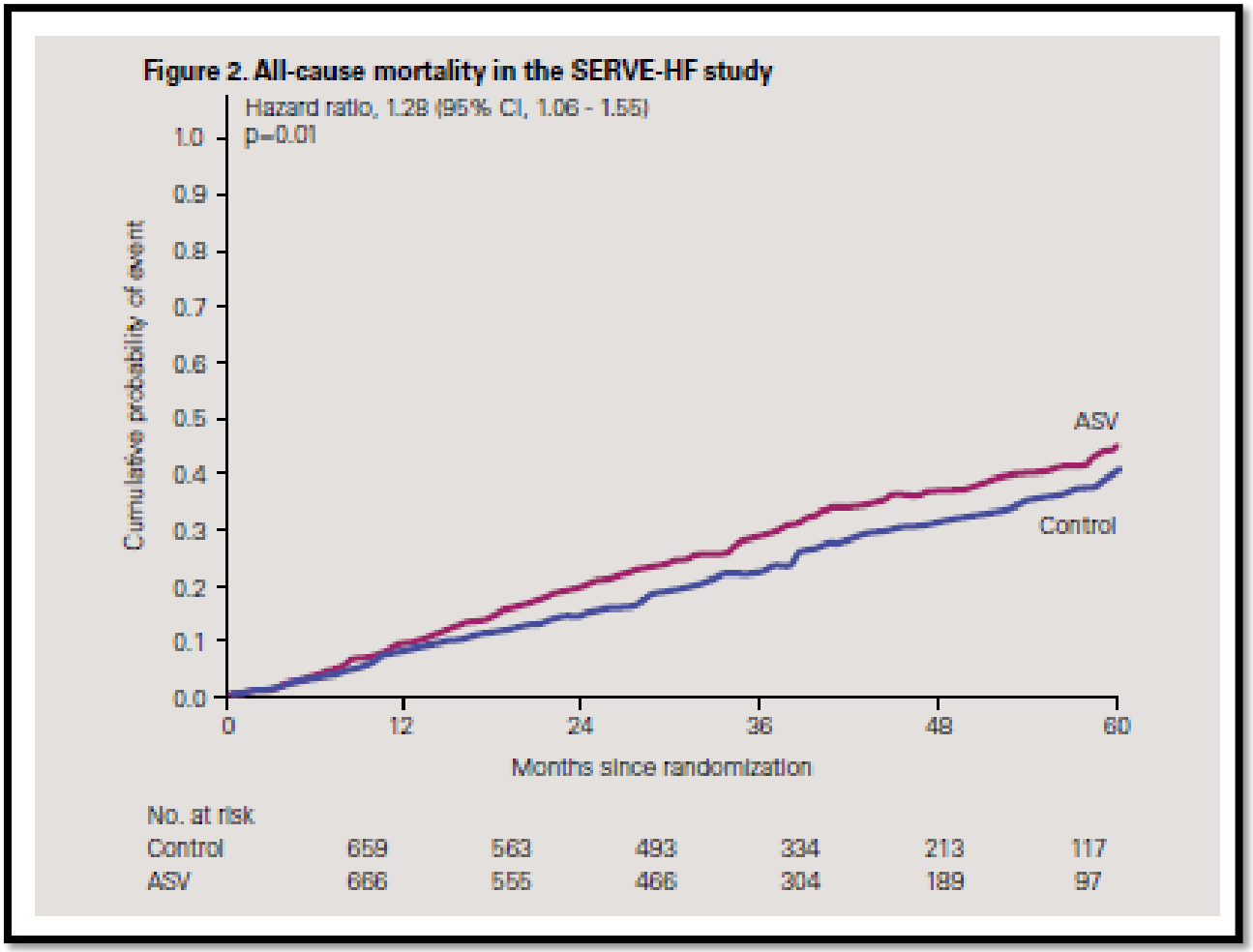


See this image and copyright information in PMC

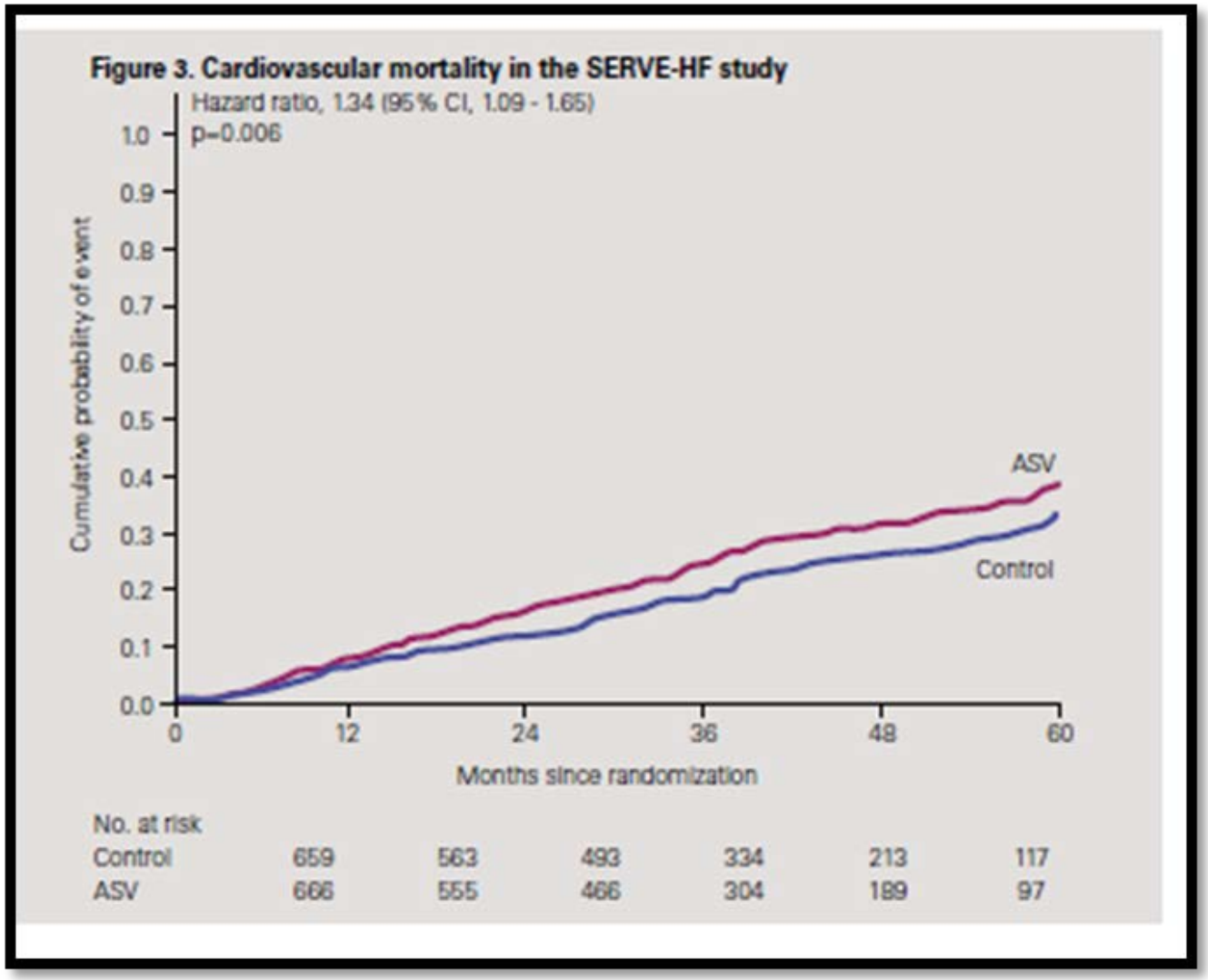
2 The Kaplan–Meier survival curve of OSA (AHI ≥ 15) combined with hypoxia ($MinSaO_2 \leq 80\%$) on MACCE-free survival in elderly subacute myocardial infarction patients during the 6-month follow-up.

Journal of Geriatric Cardiology
Online Jan 28, 2021

SERVE-HF: CSR using ASV



SERVE-HF


Figure 3. Cardiovascular mortality in the SERVE-HF study
Hazard ratio, 1.34 (95% CI, 1.09 - 1.65)
p=0.006
Cumulative probability of event
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
ASV
Control
0
12
24
36
48
60
Months since randomization
No. at risk
Control 659 563 493 334 213 117
ASV 666 555 466 304 189 97

SERVE-HF

Interpreting the SERVE-HF study results

The early and sustained increase in cardiovascular mortality seen in the ASV group in SERVE-HF was unexpected and potential pathophysiological mechanisms that might explain these findings remain to be determined. At this stage, two possibilities have been suggested.

The first is that CSA, and in particular CSR, may be a compensatory mechanism in patients with heart failure. This hypothesis has been suggested previously.[4] If this hypothesis is valid, diminishing this compensatory adaptive respiratory pattern with ASV may be detrimental in patients with heart failure. The SERVE-HF subgroup analysis results that show a positive association between the proportion of CSR and the adverse effect of ASV on the primary outcome would support this interpretation.

Secondly, it is possible that the application of positive airway pressure may impair cardiac function in at least some patients with heart failure, although it is not possible to draw any conclusions on the basis of available data.

Ejection Fraction < 45%

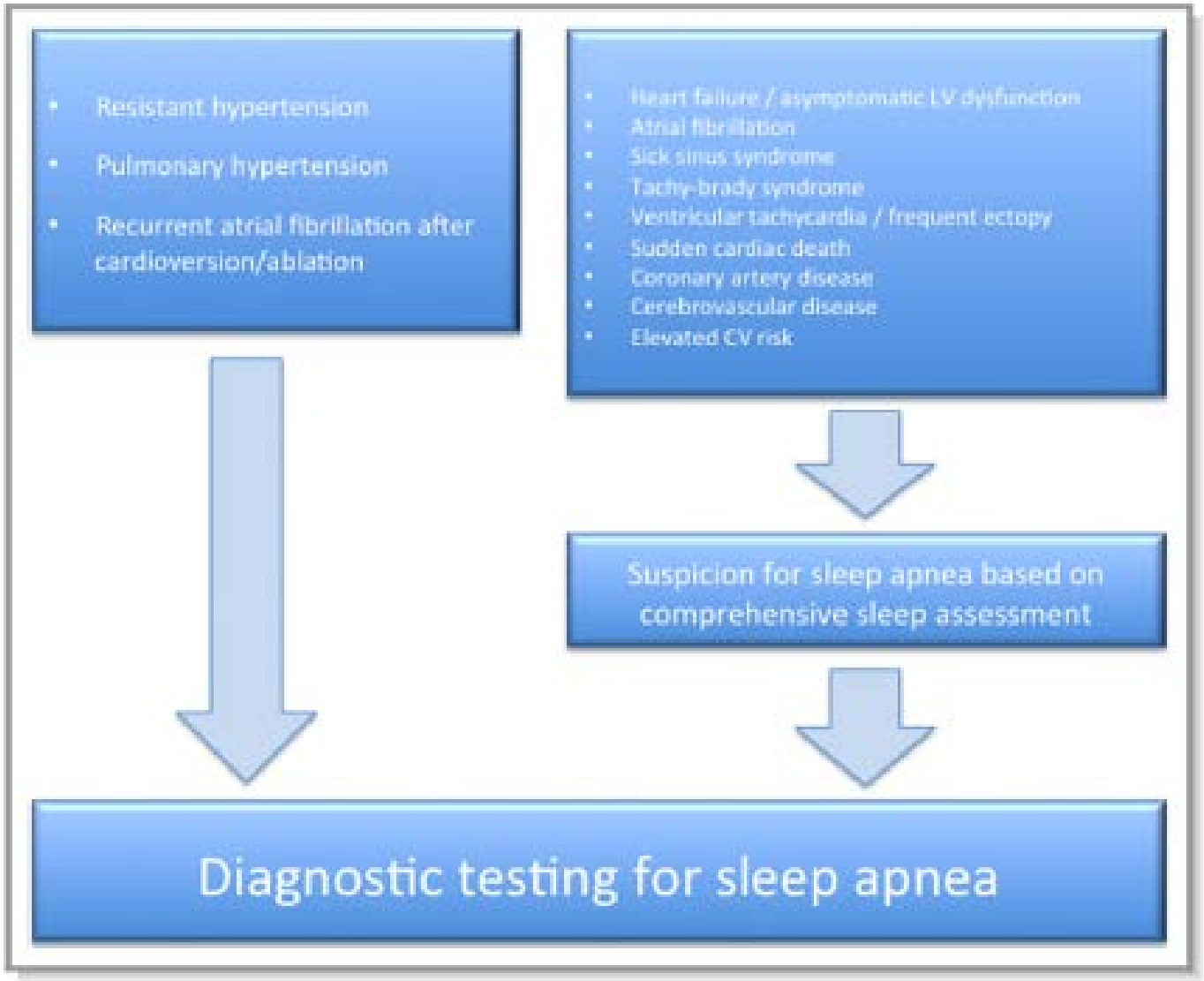
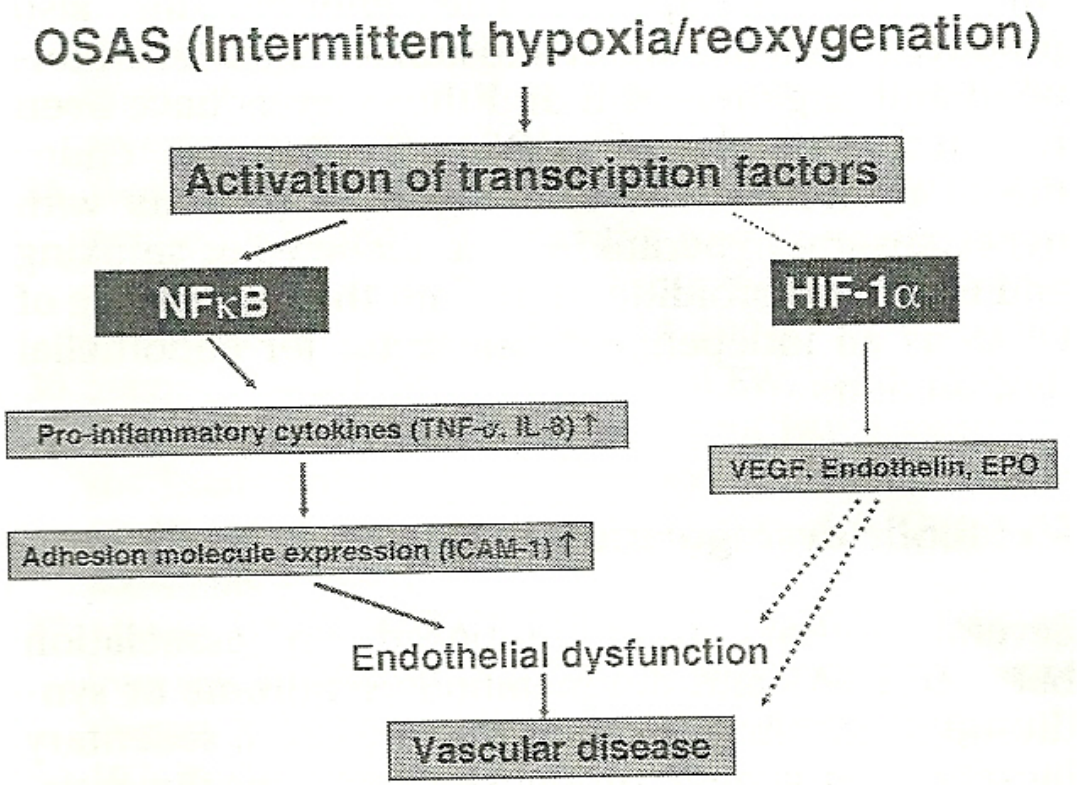


Figure 2. Proposed algorithm to select patients for formal diagnostic sleep testing based on underlying cardiovascular condition. CV indicates cardiovascular; LV, left ventricular.

J Am Heart Assoc. 2019;8:e010440. DOI: 10.1161/JAHA.118.010440.

Inflammation/Angiogenesis



Respirology 2006 McNicholas et al.

OSA and metabolic syndrome

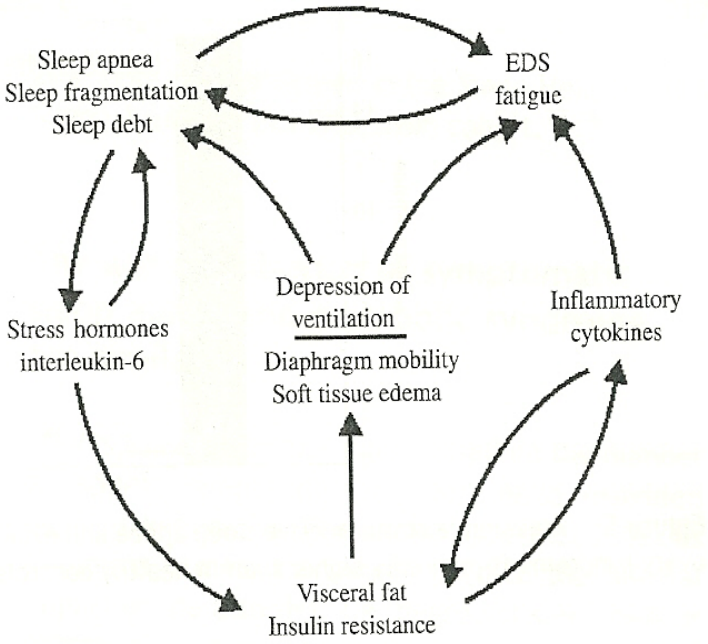


Figure 4 A heuristic model of the complex feed forward associations between visceral fat/insulin resistance, inflammatory cytokines, stress hormones, excessive daytime sleepiness and fatigue, and sleep apnea.

Vgontzas, *Sleep Medicine Reviews*, 2005

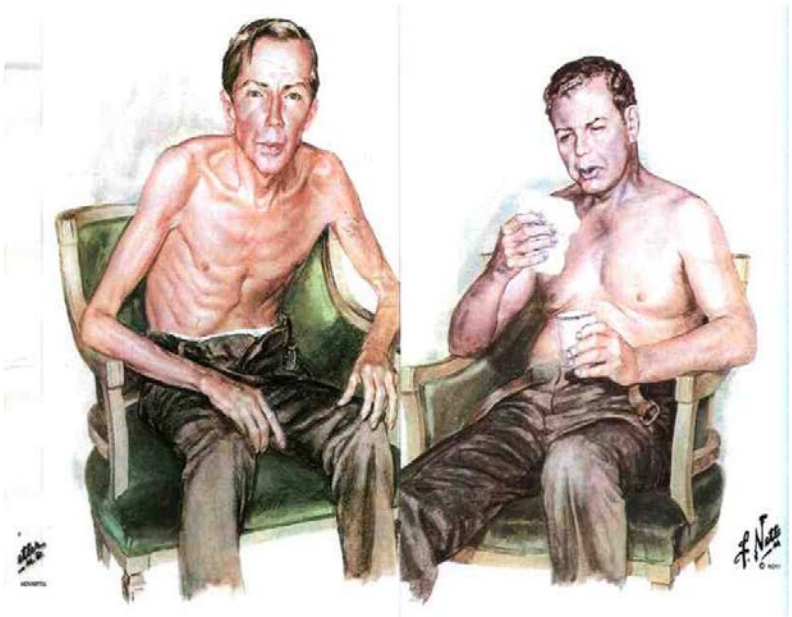
Independent of obesity, OSA is a/w:

- Insulin resistance
- Glucose intolerance
- Type 2 DM

? Intermittent hypoxia and/or recurrent arousals

CPAP may mitigate metabolic disturbance….

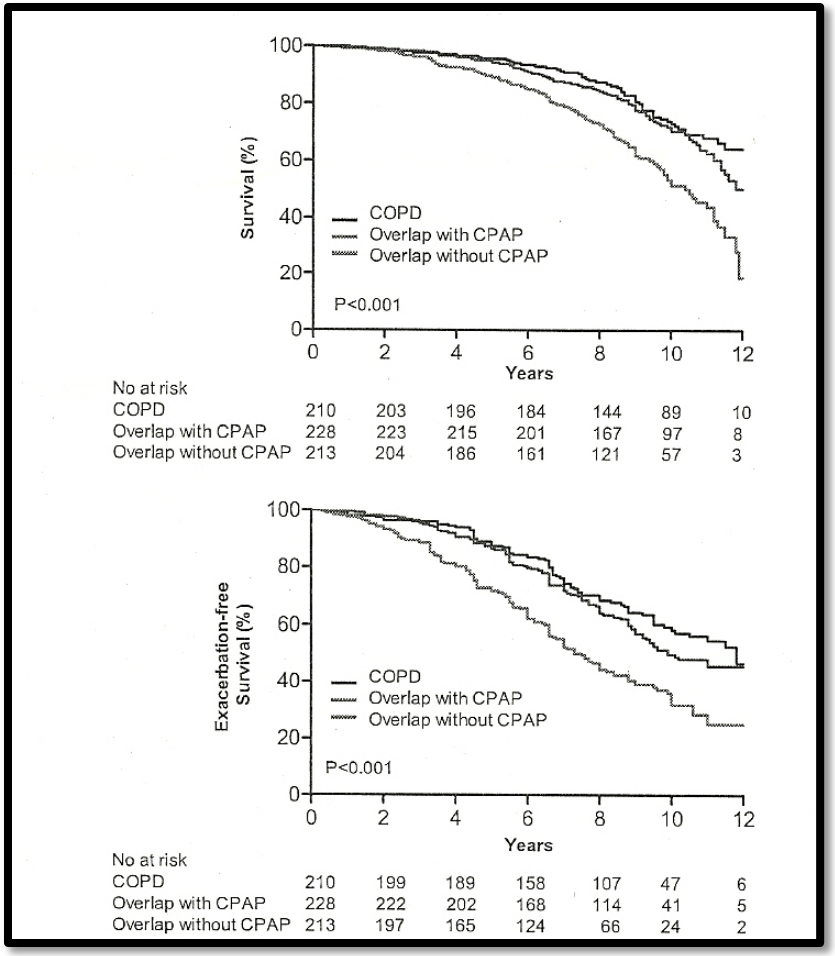
Overlap Syndrome





Overlap syndrome

- COPD/OSA a/w increased mortality
- Treating OSA reduced mortality
- More COPD exac. if overlap syndrome
- Delay in time to exac. if treated!



AJRCCM 2010

OSA and Stroke



From Shropshire.nhs.uk

OSA and Stroke

- OSA risk factor for stroke
- OSA (and CSA) common after stroke
  - OSA occurs in 60-96% of post-stroke patients
- Worse outcomes post-stroke
  - Early neurological worsening
  - Decreased functional recovery
  - Increased mortality

OSA and Stroke

- Share many risk factors
  - Male sex
  - Age
  - Obesity
  - Smoking/alcohol
- OSA causes/worsens:
  - HTN
  - DM
  - *Atrial fibrillation*
  - Carotid disease
  - Cardiac disease

Apnea and perfusion

During Apnea:

↓SBP, HR,CO, CPP



These increase at apnea termination

pii: sp-00542-15 http://dx.doi.org/10.5665/sleep.5136

EDITORIAL

Obstructive Sleep Apnea as a Candidate Unifier in Atrial Fibrillation and Cryptogenic Stroke

Commentary on Lipford et al. Associations between cardioembolic stroke and obstructive sleep apnea. SLEEP 2015;38:1699–1705.

Reena Mehra, MD, MS; Nancy Foldvary-Schaefer, DO, MS

Sleep Disorders Center, Neurological Institute, Cleveland Clinic, Cleveland, OH

Greater than 600,000 individuals are estimated to experience ischemic stroke in the United States annually.[1] Causative factors remain undetermined in up to 30% of these cases (i.e., cryptogenic stroke).[2] Given its intermittent and often asymptomatic nature, occult atrial fibrillation (AF) likely contributes to a substantial proportion of cryptogenic stroke via cardioembolism.[3–5] Current guidelines advise up to 30 days of continuous cardiac rhythm monitoring in the setting of cryptogenic stroke, defined as stroke with no readily

burden (AHI mean ~33 and median ~23). Those with OSA had a 4–6 fold higher odds of cardioembolic stroke compared to those without OSA when considering confounding variables individually in statistical models, which was marginally statistically significant in the multivariable model. Specifically, after taking into account AF, there was a 4.5-fold higher odds of cardioembolic stroke in OSA versus those with a lower AHI. Also, although a greater degree of hypoxia was observed in those with cardioembolic strokes compared to other stroke subtypes,

OSA: Direct *and* indirect effects (causes cormorbidities)
4-6 higher odds of cardioembolic stroke if OSA

NEW RESEARCH

SCIENTIFIC INVESTIGATIONS

JCSM
Journal of Clinical Sleep Medicine

Frequency of Sleep Apnea in Stroke and TIA Patients: A Meta-analysis

Karin G. Johnson, M.D.[1]; Douglas C. Johnson, M.D.[2]

[1]Baystate Medical Center, Springfield, MA; [2]Massachusetts General Hospital, Boston, MA

Study Objectives: To determine the frequency of sleep disordered breathing (SDB) in ischemic and hemorrhagic stroke and transient ischemic attack (TIA) patients by meta-analysis.

Methods: A systematic literature search using Medline, EMBASE and CINAHL and a manual review of references through December 2008 was conducted using specific search terms. The frequency of SDB stratified by apnea hypopnea index (AHI) was extracted by the author. Weighted averages using a random-effects model are reported with 95% confidence intervals.

Results: Twenty-nine articles evaluating patients with auto-CPAP, limited-channel sleep study, or full polysomnography were included in this study. In meta-analysis of 2,343 ischemic or hemorrhagic stroke and TIA patients, the frequency of SDB with AHI > 5 was 72% and with AHI > 20 was 38%. Only 7% of the SDB was primarily central apnea. There was no significant difference in SDB prevalence by event type, timing after stroke, or type of monitoring. Males had a higher percentage of SDB (AHI > 10) than females (65% compared to 48% $p = 0.001$). Patients with recurrent strokes had a higher percentage of SDB (AHI > 10) than initial strokes (74% compared to 57% $p = 0.013$). Patients with unknown etiology of stroke had a higher and cardioembolic etiology a lower percentage of SDB than other etiologies.

Conclusions: SDB is very common in stroke patients irrespective of type of stroke or timing after stroke and is typically obstructive in nature. Since clinical history alone does not identify many patients with SDB, sleep studies should be considered in all stroke and TIA patients.

Keywords: Stroke prevention, all cerebrovascular disease/strok, sleep apne, prevalence studies, screening in epidemiology

Citation: Johnson KG; Johnson DC. Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. *J Clin Sleep Med* 2010;6(2):131-137.

OSA and COVID:

BMJ Open Respiratory Research

Sleep apnoea is a risk factor for severe COVID-19

Satu Strausz,[1,2,3] Tuomo Kiiskinen,[1,4] Martin Broberg,[1] Sanni Ruotsalainen,[1] Jukka Koskela,[1,5] Adel Bachour,[6] FinnGen, Aarno Palotie,[1,5,7] Tuula Palotie,[2,3] Samuli Ripatti,[1,5,8] Hanna M. Ollila[1,5,9]

To cite: Strausz S, Kiiskinen T, Broberg M, *et al*. Sleep apnoea is a risk factor for severe COVID-19. *BMJ Open Resp Res* 2021;**8**:e000845. doi:10.1136/bmjresp-2020-000845

► Additional material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/bmjresp-2020-000845).

Received 25 November 2020

ABSTRACT

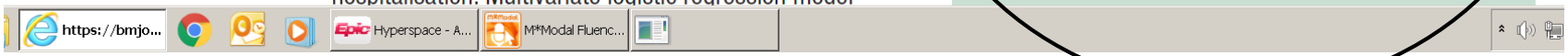
Background Obstructive sleep apnoea (OSA) is associated with higher body mass index (BMI), diabetes, older age and male gender, which are all risk factors for severe COVID-19.

We aimed to study if OSA is an independent risk factor for COVID-19 infection or for severe COVID-19.

Methods OSA diagnosis and COVID-19 infection were extracted from the hospital discharge, causes of death and infectious diseases registries in individuals who participated in the FinnGen study (n=260 405). Severe COVID-19 was defined as COVID-19 requiring hospitalisation. Multivariate logistic regression model

Key messages

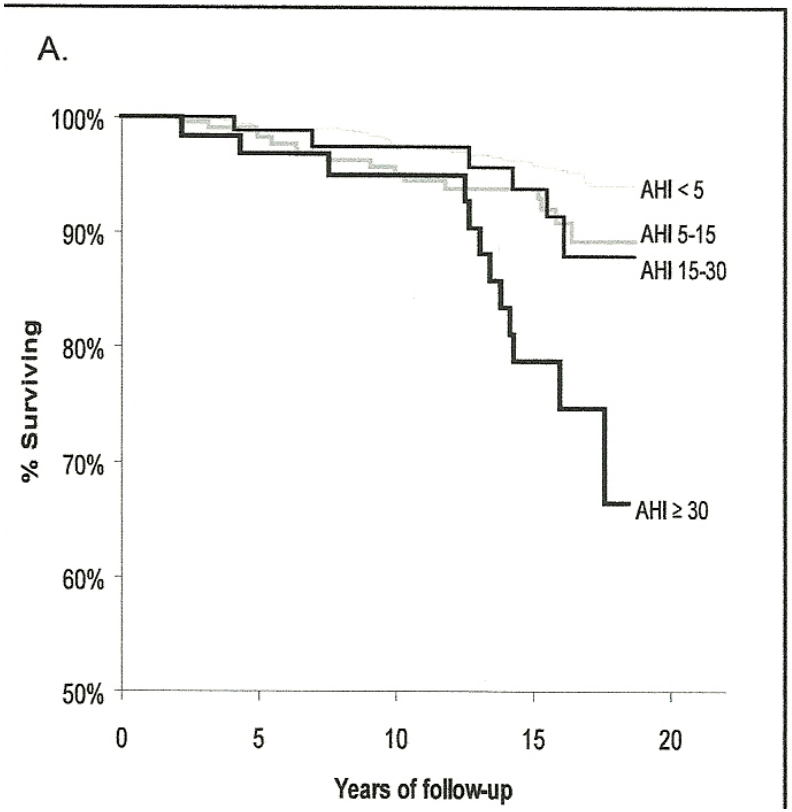
- Is obstructive sleep apnoea (OSA) an independent risk factor for severe COVID-19?
- Patients with OSA have a higher risk to be hospitalised when affected by COVID-19 than non-OSA individuals.
- In assessment of patients with suspected or confirmed COVID-19 infection, OSA should be recognised as one of the comorbidity risk factors for developing a severe form of the disease and patients with OSA with suspected or confirmed COVID-19 in-

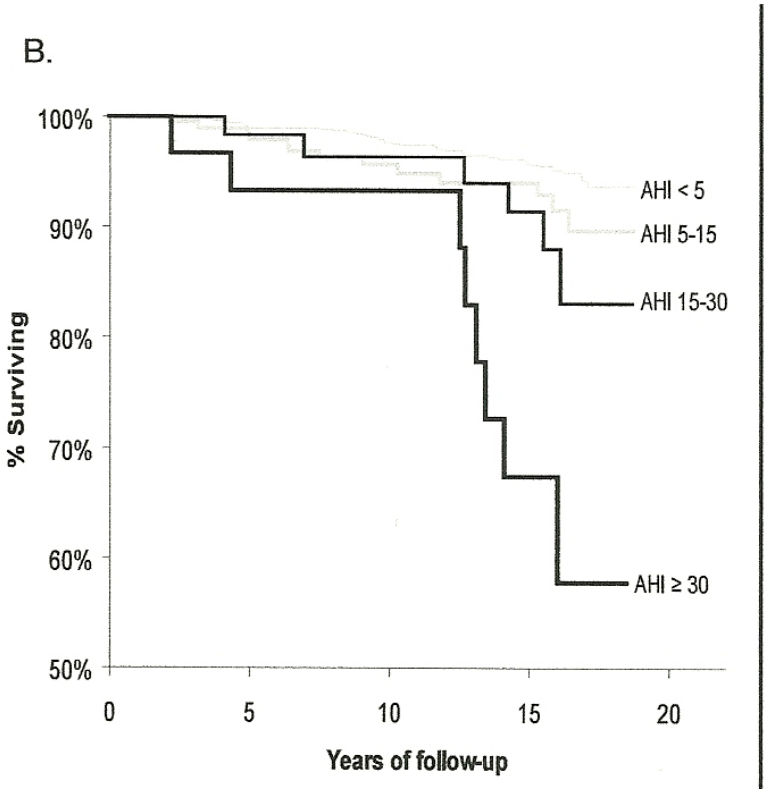


Mortality



Mortality





Kaplan-Meier estimates of survival probability for total Sample (A), and untreated sample (B)

Sleep is Money



SLEEP MEDICINE

HARVARD MEDICAL SCHOOL

The Harvard Medical School Division of Sleep Medicine is pleased to present

The Price of Fatigue:
The surprising economic costs of unmanaged sleep apnea

as an educational resource to increase awareness among the general public and with policy makers about the significance of this public health problem.

McKinsey & Company contributed to the fact base and analysis in this report. This project was funded by Sleep For America.

December 2010

Sleep is Money

Total economic costs of moderate-severe OSA

Estimated total economic cost of moderate-severe OSA	**~$65-165B+ annually in the U.S.**
▪ Diagnosis and treatment of moderate-severe OSA costs:	▪ $2 - $10B
▪ Hidden healthcare costs from moderate-severe OSA driven by: – Co-morbidities (e.g., CVD, renal disease, diabetes and depression) – Medical costs of accidents	▪ $45 - $80B
▪ OSAS-related traffic accident (*excluding medical costs captured above):*	▪ $10 - $40B
▪ OSAS-associated workplace accidents *(excluding traffic accidents and medical costs captured above):*	▪ $5 - $20B
▪ OSAS-related lost productivity costs driven by absenteeism*:	▪ $5 - $15B
▪ Additional societal impact (e.g., increased divorce rates, loss of intimacy):	▪ Not sized

*Additional presenteeism costs not directly estimated

SOURCE: Young T, Sleep, 1997, 20(9):705-706; Young T N Engl J Med 1993 (328) 1230-5; Engleman H, Sleep Med Rev, 2003, 7(1):81-99

Treatment

Multimodality therapy

Table 1—Targeting therapy to pathology in sleep apnea management

Pathophysiological target	Modality
Upper airway obstruction	Positive pressure (various), oral appliance, various soft tissue and bone-based surgeries, Provent, oral negative pressure, hypoglossal nerve stimulation, weight loss including bariatric surgery, body positioning (non-supine), lower body negative pressure
Sleep fragmentation propensity	Sleep hygiene, treating circadian phase abnormalities, sedatives
Hyporesponsive respiratory chemoreflex	Bilevel ventilation, volume-target pressure support ventilation, acetazolamide, weight loss including bariatric surgery, O_2
Hyperresponsive respiratory chemoreflex	Adaptive ventilation, sedatives, acetazolamide, O_2, CO_2 based approaches including dead space, body positioning, Provent (?), cardiac pacing, lower body negative pressure (?)
Disordered integration (opiates, brain stem pathologies)	Adaptive ventilation, O_2, CO_2 modulation

JCSM 2012;8(5):565

Also: genioglossal stimulation/Inspire therapy

Chemogenetics: 2021 and beyond

Designer Receptors Exclusively Activated by Designer Drugs Approach to Treatment of Sleep-disordered Breathing

Thomaz Fleury Curado[1,2], Huy Pho[1], Carla Freire[1,2], Mateus R. Amorim[1,3], Jordi Bonaventura[4], Lenise J. Kim[1,5], Rachel Lee[1], Meaghan E. Cabassa[1], Stone R. Streeter[1], Luiz G. Branco[3], Luiz U. Sennes[2], Kenneth Fishbein[6], Richard G. Spencer[6], Alan R. Schwartz[1,7], Michael J. Brennick[1], Michael Michaelides[4], David D. Fuller[8], and Vsevolod Y. Polotsky[1]

AJRCCM 2021; 203(1):102-110



Positive pressure therapy

"Pneumatic splint"

CPAP VS BiPAP

Auto CPAP

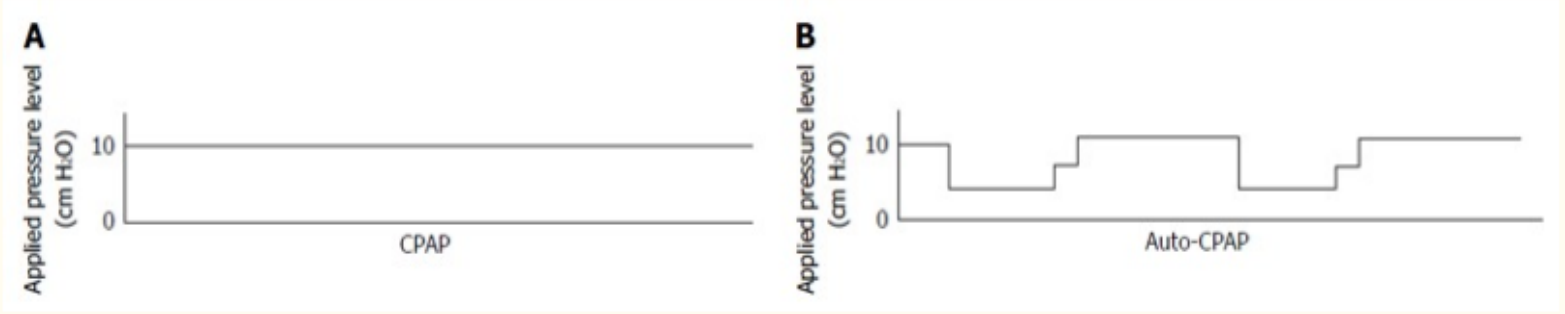


Figure 2

Differences between continuous positive airway pressure and automated continuous positive airway pressure. A: CPAP provides a constant level of positive pressure to the airway during spontaneous breathing; B: Automated CPAP devices are designed to detect various degrees of upper airway obstruction and consequently adjust the pressure level to keep the airway open. CPAP: Continuous positive airway pressure.

World J Cardio 2014 Nov26 26;6 (11):1175-1191

Positive pressure therapy works!

Table 1—*Effects of PAP Treatment*

Higher levels of evidence (multiple randomized controlled trials)
Reduction in the AHI (< 10/h)
Improvement in subjective sleepiness
Improvement in objective sleepiness
Lower levels of evidence (uncontrolled studies, smaller number of studies, or conflicting results)
Improved quality of life (vitality)
Improved nocturnal sleep quality (increased stage 3,4 sleep)
Higher level of neurocognitive function (conflicting data)
Reduced nocturnal and daytime systemic BP
Reduced pulmonary arterial pressure
Reduced risk of cardiovascular events
Reduced risk of motor vehicle accidents
Reduced nocturnal naturesis
Reduced diurnal sympathetic activity
Reduced inflammatory mediators/coagulation
Reduction in overnight hemoconcentration (Kreiger et al[77])
Decreased morning fibrinogen levels (Chin et al[78])
Reduced vascular endothelial growth factor (Lavie et al[79])
Reduced adhesion molecules and reactive oxygen species (Dyugovskaya et al[80] and Schulz et al[81])
Reduced platelet activation/aggregation (Bokinsky et al[82])
Reduced C-reactive protein and interleukin-6 (Yokoe et al[83])
Reduced atrial fibrillation recurrence after cardioversion
Improved ejection fraction in patients with congestive heart failure and OSA

Chest 2007;132

Predict CPAP compliance?

- Presence of EDS
- Severity of OSA (AHI)
- **Education/support at initiation of therapy**
- Humidification
- Bed-partner
- Mask interface
- Self-referral
- NOT pressure or Bi-level (BiPAP)

For Patients: Consequences of OSA

- Sleep Deprivation
  - Immune
  - Sexual
  - Cognition/Memory
  - Accidents
- Cardiovascular
  - Intermittent Hypoxia
  - Sympathetic surge

DM, HTN, Atrial Fibrillation

Education>Compliance>Outcomes

- Time intensive
- Specialized/RT on site
- Dashboards
- Secondary options

- CPAP compliance (old data) 50%
- AHN Center for Sleep Medicine: 80%


The End

OTHER SLEEP DISORDERS/ CODING

Jeffrey McGovern, MD, FCCP, FAASM

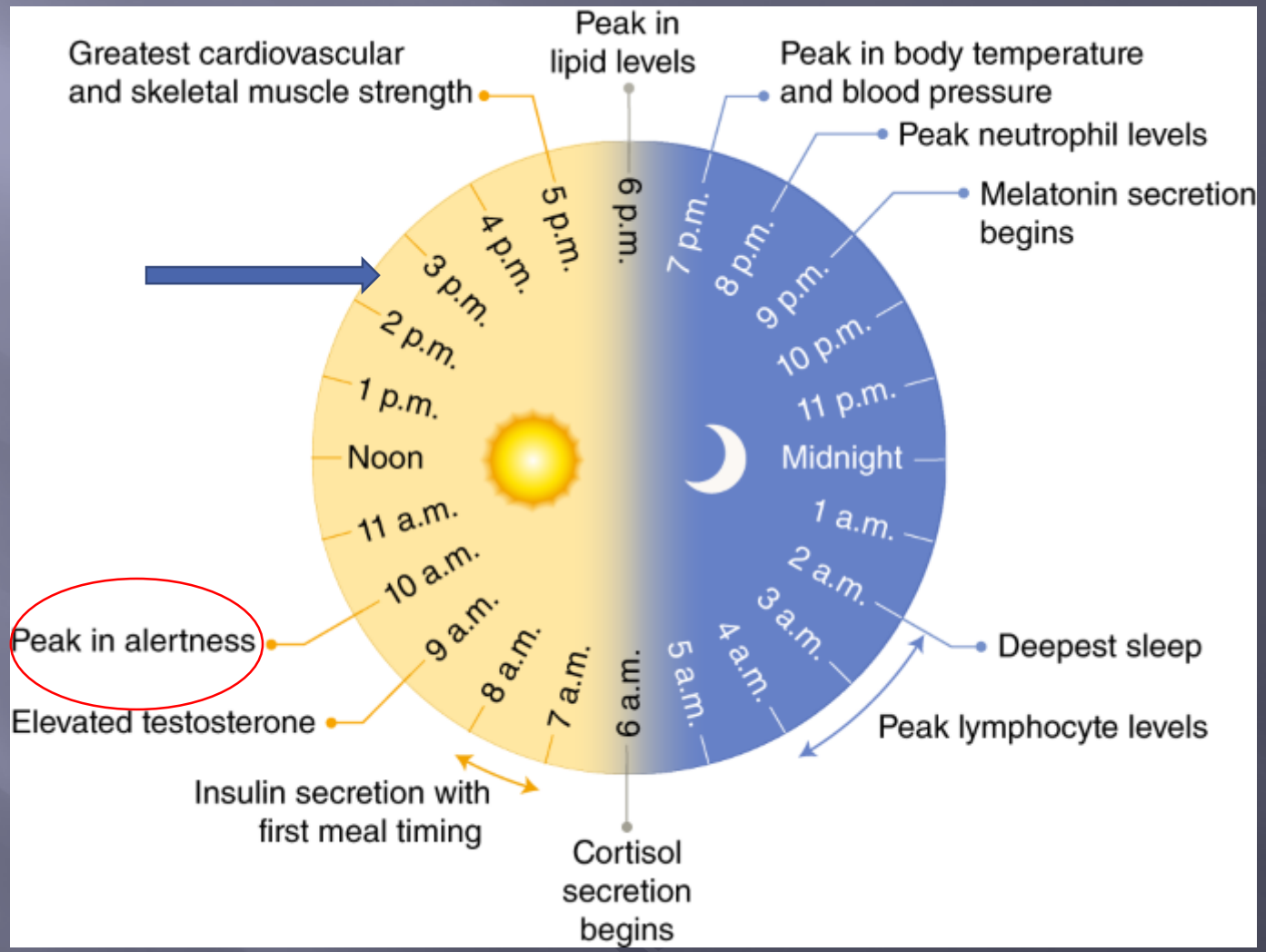
Disclosures



OTHER SLEEP DISORDERS

Review briefly sleep disorders of narcolepsy, restless legs/periodic limb movements and postgraduate fatigue

Discuss new issues and treatments for these entities


Greatest cardiovascular and skeletal muscle strength
Peak in lipid levels
Peak in body temperature and blood pressure
Peak neutrophil levels
Melatonin secretion begins
5 p.m.
6 p.m.
7 p.m.
8 p.m.
9 p.m.
10 p.m.
11 p.m.
4 p.m.
3 p.m.
2 p.m.
1 p.m.
Noon
Midnight
11 a.m.
1 a.m.
10 a.m.
2 a.m.
9 a.m.
3 a.m.
8 a.m.
4 a.m.
7 a.m.
5 a.m.
6 a.m.
Peak in alertness
Deepest sleep
Elevated testosterone
Peak lymphocyte levels
Insulin secretion with first meal timing
Cortisol secretion begins

NARCOLEPSY NT1

ICSD3

daily periods of irrepressible need to sleep or daytime lapses into sleep for at least three months

Presence of one or both:

- Cataplexy and mean sleep latency $\leq$ 8 minutes and 2 or more SOREMP (PSG or MSLT)
- CSF hypocretin-1 is either <110pg/mL or <1/3 of mean values obtained in normal subjects

Brief (< 2minutes) bilaterally symmetrical sudden loss of motor tone with retained consciousness; precipitated by strong emotions



NARCOLEPSY NT1

ICSD3

daily periods of irrepressible need to sleep or daytime lapses into sleep for at least three months

Presence of one or both:

- Cataplexy and mean sleep latency ≤ 8 minutes and 2 or more SOREMP (PSG or MSLT)
- CSF hypocretin-1 is either <110pg/mL or <1/3 of mean values obtained in normal subjects

NARCOLEPSY NT2

ICSD3
daily periods of irrepressible need to sleep or daytime lapses into sleep for at least three months
mean sleep latency < 8 minutes and 2 or more SOREMP (PSG or MSLT)
Cataplexy is absent
CSF hypocretin is > 110pg/mL or >1/3 of mean values
Hypersomnolence/MSLT findings not better explained by other causes

Narcolepsy features

- NT1
- Cataplexy and laughter
- .18% in US with M>F
- Genetics
- Bimodal (15 and 35 years)
- Deficiency in hypocretin signaling

- NT2
- No cataplexy but 10% develop
- 25% of clinic population
- Heterogeneous
- Adolescence
- Only 24% with low CSF Hcrt-1

DDX OF CNS HYPERSOMNIA

Psychiatric (can have short sleep latency in MSLT)

Kleine-Levin (derealization,hyperphagia,hypersexuality; recurrence every 18months but normal in between bouts)

Drugs(meds/withdrawal/illicit)

Medical disorders

Treatment

Practice Parameters for the Treatment of Narcolepsy and other Hypersomnias of
Central Origin
An American Academy of Sleep Medicine Report
Timothy I. Morgenthaler, MD; Vishesh K. Kapur, MD, MPH; Terry M. Brown, DO; Todd J. Swick, MD; Cathy Alessi, MD; R. Nisha Aurora, MD; Brian Boehlecke,
MD; Andrew L. Chesson Jr., MD; Leah Friedman, MA, PhD; Rama Maganti, MD; Judith Owens, MD11; Jeffrey Pancer, DDS; Rochelle Zak, MD; Standards of
Practice Committee of the AASM

Narcolepsy treatments

Modafinil	**STANDARD**
Sodium oxybate	STANDARD
Amphetamine	GUIDELINE

- The exact mechanism of action is unclear. Modafinil has been shown to significantly increase dopamine in the brain by blocking dopamine transporters; however, has a lower affinity for dopamine receptors compared to amphetamines

Narcolepsy treatments

Modafinil	STANDARD
Sodium oxybate	**STANDARD**
Amphetamine	GUIDELINE

- Sodium oxybate is derived from gamma aminobutyric acid (GABA) and acts as an inhibitory chemical transmitter in the brain. May function through specific receptors for gamma hydroxybutyrate (GHB) and GABA (B).

  Central nervous system: **Confusion** (adults: 3% to 17%), headache (≤16%), dizziness (6% to 15%)

  Drowsiness (adults: 8%), **depression** (adults: 3% to 7%), somnambulism (adults: 3% to 6%), **anxiety** (adults: 2% to 6%),

Narcolepsy treatments

Modafinil	STANDARD
Sodium oxybate	STANDARD
Amphetamine	**GUIDELINE**

- Inhibit DA and NE release and block DA and NE reuptake



CHECK THE PDMP!!!

New Meds on the block

Pitolisant

Increase CNS Histamine release

Solriamfetol

Reuptake inhibition of DA and NE

Oxybate salts

calcium, magnesium, potassium, and sodium salts with LESS salt



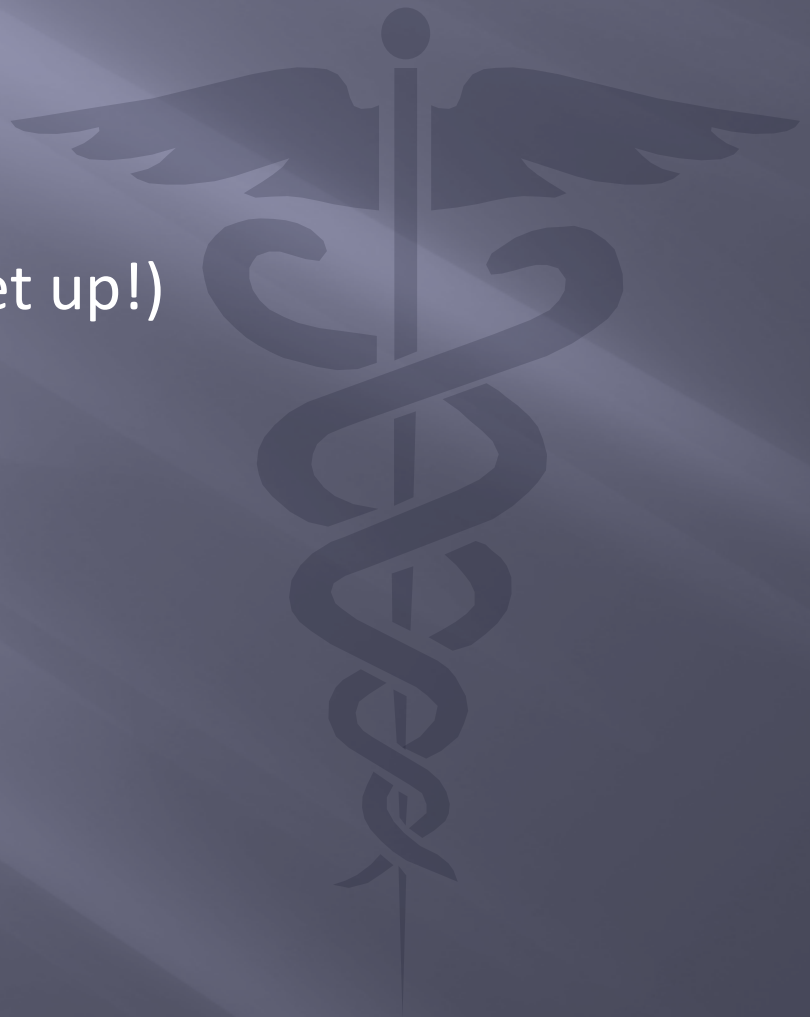
RESTLESS LEGS SYNDROME (ICSD3)

Urge to move the legs usually accompanied by uncomfortable sensation in the legs

- begin or worsen during periods of rest
- relieved partially or totally by movement
- Occur exclusively in the evening

URGE

Urge to move the legs
Rest
Relieved by movement (**G**et up!)
Circadian (**E**vening)



ASSOCIATIONS

Disturbed sleep in 60-90%

Periodic limb movements (PLM's) seen and can cause arousal from sleep

Increased prevalence of mood and anxiety disorders, ADHD (12-35%), narcolepsy, COPD, Parkinson's, OSA, DM, heart disease

RLS: DEMOGRAPHICS

Overall prevalence 5-10%

Females > males

Prevalence increases with age up to 60-70 years

RLS: PRECIPITATING FACTORS

Positive family history (early onset, complex gene-environment pattern)
Iron deficiency (serum ferritin < 50mcg/L); improved with iron
Medications (sedating antihistamines, DA antagonists, most antidepressants)
Pregnancy (2-3 times higher than general population; peak in 3rd trimester)
Chronic renal failure 2-5 times higher than general population (11-58% prevalence); improvement with kidney transplantation

RLS: ONSET AND COMPLICATIONS

Onset at any age
Familial in 3rd or 4th decade
Late onset is rapidly progressive
Impairment of health related QOL
Positive associations with RLS and cardiovascular disease (CAD) and STROKE
Increased risk of mortality in women and in CRF patients with RLS

TREATMENT

Further diagnostics studies

Avoidance measures

Behavioral and Pharmacology



DIAGNOSTICS

Sleep study?

- need to diagnose PLMD;OSA;RLS does not explain sleep disruption

Blood work

BLOOD

Hgb < 12g/dL in females; <13.5g/dL in males

Ferritin <75mcg/L (increased with inflammation and age)

TIBC >400 (decreased with inflammation and GFR)

AVOIDANCE

Nicotine*
ETOH*
Caffeine*
TCA's, SSRI's
Antihistamines
Reglan, Compazine
Antipsychotics



EXACERBATORS OF RLS

Pregnancy
ETOH
Anemia
Medications
Sleep deprivation
DM

MILD RLS (2-3 TIMES PER WEEK)

Review iron status
Evaluate secondary causes
Behavioral
- regular exercise
- sleep hygiene
- heat to legs



MODERATE TO SEVERE (>3 TIMES PER WEEK)

Evidence
Strong: pramipaxole, rotigotine, gabapentin encarbil
Moderate: ropinirole,pregabalin
Weak: Levodopa

AUGMENTATION

Seen in all DA agents

Increased RLS symptoms; earlier daily onset/other parts of the body

Change the regimen!

AUGMENTATION, CONT

Incidence
Levodopa-60%
Pramipaxole 9.2% (placebo 6%)
Ropinirole 3% (placebo 1%)
Rotigotine 1.5% (placebo 0.5%)

IMPULSE CONTROL DISORDERS (ICD) AND DOPAMINERGICS

Martinkova. Clin Neuropharmacol (2011)

2/20 patients with dopaminergic medication with pituitary adenomas with ICD's (pathological gambling, compulsive shopping, hypersexuality)



THE DAY MEDICINE CHANGES…

Libby Zion admitted 10/4/84 to NYH and died when given Demerol for agitation (was on Nardil for depression)

Death occurred before EMR's

Expert witnesses testified that they had not heard about the drug interaction

Enter Sidney Zion (attorney): death from overwork and lack of supervision of young doctors; murder charges considered but dropped

Politically motivated investigation by NY Health Commissioner followed by legislation: residents could work no longer than 24 continuous hours and no more than 80 hours per week

SLEEP, FATIGUE, AND MEDICAL TRAINING: SETTING AN AGENDA FOR OPTIMAL LEARNING AND PATIENT CARE CONFERENCE REPORT 2001,

Short term (6-12 months) and long term recommendations (>12 months)

SLEEP AND ALERTNESS IN MEDICAL INTERNS AND RESIDENTS: AN OBSERVATIONAL STUDY ON THE ROLE OF EXTENDED SHIFTS (BASNER: SLEEP 2017)

Extended overnight shifts increase the likelihood of chronic sleep restriction in interns. Reduced levels of alertness after on-call nights need to be mitigated.

MASS GEN 2018 (34 YEARS LATER!)

"All residents appear to be at risk for sleep impairment and its effects on performance, and since long work hours are a hallmark of residency training, strategies to reduce those effects are paramount," Berkowitz said. "In an era of increased recognition of and attention to physician burnout and impaired well-being, sleep hygiene is an important part of self-care that needs to be stressed."

And now for something completely different…



Revisions made by the Centers for Medicare & Medicaid Services (CMS) to its evaluation and management (E/M) codes took effect Jan. 1, 2021. The changes were based on stakeholder input gathered by the AMA Evaluation and Management Work Group, a multispecialty group with representation from the AMA/Specialty Society Relative Value Scale Update Committee (RUC) and the Current Procedural Terminology Advisory Committee.

1. History and Physical are no longer used to select an appropriate E/M code.

2. E/M code 99201 will be deleted.

3. E/M codes will be selected based on Total time or Medical Decision Making (MDM).

Number and complexity of problems addressed

Amount and/or complexity of data to be reviewed and analyzed

Risk of complications and/or morbidity or mortality of patient management

REMEMBER:

Problems

Data

Risk



5. Total time represents total time on the date of service.

Code Total Time for each code

99202 15-29 minutes of total time is spent on the date of the encounter

99203 30-44 minutes of total time is spent on the date of the encounter

99204 45-59 minutes of total time is spent on the date of the encounter

99205 60-74 minutes of total time is spent on the date of the encounter

99211 May not require the presence of a physician or other qualified health care professional. Usually, the presenting problem(s) are minimal

99212 10-19 minutes of total time is spent on the date of the encounter

99213 20-29 minutes of total time is spent on the date of the encounter

99214 30-39 minutes of total time is spent on the date of the encounter

99215 40-54 minutes of total time is spent on the date of the encounter

REMEMBER:

New patient: 15 minute increments- 15,30,45,60

Established patient: 10 minute increments-10,20,30,40

Day of service

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99202	Straightforward	**Minimal** • 1 Self-limited or minor problem	**Minimal or None**	**Minimal risk of morbidity from additional diagnostic testing or treatment**



Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99203	Low	**Low** • 2 or more self-limited or minor problems; or • 1 stable chronic illness; or • 1 acute, uncomplicated illness or injury	**Limited** ***(Must meet the requirements of at least 1 of the 2 categories):*** **Category 1: Tests and documents** Any combination of 2 from the following Review of prior external note(s) from each unique source*; Review of the result(s) of each unique test*; Ordering of each unique test* Or	**Low risk of morbidity from additional diagnostic testing or treatment**
			Category 2: Assessment requiring an independent historian(s) ***(For the categories of independent interpretation of tests and discussion of management or test interpretation, see moderate or high)***	

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99204	**Moderate**	**Moderate** • 1 or more chronic illnesses with exacerbation, progression, or side effects of treatment; or • 2 or more stable chronic illnesses; or • 1 undiagnosed new problem with uncertain prognosis; or • 1 acute illness with systemic symptoms; or • 1 acute complicated injury	**Moderate** ***(Must meet requirements of at least 1 out of 3 categories)*** **Category 1:** Tests, documents, or independent historian(s) **Any combination of 3 of the following:** • Review of prior external note(s) from each unique source; • Review of result(s) of each unique test • Ordering of each unique test • Assessment requiring an independent historian Or **Category 2:** Independent interpretation of a test performed by another physician/other qualified health care professional (not separately reported); Or **Category 3:** Discussion of management or test interpretation of external physician/other qualified health care professional/appropriate source (not separately reported)	**Moderate risk of morbidity from additional diagnostic testing or treatment** *Examples only:* • Prescription drug management • Decision regarding minor surgery with identified patient or procedure risk factors • Decision regarding elective major surgery without identified patient or procedure risk factors • Diagnosis or treatment significantly limited by social determinants of health

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99205	High	High • 1 or more chronic illnesses with severe exacerbation, progression, or side effects of treatment; or • 1 acute or chronic illness or injury that poses a threat to life or bodily function	Extensive (Must meet requirements of at least 2 out of 3 categories) Category 1: Tests, documents, or independent historian(s) Any combination of 3 of the following: • Review of prior external note(s) from each unique source; • Review of result(s) of each unique test • Ordering of each unique test • Assessment requiring an independent historian Or Category 2: Independent interpretation of a test performed by another physician/other qualified health care professional (not separately reported); Or Category 3: Discussion of management or test interpretation of external physician/other qualified health care professional/appropriate source (not separately reported)	High risk of morbidity from additional diagnostic testing or treatment Examples only: • Drug therapy requiring intensive monitoring for toxicity • Decision regarding elective major surgery with identified patient or procedure risk factors • Decision regarding emergency major surgery • Decision regarding hospitalization • Decision not to resuscitate or to de-escalate care because of poor prognosis

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99211	N/A	N/A	N/A	N/A

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99212	Straightfor ward	**Minimal** • 1 Self-limited or minor problem	**Minimal or None**	**Minimal risk of morbidity from additional diagnostic testing or treatment**

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99213	Low	**Low** • 2 or more self-limited or minor problems; or • 1 stable chronic illness; or • 1 acute, uncomplicated illness or injury	**Limited** ***(Must meet the requirements of at least 1 of the 2 categories):*** **Category 1: Tests and documents** Any combination of 2 from the following Review of prior external note(s) from each unique source*; Review of the result(s) of each unique test*; Ordering of each unique test* Or	**Low risk of morbidity from additional diagnostic testing or treatment**
			Category 2: Assessment requiring an independent historian(s) ***(For the categories of independent interpretation of tests and discussion of management or test interpretation, see moderate or high)***	

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99214	**Moderate**	**Moderate** • 1 or more chronic illnesses with exacerbation, progression, or side effects of treatment; or • 2 or more stable chronic illnesses; or • 1 undiagnosed new problem with uncertain prognosis; or • 1 acute illness with systemic symptoms; or • 1 acute complicated injury	**Moderate** ***(Must meet requirements of at least 1 out of 3 categories)*** **Category 1:** Tests, documents, or independent historian(s) **Any combination of 3 of the following:** • Review of prior external note(s) from each unique source; • Review of result(s) of each unique test • Ordering of each unique test • Assessment requiring an independent historian Or **Category 2:** Independent interpretation of a test performed by another physician/other qualified health care professional (not separately reported); Or **Category 3:** Discussion of management or test interpretation of external physician/other qualified health care professional/appropriate source (not separately reported)	**Moderate risk of morbidity from additional diagnostic testing or treatment** *Examples only:* • Prescription drug management • Decision regarding minor surgery with identified patient or procedure risk factors • Decision regarding elective major surgery without identified patient or procedure risk factors • Diagnosis or treatment significantly limited by social determinants of health

Code	Level of MDM (Based on 2 out of 3 elements of MDM)	Number and Complexity of Problems Addressed	Amount and/or Complexity of Data to be Reviewed and Analyzed *-Each unique test, order, or document contributes to the combination of 2 or combination of 3 in Category 1 below	Risk of Complications and/or Morbidity or Mortality of Patient Management
99215	High	High • 1 or more chronic illnesses with severe exacerbation, progression, or side effects of treatment; or • 1 acute or chronic illness or injury that poses a threat to life or bodily function	Extensive (Must meet requirements of at least 2 out of 3 categories) Category 1: Tests, documents, or independent historian(s) Any combination of 3 of the following: • Review of prior external note(s) from each unique source; • Review of result(s) of each unique test • Ordering of each unique test • Assessment requiring an independent historian Or Category 2: Independent interpretation of a test performed by another physician/other qualified health care professional (not separately reported); Or Category 3: Discussion of management or test interpretation of external physician/other qualified health care professional/appropriate source (not separately reported)	High risk of morbidity from additional diagnostic testing or treatment Examples only: • Drug therapy requiring intensive monitoring for toxicity • Decision regarding elective major surgery with identified patient or procedure risk factors • Decision regarding emergency major surgery • Decision regarding hospitalization • Decision not to resuscitate or to de-escalate care because of poor prognosis



Questions?



Thank you!

Lung Transplantation

Anil Singh, MD, MPH, MMM, FCCP
Executive Medical Director
Clinical Solutions, Design and Implementation
Highmark Health

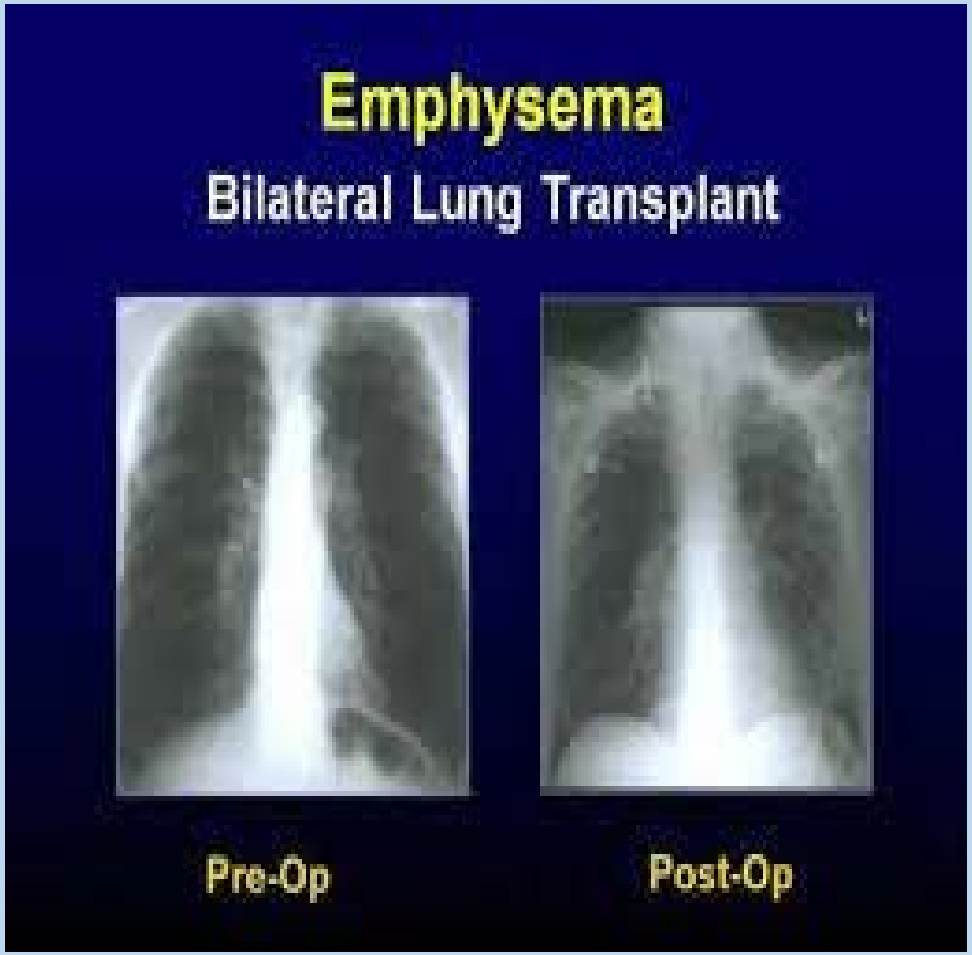
FAQ’s: lung transplant

- Improvement in lung function
- Improvement in overall quality of life
- Improvement in exercise tolerance
- 2010-2017 median survival 6.7 years



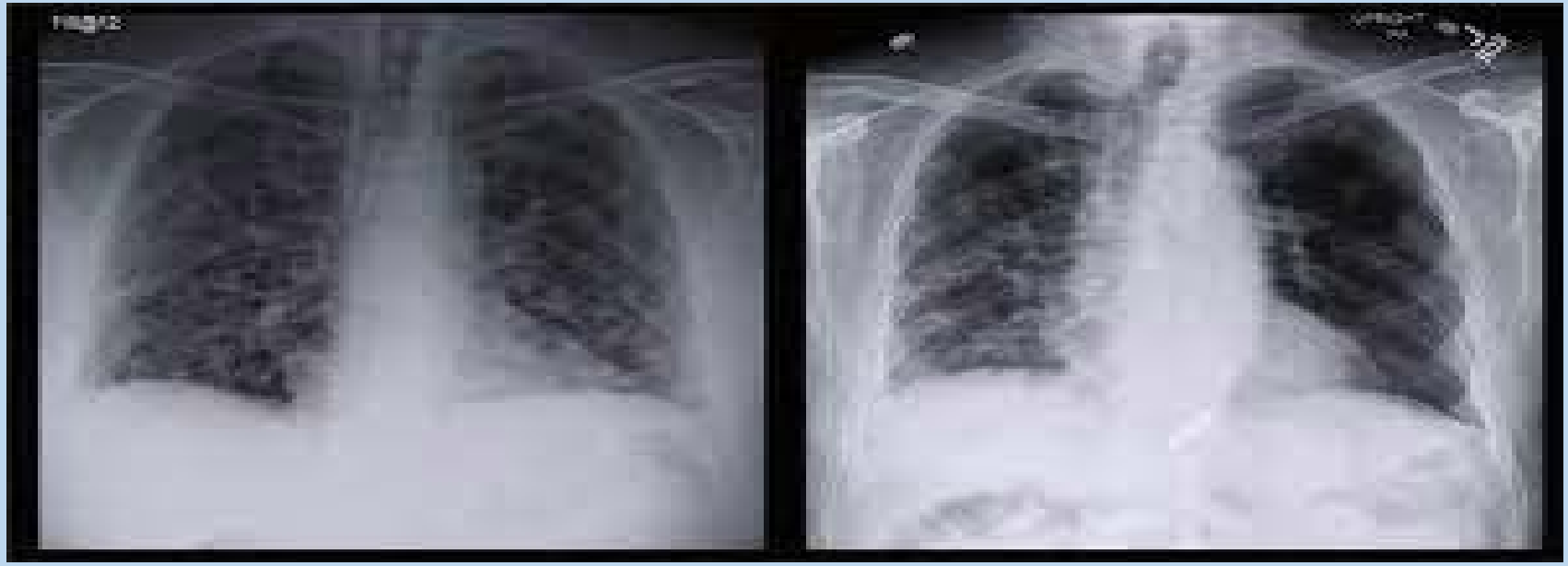
When to refer a patient?

- COPD
  - Quit smoking
  - FEV1 <30%
  - Hypercapnia
  - 6 minute walk distance < 1000 feet
  - Secondary Pulmonary HTN



When to refer?

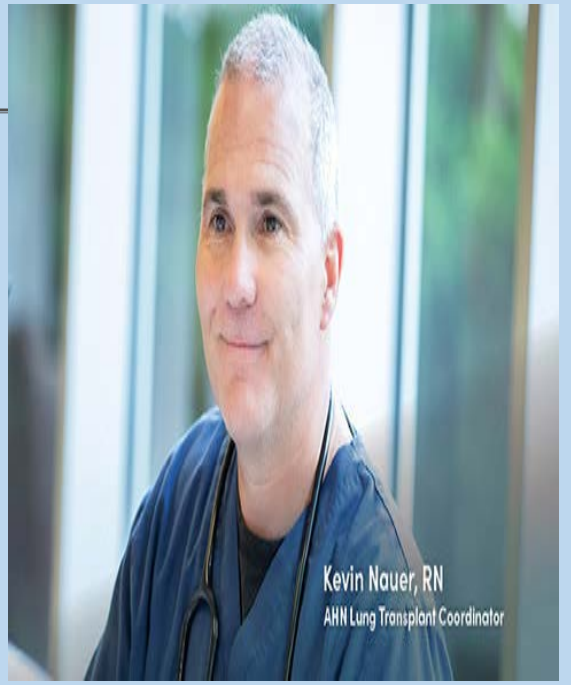
- Idiopathic Pulmonary Fibrosis with or without Connective Tissue Disease
  - FVC <50%
  - Secondary Pulmonary HTN
  - Recent hospitalization or with worsening progressive symptoms
  - Resting hypoxia



Why Johns Hopkins?

- Shortened wait times
  - most patients receiving their transplant within three months of being placed on the waitlist.
- Survival rate
  - first-year survival rate, a benchmark for long-term success, is over 93 percent, which exceeds the national average of 88.58 percent.
- Quality of life
  - Over 90 percent of patients report that they have few or no physical activity limitations and that their quality of life improved after transplant.

Lung Transplant



Formal clinical collaboration between AHN/JHM/HH to create a comprehensive lung transplant program for AHN patients.

- Pre-testing will be completed in Pittsburgh
- Evaluation will be completed in Baltimore by JHM
- Surgery by JHM and recovery (8-12 weeks) will be in Baltimore
- Post-Acute care in Pittsburgh by AHN
- Travel expenses will be covered (Highmark member)

AHN currently has 2 patients that are ready for formal evaluation by JHM in Baltimore

HIGHMARK HEALTH | AHN | JOHNS HOPKINS MEDICINE

1st Success

- **PITTSBURGH (PRWEB) FEBRUARY 02, 2021**
- Allegheny Health Network (AHN) and Johns Hopkins Medicine announced today the first successful lung transplantation as part of a unique collaboration launched last year between the two organizations.
- A 65-year-old woman from Pittsburgh with level D chronic obstructive pulmonary disease (COPD) underwent a bilateral lung transplant at The Johns Hopkins Hospital in Baltimore in September 2020 as part of the program. According to body-mass index, airflow obstruction, dyspnea, and exercise capacity (BODE) rating, level D is the most severe form of COPD, often leading to lung transplantation being considered. After a week in the hospital and six weeks of post-operative care in Baltimore, the patient returned home to Pittsburgh where she is continuing her care at AHN, with regular follow up by the Johns Hopkins team as well.

Thank you

Questions??

If you would like to contact any of the faculty with questions please feel free to email them.

Tariq Cheema, MD	tariq.cheema@ahn.org
Anil C. Singh, MD	anil.singh@ahn.org
Ahmad Alhajhusain, MD	ahmad.alhajhusain@ahn.org
Sohini Ghosh, MD	Sohini.ghosh@ahn.org
Jeffrey McGovern, MD	Jeffrey.mcgovern@ahn.org
Kevin Nauer, RN	kevin.nauer@ahn.org
Daniel A. Shade, MD	Daniel.shade@ahn.org
Benny Weksler, MD	benny.weksler@ahn.org
Tiffany Dumont, DO	tiffany.dumont@ahn.org
Amit Kaura, MD	amit.kaura@ahn.org
Timothy Mickus, MD	timothy.mickus@ahn.org
Christine Rauscher, MD	Christine.rauscher@ahn.org
Amy Schmetzer, DNP	amy.schmetzer@ahn.org
Meilin Young, MD	Meilin.young@ahn.org



Allegheny Health Network CME