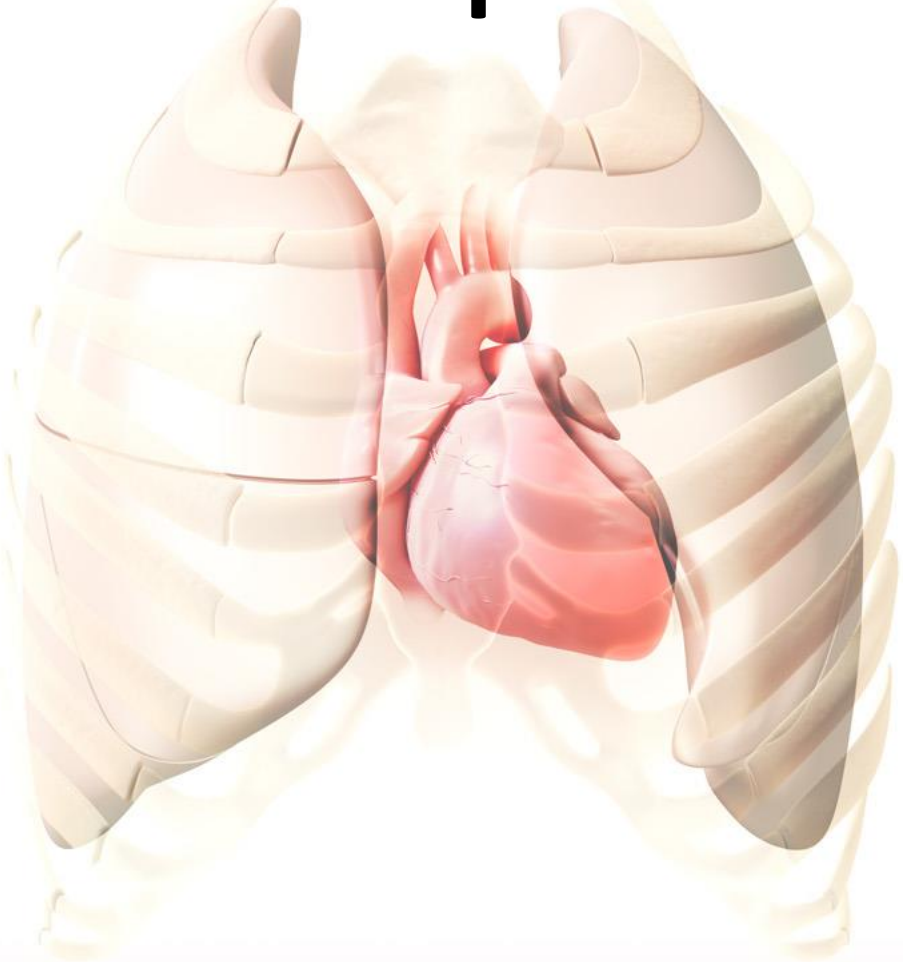
Idiopathic Pulmonary Fibrosis



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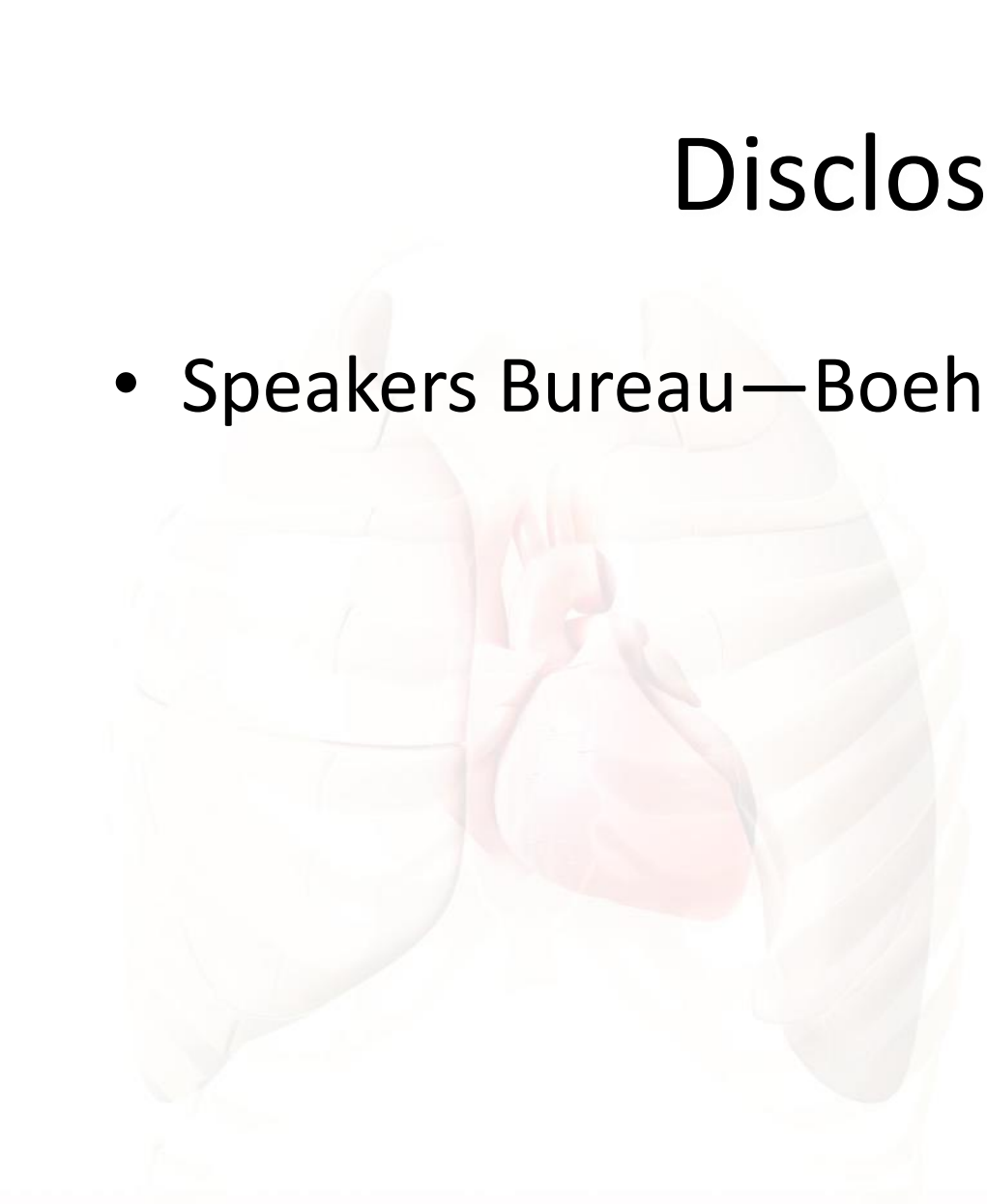
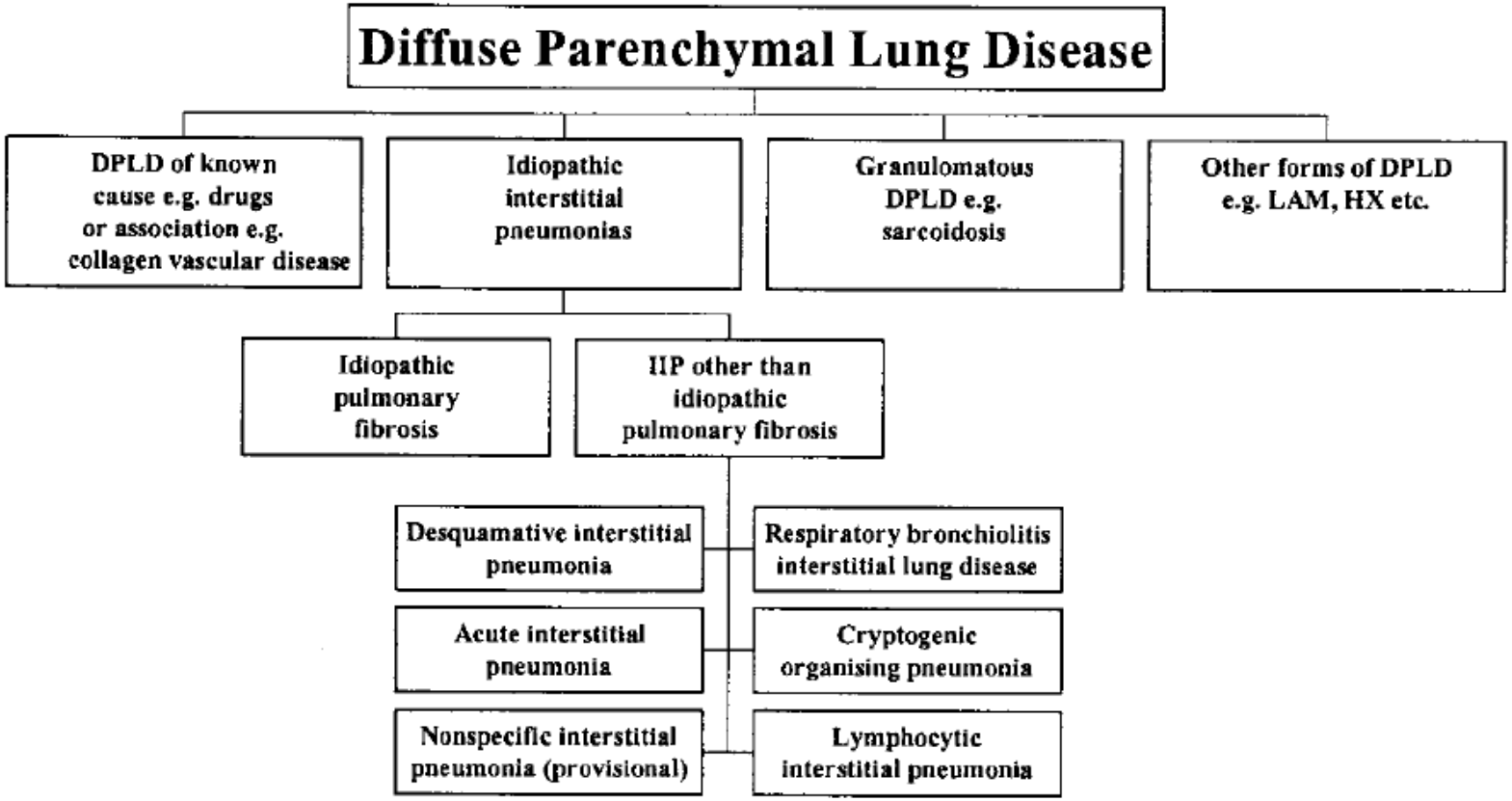
Disclosures

- Speakers Bureau—Boehringer-Ingelheim



Overview of Classification



ATS/ERS Consensus. Am J Respir Crit Care Med 2002;165:277-304

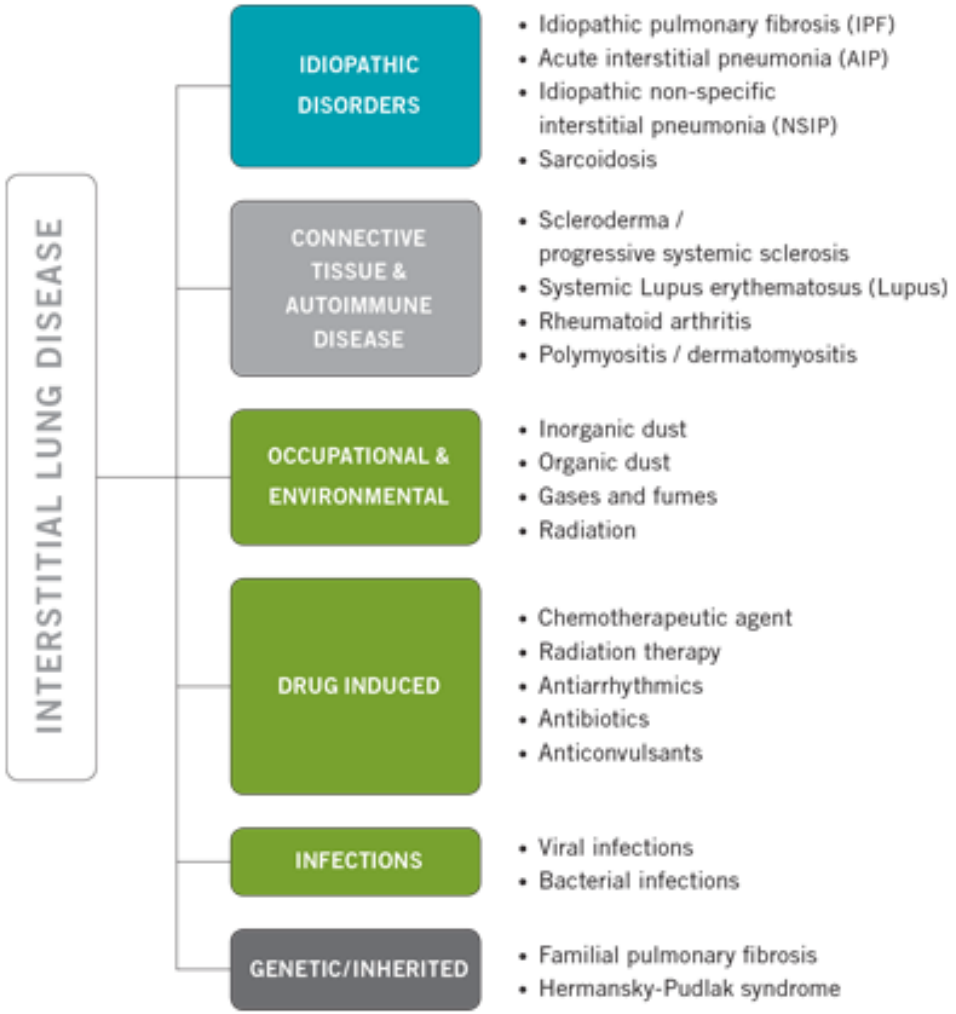


Image from the Pulmonary Fibrosis Foundation

What is IPF?

- Progressive fibrosing interstitial pneumonia.
- Alveolar epithelial cell injury→ Activation of interstitial inflammation, fibroblast proliferation with extracellular matrix collagen deposition→ Loss of lung function.

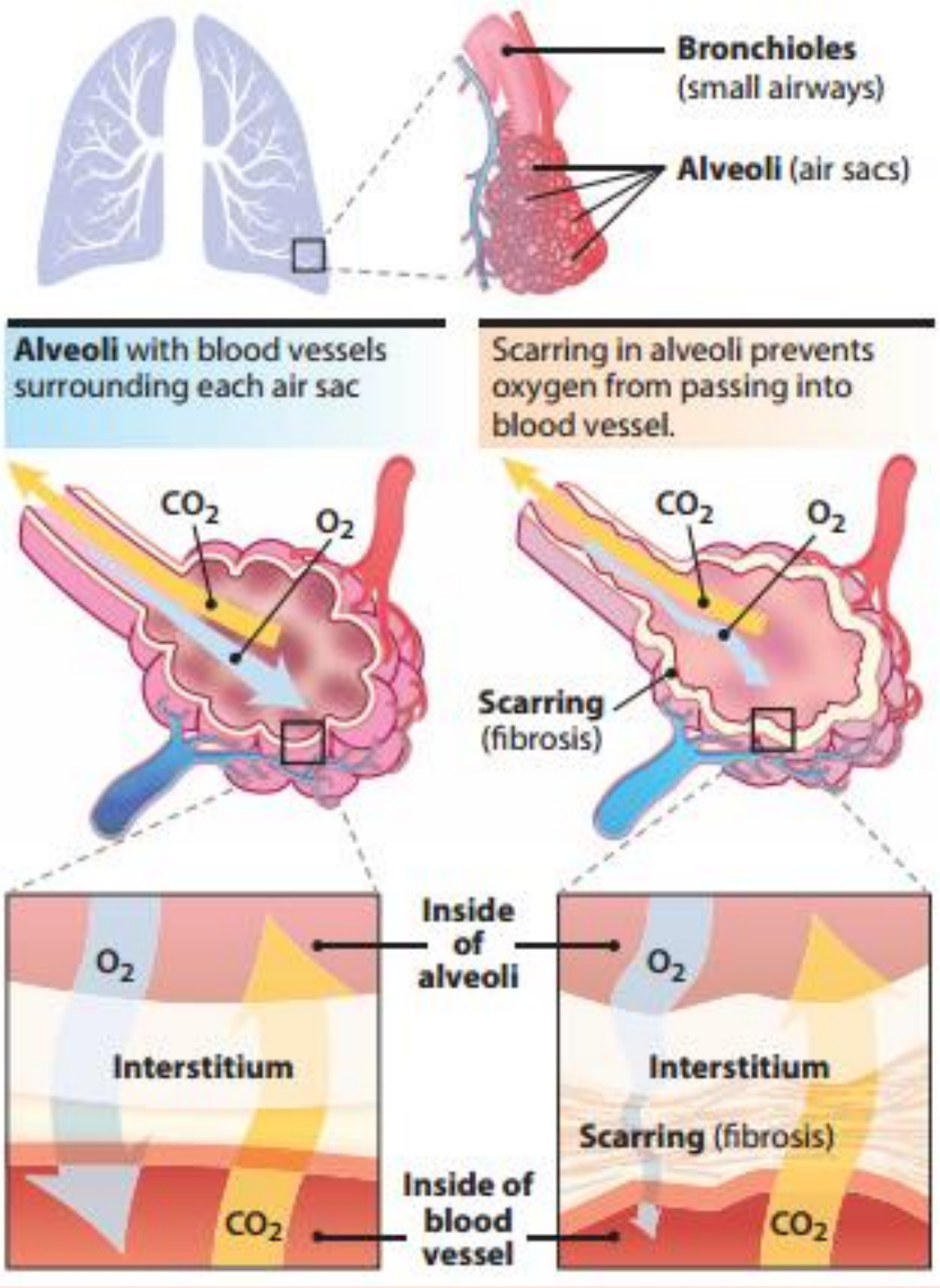
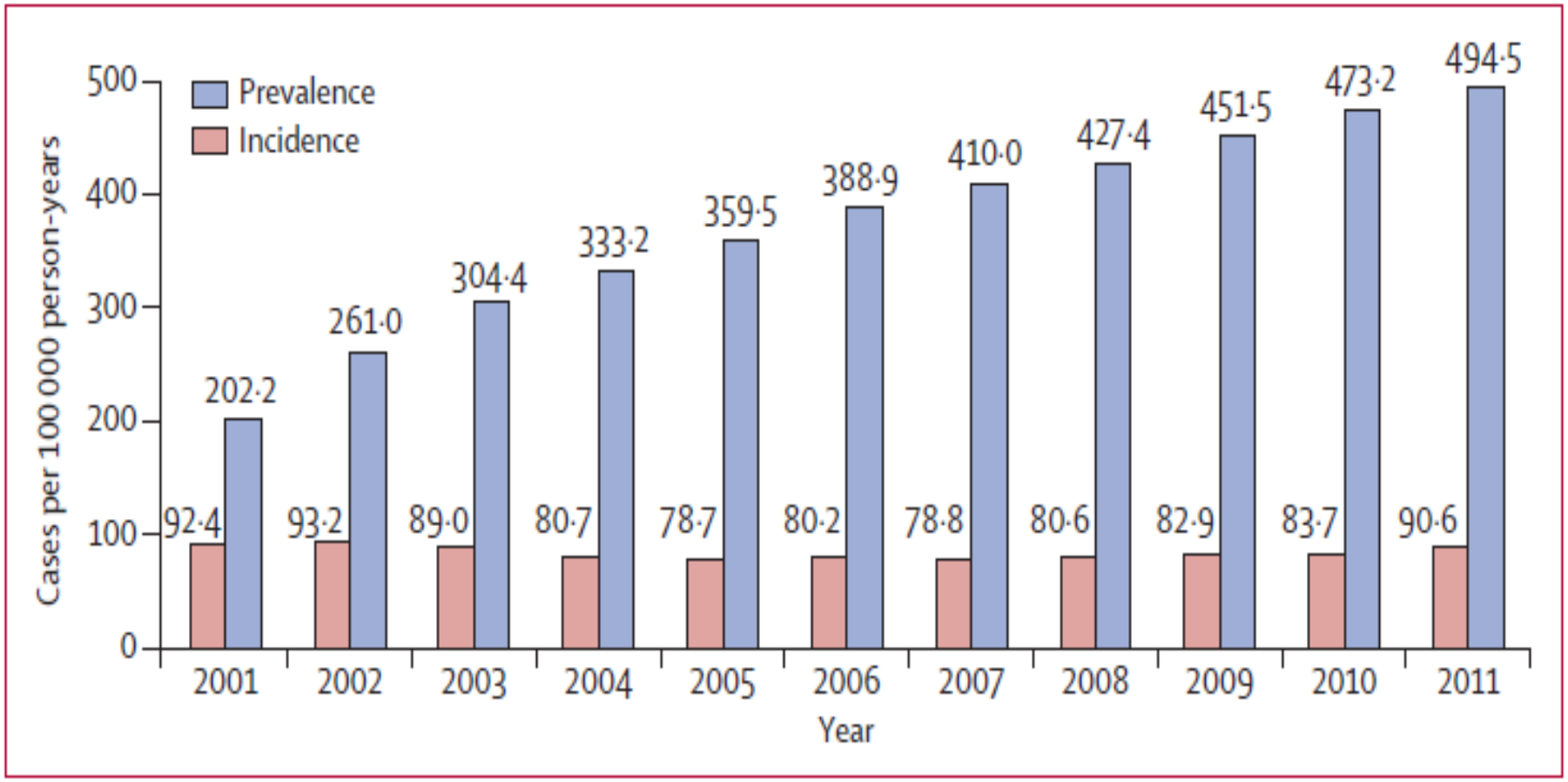


Image from the American Thoracic Society

Prevalence of IPF is Increasing

- 2011 US (Medicare) data shows 494.5 cases per 100,000 people
- Annual new diagnoses 78.7-93.2 per 100,000 people



Raghu, G, et. al. *Lancet Respir Med.* 2014;2(7):566-572

Clinical Profile

- Typically occurs in older adults, >50
- Increased incidence in males
- Smoking history
- More common in those who are Hispanic or Caucasian, rarely seen in those of African American descent
- Survival after diagnosis is typically 3-5 years, although this is impacted by factors such as age and sex

ATS/ERS/JRS/ALAT Statement. Am J Respir Crit Care Med. 2011;183:788-824
Raghu, G, et. al. *Lancet Respir Med.* 2014;2(7):566-572

Signs & Symptoms

- Chronic cough, usually dry
- Shortness of breath on exertion
- Fatigue
- May have episodes of acute exacerbations

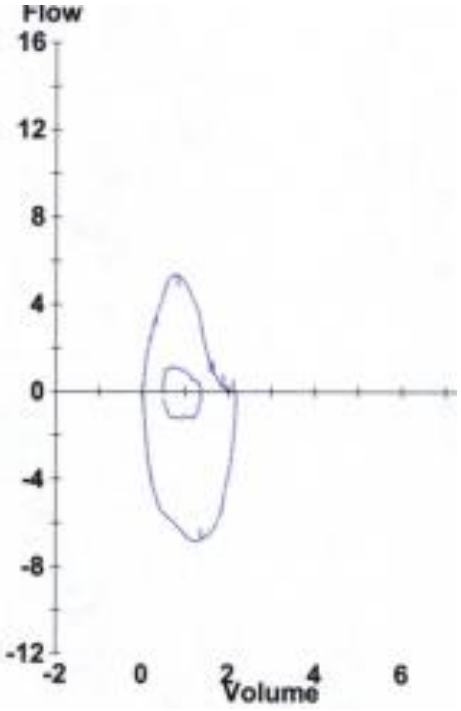
- Clubbing (widening) of the fingertips
- Basilar crackles upon lung auscultation
- Hypoxia (low oxygen)

ATS/ERS/JRS/ALAT Statement. Am J Respir Crit Care Med. 2011;183:788-824

Pulmonary function tests

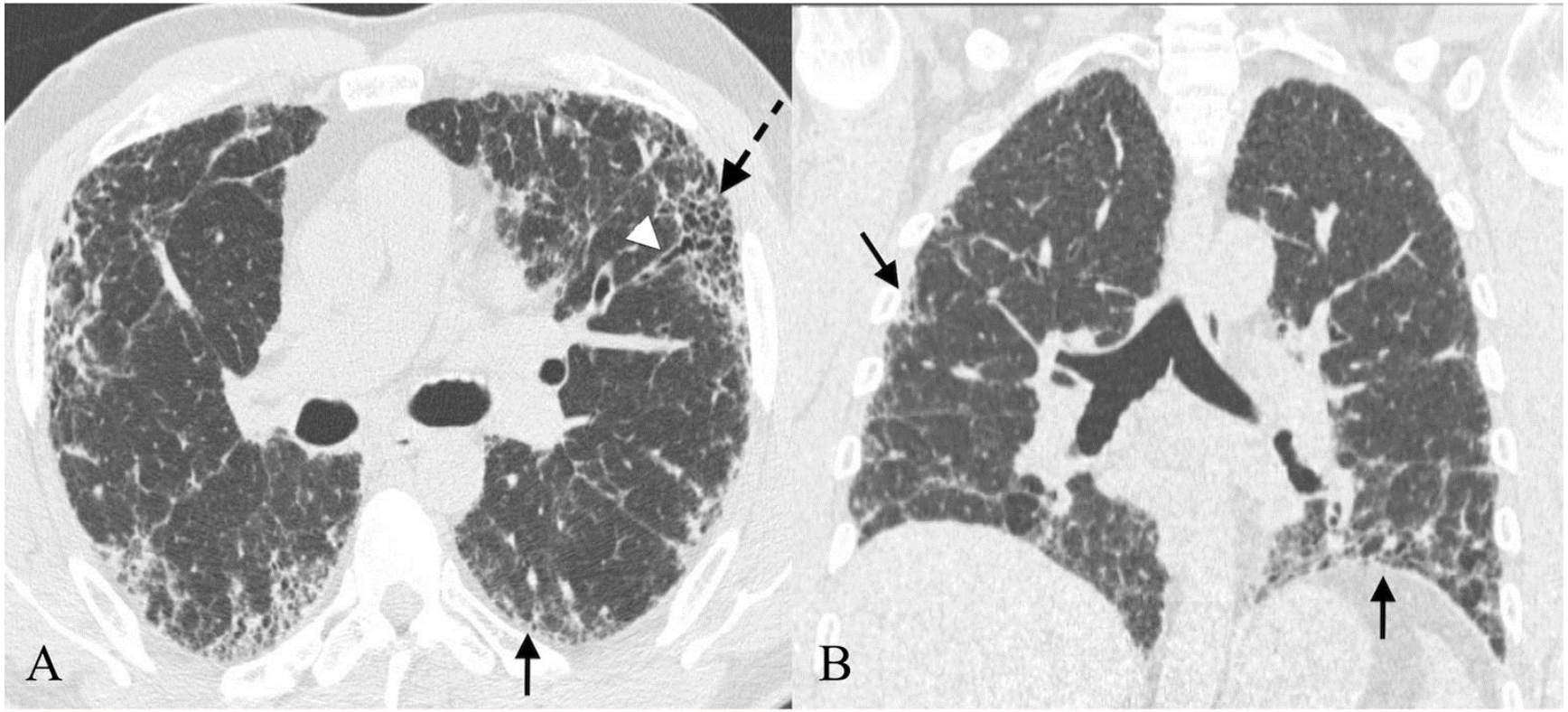
- IPF will have a restrictive pattern, rather than obstructive:
  - FVC 62%
  - FEV1 70%
  - FEV1/FVC 85%
  - TLC 61%
  - DLCO 31%

- Can have pseudonormalization of PFTs when combined: with emphysema
  - FVC 111%
  - FEV1 101%
  - FEV1/FVC 70%
  - TLC 87%
  - DLCO 36%



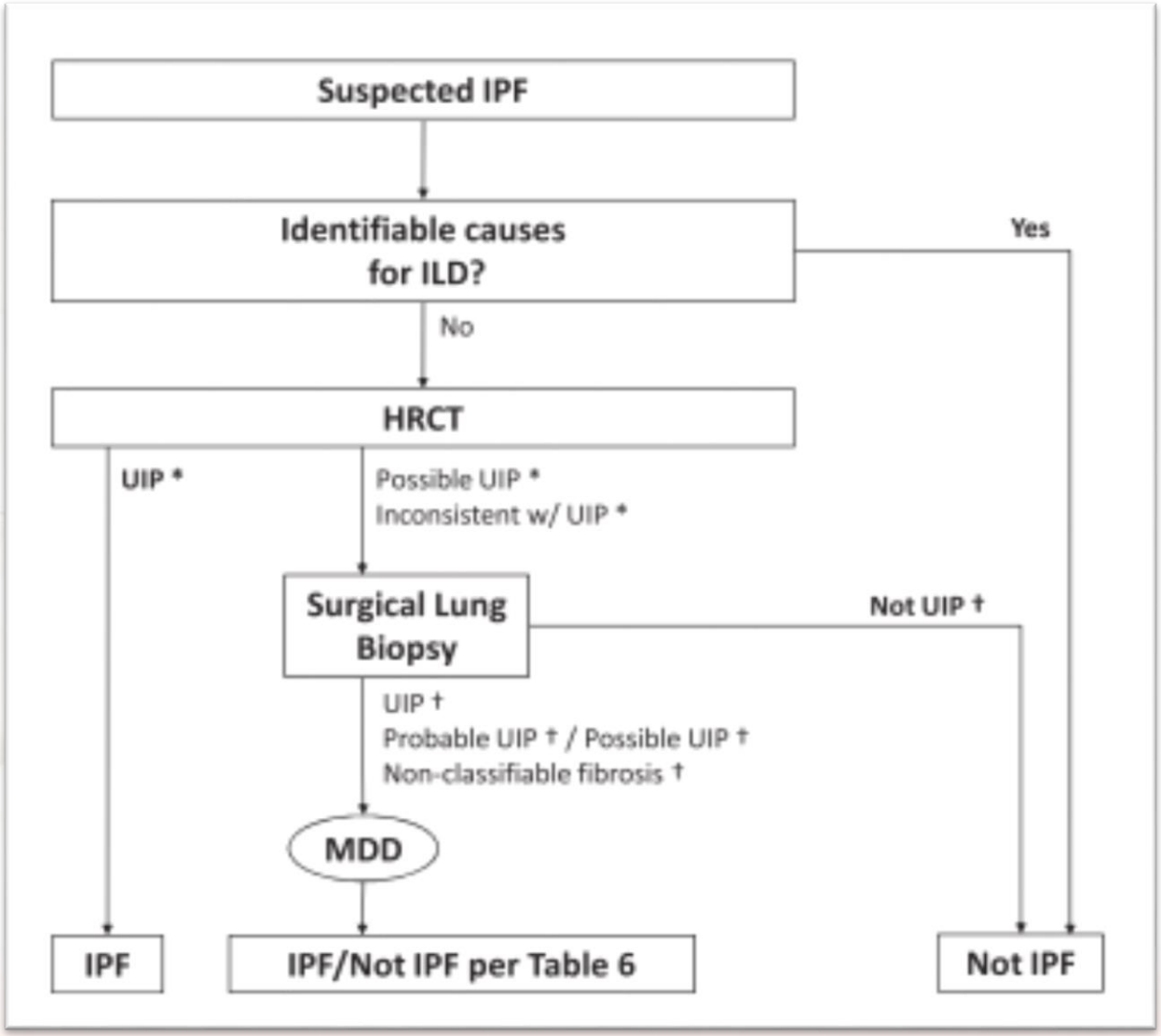
Diagnosing IPF

- Usual Interstitial Pneumonia pattern



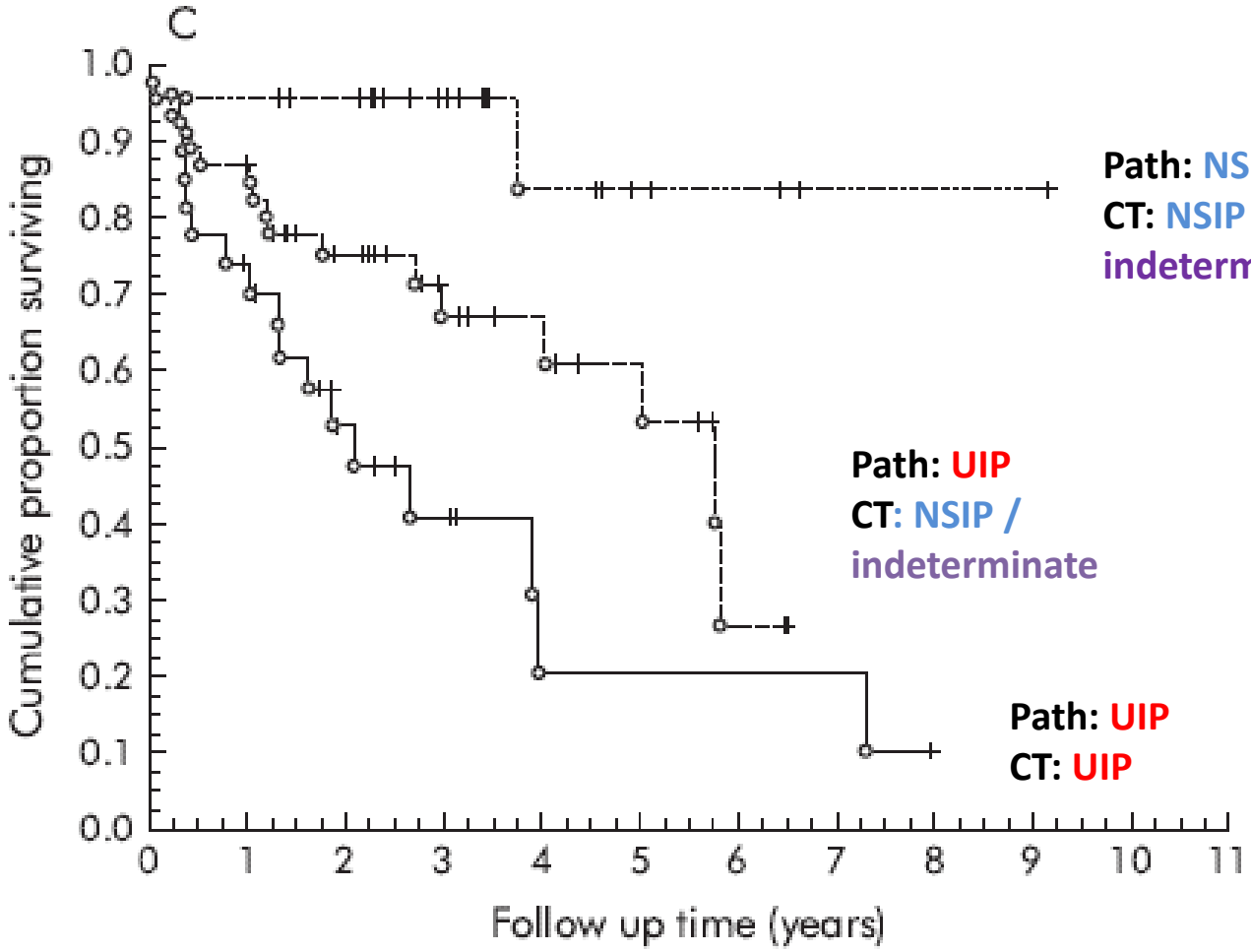
Insights Imaging. 2014;5(3):347-64

When to Biopsy



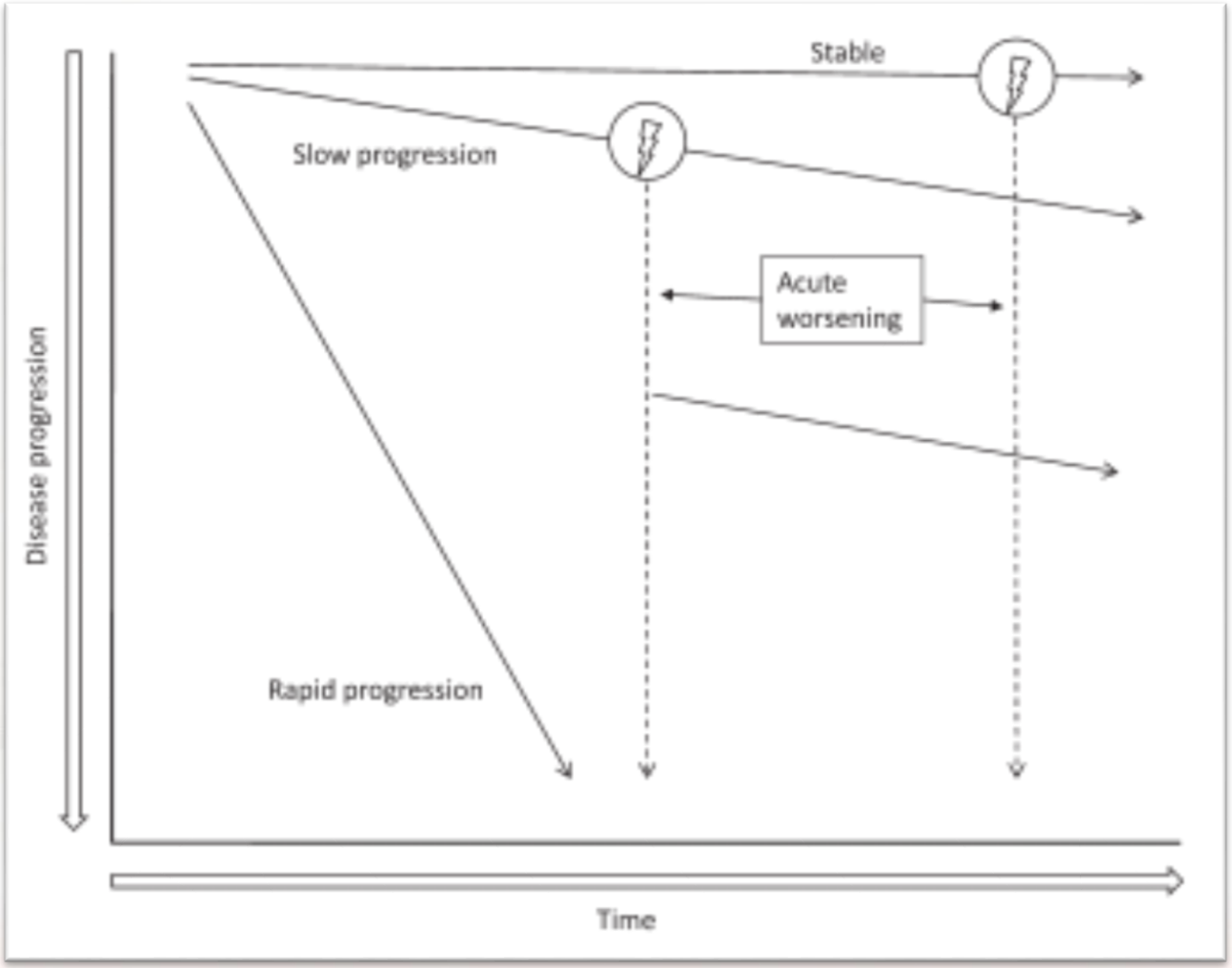
ATS/ERS/JRS/ALAT Statement. Am J Respir Crit Care Med. 2011;183:788-824

Significance of UIP on Outcomes



Thorax 2003;58:143–148

Natural History of IPF



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Pharmacologic Treatment

Pirfenidone (Esbriet)

- FDA approved in 2014 (previously used in Europe and Japan).

- Unknown mechanism of action, but is thought to interfere with the production of TGF-beta and TNF-alpha.

Trials

CAPACITY TRIALS

- Primary endpoint: percent change in FVC from baseline to 72 weeks.
- Outcome
  - -8% decline in Pirfenidone group versus -12.4% decline in the placebo group.
  - Of the patients who had decline 20% had a >10% decline in the Pirfenidone group, while 35% had a >10% decline in the placebo group.

ASCEND TRIAL

- Primary endpoint: change in FVC from baseline at 52 weeks.
- Outcome
  - Significant decline in FVC >10% occurred in 17% of patients on Esbriet and 32% of patients not on Esbriet.

King, T., et. al. N Engl J Med, 2014; 370(22). doi: 10.1056/NEJMoa1402582
Noble, P., et. al. Lancet, 2011; 377(9779). 1760-1769. doi: 10.1016/S0140-6736(11)60405-4

Pharmacologic Treatment

Nintedanib

- FDA approved in 2014.

- Blocks growth factor receptors– vascular endothelial growth factor receptor (VEGFR), fibroblast growth factor receptor (FGFR), and platelet-derived growth factor receptor (PDGFR).

Trials

TOMORROW TRIAL

- 432 patients enrolled with FVC 50% and greater.
- Primary endpoint: annual rate of decline in FVC.
  - Secondary endpoint: time to first exacerbation
- Outcome
  - Annual rate of change in FVC was 0.06L in nintedanib group versus 0.19L in placebo.
  - Incidence of acute exacerbations was lower in nintedanib group.

IMPULSIS I & II

- 1066 patients with FVC 50% and greater.
- Primary endpoint: annual rate of decline in FVC.
  - Secondary endpoint: time to first exacerbation
- Outcome:
  - Annual rate of change in FVC was -114mL with nintedanib versus -239.9mL with placebo (INPULSIS-1) and -113.6 with nintedanib versus -207.3mL with placebo (INPULSIS-2).
  - INPULSIS II: significant delay in time to first exacerbation (not significant in INPULSIS-I).

Richeldi, L. et. al. N Engl J Med. 2011; 365(12).
Richeldi, L., et. al. N Engl J Med, 2014; 70(22). 2071-2082.

Side Effects, Dosing, & Monitoring

Pirfenidone	Nintedanib
• Nausea/upper GI distress • Liver Toxicity • Photosensitivity.	• Diarrhea/lower GI distress • Liver Toxicity
• Dose in 267mg caps. Titrating dose: 1-3 caps taken three times daily.	• Dose 150mg twice daily • 100mg dosing available as well.
• Monitoring: liver function tests	• Monitoring: liver function tests

Other Treatments

- Adequate oxygen support
- Pulmonary Rehabilitation
- Control of Comorbidities
  - Reflux disease
  - Heart disease

Other Treatments

- Control of cough and symptoms
- Immunizations
- Early intervention for respiratory changes
- Early referral to lung transplantation and/or palliative care for appropriate patients

Lung Transplant

- Timing of Referral
  - Histopathologic or radiographic evidence of usual interstitial pneumonitis (UIP) or fibrosing non-specific interstitial pneumonitis (NSIP), regardless of lung function.
  - Abnormal lung function:
    - forced vital capacity (FVC) <80% predicted or
    - diffusion capacity of the lung for carbon monoxide (D_{LCO}) <40% predicted.
  - Any dyspnea or functional limitation attributable to lung disease.
  - Any oxygen requirement, even if only during exertion.

Weill, D. et. al. J Heart Lung Transplant. 2014; 34(1). 1-15

Pulmonary Fibrosis Foundation

- Established in 2000 to support and assist individuals with IPF.
- Comprised of leading medical centers with expertise in the management of ILDs.
- Support of research and establishment of pulmonary fibrosis registry.
- Information on support groups, continued education on IPF, and more.

References

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