PCP Toolkit: Interstitial Lung Disease

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I have no actual or potential conflicts of interest in relation to this presentation.

Fellowship Experience at Oregon Health & Science University

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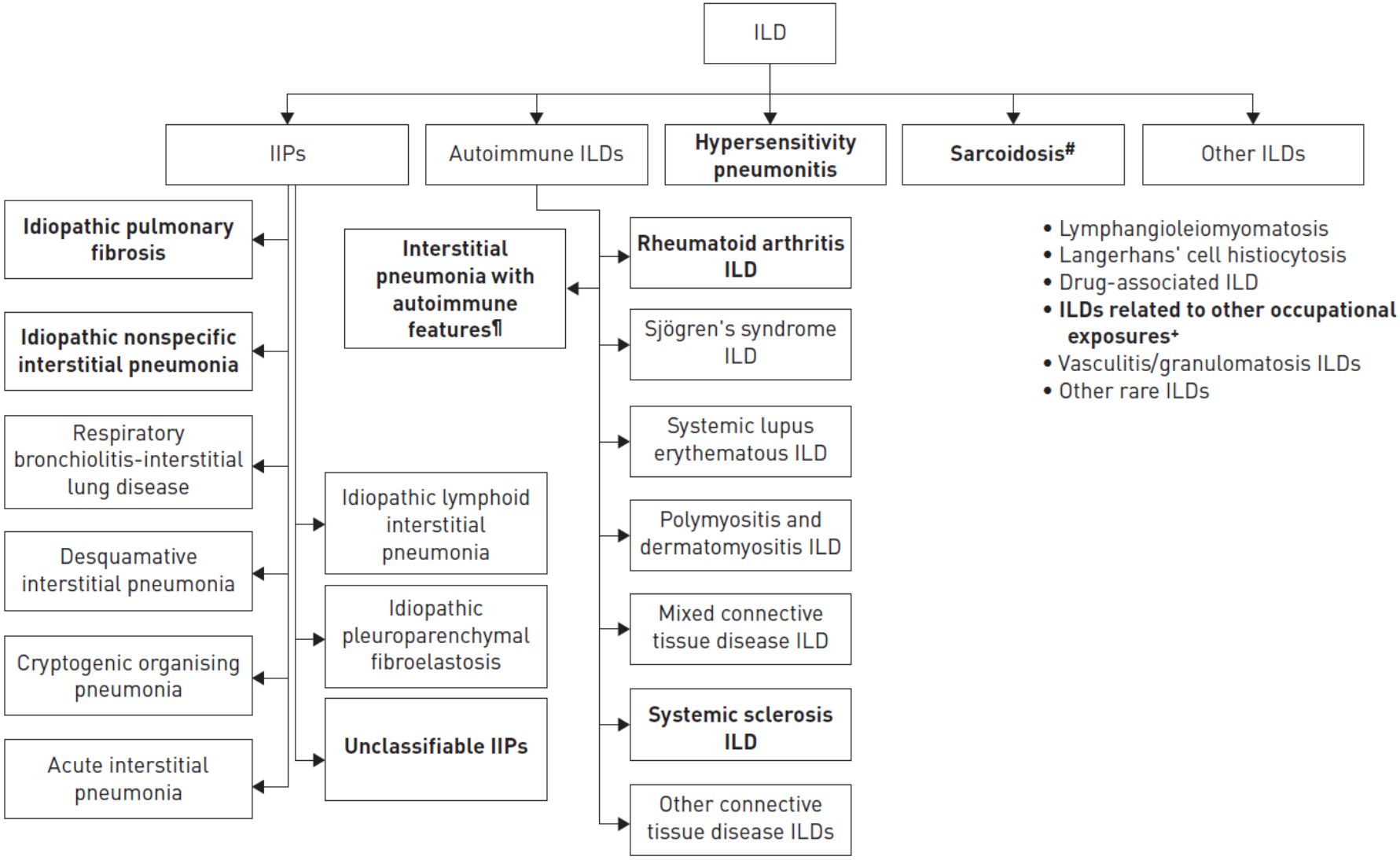
Objectives

- ✓ Provide context for how interstitial lung diseases (ILD) are organized
- ✓ Discuss the key components of the ILD evaluation
- ✓ Review the essentials of disease management

Why the Confusion? ILD Hypernym

Types of ILD



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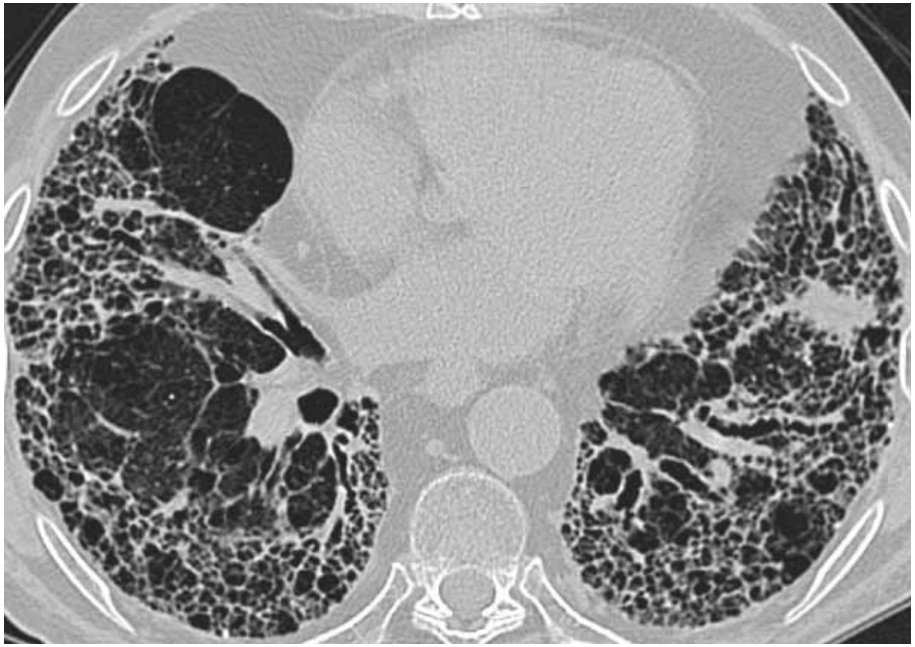
Eur Respir Rev 2018; 27: 180076

What's the Issue? Substantial Disease Burden

- Overall prevalence 76 cases per 100,000 in the US
- Idiopathic pulmonary fibrosis (IPF), connective tissue disease (CTD) associated ILD, and pulmonary sarcoidosis are the most common fibrotic ILDs
- 13-40% have a progressive fibrosing phenotype



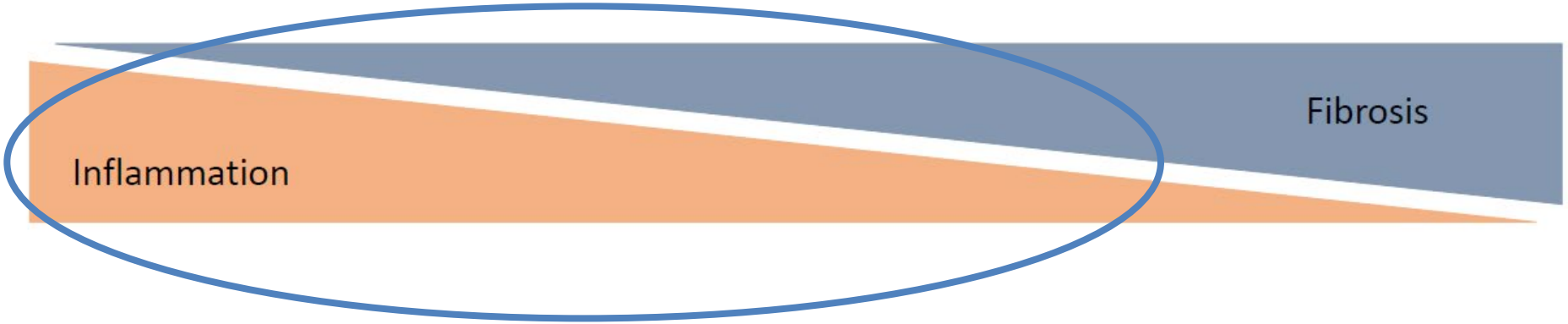
Spectrum of disease

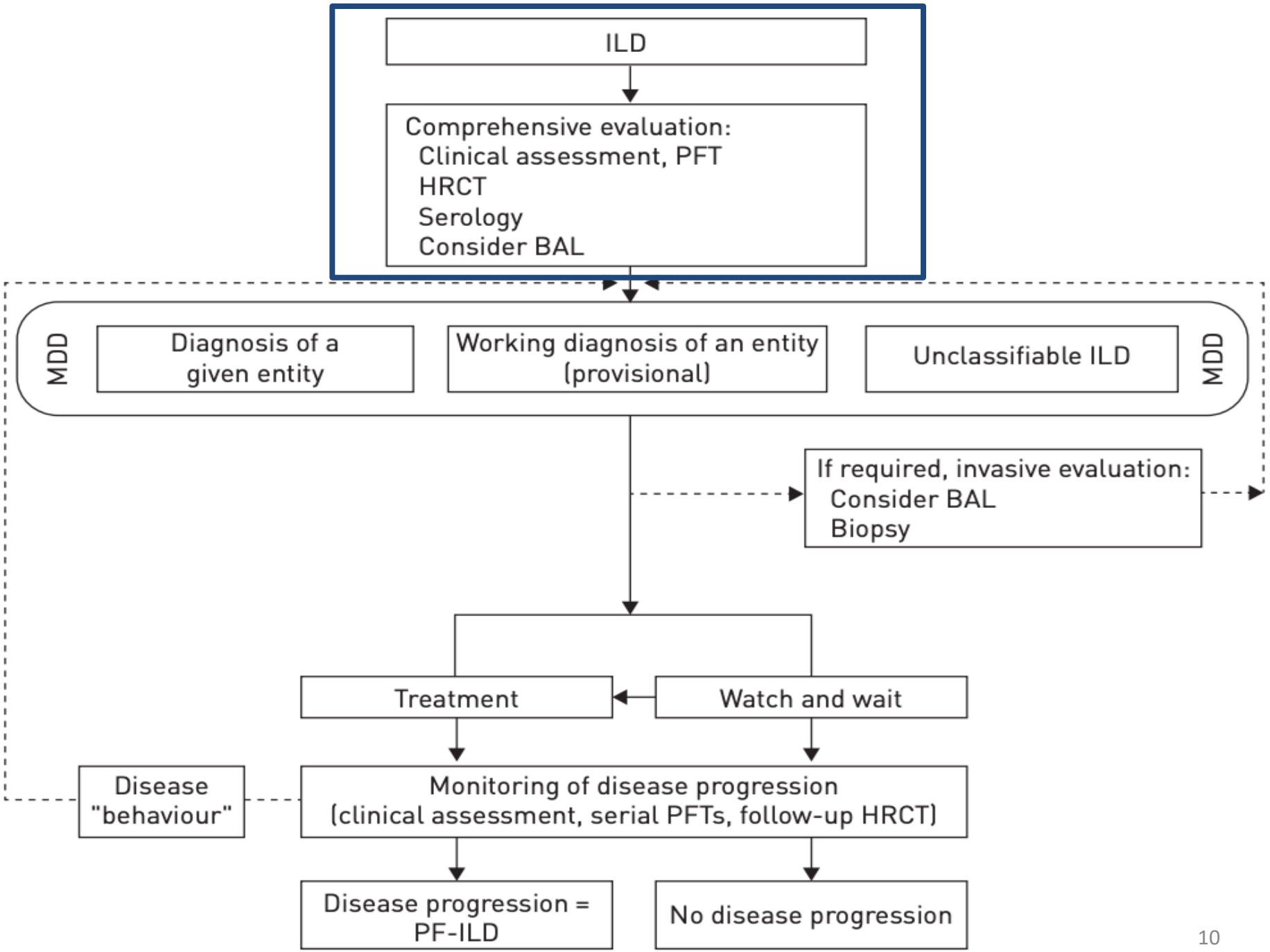
<u>Inflammatory Predominant ILDs</u>
Autoimmune ILD (most)
Hypersensitivity Pneumonitis (early)
Cryptogenic Organizing Pneumonia
Drug-induced ILD

<u>Fibrotic Predominant ILDs</u>
UIP due to Scleroderma or RA
Hypersensitivity pneumonitis (late)
Idiopathic pulmonary fibrosis
Asbestosis

Goals of the ILD evaluation

1. Diagnose early in the disease course
2. Make the correct diagnosis through a standardized, comprehensive assessment
3. Avoid unnecessary procedures
4. Treat ASAP to improve meaningful outcomes




ILD
Comprehensive evaluation:
Clinical assessment, PFT
HRCT
Serology
Consider BAL
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Diagnosis of a given entity
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Monitoring of disease progression (clinical assessment, serial PFTs, follow-up HRCT)
Disease progression = PF-ILD
No disease progression

The ILD Initial Evaluation: History

- Deep dive → dyspnea, cough, energy, level of physical activity
- Pertinent co-morbidities
  - GERD
  - Connective tissue disease
  - Cancer
- Family/Social/Medication histories (*Pneumotox.com*)
- Exposures

Examples of pertinent exposures

- Molds
- Birds
- Down feathers
- Animals
- Metal dusts
- Wood dust
- Livestock
- Stone polishing or cutting
- Occupations
- Hobbies

Chronic Hypersensitivity Pneumonitis Exposures Questionnaire

Part A: This table lists some environmental exposures that can lead to lung disease in some people. Think about places you regularly spend time and place a tick in the boxes below if you have been exposed to these on a regular basis. Places to think about are your home, workplace and any other places you regularly spend time (such as your car or basement).

- ☐ Visible or significant mold or mildew
- ☐ Musty smells
- ☐ Water damage, moisture or leaks (damp carpet, leaky plumbing)
- ☐ Humidifiers/ air conditioners with water reservoir/ swamp coolers
- ☐ Hot tubs/pools/ spas
- ☐ Down or feather products (down comforters, pillows, furniture)
- ☐ Significant vapors or gases or fumes
- ☐ Musical wind instruments (e.g. saxophone / bagpipes)
- ☐ Birds (pets, hobby, other) /bird droppings/feathers
- ☐ Farming / hay /silage
- ☐ Compost/mulch or similar organic matter
- ☐ Isocyanates (i.e. paint spraying, polyurethane foam, varnishes etc.)
- ☐ Metalworking fluids (coolants, lubricants, machine operation)
- ☐ Vegetable production (i.e. mushroom growing, onion sorting etc.)
- ☐ Food manufacturing (i.e. salami, cheese, etc)
- ☐ Wood cutting/ wood dust/ Moldy wood (e.g. cork, maple, other)

Have you been exposed to anything else which you think is important?

_____

Part B: For each exposure you indicated in Part A, please fill in the following details:

Exposure			
Date of onset of exposure (month/year)	____/____	____/____	____/____
Date of onset of symptoms (month/year)	____/____	____/____	____/____
Do symptoms improve on avoidance of this exposure?	YES / NO	YES / NO	YES / NO
How long have you been / were you exposed?	☐ < 1 month ☐ 1 – 3 months ☐ 3 – 6 months ☐ 6 – 12 months ☐ 1 – 5 years ☐ > 5 years	☐ < 1 month ☐ 1 – 3 months ☐ 3 – 6 months ☐ 6 – 12 months ☐ 1 – 5 years ☐ > 5 years	☐ < 1 month ☐ 1 – 3 months ☐ 3 – 6 months ☐ 6 – 12 months ☐ 1 – 5 years ☐ > 5 years

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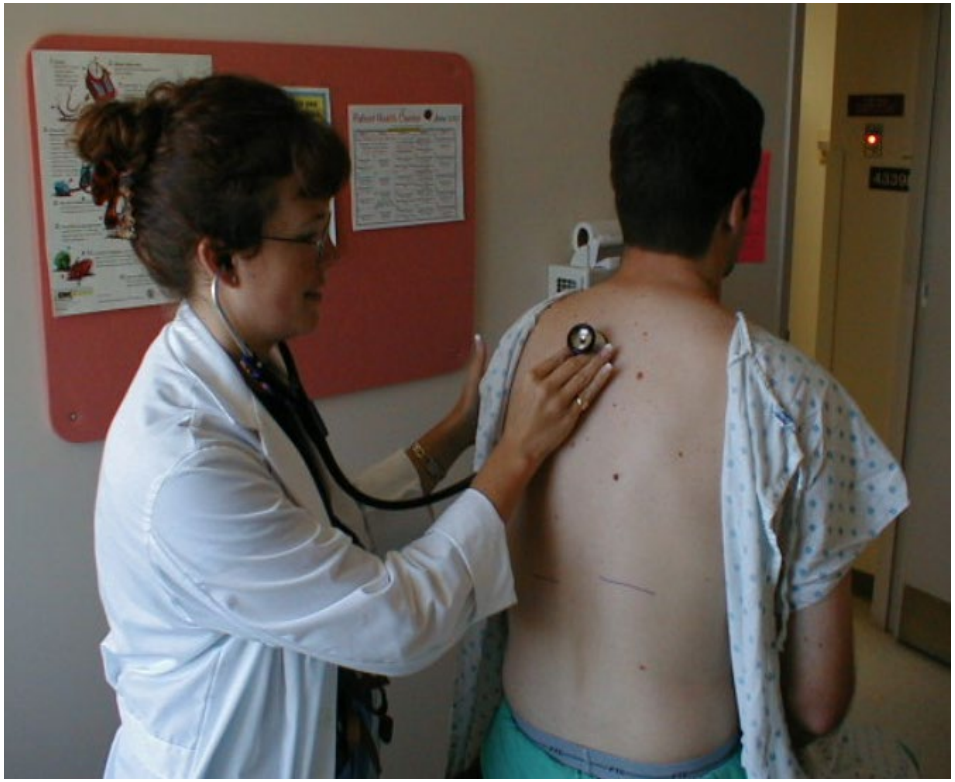
CHEST 2020;157(6):1506-1512

The ILD Initial Assessment: Physical Exam



- Fine inspiratory crackles (velcro rales)
- Squeaks
- Premature graying
- Hands, joints, and skin

The Initial ILD Assessment: Lab Studies

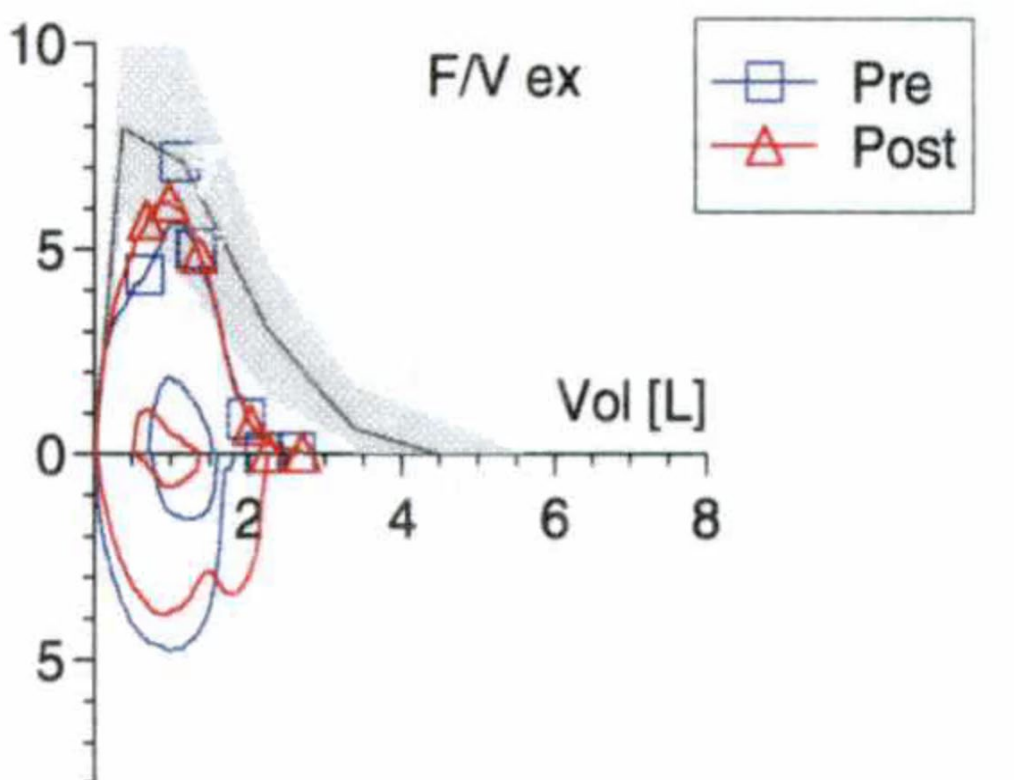
B. Serologic domain

- CRP, ESR
- ANA
- RF
- CCP
- Myositis panel

ERJ 2015. 46;976-87

Restrictive impairment and reduction in DLCO is a clinical pattern consistent with ILD

- ***Example…***
  - Normal FEV1/FVC ratio
  - FVC 2.68 L, 60%
  - TLC 4.08 L, 58%
  - DLCO ml(mmHg) 5.3 16%



ILD-screen score > 8 = high-risk patient for ILD

TABLE 4] Prospectively Applied ILD-Screen Performance Stratified According to ILD Subtype

Variable	ILD-Screen		% Correctly Classified
	Negative	Positive	
ILD classification			
Fibrotic ILD	0	34	100
Nonfibrotic ILD/ILAs	13	16	55
Diagnosis			
Idiopathic pulmonary fibrosis	0	6	100
Connective tissue disease-associated ILD	1	8	89
Unclassifiable fibrotic ILD	0	10	100
Unclassifiable nonfibrotic ILAs	5	13	72
Smoking-related ILD	4	5	56
Other ILD	3	8	73
Total	13	50	79

ILAs = interstitial lung abnormalities. See Table 1 legend for expansion of other abbreviation.

CHEST 2020. 158(2):620-29

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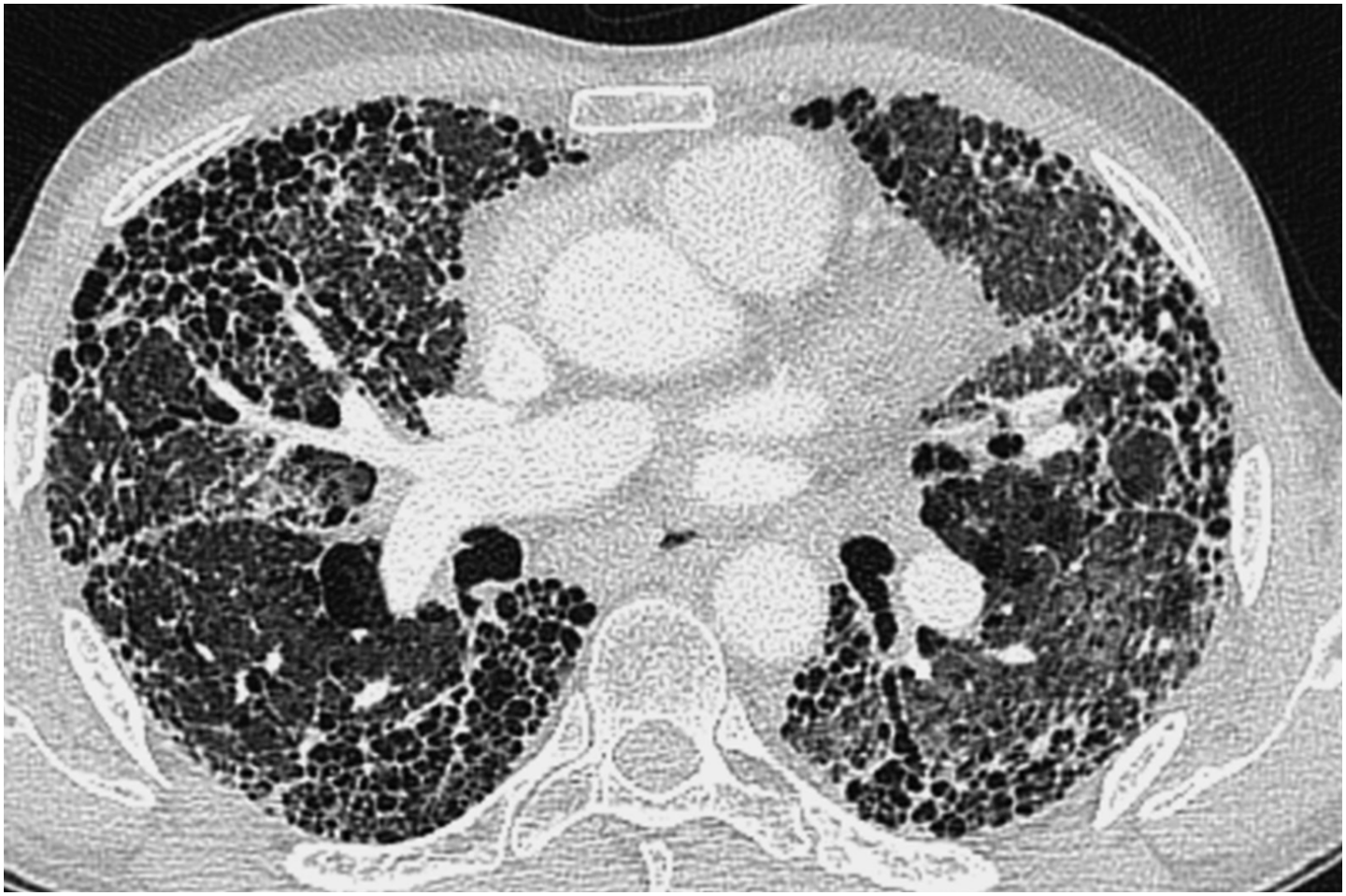
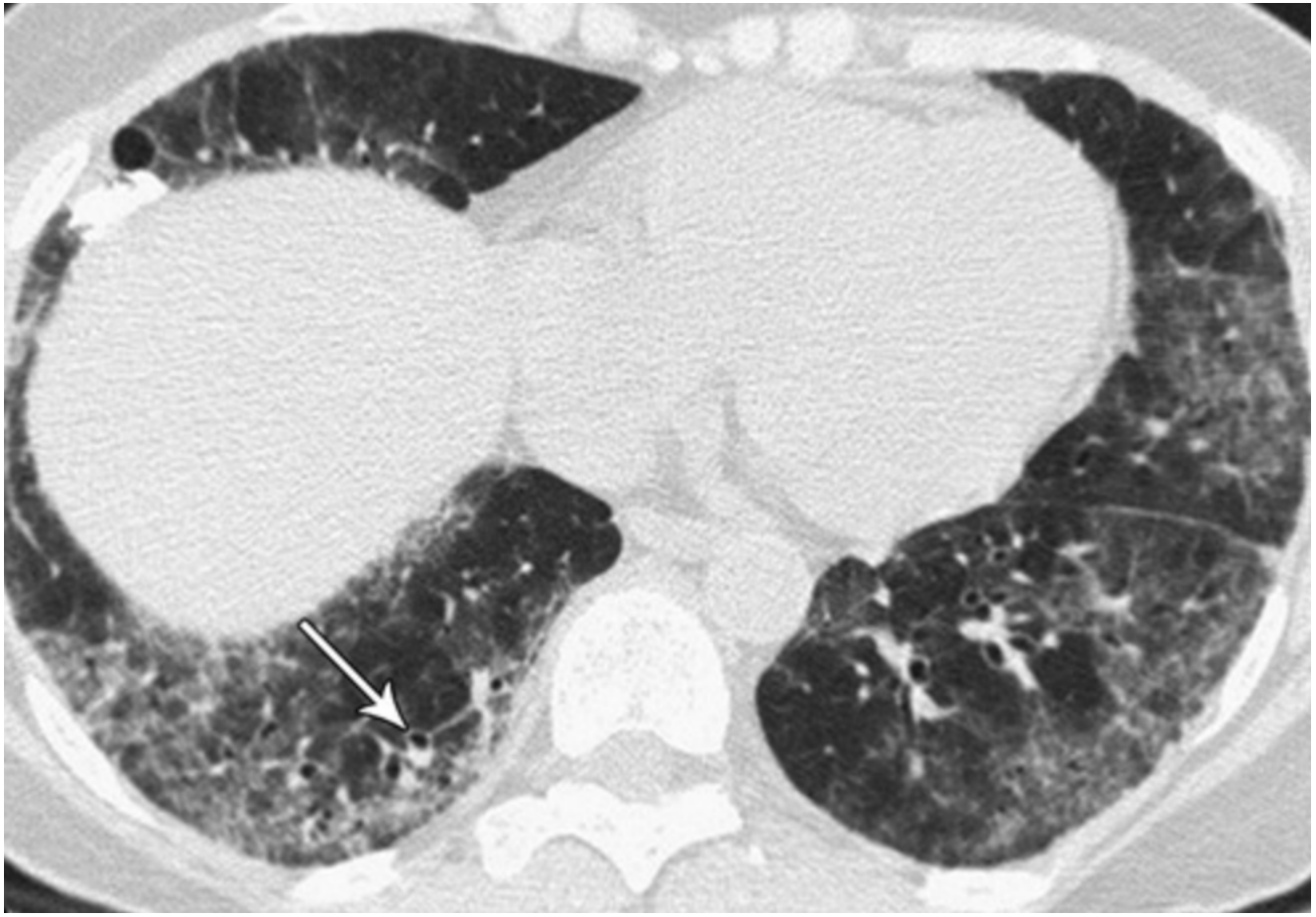
The Initial ILD Assessment: Chest Imaging

- High-resolution CT scan
  - Prone positioning
  - Expiratory phase
- Obtain all previous chest imaging available for personal review

The Initial ILD Assessment: Chest Imaging→ IPF



The Initial ILD Assessment: Chest Imaging→ Non-specific Interstitial Pneumonia



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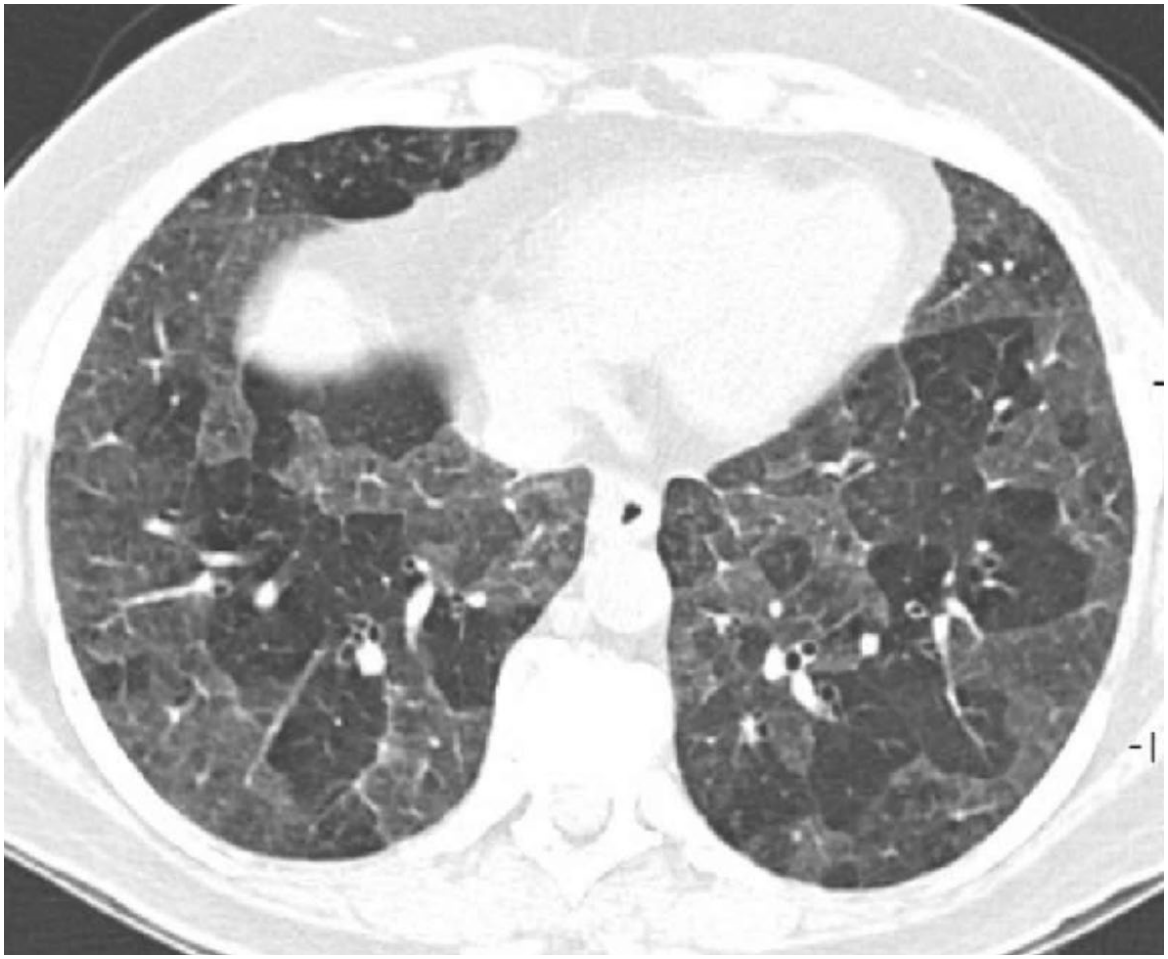
The Initial ILD Assessment: Chest Imaging→ Hypersensitivity Pneumonitis



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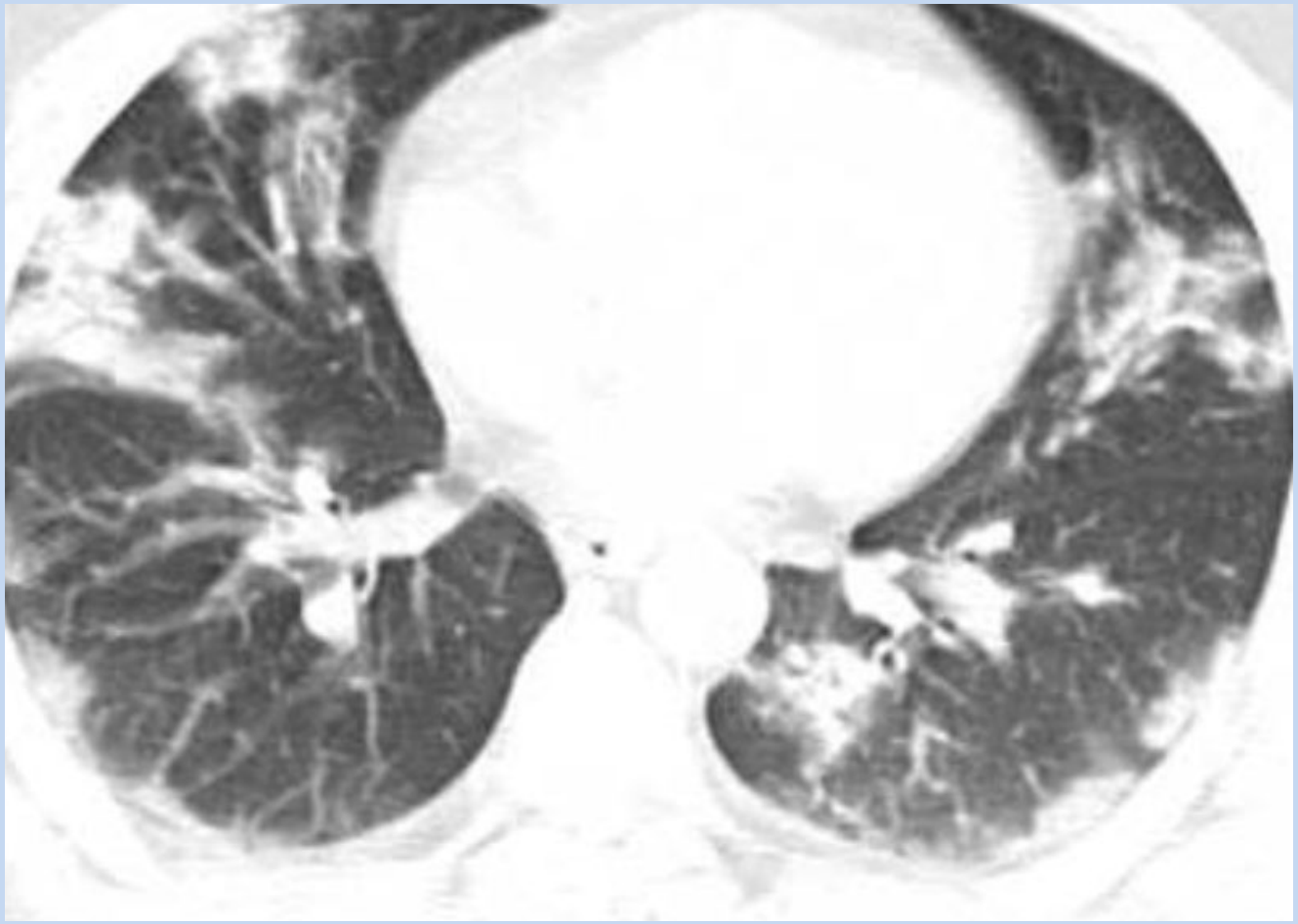
The Initial ILD Assessment: Chest Imaging→ Organizing Pneumonia



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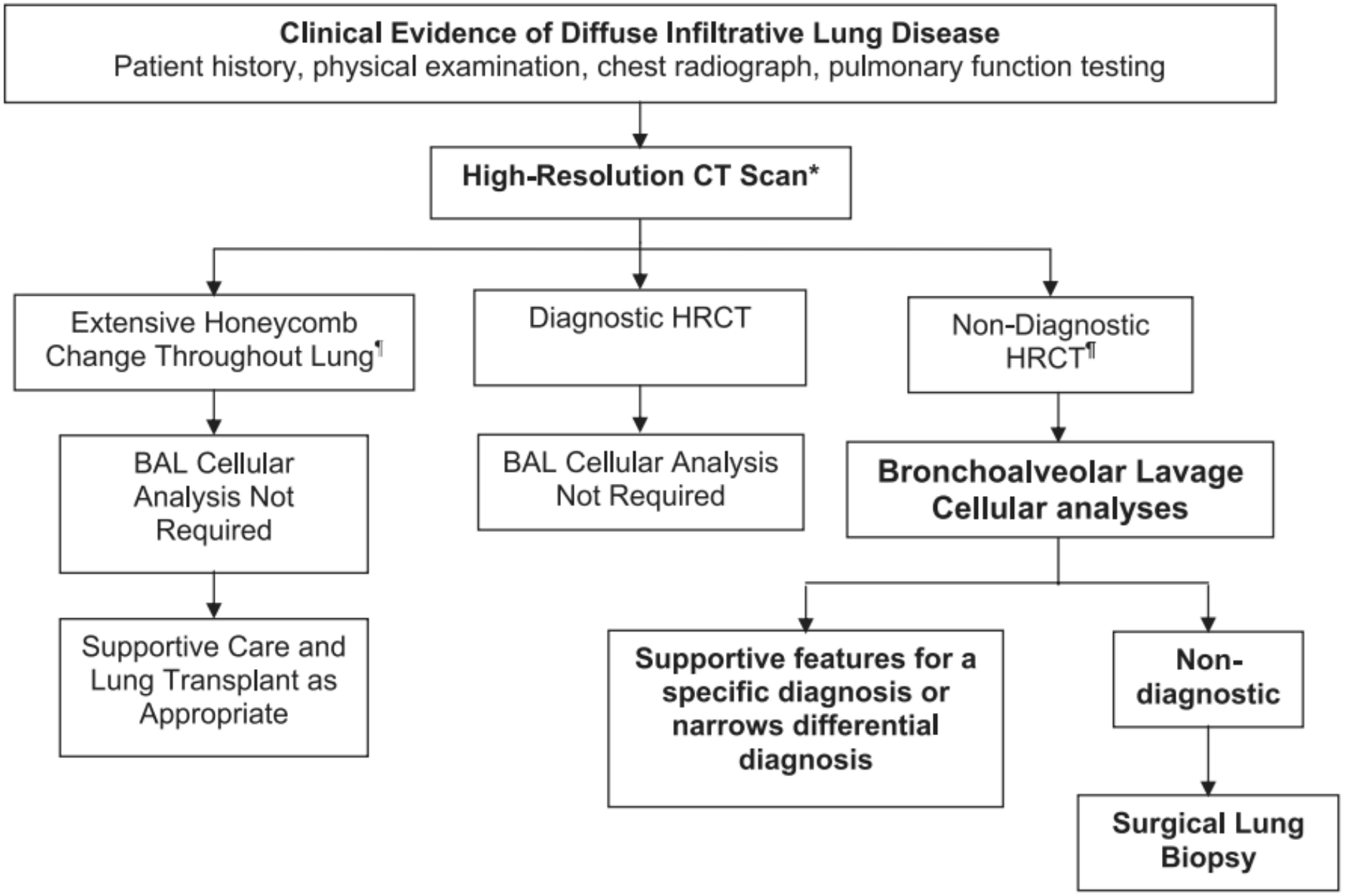

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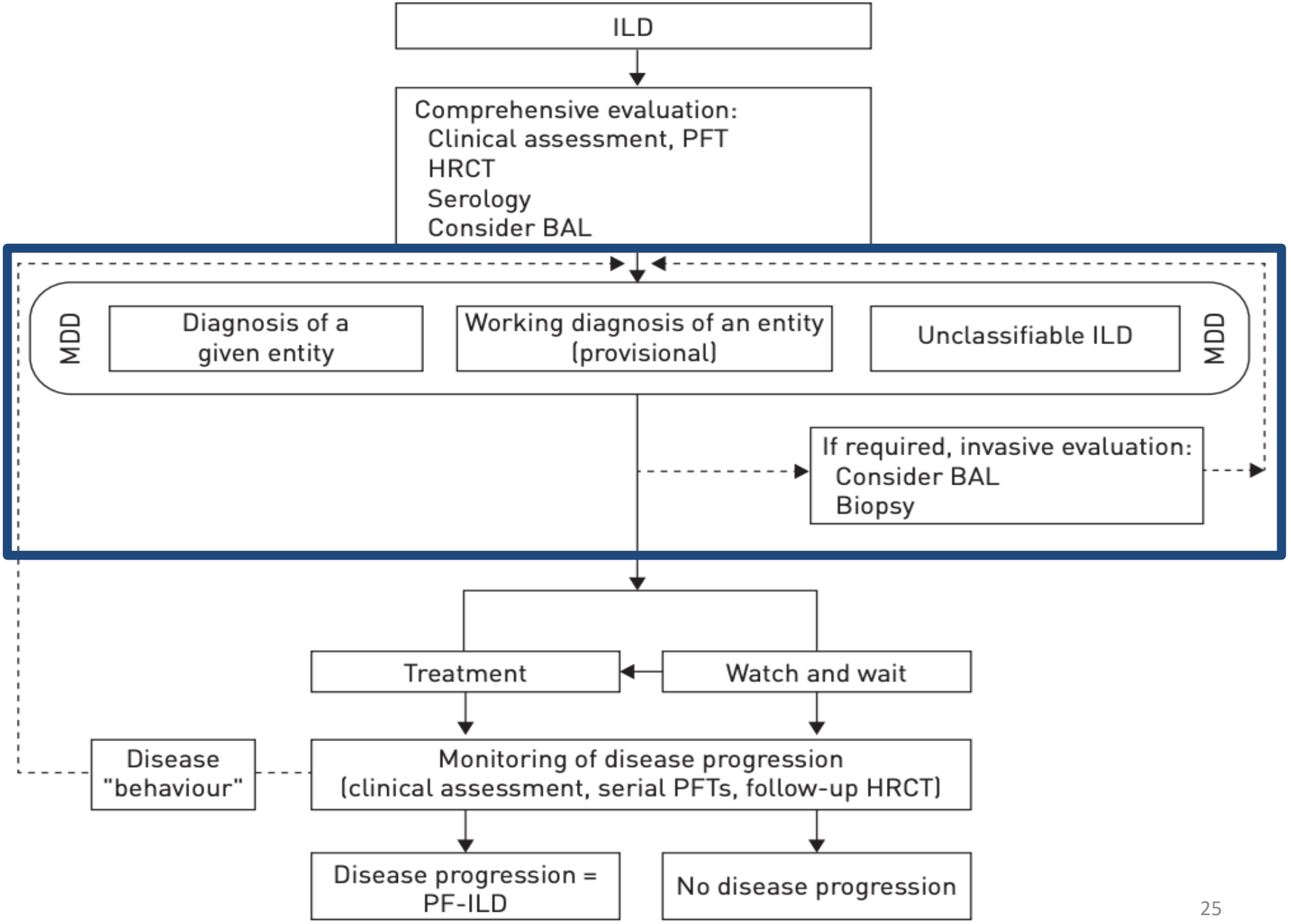
Bronchoalveolar Lavage Cellularity

TABLE 1 Bronchoalveolar lavage (BAL) findings that are useful in interstitial lung disease diagnosis

BAL finding	Consistent interpretation/suggested diagnosis
Eosinophils ⩾25%	Eosinophilic pneumonia
Lymphocytes ⩾25%	Sarcoidosis, HP, cellular NSIP, drug reaction, CBD, LIP, lymphoproliferative disorder
Neutrophils ⩾50%	AIP, DAD, AEIPF, pulmonary infection
Bloody fluid	Pulmonary haemorrhage, DAH
High haemosiderin score	DAH, DAD
CD1a+ cells >4%	PLCH
Milky BAL fluid with PAS-positive amorphous debris	PAP
Monotypic lymphocytes	Pulmonary lymphomatous malignancy
Malignant cells	Pulmonary malignancy
Squamous epithelial cells >5%	Unsuitable sample due to upper airway secretion contamination
Bronchial epithelial cells >5%	BAL sample may be unsuitable for cell analysis

ERJ 2011. 38(4):761-69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Multi-disciplinary Discussion (MDD)

History

Exposures

PFTs

Imaging

Pulmonologist
Chest radiologist
Pulmonary pathologist

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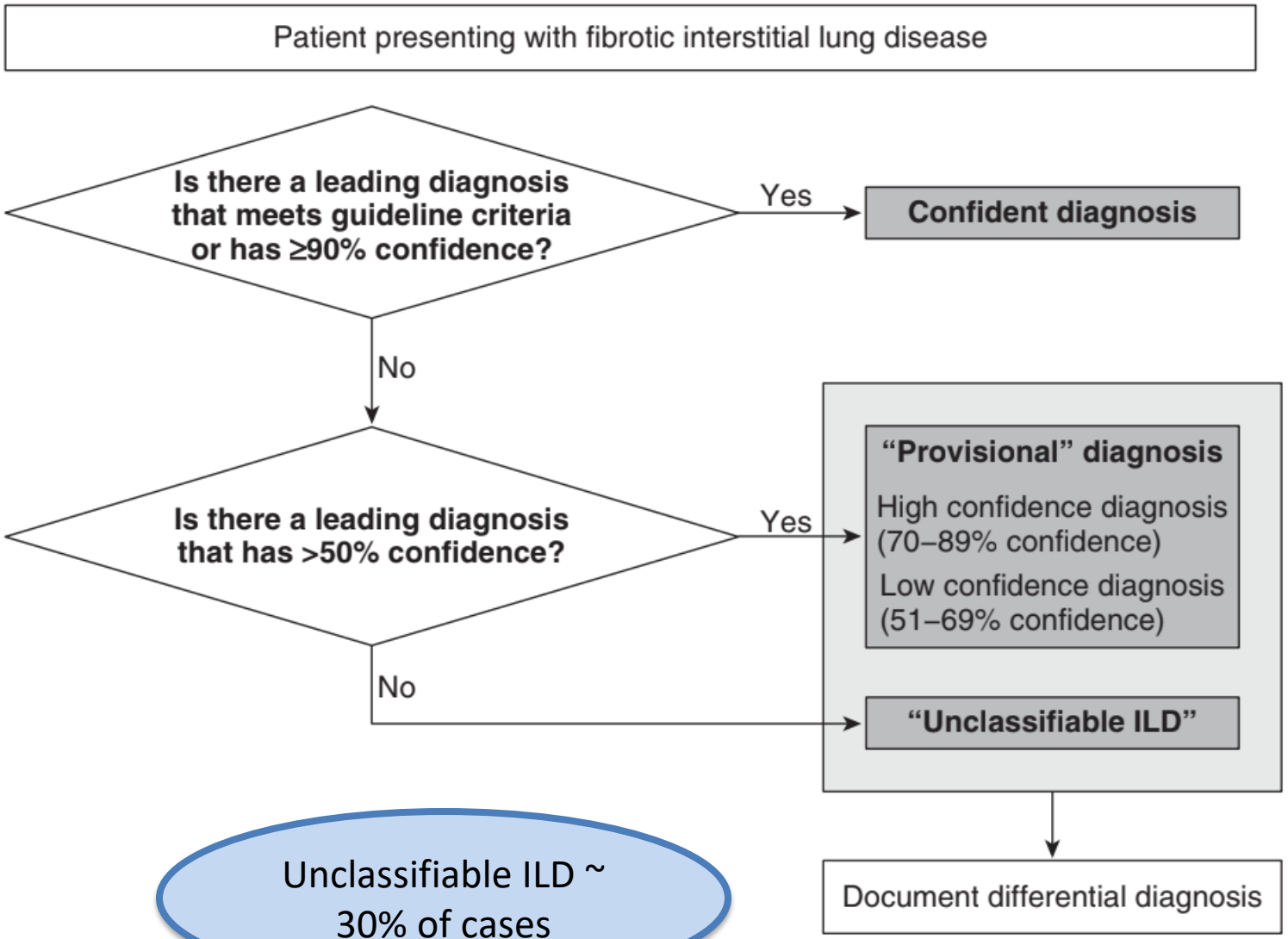
Accurate diagnosis is critically important because of the prognostic and therapeutic implications



Unclassifiable ILD ~ 30% of cases

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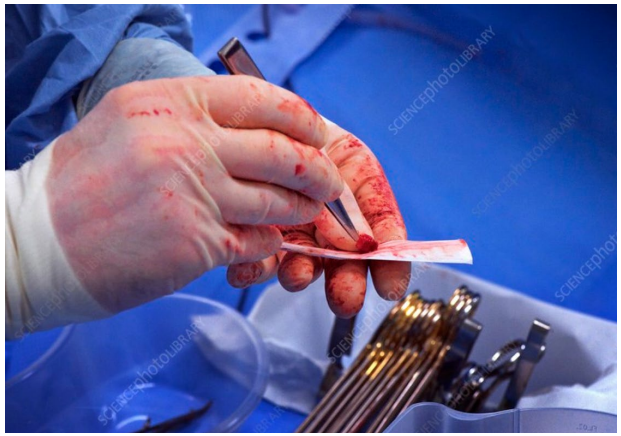
Surgical Lung Biopsy- Upsides Outweigh the Downsides?

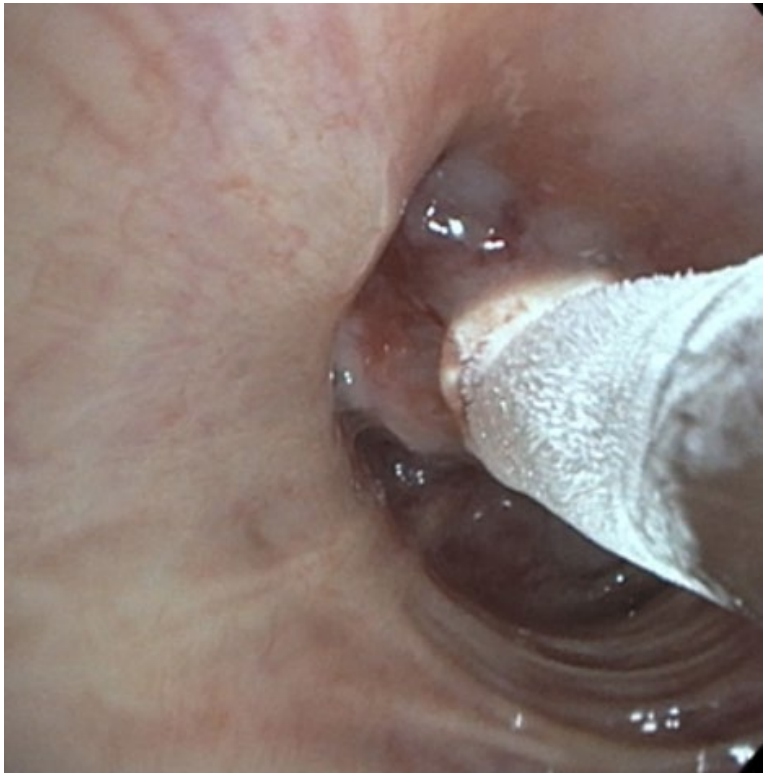
- 1-7% mortality
- Those at risk…
  - Poor cardiopulmonary reserve
  - Advanced age
  - Comorbid disease



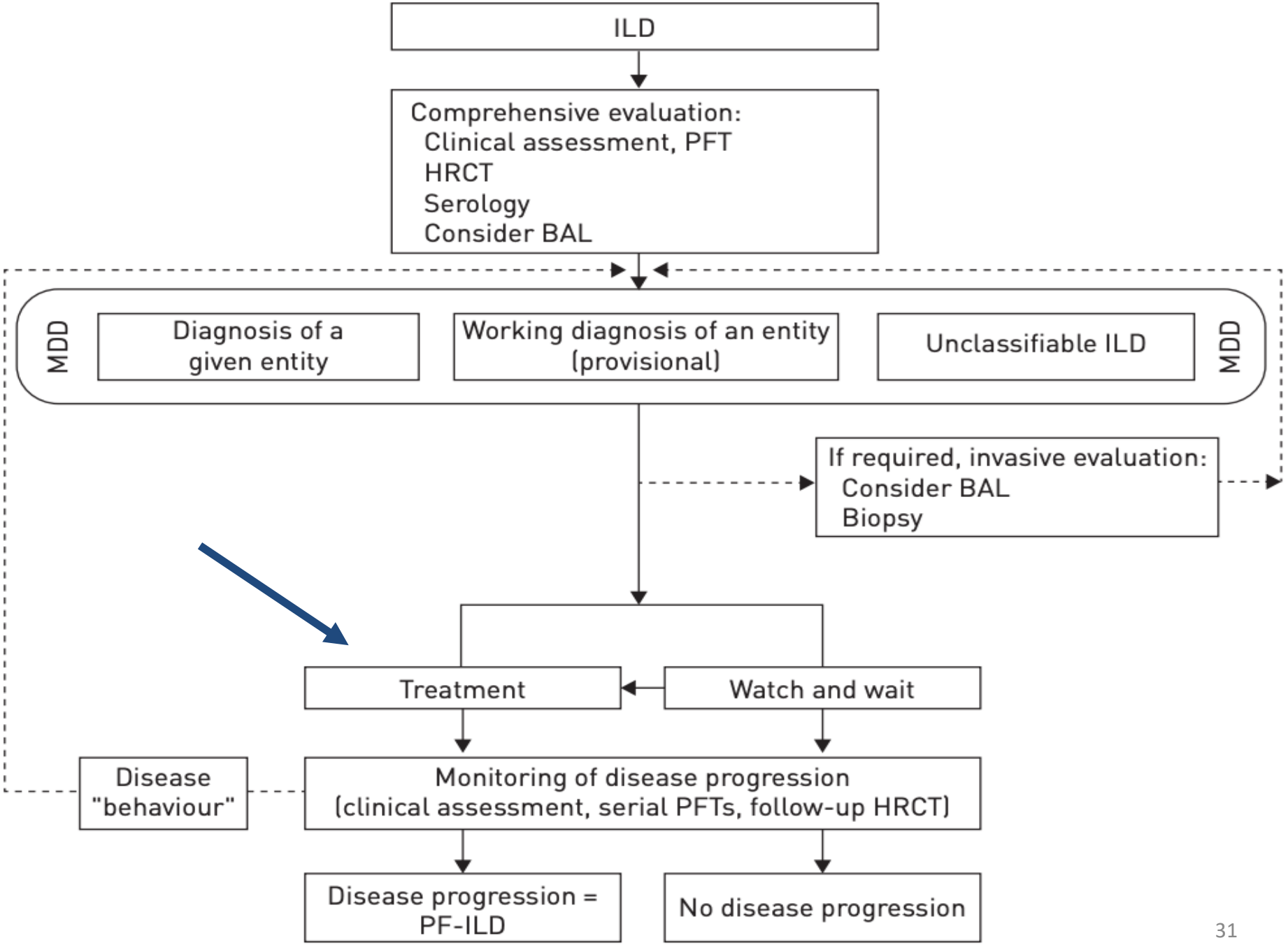
- Complications (~6%) include exacerbations, bleeding, prolonged air leak, neuropathic pain, delayed wound healing
- Decision to perform SLB should be made in the context of an ILD multi-disciplinary discussion

New Kid on the Block: Cryobiopsy

- Obtain large pieces of lung tissue with intact parenchymal architecture
- Lower complication rate than surgical lung biopsy?
  - Pneumothorax (20%)
  - Bleeding (9%-20%)
- Guidelines do not recommend for or against its use outside the research setting



ILD MDD…again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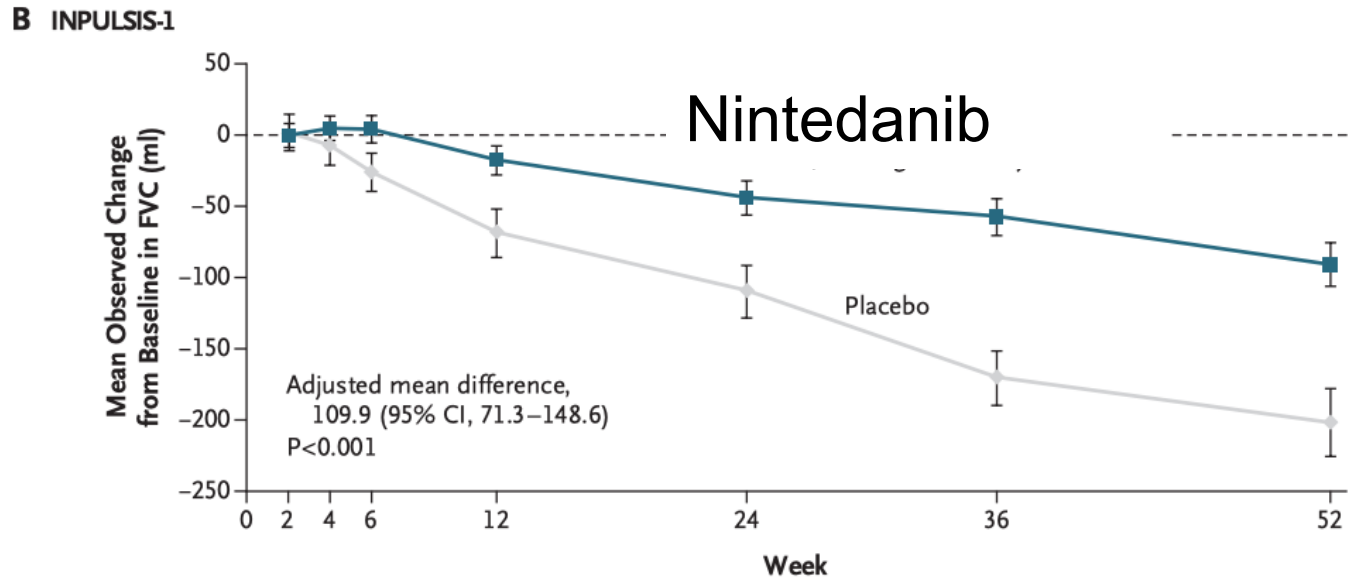
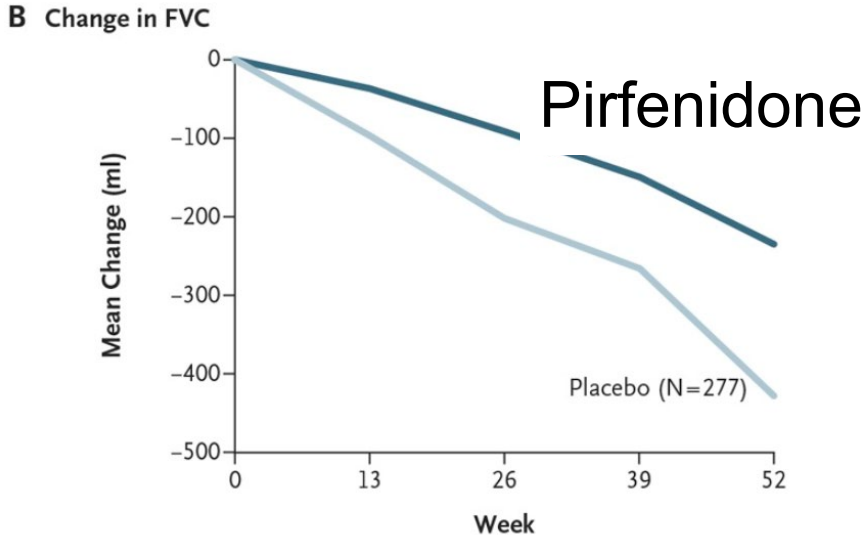
IPF Pharmacology: Anti-Fibrotic Therapies





Side effects include…

- Diarrhea
- Nausea
- Transaminitis
- Photosensitivity (pirfenidone)

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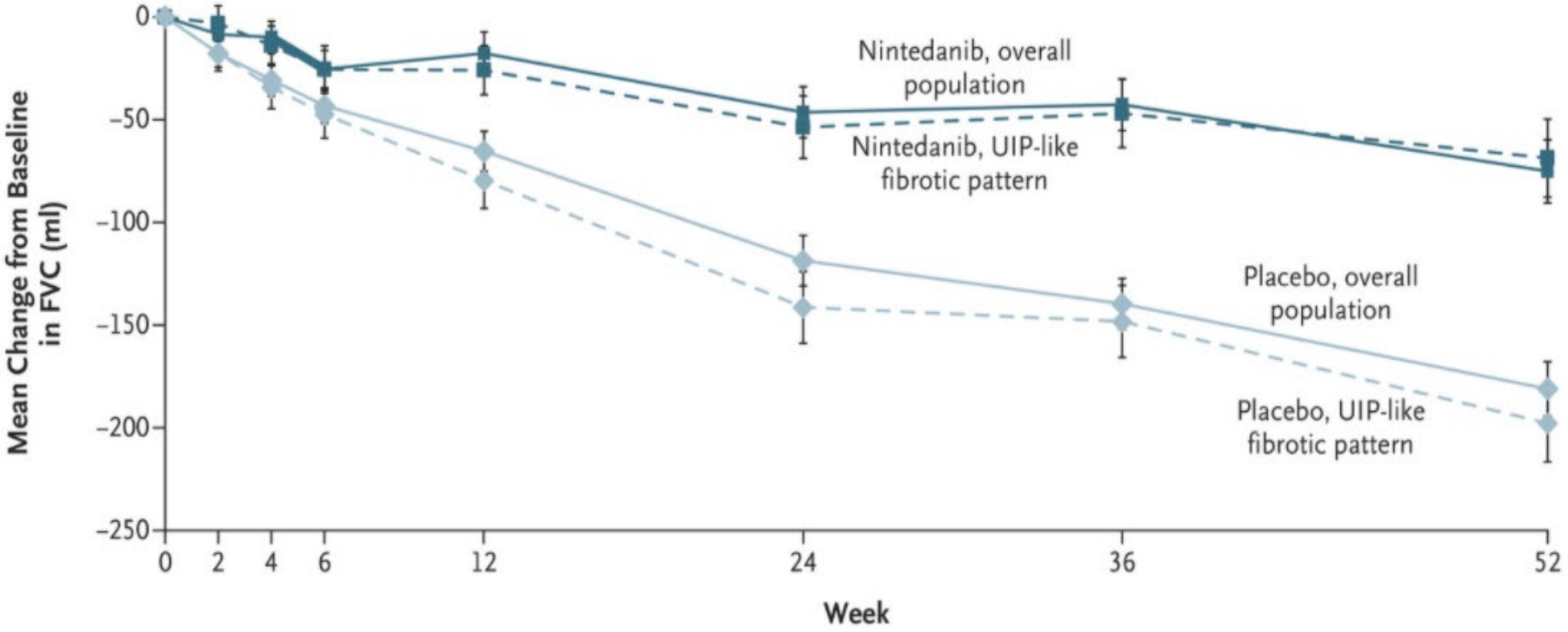
INPULSIS trial NEJM 2014, ASCEND trial NEJM 2014

Progressive Fibrotic-ILD: Nintedanib Seems Efficacious

1. Decline in FVC > 10%
2. Decline in FVC 5-10% + worsening symptoms
3. Increased fibrosis on CT + worsening symptoms



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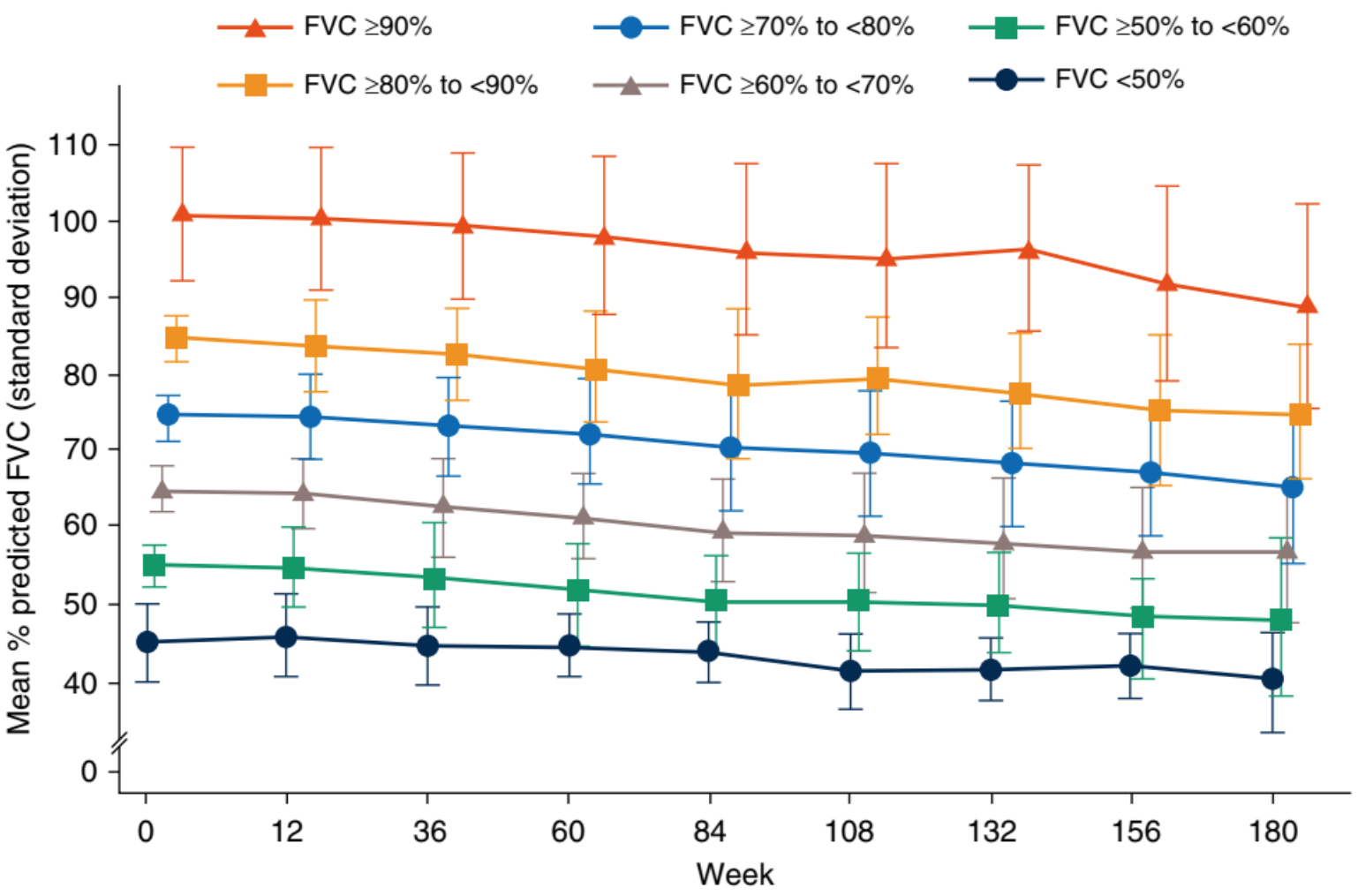
INBUILD trial *NEJM* 2019
DOI: 10.1056/NEJMoa1908681

Early Initiation At the Time of Diagnosis…Makes Sense



AnnalsATS 2019. 16(7):927-29

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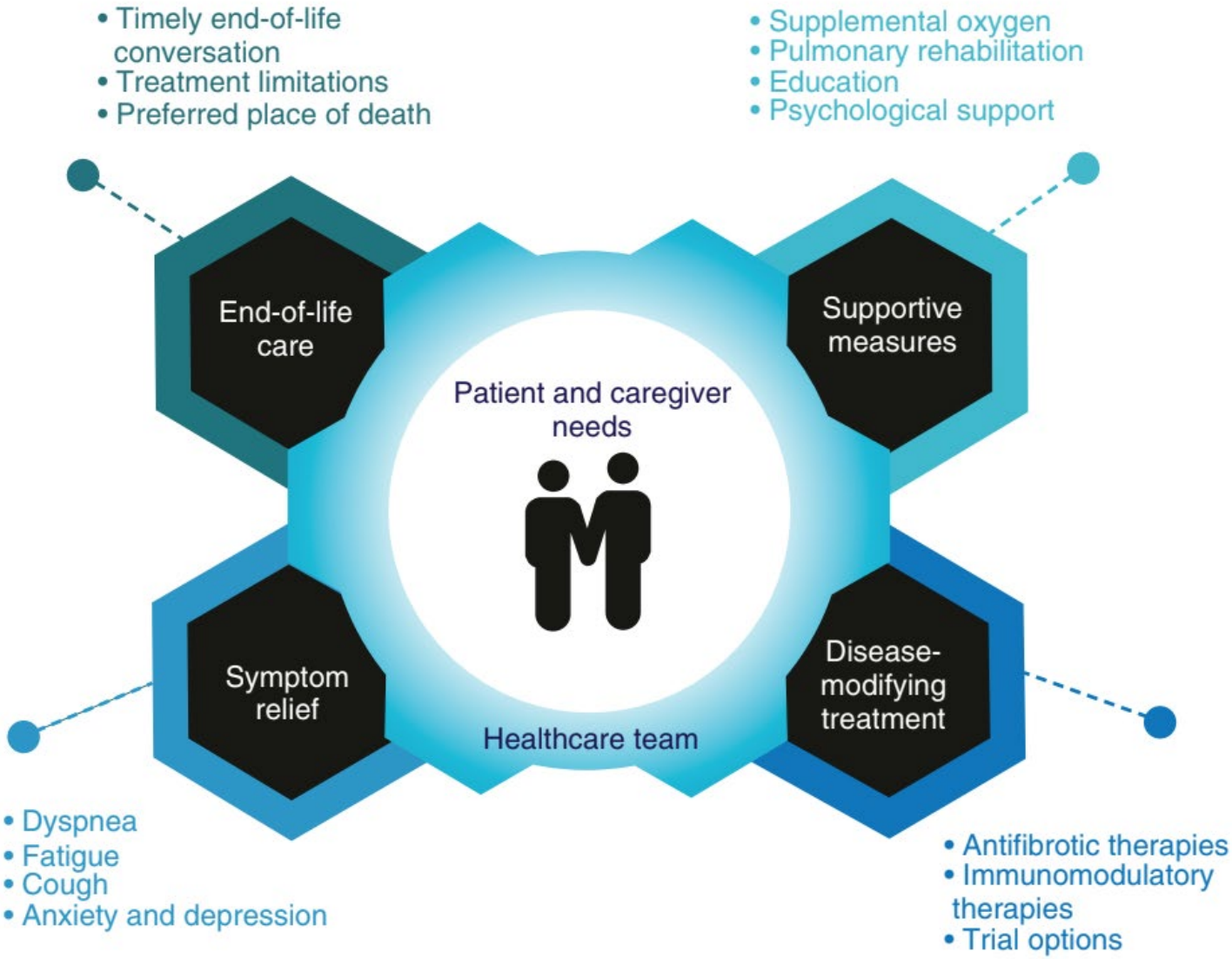
Comprehensive Supportive Care



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AJRCCM 2019. 200(2):152-59

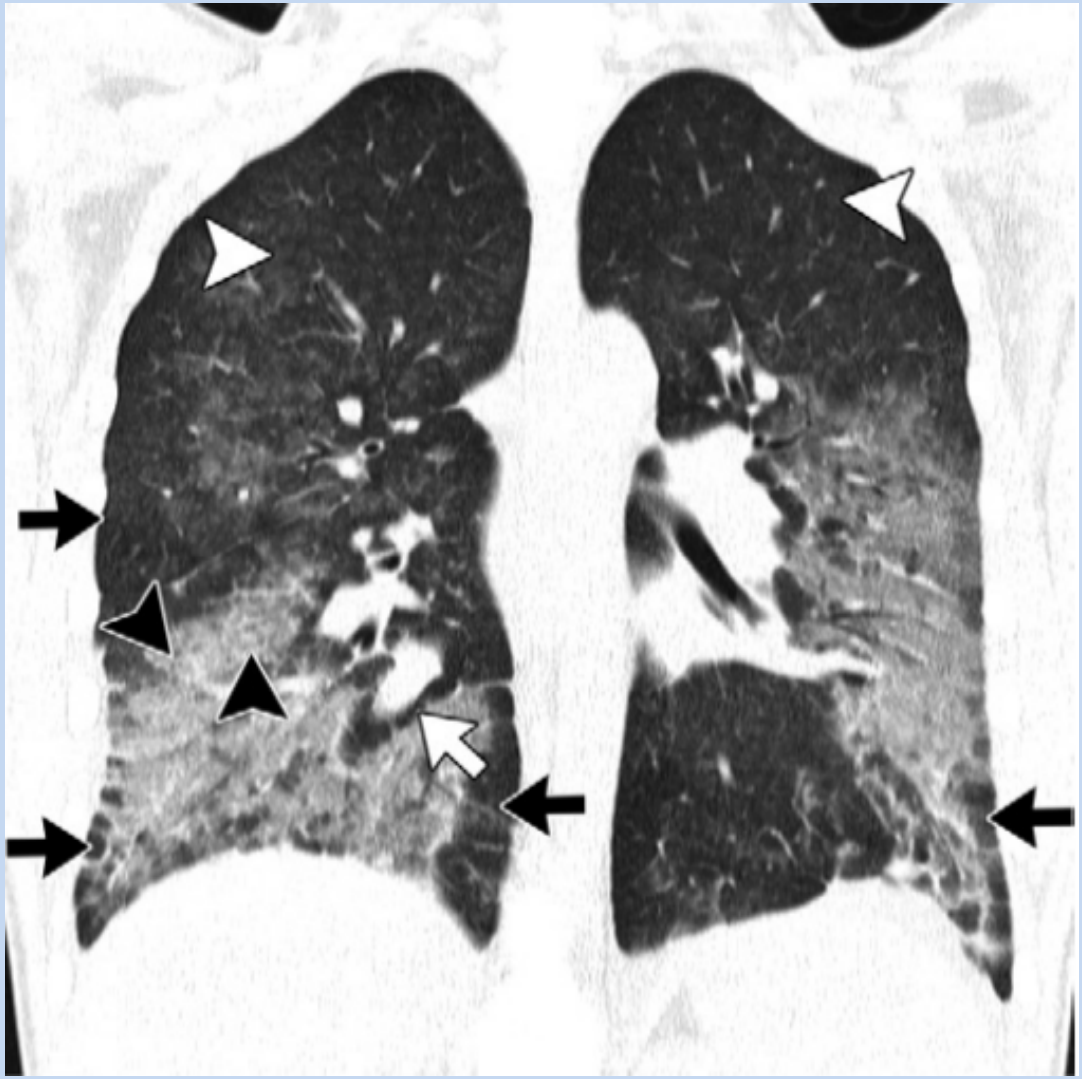
ILD Program: Provide Comprehensive Supportive Care

1. Standardized evaluation
   - Discuss case at the ILD MDD
   - Arrange procedures
2. Initiate anti-fibrotic therapy
3. Advise engagement in the ILD support group
4. Communicate with all associated healthcare providers
5. Ensure patients understand the diagnosis and prognosis

Sample Case

- 35 year old man with an unremarkable past medical history presents to clinic for progressive exertional dyspnea and dry cough x 6 weeks
- Exposures- e-cigarettes x 1 year, works as a chef
- Blood tests - negative CTD studies, eosinophils 0.2%, CRP 100
- PFTs- mild restrictive physiology and moderate reduction in DLCO

Chest CT: Organizing Pneumonia



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ILD MDD

- **Consensus diagnosis:** EVALI (organizing pneumonia phenotype)
- **Recommendations:**
  - Prednisone 1 mg/kg x 30 days, taper by 5 mg every 7 days following
  - PCP prophylaxis
  - Stop vaping
  - Repeat imaging and PFTs following steroid taper

Electronic Cigarette or Vaping Associated Lung Injury (EVALI)

- Most dramatic rise in adolescents
- E-cigarette vaping aerosols → free radicals → lung injury
- Steroid responsive ILD

Table 1: Summary of Histopathologic Features in Vaping-associated Lung Injury

Feature	Cases
Injury pattern(s)	
Organizing pneumonia	19/25 (76)
Acute fibrinous pneumonitis with organization	12/25 (48)
Diffuse alveolar damage, acute and organizing	6/25 (24)
Other histologic features	
Foamy or vacuolated macrophages	21/25 (84)
Foamy or vacuolated pneumocytes	17/17 (100)
Intra-alveolar fibrin	22/25 (88)
Bronchiolitis	7/9 (78)
Bronchiolar mucosal ulceration	6/9 (67)
Interstitial edema	11/17 (65)
Neutrophilic inflammation	10/25 (40)
Chronic interstitial inflammation	14/25 (56)
Pigmented macrophages	7/17 (41)
Eosinophils, rare	7/25 (28)
Granulomas	0/25 (0)
Exogenous lipoid pneumonia	0/25 (0)

Radiology 2020. 294(3):491-505

ILD…In a Nutshell

- In summary…
  - ILD groups include exposure-related, CTD, granulomatous disease, and idiopathic
  - Diagnosis is often challenging but we are more precise as a team
  - Comprehensive supportive care is essential to help patients live as well as possible for as long as possible

Mahalo, any questions?

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