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Update on Idiopathic Pulmonary Fibrosis – What you need to know

Nazia Chaudhuri on behalf of NI ILD Network
Respiratory Consultant with Specialist Interest in ILD

https://pure.ulster.ac.uk/en/persons/nazia-chaudhuri
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Web of Science: https://www.webofscience.com/wos/author/record/J-4517-2019
Twitter: @ILDIPFDoc_NI



OBJECTIVES:

- Case illustration of patient with IPF
- Why its important to diagnose early
- What the new treatments are and potential side effects
- How to manage breathlessness, cough
- End of life care



65 year old male

Known COPD ETT 400yards normally

SOB progressive for 6 months

Dry cough

Smoker

PMH: MI 5 years ago

Poor response to inhaler therapy

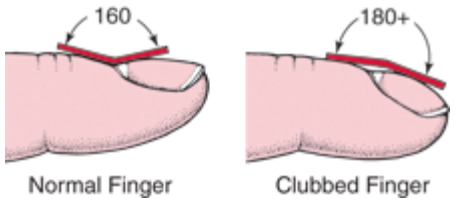
Little improvement with frusemide

No asbestos exposure

No eye problems; skin changes; dysphagia

Examination:

- Completing sentences
- Sats 92%
- Nail clubbing
  - 25-50%





- Bibasal Inspiratory Crepitations – Velcro like

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- Over 45 years old
- Persistent SOB
- Persistent Cough
- Velcro crackles
- Normal or Restrictive Spirometry

Idiopathic pulmonary fibrosis: the diagnosis and management of suspected idiopathic pulmonary fibrosis

Issued: June 2013

NICE clinical guideline 163
guidance.nice.org.uk/cg163



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- THINK ILD
- THINK IPF

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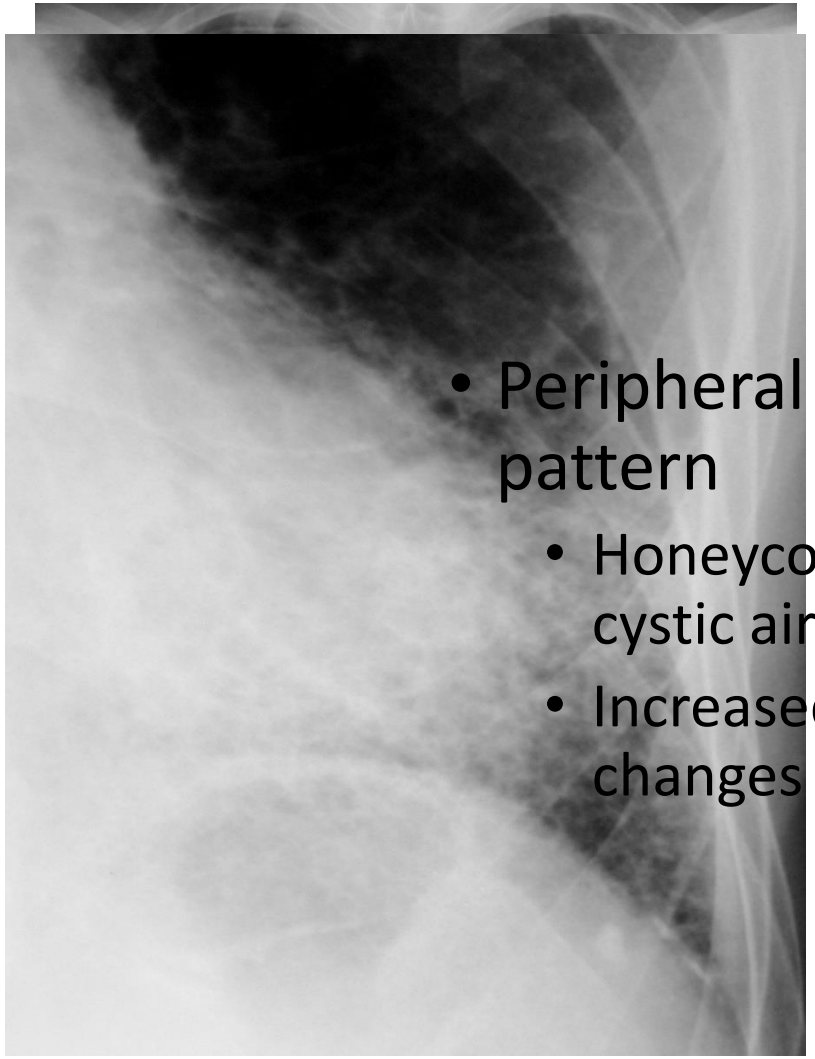
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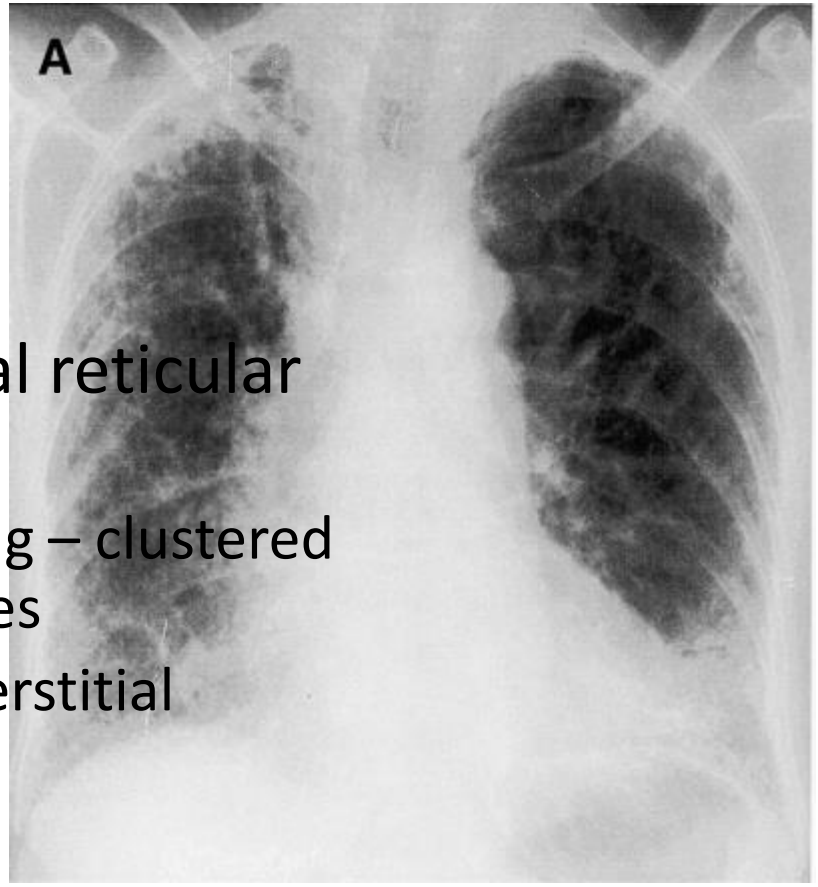
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CxR:





- Peripheral basal reticular pattern
  - Honeycombing – clustered cystic airspaces
  - Increased interstitial changes

CW5 6ED Technician: IAN WALLER

Age: 72 Gender: Male Ht(cm): 179 Wt(kg): 89.4 BMI: 27.90 Race: CAUCASIAN

SR range: Normal -1.645 to 1.645 Mild +/- 1.65-2.50 Moderate +/- 2.51-3.50 Severe +/- >3.50

P

Date: 11/06/12 14:47

Bronchodilator administered:

Spirometry

		Ref	Pre Meas	Pre % Ref	SR	Post Meas	Post % Chg
FEV1	Liters	3.12	(2.19)	(70)	-1.82		
FVC	Liters	4.09	(2.75)	(67)	-2.20		
VC	Liters	4.25	(2.77)	(65)	-2.65		
FEV1/FVC%		74	80		0.75		
FEV1/SVC%		74	79		0.67		

Flow Volume Loop

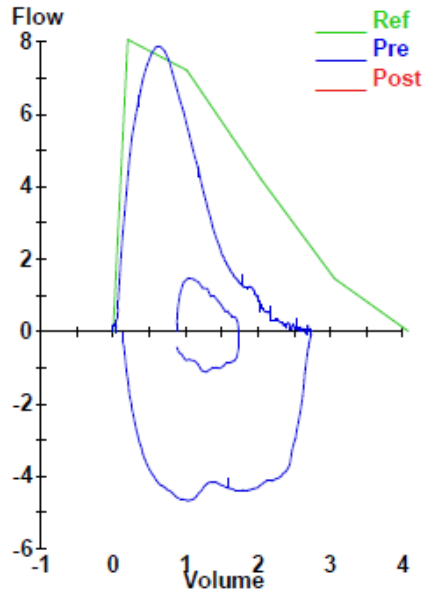
PEF	L/sec	8.06	(10.35)	(128)	1.90		
FEF25%	L/sec	7.21	7.21	100	-0.00		
FEF50%	L/sec	4.21	3.80	90	-0.19		
FEF75%	L/sec	1.45	0.72	50	-0.94		
FEF25-75%	L/sec	3.08	2.14	69	-0.91		
PIF	L/sec		4.68				

Lung Volumes

FRC (N2 Washout)		3.76	2.93	78	-1.38		
TLC (N2 Washout)	Litres	7.22	4.50	62	-3.90		
RV (N2 Washout)	Litres	2.70	1.73	64	-2.37		
RV/TLC	%	42	38				

Diffusion

DLCO	mmol/kPa.min	8.9	(4.1)	(46)	-3.39		
DL Adj	mmol/kPa.min	8.9	(4.1)	(46)	-3.39		
VA	Liters		3.58				
KCO	DLCO/L	1.23	1.15	94			
KCO Adj		1.23	1.15	94			

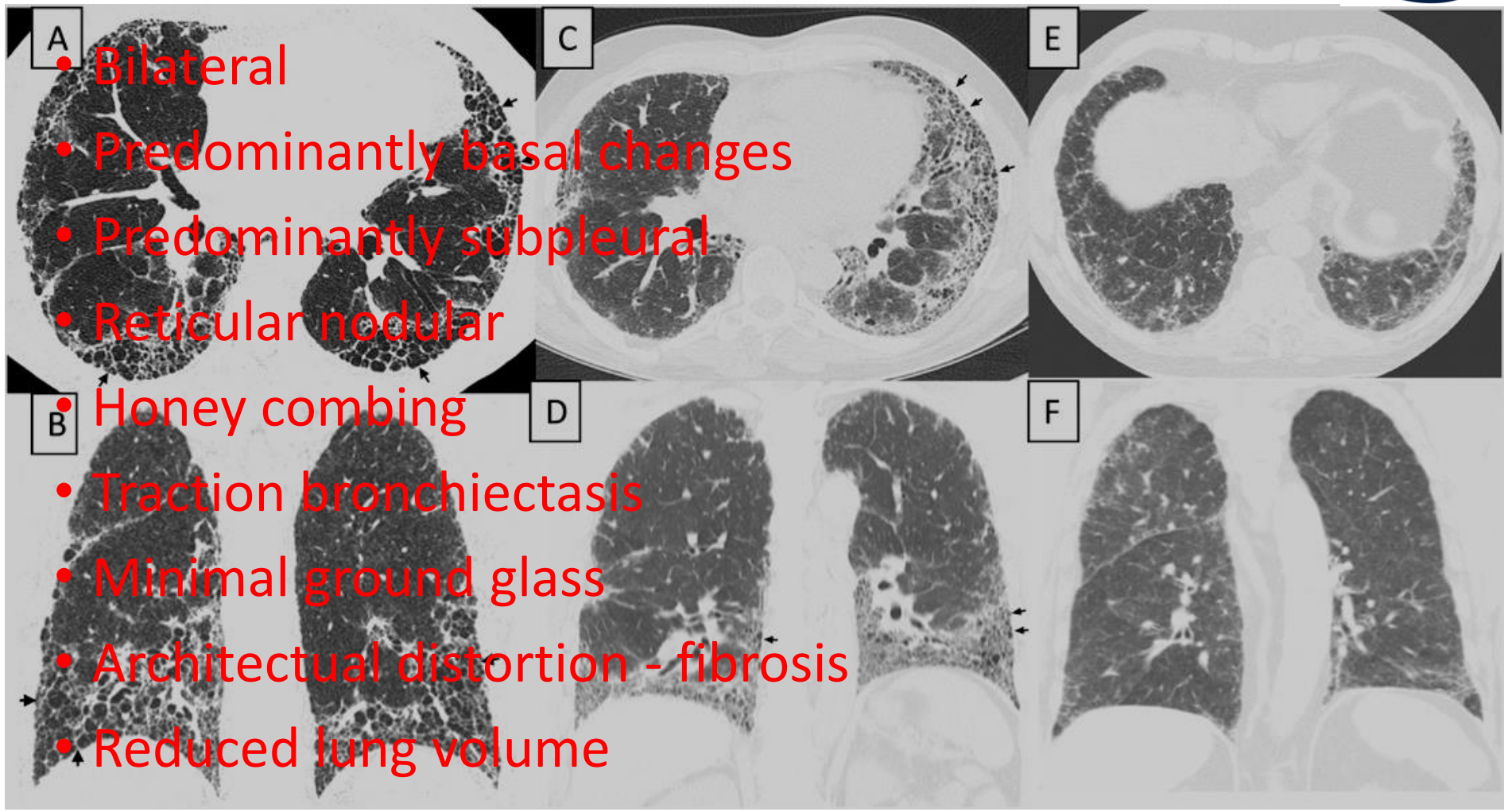


Capillary Blood Gases onAIR

SaO2	95.0 %	pH			
pO2	kPa	BE	mmol/l	Hb	g/dL
pCO2	kPa	HCO3	mmol/l		

Other Tests / Technical Comments

HRCT:

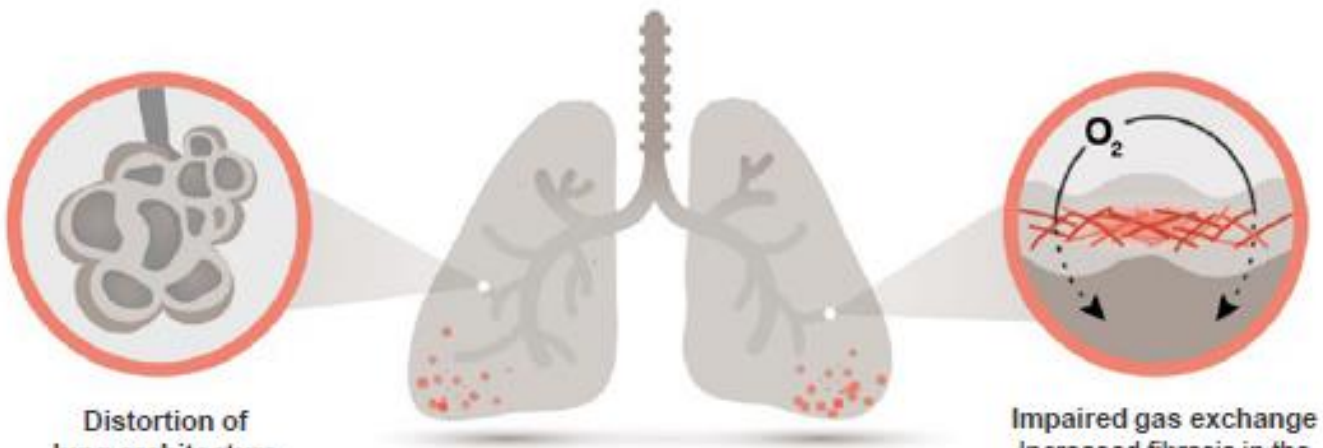


- Bilateral
- Predominantly basal changes
- Predominantly subpleural
- Reticular nodular
- Honey combing
- Traction bronchiectasis
- Minimal ground glass
- Architectual distortion - fibrosis
- Reduced lung volume

What is interstitial lung disease?

Interstitial lung diseases (ILDs) are a heterogenous group of lung disorders that vary in aetiology[1]

- There are over 200 types of ILD of known and unknown causes[1,2]
- Many ILDs are fibrotic and progressive[3,4]
- Individual fibrotic ILDs are rare, but collectively they affect approximately 70,000 people in the UK[5,6]
- Fibrotic ILDs are characterised by irreversible scarring of lung tissue, known as pulmonary fibrosis[7,8]



ILD, interstitial lung disease.

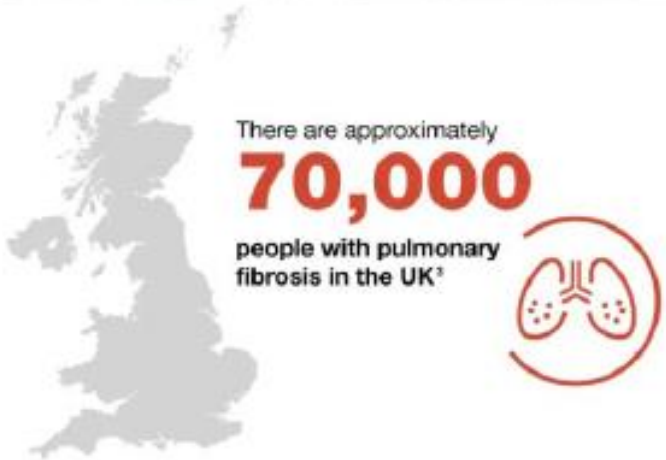
1. Oldham JM and Noth I. *Respir Med* 2014;108:819–829; 2. Cottin V et al. *Eur Respir Rev* 2018;27:180076; 3. Wijsenbeek M et al. *Curr Med Res Opin* 2019;35:2015–2024; 4. Cottin V et al. *Eur Respir Rev* 2019;28:180100; 5. Wijsenbeek M and Cottin V. *N Engl J Med* 2020;383:958–968; 6. Action for Pulmonary Fibrosis. Experience of pulmonary fibrosis in the UK. Available at www.actionpf.org/news/people-with-lived-experience-of-pf-at-the-heart-ofsurvey-set-to-influence-change (accessed September 2024); 7. Wollin L et al. *Eur Respir Rev J* 2019;54:1900161; 8. Selman M et al. *Ann Intern Med* 2001;134:136–151; 9. Wells AU and Denton CP. *Nat Rev Rheumatol* 2014;10:728–739; 10. Bagnato G and Harari S. *Eur Respir Rev* 2015;24:102–114; 11. Kolb M and Vasakova M. *Respir Res* 2019;20:57.

Individual fibrotic ILDs are rare, but collectively they affect a considerable number of people in the UK



IPF is the most common ILD[4,5]

- Around 32,500 people in the UK live with IPF[4]
- There are 6,000 new cases of IPF diagn
  the UK[3]
- In the UK, people with IPF have a life expectancy of 3–5 years[3]
- 1 in 100 of all deaths in the UK are due to IPF[4]

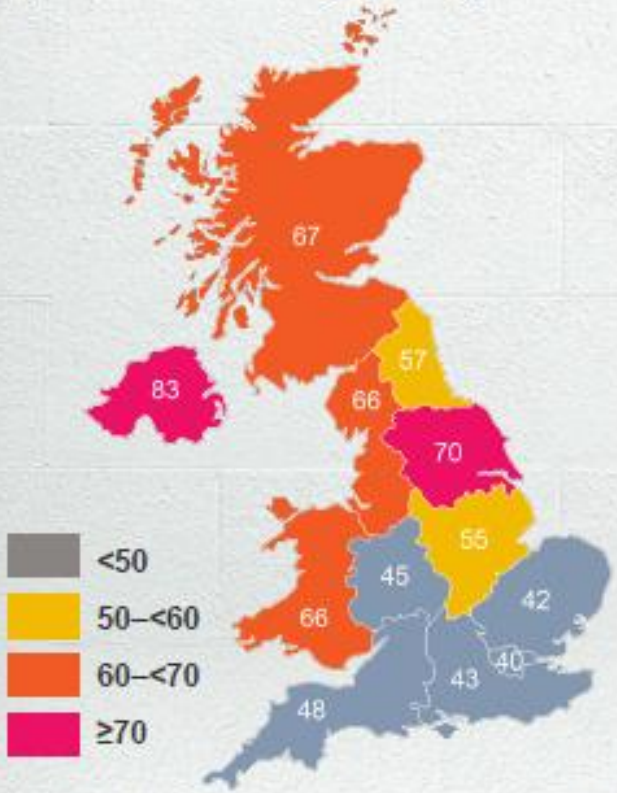




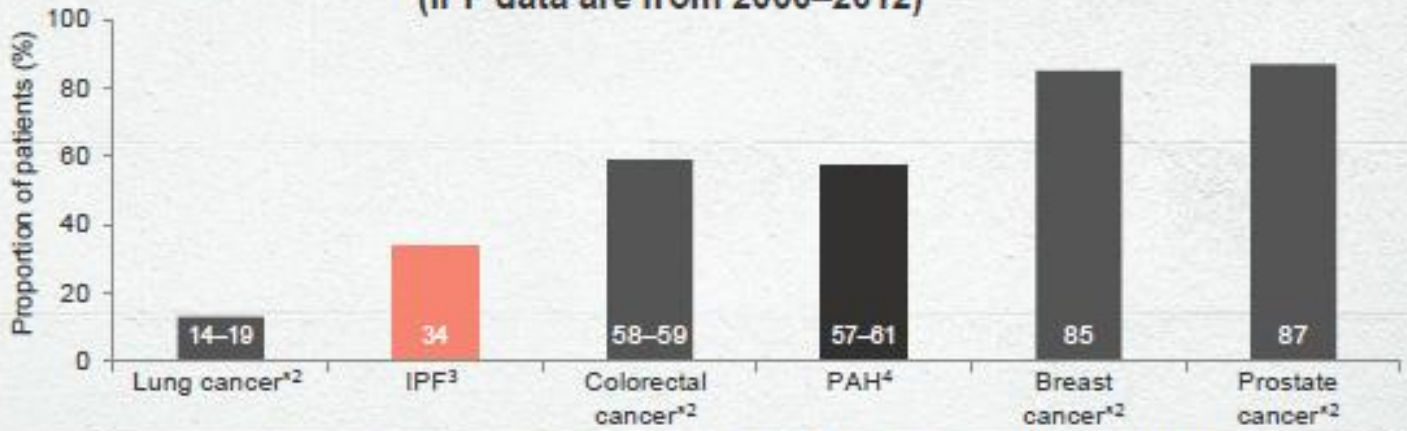
IPF prevalence displays regional variation in the UK, and is associated with high morbidity and mortality



Number of people per 100,000 ever diagnosed with IPF by UK region in 2012[1]



5-year survival rate of IPF in comparison with other conditions (IPF data are from 2000–2012)



Prevalence (%) of comorbidities in people with IPF at presentation in BTS ILD registry 2013–2021[5]

Gastro-oesophageal disease (24.4%)

Known hiatus hernia (8.3%)

Diabetes (24.4%)

Lung cancer (0.7%)

Signs and symptoms of ILD





Persistent breathlessness on exertion[1–3]



Persistent dry cough[1–3]



Bilateral inspiratory crackles[1,4]



Finger clubbing (widening and rounding of fingertips)[1,3]



Loss of appetite and weight loss[2,3]



Fatigue[2,3]

- **Breathlessness** and **cough** are the most common symptoms reported in patients with ILD[2]
- Early symptoms, such as cough and breathlessness, are non-specific and may precede diagnosis by **up to 2 years**[4]

Auscultation can provide vital information about an ILD[1–3]

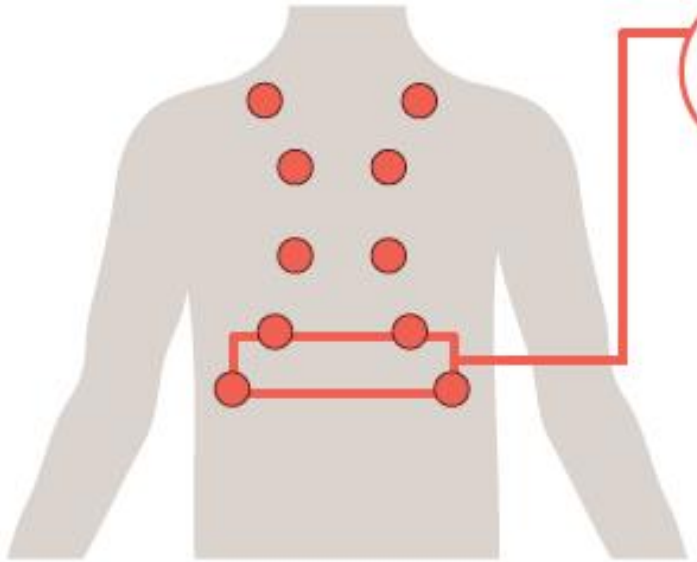


- Dry inspiratory crackles at the base of the lung can be a key indicator of ILD[1–3]
- They can typically be heard during middle-to-late inspiration, do not clear with a cough and have a short duration[2]

Sounds like



A particularly distinctive feature of the dry inspiratory crackles associated with fibrotic ILD is their similarity to the sound of VELCRO® being peeled apart[2,3]



Listen for dry inspiratory crackles at the bases of the lungs[1–3]

Scan below to take the 'Sounds of ILD' challenge

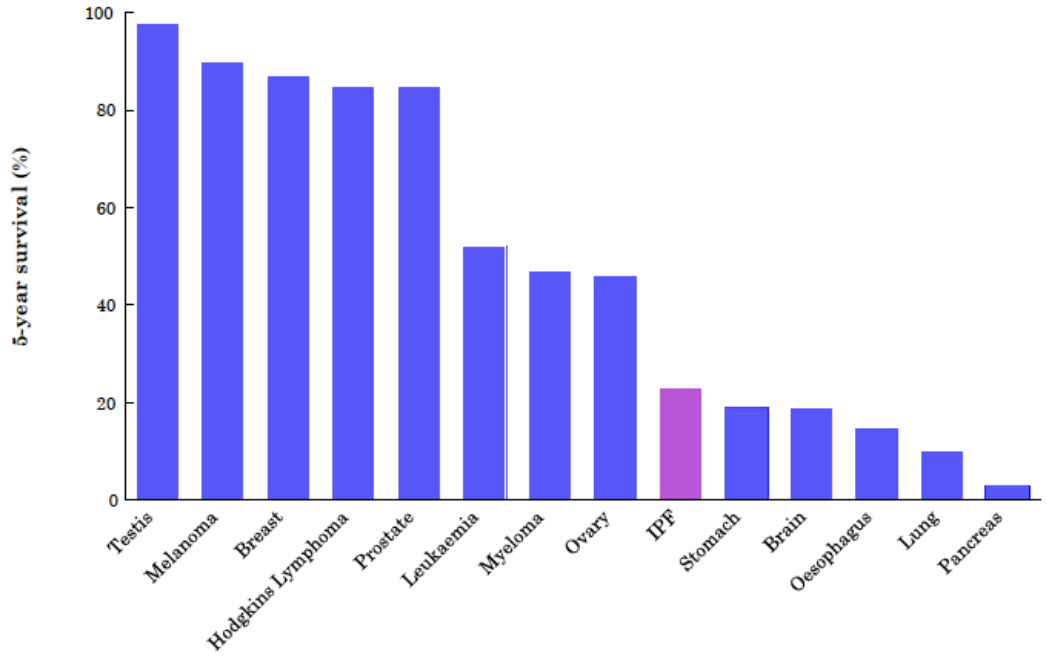
The 'Sounds of ILD' challenge allows you to practice identifying various respiratory conditions including IPF and fibrotic ILDs

Listen to and compare dry inspiratory crackles of a person with ILD with other breath sounds

- Dry inspiratory crackles in ILD
- Breath sounds of COPD
- Healthy breath sounds

The Challenges in ILD Diagnosis

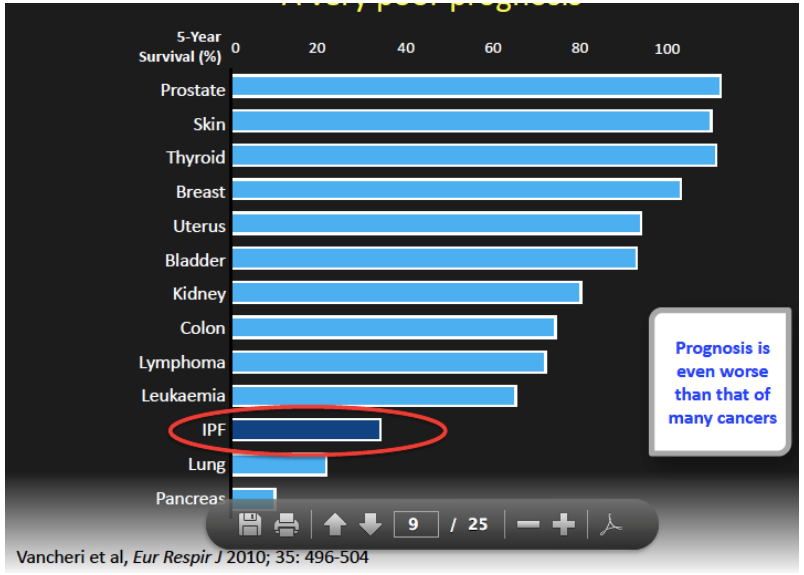
- **Early Diagnosis** is paramount in a disease with worst outcomes than most cancers.



Source: Adapted from Cancer Research UK, England and Wales survival (2010-2011), 2014

IPF

- US approx 150,000IPF patients
- 14-43 IPF cases per 100,000
- UK 8-9 per 100,000
- 5% increase incidence year on year



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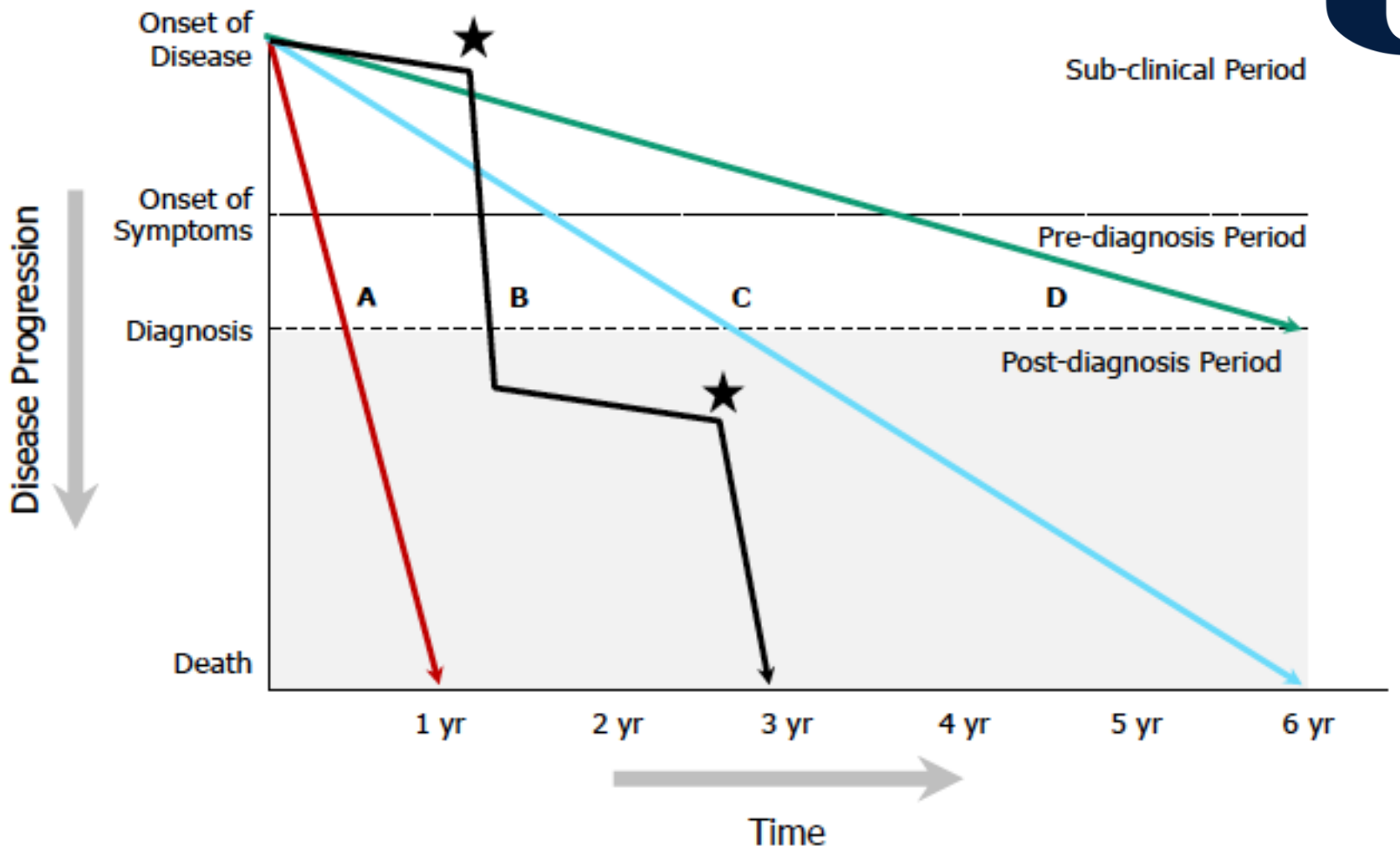
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- Median survival 3-5 years after diagnosis
- Estimated 5 year survival 37%
- Accurate and early diagnosis often delayed on average 1-2 years from onset of symptoms
  - Early symptoms non-specific and similar to other respiratory diseases



IPF DISEASE PROGRESSION



Adapted from Ley B et al, Am J Respir Crit Care Med 2011

Ave life expect 3-5 years
37% 3 year survival

The Challenges in ILD Diagnosis

- **Equal access** to treatments:
- Antifibrotics access
- Pulmonary rehabilitation and oxygen provisions vary
- Transplant

Maher et al. BMC Pulmonary Medicine (2017) 17:124
DOI 10.1186/s12890-017-0468-5

BMC Pulmonary Medicine

RESEARCH ARTICLE Open Access

Unmet needs in the treatment of idiopathic pulmonary fibrosis—insights from patient chart review in five European countries

Toby M. Maher[1,8*], Maria Molina-Molina[2], Anne-Marie Russell[1], Francesco Bonella[3], Stéphane Jouneau[4], Elena Ripamonti[5], Judit Axmann[6] and Carlo Vancheri[7]

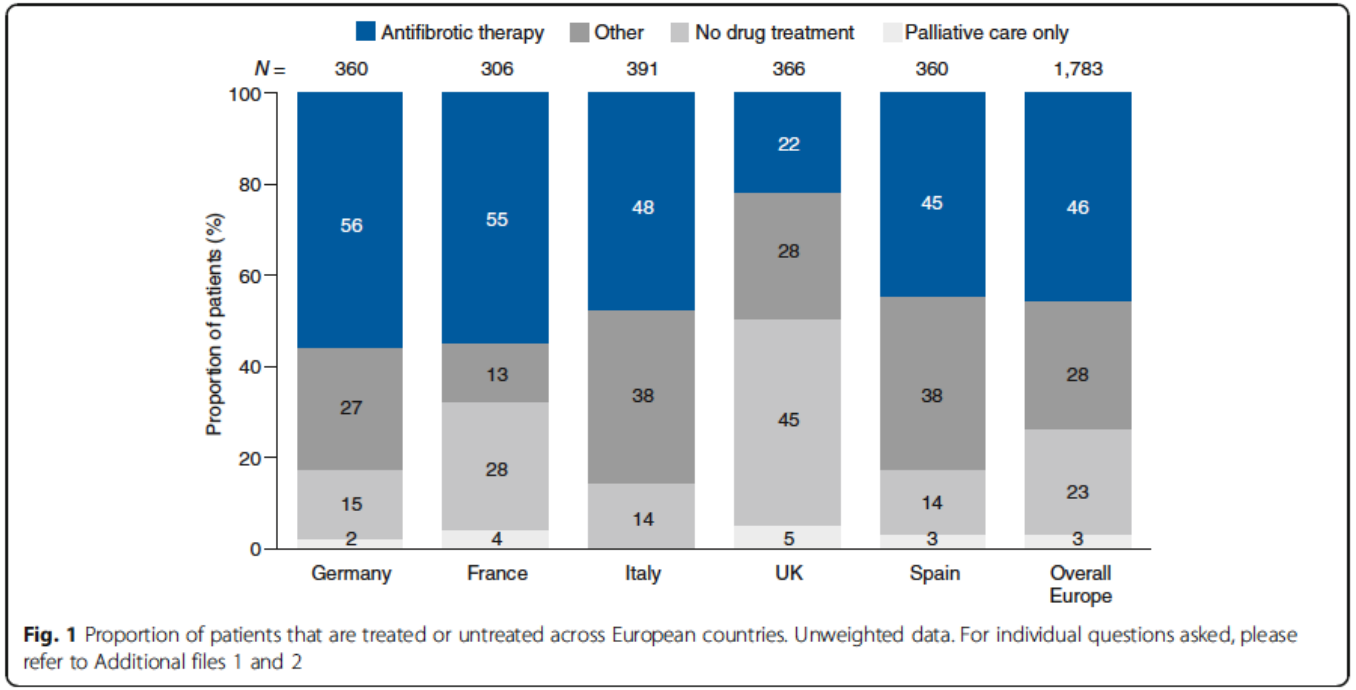
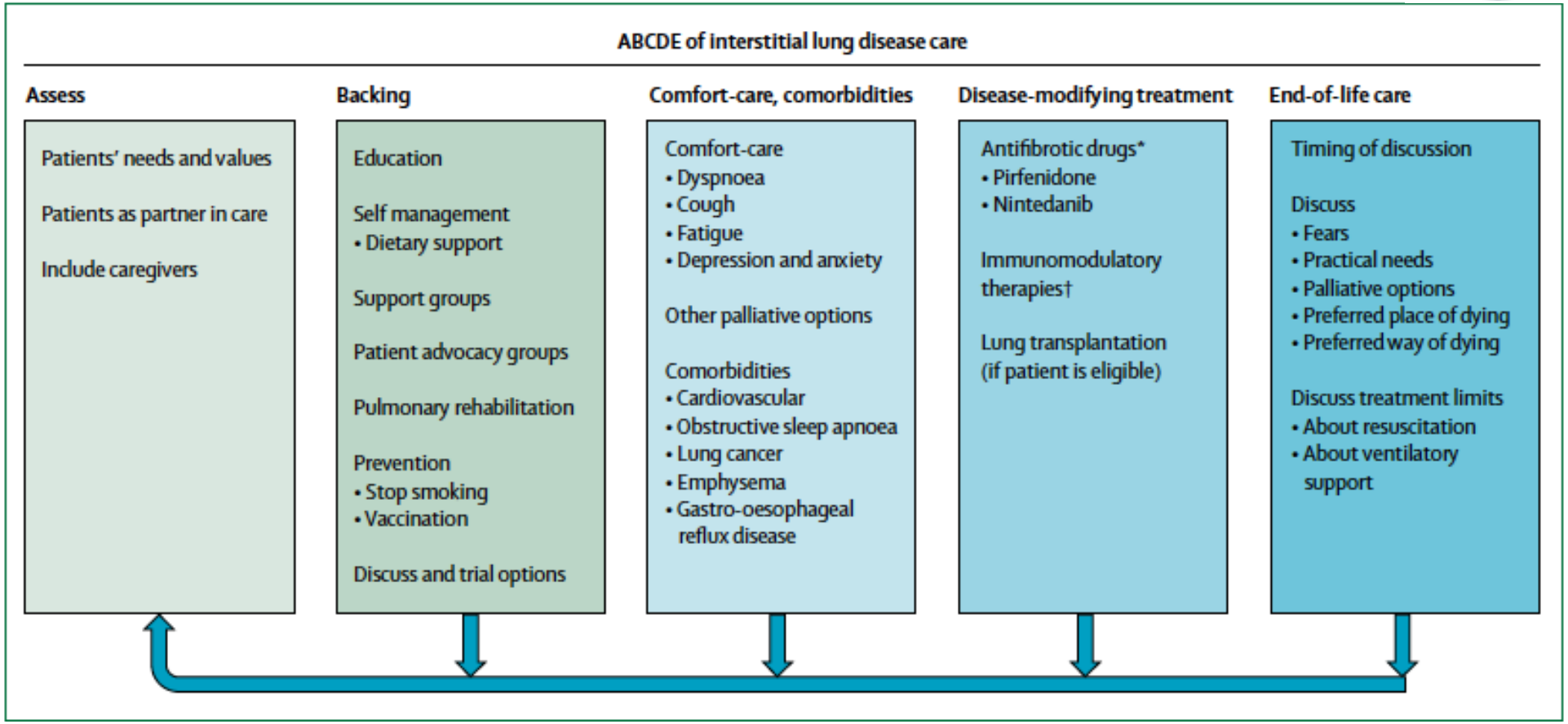


Fig. 1 Proportion of patients that are treated or untreated across European countries. Unweighted data. For individual questions asked, please refer to Additional files 1 and 2



Palliative care in interstitial lung disease: living well

Michael Kreuter, Elisabeth Bendstrup*, Anne-Marie Russell*, Sabrina Bajwah, Kathleen Lindell, Yochai Adir, Crystal E Brown, Greg Calligaro, Nicola Cassidy, Tamera J Corte, Klaus Geissler, Azza Adel Hassan, Kerri A Johannson, Ronaldo Kairalla, Martin Kolb, Yasuhiro Kondoh, Sylvia Quadrelli, Jeff Swigris, Zarir Udwadia, Athol Wells†, Marlies Wijsenbeek†*

Lancet Respir Med 2017

Published Online
October 12, 2017
http://dx.doi.org/10.1016/
S2213-2600(17)30383-1

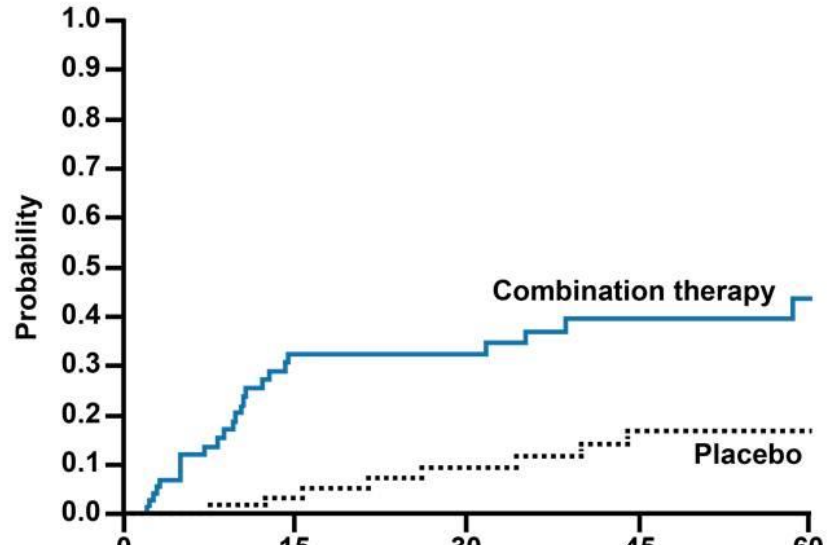
Management of IPF:

- Holistic approach
- Education
- Non-pharmacological
  - Pulmonary rehabilitation
- Infection prevention
  - vaccinations
- Palliative care
- Comorbidities
- Transplant in small minority
- Pharmacological



Immunosuppression KILL patients with IPF

PANTHER-IPF: Time to Death or Hospitalization



Number at Risk					
Combination therapy	77	40	29	23	10
Placebo	78	55	42	26	16

Idiopathic Pulmonary Fibrosis Clinical Research Network, et al. *N Engl J Med*. 2012;366:1968-1977.

THE PRESENT:

- Pirfenidone - anti-inflammatory/antifibrotic
  - 3 RCTs CAPACITY and ASCEND
- Nintedanib - Tyrosine kinase inhibitor
  - 2 RCTs INPULSIS

- SLOW rate of Decline in IPF – FVC
- Improve survival – pirfenidone only

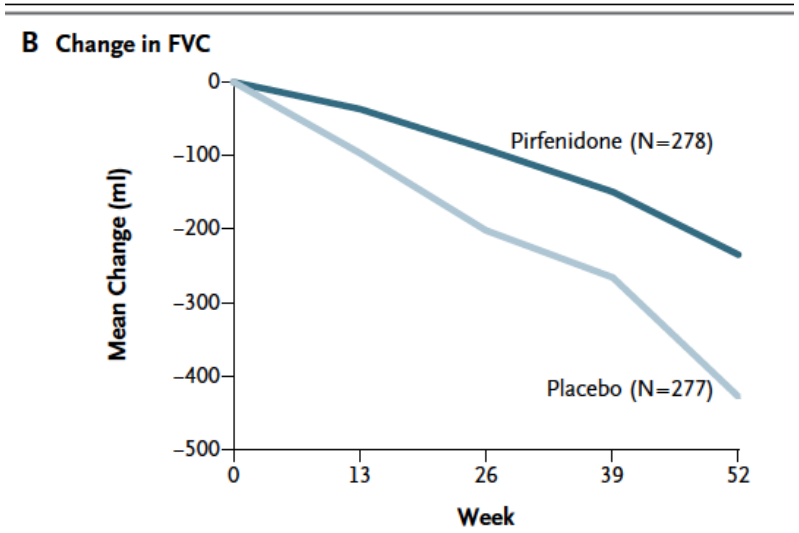
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PIRFENIDONE

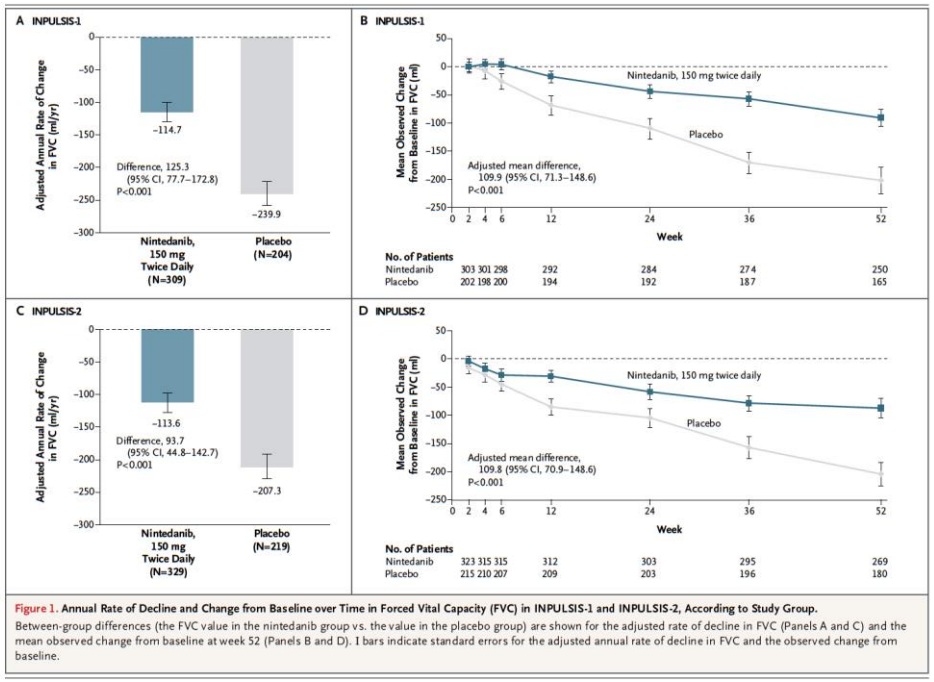


Figure 1. **Annual Rate of Decline and Change from Baseline over Time in Forced Vital Capacity (FVC) in INPULSIS-1 and INPULSIS-2, According to Study Group.**
Between-group differences (the FVC value in the nintedanib group vs. the value in the placebo group) are shown for the adjusted rate of decline in FVC (Panels A and C) and the mean observed change from baseline at week 52 (Panels B and D). I bars indicate standard errors for the adjusted annual rate of decline in FVC and the observed change from baseline.

NINTEDANIB

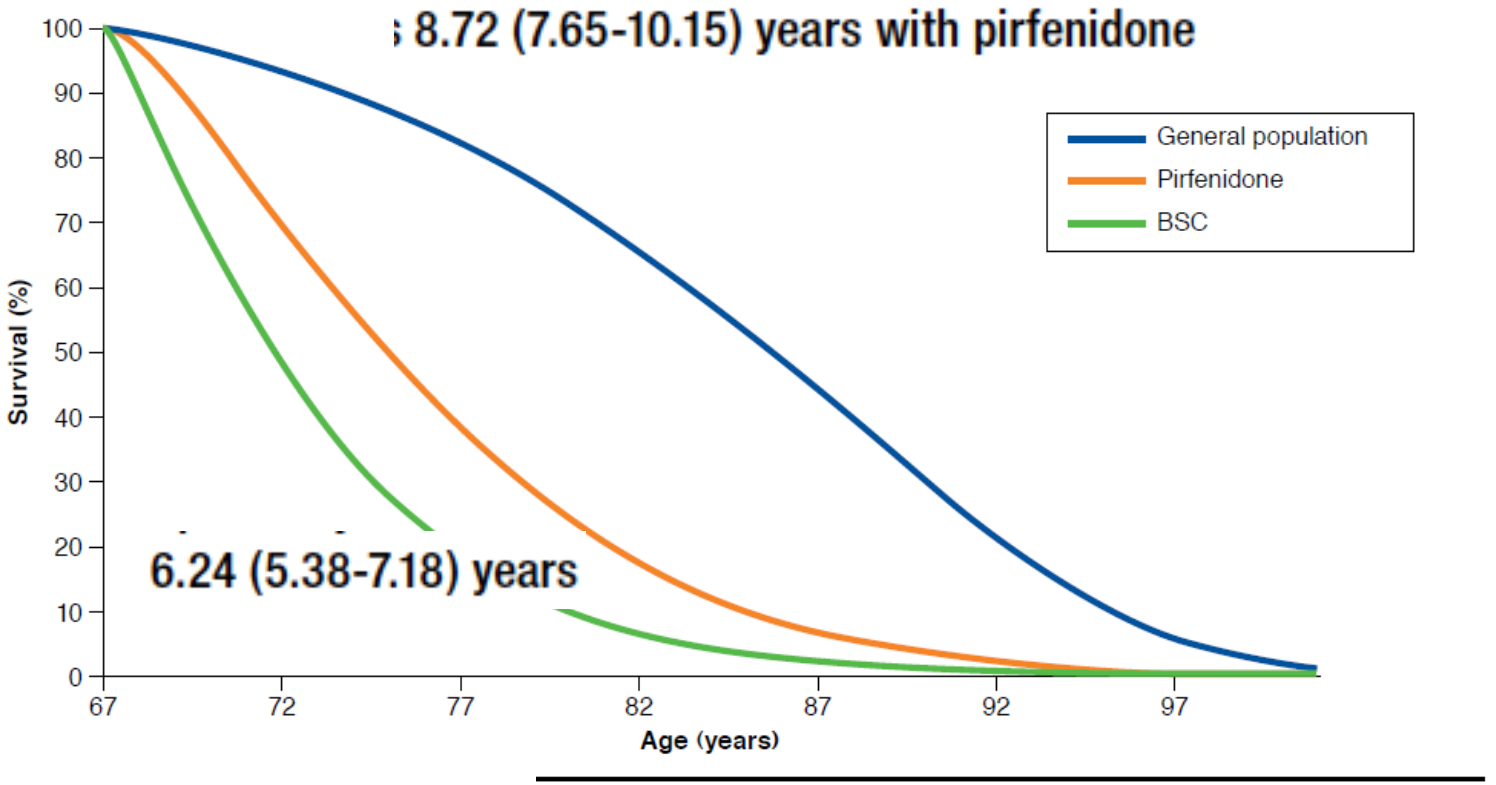
Table 3. Adverse Events.*

Adverse Event	Pirfenidone (N=278)	Placebo (N=277)
	no. of patients (%)	
Cough	70 (25.2)	82 (29.6)
Nausea	100 (36.0)	37 (13.4)
Headache	72 (25.9)	64 (23.1)
Diarrhea	62 (22.3)	60 (21.7)
Upper respiratory tract infection	61 (21.9)	56 (20.2)
Fatigue	58 (20.9)	48 (17.3)
Rash	78 (28.1)	24 (8.7)
Dyspnea	41 (14.7)	49 (17.7)
Dizziness	49 (17.6)	36 (13.0)
Idiopathic pulmonary fibrosis†	26 (9.4)	50 (18.1)
Bronchitis	39 (14.0)	36 (13.0)
Constipation	32 (11.5)	38 (13.7)
Back pain	30 (10.8)	37 (13.4)
Dyspepsia	49 (17.6)	17 (6.1)
Nasopharyngitis	33 (11.9)	30 (10.8)
Anorexia	44 (15.8)	18 (6.5)
Vomiting	36 (12.9)	24 (8.7)
Decrease in weight	35 (12.6)	22 (7.9)
Gastroesophageal reflux	33 (11.9)	18 (6.5)
Insomnia	31 (11.2)	18 (6.5)

Table 3. Adverse Events.

Event	INPULSIS-1		INPULSIS-2	
	Nintedanib (N=309)	Placebo (N=204)	Nintedanib (N=329)	Placebo (N=219)
	number of patients (percent)			
Any adverse event	298 (96.4)	181 (88.7)	311 (94.5)	198 (90.4)
Any adverse event, excluding progression of idiopathic pulmonary fibrosis*	296 (95.8)	179 (87.7)	311 (94.5)	197 (90.0)
Most frequent adverse events†				
Diarrhea	190 (61.5)	38 (18.6)	208 (63.2)	40 (18.3)
Nausea	70 (22.7)	12 (5.9)	86 (26.1)	16 (7.3)
Nasopharyngitis	39 (12.6)	34 (16.7)	48 (14.6)	34 (15.5)
Cough	47 (15.2)	26 (12.7)	38 (11.6)	31 (14.2)
Progression of idiopathic pulmonary fibrosis*	31 (10.0)	21 (10.3)	33 (10.0)	40 (18.3)
Bronchitis	36 (11.7)	28 (13.7)	31 (9.4)	17 (7.8)
Upper respiratory tract infection	28 (9.1)	18 (8.8)	30 (9.1)	24 (11.0)
Dyspnea	22 (7.1)	23 (11.3)	27 (8.2)	25 (11.4)
Decreased appetite	26 (8.4)	14 (6.9)	42 (12.8)	10 (4.6)
Vomiting	40 (12.9)	4 (2.0)	34 (10.3)	7 (3.2)
Weight loss	25 (8.1)	13 (6.4)	37 (11.2)	2 (0.9)
Severe adverse events‡	81 (26.2)	37 (18.1)	93 (28.3)	62 (28.3)
Serious adverse events‡	96 (31.1)	55 (27.0)	98 (29.8)	72 (32.9)
Fatal adverse events	12 (3.9)	10 (4.9)	25 (7.6)	21 (9.6)
Adverse events leading to treatment discontinuation§	65 (21.0)	22 (10.8)	58 (17.6)	33 (15.1)
Gastrointestinal disorders	26 (8.4)	3 (1.5)	21 (6.4)	2 (0.9)
Respiratory, thoracic, and mediastinal disorders	12 (3.9)	10 (4.9)	8 (2.4)	18 (8.2)
Investigation results¶	10 (3.2)	1 (0.5)	8 (2.4)	1 (0.5)
Cardiac disorders	5 (1.6)	4 (2.0)	2 (0.6)	3 (1.4)
General disorders and conditions involving site of study-drug administration‖	8 (2.6)	3 (1.5)	2 (0.6)	1 (0.5)

Pirfenidone improves life expectancy by 2.47 years compared with BSC.

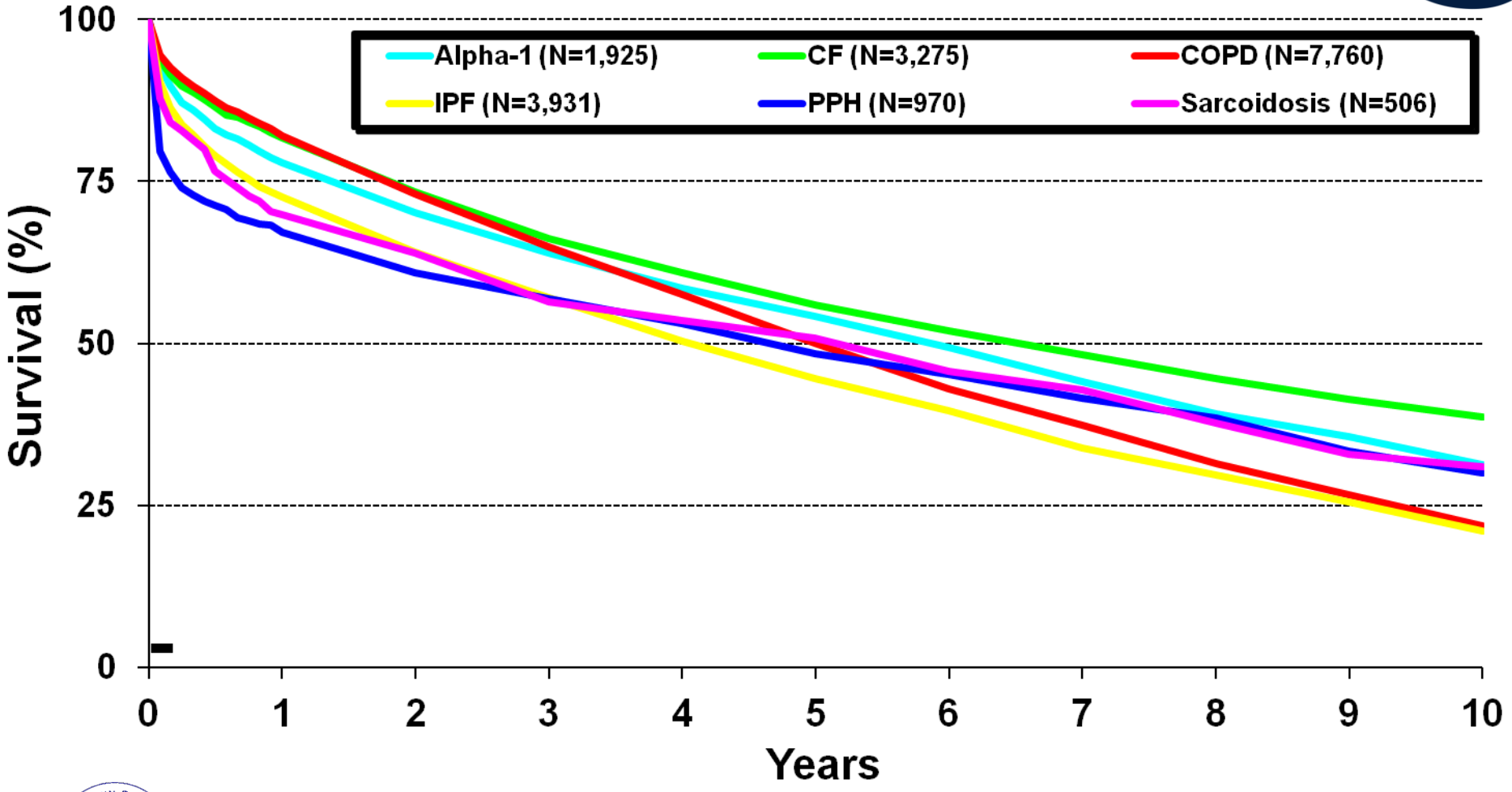


Predicting Life Expectancy for Pirfenidone in Idiopathic Pulmonary Fibrosis

Mark Fisher, MSc; Steven D. Nathan, MD; Christian Hill, BSc; Jade Marshall, MSc; Fred Dejonckheere, MD; Per-Olof Thuresson, MSc; and Toby M. Maher, MD

ADULT LUNG TRANSPLANTATION

Kaplan-Meier Survival By Diagnosis (Transplants: January 1990 – June 2006)



ISHLT

2008

J Heart Lung Transplant 2008;27: 937-983



71-year-old female

Presented with:

- 8-month history of progressive breathlessness

Past medical history:

- Hypertension, TIA and recurrent UTI

Drug history:

- Ramipril
- Clopidogrel
- Nitrofurantoin
- Simvastatin

Patient pathway to specialist centre:

- No response to several courses of antibiotics in primary care
- 3/12 before admission to hospital with worsening SOB
- Treated as atypical pneumonia with broad spectrum antibiotics
  - No improvement observed
- Referred to cardiology as increasingly desperate
- Respiratory expedite requested…



Physical findings

- Afebrile throughout
- Bilateral inspiratory coarse crackles on auscultation



Investigations

- Chest X-ray and CT scan reported as atypical infection
- Coronary angiogram



Oxygen tests

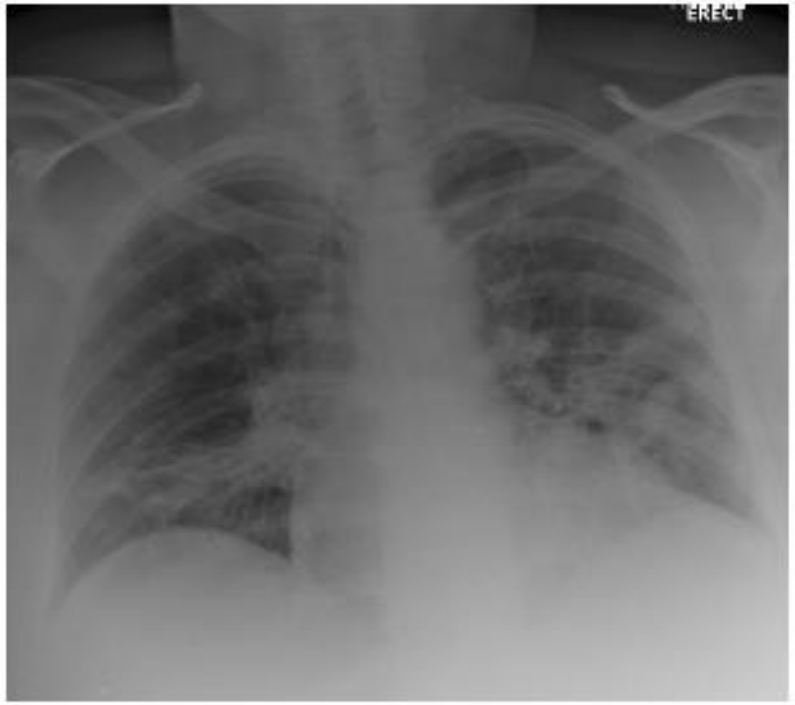
- O_2 sats 92% on room air



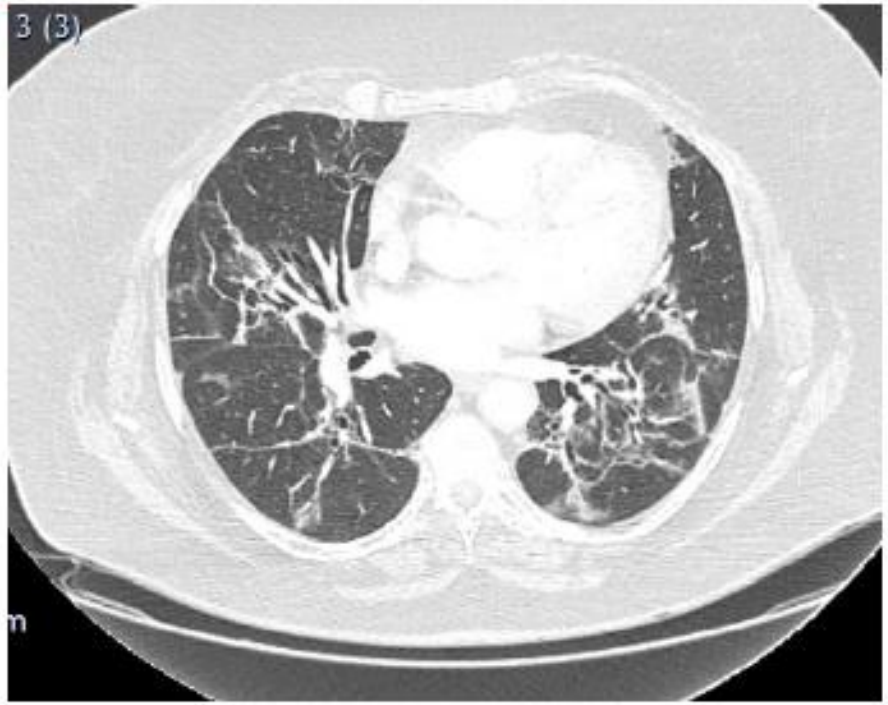
Blood tests

- WBC 10
- CRP 30 mg/dL
- Normal eosinophils levels
- Normal renal and liver function
- Normal BNP

Chest x-ray



HRCT



What is the likely diagnosis here?

A. Antibiotic-resistant pneumonia
B. Cardiac failure
C. Lung cancer
D. Drug-related ILD
E. Idiopathic pulmonary fibrosis

Nitrofurantoin lung disease



- Although rare, nitrofurantoin-induced lung injury is one of the most commonly reported drug-induced ILDs[1]
- Typically, experienced in elderly women (aged 70+ years) after a year of treatment[1,2]
- CT appearances can vary but typically similar to an organising pneumonia pattern[1]
- Key treatment is drug cessation, and most patients improve (as observed in this patient case study)[1]
- Steroids may be prescribed if severe respiratory impairment is experienced[1]
- Diagnostic delay is very common due to poor awareness of disease[1,2]

Does slowly progressive SOB for several months really fit with 'atypical pneumonia' as diagnosed in hospital?[2]

This patient case study reinforces the central role of history taking in diagnosing ILD and the safety net of primary care in taking a longer view of symptoms and treatment failure/response[2]

Surely get a scan and take it from there?



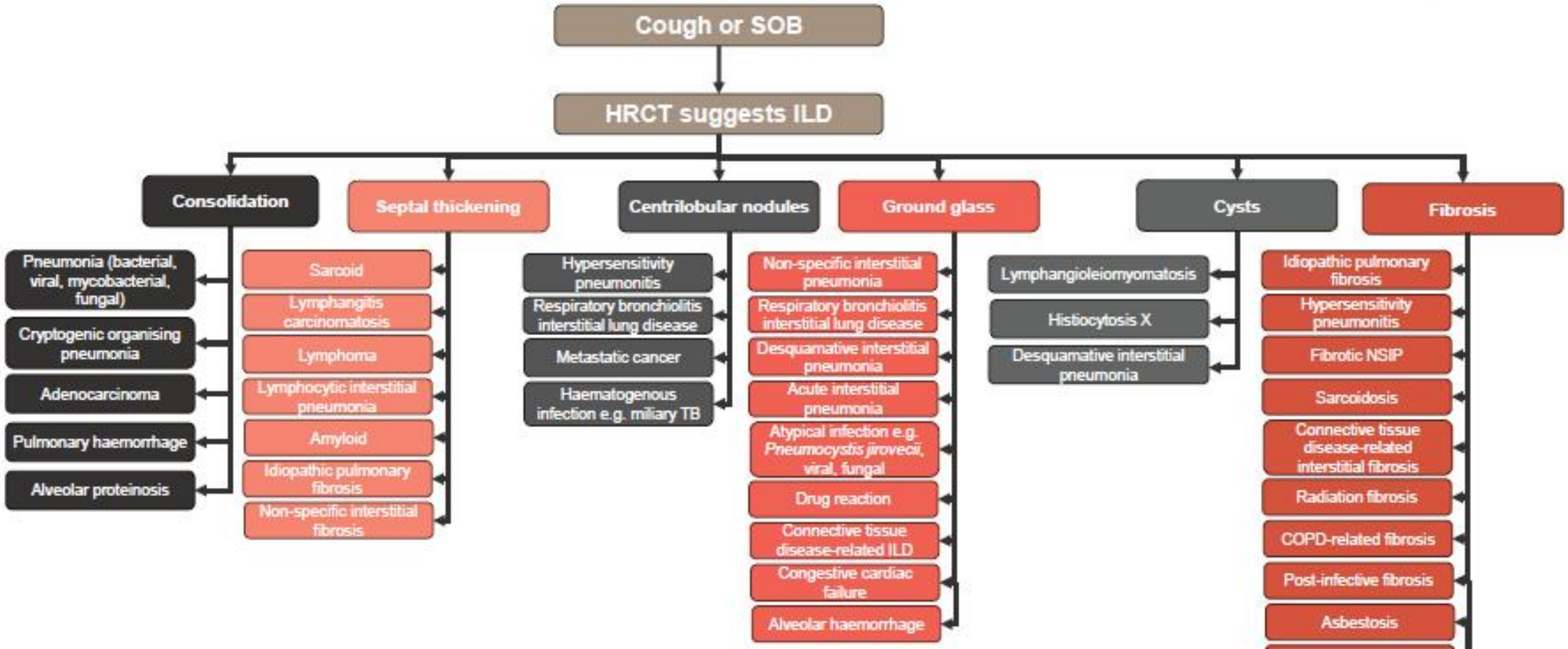


Figure has been provided by speaker and created from their own experience.

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Treatment Options









Potential side effects with anti-fibrotics

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- Nausea/Vomiting
- Loss of / reduced appetite
- Weight loss
- Rash
- Stomach pain
- Upper respiratory tract infection
- Diarrhoea
- Fatigue
- Headache
- Indigestion
- Dizziness



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Diarrhoea



Dietary advice - always ensure you are taking the medication as instructed, with food either in the middle of the meal or immediately after food, and with a good glass of water.



Dietary changes – it may require a change in eating habits. Think about reducing high fibre foods or cutting out fatty/greasy foods.

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Change in dietary habits

- It is good to take a good breakfast high in protein
- Try frequent small meals over the course of the day
- Take Low fibre foods such as bananas, eggs, chicken or fish.
- No more than 14 units of alcohol weekly

Loperamide
Imodium®

- 1 tablet = 2mg
- Can use up to 8mg in 24hrs
- Monitor for effect and reduce dose as required
- May not need to take daily





Nausea & Vomiting

Manage early!

Anti-emetic prescription – Metoclopramide, 5 days only

Long Term Management

- Cyclizine 50mg TID
- Ondansetron 4mg BD (avoid in presence of prolonged QT)

- Dietary considerations – ALWAYS WITH FOOD and a glass of water!



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Photosensitivity with Pirfenidone !



Daily application of factor 50 sunblock

Keeping covered – wear hat , long sleeves





Managing Breathlessness

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- Oromorph
- MST
- Pulmonary Rehab
- Hand Held Fan
- Oxygen
- Breathing Techniques

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COUGH

Treatments which may be offered include:

Proton pump inhibitors (acid reflux)

GI motility agent (non-acid reflux)

Inhaled steroid (eosinophilic cough)

Oramorph (cough hypersensitivity)

Codeine Phosphate Linctus

Gabapentin (an anticonvulsant medicine)

Mucolytic therapy.



‘I try not to do things that trigger my cough, which is everything. I'm embarrassed with other people's reactions as they don't understand my condition’.

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Reduced Appetite & Weight Loss

Dietary Supplements

Dietitian referral



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Oxygen Therapy







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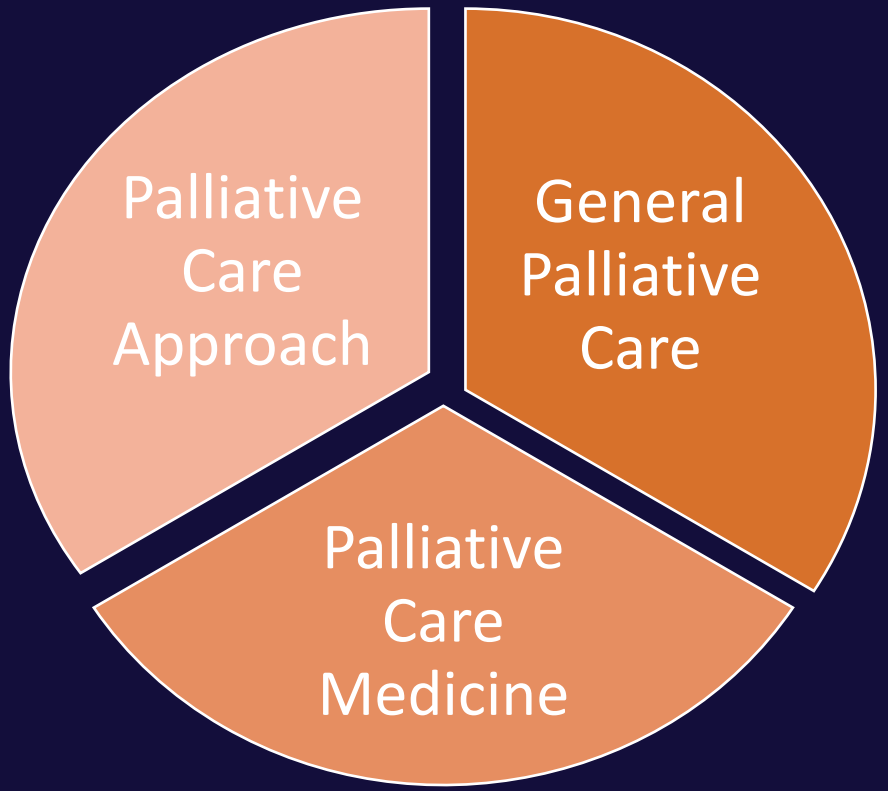
"The goals of palliative care are to prevent and relieve suffering, support the best quality of life for patients and their families, and encourage discussions regarding end-of-life preferences."

"Palliative care involves management of symptoms, which is relevant even in patients with mild to moderate disease."



Types of Palliative Care

Palliative Care Approach
Offered by all HCPs

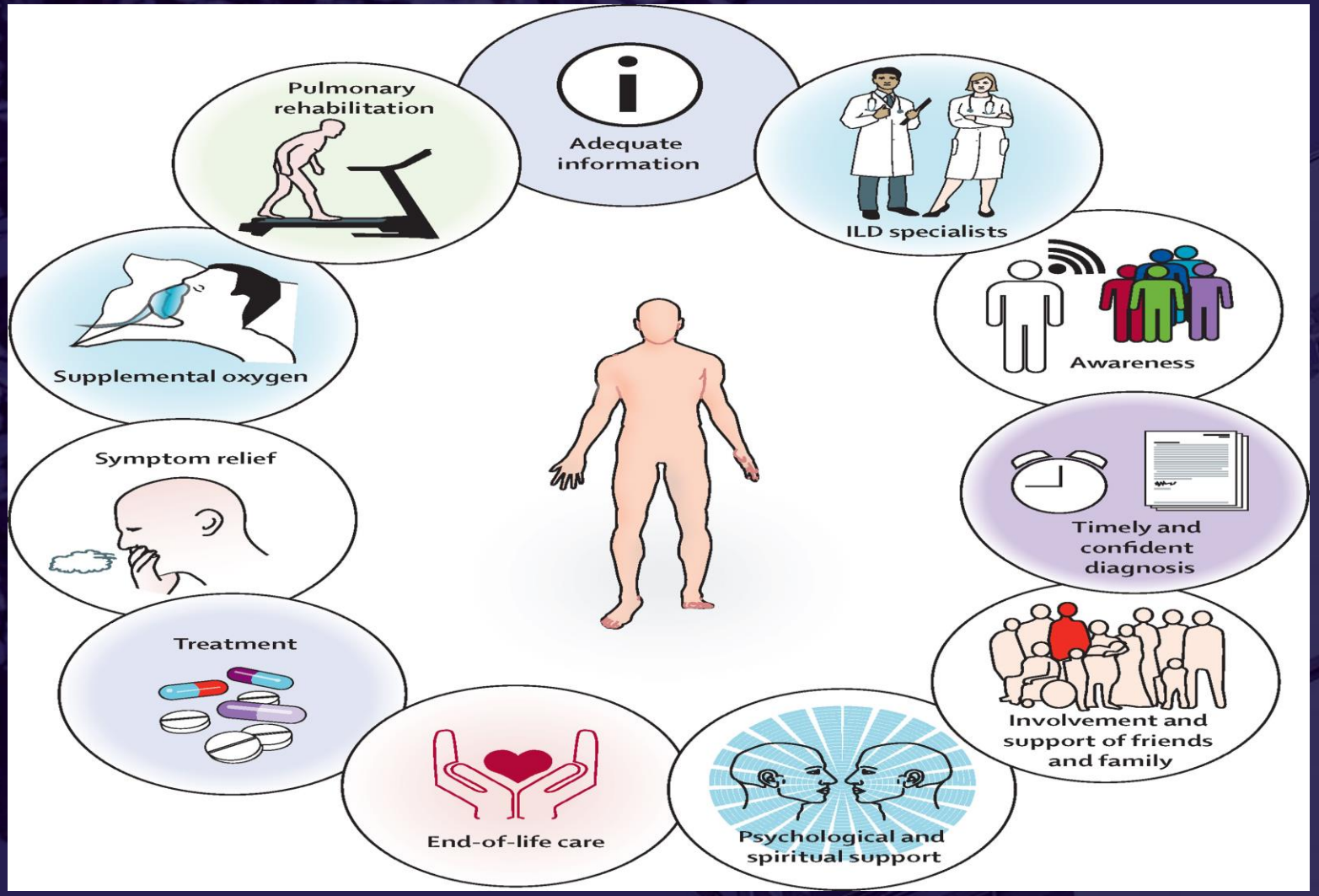


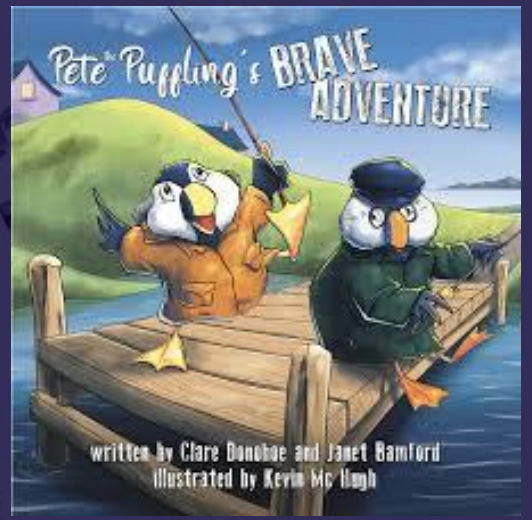
General Palliative Care

Arranged by respiratory teams with additional training

Palliative Medicine
Led by specialised palliative care teams; delivered at home
or in a hospital/hospice

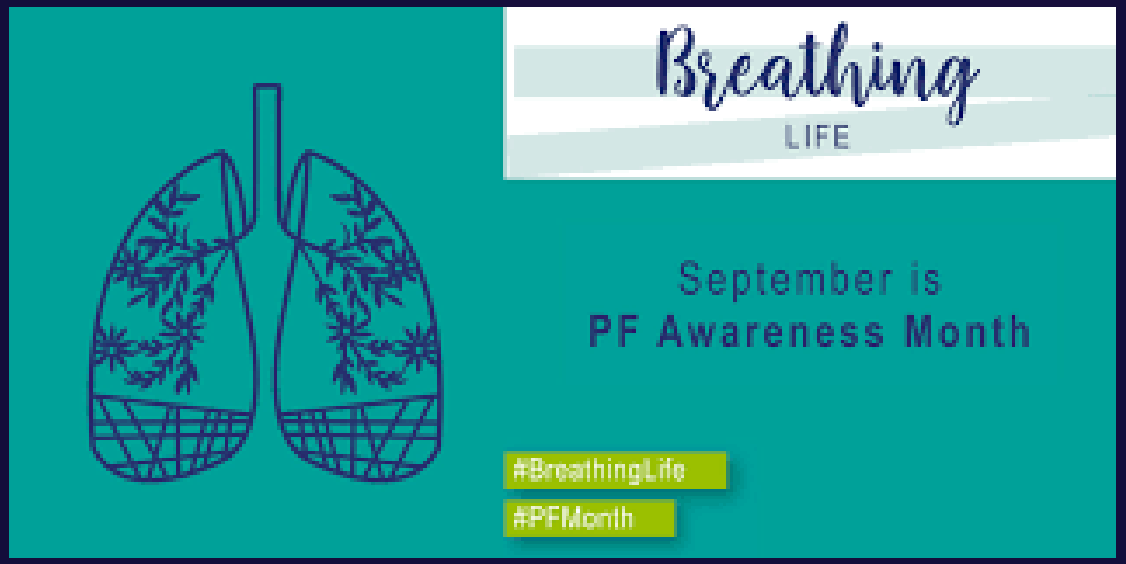
Patient journey





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Take Home message

