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Convegno di presentazione della versione italiana delle linee guida per la diagnosi di fibrosi polmonare idiopatica

1 Febbraio 2020

Hotel Enterprise Milano

Linee guida ufficiali ATS/ERS/JRS/ALAT per la pratica clinica

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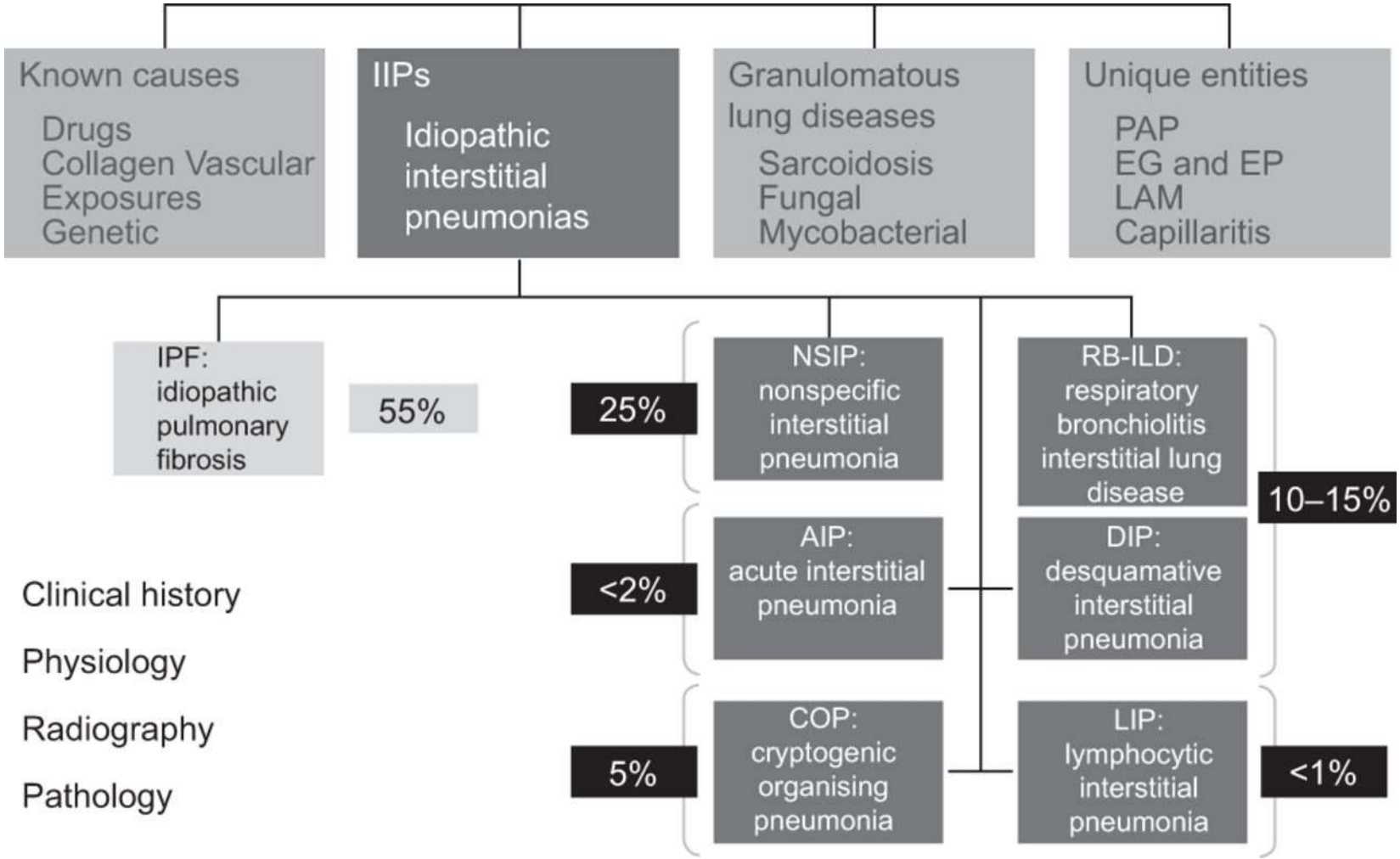
Hotel Enterprise Milano

La Diagnosi Clinica

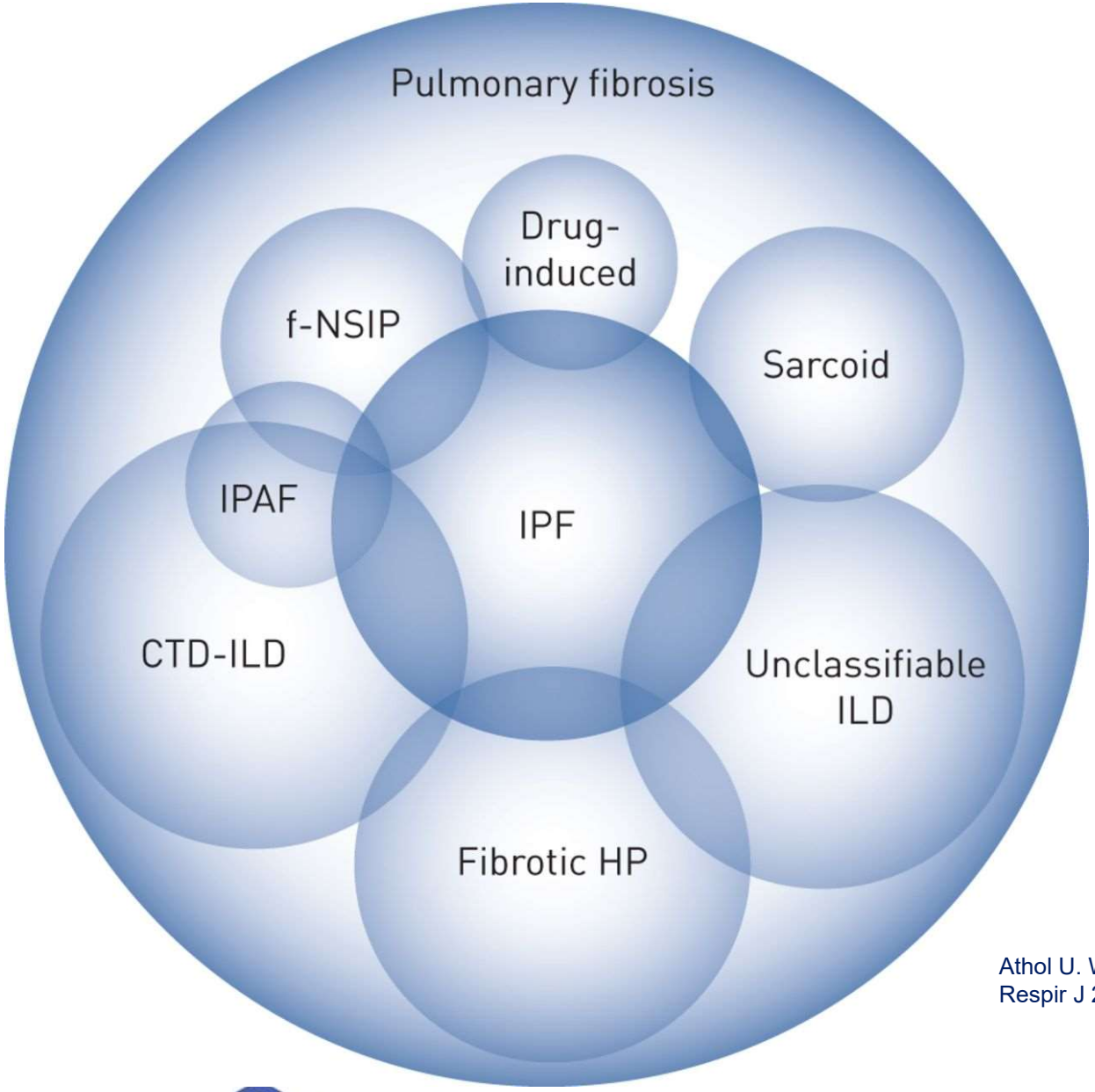
Francesco Varone

UOC Pneumologia
Fondazione Policlinico A. Gemelli IRCCS
Roma

Classification of interstitial lung disease



Athol U. Wells Eur Respir Rev 2013;22:158-162

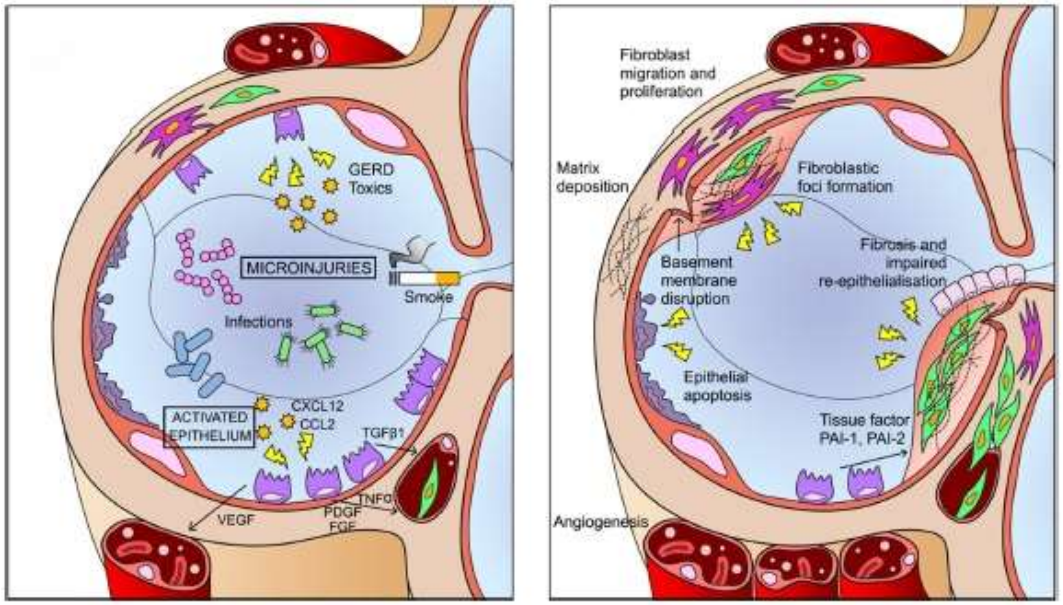


Athol U. Wells et al. Eur Respir J 2018;51:1800692

An Official ATS/ERS/JRS/ALAT Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management

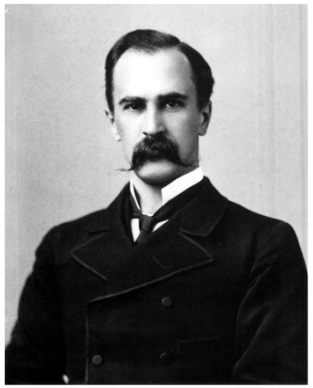
IPF is a specific form of chronic, progressive, fibrosing interstitial pneumonia of unknown cause.

It occurs primarily in older adults, is limited to the lungs, and is defined by the histopathologic and/or radiologic pattern of UIP



Sgalla *et al. Respiratory Research* (2018) 19:32
https://doi.org/10.1186/s12931-018-0730-2

Am J Respir Crit Care Med Vol 183. pp 788–824, 2011
DOI: 10.1164/rccm.2009-040GL
Internet address: www.atsjournals.org



William Osler

''Cirrhosis of the Lung''

Hamman and Rich

«Acute diffuse interstitial fibrosis of the lung»

Liebow and Carrington

Usual Interstitial Pneumonia (UIP)

Bronchiolitis interstitial pneumonia

Desquamative interstitial pneumonia (DIP)

Lymphoid interstitial pneumonia (LIP)

giant cell interstitial pneumonia (GIP)

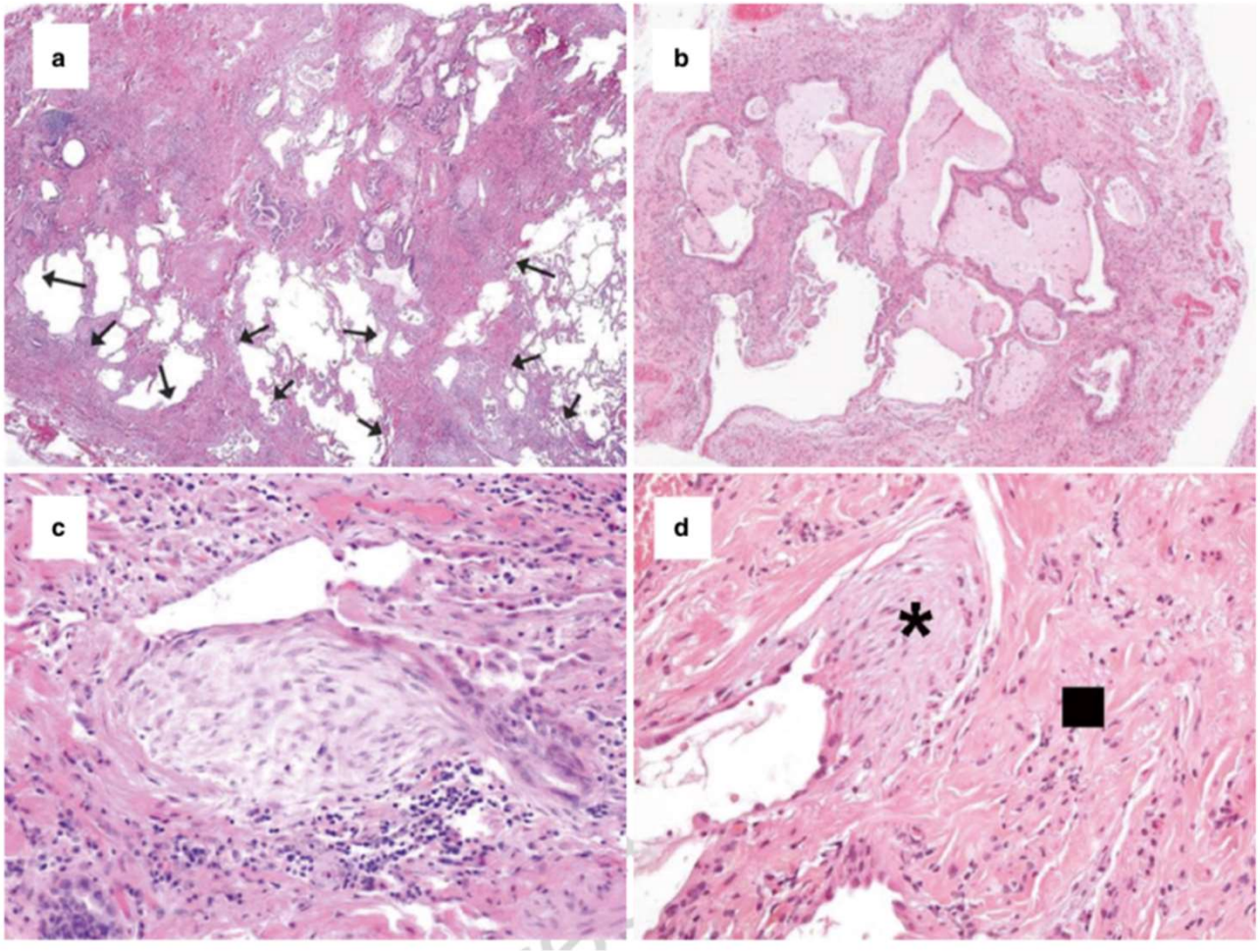
Katzenstein, Myers

UIP, NSIP, DIP, RB-ILD, AIP

IPF clinical-radiological-pathological correlations

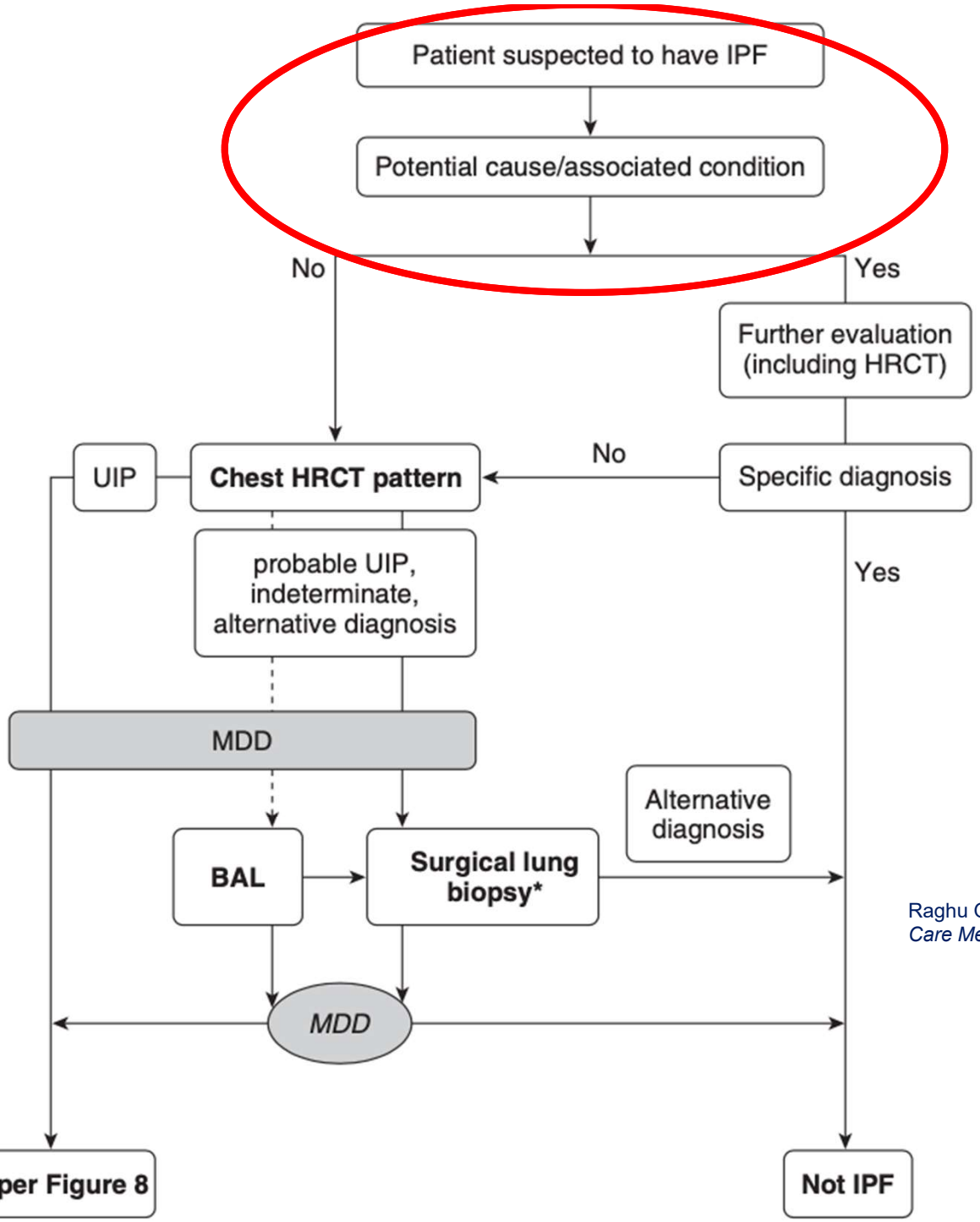
Collard HR, King TE; Arch Intern Med. 2003 Jan 13;163(1):17-29.

1892 1944 1969 1998 2011-present



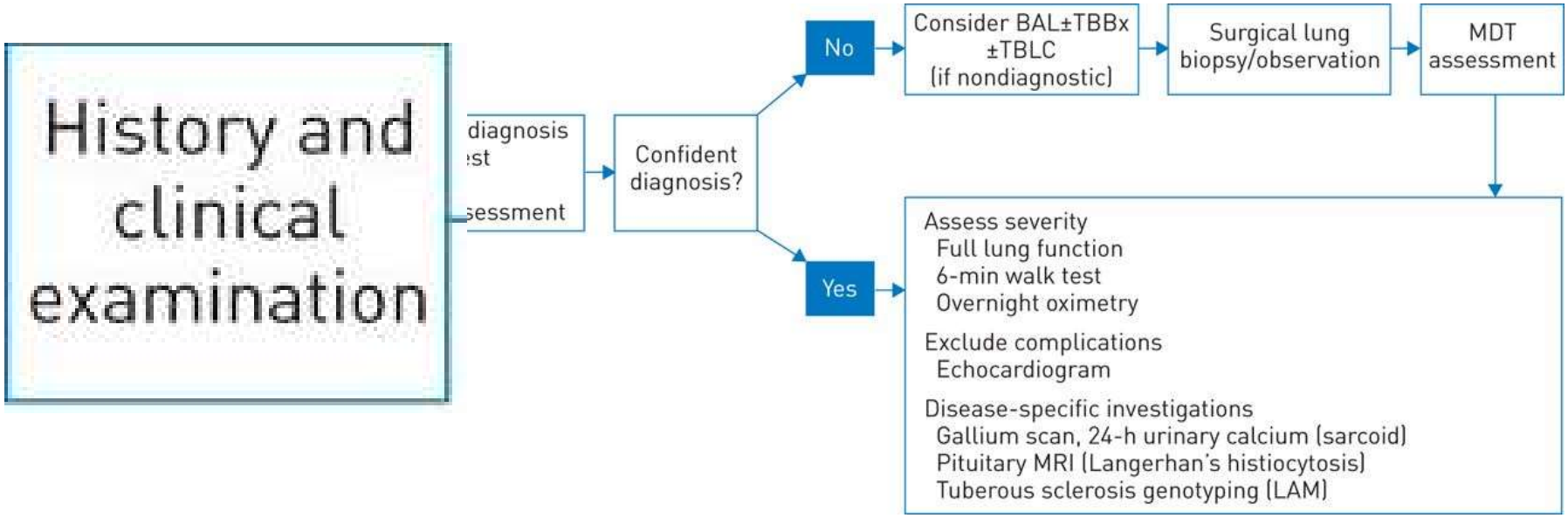
- **Dense fibrosis with architectural distortion (i.e., destructive scarring and/or honeycombing)**
- **Predominant subpleural and/or paraseptal distribution of fibrosis**
- **Patchy involvement of lung parenchyma by fibrosis**
- **Fibroblast foci**
- **Absence of features to suggest an alternate diagnosis**

Pulmonary Fibrosis and the Many Faces of UIP Springer-Verlag London 2015
Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68



Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68

Diagnostic workup



S. Tomassetti et al; Eur Respir Rev 2015; 24: 69–77cc

Anamnesis

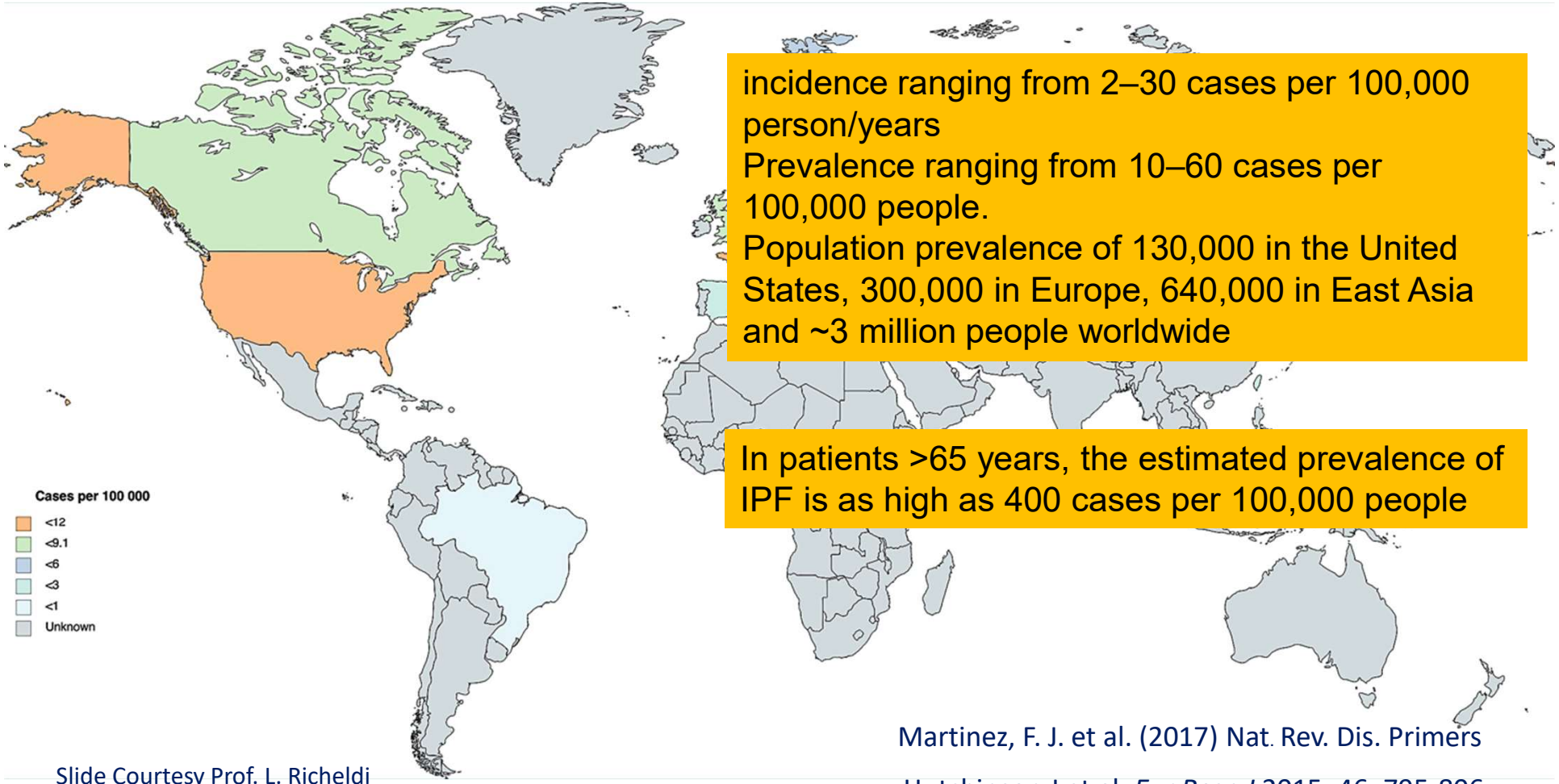
"A thorough and comprehensive history may provide invaluable information that can suggest certain entities and provide suspicion that a patient may have a specific diagnosis"

- Age
- Sex
- Smoking History
- Onset of Symptoms (Cough, Dyspnea, etc.)
- Other Symptoms (Fever, weight loss, Myalgias, etc)
- Comorbidities (GERD, Diabetes, Cardiovascular, etc)
- Family History
- Exposures
- Pets
- Drugs

KC Meyer Translational Respiratory Medicine 2014, 2:4

Epidemiology

Worldwide Incidence



incidence ranging from 2–30 cases per 100,000 person/years
Prevalence ranging from 10–60 cases per 100,000 people.
Population prevalence of 130,000 in the United States, 300,000 in Europe, 640,000 in East Asia and ~3 million people worldwide

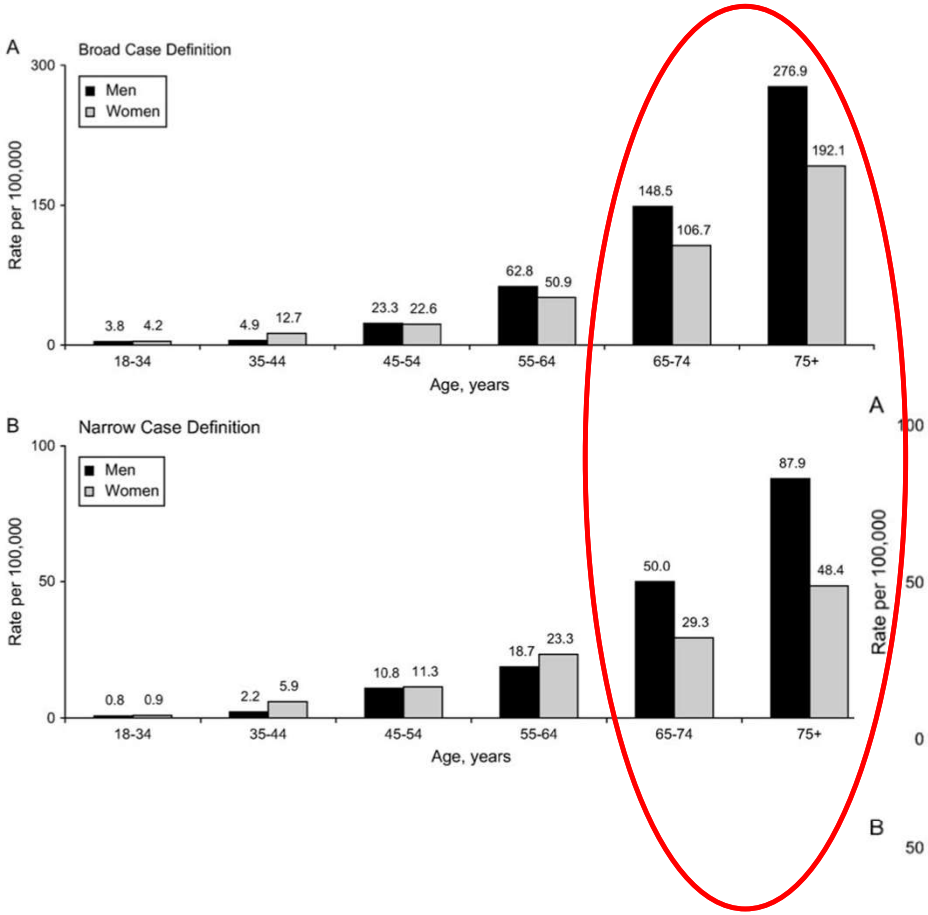
In patients >65 years, the estimated prevalence of IPF is as high as 400 cases per 100,000 people

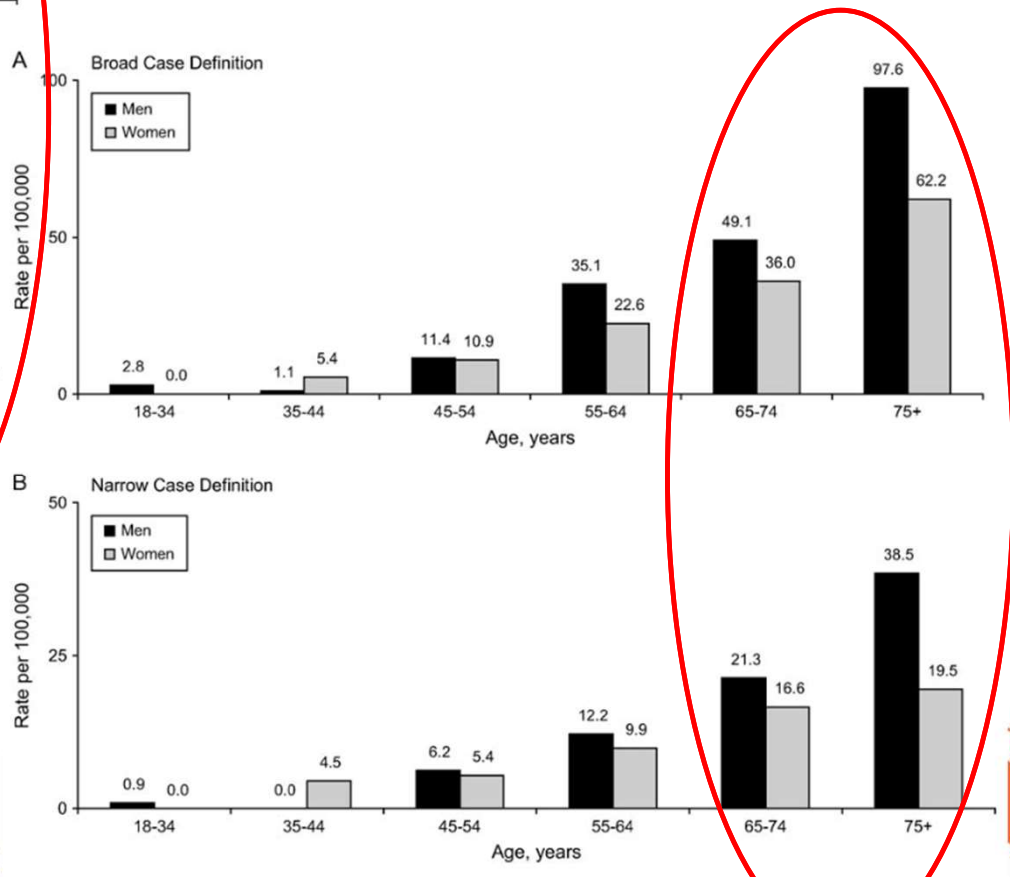
Martinez, F. J. et al. (2017) Nat. Rev. Dis. Primers

Hutchinson J et al, *Eur Resp J* 2015; 46: 795-806

Slide Courtesy Prof. L. Richeldi

Incidence and Prevalence of Idiopathic Pulmonary Fibrosis

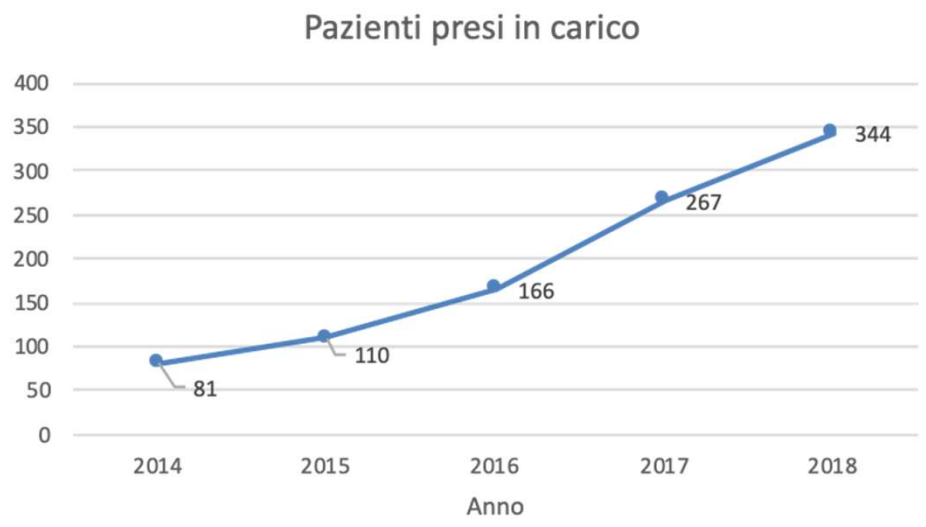




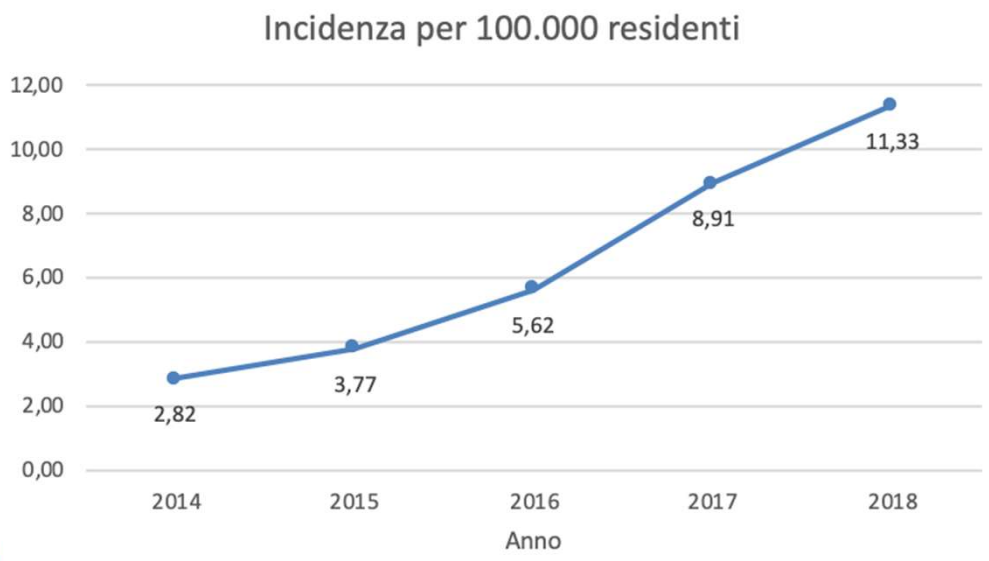
Raghu G, et al. *Am J Respir Crit Care Med*. 2006;174(7):810–816

I pazienti con IPF nella Regione Lazio

Aumento nel numero di pazienti presi in carico in ogni anno dai centri IPF

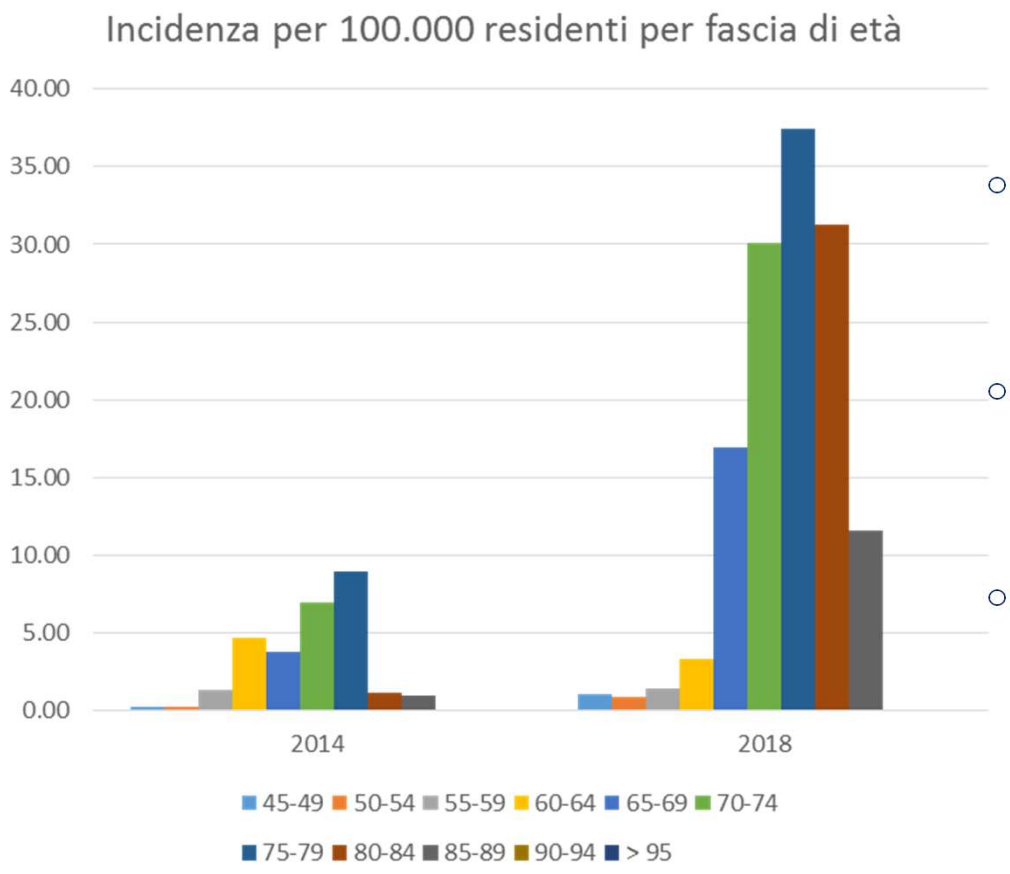


- Si è passati dagli 81 pazienti del 2014 ai 344 nel 2018, con un tasso di incremento annuo medio del 44%.
- Gli incrementi maggiori nel numero annuo di pazienti presi in carico si sono avuti negli ultimi due anni (2017-2018).
- Anche analizzando il tasso di incidenza (pazienti presi in carico/popolazione residente con età ≥ 45 anni) emerge un trend crescente.



Varone F et al Poster AIPO 2019

I pazienti con IPF nella Regione Lazio



Aumento nel numero di pazienti presi in carico con età > 65 anni

- La quota parte di over 75 anni tende a crescere negli anni (30.9% del 2014 vs. 50.1% dei casi nel 2018).
- In pochi casi i pazienti con diagnosi di IPF hanno un'età inferiore ai 45 anni (max annuo 1.2%, 0.3% nel 2018).
- Negli anni considerati emerge un aumento del **tasso di incidenza** (per 100.000 residente) **per le fasce di età ≥ 65 anni**.

Varone F et al Poster AIPO 2019

Clinical Predictors of a Diagnosis of Idiopathic Pulmonary Fibrosis

Charlene D. Fell[1], Fernando J. Martinez[2], Lyrica X. Liu[3], Susan Murray[3], MeiLan K. Han[2], Ella A. Kazerooni[4], Barry H. Gross[4], Jeffrey Myers[5], William D. Travis[6], Thomas V. Colby[7], Galen B. Toews[2], and Kevin R. Flaherty[2]

Am J Respir Crit Care Med.
2010;181(8):832–837

Data from 97 patients with biopsy-proven IPF and 38 patients with other IIPs

TABLE 3. UNIVARIATE LOGISTIC REGRESSION MODELS OF VARIABLES PREDICTING A DIAGNOSIS OF IDIOPATHIC PULMONARY FIBROSIS

	OR (95% CI)	*P* Value
Age	1.11 (1.06, 1.16)	<0.0001
Male sex	1.96 (0.92, 4.19)	0.08
Ever smoker	1.28 (0.58, 2.80)	0.54
HRCT score		
HRCT alveolar score	0.61 (0.43, 0.87)	0.007
HRCT interstitial score	17.20 (5.41, 54.70)	<0.0001
Pulmonary function		
FVC % predicted	0.18 (0.02, 1.59)	0.12
DL_{CO} % predicted	0.48 (0.04, 6.01)	0.57
6MWT Variables		
Desaturation <88%	0.63 (0.20, 1.93)	0.41
Distance per 1,000 ft	1.06 (0.35, 3.26)	0.91

Definition of abbreviations: CI = confidence interval; D_{LCO} = diffusion capacity for carbon monoxide; HRCT = high-resolution computed tomography scan of the chest; OR = odds ratio; 6MWT = 6-minute walk test.

TABLE 4. POSITIVE PREDICTIVE VALUE, SPECIFICITY, SENSITIVITY, AND NEGATIVE PREDICTIVE VALUE WHEN CLASSIFYING PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS BASED ON BEING AT LEAST AS OLD AS THE AGE INDICATED

Age (*yr*)	PPV	Specificity	Sensitivity	NPV
30	72	0	100	NA
35	72	5	99	67
40	74	11	98	67
45	74	16	95	55
50	78	34	92	62
55	83	58	80	54
60	87	76	61	43
65	91	89	43	38
70	95	97	21	32
75	100	100	6	29
80	100	100	1	28

Definition of abbreviations: NA = not applicable; NPV = negative predictive value; PPV = positive predictive value.
Data expressed as percentages.

The Aging Lung

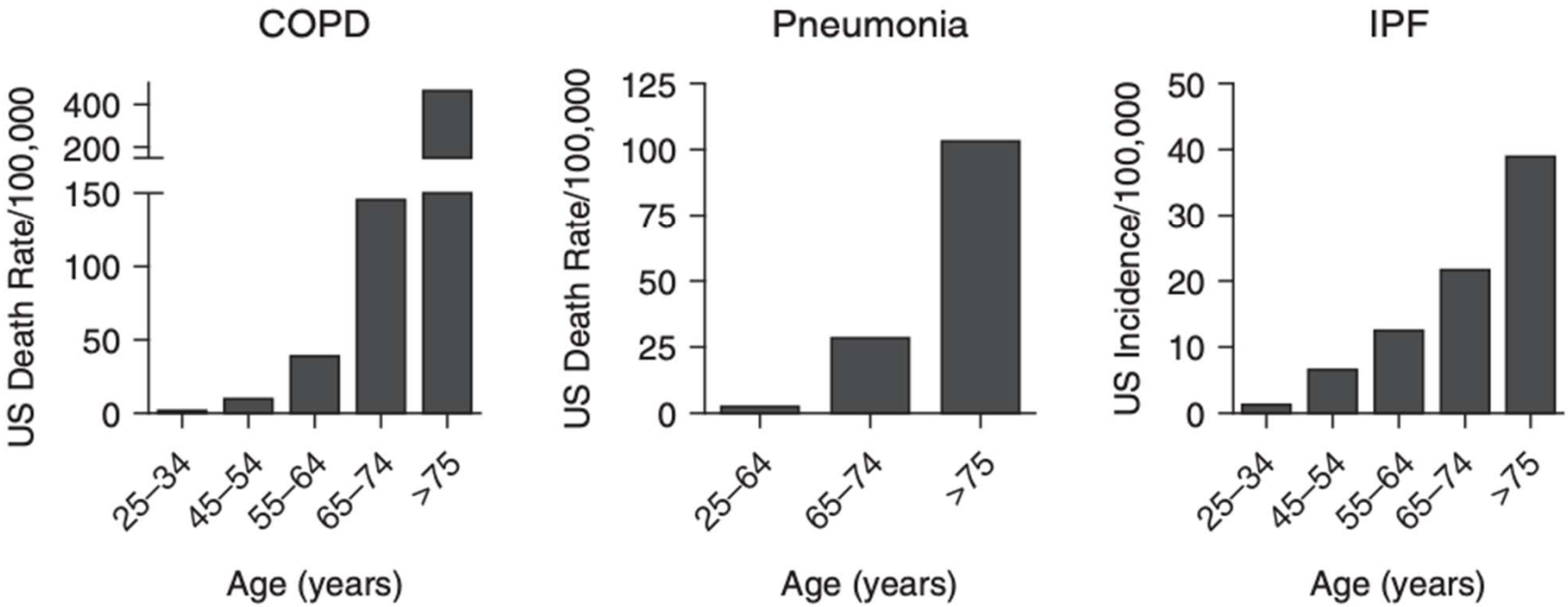


Figure 1. Lung disease is more common in the elderly. Estimates of annual U.S. death rates for chronic obstructive pulmonary disease (COPD) and pneumonia and the estimated annual incidence rate for idiopathic pulmonary fibrosis (IPF) are shown. Data from References 4, 107, and 108.

Thannickal VJ et al, AJRCCM, Volume 191 Number 3 February 1 2015

Cigarette Smoking: A Risk Factor for Idiopathic Pulmonary Fibrosis

KATHY B. BAUMGARTNER, JONATHAN M. SAMET, CHRISTINE A. STIDLEY, THOMAS V. COLBY, JAMES A. WALDRON, and COLLABORATING CENTERS

Division of Epidemiology and Cancer Control, University of New Mexico Health Sciences Center, and Department of Family and Community Medicine, University of New Mexico School of Medicine, Albuquerque, New Mexico; Department of Epidemiology, School of Hygiene and Public Health, Johns Hopkins University, Baltimore, Maryland; Department of Laboratory Medicine and Pathology, Mayo Clinic Scottsdale, Scottsdale, Arizona; and Department of Pathology, University of Arkansas for Medical Sciences, Little Rock, Arkansas

TABLE 4

ODDS RATIOS AND 95% CONFIDENCE INTERVALS FOR SMOKING VARIABLES ADJUSTED FOR AGE

Characteristic	No. Cases	No. Controls	OR	CI
Cigarettes				
Never	69	183	1.00	–
Ever	179	308	1.59	(1.1–2.4)
Smoking status				
Never	69	183	1.00	–
Former	137	205	1.90	(1.3–2.9)
Current	42	103	1.06	(0.6–1.8)
Cigarette type*				
Mostly filtered	67	109	1.00	–
Mixed	66	117	1.02	(0.6–1.7)
Mostly nonfiltered	43	76	0.78	(0.4–1.4)
Pack-yr*				
⩽ 20	51	121	1.00	–
21–40	68	73	2.26	(1.3–3.8)
> 40	57	108	1.12	(0.7–1.9)

* Smokers only; missing data for nine subjects.

Am J Respir Crit Care Med. 1997;155(1):242–248.

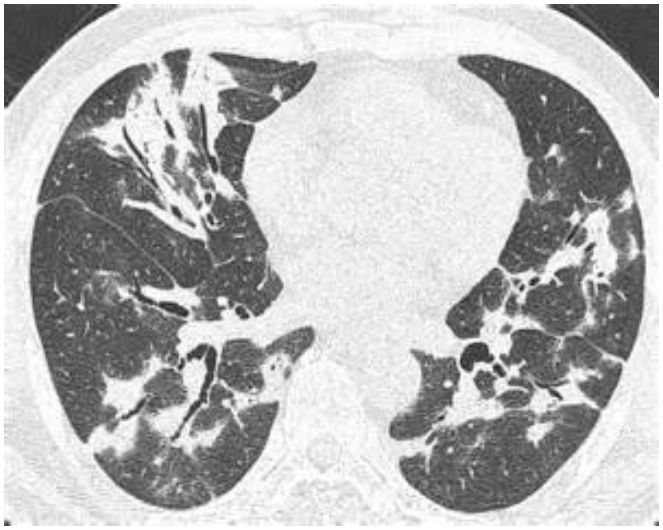
TABLE 1 Patient characteristics and risk factors in the total cohort by idiopathic pulmonary fibrosis (IPF) disease duration

	Patients	Total cohort	Subgroups		
			Prevalent IPF#	Incident IPF¶	p-value
Patients		502	331	171	
Males	502	391 (77.9)	243 (73.4)	148 (86.6)	0.001
Age years	502	68.7±9.4	67.5±9.8	71.0±8.0	<0.001
Body mass index kg·m^{-2}	502	27.6±4.1	27.4±4.2	28.2±3.8	0.048
Smoking status	502				
Never		195 (38.8)	140 (42.3)	55 (32.2)	0.087
Previous		302 (60.2)	188 (56.8)	114 (66.7)	
Current		5 (1.0)	3 (0.9)	2 (1.2)	
6-min walk distance m	502	267.6±199.7	266.7±198.7	269.4±202.1	0.886
Symptom duration months	458	46.9±52.5	57.6±54.4	27.2±42.3	<0.001
Disease duration months	498	27.6±41.9	41.3±46.2	1.4±2.0	0.036
Risk factors	502				
Environmental exposure		136 (27.1)	80 (24.2)	56 (32.8)	0.028
Gastro-oesophageal reflux		148 (29.5)	106 (32.0)	42 (24.6)	0.136
Genetic predisposition		20 (4.0)	13 (3.9)	7 (4.1)	0.887
Exposure to drugs associated with IPF		8 (1.6)	5 (1.5)	3 (1.8)	0.309

Data are presented as n, n (%) or mean±SD, unless otherwise stated. #: duration since diagnosis ≥6 months; ¶: duration since diagnosis <6 months.

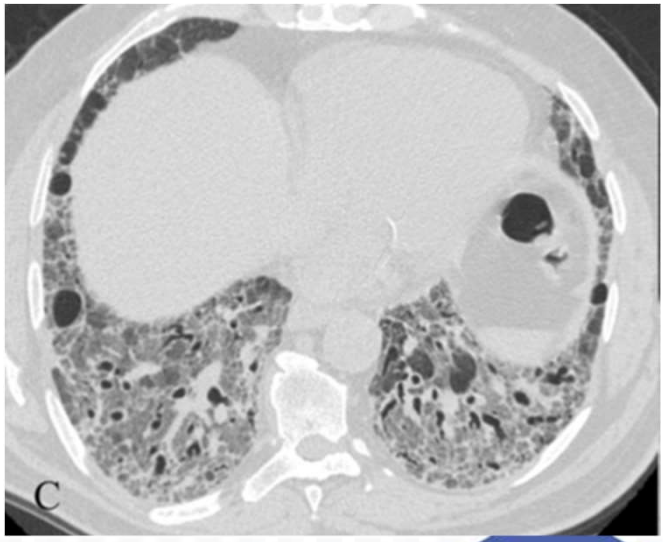
Behr J et al, Eur Respir J. 2015 Jul;46(1):186-96.

Onset of Symptoms



ACUTE

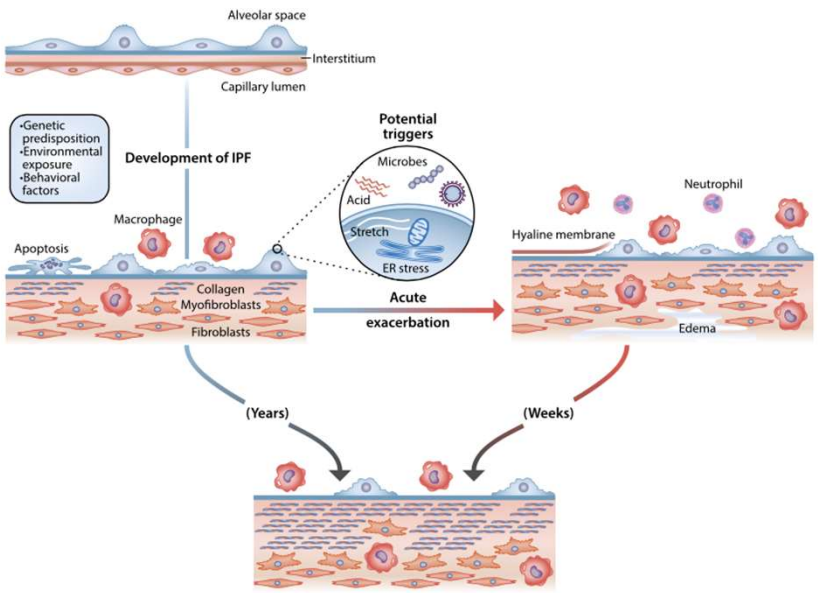
- AIP
- Acute HP, Acute EP
- Drug Reaction
- COP
- CTD (e.g acute lupus capillaritis)
- DAH

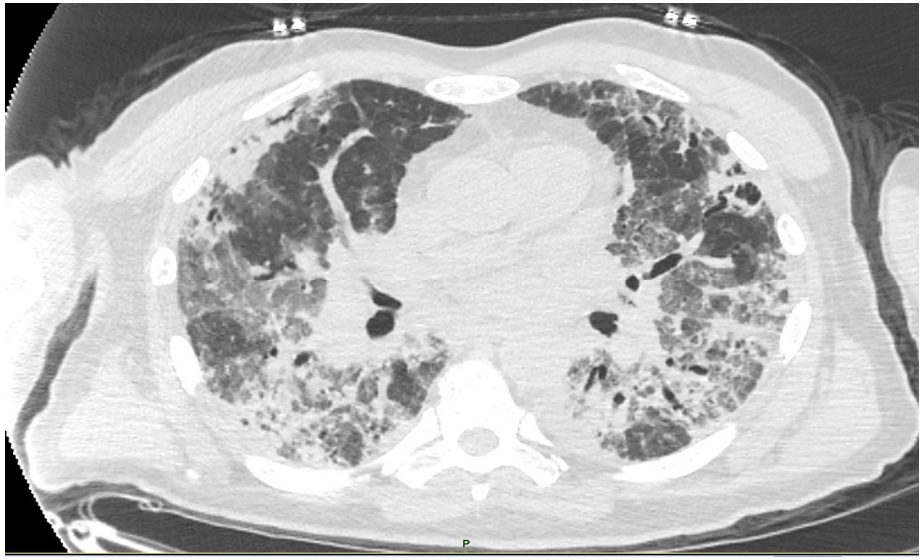


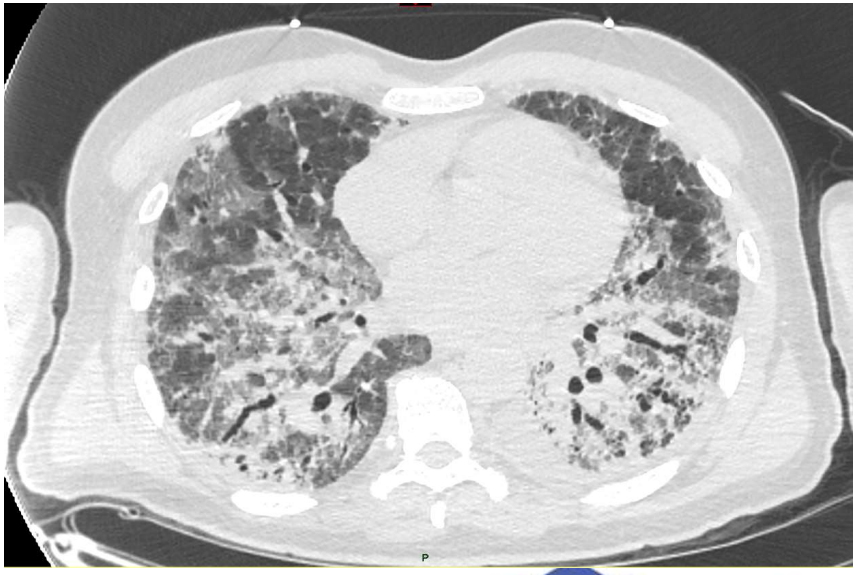
CHRONIC

- IPF
- NSIP
- CTD-ILD
- CHP
- CEP
- Sarcoidosis

KC Meyer Translational Respiratory Medicine 2014, 2:4







Am J Respir Crit Care Med. 2016 Aug 1;194(3):265-75. doi: 10.1164/rccm.201604-0801CI

Comorbidities

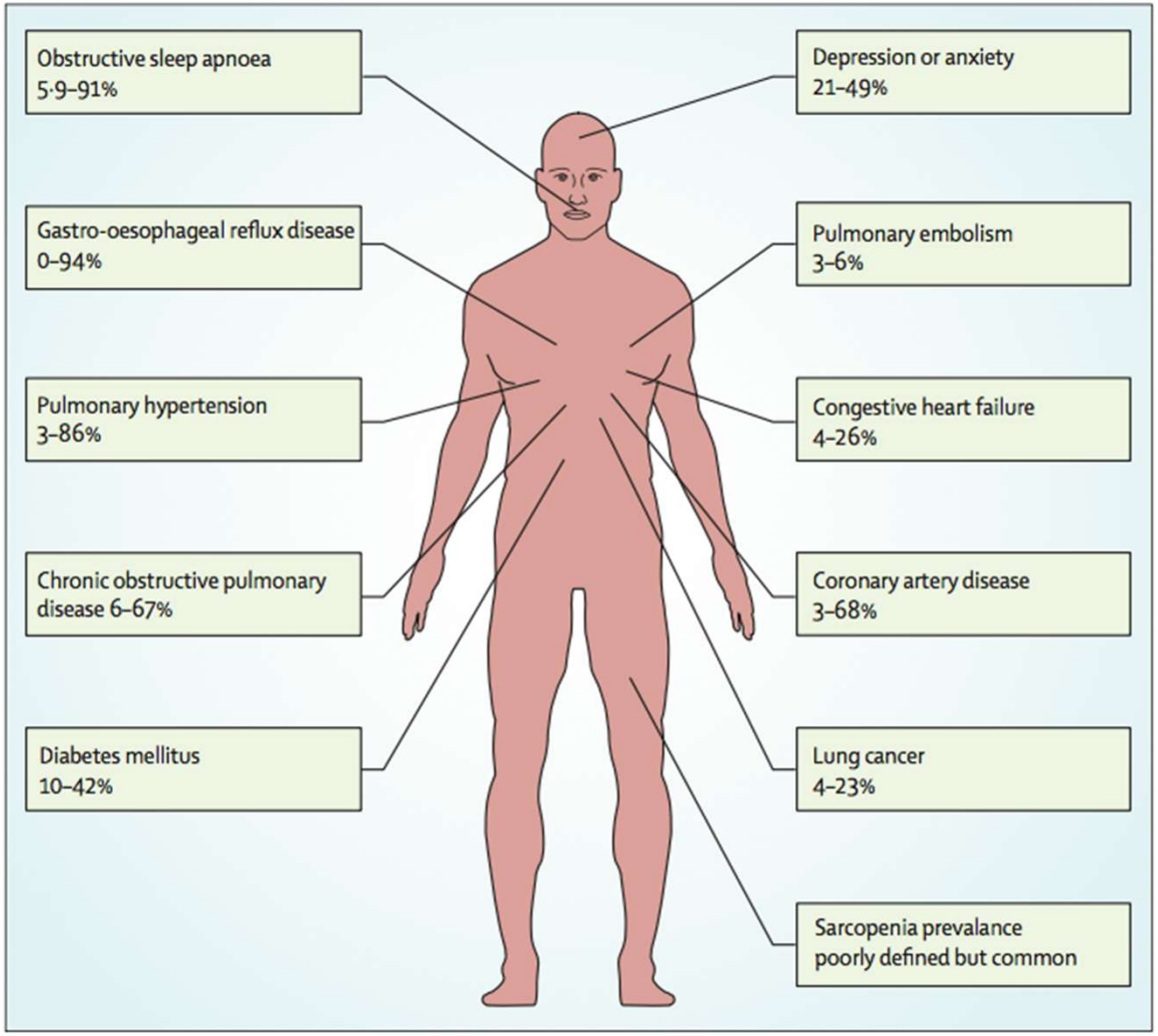


Figure 1: **Prevalence of the various comorbidities of idiopathic pulmonary fibrosis**

King CS, Nathan SD, Lancet Resp Med ,2016 doi.org/10.1016/S2213-2600(16)30222-3

Comorbidities

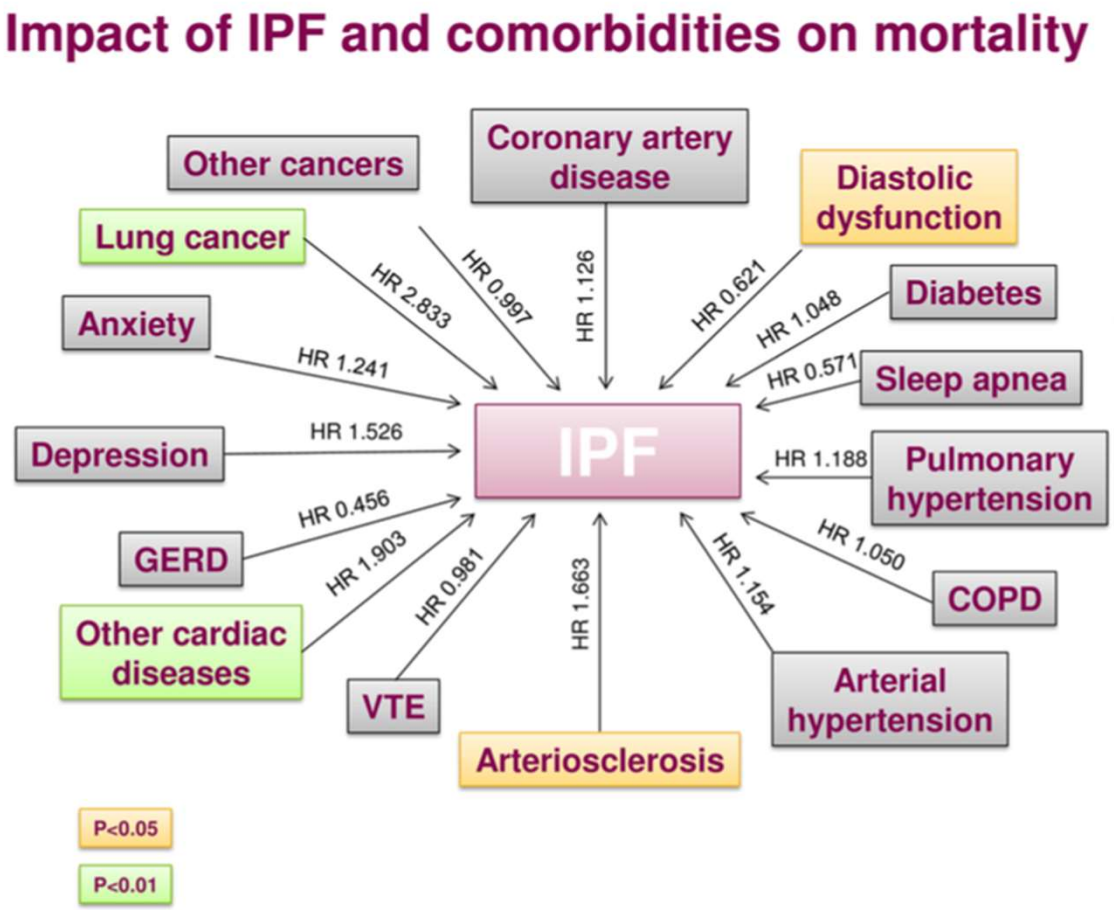


Fig 5. Impact of idiopathic pulmonary fibrosis and comorbidities on mortality. Hazard ratios (HR) have been determined using a predictive multivariate Cox proportional hazards regression model.

Kreuter M, et al PLOS ONE | DOI:10.1371/journal.pone.0151425 March 29, 2016

The Impact of Lung Cancer on Survival of Idiopathic Pulmonary Fibrosis

CHEST

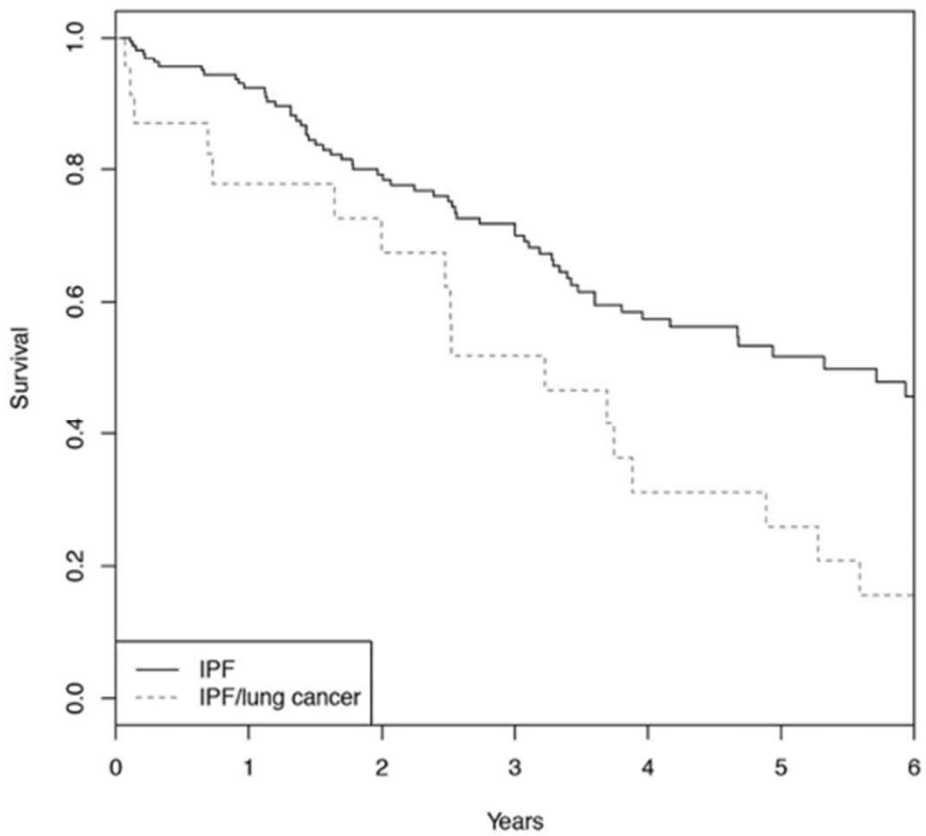


Figure 3 – *Survival curve of patients with IPF with and without LC (time 0 is diagnosis of IPF for both groups). One-y and 3-y survival among the two groups were 78% and 52% in the study group and 92% and 70% in the control group, respectively, by Kaplan-Meier analysis. IPF = idiopathic pulmonary fibrosis. See Figure 2 legend for expansion of other abbreviation.*

S. Tomassetti et al, Chest 2015; 147(1):157-164

Exposures

Metal dusts

Wood dusts

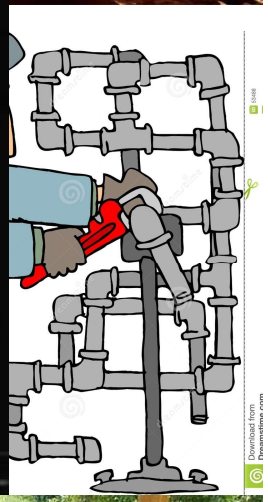
Silica

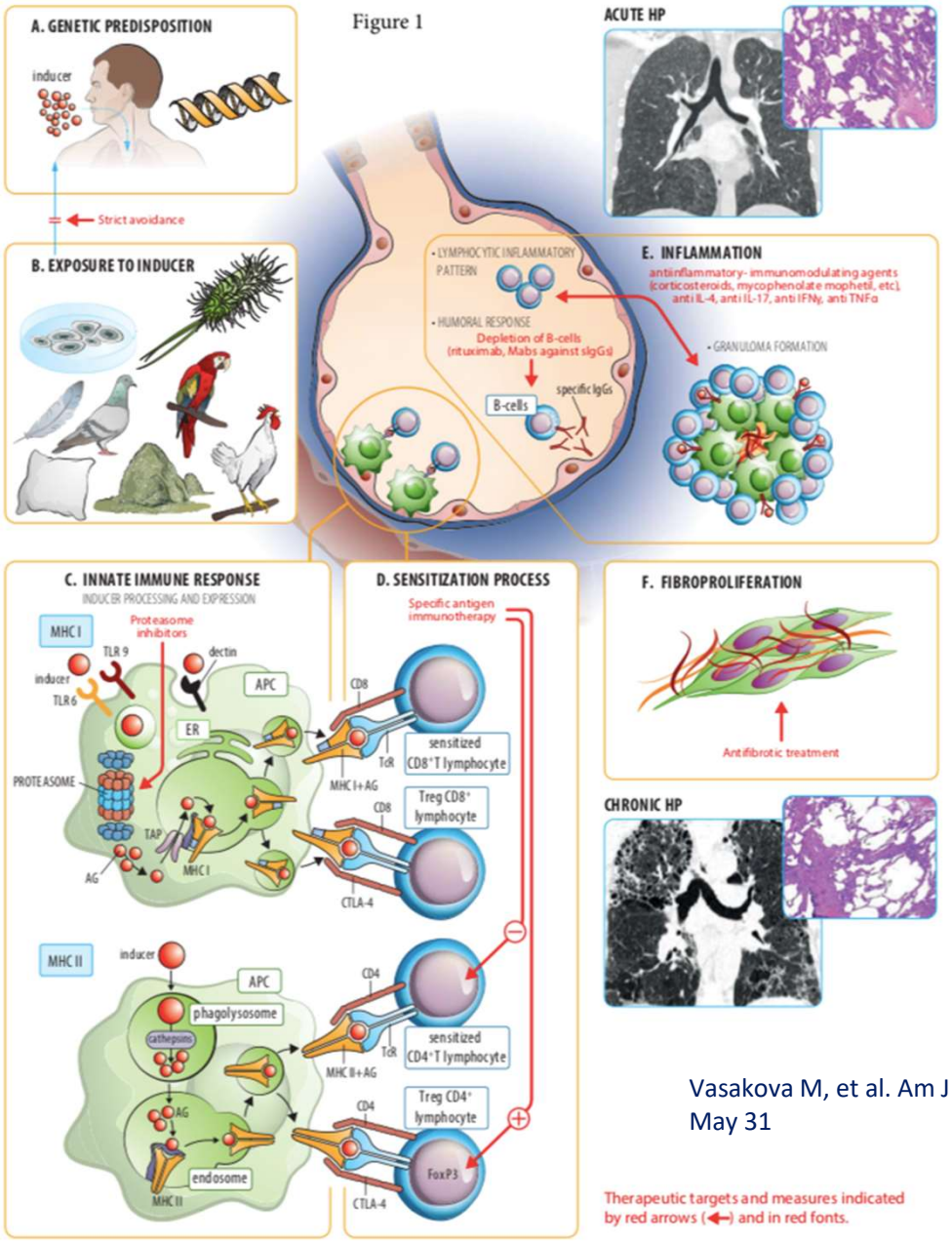
Asbestos

Fungal, bacterial, protozoal, and animal proteins

Molds

Isocyanates found in paints, foams, and sealants



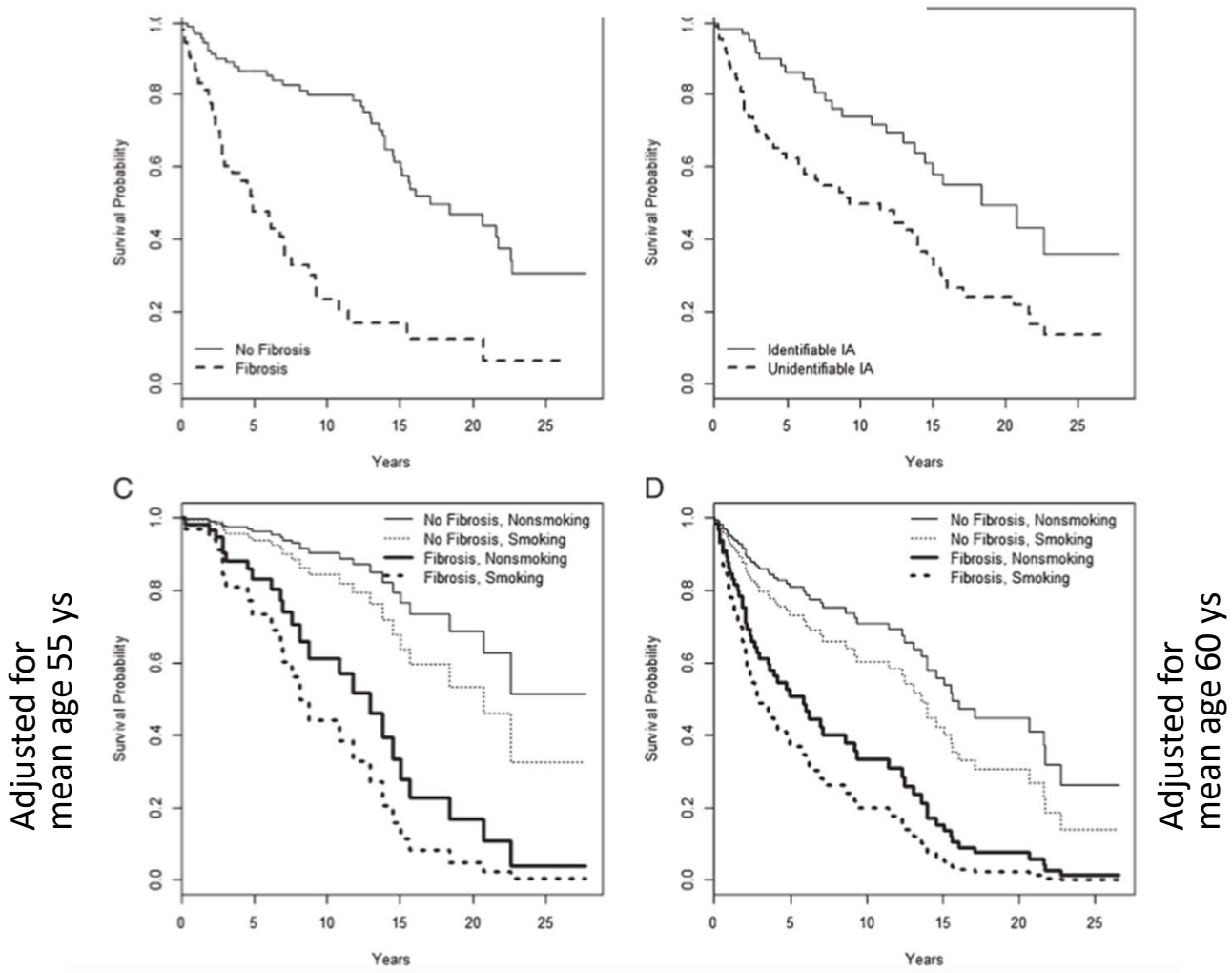


Vasakova M, et al. Am J Respir Crit Care Med. 2019 May 31

Therapeutic targets and measures indicated by red arrows (←) and in red fonts.

Identifying an Inciting Antigen Is Associated With Improved Survival in Patients With Chronic Hypersensitivity Pneumonitis

142 consecutive adult patients



Chest. 2013 Nov;144(5):1644-1651

Familial pulmonary fibrosis is the strongest risk factor for idiopathic pulmonary fibrosis

Table 2 Family history of pulmonary fibrosis and comorbidities of cases and controls.

Characteristic	IPF cases[a] (n = 100)	Control subjects[a] (n = 263)	OR (CI95%)
Familial IPF (parent and/or sibling)	20 (20.0)	7 (2.7)	9.1(3.7–22.4) $p < 0.0001$
Past gastroesophageal reflux	23 (23.0)	23 (8.7)	3.1 (1.7–5.9) $p < 0.0001$
Past gastritis	40 (40.0)	66 (25.1)	1.9 (1.2–3.2) $p = 0.006$
Type 2 diabetes mellitus	30 (30.0)	50 (19.0)	1.8 (1.1–3.1) $p = 0.02$
Past or current cardiac disease	13 (13.0)	17 (6.5)	2.2 (1–4.6) $p = 0.05$

[a] Data correspond to n (%).

Table 3 Crude and adjusted odds ratios for IPF.

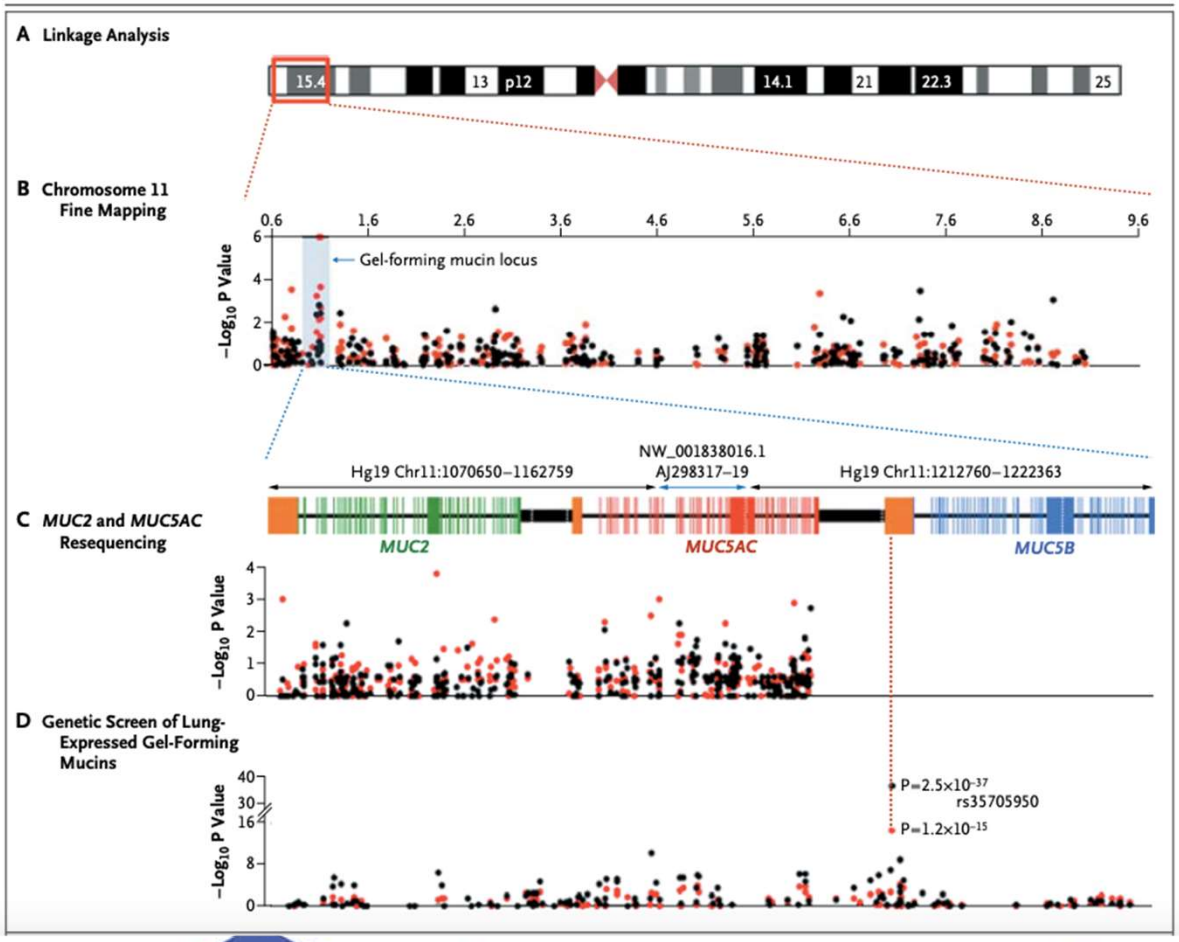
Variable	Crude OR (95% CI)	Adjusted OR (95% CI)
Parent or sibling with IPF	9.1 (3.7–22.4) $p < 0.0001$	6.1 (2.3–15.9) $p < 0.0001$
Former smoker	2.7 (1.7–4.4) $p < 0.0001$	2.5 (1.4–4.6) $p = 0.003$
Past or current occupational exposure to dusts, smokes, gases or chemicals	2.4 (1.4–4.0) $p = 0.001$	2.8 (1.5–5.5) $p = 0.002$
Past or current gastroesophageal reflux	3.1 (1.7–5.9) $p < 0.0001$	2.9 (1.3–6.6) $p = 0.007$
Type 2 diabetes	1.8 (1.1–3.1) $p = 0.02$	1.6 (0.9–3.0) $p = 0.1$

García-Sancho C, et al *Respir Med*. 2011;105(12):1902–1907.

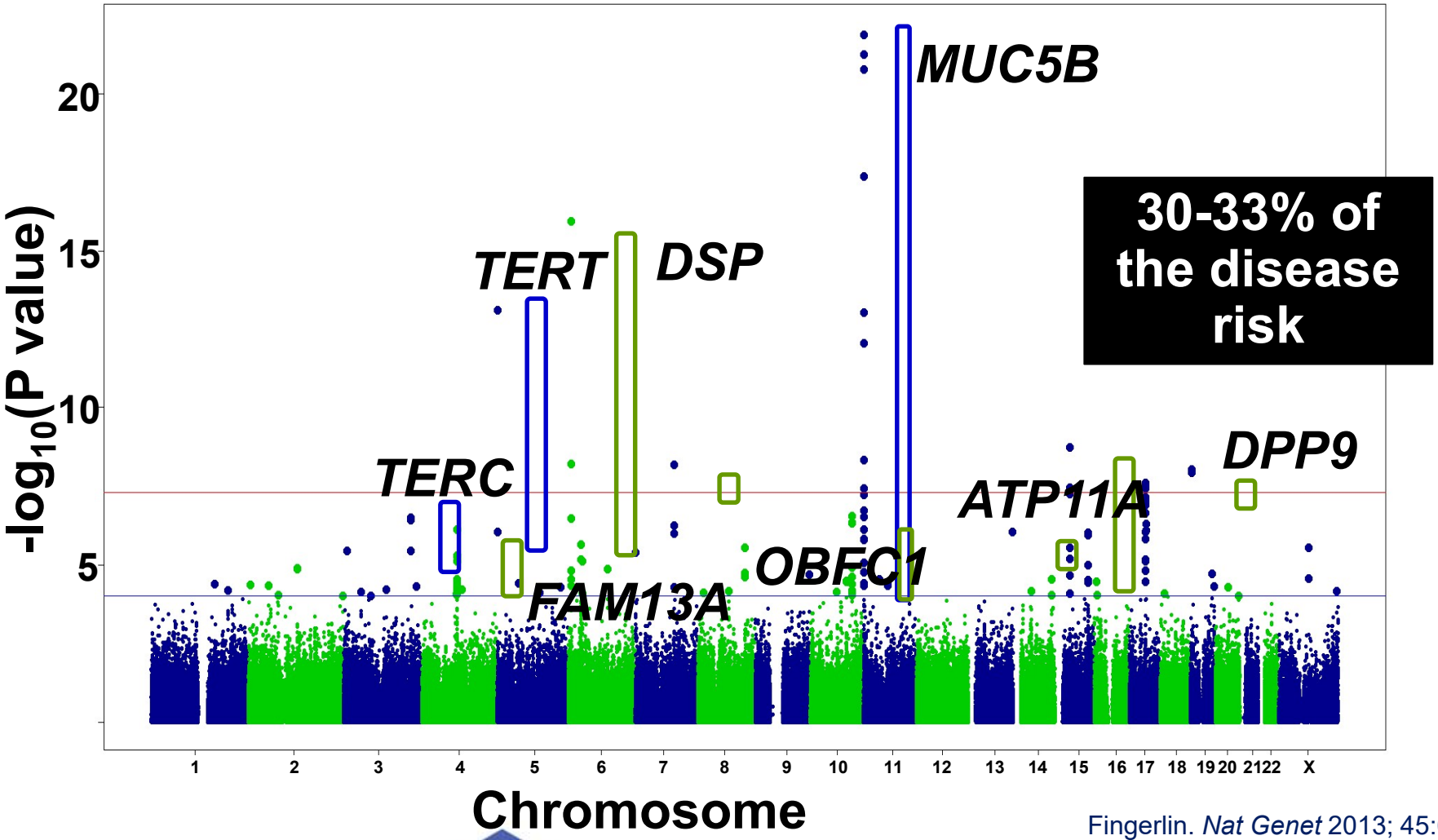
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

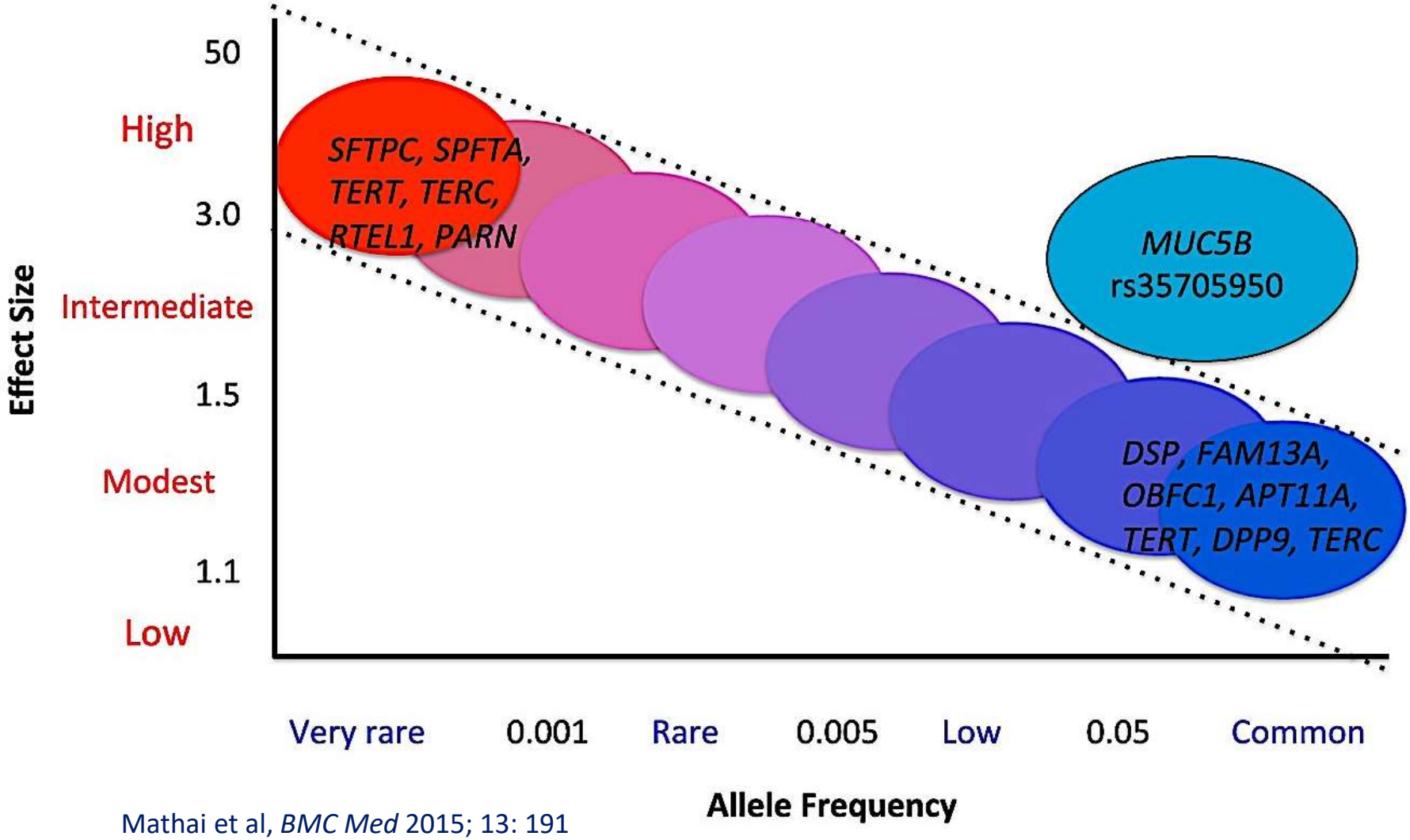
A Common *MUC5B* Promoter Polymorphism and Pulmonary Fibrosis



Genome Wide Association Study in IIP



Fingerlin. *Nat Genet* 2013; 45:613

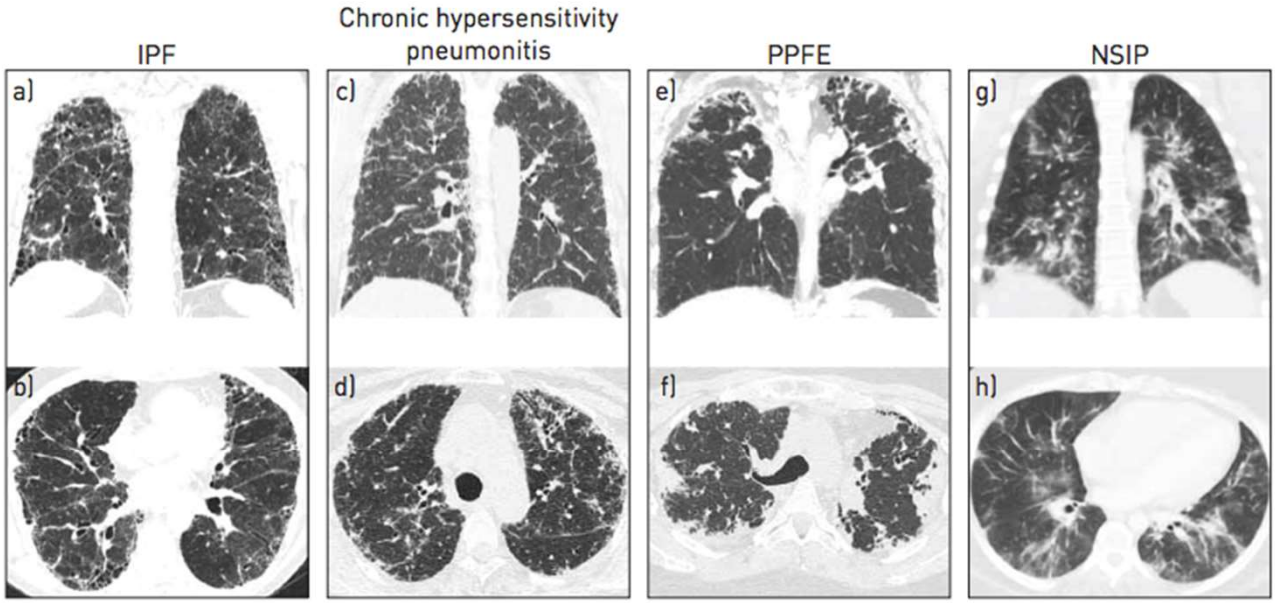


Mathai et al, *BMC Med* 2015; 13: 191

Telomeropathy

TERT
TERC
RTEL1

PARN



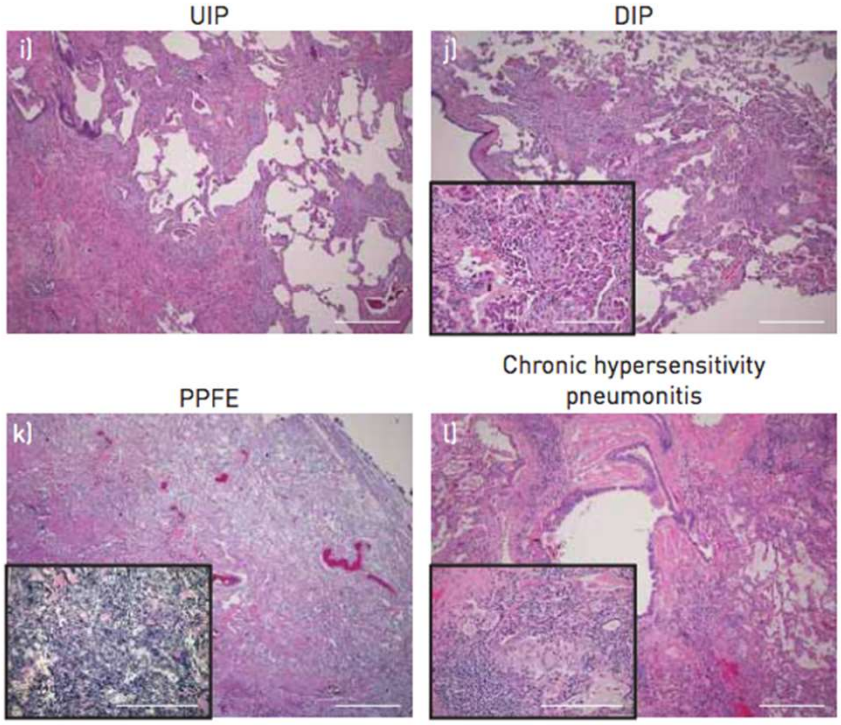
Table

Table 1. Key Personal and Family History Elements	
	Short Telomere Syndromes
Adult ILD	++
Premature greying*	++
Cryptogenic cirrhosis	++
Aplastic Anemia	++
Myelodysplasia/Leukemia	+

Newton CA, et al. Eur Respir J. 2016;48(6):1710–1720

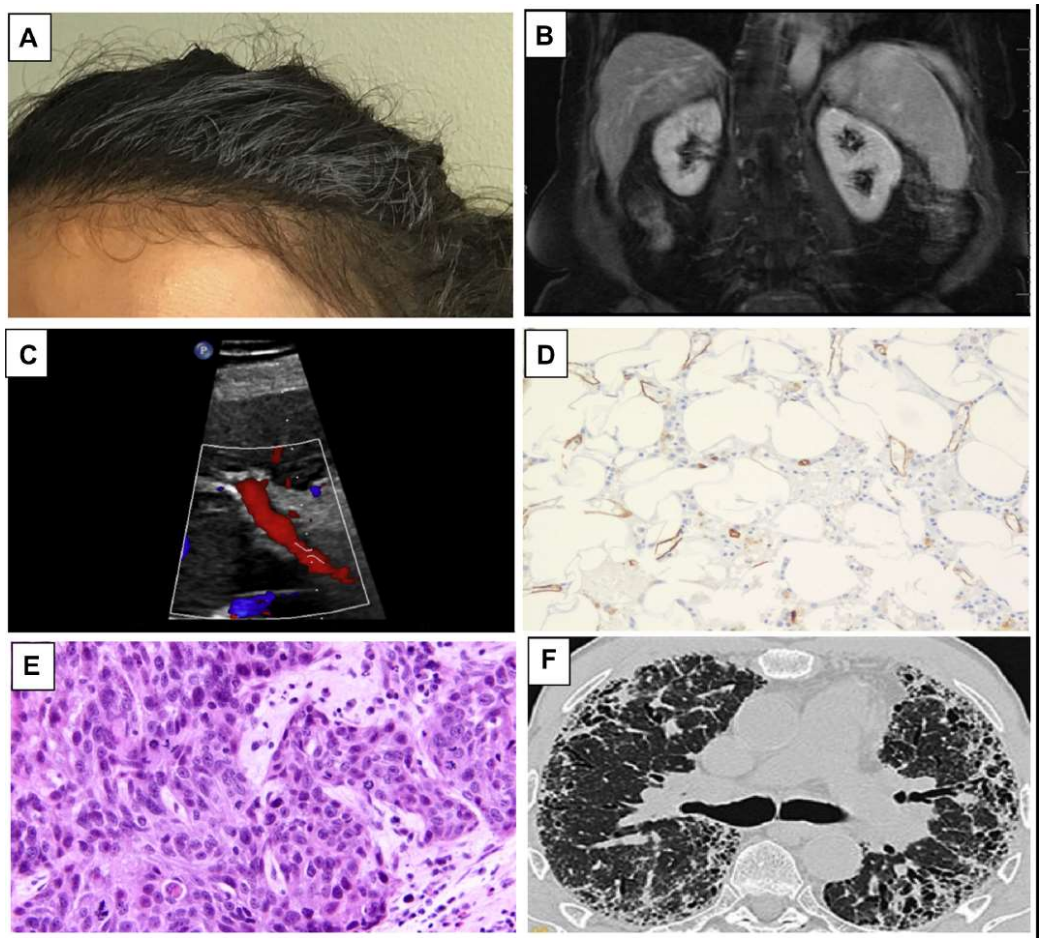
Family members with same *TERT* mutation

Family members with same *TERC* mutation



Integrating Genomics Into Management of Fibrotic Interstitial Lung Disease

CHEST



Adegunsoye A, et al. Chest. 2019;155(5):1026–1040

Drugs

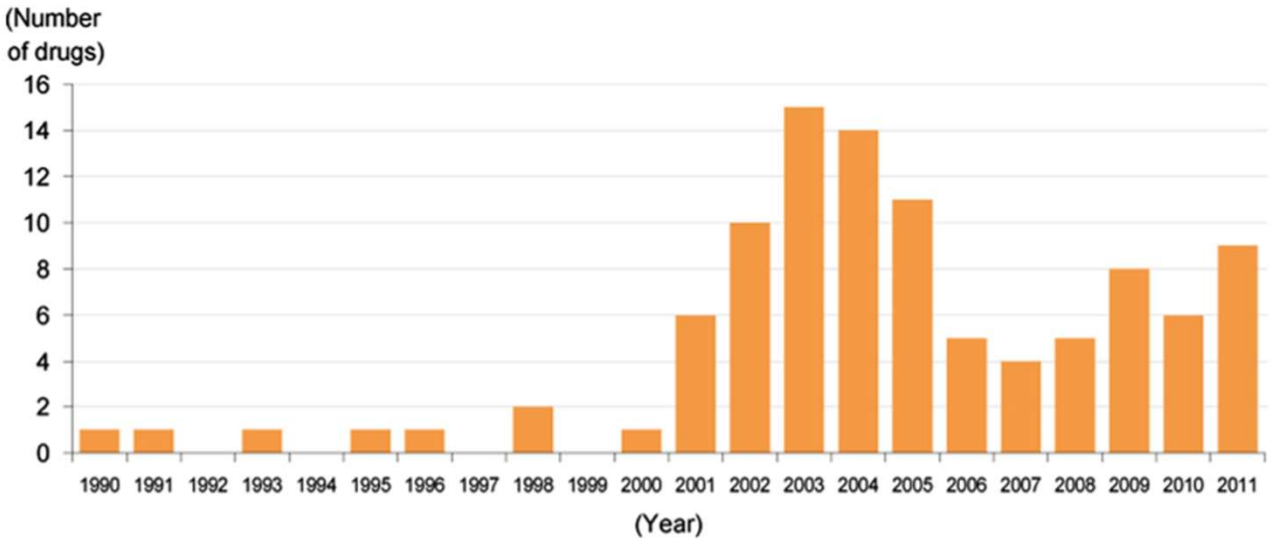
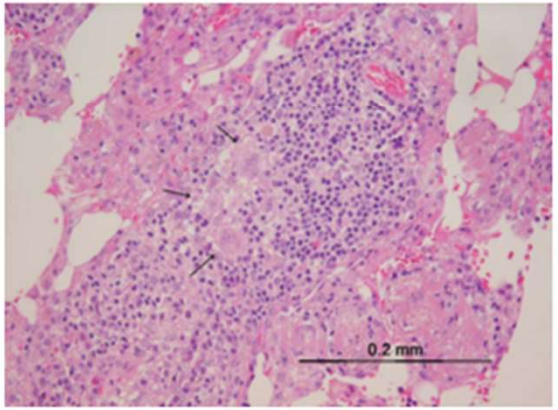


Fig. 1 – Number of drugs that have been reported to cause drug-induced (interstitial) pneumonia. The number of drugs that have been reported to cause drug-induced (interstitial) pneumonia between 1990 and 2011 according to data reported in the Pharmaceuticals and Medical Devices Safety Information (Pharmaceutical and Food Safety Bureau, Ministry of Health, Labour & Welfare) is shown.

Kubo K, et al. Respiratory investigation 51 (2013) 260–277

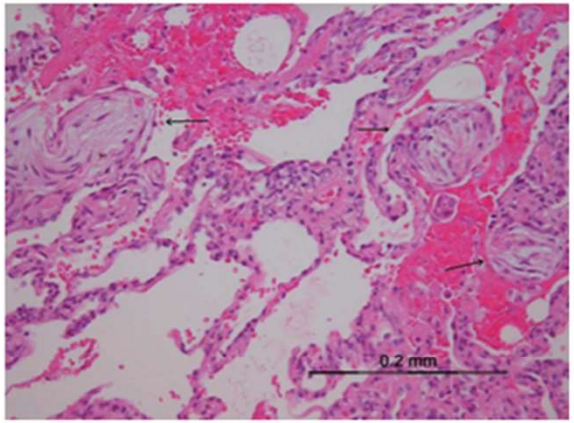
Schwaiblmair M et al, The Open Respiratory Medicine Journal, 2012, 6, 63-74

(a)



HP

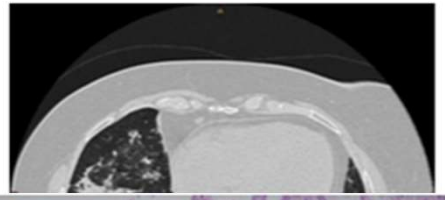
(b)

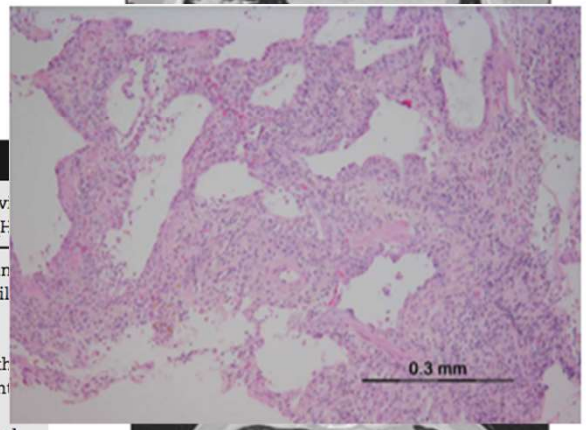


OP

NSIP

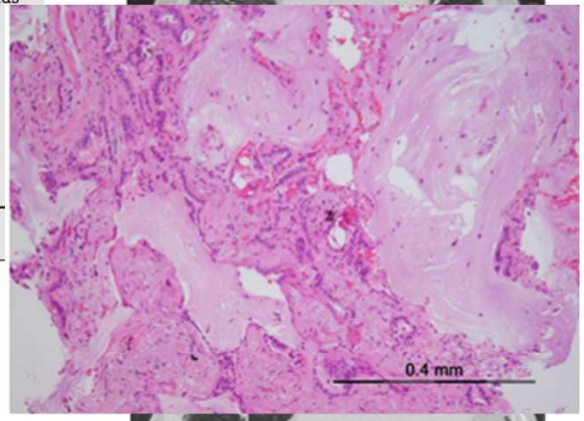
(a)

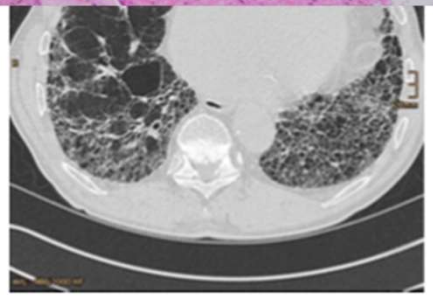




lmonary disease.		
inophilic umonia (EP)	Organizing pneumonia (OP)	Hypersensitiv pneumonia (H
fuse infiltrative dows or ground ss opacities dominantly in the iphery	Multiple, nonsegmental infiltrates in both lung fields	Decreased lun volume and il defined interstitial shadows in th basal segmen both lungs
und glass opacities, ltrative shadows, lule-like shadows, diastinal nphadenopathy, ural effusion, erlobular septum, l thickening of ncho-vascular ndles	Nodular shadows, patchy shadows, ground glass opacities, and reversed halo sign in the subpleura or along the broncho-vascular bundles	Diffuse ground glass opacities in both lung fields

UIP



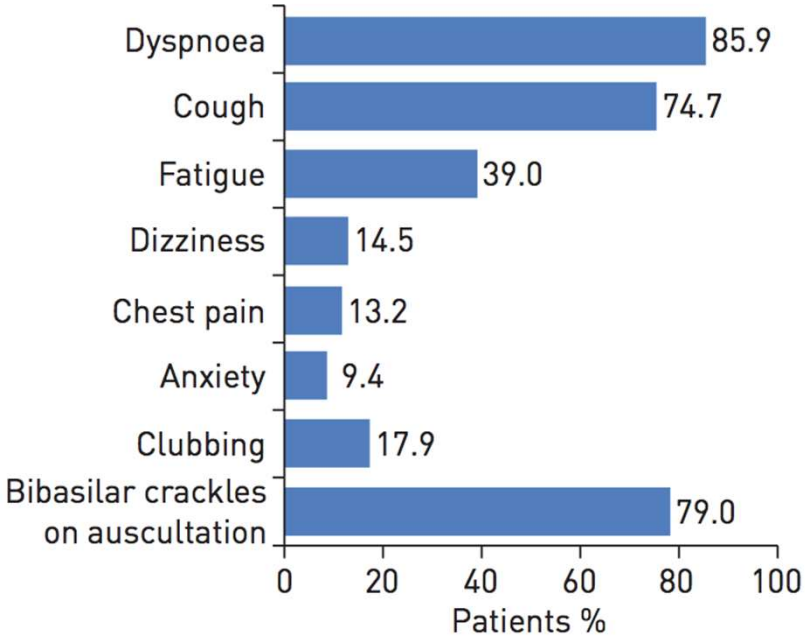


Kubo K, et al. Respiratory investigation 51 (2013) 260–277

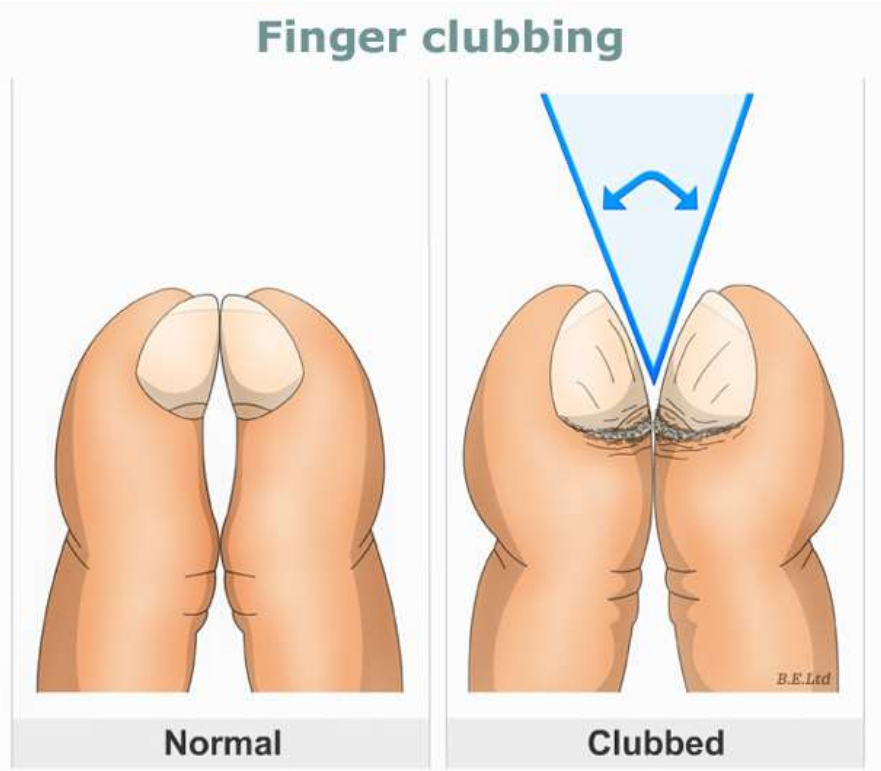
Schwaiblmair M et al, The Open Respiratory Medicine Journal, 2012, 6, 63-74

Physical Examination

- No specific sign for IPF
- Velcro crackles
- Clubbing
- Cianosis



Behr J et al, Eur Respir J. 2015 Jul;46(1):186-96.



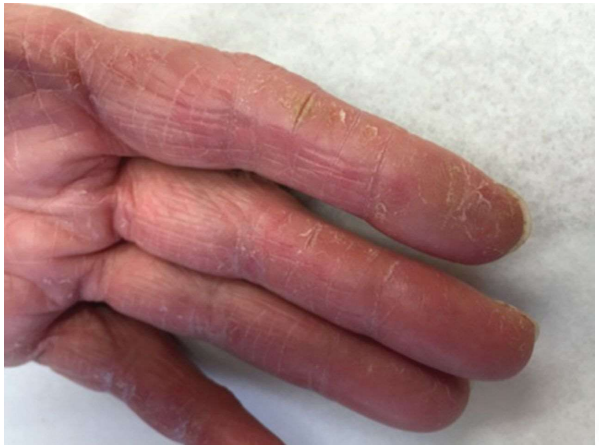
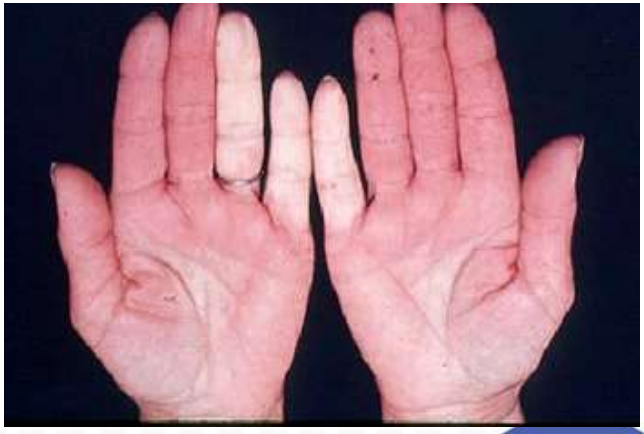


Table 3. Useful antibodies for CTD-ILD assessment [30]

Autoantibody	Commonly associated CTD
High-titer ANA (≥1:320 titer)	Many
High-titer RF (≥60 IU/ml)	RA, SjS, SLE
Anti-CCP	RA
Anti-centromere	SSc
Anti-nucleolar ANA	SSc
Anti-Ro (SSA)	Many
Anti-La (SSB)	SLE, SjS
Anti-Smith	SLE
Anti-ribonucleoprotein	SLE, MCTD
Anti-dsDNA	SLE
Anti-topoisomerase (Scl-70)	SSc
Anti-tRNA synthetase antibodies	PM/DM (anti-synthetase syndrome)
Anti-PM-Scl	SSc/myositis overlap
Anti-Th/To	SSc
Anti-U3 ribonucleoprotein	SSc
Anti-MDA-5 (CADM)	Clinical amyopathic dermatomyositis

SLE = Systemic lupus erythematosus; MCTD = mixed connective tissue disease.



KC Meyer Translational Respiratory Medicine 2014, 2:4

Serological testing for excluding connective tissue disease

2018 guidelines[1]	
Recommendation	Serological testing to exclude connective tissue diseases as a potential cause of ILD
Rationale	Exclusion of other causes of ILD, including connective tissue disease-ILD are mandatory for a diagnosis of IPF and routine serological testing is the best way to do this

2011 guidelines[2]	Diagnosis of IPF requires exclusion of other known causes of ILD (eg domestic and occupational environmental exposures, connective tissue disease, and drug toxicity)
Fleischner Society[3]	A systematic assessment for connective tissue disease is necessary for an IPF diagnosis. Serological findings can suggest an autoimmune disorder eg mixed-connective tissue disease

ILD, interstitial lung disease; IPF, idiopathic pulmonary fibrosis

1. Raghu G *et al. Am J Respir Crit Care Med* 2018;198:e44–e68; 2. Raghu G *et al. Am J Respir Crit Care Med* 2011;183:788–824; 3. Lynch DA *et al. Lancet Respir Med* 2018;6:138–153

Connective Tissue Disease Associated Interstitial Lung Disease

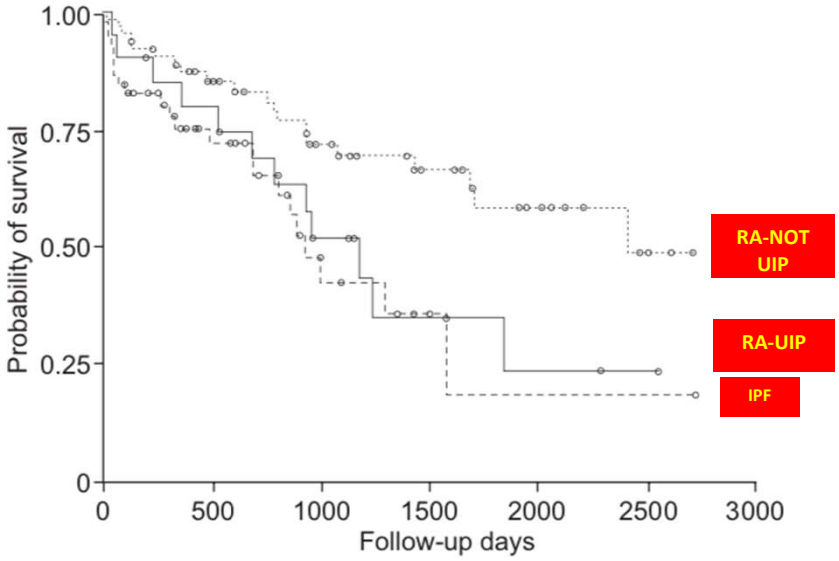
Connective Tissue Disease	Type of ILD	Estimated Prevalence of ILD	CTD is Occult
Dermatomyositis Polymyositis Anti-synthetase syndrome	NSIP with OP NSIP OP UIP	40%	Often
Sjogren's syndrome	NSIP UIP LIP	Up to 40%	Less often
Systemic sclerosis	NSIP UIP	50% (80% subclinical)	Less often
Rheumatoid arthritis	UIP NSIP OP	50% (80% subclinical)	Less often
Interstitial pneumonia with autoimmune features	NSIP OP NSIP/OP UIP	10% (30% subclinical)	Often

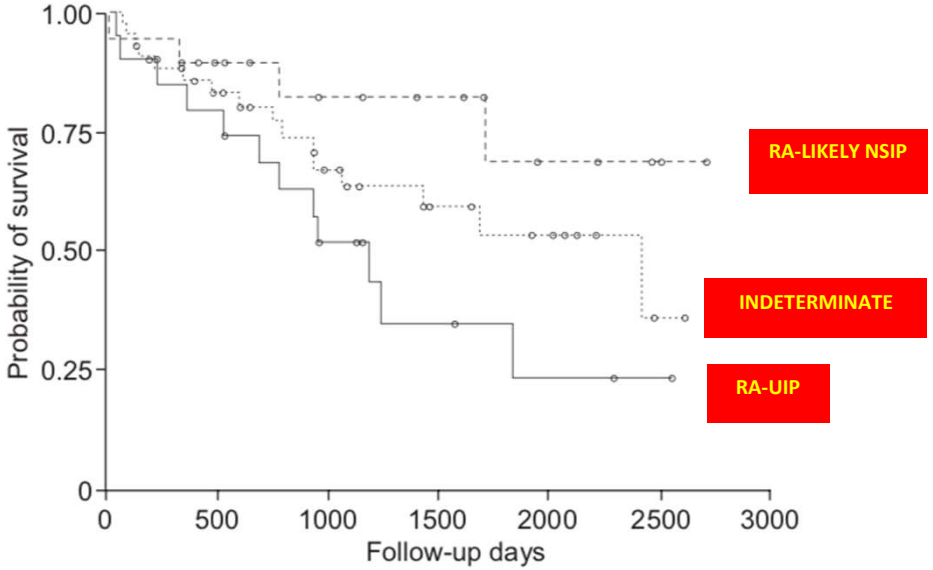
CTD: Connective tissue disease; ILD: Interstitial lung disease; LIP: Lymphocytic interstitial pneumonia; OP: Organizing pneumonia; UIP: Usual interstitial pneumonia.

Raghu G et al. Am J Respir Crit Care Med 2018;198:e44–e68; 2

Usual interstitial pneumonia in rheumatoid arthritis-associated interstitial lung disease

E.J. Kim*, B.M. Elicker#, F. Maldonado¶, W.R. Webb#, J.H. Ryu¶, J.H. Van Uden#, J.S. Lee*, T.E. King Jr* and H.R. Collard*





Eur Respir J 2010; 35: 1322–1328

Connective Tissue Disease Associated Interstitial Lung Disease

Connective Tissue Disease	Laboratory Workup
All Patients with newly identified ILD	CRP (C-reactive protein), erythrocyte sedimentation rate, antinuclear antibodies (by immunofluorescence), rheumatoid factor, myositis panel, and anti–cyclic citrullinated peptide
Suspected Myositis	CPK, myoglobin, aldolase, antisynthetase antibodies (Jo-1 and others if available), anti–MDA5, anti– Mi-2, anti-NXP2), anti–TIF1-g, anti-SRP, anti-HMGCR, anti-SAE, anti-U1RNP, anti-PM/Scl75, anti-PM/ Scl100, and anti-Ku
Suspected Systemic sclerosis	anti–Scl-70/topoisomerase-1, anti-centromere, anti-RNA polymerase III, anti-U1RNP, anti-Th/To, anti-PMScl, U3 RNP (fibrillarin), and anti-Ku
Suspected Sjogren's syndrome	anti-SSA/Ro (Sjogren-specific antibody A) and anti-SSB/La
Suspected Vasculitis	anti- cytoplasmic antibodies

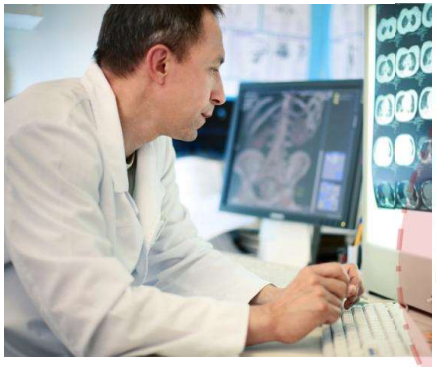
Raghu G et al. Am J Respir Crit Care Med 2018;198:e44–e68; 2

Rheumatologic Evaluation

Table 2. Suggested categories of ILD patients that require further rheumatologic evaluation [30]

1.	Women, particularly those younger than 50 years
2.	Any patient with extrathoracic manifestations highly suggestive of CTD i.e., Raynaud's phenomenon, esophageal hypomotility, inflammatory arthritis of the metacarpal-phalangeal joints or wrists, digital edema, or symptomatic KCS
3.	All cases of NSIP, LIP, or any ILD pattern with secondary histopathology features that might suggest CTD i.e., extensive pleuritis, dense perivascular collagen, lymphoid aggregates with germinal center formation, prominent plasmacytic infiltration
4.	Patients with a positive ANA or RF in high titer (generally considered to be ANA >1:320 or RF >60 IU/ml), a nucleolar-staining ANA at any titer, or any positive autoantibody specific as to a particular CTD i.e., anti-CCP, anti-Scl-70, anti-Ro, anti-La, anti-dsDNA, anti-Smith, anti-RNP, anti-tRNA synthetase

Fischer/Lee/Cottin Respiration 2015;90:177–184 DOI: 10.1159/000440665



Convegno di presentazione della versione italiana delle linee guida per la diagnosi di fibrosi polmonare idiopatica

Linee guida ufficiali ATS/ERS/JRS/ALAT per la pratica clinica

1 Febbraio 2020

Hotel Enterprise Milano

SOCIETÀ ITALIANA DI PNEUMOLOGIA

ITS ITALIAN THORACIC SOCIETY

AIPO ASSOCIAZIONE ITALIANA PNEUMOLOGI OSPEDALIERI

Idiopathic Interstitial Pneumonia

What Is the Effect of a Multidisciplinary Approach to Diagnosis?

TABLE 3. INTEROBSERVER AGREEMENT AT EACH DIAGNOSTIC STEP

Step	Clinicians [κ (95% CI)]	Radiologists [κ (95% CI)]	Clinicians–Radiologists [κ (95% CI)]	All Observers [κ (95% CI)]
1	0.41 (0.29, 0.52)	0.72 (0.57, 0.86)	0.39 (0.29, 0.49)	NA
2	0.51 (0.37, 0.64)	0.80 (0.67, 0.93)	0.44 (0.34, 0.54)	NA
3	0.67 (0.54, 0.79)	0.78 (0.65, 0.91)	0.55 (0.44, 0.66)	NA
4	0.75 (0.64, 0.86)	0.84 (0.72, 0.96)	0.78 (0.70, 0.86)	0.79 (0.71, 0.86)
5	0.86 (0.76, 0.95)	0.90 (0.80, 0.99)	0.88 (0.81, 0.96)	0.88 (0.81, 0.94)

Definition of abbreviations: CI = confidence interval for corresponding statistic; NA = not applicable.

TABLE 5. AGREEMENT OF CLINICIANS AND RADIOLOGISTS WITH PATHOLOGIST IMPRESSION

	Clinicians			Radiologists	
Step	A [κ (95% CI)]	B [κ (95% CI)]	C [κ (95% CI)]	A [κ (95% CI)]	B [κ (95% CI)]
1	0.22 (0.07, 0.36)	0.22 (0.09, 0.36)	0.38 (0.23, 0.54)	0.09 (0.0, 0.21)	0.14 (0.02, 0.27)
2	0.34 (0.20, 0.48)	0.20 (0.05, 0.34)	0.39 (0.24, 0.55)	0.12 (0.0, 0.26)	0.17 (0.04, 0.30)
3	0.34 (0.20, 0.48)	0.32 (0.17, 0.47)	0.39 (0.23, 0.54)	0.13 (0.0, 0.26)	0.19 (0.05, 0.32)
4	0.76 (0.63, 0.88)	0.79 (0.67, 0.91)	0.74 (0.61, 0.88)	0.81 (0.69, 0.94)	0.92 (0.84, 1.00)
5	0.89 (0.80, 0.99)	0.78 (0.65, 0.91)	0.89 (0.79, 0.99)	0.87 (0.76, 0.97)	0.92 (0.84, 1.00)

The consensus diagnosis of the pathologists without clinical or radiographic information (Table 2) was used for Steps 1–3. The consensus diagnosis of the pathologists after hearing the clinical/radiographic information and after a final group discussion (Table 1) was used for Steps 4 and 5, respectively.

Flaherty KR, et al AJRCCM. 2004;170(8):904–910

Multicentre evaluation of multidisciplinary team meeting agreement on diagnosis in diffuse parenchymal lung disease: a case-cohort study

Simon L F Walsh, Athol U Wells, Sujal R Desai, Venerino Poletti, Sara Piciucchi, Alessandra Dubini, Hilario Nunes, Dominique Valeyre, Pierre Y Brillet, Marianne Kambouchner, António Morais, José M Pereira, Conceição Souto Moura, Jan C Grutters, Daniel A van den Heuvel, Hendrik W van Es, Matthijs F van Oosterhout, Cornelis A Seldenrijk, Elisabeth Bendstrup, Finn Rasmussen, Line B Madsen, Bibek Gooptu, Sabine Pomplun, Hiroyuki Taniguchi, Junya Fukuoka, Takeshi Johkoh, Andrew G Nicholson, Charlie Sayer, Lilian Edmunds, Joseph Jacob, Maria A Kokosi, Jeffrey L Myers, Kevin R Flaherty, David M Hansell

	Clinicians (κ)		Radiologists (κ)		Pathologists (κ)		MDTM (κ)	
	Total (n=70)	No biopsy (n=48)	Total (n=70)	No biopsy (n=48)	Total (n=70)	No biopsy (n=48)	Total (n=70)	No biopsy (n=48)
Overall total	0·45	0·50	0·33	0·31	0·31	··	0·50	0·57
Idiopathic pulmonary fibrosis total	0·59	0·71	0·46	0·42	0·46	··	0·60	0·70
Non-specific interstitial pneumonia total	0·19	0·19	0·25	0·25	0·23	··	0·25	0·25
Connective tissue disease-related interstitial lung disease total	0·57	0·62	0·10	0·11	0·22	··	0·64	0·73
Hypersensitivity pneumonitis total	0·25	0·38	0·27	0·22	0·20	··	0·24	0·31

MDTM=multidisciplinary team meeting.

Table 3: **Unweighted kappa values (κ) for clinicians, radiologists, pathologists, and inter-multidisciplinary team meeting agreement on individual diagnoses of diffuse parenchymal lung disease**

Lancet Respir Med. 2016 Jul;4(7):557-65.

Cosgrove et al. BMC Pulmonary Medicine (2018) 18:9
DOI 10.1186/s12890-017-0560-x

BMC Pulmonary Medicine

RESEARCH ARTICLE Open Access

Barriers to timely diagnosis of interstitial lung disease in the real world: the INTENSITY survey

Gregory P. Cosgrove[1,2*], Pauline Bianchi[3], Sherry Danese[4] and David J. Lederer[2,5]

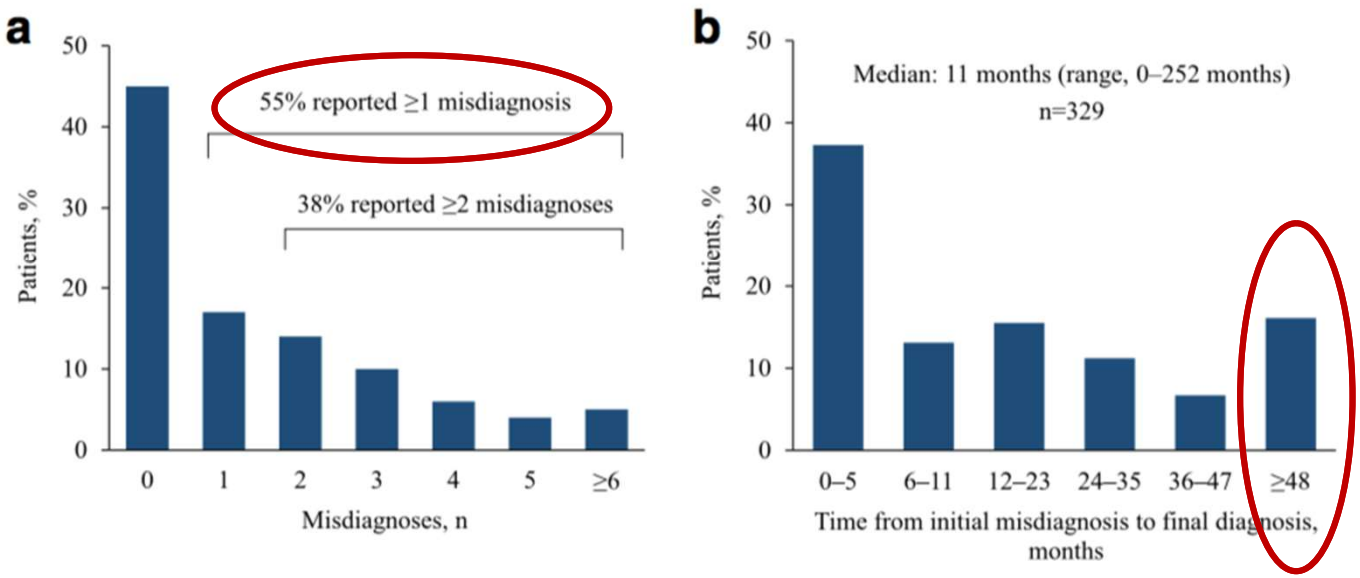


Fig. 2 Reported frequency of misdiagnosis (**a**) and time from initial misdiagnosis to final diagnosis (**b**)

Cosgrove et al. BMC Pulmonary Medicine (2018) 18:9
DOI 10.1186/s12890-017-0560-x

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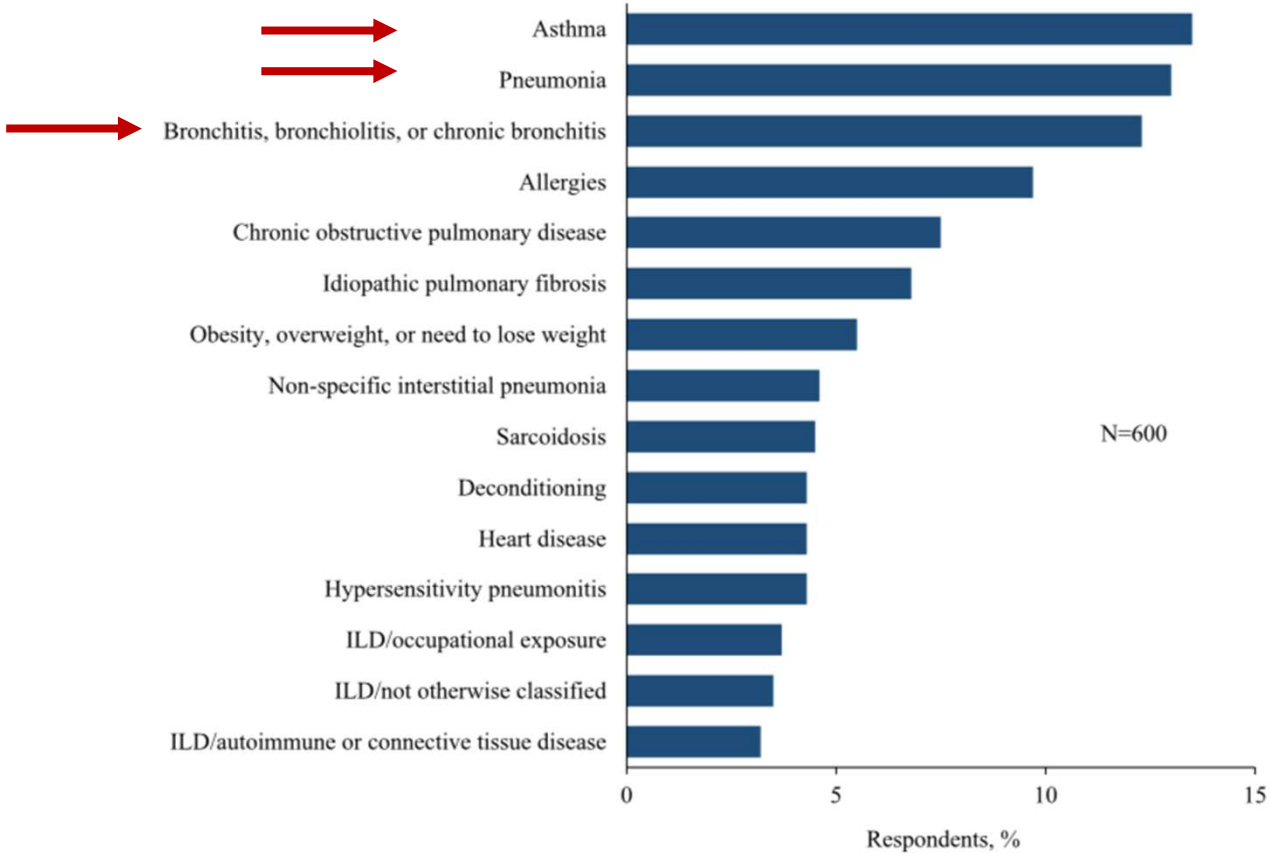
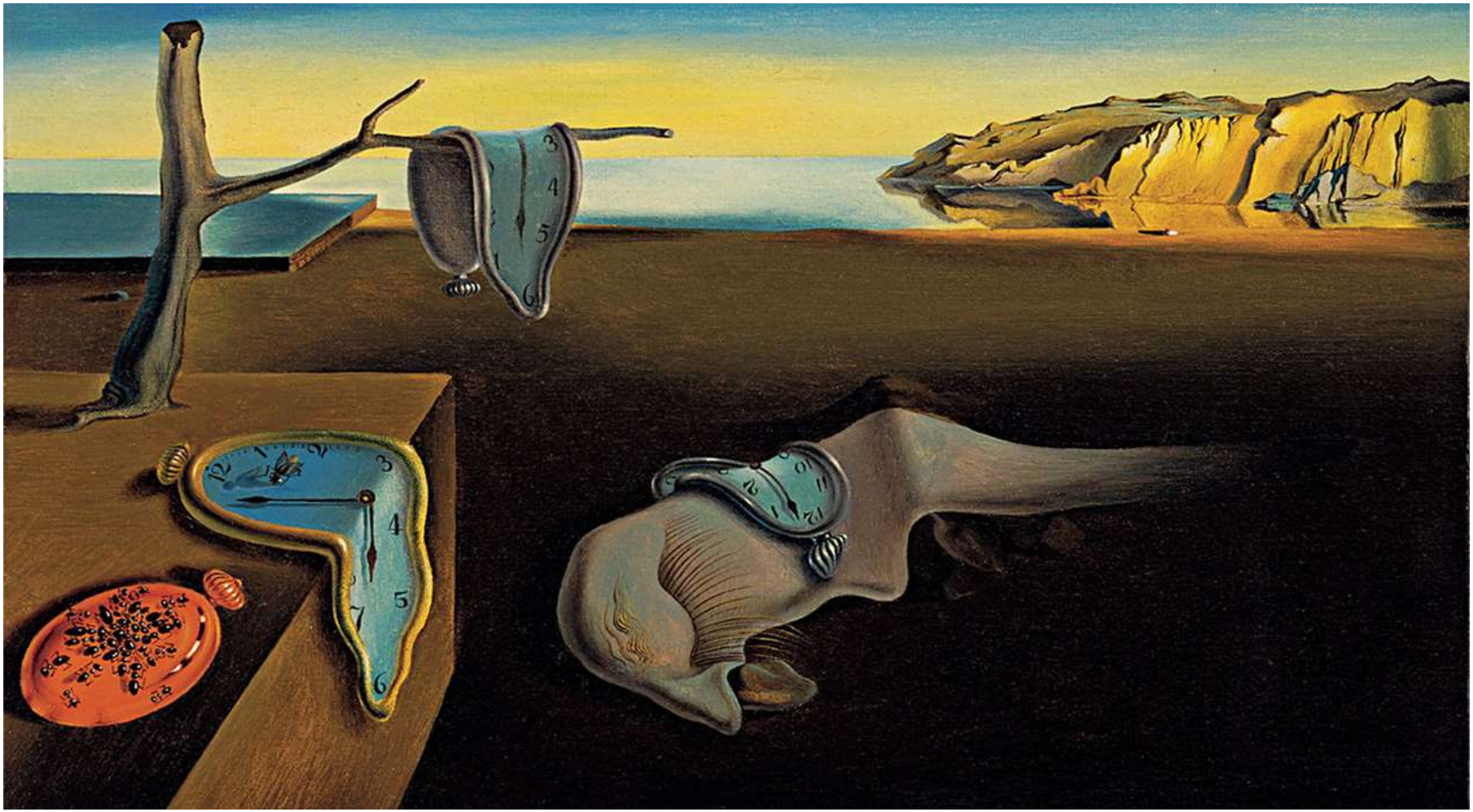


Fig. 3 Most commonly reported misdiagnoses (reported by > 3% of respondents). *ILD* = interstitial lung disease

TIME



Conclusions

- IPF diagnosis should be considered in all adult patients with unexplained chronic exertional dyspnea, cough, bibasilar inspiratory crackles, and/or digital clubbing that occur without constitutional or other symptoms that suggest a multisystem disease

- Clinical context is fundamental (age>60 ys, male predominant, smoking history frequent)

- No specific sign and/or symptoms

- Misdiagnosis is frequent

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