# FROM ARK TO MARS: IDIOPATHIC PULMONARY FIBROSIS

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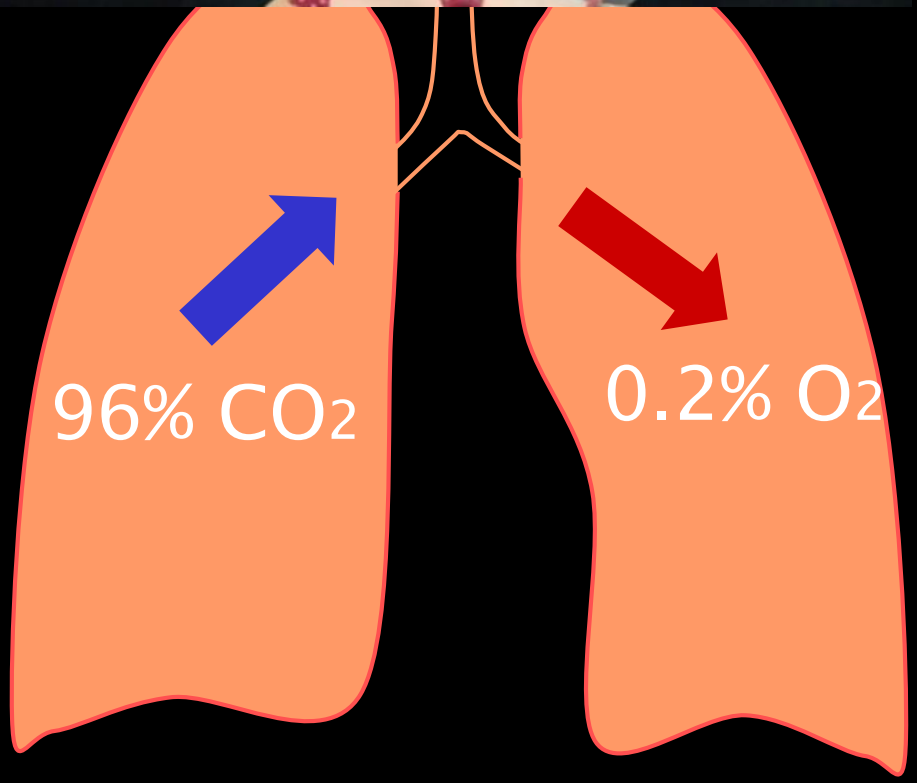
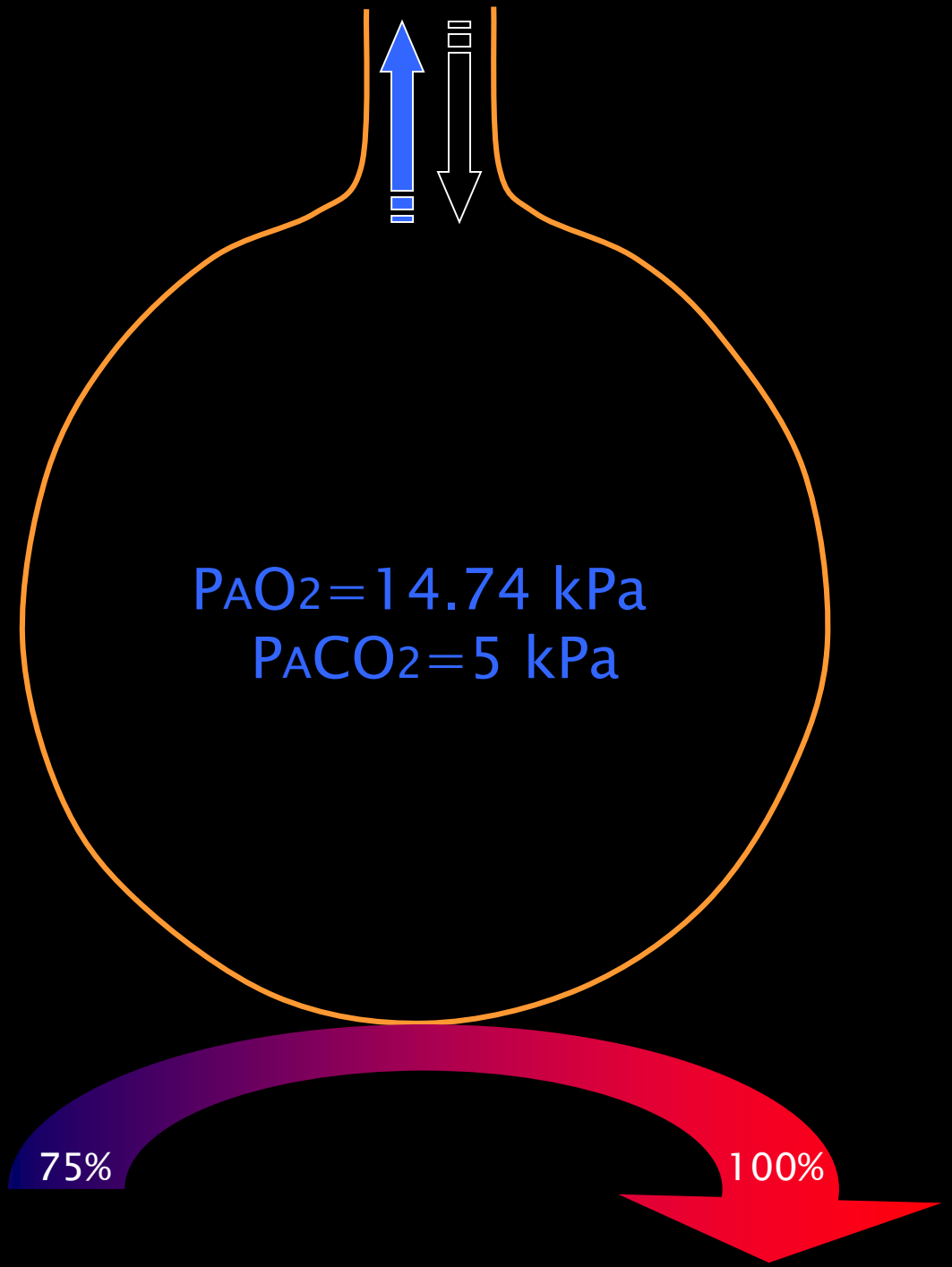
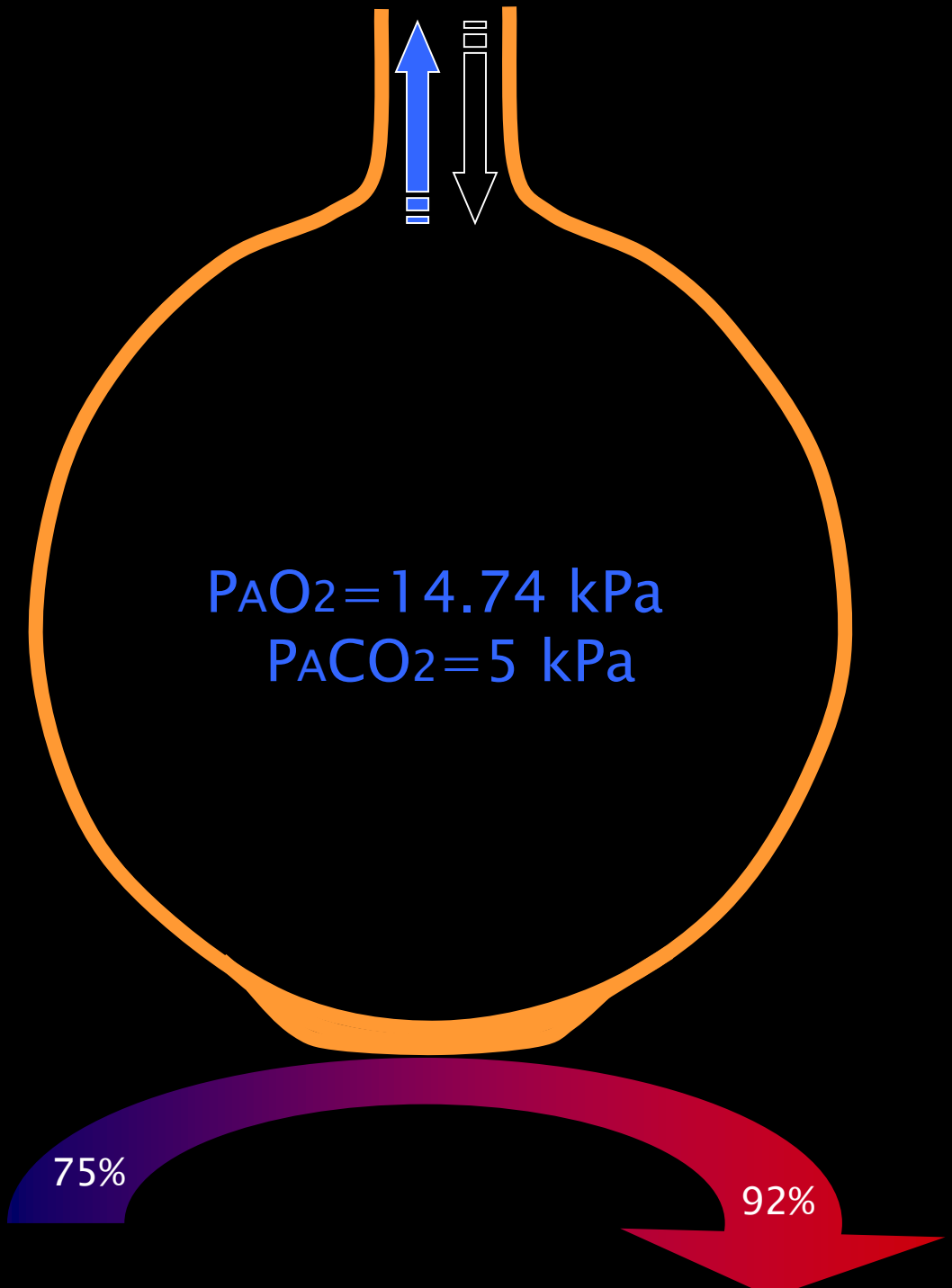
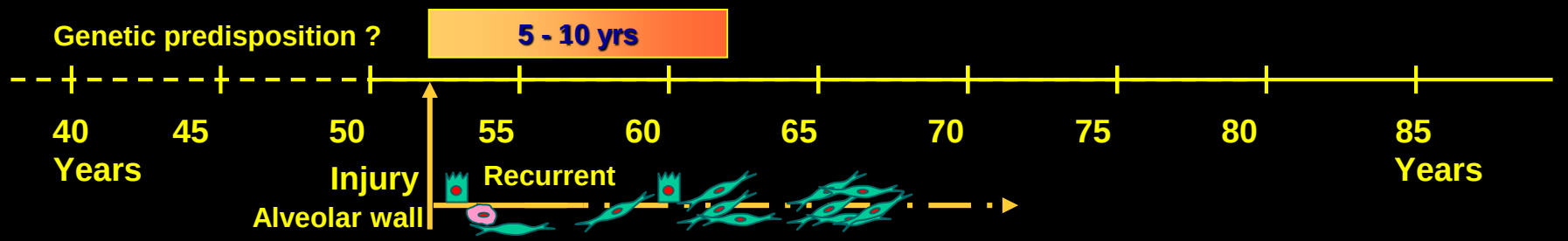
North Bristol Lung Centre
Southmead Hospital

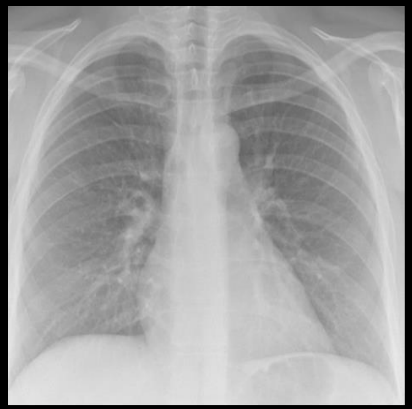
# Quiz: The Romans named Mars after God of War?

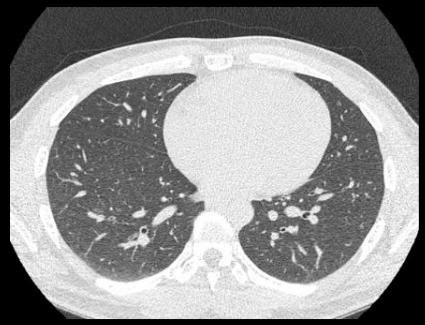

96% $CO_2$
0.2% $O_2$

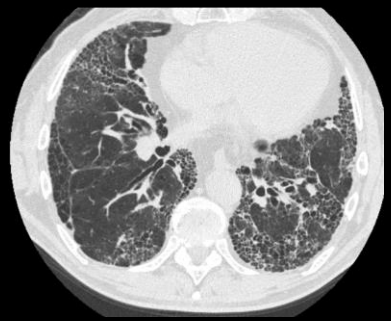

$P_AO_2$=14.74 kPa
$P_ACO_2$=5 kPa
75%
100%

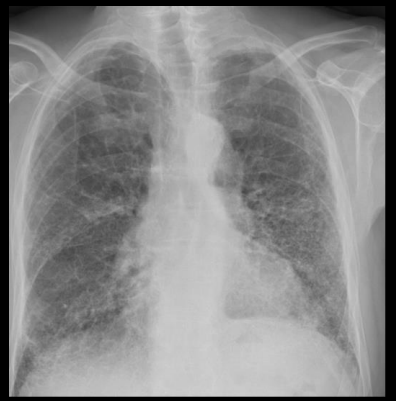

$P_AO_2$=14.74 kPa
$P_ACO_2$=5 kPa
75%
92%


Genetic predisposition ?
5 - 10 yrs
40
Years
45
50
55
60
65
70
75
80
85
Years
Injury
Recurrent
Alveolar wall



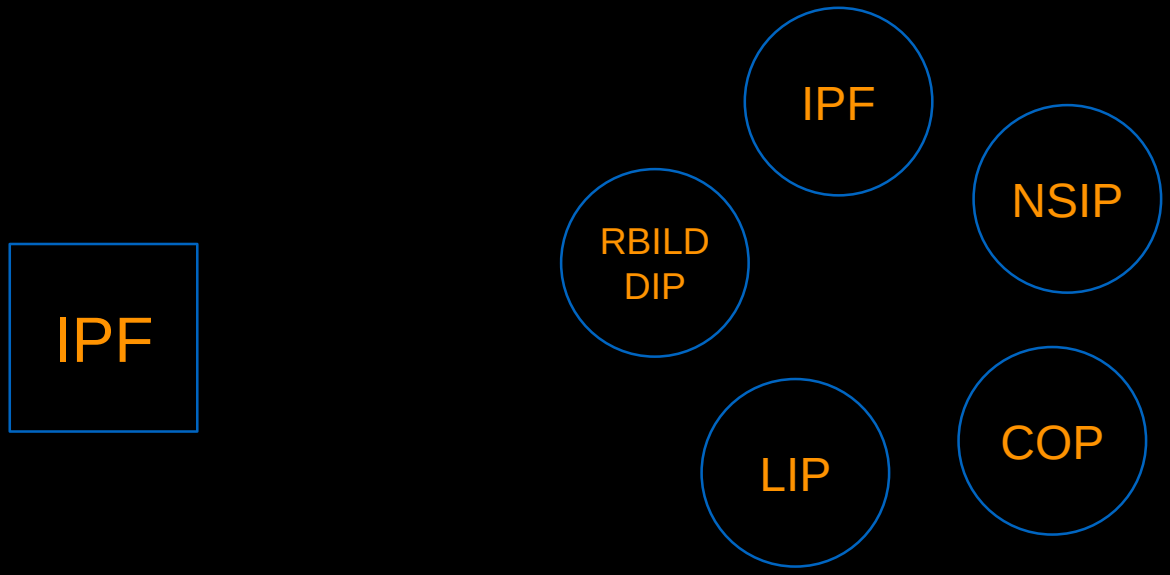






- 1898- Rindfleisch
  - Necropsy of 40 year old clergy man who had a worsening cough and dyspnoea. The author found hypertrophied right ventricle and small stiff lung without pleural adhesions. Lung interstitial contained an enormous amount of fibrous tissue with round cells as well as multiple cysts: ***cirrhosis cystic pulmonum***
- 1907- Sandoz
  - Twin sisters with progressively worsening cough and dyspnoea. Stiff ventricle and small stiff lungs with widened and thickened bronchiole and an increased amount of interstitial tissue but no pleural adhesions: first case of familial IPF
- 1933- Hamman and Rich
  - Acute interstitial fibrosis of lung: extreme dyspnoea, cyanosis and cough. Death occurred between 31 days and 24 weeks of admission. Inflammatory cells and excessive proliferation of fibrous tissue in the interstitium. Necrosis of alveolar and bronchiolar walls.

# Lumpers to Splitters




1970s Lumpers

1990s Splitters

# Fibrotic Lung Disease

## Inhaled substances

Asbestosis
Hypersensitivity pneumonitis

## Resulting from infection

Pneumonia
Tuberculosis

## Connective tissue or Rheumatological disorder

Rheumatoid arthritis
Systemic sclerosis

## Unknown cause

IPF
Sarcoid

# Objectives

Step 1
- History and Examination

Step 2
- Imaging

Step 3
- Pathology and Biopsies

Step 4
- Multidisciplinary Meeting

Step 5
- Treatment

Step 1

# •History

- Important to acquire a detailed medical history
- Need to exclude:
  - Environmental exposures
  - Extra pulmonary symptoms
  - Family Medical history
- Essential to exclude hypersensitive pneumonitis and CTD

# Case: Presenting Complaint

- 76 years; 2012
- An ex-smoker of 36 years; he previously smoked 40cigs/day for 15 years
- Married to a nurse practitioner
- ‘Choking’ cough
  - predominantly at night time and mornings
  - dry and non-productive
- Insidious onset of Shortness of breath

- Shortness of breath
  - Reduced walking distance on flat <1 mile on flat
  - Difficulty with inclines.
  - His MRC dyspnoea score is 3 (walks slower than contemporaries on level ground because of breathlessness, or has to stop for breath when walking at own pace).
- Locum GP: Persistent Lower respiratory infection
  - antibiotics but no resolution of symptoms.

- Weight loss and loss of appetite
- Denied cardiac symptoms, in particular chest pain, palpitations, ankle swelling and paroxysmal nocturnal dyspnoea.
- Used 3 pillows to sleep.
- Symptoms of gastro-oesophageal reflux disease
- No suspect drugs
- No evidence of cracking and fissuring of fingers, Raynauds, joint pain and swelling
- No pets (birds), stuffed bird feathers pillows etc

Step 1

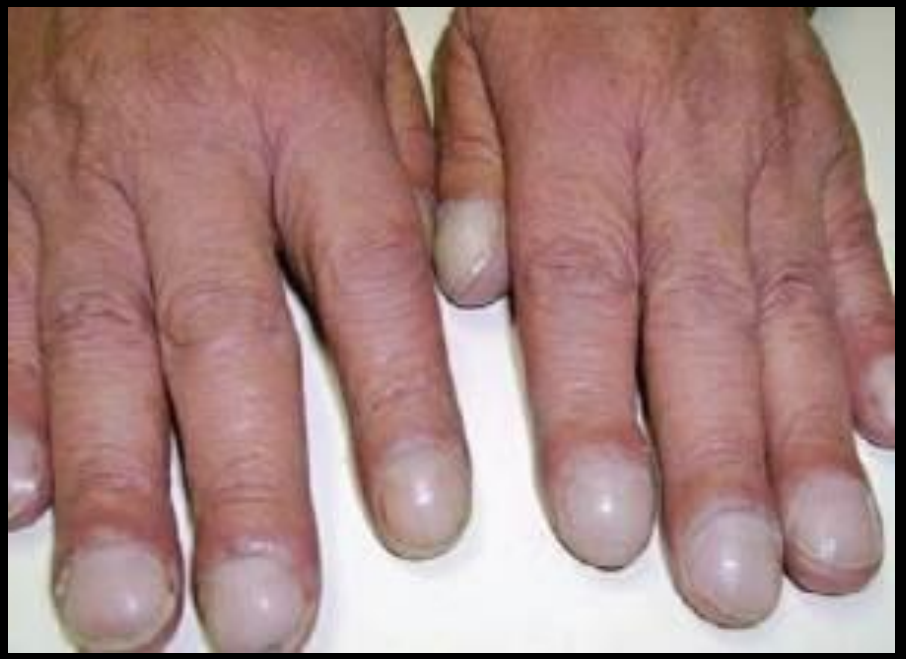
# •Examination

- Blood pressure was 148/80mmHg, oxygen saturations (at RA) was 93%, pulse rate 88 beats/minute. BMI was 22 kg/m2.
- He had evidence of clubbing.
- There were no skin and musculoskeletal features
- There was no elevated JVP nor ankle swelling. Cardiovascular examination was normal

# Quiz

Clubbing of the fingers develops in what percentage of IPF patients?

1. 80-100%
2. 25-50%
3. <25%
4. 0%



American Thoracic Society/European Respiratory Society. Am J Respir Crit Care Med 2002;165:277-304; 2. Raghu G et al. Am J Respir Crit Care Med 2011;183:788-824;
Image courtesy of: commons.wikimedia.org/wiki/File: Acopaquia.jpg

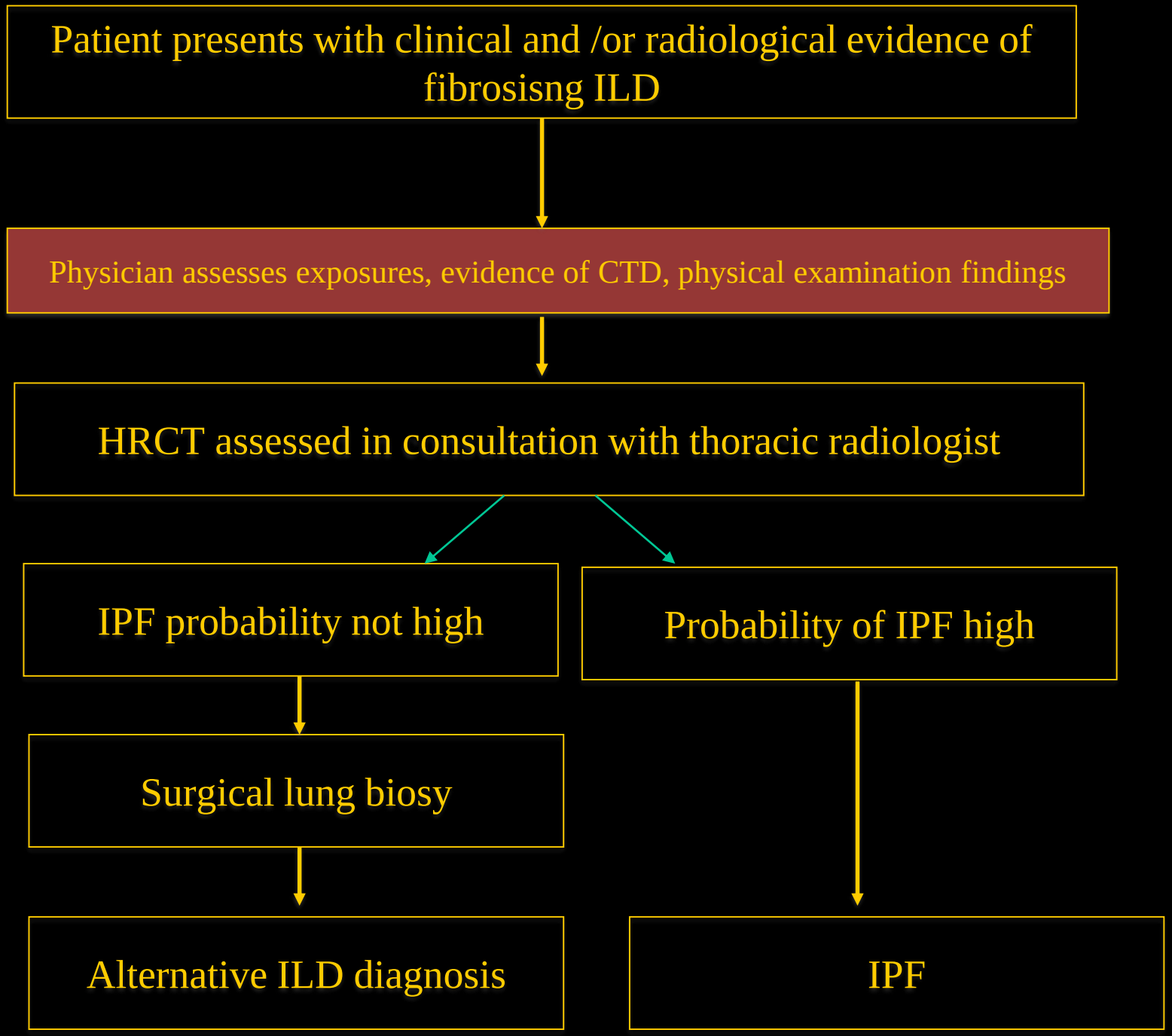
# Quiz 3

# Auscultation

- Lung auscultation is the only method of recognising IPF early
- Crackles are
  - detected during slow deep breaths
  - Discontinuous, short explosive non-musical sounds during inspiration
  - Best heard over dependant lung regions
  - Sometimes associated with expiratory crackles

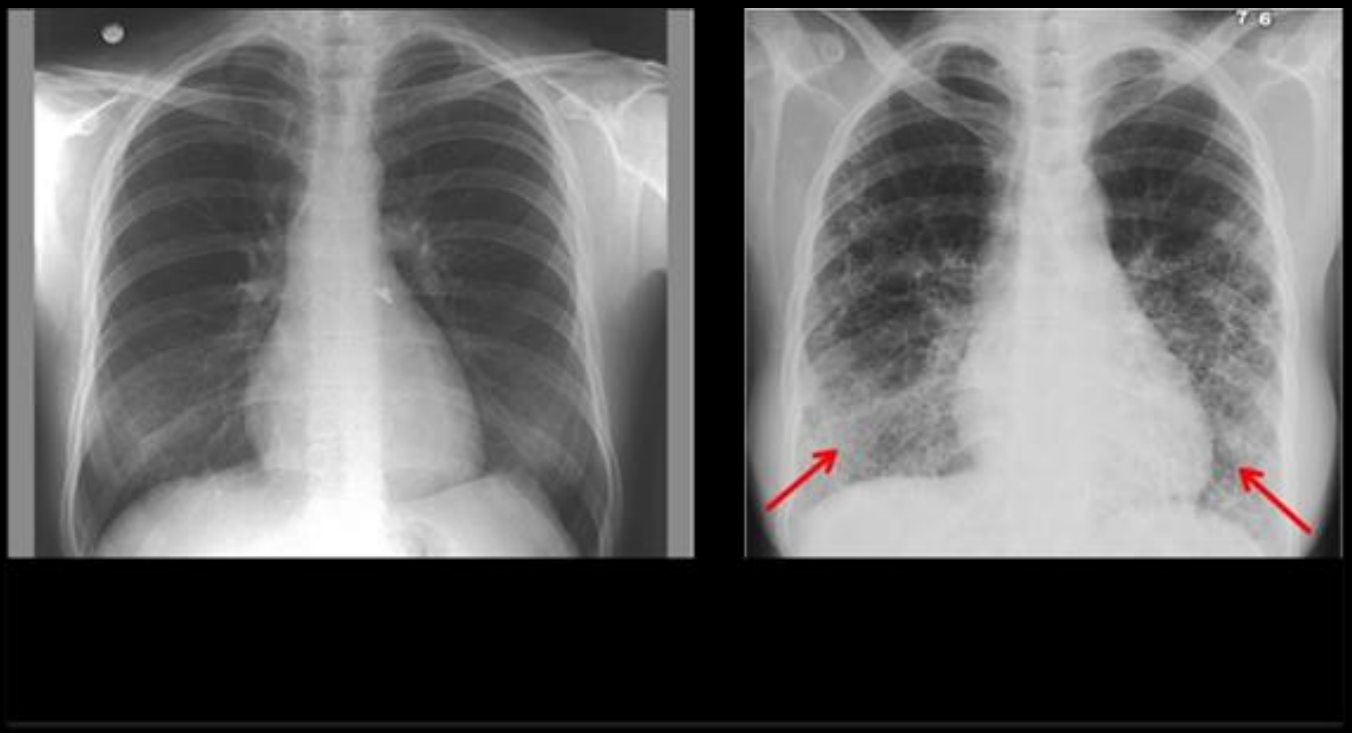
# Ascultation

- Velcro crackles:
  - Present in 63% of ILD patients and 100% of IPF patients
  - Associated with UIP or possible UIP on multivariate analysis

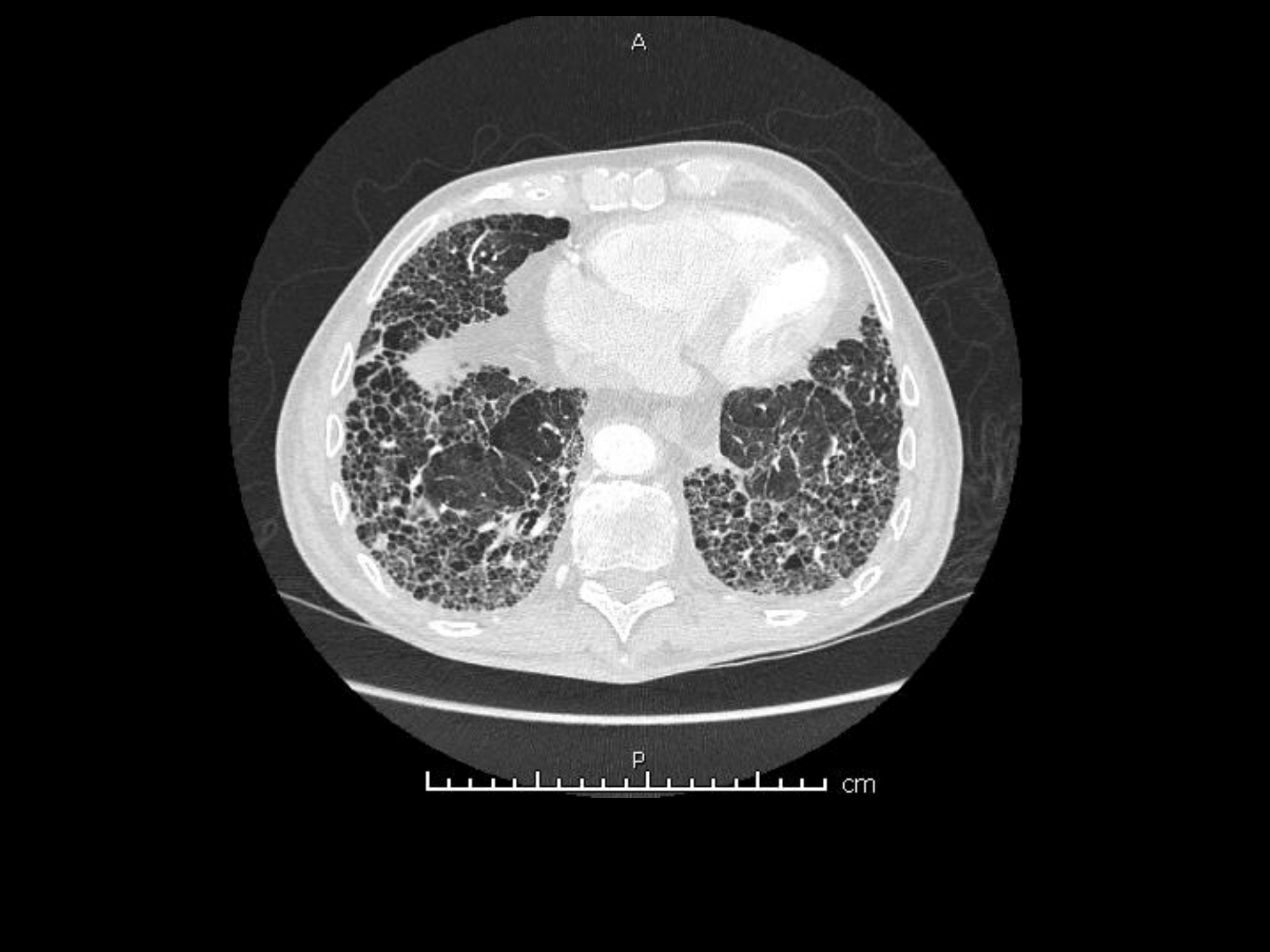

Patient presents with clinical and /or radiological evidence of fibrosisng ILD
Physician assesses exposures, evidence of CTD, physical examination findings
HRCT assessed in consultation with thoracic radiologist
IPF probability not high
Probability of IPF high
Surgical lung biosy
Alternative ILD diagnosis
IPF

Step 3

# •Radiology



Radiography lacks diagnostic accuracy for IPF with a sensitivity of < 50%


A
P
cm

# HRCT findings

**UIP Pattern (all 4 features)**

- Sub pleural, basal predominance
- Reticular abnormality
- Honeycombing with or without traction bronchiectasis
- Absence of

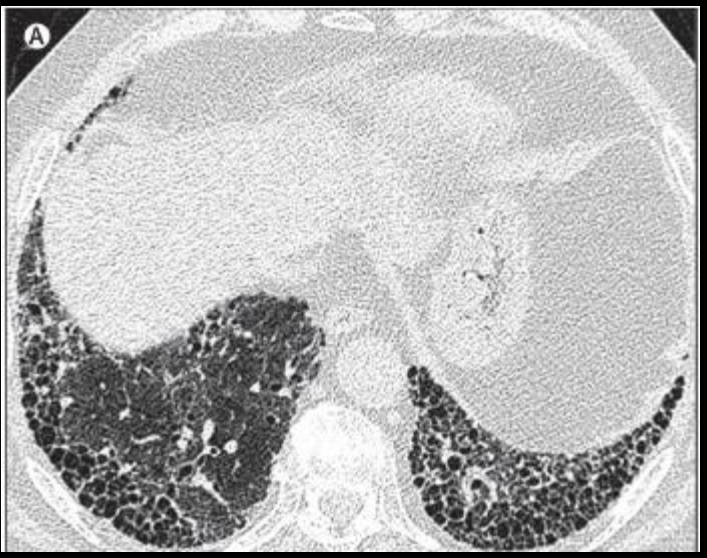
**Possible UIP pattern (all 3)**

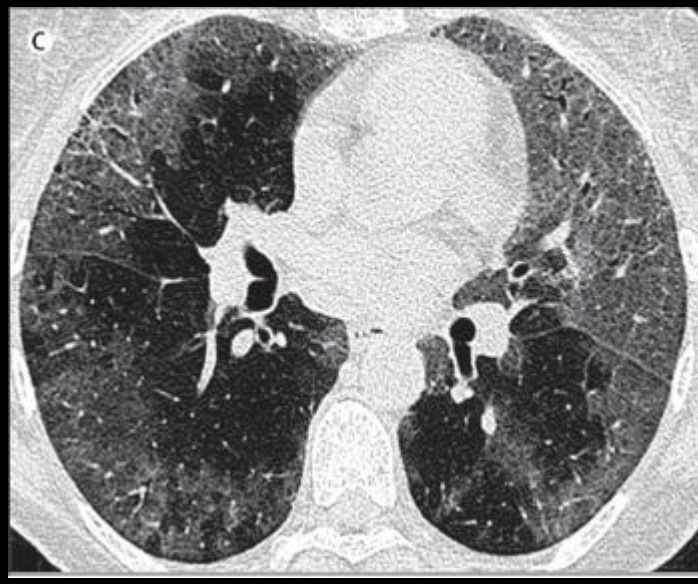
- Sub pleural, basal predominance
- Reticular abnormality
- Absence of

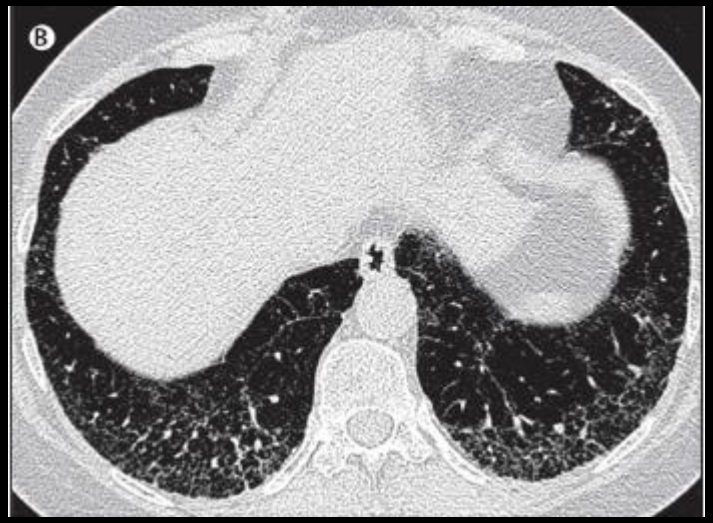
**Absence of**

- Upper or mid-lung predominance
- Peri-bronchovascular predominance
- Extensive ground glass abnormality
- Profuse micro nodules
- Discrete cysts
- Diffuse mosaic attenuation/air trapping
- Consolidation in in bronchopulmonary segments/lobes

# Quiz



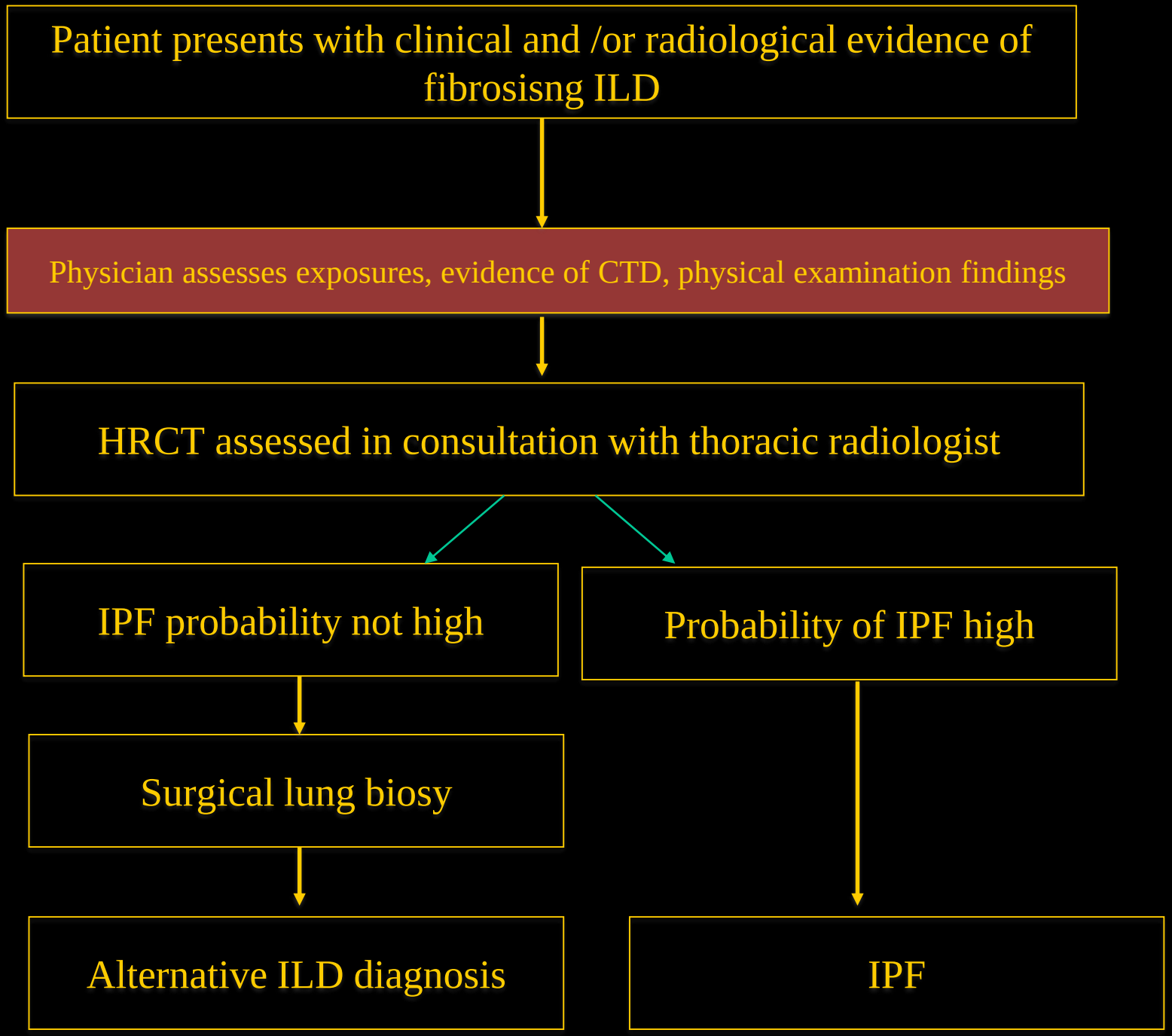



# In the absence of honeycombing

- If patient has a clinical presentation of IPF/suspect IPF but HRCT diagnosis was possible UIP then certain features can aid diagnosis:
  - Presence of reticulation
  - Absence of ground-glass opacification
  - Older age (>50 years)
  - Male sex
  - Traction bronchiectasis score of >4

1. Salisbury ML et al. *Respir Med.* 2016;118:88-95.
2. Brownell R et al. *Thorax.* 2017;72:424-429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IPF probability not high
Probability of IPF high
Surgical lung biosy
Alternative ILD diagnosis
IPF

Step 4

- Pathology

# Who should have a VATS lung biopsy

**Consider lung biopsy in**

- Patients with ILD and HRCT pattern of possible UIP or inconsistent with UIP who
  - Want to establish diagnosis of IPF or evaluate prognosis
  - Are eligible for medical therapy, clinical trial, and/or lung transplantation

**Risk of lung biopsy is too high in patients with**

- Comorbidities
- Age greater than  70-75 years
- Advanced disease
- Severe pulmonary hypertension
- Acute exacerbation or accelerated decline


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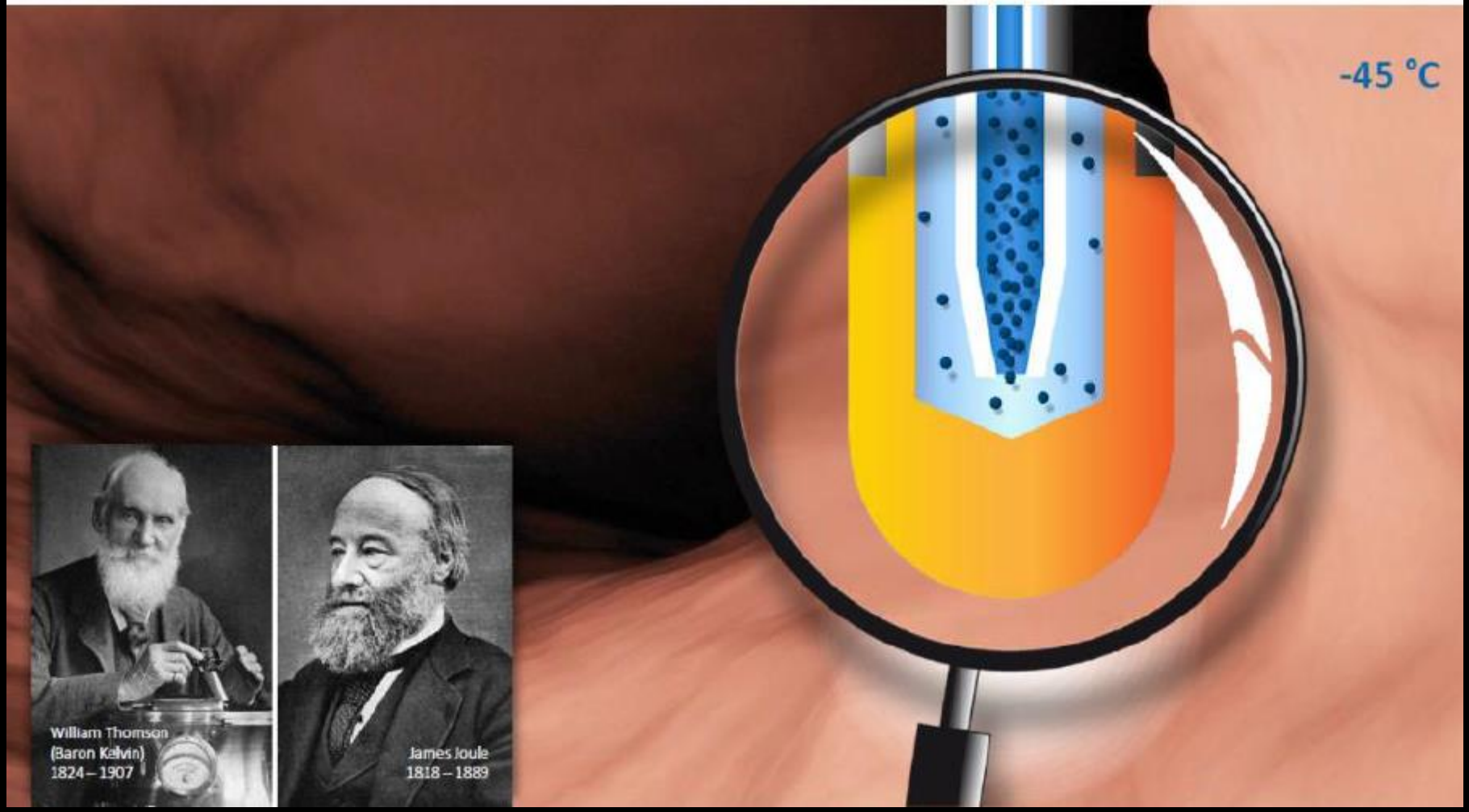
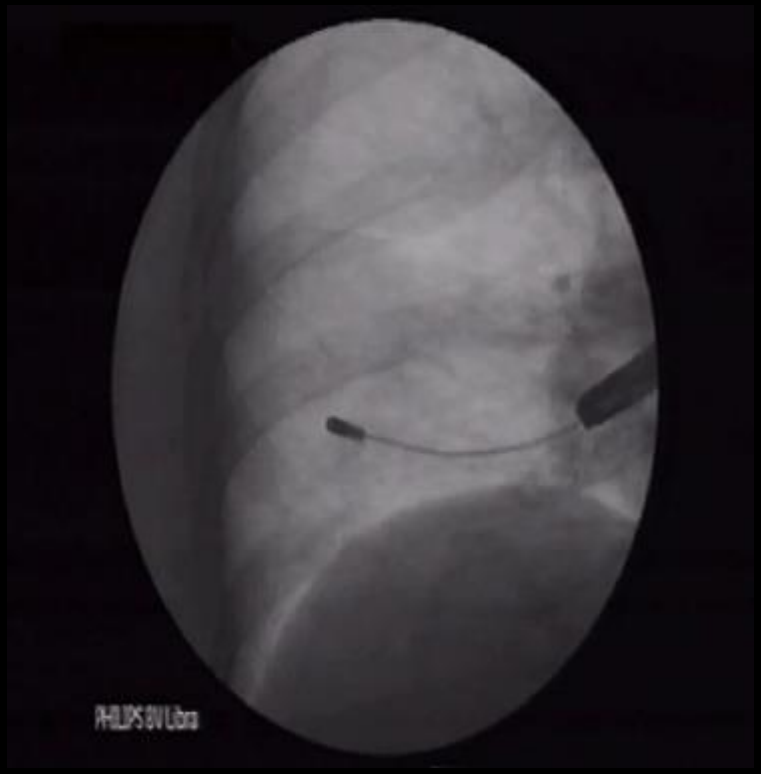
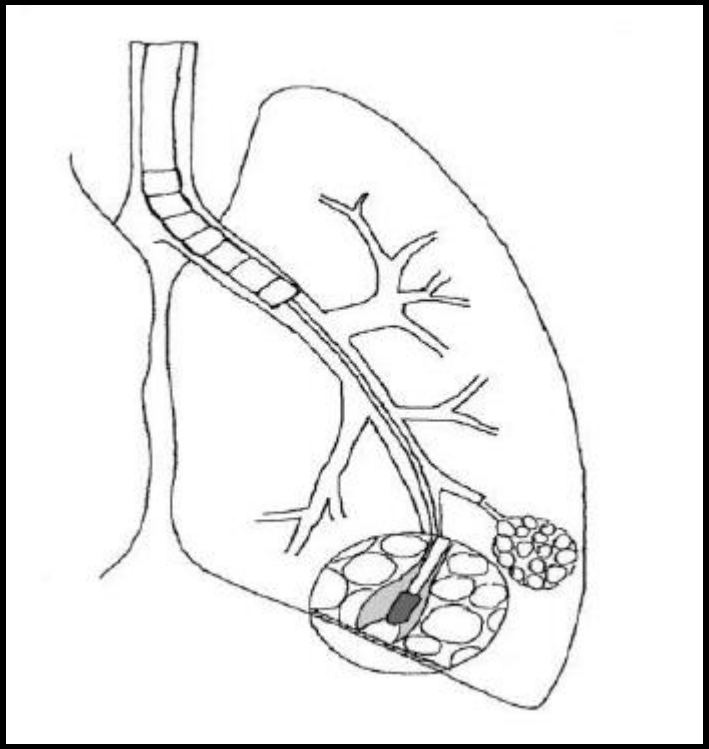
# Joule Thomson Effect

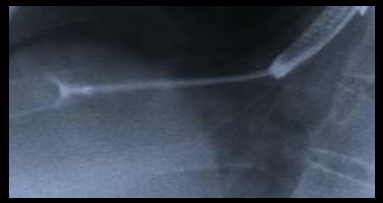


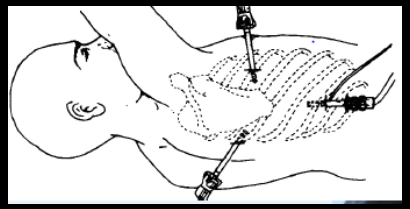

The gas at the tip expands due to the sudden difference in pressure , resulting in a drop in temperature at the tip of the probe

# The technique

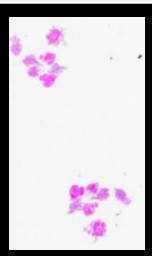


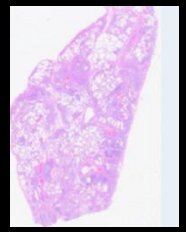


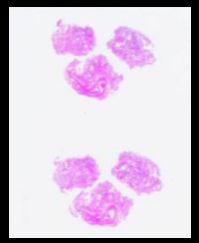




| | Transbronchial | VATS | Cryobiopsy |
|---|---|---|---|
| Sedation | LA/GA | GA | LA/GA |
| Biopsy size (mm) | 2-3 | 30-50 | 5-15 |
| Diagnostic precision | 30-50% | 80-95% | 85% |
| Mortality (%) | <1 | 2.3-4 | 0.1-1.7 |
| Severe Bleeding (%) | 5-10 | <10 | 10-20 |
| Pneumothorax | <10 | 100 | 20-30 |
| Days hospitalization | 1 | 3-6 | 1 |
| Artefact (Constriction/Crush) | + | - | - |

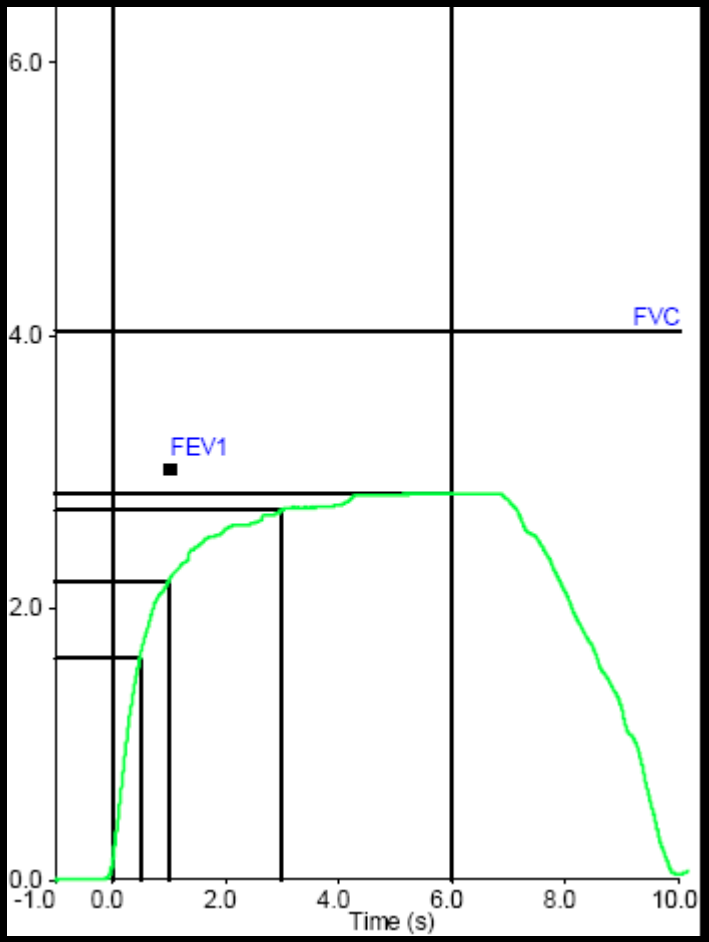







Sharp C, Adamali, H, Medford A. QJM. 2017; 110: 207-214
Dhooria S et al. Respir Care. 2016;61(5):700-12.
Tomassetti S et al. AJRCCM. 2016;193(7):745-52.
Ravaglia C et al. Respiration. 2016;91(3):215-27.
Johannson KA et al

# Quiz

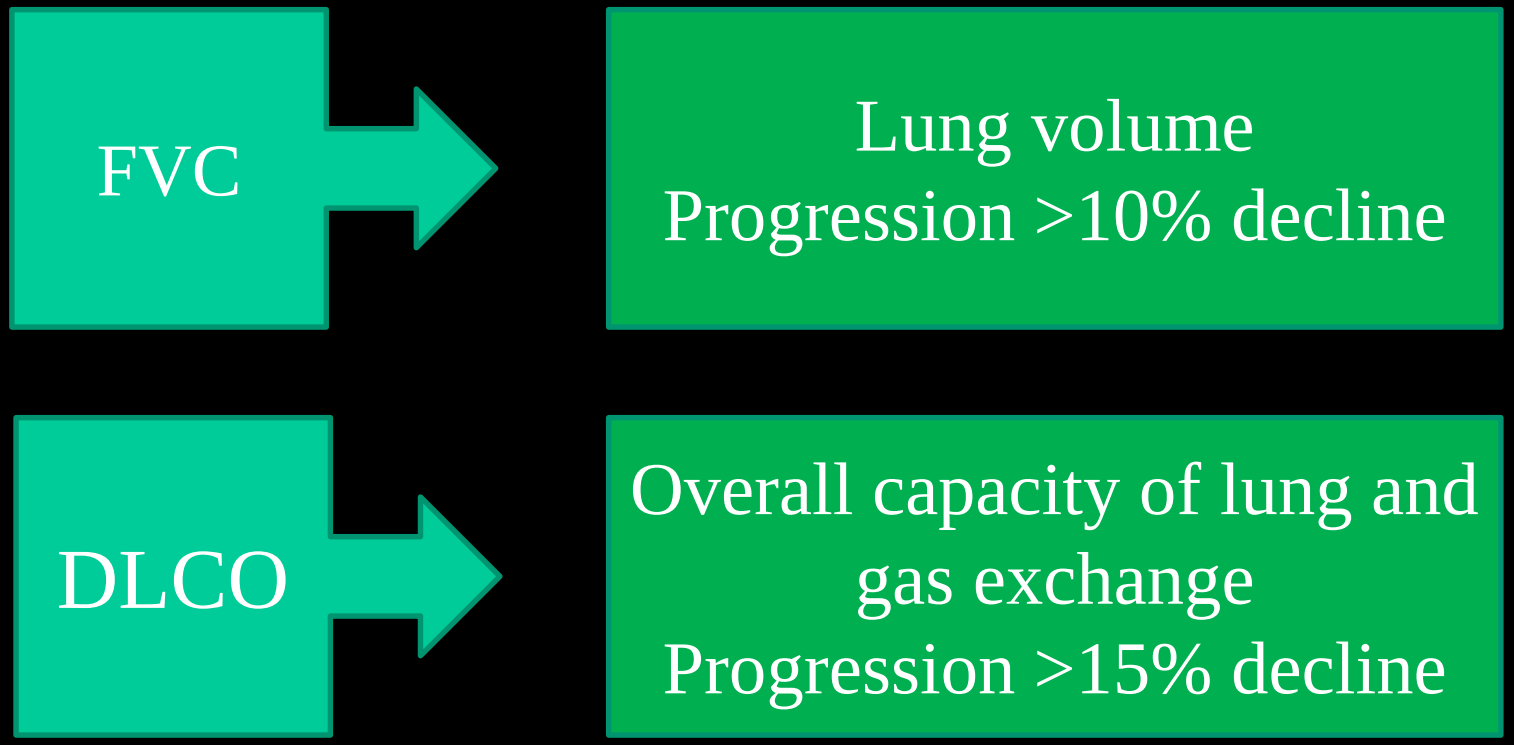



| | Units | Predicted Range | Pre Observed | Pre % Predicted | Pre SR |
|---|---|---|---|---|---|
| FRC | L,btps | 2.83 - 4.80 | 3.01 | 79 < | -1.34 |
| RV | L,btps | 2.15 - 3.50 | 1.56 < | 55 < | -3.08 |
| TLC | L,btps | 6.15 - 8.45 | 4.38 < | 60 < | -4.17 |
| RV/TLC | % | 35 - 53 | 36 | 81 | -1.54 |

## Transfer Factor

| | Units | Predicted Range | Pre Observed | Pre % Predicted | Pre SR |
|---|---|---|---|---|---|
| TLco | mmol/min/kPa,stpd | 6.57 - 11.21 | 2.94 < | 33 < | -4.22 |
| TLcoHb | mmol/min/kPa,stpd | 6.57 - 11.21 | 2.94 < | 33 < | -4.22 |
| VAsb | L,btps | 6.15 - 8.45 | 4.03 < | 55 < | -4.67 |
| KCO | mmol/min/kPa/L,stpd | 0.77 - 1.66 | 0.73 < | 60 < | -1.81 |
| KCOHb | mmol/min/kPa/L,stpd | 0.77 - 1.66 | 0.73 < | 60 < | -1.81 |
| Hgb | g/dl | 13.50 - 17.50 | 14.60 | | |

# Lung function impairment is associated with higher risk mortality




King TE Jr et al. *Am J Respir Crit Care Med.* 2014;189:825-831

# Serological testing

- Occult CTD
- Older patients (>55 years) have circulating evidence of autoimmunity
- 67 IPF vs 21 age matched controls: 1 positive autoantibody
- IPAF

| | |
|---|---|
| **SS-A(Ro-60)** | Negative |
| **SS-B(La)** | Negative |
| **RNP** | Negative |
| **Sm** | Negative |
| **Jo1** | Negative |
| **CCP** | Negative |
| **SCLER70** | Negative |

Nielson et al., BMJ. 2012; 345:e5244.
Lee et al., Respir Med. 2013; 107:249–55

# Diagnosis of chronic HP

High index of suspicion based on a thorough history and evolving data from imaging and pathological findings

- Specific IgG to known antigens,
- Cultures from specimens obtained from the patient's environment
- Bronchoalveolar lavage cellular analyses
- Bronchoprovocation test for a specific or suspected antigen,
- Bronchoalveolar lavage lymphocytosis

Step 5

# • MDT: General and CTD

## Clinical

History
Physical
Laboratory
PFTs
6MWT
Bronchoscopy

## Radiology (PACS)

Chest X-ray
HRCT

## Pathology (Central)

VATS Biopsy
Open lung biopsy

Primary care physicians

ILD Consultants

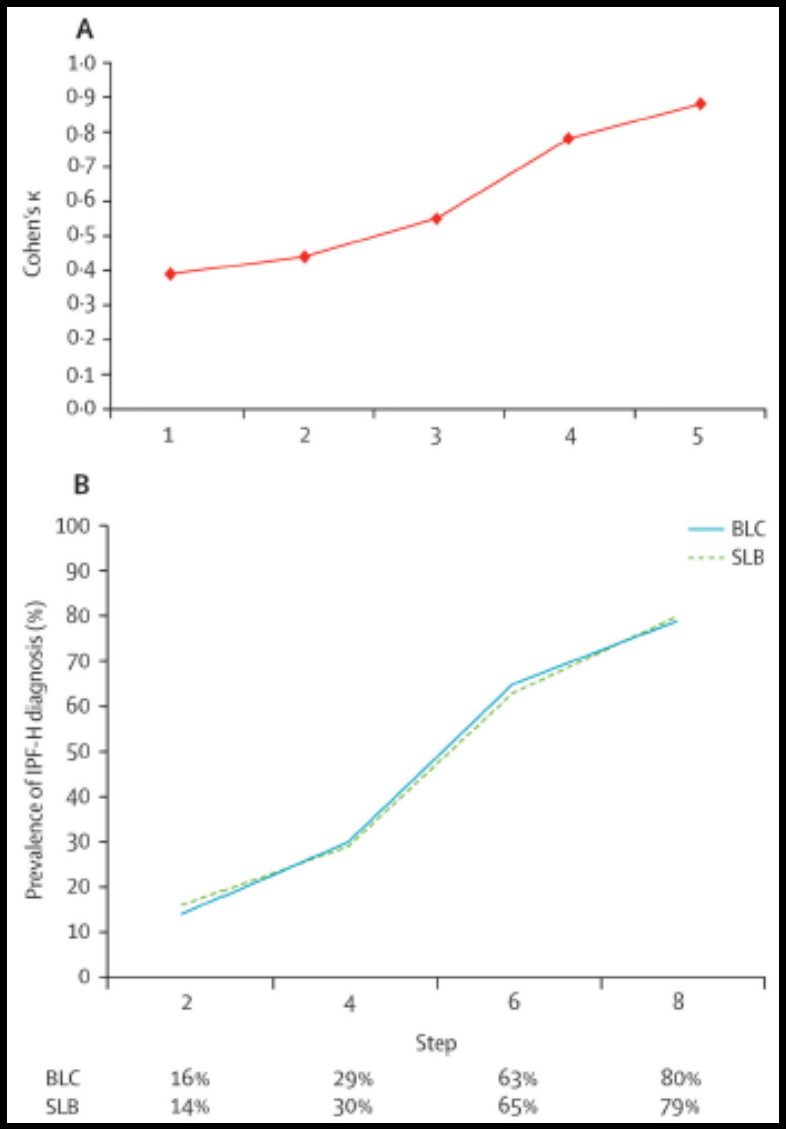
Specialist Nurse/ Pharmacist

Radiologists

Pathologist

BILD MDT

South West Regional ILD Network




**Step 1**: individual assessment of high-resolution CT data alone.
**Step 2**: individual assessment of high-resolution CT plus clinical data.
**Step 3**: group discussion of high-resolution CT plus clinical data.
**Step 4:** group discussion of high-resolution CT, clinical, and surgical lung biopsy data.
**Step 5:** consensus diagnosis among all participants.

Step 2: addition of clinical and radiological data.
Step 4: addition of bronchoalveolar lavage data.
Step 6: addition of biopsy data.
Step 8: addition of follow-up data

Lancet Respir Med. 2017 January ; 5(1): 61–71.
Am J Respir Crit Care Med. 2004; 170:904–10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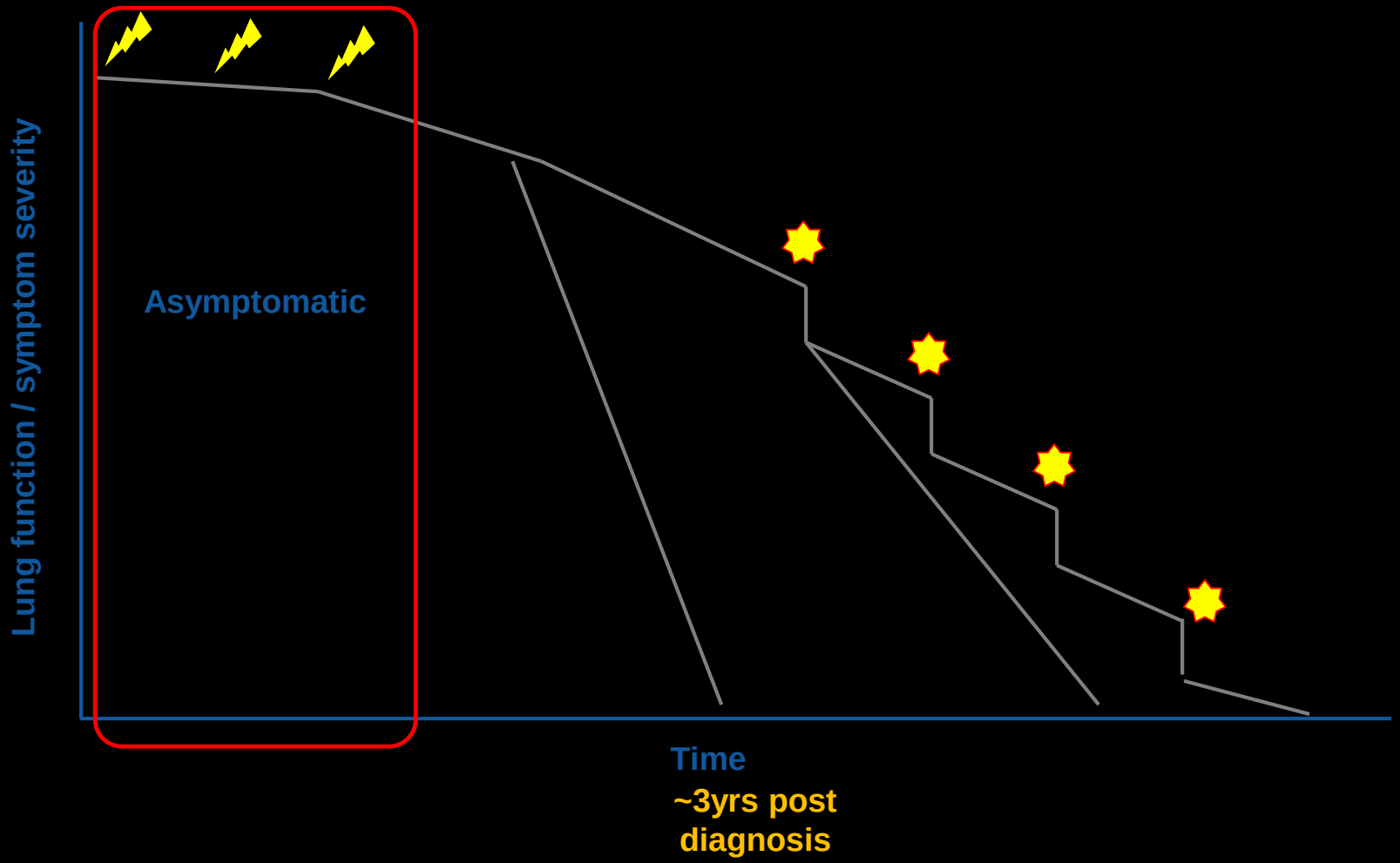
# Future Prognostic Biomarkers

Biomarkers: able to prognosticate if patient are going to remain stable or progress or if the patient on a particular type of treatment are going to respond:

- Radiographic predictors: HRCT-ground glass opacities, consolidation, reticulation, reticulation and honeycombing
- Physiological predictors: FVC, TLco, DLco, Exercise testing
- Blood markers: BNP, albumin levels, KL6, surfactant proteins, CCl-18, CCL-2, CCL-17, CCL-22, fibrocytes, BAL (neutrophil percentage)

# IPF – natural history

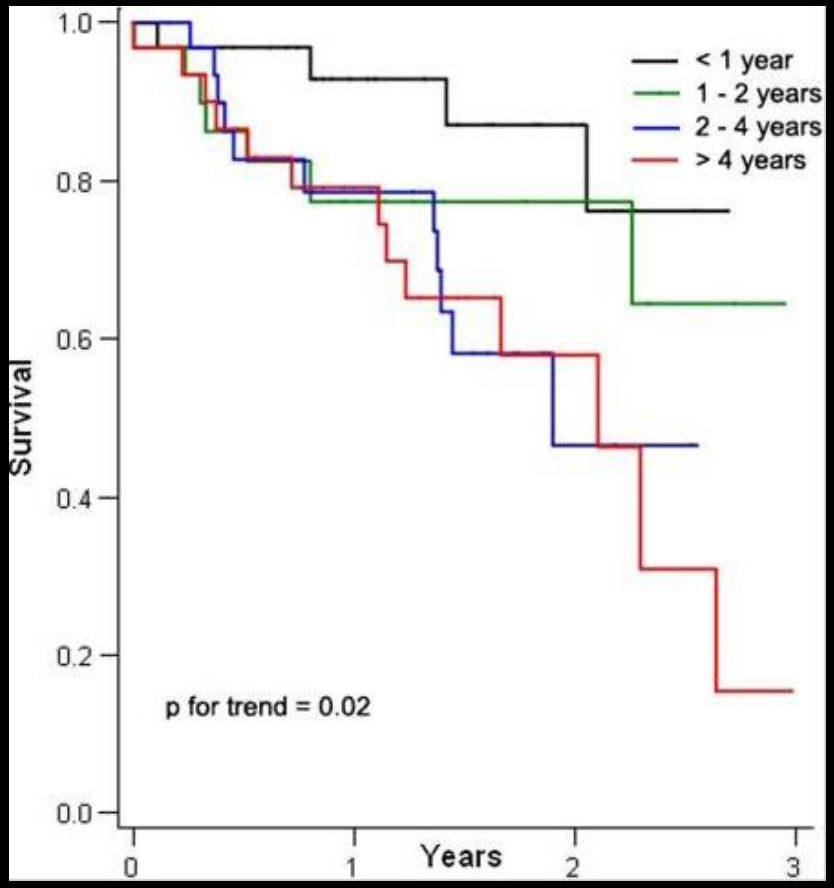


# Quiz

Acute exacerbation carry a mortality of _____ % 1 month mortality

1. 10%
2. 30%
3. 50%
4. 70%

# Delayed Diagnosis to Tertiary Centres leads to worse outcome




Lamas DJ et al. *Am J Respir Crit Care Med.* 2011;184:842-847.

# Quiz

For each year the diagnosis of IPF is delayed, lung function is decreased by:

1. 10%
2. 20%
3. 50%
4. 70%

Step 6

# •Treatments

- Referral to an ILD centre
- Secure early accurate diagnosis
- Engage, Educate, Empower
- Prescribe effective treatments to slow progression of disease
- Consider ongoing clinical trials for potential new therapies
- List for lung transplantation
- Participate in support group

The NEW ENGLAND JOURNAL of MEDICINE

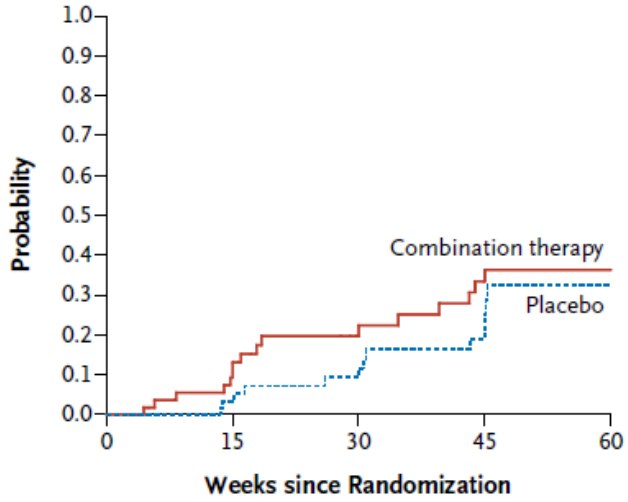
ORIGINAL ARTICLE

# Prednisone, Azathioprine, and N-Acetylcysteine for Pulmonary Fibrosis

The Idiopathic Pulmonary Fibrosis Clinical Research Network*

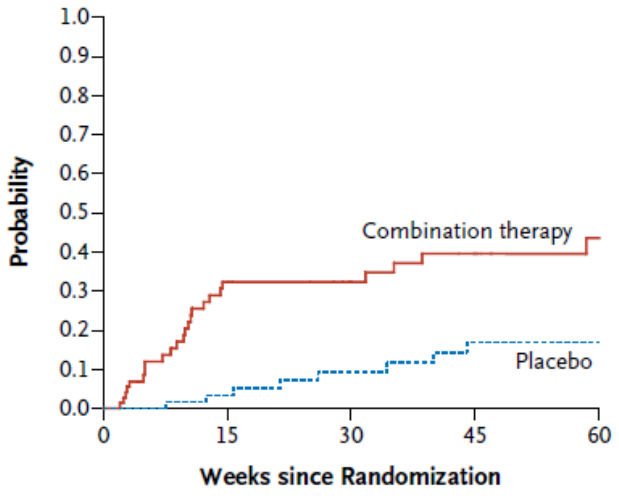
ABSTRACT

**B** Time to Death or Disease Progression




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Combination therapy | 77 | 46 | 29 | 22 | 12 |
| Placebo | 78 | 55 | 39 | 24 | 11 |

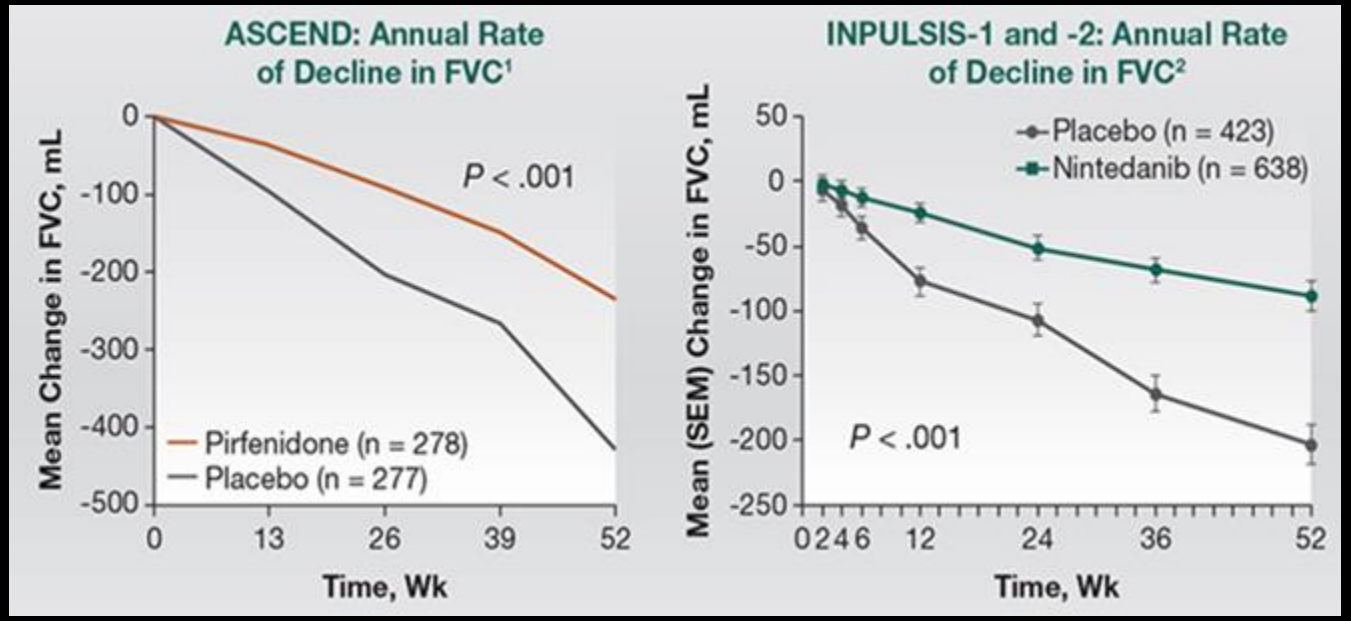
**C** Time to Death or Hospitalization




| No. at Risk | | | | | |
|---|---|---|---|---|---|
| Combination therapy | 77 | 40 | 29 | 23 | 10 |
| Placebo | 78 | 55 | 42 | 26 | 16 |

*N Engl J Med* 2012;366:1968-1977

# Pirfenidone vs Nintedanib




King TE et al; ASCEND Study Group. *N Engl J Med.* 2014;370:2083-2092
Richeldi L et al; INPULSIS Trial Investigators. *N Engl J Med.* 2014;370:2071-2082.

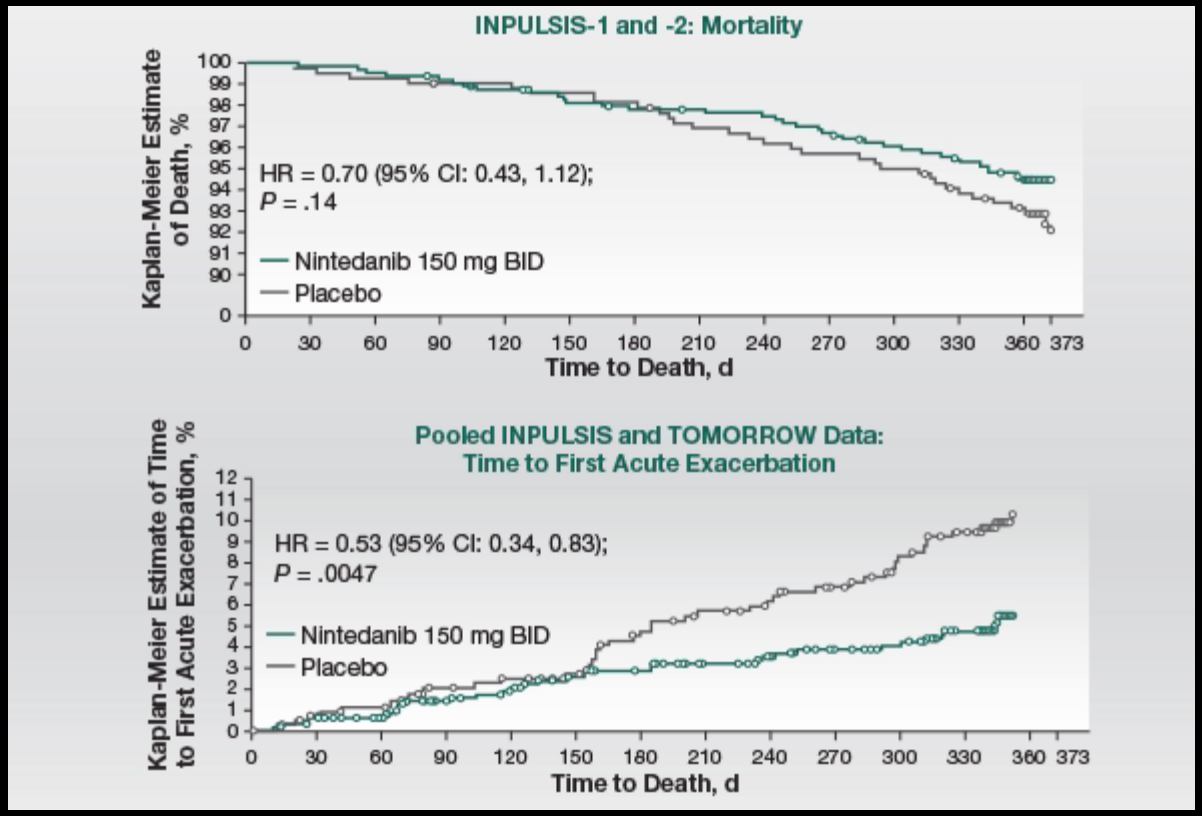
# Pirfenidone and Mortality

- Week 52, the relative risk of death for all four mortality outcomes was significantly lower in the pirfenidone group than in the placebo group in the pooled population
  - all-cause mortality hazard ratio [HR] 0·52 [95% CI 0·31-0·87; p=0·0107]
  - treatment-emergent all-cause mortality 0·45 [0·24-0·83; 0·0094]
  - idiopathic-pulmonary-fibrosis-related mortality 0·35 [0·17-0·72; 0·0029]
  - treatment-emergent idiopathic-pulmonary-fibrosis-related mortality 0·32 [0·14-0·76; 0·0061]).

- Over 120 weeks significant differences in the pooled analysis favoring pirfenidone therapy compared with placebo
  - treatment-emergent all-cause mortality (p=0·0420)
  - idiopathic-pulmonary-fibrosis-related mortality (0·0237),
  - treatment-emergent idiopathic-pulmonary-fibrosis-related (0·0132) mortality

Lancet Respir Med. 2017 Jan;5(1):33-41

# Nintedanib and Mortality




Richeldi L et al; INPULSIS Trial Investigators. *N Engl J Med.* 2014;370:2071-2082

Quiz: Based on ASCEND AND INPULSIS, the reduction in lung function would be?

1. Same as placebo
2. 25% less than placebo
3. 50% less than placebo
4. 75% less than placebo

# Comparison of Treatments

**Pirfenidone**

- 9 pills

- Nausea
- Rash
- Diarrhoea
- Fatigue
- Dyspepsia
- Anorexia
- Headache
- Photosensitivity

**Nintedanib**

- 2 pills

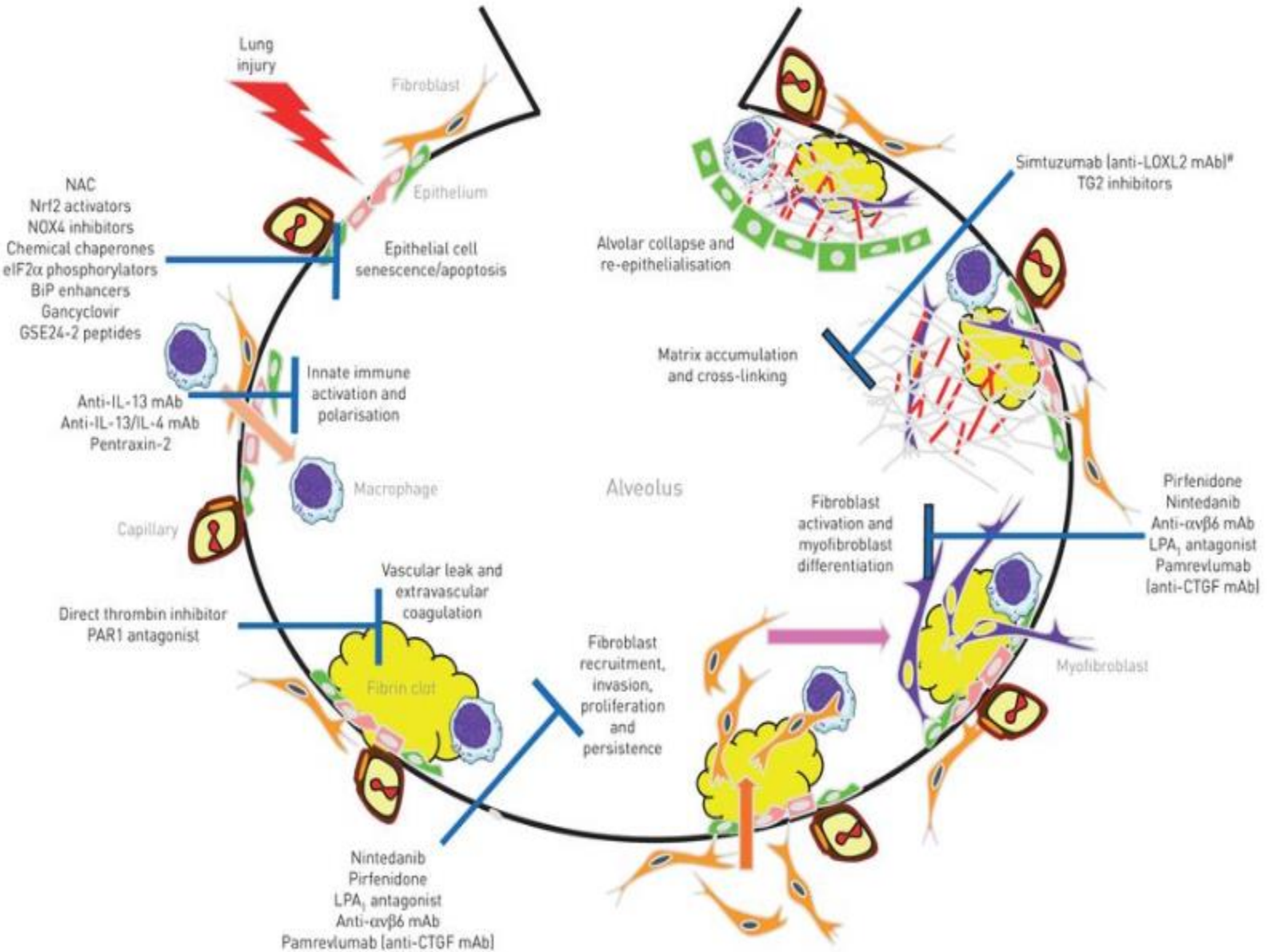
- Diarrhoea
- Nausea and vomiting
- Abdominal pain
- Decreased appetite
- Weight decreased
- Hepatic enzymes increase


40 MISSIONS LAUNCHED...
BUT ONLY 18 SUCCESSFUL

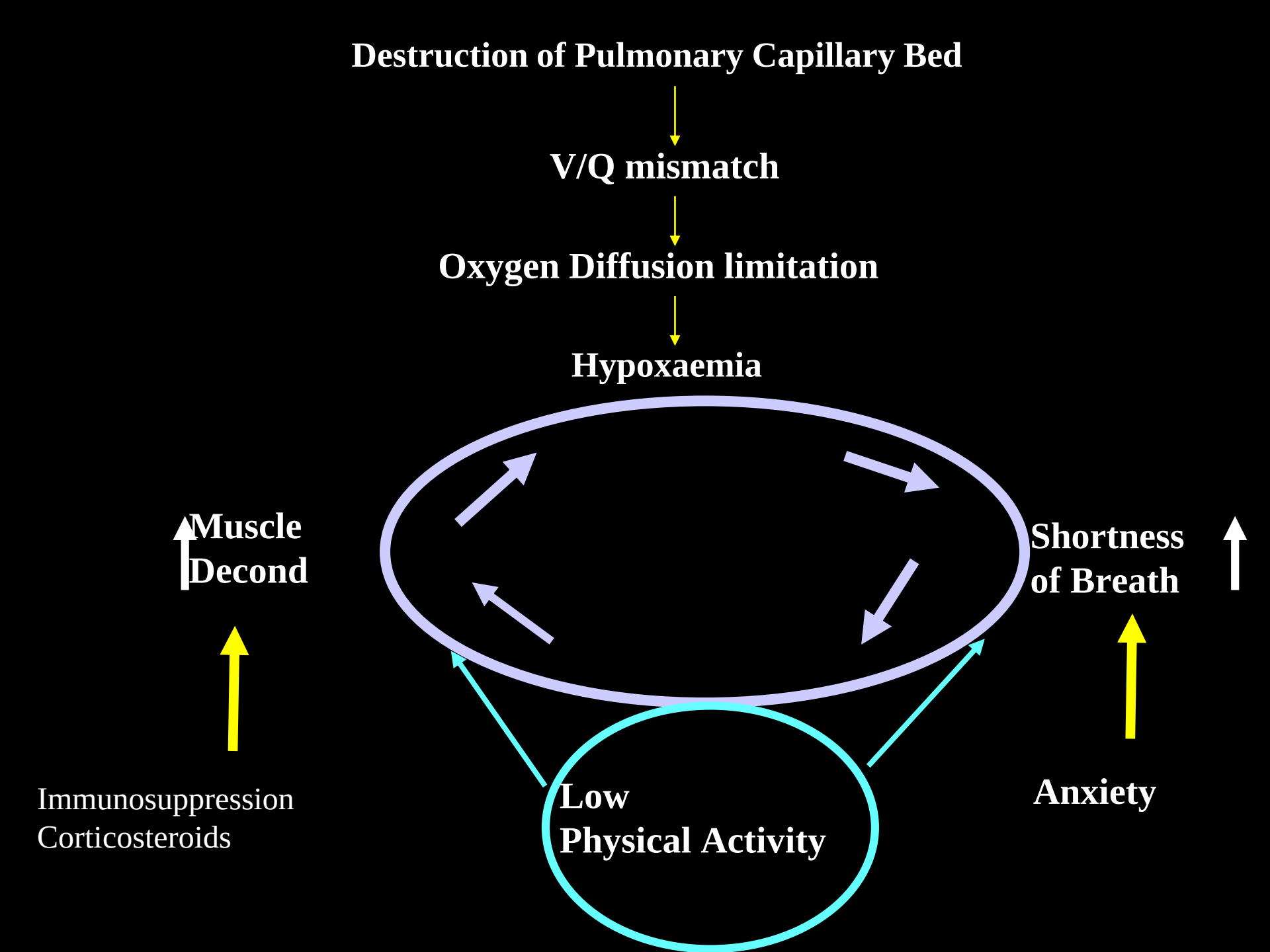
| | | |
|---|---|---|
| **New and revised recommendations** | | |
| Anticoagulation (warfarin) | Strong recommendation against use‖ | Conditional recommendation against use‡ |
| Combination prednisone+azathioprine+*N*-acetylcysteine | Strong recommendation against use¶ | Conditional recommendation against use |
| Selective endothelin receptor antagonist (ambrisentan) | Strong recommendation against use¶ | Not addressed |
| Imatinib, a tyrosine kinase inhibitor with one target | Strong recommendation against use‖ | Not addressed |
| Nintedanib, a tyrosine kinase inhibitor with multiple targets | Conditional recommendation for use‖ | Not addressed |
| Pirfenidone | Conditional recommendation for use‖ | Conditional recommendation against use¶ |
| Dual endothelin receptor antagonists (macitentan, bosentan) | Conditional recommendation against use¶ | Strong recommendation against use‖ |
| Phosphodiesterase-5 inhibitor (sildenafil) | Conditional recommendation against use‖ | Not addressed |
| **Unchanged recommendations** | | |
| Antiacid therapy | Conditional recommendation for use‡ | Conditional recommendation for use‡ |
| *N*-acetylcysteine monotherapy | Conditional recommendation against use¶ | Conditional recommendation against use¶ |
| Antipulmonary hypertension therapy for idiopathic pulmonary fibrosis-associated pulmonary hypertension | Reassessment of the previous recommendation was deferred | Conditional recommendation against use‡ |
| Lung transplantation: single *versus* bilateral lung transplantation | Formulation of a recommendation for single *versus* bilateral lung transplantation was deferred | Not addressed |

# New direction

- *S*tall disease progression and reverse the disease process before the pulmonary parenchyma progresses to irreversible honeycombing.


Lung injury
Fibroblast
Epithelium
NAC
Nrf2 activators
NOX4 inhibitors
Chemical chaperones
eIF2α phosphorylators
BiP enhancers
Gancyclovir
GSE24-2 peptides
Epithelial cell senescence/apoptosis
Innate immune activation and polarisation
Anti-IL-13 mAb
Anti-IL-13/IL-4 mAb
Pentraxin-2
Macrophage
Capillary
Alveolus
Vascular leak and extravascular coagulation
Direct thrombin inhibitor
PAR1 antagonist
Fibrin clot
Fibroblast recruitment, invasion, proliferation and persistence
Nintedanib
Pirfenidone
LPA1 antagonist
Anti-αvβ6 mAb
Pamrevlumab (anti-CTGF mAb)
Alvolar collapse and re-epithelialisation
Simtuzumab (anti-LOXL2 mAb)#
TG2 inhibitors
Matrix accumulation and cross-linking
Fibroblast activation and myofibroblast differentiation
Pirfenidone
Nintedanib
Anti-αvβ6 mAb
LPA1 antagonist
Pamrevlumab (anti-CTGF mAb)
Myofibroblast

What about pulmonary rehab?

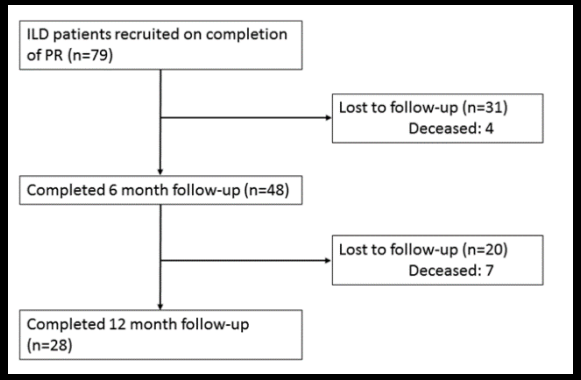

Destruction of Pulmonary Capillary Bed
V/Q mismatch
Oxygen Diffusion limitation
Hypoxaemia
Muscle Decond
Shortness of Breath
Immunosuppression
Corticosteroids
Low Physical Activity
Anxiety

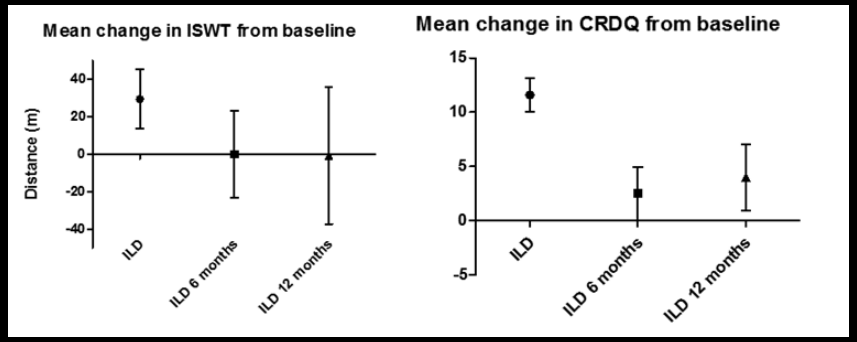
| | Disease type | Study design | Number of patients | Duration | Change in 6MWT distance | Outcomes |
|---|---|---|---|---|---|---|
| Vainshelboim et al (2014)[112] | IPF | RCT | 32 | 12 weeks | 81 m* | Improved dyspnoea and QOL |
| Jastrzebski et al (2006)[113] | ILD (67·7% IPF) | Prospective | 31 | 6 weeks | Not reported | Improved QOL and dyspnoea |
| Nishiyama et al (2008)[114] | IPF | RCT | 28 | 10 weeks | 46·3 m* | Improved QOL |
| Holland et al (2008)[115] | ILD (59·6% IPF) | RCT | 57 | 8 weeks | 35 m* | Improved exercise capacity and symptoms |
| Ferreira et al (2009)[116] | ILD (around 50% IPF) | Retrospective | 99 | 6–8 weeks | 56 m* | Improved dyspnoea |
| Ozalevli et al (2010)[117] | IPF | Prospective | 17 | 12 weeks | 45 m* | Improved QOL; home based |
| Rammaert et al (2011)[118] | IPF | Prospective | 17 | 8 weeks | No change | Improved dyspnoea and endurance; home based |
| Kozu et al (2011)[119] | IPF | Prospective | 65 | 8 weeks | Variable | Improved 6MWT and decreased hospital admissions if MRC dyspnoea 2 or 3 |
| Kozu et al (2011)[120] | IPF (50%) and COPD (50%) | Prospective | 90 | 8 weeks | 16·2 m* | Improved dyspnoea; benefits not maintained at 6 months |
| Swigris et al (2011)[121] | IPF | Prospective | 21 | 6 weeks | 61·6 m* | Improved fatigue |
| Huppmann et al (2013)[122] | ILD (50% IPF) | Observational | 402 | 4 weeks | 46 m* | Improved QOL |
| Jackson et al (2014)[123] | IPF | RCT | 21 | 3 months | No change | Increase in exercise time |

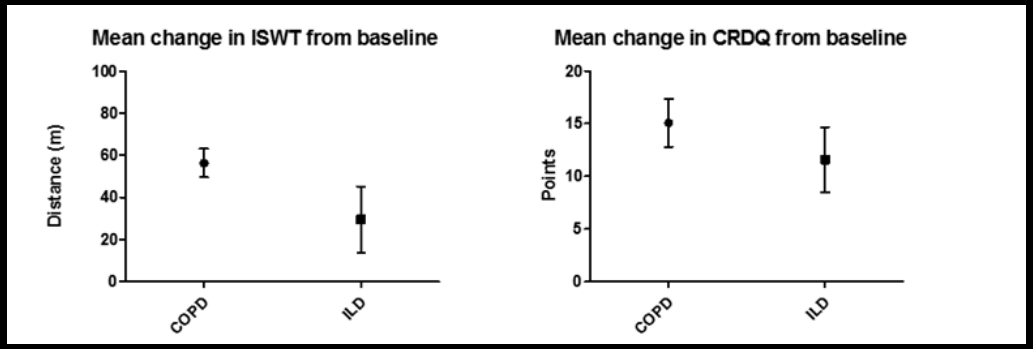
# Duration of benefit following completion of pulmonary rehabilitation in interstitial lung disease—an observational study

C. Sharp, M. McCabe, M.J. Hussain, J.W. Dodd, H. Lamb, H. Adamali, A.B Millar, D. Smith

DOI: http://dx.doi.org/10.1093/qjmed/hcw105 hcw105 First published online: 10 July 2016



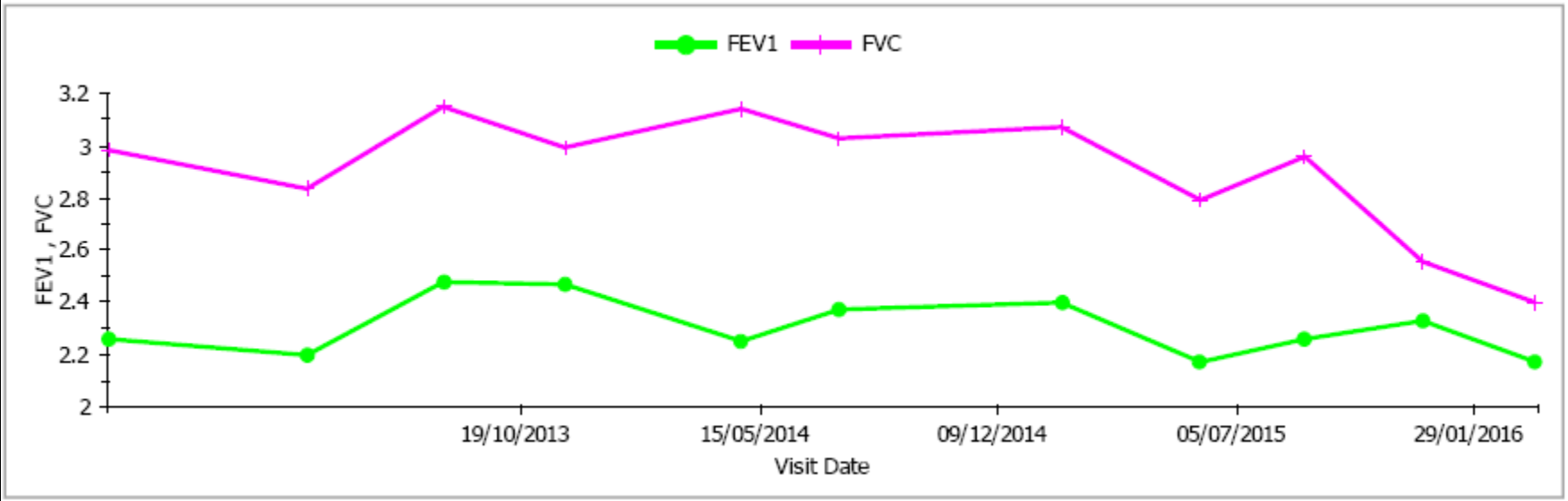




Standard PR gives initial benefits in participants with ILD who complete the course, however these are not sustained. Tailored approaches to this group would be appreciated by this group and should be explored.

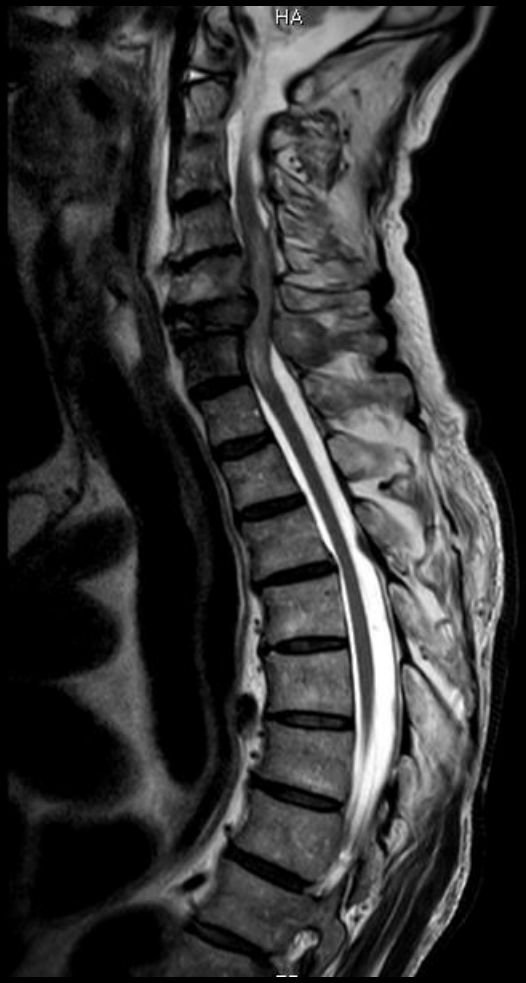
What about oxygen therapy?

- Cochrane Review (2016)
  - no evidence to support or refute the use of ambulatory or short burst oxygen in ILD due to the limited number of limited studies and data
- AMBOX study (2017)
  - Ambulatory oxygen was associated with significant improved health status (>50% IPF patients)

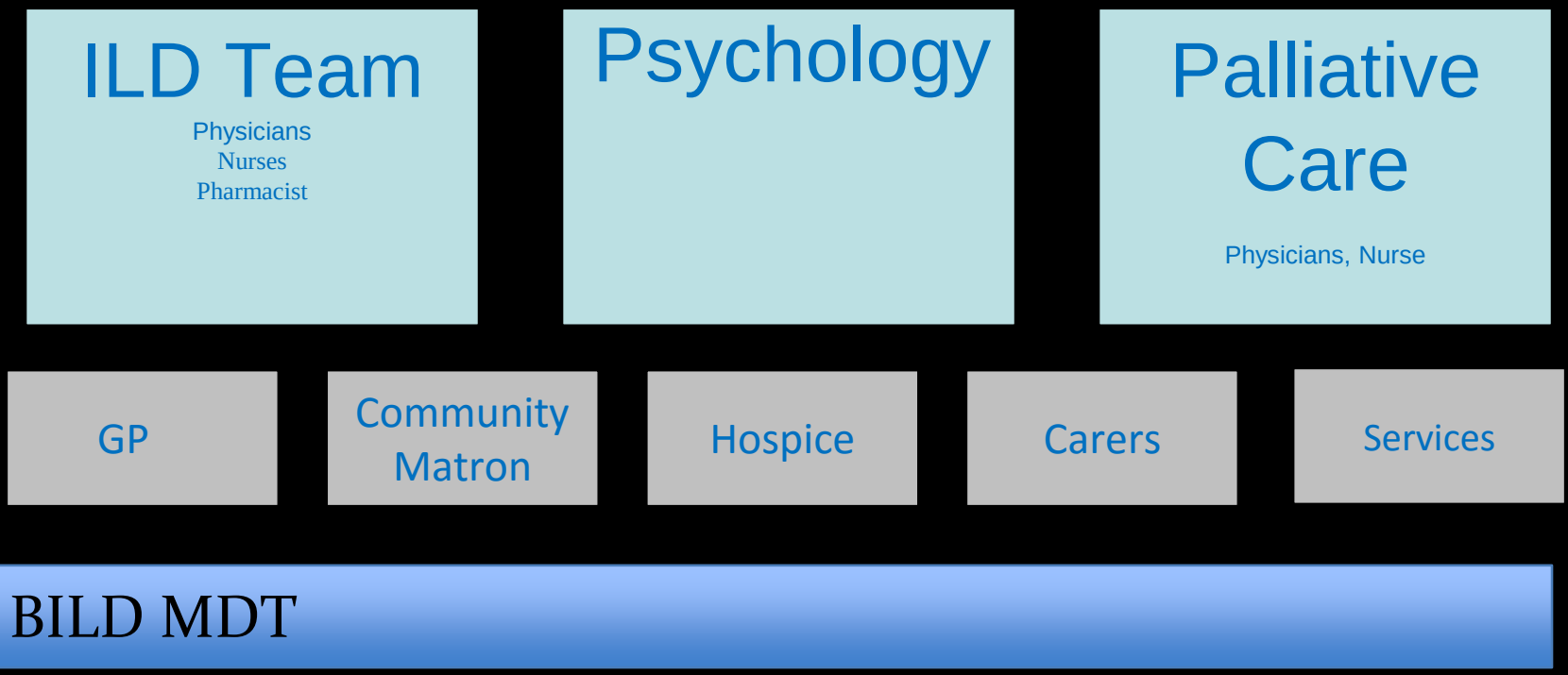
# Our patient


FEV1
FVC
3.2
3
2.8
2.6
2.4
2.2
2
FEV1, FVC
19/10/2013
15/05/2014
09/12/2014
05/07/2015
29/01/2016
Visit Date

# May 2016



# Palliative/Pyschology/ILD MDT



# Development of tools to facilitate palliative and supportive care referral for patients with idiopathic pulmonary fibrosis

Decisions related to end of life and supportive care are poorly documented in IPF, even in those with advanced disease in the period immediately before their death.

Explore the proportion of IPF patients with documented decisions around supportive and end of life care

Assess the impact of a supportive care decision aid tool for clinicians managing

Sharp C, Lamb H, Jordan N, et al BMJ Supportive & Palliative Care Published Online First: 30 June 2017. doi: 10.1136/bmjspcare-2017-001330

Underlying Respiratory Diagnosis: Choose an item.

Following review in the interstitial lung disease clinic today, this screening tool was used to assess possible supportive care needs for this patient. Please find below the assessment and the outcomes enacted.

Identified features demonstrate worsening ILD in the absence of any reversible causes such as infection, and should guide the assessor towards recognising the patient has advanced disease.

**Significant change in functional status:**

- Requiring increasing assistance for personal needs ☐No ☐Yes
- Decrease in exercise tolerance ☐No ☐Yes
- Confined to chair for more than 50% of the waking day ☐No ☐Yes

**Significant respiratory factors:**

- Referral for transplant assessment ☐No ☐Yes
- Acute exacerbation managed at home/hospital in past 3/12 ☐No ☐Yes
- New LTOT requirement ☐No ☐Yes
- TLCO < 40% ☐No ☐Yes
- 6MWD <207m[1] or So2 nadir <85% ☐No ☐Yes
- FVC decline ≥ 10% ☐No ☐Yes
- TLCO decline ≥ 15% ☐No ☐Yes
- BNP >300 or severe pulmonary hypertension on echocardiogram[2] ☐No ☐Yes

Discuss outcome of screening with patient: ☐Yes ☐No

Outcome: Request patient details entered onto GP supportive care register ☐Yes ☐No

Refer for FAB course: ☐Yes ☐No

Refer for community matron input: ☐Yes ☐No

Refer to St Peters hospice community team: ☐Yes ☐No

DNAR completed: ☐Yes ☐No

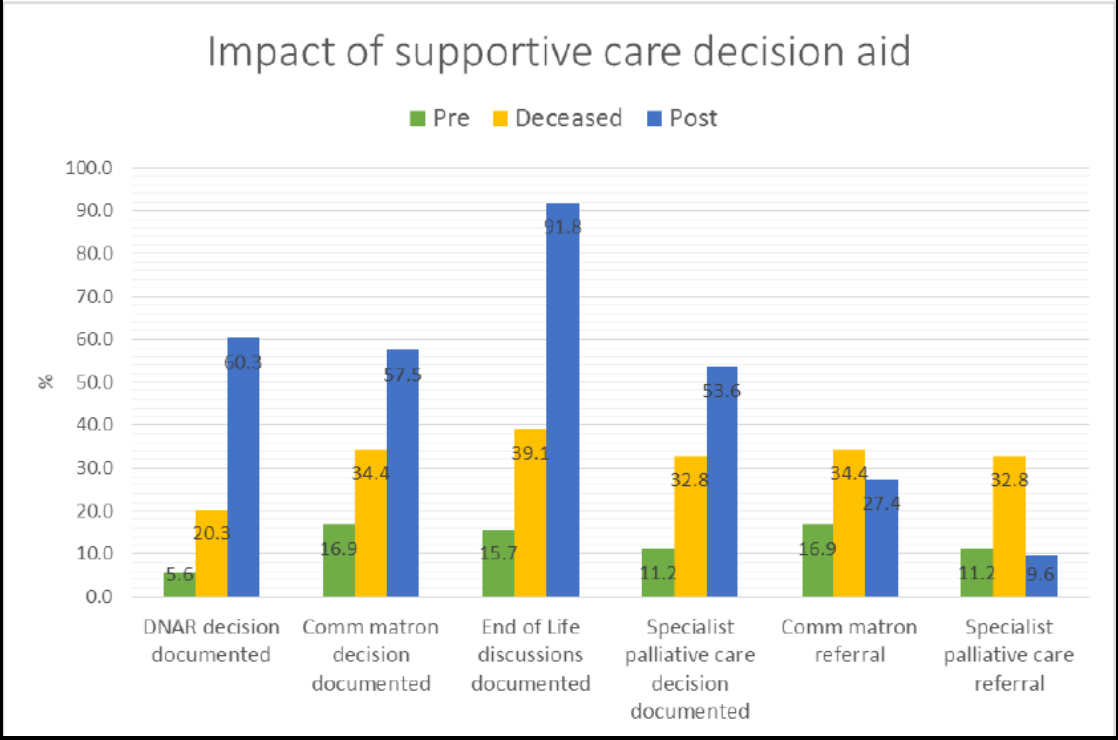
Copy of DNAR to patient ☐ GP ☐ faxed to GWAS ☐

**Table 1 – Demographic and physiological parameters for the three cohorts of patients**

| | Before | n=89 | Deceased | n=64 | After | n=73 | Significance |
|---|---|---|---|---|---|---|---|
| | Mean | SD | Mean | SD | Mean | SD | |
| Age | 75.0 | 7.7 | 75.4 | 10.0 | 74.0 | 7.7 | NS |
| FVC (%) | 79.2 | 20.8 | 68.5 | 19.2 | 81.9 | 19.6 | <0.001 |
| DLCO (%) | 48.5 | 15.6 | 35.8 | 15.5 | 47.4 | 15.5 | <0.001 |
| 6MWD (m) | 298.3 | 95.4 | 217.6 | 102.2 | 308.9 | 98.6 | <0.001 |
| CPI score | 45.0 | 13.5 | 56.4 | 12.9 | 45.6 | 13.3 | <0.001 |

**Table 2 – Characteristics of the three cohorts.**

| | Pre N=89 | Deceased N=64 | After N=73 | |
|---|---|---|---|---|
| | % | % | % | |
| Male | 80.9 | 82.8 | 78.1 | NS |
| FVC <50% | 3.4 | 12.5 | 4.2 | NS |
| DLCO <35% (or unable) | 28.1 | 32.8 | 22.5 | NS |
| FVC fall | 14.8 | 16.0 | 4.9 | NS |
| DLCO fall | 5.5 | 12.5 | 0.0 | 0.005 |
| Desaturation | 78.8 | 74.0 | 67.2 | NS |
| PH | 14.6 | 32.8 | 19.2 | NS |
| LTOT | 37.1 | 45.3 | 20.5 | 0.002 |
| Admission <6months | 10.1 | 6.3 | 6.8 | NS |
| Mortality | 5.6 | 100.0 | 4.1 | N/A |
| GAP stage I | 68.5 | 45.3 | 84.5 | <0.001 |
| Out of area referrals | 23.6 | 23.4 | 24.7 | NS |

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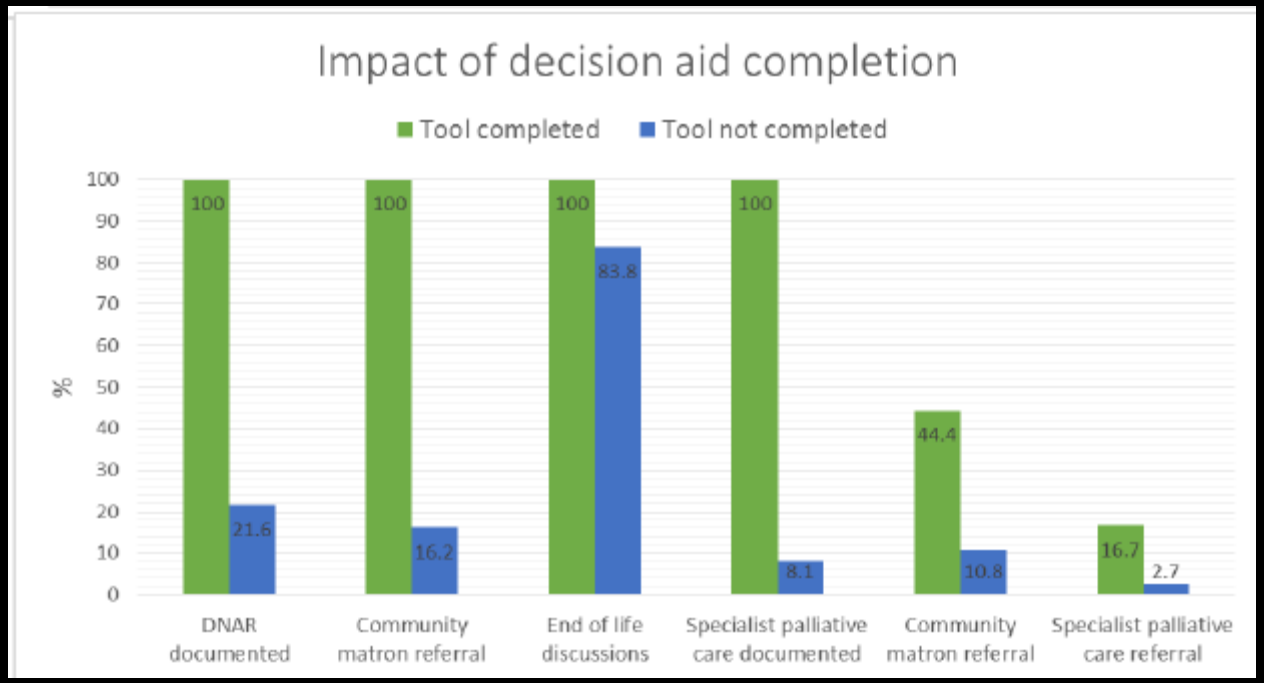


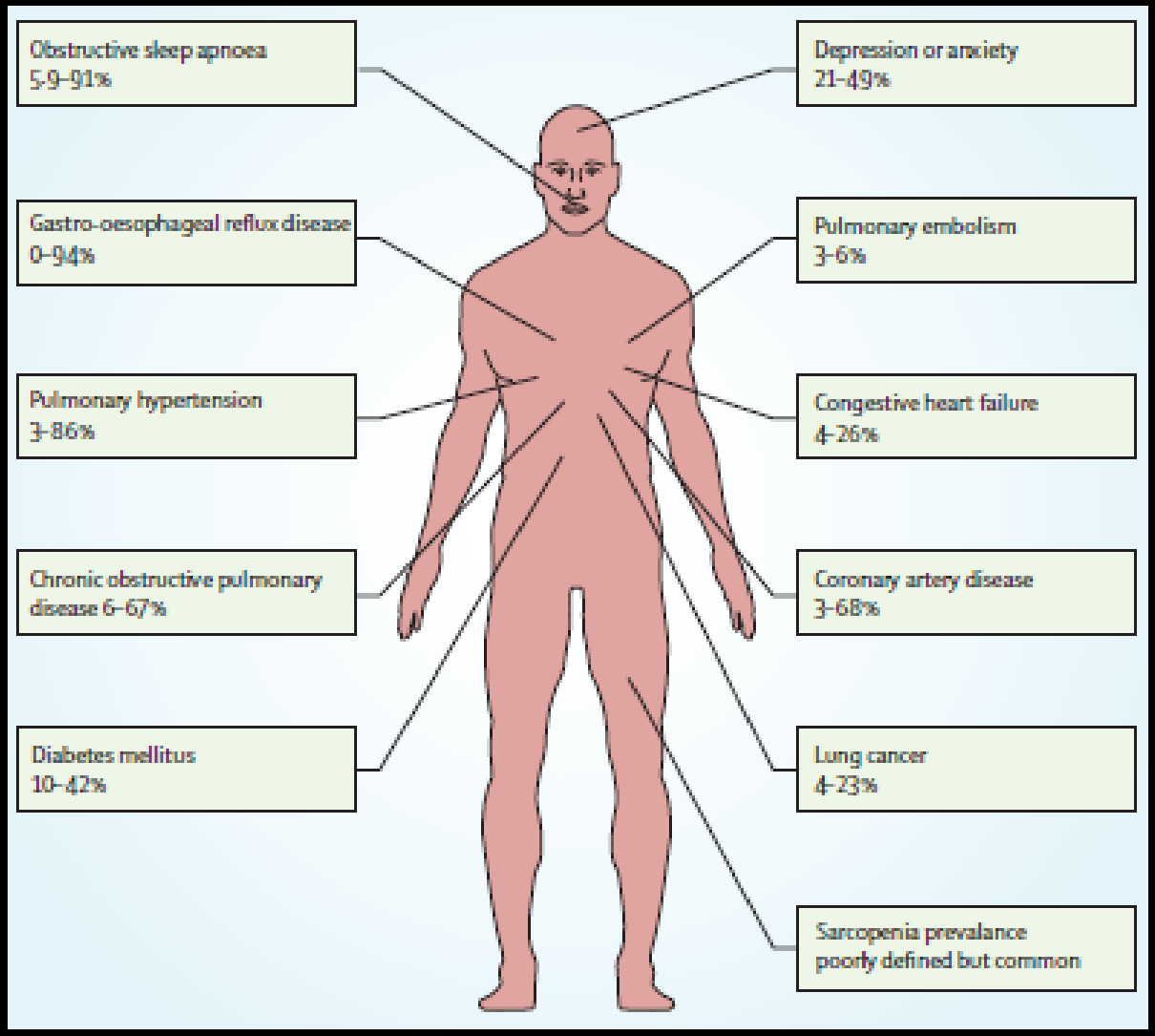

Sharp C, Lamb H, Jordan N, et al BMJ Supportive & Palliative Care Published Online First: 30 June 2017. doi: 10.1136/bmjspcare-2017-001330

A simple decision aid tool resulted in improved documentation of decisions related to supportive care and discussions around end of life in patients with IPF.

There was also an increase in the frequency of documentation of end of life discussions even without completion of this decision aid. The decision aid also resulted in an increase in the rates of referral to community matron or specialist palliative care.

This simple tool was an effective means to increase awareness of patients palliative care needs, however multidisciplinary feedback has suggested refinement to make this more patient-led and symptom focussed.

# Comorbidities in IPF patients



| | | |
|---|---|---|
| Pulmonary hypertension | Adversely affects functional status and survival; consider PH-IPF in patients with severe exertional desaturation, markedly reduced DLCO, or 6MWT distance | Treatment has not been shown to be helpful and might be associated with harm; we recommend vasodilator therapy only be used in RCTs or at expert centres |
| Combined pulmonary fibrosis and emphysema | High incidence of lung cancer and pulmonary hypertension; diagnosed by CT findings | Trial of bronchodilator therapy is reasonable; consider antifibrotic therapy |
| Lung cancer | Associated with poor survival; often presents as lower lung nodules on periphery of fibrosis | Optimal treatment strategies are poorly defined; carefully selected patients might be candidates for surgical resection |
| Gastro-oesophageal reflux disease | Highly prevalent in IPF; possible cause of IPF | Mixed data regarding the effect of antacid therapy on IPF outcomes; trial of antireflux surgery is currently enrolling |
| Cardiac disease | High prevalence of coronary disease, CHF, and cardiac arrhythmias in the IPF population | Consider ischaemia assessment or CHF in the differential diagnosis of dyspnoea in patients with IPF; standard management strategies for these conditions apply to the population with IPF |
| Venous thromboembolism | Higher incidence of VTE in patients with IPF than in the general population | Anticoagulation should be prescribed when there is a clinical indication; optimal anticoagulant for patients with IPF has not yet been determined |
| Depression and anxiety | Affects around a third of patients with IPF; can contribute to increased symptoms | Screen all patients with IPF for depression; treatment with antidepressant medications and counselling is reasonable; pulmonary rehabilitation might improve symptoms |
| Deconditioning | Commonly encountered; severe deconditioning is associated with a high risk of death | Pulmonary rehabilitation improves functional status and QOL |
| Sleep-disordered breathing | OSA affects most patients with IPF; poor sleep from OSA, nocturnal cough, and hypoxia is common | Refer all patients with IPF for sleep study; treatment with OSA when diagnosed with CPAP |
| Diabetes | Higher prevalence of diabetes in patients with IPF than in matched controls | Effects of glycaemic control on IPF progression are unknown; standard management of diabetes for patients with IPF |

# Summary

- Its is critical to secure early and accurate diagnosis
- Its imperative to slow the rate of disease decline
- Its important to manage symptom burden
- Its important to have access to MDT
- IPF patients must have access to treatments including anti-fibrotic, new clinical trials, pulmonary rehabilitation and lung transplantation.