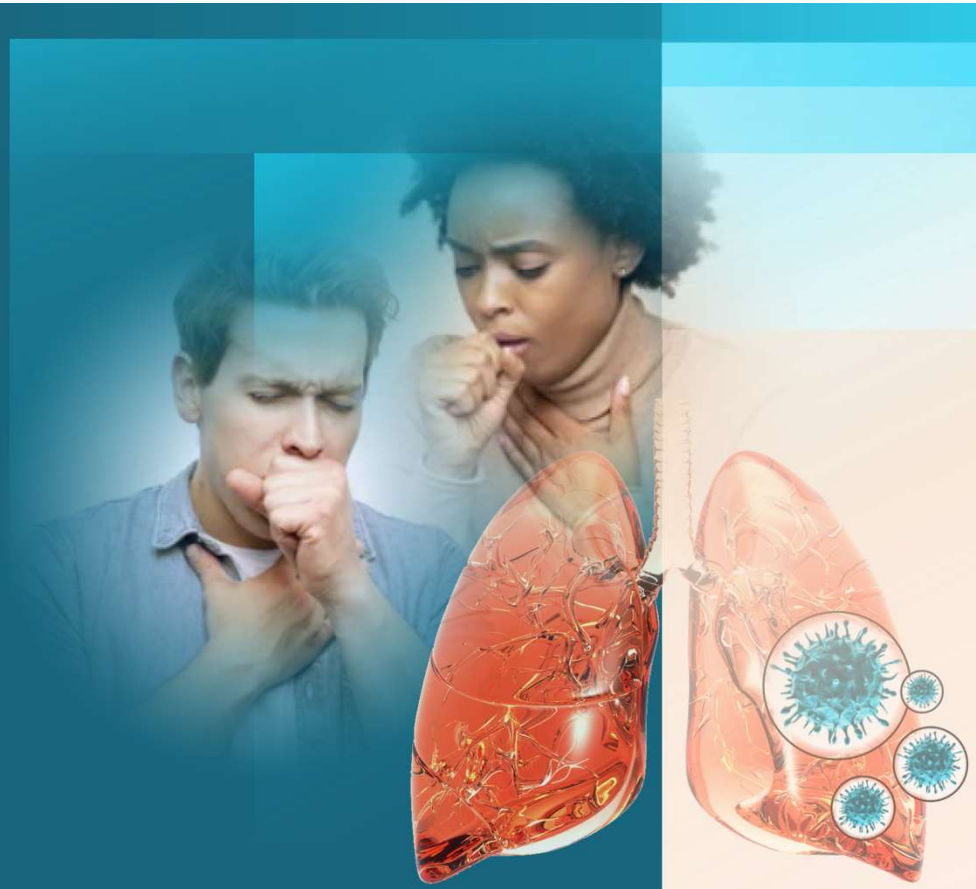

Struggling to Breathe:

The Patient Journey to Diagnosis and Treatment of Interstitial Lung Disease

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Learning Objectives

1. Define the epidemiology, disease burden, and signs and symptoms of interstitial lung disease (ILD).
2. Identify risk factors and/or comorbidities associated with ILD.
3. Identify strategies for timely and accurate ILD diagnosis and referral, including the use of appropriate tests and procedures.
4. Commit to strategies optimizing interprofessional, multidisciplinary communication among patients, caregivers, and the health care team that is culturally and linguistically appropriate.
5. Discuss aspects of the socioeconomic and health disparities impacting optimal ILD management.

Video Vignette: Joel's Diagnosis Story

Interstitial Lung Disease (ILD) Introduction

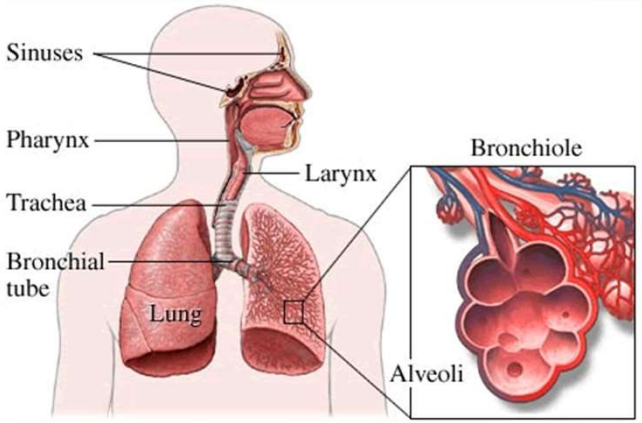
Interstitial Lung Disease: A Heterogenous Group!

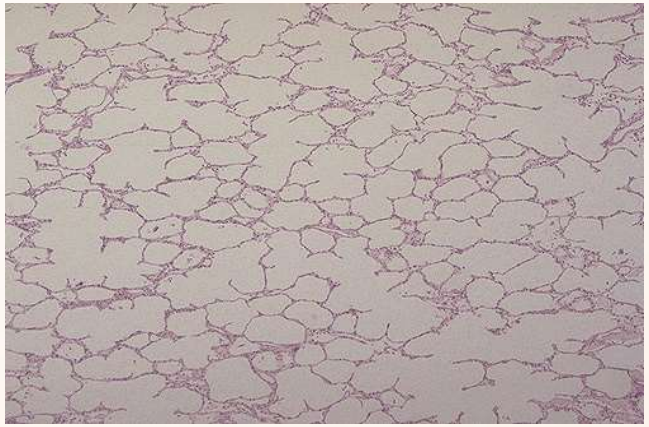
Interstitial Lung Disease

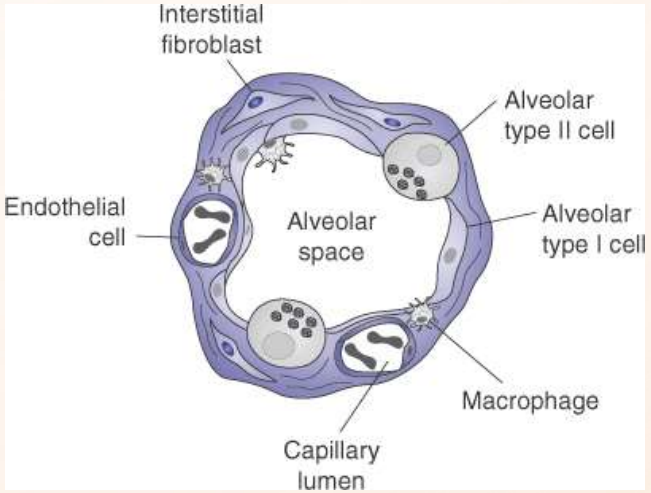
- Idiopathic Interstitial Pneumonias
  - Familial (e.g., Telomerase mutations)
  - Nonfamilial
    - Smoking-Related
      - RB-ILD
      - DIP
    - Acute/Subacute
      - COP
      - AIP
    - Chronic/Fibrosing
      - IPF
      - NSIP
- Occupational/Environmental/ Drugs (e.g., asbestos)
- Systemic Disease (e.g., RA, scleroderma)
- Granulomatous Disease (e.g., sarcoidosis)
- Other Rare Causes (e.g., LAM, PLCH)

RA = Rheumatoid arthritis; LAM = Lymphangioleiomyomatosis; PLCH = Pulmonary Langerhans cell histiocytosis; RB-ILD = Respiratory bronchiolitis ILD; DIP = Desquamative interstitial pneumonia; COP = Cryptogenic organizing pneumonia; AIP= Acute interstitial pneumonia; NSIP = Nonspecific interstitial pneumonia

The Distal Human Lung Is Composed of Delicate Alveoli Required for Gas Exchange





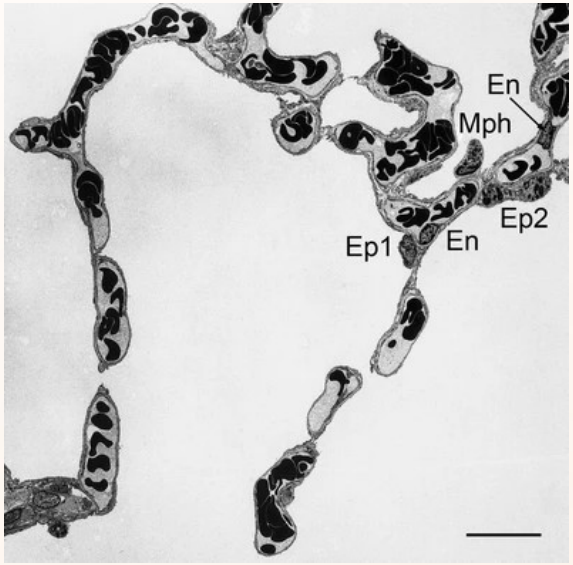


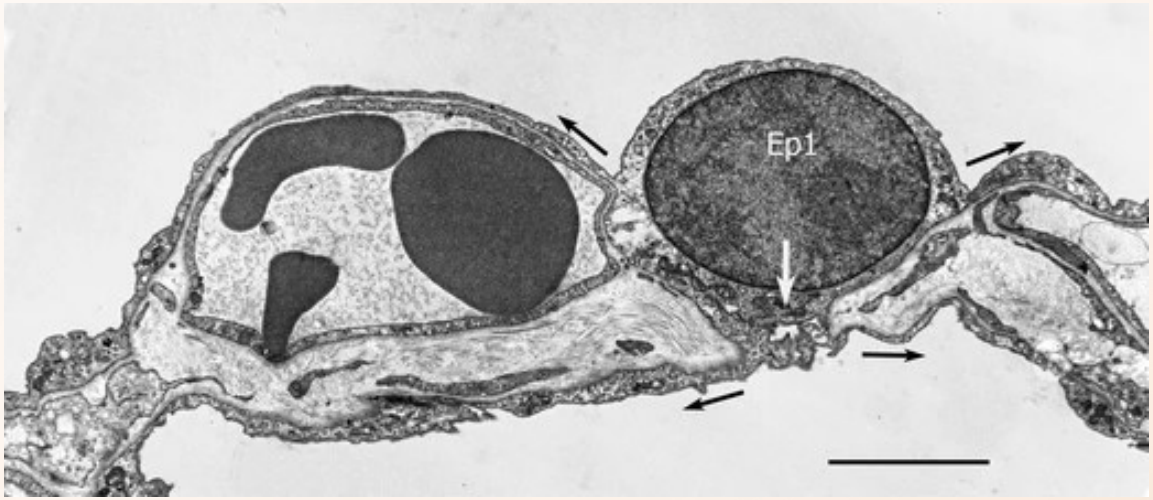
- Alveolar type 1 cells are responsible for gas exchange with capillaries.
- Alveolar type 2 cells secrete surfactant.
- There is a subtle interstitial space underlying the epithelium that normally is very small and contains infrequent fibroblasts.

Image credits: webpath.med.Utah.edu, Quizlet.com

Electron Micrograph of the Alveolar-Capillary Interface

Flat, large, and very thin alveolar type 1 cells wrap endothelial capillary cells to allow gas exchange.





Weibel ER. Lung morphometry: the link between structure and function. *Cell Tissue Res.* 2017;367:413-426.
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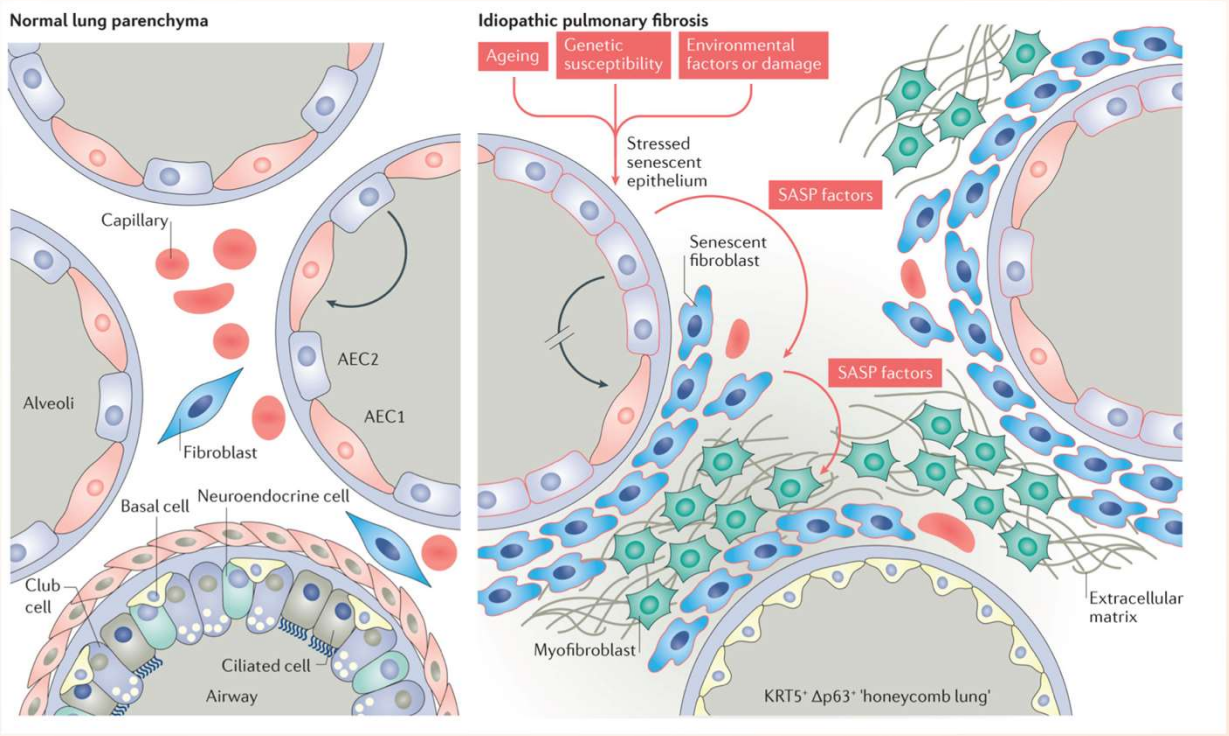
Mechanisms of Idiopathic Pulmonary Fibrosis (IPF)

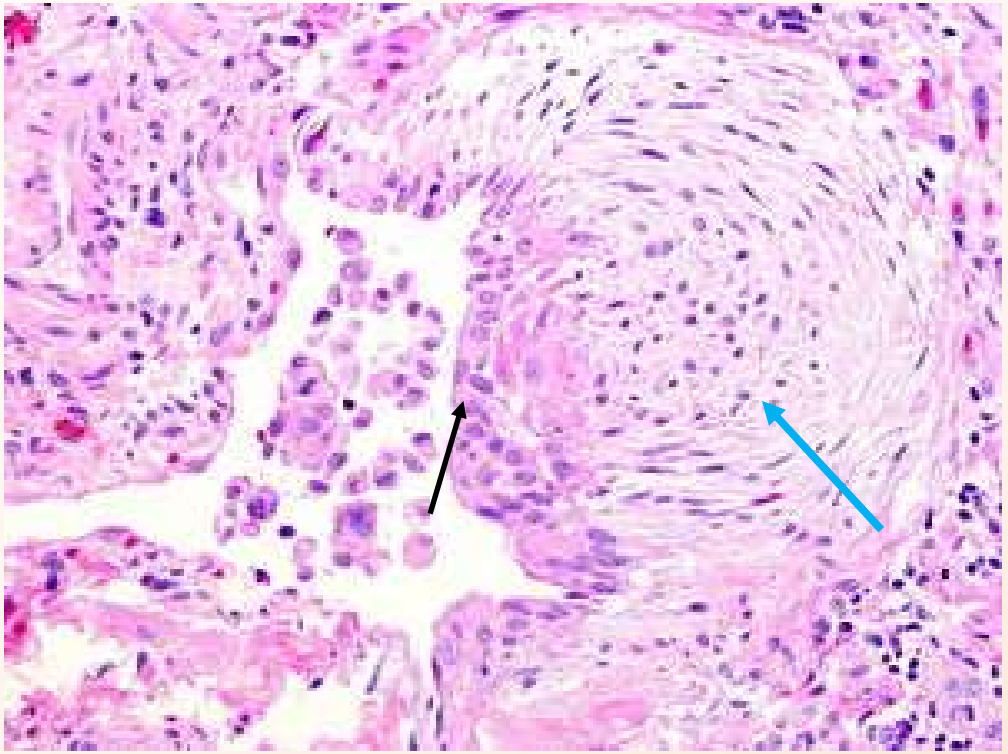
- Cyclical injury to the distal lung, in particular alveolar type 2 cells
- Eventually leads to abnormal cell behaviors and activation of the fibroblast compartment
- This includes proliferation of myofibroblasts that drive fibrotic remodeling.
- The pattern seen histologically is described as usual interstitial pneumonia (UIP).



Nat Rev Drug Discov. 2017 October 30;16(11):810. doi:10.1038/nrd.2017.225.

Histological Features of UIP

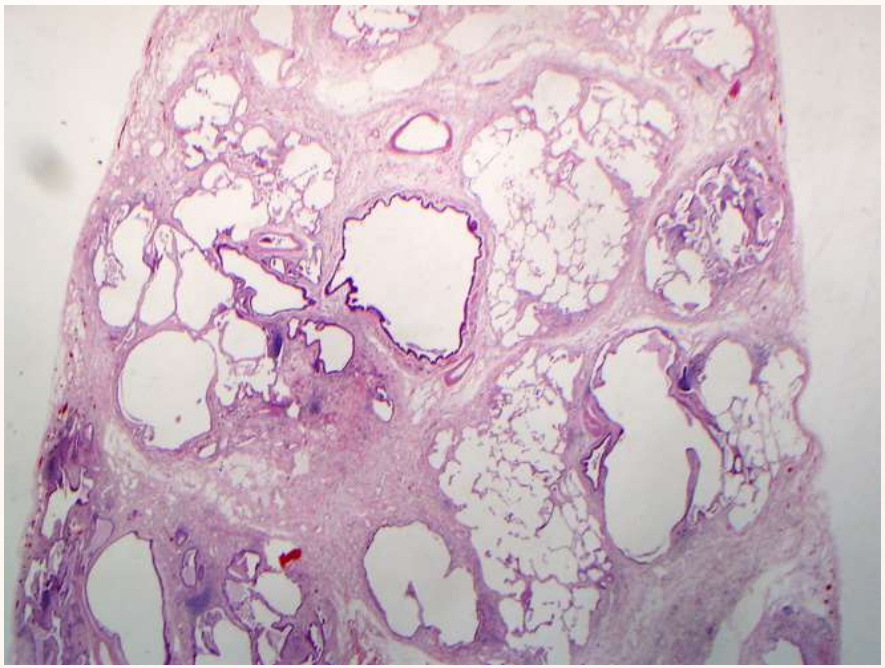
- Fibroblastic foci are a key finding in IPF
- Accumulation of myofibroblasts in the interstitium and typically immediately adjacent to atypical alveolar type 2 cells

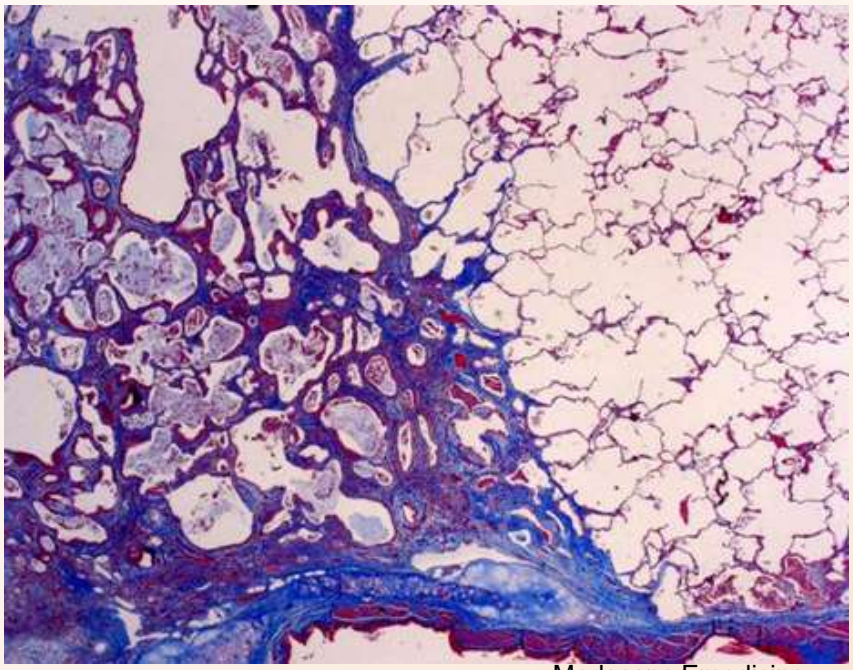


Wikimedia commons

Histological Features of UIP

- Subpleural process
- Dense fibrotic bands
- Bronchiolization (i.e., cystic structures lined with airway like cells)
- Heterogeneity: very abnormal areas adjacent to seemingly normal lung

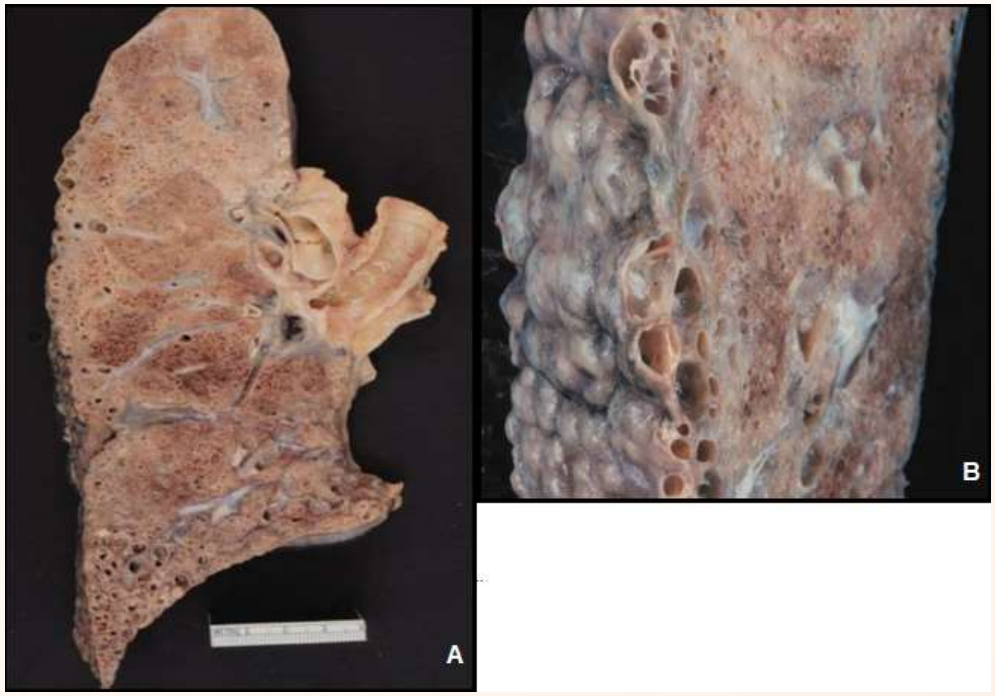




Medscape Emedicine

Macroscopic Appearance of the Lung in UIP/IPF

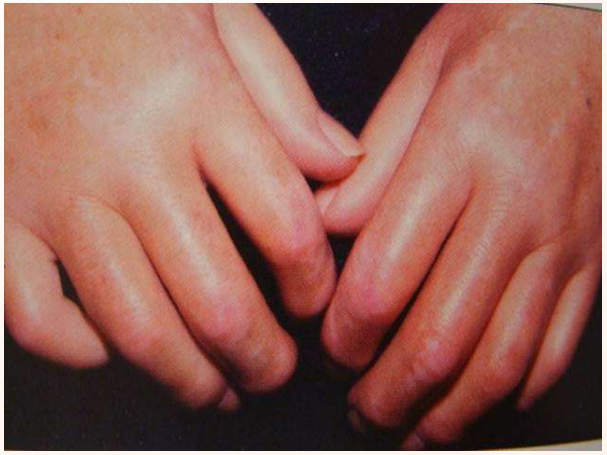
- Fibrosis and cysts in a subpleural and basilar distribution
- Dilated airways – traction bronchiectasis
- Small lung volumes



ILD in Systemic Diseases: Important to Evaluate for Underlying Connective Tissue Disease

- Scleroderma (scl-70) (NSIP>UIP)
- Lupus (ANA, anti-ds DNA, anti-Sm)
- Rheumatoid arthritis (RF) (NSIP, UIP, COP)
- Dermatomyositis (jo-1 antibodies) (NSIP, UIP)

Sclerodactyly



Raynaud's syndrome

Gottron's papules

Drug/Occupational/Environmental Exposures

- Asbestos
- Silica
- Chemotherapeutic agents
- Other drug reactions (nitrofurantoin, amiodarone)
- Organic antigens associated with hypersensitivity pneumonitis
  - Extensive list; birds, antigens, and agriculture among most frequent causes

Strategies for Timely and Accurate Diagnosis and Referral

Audience Polling Question 1

How confident are you in your ability to diagnose ILD in your practice?
(5 = very confident, 1 = not at all confident, please select one)

How confident are you in knowing when to refer your patients with ILD to a pulmonary specialist?
(5 = very confident, 1 = not at all confident, please select one)

High-Resolution CT Chest Patterns in Idiopathic Pulmonary Fibrosis (UIP)

UIP

- Subpleural and basal predominant; distribution is often heterogeneous
- Honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis

Probable UIP

- Subpleural and basal predominant; distribution is often heterogeneous
- Reticular pattern with peripheral traction bronchiectasis or bronchiolectasis
- May have mild GGO

Indeterminate for UIP

- Subpleural and basal predominant
- Subtle reticulation; may have mild GGO or distortion ("early UIP pattern")
- CT features and/or distribution of lung fibrosis that do not suggest any specific etiology ("truly indeterminate for UIP")

Alternative Diagnosis

- Findings suggestive of another diagnosis, including:

CT Features

- Cysts
- Marked mosaic attenuation
- Predominant GGO
- Profuse micronodules
- Centrilobular nodules
- Nodules
- Consolidation

Predominent distribution

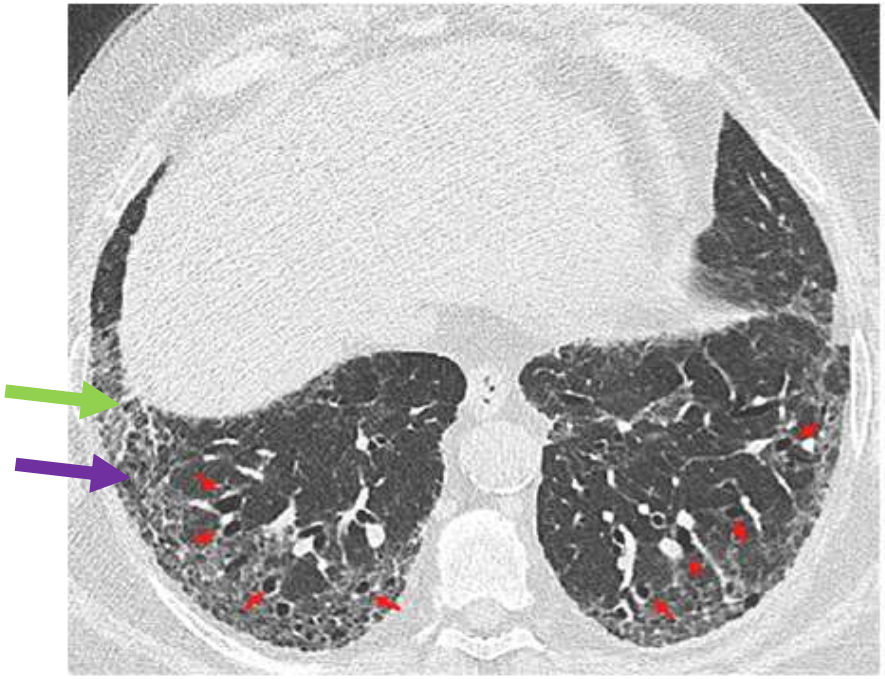
- Peribronchovascular
- Perilymphatic
- Upper or mid-lung

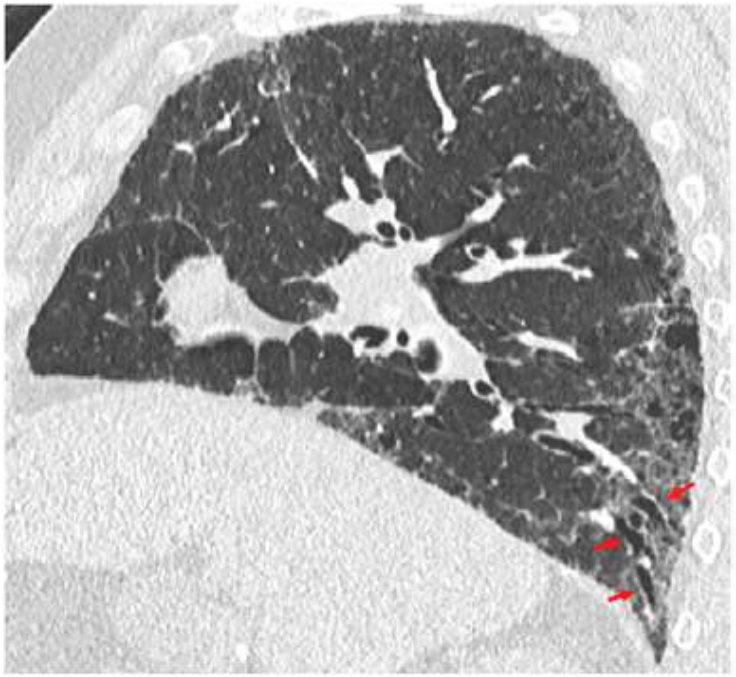
Other

- Pleural plaques (consider asbestosis)
- Dilated esophagus (consider CTD)
- Distal clavicular erosions (consider other etiologies)
- Pleural effusions, pleural thickening (consider CTD/drugs)

American Thoracic Society. IPF: Update 2021. Available at: https://www.thoracic.org/education-center/ild/pdf/ats-pocket-guide_2021_redesign_r2.pdf

Reticulations, Traction Bronchiectasis, and Distribution in the Lung

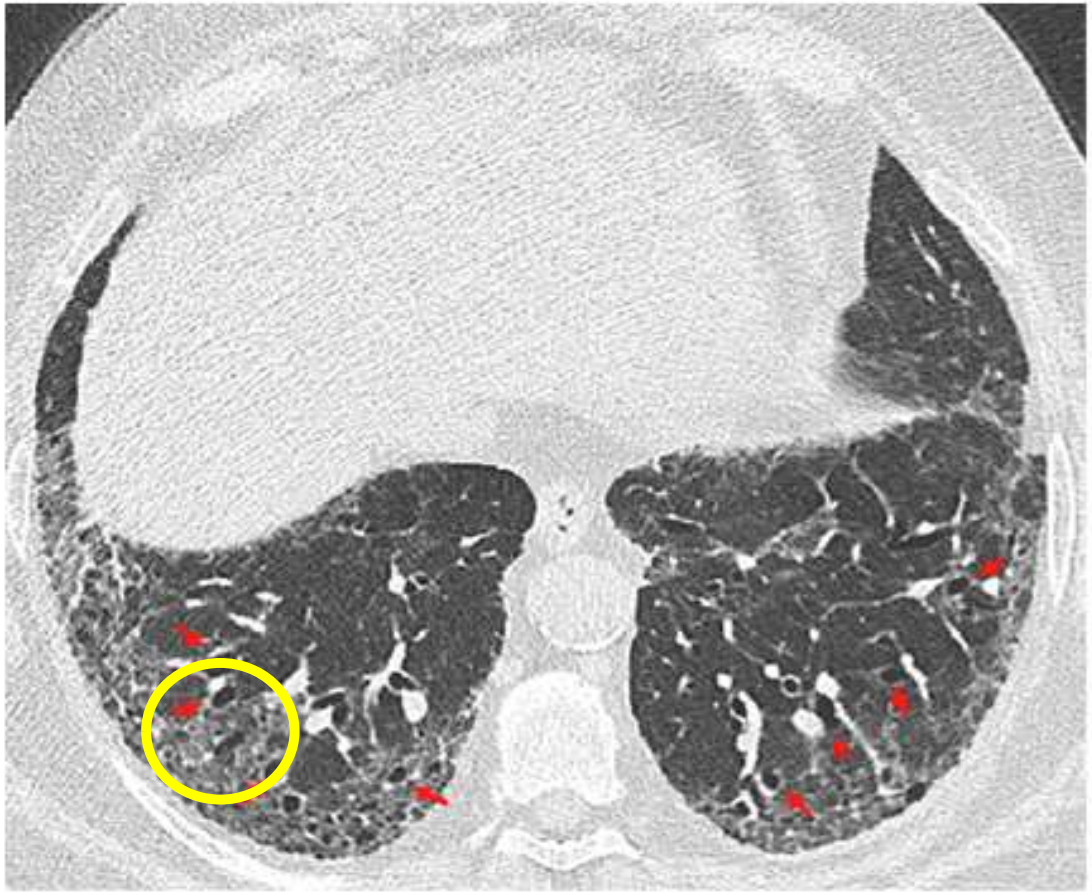




Traction bronchiectasis
Septal thickening
Reticulations
} Fibrotic changes

Distribution
- Subpleural
- Basilar predominant

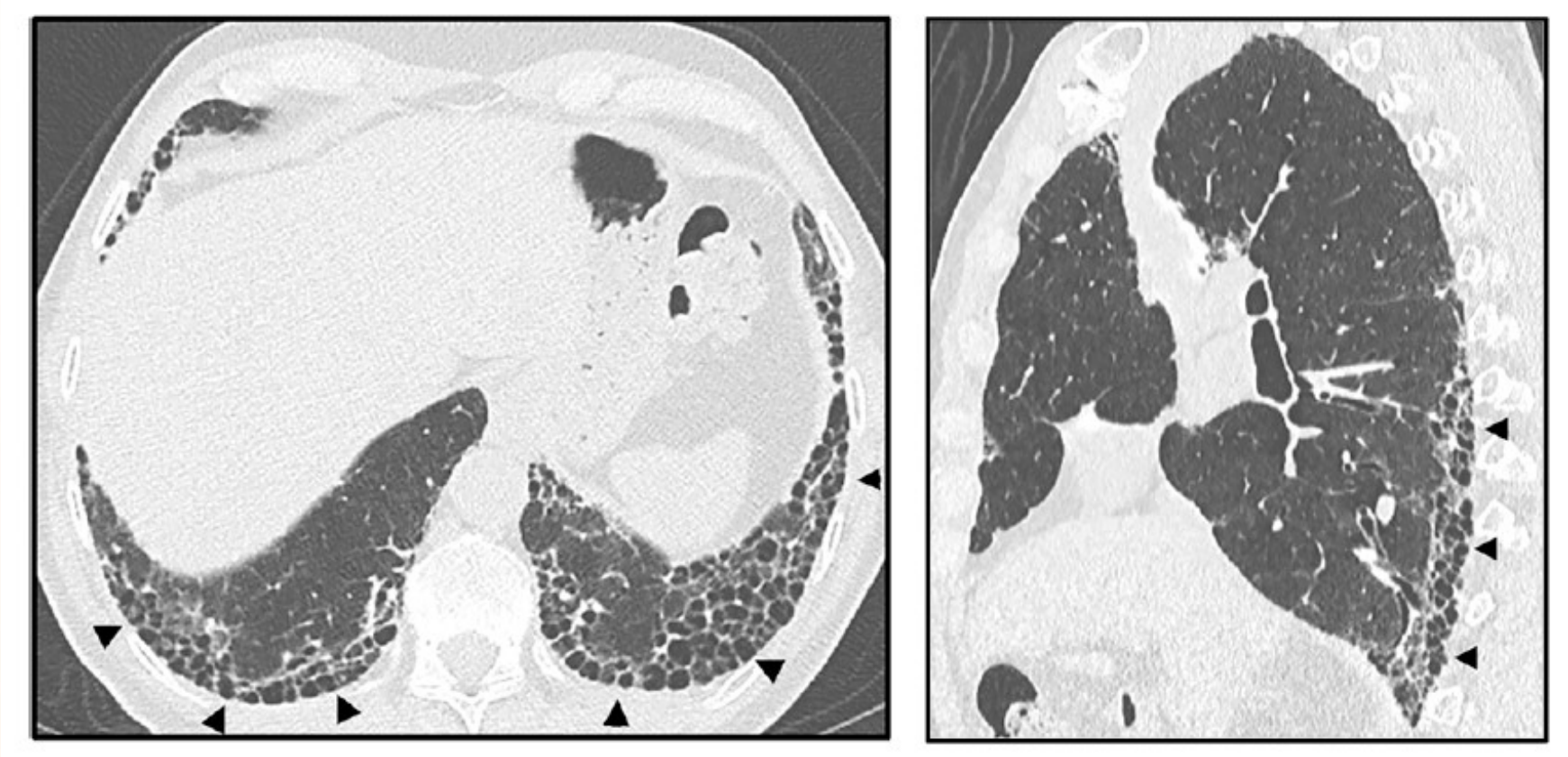
Lack of Atypical Features such as Ground Glass Opacity



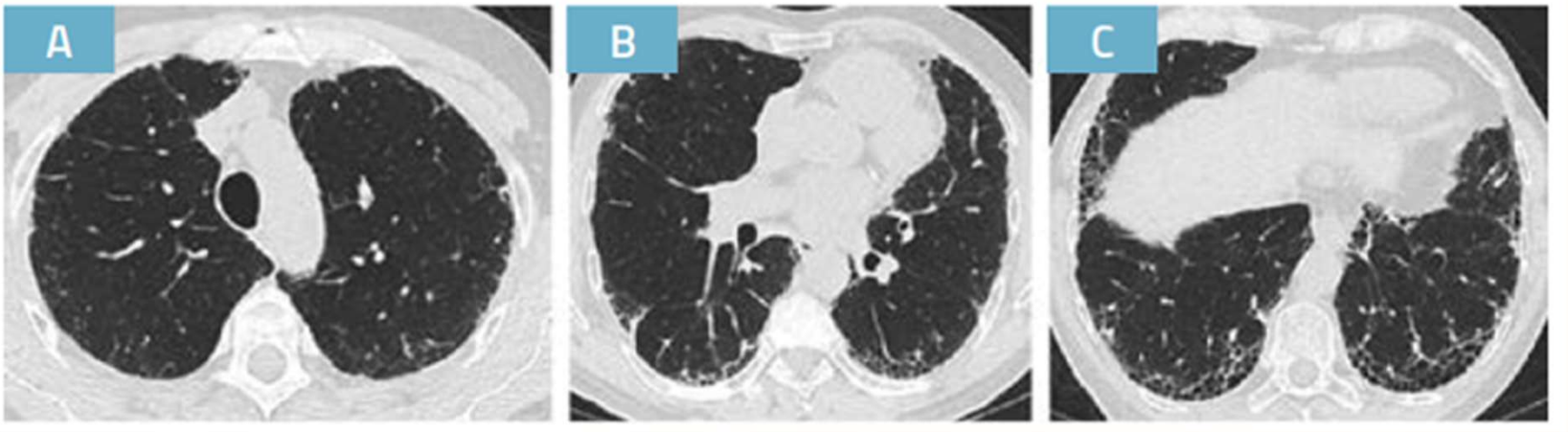
- Ground glass opacities (GGOs) suggest more subtle abnormalities in the alveoli including inflammation and are minimal in UIP
- Moderate or more GGOs suggest an alternative diagnosis

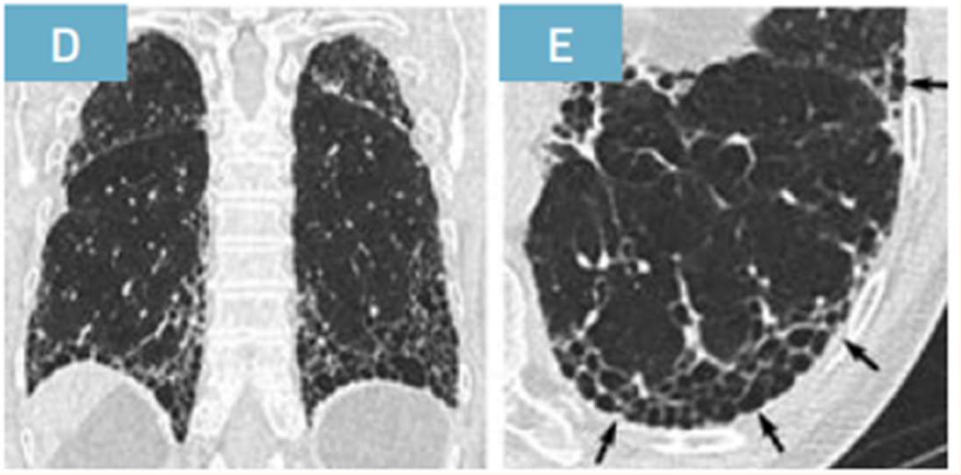
Raghu G, et al. *Am J Respir Crit Care Med*. 2022;205(9):e18-e47.

Honeycomb Cysts



UIP Pattern

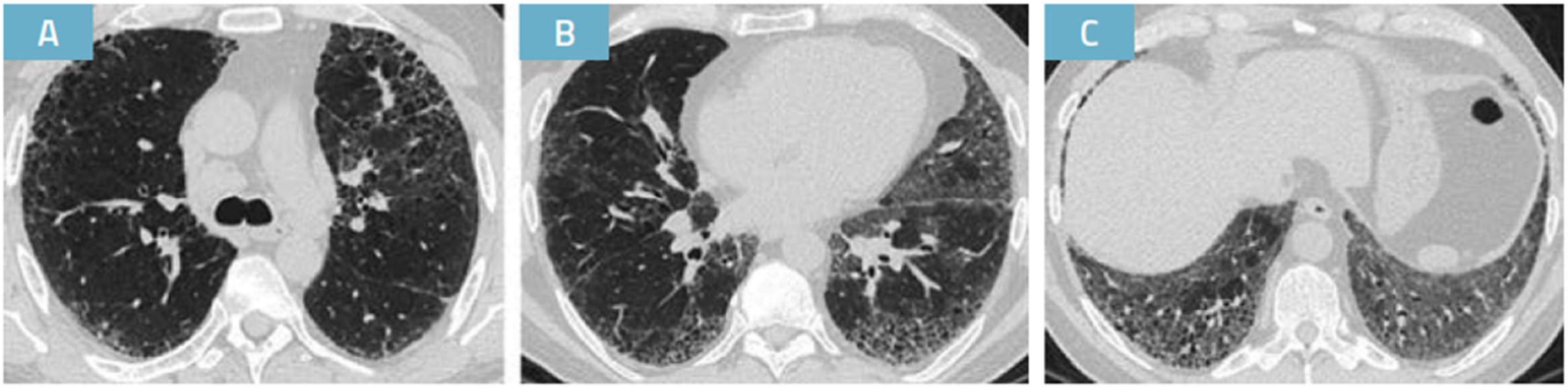




- A–C (transverse CT section) and D (coronal reconstruction) illustrating presence of honeycombing with subpleural and basal predominance, and mild ground-glass opacity.
- E: Magnified view of left lower lobe showing honeycombing, consisting of clustered cystic airspaces with well-defined walls and variable diameters, seen in single or multiple layers (arrows).

American Thoracic Society. IPF: Update 2021. Available at: https://www.thoracic.org/education-center/ild/pdf/ats-pocket-guide_2021_redesign_r2.pdf

Indeterminate for UIP Pattern



- Transverse CT sections: extensive lung filtration combining honeycombing, mild-to-marked GGO, asymmetrical distribution b/w both lungs, and no subpleural predominance.

American Thoracic Society. IPF: Update 2021. Available at: https://www.thoracic.org/education-center/ild/pdf/ats-pocket-guide_2021_redesign_r2.pdf

Interstitial Lung Disease: A Heterogenous Group!

Interstitial Lung Disease

- Idiopathic Interstitial Pneumonias
  - Familial (e.g., SFTPC mutations TERT mutations)
  - Nonfamilial
    - Smoking-Related
      - RB-ILD
      - DIP
    - Acute/Subacute
      - COP
      - AIP
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- Other rare causes (e.g., LAM, PLCH)

RA = Rheumatoid arthritis; LAM = Lymphangioleiomyomatosis; PLCH = Pulmonary Langerhans cell histiocytosis; RB-ILD = Respiratory bronchiolitis ILD; DIP = Desquamative interstitial pneumonia; COP = Cryptogenic organizing pneumonia; AIP= Acute interstitial pneumonia; NSIP = Nonspecific interstitial pneumonia

Summary

-Interstitial Lung Disease describes a heterogenous group of conditions of variable cause

-The most common symptoms are shortness of breath and cough which are very non-specific

-Primary care physicians should have ILD in their differential diagnosis, but the complexity can be challenging

-Detailed history or exposures (occupational, environmental) and a detailed assessment for connective tissue disease are important factors in the work up of any patient suspected of having ILD.

-CT chest patterns are important factors in ILD and with the increasing frequency of imaging being performed, abnormalities are frequently detected.

-Diagnosis of ILD and referral to a specialist are often delayed.

Case Study
Clinical Visit 1

Visit 1: 57-Year-Old Male Presents to Primary Care Physician for Evaluation

Past Medical History
- HTN: Well controlled for years
- Hypercholesterolemia

Medications
- Atorvastatin 40 mg daily
- Lisinopril 40

Social History
- Occupation: Real estate agent
- Tobacco use: Lifelong nonsmoker
- Alcohol use: Rare alcohol use, 1 glass/week
- No drugs

Family History
- Father with coronary artery disease at age 52
- His two siblings are healthy

Visit 1: Dialogue/Role Play

JW: *What brings you in today?*

AB: *Hey Doc, well you know I've always been active-biking, hiking, long workouts, racquetball. So, I was a little concerned when as I started a workout last week and just a couple minutes into my routine I became very winded. I thought to myself, I can't be that out of shape. It was just weird. So, I thought I'd come and see you.*

JW: *Thanks for coming in. This does sound unusual for you. Could you tell me a little bit more about feeling winded?*

AB: *I really only notice it when I am doing heavy activity. In fact, this morning when I was on my morning bike ride, after about a half a mile I got pretty short of breath. I had to stop and catch my breath. I was probably standing on the roadside for 5 or 6 minutes just trying to catch my breath.*

JW: *Have you ever noticed being winded before?*

AB: *No, this sensation that I been having is new for me.*

JW: *When this shortness of breath happens—say, this morning, for example—does it come on suddenly?*

AB: *I would say more gradually. It's not immediate—it usually develops over the course of a few minutes.*

JW: *If you can think back, did you have any limitations with biking or hiking 2 months ago?*

Visit 1: Dialogue/Role Play (cont.)

AB: *Now that you mention it, I was finding myself not able to go as long as I did in the past on the bike. I did not notice it at that time.*

JW: *Do you get any shortness of breath while at rest?*

AB: *No, fortunately I have not had any symptoms while sitting around the house. I am actually also probably a little winded after going up the flight of stairs in my house.*

JW: *Have you had any other symptoms like chest pain, palpitations, or swelling in your legs?*

AB: *No, no chest pain. Occasionally my chest feels a little bit weird. My chest feels very congested each morning, like a chest cold. I have been coughing up mucus, though it's white in color*.

JW: *Have you noticed any bleeding from anywhere or any black stools?*

AB: *I did have that stomach ulcer many years ago but has not had any of those symptoms since. My stools have been normal.*

JW: *Have you been sick at all the last couple months with fever, cough, and/or any cold symptoms?*

AB: *I did have COVID last year, many months ago. I feel like I did recover from it fully. Otherwise, I have been feeling relatively well other than what I have already mentioned*.

Visit 1: Summary of History

- 57-yo male with HTN and high cholesterol presents with subacute dyspnea on exertion over the last 2 to 3 mo. The dyspnea is with exertion only; however, it appears to be progressing over time.
- The differential of dyspnea on exertion is broad.[1]
- Considering his cardiac risk factors including family hx of CAD, HTN, and high cholesterol, this could be a presentation of cardiac ischemia even in the absence of any chest pain.
- Severe anemia can cause dyspnea. In a 57-yo male, most common cause of anemia would be occult GI blood loss. The lack of reported black stools argues against an upper GI blood source, however, severe anemia remains in the differential at this point.
- CHF is a common cause of dyspnea on exertion.
  - No reported symptoms of fluid overload or positional dyspnea such as orthopnea or paroxysmal nocturnal dyspnea.
  - He does have a risk factor for HF (HTN); however, he has no obvious risk factors including heavy alcohol use or other toxins, T2DM, CAD, or recent viral illnesses.
- PE is always in the differential of a patient with dyspnea. Considering the chronicity of his symptoms, chronic PE is a possibility. He has no known risk factors for PE.
- The next step would be to further investigate his cough symptoms.

1: Parshall MB, et al. *Am J Respir Crit Care Med.* 2012;185:435.

Visit 1: Dialogue/Role Play (cont.)

JW: *So, tell me more about your cough.*

AB: *Well, I have noticed the cough for the last 8–10 weeks. It comes and goes. It is sometimes dry but sometimes has some white mucus.*

JW: *Is it worse at night? Is there anything that triggers it? Have you seen any blood? Have you been losing weight?*

AB: *The cough seems to just come and go. There is nothing particular that sets it off. I may have lost a couple of pounds, but my weight has been pretty stable. No, fortunately I have not seen any blood. If I had, I would have come in sooner*.

JW: *Do you have any history of lung disease like asthma as a child? I know that you mentioned you have never smoked tobacco, but do you smoke any other substances or vape?*

AB: *No, I have never smoked anything. I was pretty healthy as a child*.

JW: *Since I met you 10 years ago, you have always been a real estate agent. Had you had any occupations in the past when you had exposure to any chemicals or other toxins like asbestos?*

AB: *I did some landscaping work as a teenager but otherwise I have been selling properties all of my life*.

Visit 1: Clinical Decision Making

- Patient's cough symptoms appear to coincide with dyspnea on exertion. There could be more than one condition, but these two symptoms are likely related.
- As I think about this patient's now chronic cough, there are multiple possibilities.[1]
- As with dyspnea, CHF is a common cause of chronic cough.
- The patient denies hemoptysis or weight loss; but malignancy in the chest cavity remains a possibility.
- GERD is a common cause of chronic cough sometimes in the absence of reflux symptoms. Adult-onset asthma is unusual, particularly without childhood asthma. There can be some respiratory complaints with GERD, but this degree of dyspnea will be highly unusual.
- Conditions that cause both dyspnea and cough: (1) COPD and (2) ILD. Pt is a lifelong nonsmoker making COPD less likely, but still a possibility (e.g., alpha-1 antitrypsin deficiency).
- ILD has multiple causes including many cases being idiopathic.
  - Diagnosis can be difficult as symptoms are subtle.
  - At this point, there is nothing pointing to a definitive diagnosis of ILD, but it must be kept in the differential of any patient with cough and dyspnea.
- Next steps: Perform a physical exam, focusing on the cardiac and pulmonary components of the exam.

1: Irwin RS, et al. *Chest.* 2014;146:885.

Visit 1: Physical Examination

- Patient is resting comfortably in no apparent distress.
  - BP: 132/82
  - Pulse: 98
  - Respirations: 18, 96% on room air
  - Temp: 98.5°F
- Throat is clear. Neck is supple without lymphadenopathy. Jugular venous pressure is at 6 cm.
- CV: Heart is regular rhythm with normal S1 and S2; no murmurs.
- Lungs: Good air movement with equal breath sounds; occasional fine expiratory crackles at the bases.
- Abdomen: Soft and nontender
- Extremities: Well-perfused with no edema

Visit 1: Clinical Decision Making

Initial Thoughts on Physical Exam

- Respiratory rate (18) is slightly increased.
- O_2 saturation is WNL; no evidence of fluid overload; a few expiratory crackles that may or may not be significant.

What's next?

- At this point, proceed with performing additional diagnostic testing
  - CBC to assess for anemia.
  - Creatinine to assess for any underlying renal sufficiency.
  - EKG to assess for a recent myocardial event.
  - Chest x-ray to evaluate for any masses or other pathology (pleural effusion, pulmonary edema, parenchymal, or interstitial disease).
  - BNP to screen for CHF.
  - Review of the chart reveals he is up-to-date on colon cancer screening (low concern for an occult source of blood loss.
- Schedule return visit to assess symptoms and review test results.

Case Study
Clinical Visit 2

Visit 2 (Two Weeks Later): Dialogue/Role Play

JW: *So how have you been feeling*?

AB: *I have been feeling about the same. I still get shortness of breath when I am riding a bike or walking. The cough is about the same*.

JW: *Have you noticed anything new or different*?

AB: *Nope.*

Visit 2: Review of Test Results

On this visit, examination is essentially unchanged; notable for a slightly increased respiratory rate (18) and oxygen saturation of now 95%.

Test Results

- CBC: Normal
- Renal function: Normal
- EKG: Normal sinus rhythm without any evidence of recent MI or ongoing cardiac ischemia
- Chest x-ray: Normal
- BNP: Low (within the normal range)

Visit 2: Clinical Decision Making

- With cardiac ischemia still being in the differential and a “not to miss diagnosis,” proceed with ordering a cardiac stress test.
- Low suspicion for CHF (no evidence of CHF on exam and patient has a normal BNP): I would not perform an echocardiogram at this point.[1]
- With ongoing dyspnea and fine crackles on exam, an underlying lung process is higher on the differential.
- Normal chest x-ray does not rule out an underlying pulmonary etiology.
- Next step: order pulmonary function tests to assess presence of an obstructive/interstitial process.

1: Cowie MR, et al. *Lancet.* 1997;250:1349.

Visit 2: Dialogue/Role Play (cont.)

JW: *So, your blood tests and x-ray all look good. It's good news that we didn't find anything wrong so far, I think it's important we proceed with some additional tests of your lungs and heart. I will see you in my office after we get these test results back.*

AB: *Okay sounds good. Keep me posted.*

Case Study
Clinical Visit 3

Visit 3 (Two Weeks Later): Dialogue/Role Play

The patient returns 2 weeks later to follow-up on his dyspnea and cough.

JW: *So how have you been feeling?*

AB: *I think, I'm actually feeling a little bit worse. I am getting more winded and note that I get shortness of breath more easily when I am doing things around the house.*

Visit 3: Summary

- Physical exam remains the same.
- Oxygen saturation after 50 feet of ambulation drops to 92%.
- Cardiac stress test reveals poor exercise tolerance, however, no evidence of cardiac ischemia.
- Pulmonary function test reveals no evidence of obstruction, however, there are moderately decreased lung volumes with a decreased DLCO.

DLCO: Diffusing capacity of the lungs for carbon monoxide

Visit 3: Dialogue/Role Play (cont.)

JW: *I'm sorry that you're not feeling any better. In fact, I'm actually a little worried you're feeling a little worse.*

AB: *Yes, I'm worried too. There is definitely something going on. What you think it could be?*

JW: *Based on the testing so far and the fact you have a low oxygen saturation level when you walk around, I am concerned about a lung cause for your symptoms. Your lung function test do not show any evidence of emphysema or asthma, but they do show that you may have something preventing your lungs from absorbing oxygen.*

There is no particular medication that I can give you right now until we sort this out further. I would like to talk to my lung doctor colleague, Dr. Hawkins about the next steps. And one of us will let you know what our plan is.

AB: *Ok, that is not great news, but I am glad you have a colleague to consult.*

Case Study
PCP Case Review with Pulmonologist

Discussion: Dr. Worcester and Dr. Hawkins

JW: *I have a 57-year-old male with progressive dyspnea and cough over the last 2 to 3 months. He has no known lung history and is a lifelong nonsmoker. I found on the last visit that he does desaturate when he ambulates. I have done blood work, chest x-ray, EKG, cardiac stress test, and pulmonary function test. Based on the history and results, I have a very low suspicion for a cardiac cause. His chest x-ray is clear but his pulmonary function tests are abnormal. He has decreased lung volumes and a decreased DLCO. I am concerned about an interstitial process. The patient is worried as he has been an active person up until this point. What would you suggest as the next steps?*

FH: *Thanks for the clear summary, Dr. Worcester. As you know, shortness of breath and cough are such common symptoms and can be caused by such a wide variety of diseases ranging from mild and self-limiting to chronic and progressive. It is essential to try to identify patients with a potentially more serious diagnosis. Ruling out cardiac disease in a 57-year-old man is an important step. The ambulatory oximetry is an important test that can be performed in most clinical settings. Despite the normal chest x-ray, in this case the desaturation noted on oximetry suggests that there is significant pulmonary/vascular pathology and establishes the need for further testing. The pulmonary function tests confirm abnormal lung function: restriction and a decreased DLCO. Based on these results, I would recommend obtaining more definitive imaging of the chest and additional history.*

JW: *Is there any particular imaging study you recommend?*

Discussion: Dr. Worcester and Dr. Hawkins (cont.)

FH: *Yes, I recommend a high-resolution CT scan of the chest as the definitive radiological study when interstitial lung disease is being considered. Depending on your institution, you may have to specifically request prone views and inspiratory and expiratory views. The prone views help to differentiate changes caused by simple atelectasis from real parenchymal disease. The expiratory scans may help identify air trapping that might inform the decision making.*

JW: *What about the additional history you mentioned?*

FH: *In individuals suspected or confirmed to have ILD it is important to assess for potential causes. Typically, we would take a careful history of any environmental or occupational exposures. The list of factors associated with ILD is lengthy but occupational causes include working in construction, agricultural, factory or mines, for example. Environmental exposures include birds, pets, air conditioners, and humidifiers. A current or past history of smoking is important and it is helpful to know that our patient is a nonsmoker. Prior medication use is also relevant as certain medications can cause ILD. Finally, we are increasingly aware of genetic predispositions to ILD. A careful history of lung disease amongst family members is also important. If the patient has ILD, we will take a detailed history in the ILD clinic. We will also screen for a history or any physical signs of connective tissue disease.*

Discussion: Dr. Worcester and Dr. Hawkins (cont.)

JW: *Should I refer this patient to a pulmonologist and what will the next steps be?*

FH: *If the high-resolution chest CT confirms the presence of interstitial lung disease, then the patient should definitely be referred to a pulmonologist. In larger academic centers, there are typically pulmonologists who specialize in ILD. Since ILD refers to a broad range of diseases with different causes, treatment options, and prognoses, it is important to make a more definitive diagnosis. To do so, it is recommended that the case be reviewed by a multidisciplinary team of health care professionals typically composed of pulmonologists, chest radiologists, pathologists, and sometimes thoracic surgeons and rheumatologists. This approach has been shown to improve diagnostic accuracy. Based on the medical history and the radiographic features seen on high-resolution chest CT the multidisciplinary team evaluates the likelihood that this is classic or idiopathic pulmonary fibrosis (IPF) or is indeterminate or unlikely to be IPF based on guidelines including from the American Thoracic Society.*

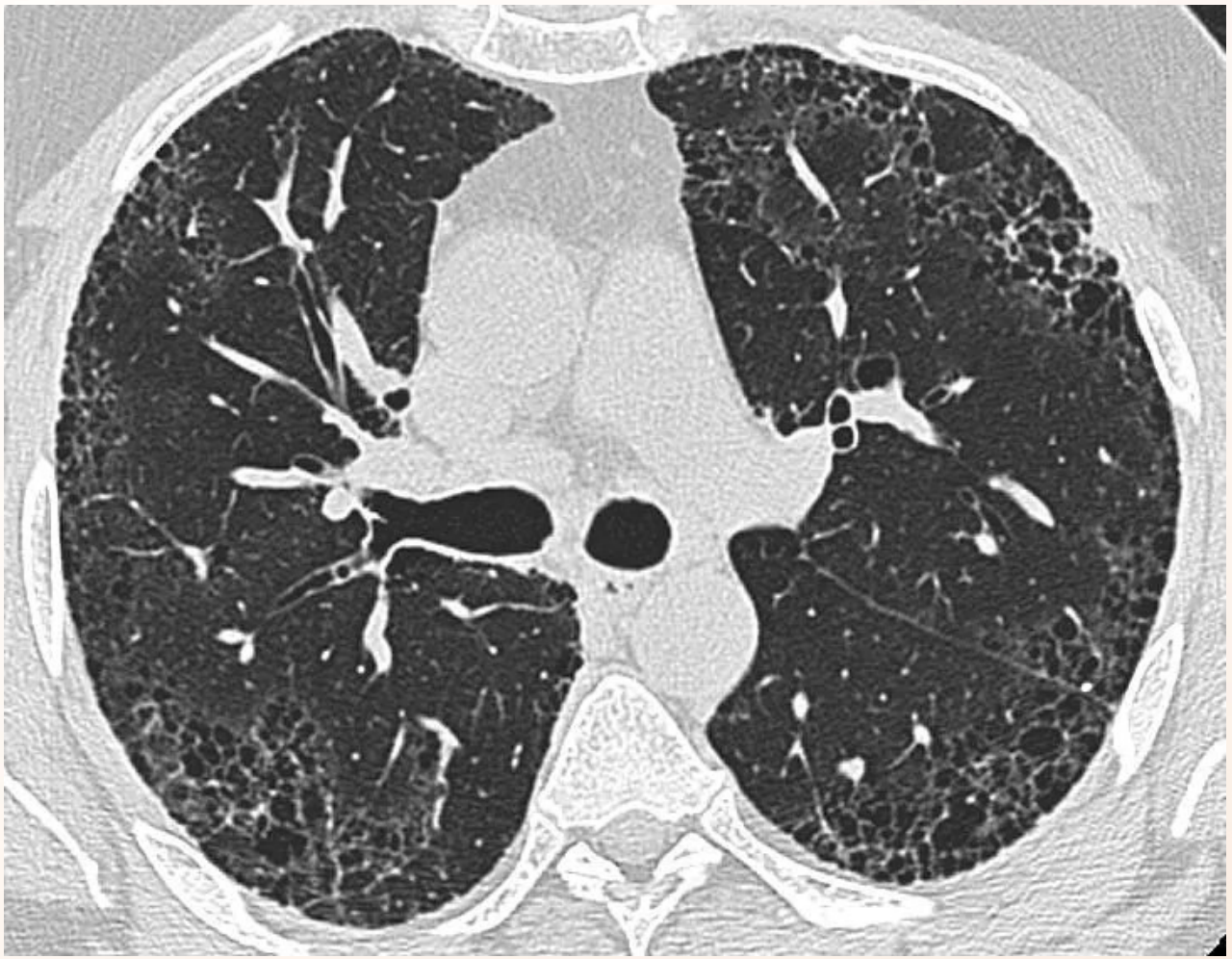
JW: *What should the patient expect if the team diagnoses classic IPF?*

Discussion: Dr. Worcester and Dr. Hawkins (cont.)

FH: *If the CT scan has the classic features of IPF—called the 'usual interstitial pneumonia' (UIP) pattern—and lacks atypical clinical or radiographic features, we diagnose IPF. We assess for the need for supplemental oxygen and recommend pulmonary rehabilitation. After educating the patient on the specific diagnosis we typically recommend treatment with an antifibrotic agent for most patients. There is no cure yet for IPF and patients will lose lung function at a variable rate. Two medications, nintedanib and pirfenidone were demonstrated to slow the rate of lung function decline. If the patient does not have liver disease, we start one of these medications. We monitor their liver function every month at first and since both medications cause gastrointestinal side effects, we follow them closely to help with symptom management.*

JW: *What if the patient has a different ILD?*

FH: *It is really important to differentiate IPF from other ILDs. Some other forms of ILD have the potential to respond well to treatment. If the multidisciplinary team suspects an alternative diagnosis, typically some sort of biopsy will be required. This could be via bronchoscopy or may entail a surgical lung biopsy. If a connective tissue disease is suspected, we would recommend evaluation by our rheumatology colleagues and obtain serologies for autoimmune diseases. Connective tissue disease associated-ILD is typically treated with immunosuppressing agents. If there is evidence of fibrosis and progressive loss of lung function, then an antifibrotic might also be used based on the INBUILD study.*



Visit 3: Clinical Decision Making

HRCT Results

- Scattered reticular opacities
- Honeycombing seen affecting the lung, primarily in the lower lobes
- Lung architectural distortion in the lower lobes
- No mass or lymphadenopathy

- At this point, CT findings are consistent with ILD in a UIP pattern.
- Potential causes? Pt is a lifelong nonsmoker, has no occupational exposures or environmental factors, no symptoms of connective tissue disease, no offending medications, and no family history of lung disease.
- With CT findings and absence of any other clinical findings leaning toward another cause, this patient likely has IPF.[1]
- The patient is referred to a pulmonologist.

1: Raghu G, et al. *Am J Respir Crit Care Med*. 2022;205(9):e18-e47.

Case Study: Visit 4
Dialogue/Role Play
Dialogue with Pulmonologist After Referral

Visit 4: Dialogue/Role Play
Patient–Pulmonologist After Referral

FH: *It's a pleasure to meet you. I am a pulmonologist and I specialize in the care of patients with interstitial lung disease. Your PCP contacted me about your case I have reviewed your records, your CT scan, and the results of your breathing tests. But first, if it is OK with you, I would like to confirm that I have the details of your case correct and make sure I have not missed any important information about potential exposures such as occupational, medications, or environmental. And I'd also like to review your family history with you.*

AB: *Sure, absolutely.*

Pause…..move to discussion

FH: *Well, piecing everything together I think the cause of your symptoms is idiopathic pulmonary fibrosis. Would you like me to explain a little more about this diagnosis?*

AB: *Yes, please. I read about it on the internet after my PCP brought up the diagnosis on my last visit.*

FH: *IPF is a progressive fibrotic lung disease. By that, I mean there is a build-up of scar tissue in the lungs, which leads to issues with breathing. We don't know exactly what causes it yet, but age and smoking are risk factors. Your CT scan shows the findings that are typical for this diagnosis, so I don't think a biopsy is needed.*

Visit 4: Dialogue/Role Play (cont.)
Patient-Pulmonologist After Referral

AB: *So can I expect my symptoms to get worse?*

FH: *I realize it can be pretty scary to talk about this. Typically, the scar tissue does get worse over time, but it can vary quite a bit from person to person. One of the first things I recommend is that you come to see me again in a few months and we'll repeat your breathing tests and see how you are feeling. This way we will figure out if the fibrosis or scaring is progressing.*

AB: *Okay, what if it is progressing?*

FH: *In that case, I would recommend treating you with a type of medication called an antifibrotic. These medications were approved relatively recently, and the clinical trials showed that they slowed the progression of the lung disease. We have many patients with IPF in our clinic and most are taking these medications.*

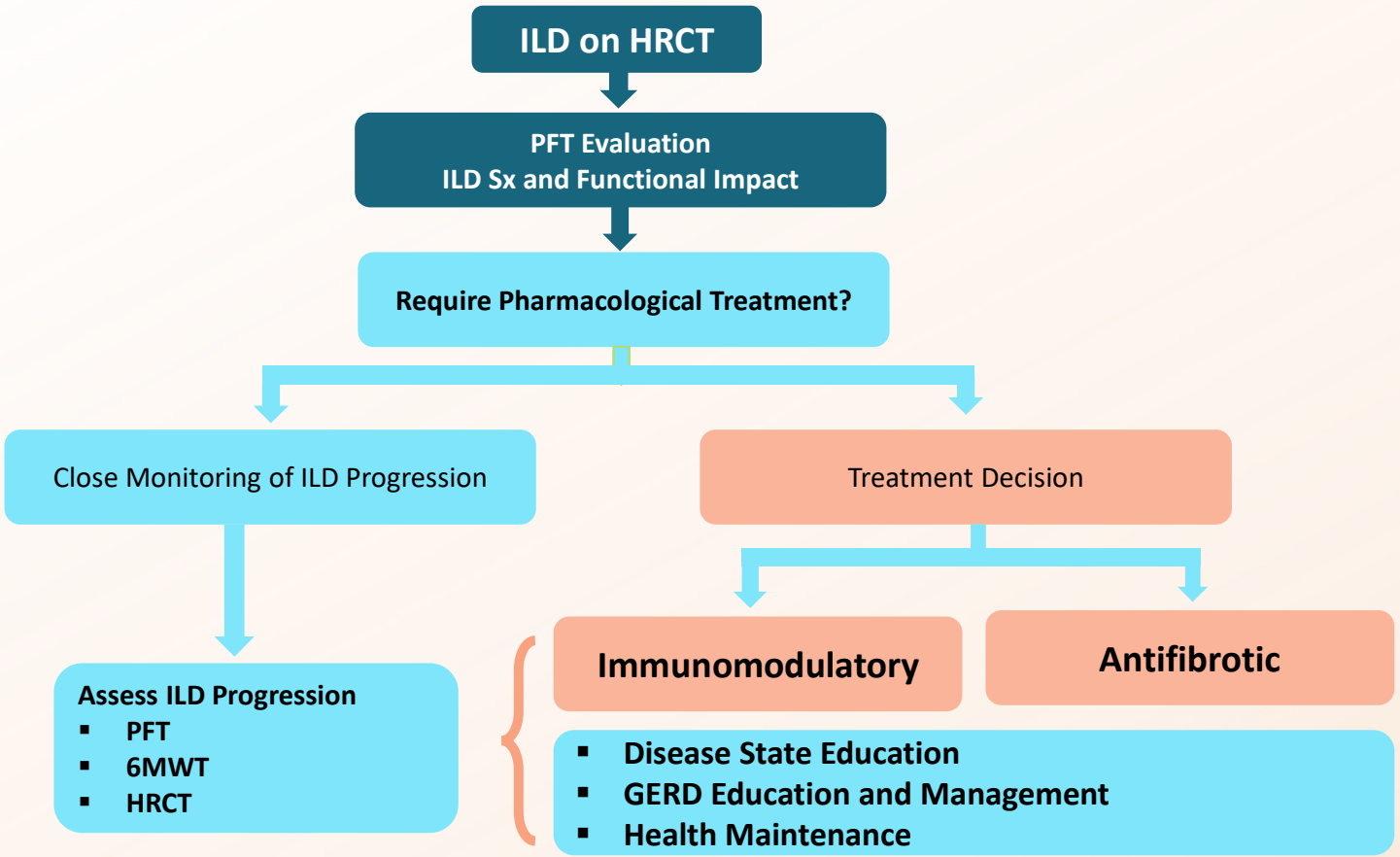
AB: *If there is something I can do to prevent this from getting worse, I am all ears. Are there side effects I should be worried about? What else can I do for IPF?*

FH: *Great questions. I would like you to meet our pharmacist and our nurse to help with answering these questions.*

Video Vignette: Andrew's Quality of Life

IPF Treatments: Managing Expectations, Optimizing Team-Based Care, and Addressing Socioeconomic and Health Disparities

Conceptual Framework for ILD Management



Modified from American College of Rheumatology: Dinesh K et al. 2022 Jan;74(1):13-27. doi: 10.1002/art.41933. Epub 2021 Nov 10

ILD Treatment

Pharmacologic

- Corticosteroids
- Immunosuppressives
- Immunomodulators
- Antioxidants
- Antibody treatment
- Antifibrotics
- Others (e.g., IV immunoglobulin)

Nonpharmacologic

- Pulmonary rehabilitation
- Oxygen therapy
- Surgery (lung transplant)
- Palliative/supportive care

Pirfenidone: FDA-Approved Antifibrotic

The NEW ENGLAND JOURNAL of MEDICINE

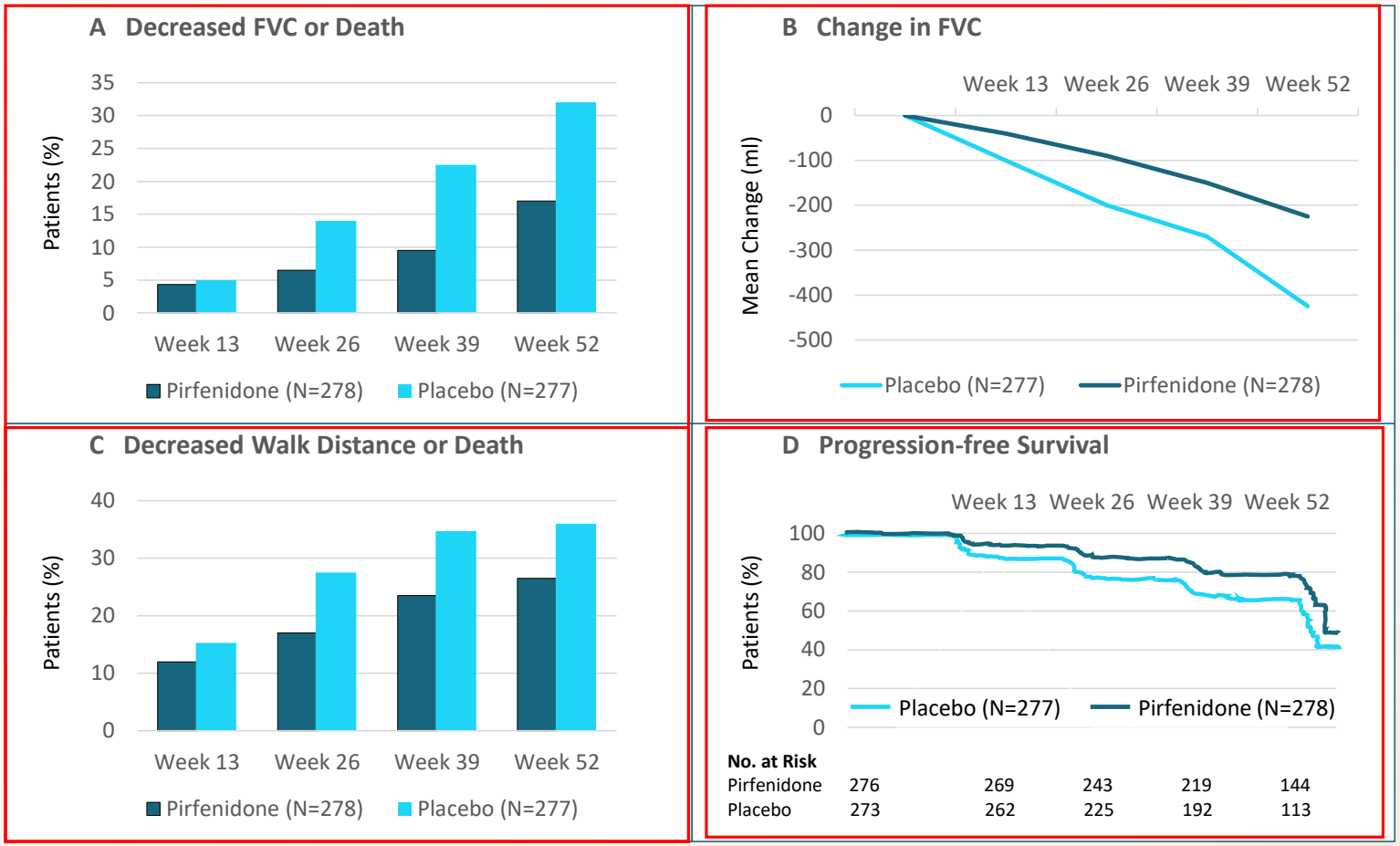
ORIGINAL ARTICLE

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*

King TE Jr et al. *N Engl J Med*. 2014;370:2083-92.

Primary/Key Secondary Efficacy Outcomes Over 52 Weeks



King TE Jr, et al. *N Engl J Med.* 2014;370:2083-92.

Nintedanib: FDA-Approved Antifibrotic

The NEW ENGLAND JOURNAL of MEDICINE

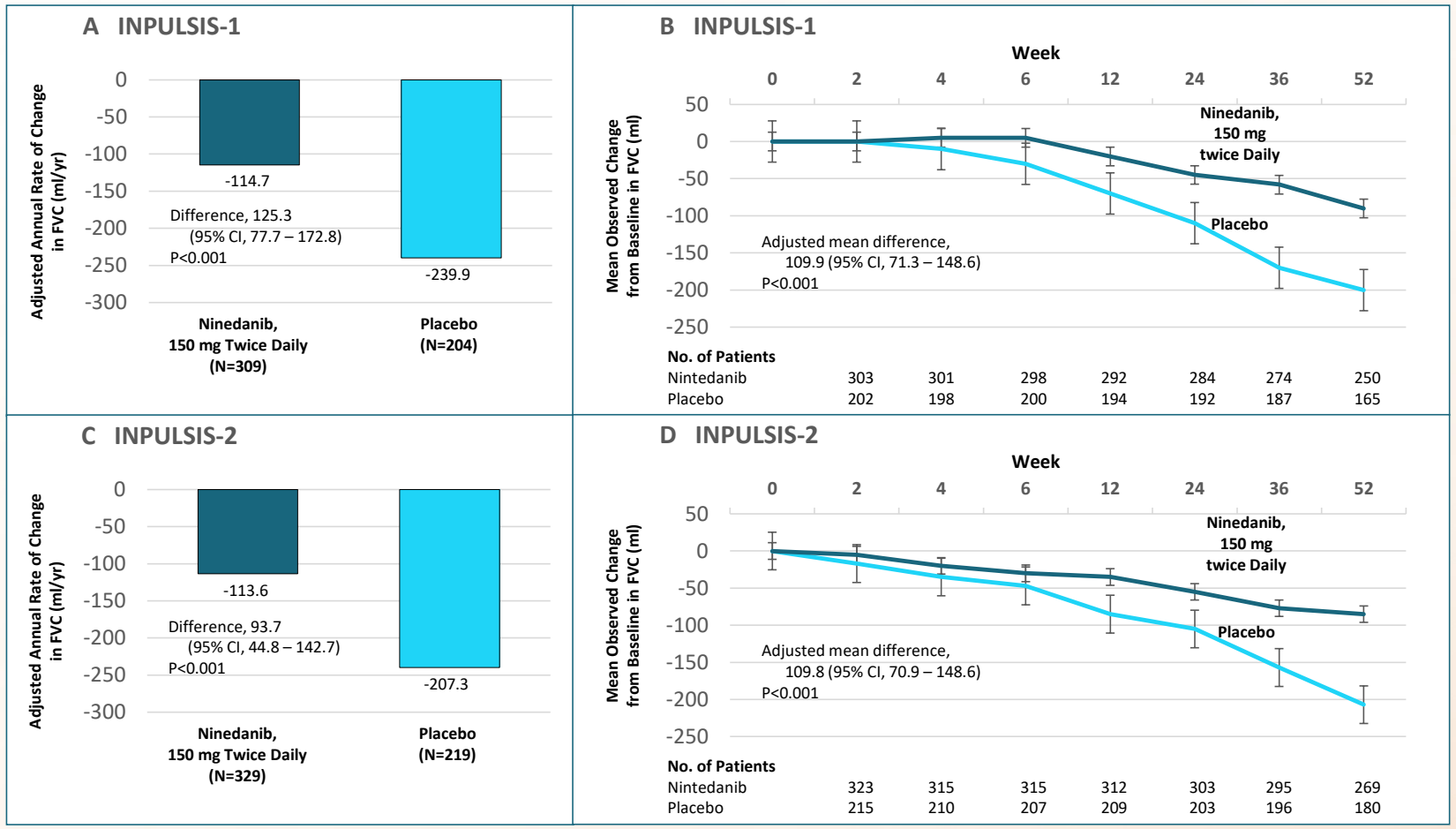
ESTABLISHED IN 1812 MAY 29, 2014 VOL. 370 NO. 22

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*

Richeldi L et al. N Engl J Med. 2014; 370: 2071-82.

Primary Efficacy Outcomes Over 52 Weeks



Richeldi L, et al. *N Engl J Med.* 2014;370:2071-82.

Mycophenolate and Cyclophosphamide Improve Skin Fibrosis and Pulmonary Function

Mean changes of ppFVC and mRSS from baseline to 24 months

	CYC			MMF			ΔMMF - ΔCYC	
	N	Change	95% CI	N	Change	95% CI	Δ	95% CI
ppFVC	**51**	2.88	1.19 to 4.58	**53**	2.19	0.53 to 3.84	−0.70	−3.1 to 1.7
mRSS	**53**	−5.35	−6.9 to −3.8	**53**	−4.9	−6.4 to −3.4	0.45	−1.7 to 2.6

Tashkin DP, et al. *Lancet Respir Med*. 2016 Sep;4(9):708-719. doi: 10.1016/S2213-2600(16)30152-7

Tocilizumab and Rituximab Slows Lung Function Decline; But Only Rituximab Improves mRSS

	Change from baseline @ 48 weeks				Change from baseline @ 24 weeks			
	Tocilizumab (FocuSSed)				Rituximab (DESIRES)			
	Tx Arm	Placebo	Difference 95% CI	pValue	Tx Arm	Placebo	Difference 95% CI	pValue
mRSS	−6.1	−4.4	−1.7 (−3.8 to 0.3)	0.1	−6.3	2.14	−8.44 (−11.0 to −5.88)	<0.0001
ppFVC	−0.4%	−4.6%	4.2% (2.0 to 6.4)	0.0002	0.09%	−2.87%	2.96% (0.08 to 5.84)	0.04

mRSS = modified Rodnan skin score; FVC = forced vital capacity; ppFVC = percent predicted forced vital capacity

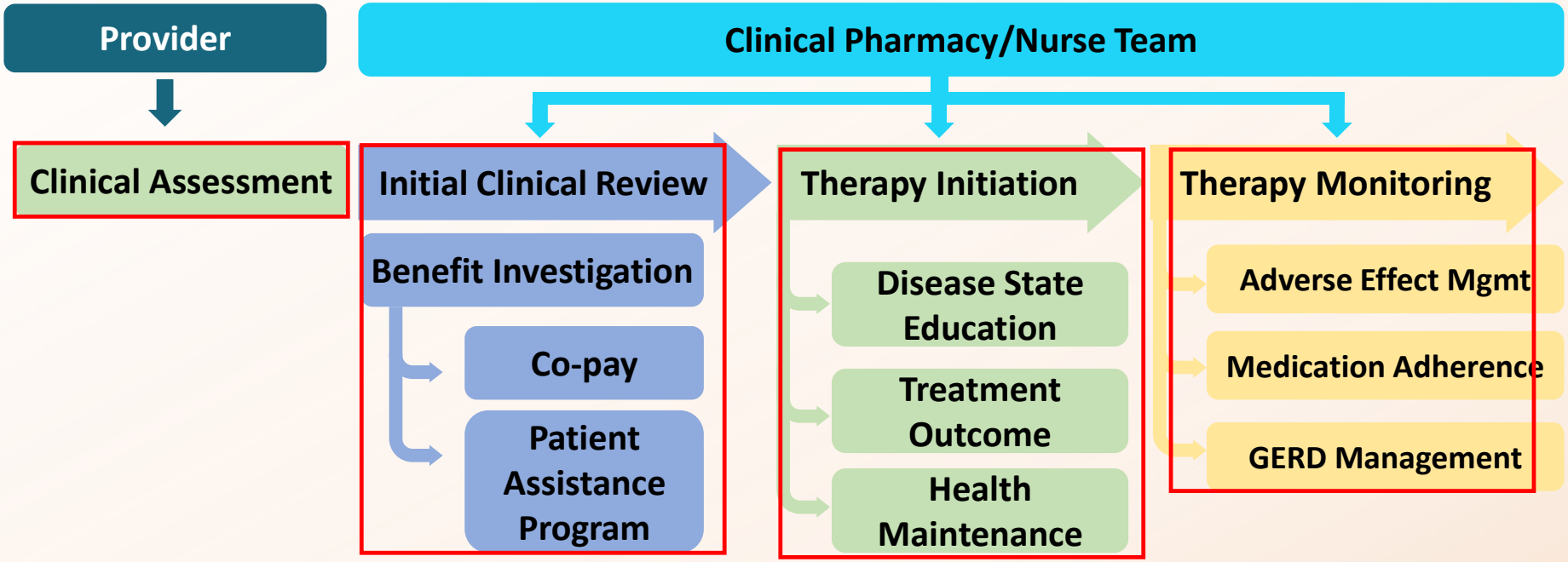
Khanna D, et al. *Lancet Respir Med*. 2020 Oct;8(10):e75. Erratum in: *Lancet Respir Med*. 2021 Mar;9(3):e29.
Ebata S, et al. *Lancet Rheumatology.* 2021 July;3(7):E489-E497.

Video Vignette 3
Joel, 55-year-old patient, Treatment

Intro: In this vignette Joel describes his experience with biologic therapy.

Multidisciplinary Care Team in ILD Management

The Boston Medical Center Model



Therapy Safety and Efficacy Monitoring

- Most common adverse effects:
  - Diarrhea
  - Nausea
  - Vomiting

- Month 1: Once a week adverse effect monitoring and management follow-up
- Months 2 and 3: once a month safety monitoring follow-up
- Post month 3: As needed follow-up

Racial Disparities in IPF Care

- Black patients are generally less likely to receive diagnostic medical imaging, especially CT scans.
  - In resource-poor settings, limited access to chest CT and spirometry impedes early diagnosis.
- Structural inequities and implicit bias in the health care system impacts medical care received by Blacks and delays time to diagnosis.
- Black individuals may be uninsured or underinsured and lack access to high-quality primary care precluding their ability to obtain diagnostic tests or be referred for subspecialty pulmonology care.
- This leads to prolonged referral time and further delay in diagnosis/treatment.
- Pulmonary fibrosis increases by ~2% for each year that the diagnosis remains delayed and is associated with higher mortality.
- Underserved communities

Adegunsoye A, et al. *Arch Bronconeumol*. 2022;58(8):590-2.

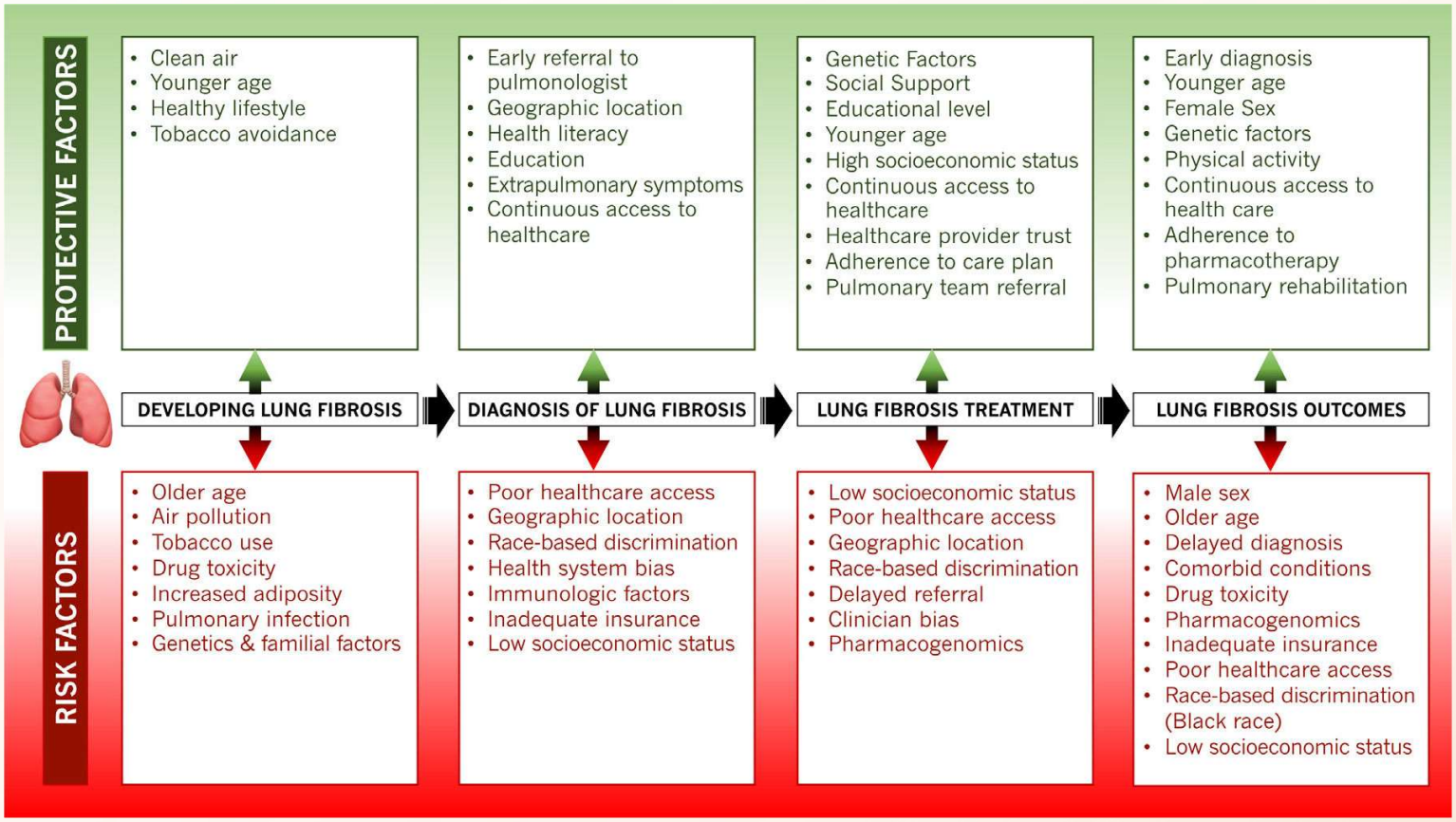
Racial Disparities in IPF Care

Black individuals may also have reduced access to treatment options due to:

- Lower rates of trial enrollment
- Lower physician prescribing
- Difficulty obtaining high-cost medications

Geller SE, et al. *Acad Med*. 2018;93:630–5.

Risk Factors and Protective Factors for IPF Across the Disease Course



Core Strategies for Improving Team-Based Care and Overcoming Disparities

- Provide tools for helping patients cope with their diagnosis and managing expectations regarding the goals of ILD treatment and prognosis.
- Implement strategies to increase interprofessional and multidisciplinary communication and coordination of care.
- Increase communication among patients, caregivers, and the health care team.
- Address racial disparities and provide care in a culturally and linguistically appropriate way.
- Implement strategies to overcome socioeconomic, racial, and health disparities through a multidisciplinary and interprofessional approach to ILD management.

A Coordinated Multidisciplinary Approach for IPF Care

- Pulmonology
- Primary Care
- Radiology
- Clinical Nursing
- Pharmacy
- Laboratory

The Multidisciplinary Clinical team provides integrated care between pulmonology, primary care, radiology, nursing, pharmacy, and laboratory with dedicated social work and patient navigator support as needed.

This program is an integral part of the Boston University IPF clinic; consolidate the clinical program and build translational research capabilities to advance new product concepts into clinical testing.

Audience Polling Question 2

After participating in this program how confident are you in your ability to diagnose ILD in your practice?
(5 = very confident, 1 = not at all confident, please select one)

After participating in this program how confident are you in knowing when to refer your patients with ILD to a pulmonary specialist?
(5 = very confident, 1 = not at all confident, please select one)

Summary

- ILD is a heterogenous group—a spectrum—of fibrotic lung diseases.
- Timely and accurate ILD diagnosis and referral are keys to improved outcomes for all ILD populations.
- Enhanced care of medication management across races requires:
  - Recognition of racial disparities
  - Care that is tailored to a specific race or culture
  - A coordinated multidisciplinary approach
  - Improved patient–clinician and clinician–clinician communication

Thank you for your attention.

Please complete the evaluation and posttest in order to claim your certificate of credit.