Supplementary Material

METHODS

Case definition and inclusion criteria

Patients with potential IPF cases were identified via Read Codes (the clinical coding system within UK general practice) and free-text within clinical records for IPF diagnosis and/or IPF-related medication (Pirfenidone and Nintedanib). The Read Codes and free-text search terms for identifying IPF diagnosis and medication are listed below. This group of patients are subsequently referred to as the overall IPF patients group.

A subset of patients who had a code for a consultation to a chest specialist prior to IPF diagnosis (code for specialist consultation allowed until up to 60 days period after the diagnosis) was identified as the primary analysis population. This group of patients was defined to select for patients with a more confident diagnosis for IPF, as IPF diagnosis is difficult to make and non-IPF patients may be erroneously assigned with IPF diagnosis codes. Read Codes used to identify chest specialist consultation are listed below.

Selection of signs, symptoms and clinical features

At the initial stage of the study, a manual review was conducted for all Read Codes and free-text records from the first record date from a sample of 40 IPF patients consisting of:

1) A convenient sample of 25 registered patients from 2 GP practices with at least one IPF diagnosis code, and
2) All patients with Pirfenidone or Nintedanib prescription (n=15).

This was to identify IPF related signs and symptoms present within the patient records. Signs and symptoms potentially related to IPF were shortlisted by the research team including a UK general practitioner for data extraction as Read Codes or free text in the full study sample. The following signs and symptoms were selected: clubbed fingers, cough, crackles, dry cough, dyspnoea (shortness of breath), fatigue/malaise, loss of appetite, and weight loss.

A second round of manual review of all Read Codes related to other clinical features identified from the overall IPF patients group was also conducted by 2 general practitioners with a special interest in respiratory medicine involved with the study (RJ and DP). This was to select for clinical features relevant to IPF. The following clinical features were selected: chest examination, chest/respiratory infection, chest specialist consultation, chest symptoms, chest CT-scan conducted, chest X-ray conducted, COPD diagnosis, COPD exacerbation, fibrosis diagnosis, interstitial lung disease diagnosis, lung function test, smoking status, and sputum test.

List of Read Codes and free-text string used to identify IPF:

IPF diagnosis

Specific codes	
H563.	Idiopathic fibrosing alveolitis
H5630	Alveolar capillary block
XE0Yb	Cryptogenic fibrosing alveolitis
H563z	Idiopathic fibrosing alveolitis NOS
H5633 or X102v	Usual interstitial pneumonitis

Broad codes	
H5631	Diffuse pulmonary fibrosis
H5632	Pulmonary fibrosis
XE0Zr	Hamman-Rich syndrome

Search terms in free text

" ipf "
" urtipf "

" idiop" AND " pulm" AND " fib"

IPF Medication

h8M..	PIRFENIDONE
h8M1.	ESBRIET 267mg capsules
h8M2.	PIRFENIDONE 267mg capsules
hhq..	NINTEDANIB
hhq1.	VARGATEF 100mg capsules
hhq2.	VARGATEF 150mg capsules
hhq3.	NINTEDANIB 100mg capsules
hhq4.	NINTEDANIB 150mg capsules
hhq5.	OFEV 100mg capsules
hhq6.	OFEV 150mg capsules

Search terms in free text

"Pirfenidone"
"Esbriet"
"Nintedanib"
"vargatef"
"ofev"

List of Read Codes and free-text string used to identify signs and symptoms:

Clubbed fingers

Read code

2G28.	O/E - hands - finger clubbing
R015.	[D]Clubbing of fingers
X75vj	Clubbing of nail
X75vl	Pseudo-clubbing
XM0z5	Clubbing of fingers/toes [D]
Xa1zM	Finger clubbing

Search terms in free text

"club" AND ("finger" or "toe" or "digit" or "nail")
"clubbing"

Cough

Read code

171..	C/O - cough
1712.	Dry cough
1713.	Productive cough -clear sputum
1714.	Productive cough -green sputum
1715.	Productive cough-yellow sputum
1716.	Productive cough NOS
1717.	Night cough present
1718.	Night cough absent
1719.	Chesty cough
171A.	Chronic cough
171C.	Morning cough
171D.	Evening cough
171E.	Unexplained cough
171G.	Bovine cough
171J.	Reflux cough
171K.	Barking cough
171L.	Cough on exercise
171Z.	Cough symptom NOS
173B.	Nocturnal cough / wheeze
R062.	[D]Cough
R0621	[D]Episodic dry cough
X76Hy	Productive cough
X76Hz	Nocturnal cough
X76I0	Cough when swallowing
XE0qn	Cough
XE0qo	Productive cough NOS
XM1QR	Spasmodic cough
Xa2kc	Persistent cough
Xa6a9	Increasing frequency of cough
Xa7mD	Allergic cough
Xa7u9	Brassy cough
Xa7uA	Bovine cough
Xa7uB	Effective cough
XaBmo	Cough on exercise
XaFwR	Unexplained cough
XaLCS	Reflux cough
XaYYO	Episodic dry cough

Search terms in free text

"cough"

Crackles

Read code

X76Il	Moist crackles

X76Im	Bubbling crackles
X76In	Post-tussive crackles
XM02C	Coarse respiratory crackles
XM02D	Fine respiratory crackles
XM08B	Respiratory crackles
Xa7uv	Inspiratory crackles
Xa7uw	Expiratory crackles

Search terms in free text

"crackles"
"velcro"

Dry cough

Read code

1712.	Dry cough
R0621	[D]Episodic dry cough
XaYYO	Episodic dry cough

Search terms in free text

"cough" AND "dry"

Dyspnoea

Read code

173..	Breathlessness
1732.	Breathless - moderate exertion
1733.	Breathless - mild exertion
1734.	Breathless - at rest
1735.	Breathless - lying flat
1739.	Shortness of breath
173C.	Short of breath on exertion
173F.	Short of breath dressing/undressing
173I.	MRC Breathlessness Scale: grade 2
173J.	MRC Breathlessness Scale: grade 3
173K.	MRC Breathlessness Scale: grade 4
173L.	MRC Breathlessness Scale: grade 5
X76Gz	Dyspnoea on exertion
XE0qq	Dyspnoea
XE0qr	Orthopnoea
XaIQ2	Short of breath dressing/undressing

XaIUl	MRC Breathlessness Scale: grade 2
XaIUm	MRC Breathlessness Scale: grade 3
XaIUn	MRC Breathlessness Scale: grade 4
XaIUo	MRC Breathlessness Scale: grade 5

Search terms in free text

"dyspnoea" OR "dyspnea" OR "breathless" OR "sob" OR "orthopnea" OR "orthopnoea" OR "platypnea" OR "platypnoea"
"short" AND "breath"

Fatigue or malaise

Read code

168..	Tiredness symptom
1682.	Fatigue
1683.	Tired all the time
1684.	Malaise/lethargy
1688.	Exhaustion
168Z.	Tiredness symptom NOS
R007.	[D]Malaise and fatigue
R0070	[D]Malaise
R0071	[D]Fatigue
R0072	[D]Asthenia NOS
R0073	[D]Lethargy
R0075	[D]Tiredness
R007z	[D]Malaise and fatigue NOS
R202.	[D]Senile asthenia
R203.	[D]Senile debility
R204.	[D]Senile exhaustion
R2y3.	[D]Debility, unspecified
X70xR	Exhaustion - physiological
X76Ae	Exhaustion
XE0qj	Tiredness symptom
XE0qk	Tired all the time
XE0ql	Malaise/lethargy
XE0uN	[Tiredness], [fatigue], [lethargy] or [malaise] symptom
XE0uP	(Malaise: [/lethargy] or [debility]) or (overwork) or (postv
XE1aa	(Nerv debil - neurasth) or (nerv exhaus) or (tired all time)
XE2y5	[D]Debility, unspecified
XM06l	Malaise and fatigue
XM06o	Lethargy
XM09P	Senile asthenia
XM09Q	Senile debility
XM09R	Senile exhaustion
XM0Ce	C/O - debility - malaise

XM0D3	Fatigue - symptom
XM0D5	C/O - tired all the time
XM0yx	Asthenia [D]
XM1AV	Asthenia
Xa96S	Tiredness

Search terms in free text

"fatigue"
"malaise"
"tiredness"
"tired all the time"
"somnolence"
"lethargy"
"discomfort"
"muzzy head"
"debility"
"heavy legs"
"heavy feeling"
"tearful"

Loss of appetite

Read code

1612.	Appetite loss - anorexia
1615.	Reduced appetite
E2756	Non-organic loss of appetite
Eu50y	[X]Other eating disorders
R0300	[D]Appetite loss
X76cJ	Loss of appetite - symptom
XE24f	Appetite loss - anorexia
XM07Y	Loss of appetite

Search terms in free text

("loss" OR "reduc") AND "appet"
"anorexia"
"appetite"

Weight loss

Read code

1623.	Weight decreasing
1625.	Abnormal weight loss
1627.	Unintentional weight loss

1D1A.	Complaining of weight loss
R032.	[D]Abnormal loss of weight
XE0uH	Weight loss (& abnormal)
XaQgK	Unexplained weight loss
XaXTs	Unintentional weight loss

Search terms in free text

("weight" OR "wt") AND ("loss" OR "decreas" OR "abno" OR "unexp")

List of Read Codes used to identify clinical features:

Chest specialist consultation (used for patient selection)

9N2g.	Seen by respiratory physician
9Nk7.	Seen in respiratory clinic
XaASl	Seen by respiratory physician
8H4C.	Referred to chest physician
8H4g.	Referral to respiratory physician
XaONr	Seen in respiratory clinic
XaAfm	Referral to respiratory physician
9N1b.	Seen in chest clinic
744Bz	Rigid diagnostic bronchoscopy NOS
9N0u.	Seen in community respiratory clinic
8HVR.	Private referral to chest physician
XaAfk	Referral to chest physician

Chest examination

Read code

23...	Examn. of respiratory system
X774f	Respiratory rate
2315	Resp. system examined - NAD
XM1Ue	O/E - chest examination normal
23G..	Chest clear
XM0CK	O/E - chest findings
Xa83j	Chest clear

Chest/respiratory infection

Read code

H06z0	Chest infection NOS
XE0Xs	Chest infection NOS
H0...	Acute respiratory infections

H06z1	Lower resp tract infection
X1004	Infection of lower respiratory tract
2E31.	O/E - temperature normal
H062.	Acute lower respiratory tract infection
XM1QW	Respiratory tract infection
XE0Xt	Acute lower respiratory tract infection
H30..	Bronchitis unspecified
H0z..	Acute respiratory infection NOS
XM1QX	Acute wheezy bronchitis
H06z2	Recurrent chest infection

Chest symptoms

Read code

182..	Chest pain
23D3.	O/E - coarse crepitations
23D4.	O/E - fine crepitations
1828	Atypical chest pain
R065A	[D]Musculoskeletal chest pain
182Z.	Chest pain NOS
1825	Pleuritic pain
R065.	[D]Chest pain
R0658	[D]Chest tightness
23D..	O/E - adventitious sounds
R065B	[D]Non cardiac chest pain
182C.	Chest wall pain
182A.	Chest pain on exertion
R065z	[D]Chest pain NOS
XSJF8	Chest wall pain
9N0f.	Seen in rapid access chest pain clinic
1824	Anterior chest wall pain
1822	Central chest pain
8HTJ.	Referral to rapid access chest pain clinic
Xa2kY	Basal crepitations

Chest CT-scan

Read code

5678	CAT scan - thorax
56780	CT (computed tomography) of chest and abdomen
7P040	Computed tomography of chest
56781	CT (computed tomography) of chest, abdomen and pelvis

Chest X-ray

Read code

535..	Standard chest X-ray
5353	Standard chest X-ray abnormal
5352	Standard chest X-ray normal
5351	Standard chest X-ray requested
7P042	Plain x-ray of chest
535Z.	Standard chest X-ray NOS
68C1.	Screening chest X-ray

COPD diagnosis

Read code

H3...	Chronic obstructive pulmonary disease

COPD exacerbation

Read code

H3122	Acute exacerbation of chronic obstructive airways disease

Fibrosis diagnosis

Read code	Read term
23E5.	O/E - fibrosis of lung present

ILD diagnosis

Read code	Read term
H58y3	Interstitial lung disease NEC
X102V	Interstitial lung disease

Lung function test

Read code	Read term
3396	Forced vital capacity - FVC
339R.	FEV1/FVC percent
339S.	Percent predicted FEV1
339M.	FEV1/FVC ratio
XaEFz	Percent predicted FEV1
XaEFy	FEV1/FVC percent
339P.	Expected FEV1

339Q.	Expected FVC
339i.	FVC/Expected FVC percent
3386	Lung vital capacity
339b.	FEV1 after bronchodilation
3371	Lung function testing done
337..	Lung function testing
339a.	FEV1 before bronchodilation
XaCJK	Expected FEV1
XaCJL	Expected FVC
339m.	FEV1/FVC ratio after bronchodilator
339h.	FVC after bronchodilation
XaIxR	FEV1 after bronchodilation
3373	Lung function testing normal
XaJ9E	FEV1/FVC ratio after bronchodilator
339N.	Expected FEV1/FVC ratio
XaJ5w	FVC/Expected FVC percent
XaJ9D	FEV1/FVC ratio before bronchodilator
XaJ3K	FVC after bronchodilation
3377	Lung function restrictive
3399	FEV1/FVC ratio abnormal
339T.	FEV1/FVC > 70% of predicted
339l.	FEV1/FVC ratio before bronchodilator
XaF6d	FEV1/FVC < 70% of predicted
3398	FEV1/FVC ratio normal
339E.	More than 80% of predicted peak flow rate
33960	FVC - forced vital capacity normal
339F.	60-80% of predicted peak flow rate
339U.	FEV1/FVC < 70% of predicted
XaCFR	Expected FEV1/FVC ratio
Xab2f	Percentage of predicted FVC after bronchodilation
XaF6e	FEV1/FVC > 70% of predicted

Smoking status

Read code

XE0oh	Never smoked tobacco

Sputum test

Read code

4JF5.	Sputum sent for C/S
X76IB	Clear sputum
4E2A.	Sputum appearance
4E11.	Sputum sent for examination
X76I5	Volume of sputum

4E3..	Sputum microscopy
XE0qp	Blood in sputum - haemoptysis
4E...	Sputum examination
4E2E3	Scanty sputum
4E4..	Sputum culture

List of Read Codes for other baseline chronic respiratory diseases (excluding cancer)

Read code	
23E5.	O/E - fibrosis of lung
A114.	Tuberculous fibrosis of lung
A115.	Tuberculous bronchiectasis
A1202	Tuberculous hydrothorax
A7899	HIV disease resulting in lymphoid interstitial pneumonitis
AD50.	Sarcoidosis of lung
AD52.	Sarcoidosis of lung with sarcoidosis of lymph nodes
AD54.	Sarcoidosis of inferior turbinates
C10N1	Cystic fibrosis related diabetes mellitus
C370.	Cystic fibrosis
C3700	Cystic fibrosis with no meconium ileus
C3701	Cystic fibrosis with meconium ileus
C3702	Cystic fibrosis with pulmonary manifestations
C3703	Cystic fibrosis with intestinal manifestations
C3704	Arthropathy in cystic fibrosis
C3705	Cystic fibrosis with distal intestinal obstruction syndrome
C3707	Liver disease due to cystic fibrosis
C3708	Cystic fibrosis related cirrhosis
C3709	Exacerbation of cystic fibrosis
C370y	Cystic fibrosis with other manifestations
C370z	Cystic fibrosis NOS
H34..	Bronchiectasis
H340.	Recurrent bronchiectasis
H341.	Post-infective bronchiectasis
H34z.	Bronchiectasis NOS
H35..	Hypersensitivity pneumonitis
H350.	Farmers' lung
H351.	Bagassosis
H352.	Bird-fancier's lung
H3520	Budgerigar-fanciers' lung
H3521	Pigeon-fanciers' lung
H352z	Bird-fancier's lung NOS
H353.	Suberosis (cork-handlers' lung)
H354.	Malt workers' lung
H355.	Mushroom workers' lung
H356.	Maple bark strippers' lung
H35y.	Other allergic alveolitis
H35y0	Cheese-washers' lung
H35y1	Coffee-workers' lung
H35y2	Fish-meal workers' lung
H35y3	Furriers' lung
H35y4	Grain-handlers' disease
H35y5	Pituitary snuff-takers' disease
H35y6	Sequoiosis (red-cedar asthma)

H35y7	Wood asthma
H35y8	Air-conditioner and humidifier lung
H35yz	Other allergic alveolitis NOS
H35z0	Allergic extrinsic alveolitis NOS
H35z1	Hypersensitivity pneumonitis NOS
H4...	Lung disease due to external agents
H40..	Coal workers' pneumoconiosis
H41..	Asbestosis
H410.	Pleural plaque disease due to asbestosis
H41z.	Asbestosis NOS
H42..	Silica and silicate pneumoconiosis
H420.	Talc pneumoconiosis
H421.	Simple silicosis
H422.	Complicated silicosis
H423.	Massive silicotic fibrosis
H42z.	Silica pneumoconiosis NOS
H43..	Pneumoconiosis due to other inorganic dust
H430.	Aluminosis of lung
H431.	Bauxite fibrosis of lung
H432.	Berylliosis
H433.	Graphite fibrosis of lung
H434.	Siderosis
H435.	Stannosis
H43z.	Pneumoconiosis due to inorganic dust NOS
H44..	Pneumopathy due to inhalation of other dust
H440.	Byssinosis
H441.	Cannabinosis
H442.	Flax-dressers' disease
H44z.	Pneumopathy due to inhalation of other dust NOS
H45..	Pneumoconiosis NOS
H450.	Pneumoconiosis associated with tuberculosis
H46..	Respiratory disease due to chemical fumes and vapours
H462.	Upper respiratory inflammation due to chemical fumes
H464.	Chronic respiratory conditions due to chemical fumes
H4641	Obliterative bronchiolitis due to chemical fumes
H4642	Chronic pulmonary fibrosis due to chemical fumes
H464z	Chronic respiratory conditions due to chemical fumes NOS
H465.	Chemical-induced pulmonary oedema
H46z.	Respiratory conditions due to chemical fumes NOS
H46z0	Silo-fillers' disease
H46zz	Respiratory conditions due to chemical fumes NOS
H4710	Lipoid pneumonia (exogenous)
H48..	Progressive massive fibrosis
H4y..	Other specified lung diseases due to external agent
H4y1.	Chronic pulmonary radiation disease
H4y10	Chronic pulmonary fibrosis following radiation
H4y1z	Chronic pulmonary radiation disease NOS
H4y2.	Drug-induced interstitial lung disorders
H4y21	Chronic drug-induced interstitial lung disorders
H4yy.	Other external agent causing respiratory condition
H4yz.	External agent causing respiratory conditions NOS
H4z..	Lung disease due to external agents NOS
H5000	Empyema necessitans
H5001	Empyema with bronchopleural fistula
H5002	Empyema with hepatopleural fistula
H5003	Empyema with mediastinal fistula

H5004	Empyema with pleural fistula NOS
H5005	Empyema with thoracic fistula NOS
H5010	Loculated empyema
H5012	Pleural empyema
H5013	Lung empyema NOS
H5015	Pyopneumothorax
H510C	Pleural plaque
H51y.	Other pleural effusion excluding mention of tuberculosis
H51y0	Encysted pleurisy
H51y7	Malignant pleural effusion
H51yz	Other pleural effusion
H51z.	Pleural effusion NOS
H54..	Pulmonary congestion and hypostasis
H540.	Pulmonary hypostasis
H540z	Pulmonary hypostasis NOS
H5410	Chronic pulmonary oedema
H541z	Pulmonary oedema NOS
H54z.	Pulmonary congestion and hypostasis NOS
H55..	Postinflammatory pulmonary fibrosis
H56..	Other alveolar and parietoalveolar disease
H560.	Pulmonary alveolar proteinosis
H561.	Idiopathic pulmonary haemosiderosis
H562.	Pulmonary alveolar microlithiasis
H563.	Idiopathic pulmonary fibrosis
H5630	Alveolar capillary block
H5631	Diffuse pulmonary fibrosis
H5632	Pulmonary fibrosis
H5633	Usual interstitial pneumonitis
H563z	Idiopathic fibrosing alveolitis NOS
H56yz	Other alveolar and parietoalveolar disease NOS
H56z.	Alveolar and parietoalveolar disease NOS
H57y0	Pulmonary amyloidosis
H57y2	Pulmonary sarcoidosis
H583.	Pulmonary eosinophilia
H5830	Loeffler's syndrome
H5831	Tropical eosinophilia
H583z	Pulmonary eosinophilia NOS
H5840	Postoperative pulmonary oedema
H5850	Pulmonary insufficiency following shock
H5851	Pulmonary insufficiency following surgery
H5852	Pulmonary insufficiency following trauma
H585z	Trauma and postoperative pulmonary insufficiency NOS
H58y0	Broncholithiasis
H58y3	Interstitial lung disease NEC
H58y5	Respiratory bronchiolitis associated interstitial lung disease
H58y6	Interstitial lung disease due to collagen vascular disease
H58y7	Interstitial lung disease due to connective tissue disease
H5X..	Pleural condition, unspecified
H5y30	Fibrosis of mediastinum
Hy02.	Chronic pulmonary insufficiency following surgery
Hyu4.	[X]Lung diseases due to external agents
Hyu40	[X]Pneumoconiosis due to other dust containing silica
Hyu41	[X]Pneumoconiosis due to other specified inorganic dusts
Hyu42	[X]Airway disease due to other specific organic dusts
Hyu43	[X]Hypersensitivity pneumonitis due to other organic dusts

Hyu44	[X]Upper respiratory inflammation due to chemicals, gases, fumes and vapours, not elsewhere classified
Hyu46	[X]Other respiratory conditions due to chemicals, gases, fumes and vapours
Hyu48	[X]Chronic and other pulmonary manifestations due to radiation
Hyu49	[X]Respiratory conditions due to other specified external agents
Hyu4A	[X]Respiratory conditions due to unspecified external agent
Hyu5.	[X]Other respiratory diseases principally affecting the interstitium
Hyu50	[X]Other interstitial pulmonary diseases with fibrosis
Hyu51	[X]Other specified interstitial pulmonary diseases
Hyu6.	[X]Suppurative and necrotic conditions of the lower respiratory tract
Hyu70	[X]Pleural effusion in conditions classified elsewhere
P861.	Congenital bronchiectasis
PK35.	Kartageners syndrome
SP130	Mendelson's syndrome as a complication of care
X00lU	Nasal sarcoidosis
X00nm	Laryngeal sarcoidosis
X100l	Congenital cystic bronchiectasis
X100m	Acquired bronchiectasis
X100n	Idiopathic bronchiectasis
X100o	Obstructive bronchiectasis
X100p	Toxin-induced bronchiectasis
X100q	Bronchiectasis due to toxic aspiration
X100r	Bronchiectasis due to toxic inhalation
X100t	Post-lung transplantation bronchiectasis
X100V	Chronic pulmonary coccidioidomycosis
X1012	Benign asbestos pleural effusion
X1013	Drug-induced pleural effusion
X1014	Meigs syndrome
X101a	Primary ciliary dyskinesia due to transposition of ciliary microtubules
X101b	Immotile cilia syndrome due to defective radial spokes
X101c	Immotile cilia syndrome due to excessively long cilia
X101d	Young's syndrome
X101e	Rutland ciliary disorientation syndrome
X101T	Pleural plaque
X101U	Asbestos-induced pleural plaque
X101Z	Polynesian bronchiectasis
X102b	High altitude pulmonary oedema
X102c	Post-upper airway obstruction pulmonary oedema
X102d	Toxic pulmonary oedema
X102e	Chemical-induced pulmonary oedema
X102F	Allergic bronchopulmonary aspergillosis
X102g	Oxygen-induced pulmonary oedema
X102H	Cryptogenic pulmonary eosinophilia
X102h	Fluid overload pulmonary oedema
X102I	Pulmonary histiocytosis X
X102i	Uraemic pulmonary oedema
X102J	Animal handlers' lung
X102K	Dog house disease
X102k	Seasonal cryptogenic organising pneumonia with biochemical cholestasis
X102L	Dry rot lung
X102l	Diffuse infiltrative lung disease
X102M	Lycoperdonosis
X102N	Wheat weevil disease
X102n	Idiopathic diffuse pulmonary ossification
X102O	New Guinea lung
X102o	Micronodular pulmonary ossification

X102P	Paprika splitters' lung
X102p	Diffuse pulmonary neurofibromatosis
X102Q	Pyrethrum alveolitis
X102q	Pulmonary tuberose sclerosis
X102R	Rodent handlers' lung
X102S	Sewage workers' lung
X102s	Pulmonary lipid storage disease
X102T	Summer-type hypersensitivity pneumonitis
X102t	Bronchocentric granulomatosis
X102U	Vineyard sprayers' lung
X102u	Fibrosis of lung
X102V	Interstitial lung disease
X102v	Usual interstitial pneumonitis
X102w	Desquamative interstitial pneumonitis
X102x	Lymphoid interstitial pneumonitis
X102y	Giant cell interstitial pneumonitis
X102Z	Neurogenic pulmonary oedema
X1030	Toxic diffuse interstitial pulmonary fibrosis
X1031	Drug-induced diffuse interstitial pulmonary fibrosis
X1032	Localised pulmonary fibrosis
X1033	Mediastinal radiation fibrosis
X103a	Erionite pneumoconiosis
X103b	Kaolin pneumoconiosis
X103c	Metal pneumoconiosis
X103d	Antimony pneumoconiosis
X103e	Argyro-siderosis
X103f	Barium pneumoconiosis
X103G	Radiation-induced fibrous mediastinitis
X103i	Chronic berylliosis
X103j	Cerium pneumoconiosis
X103k	Hard metal pneumoconiosis
X103l	Nickel pneumoconiosis
X103m	Thorium pneumoconiosis
X103N	Mediastinal lymph node sarcoidosis
X103n	Zirconium pneumoconiosis
X103o	Mica pneumoconiosis
X103p	Mixed mineral dust pneumoconiosis
X103q	Liparosis
X103r	Slate pneumoconiosis
X103s	Diatomite pneumoconiosis
X103v	Chronic silicosis
X103W	Simple pneumoconiosis
X103w	Silicotuberculosis
X103X	Complicated pneumoconiosis
X103x	Wollastonite pneumoconiosis
X103Y	Rheumatoid pneumoconiosis
X103Z	Bentonite pneumoconiosis
X1043	Stage 1 pulmonary sarcoidosis
X1044	Stage 2 pulmonary sarcoidosis
X1045	Stage 3 pulmonary sarcoidosis
X1046	Stage 4 pulmonary sarcoidosis
X1047	Endobronchial sarcoidosis
X1048	Necrotising sarcoid granulomatosis
X1049	Sarcoid pulmonary calcification
X20GM	Nasopharyngeal sarcoidosis
X309R	Cystic fibrosis of pancreas

X70Qb	Chronic necrotising pulmonary aspergillosis
X70Ra	Chronic pulmonary African histoplasmosis
X70Rg	Chronic pulmonary blastomycosis
Xa08A	Chronic pulmonary insufficiency of prematurity
Xa0IL	Malignant pleural effusion
Xa0kb	Tropical pulmonary eosinophilia
Xa0lb	Pleural effusion
Xa0Xi	Pulmonary lymphangioleiomyomatosis
Xa6YO	Pulmonary oedema
Xa9Bw	Pneumoconiosis
Xa9By	Diffuse pulmonary calcinosis
Xaa7C	Eosinophilic bronchitis
XaB1L	Haemorrhagic pleural effusion
XaBDb	Cystic fibrosis with other manifestations
XaCL7	Sarcoidosis of inferior turbinates
XaJlX	[X]Hepatopulmonary syndrome
XaMzI	Cystic fibrosis related diabetes mellitus
XaREa	Liver disease due to cystic fibrosis
XaREX	Arthropathy in cystic fibrosis
XaREZ	Cystic fibrosis with distal intestinal obstruction syndrome
XaXlE	Respiratory bronchiolitis associated interstitial lung disease
XaXlF	Interstitial lung disease due to collagen vascular disease
XaXlJ	Interstitial lung disease due to connective tissue disease
XaZr7	Exacerbation of cystic fibrosis
XE0Ya	Post-inflammatory pulmonary fibrosis
XE0Yb	Cryptogenic fibrosing alveolitis
XE0Yd	Trauma and postoperative pulmonary insufficiency
XE0Ye	Adult respiratory distress syndrome
XE0YY	Lung disease due to external agents
XE0Zn	Lung: [pulmonary oedema NOS] or [congestion]
XE0Zr	Idiopath. fibrosing alveolitis (& Hamman-Rich syndrome)
XE0ZZ	(Pneumoconiosis NOS) or (siderosis)
XE2wL	Tuberculous pleural empyema
XE2wM	Pleural empyema
XE2wN	Pleural empyema with fistula
XE2wP	Pleural empyema with no fistula
XE2wR	Pleural empyema NOS

RESULTS

Supplementary Table E1. Baseline demographic patient characteristics and procedures conducted within the overall IPF patients (n=1,116).

Variable*	Overall IPF patients
Age (years), • mean (SD) • median (IQR)	 74.8 (10.0) 76.0 (69.0; 82.0)
Male gender	706 (60.5)
BMI • % non-missing • <18.5 • 18.5 - <25 • 25 - <30 • ≥30	 1,112 (95.4) 23 (2.1) 343 (30.9) 443 (39.8) 303 (27.2)
Smoking status • n (% non-missing) • Current smoker • Ex-smoker • Never smoked	 1,119 (96.0) 110 (9.8) 604 (54.0) 405 (36.2)
Asthma diagnosis†	53 (4.5)
COPD diagnosis†	35 (3.0)
Respiratory tract cancer	1 (0.1)
Other chronic respiratory diseases (excl. cancer)	26 (2.2)
Lung function test conducted • 90 days prior diagnosis • 365 days prior diagnosis	 198 (17.0) 355 (30.4)
*Numbers are presented as n (%) unless specified. †First diagnostic code recorded ever prior and up to index date.	

Supplementary Table E2. Presence of signs & symptoms in the year prior to IPF diagnosis, identified via Read Codes only or with the addition of free-text, in both overall IPF patients and patients with chest specialist consultation followed by IPF diagnosis.

	All patients with IPF (N=1,166)		Consultation followed by diagnosis (N=462)	
Signs and symptom*	**Read Codes and Free-text**	**Read Codes only**	**Read Codes and Free-text**	**Read Codes only**
Dyspnoea	483 (41.4)	361 (31.0)	225 (48.7)	162 (35.1)
Cough	457 (39.2)†	371 (31.8)‡	189 (40.9)§	149 (32.3)‖
Fatigue or malaise	65 (5.6)	39 (3.3)	22 (4.8)	13 (2.8)
Weight loss	45 (3.9)	30 (2.6)	19 (4.1)	16 (3.5)
Crackles	28 (2.4)	1 (0.1)	14 (3.0)	0 (0.0)
Loss of appetite	25 (2.1)	14 (1.2)	13 (2.8)	7 (1.5)
Clubbed fingers	5 (0.4)	4 (0.3)	2 (0.4)	1 (0.2)

*Numbers are presented as n (%) unless specified. †, ‡, §, ‖Include 54 (4.6%), 40 (3.4%), 25 (5.4%), and 18 (3.9%) dry cough respectively.

Supplementary Table E3. Prevalence (n[%]) of each component of respiratory consultation and respiratory test before chest specialist consultation prior to IPF diagnosis (n=462).

Variable	90 days	365 days
Respiratory consultations (overall)	**238 (51.5)**	**360 (77.9)**
Clubbed fingers	1 (0.2)	2 (0.4)
Cough	108 (23.4)	196 (42.4)
Crackles	7 (1.5)	13 (2.8)
Dyspnoea	142 (30.7)	226 (48.9)
Sputum	9 (1.9)	13 (2.8)
Chest symptom	33 (7.1)	52 (11.3)
Chest/respiratory infection	73 (15.8)	130 (28.1)
Respiratory tests (overall)	**176 (38.1)**	**283 (61.3)**
Chest X-ray	102 (22.1)	191 (41.3)
Chest CT-Scan	7 (1.5)	8 (1.7)
Lung function test	89 (19.3)	150 (32.5)
Chest examination	12 (2.6)	22 (4.8)

Supplementary Table E4. History of respiratory consultation and respiratory test in period before diagnosis or chest specialist consultation in all patients with IPF diagnosis or medication (n=1,166)*

Variable	Frequency, n (%)
Respiratory consultation†	
• within 90 days prior diagnosis or consultation	543 (46.6)
• within 365 days prior diagnosis or consultation	850 (72.9)
Respiratory tests conducted‡	
• within 90 days prior diagnosis or consultation	395 (33.9)
• within 365 days prior diagnosis or consultation	636 (54.5)

*Frequency expressed as n (%). †Codes for chest/respiratory infection, chest symptoms, clubbed fingers, cough, crackles, dyspnoea, or sputum or wheeze. ‡Codes for chest X-ray, chest CT scan, lung function test and chest examination.

Supplementary Table E5. Co-occurrence of signs and symptoms in the one-year period up to IPF diagnosis – All IPF patients (n=1,166)

Clubbed fingers	Cough	Crackles	Dry cough	Dyspnoea	Fatigue or malaise	Loss of appetite	Weight loss	Patients	%	Cumulative %
								412	35.3	35.3
				■				225	19.3	54.6
	■							177	15.2	69.8
	■			■				162	13.9	83.7
	■		■					23	2.0	85.7
	■		■	■				23	2.0	87.7
	■			■	■			18	1.5	89.2
							■	17	1.5	90.7
				■	■			13	1.1	91.8
					■			10	0.9	92.6
	■						■	8	0.7	93.3
	■				■			8	0.7	94.0
		■						8	0.7	94.7
	■	■		■				7	0.6	95.3
						■		4	0.3	95.6
	■	■						4	0.3	96.0
	■			■		■		4	0.3	96.3
■								3	0.3	96.6
				■		■		3	0.3	96.8
		■		■				3	0.3	97.1
				■			■	3	0.3	97.3
	■					■		2	0.2	97.5
	■					■	■	2	0.2	97.7
	■	■		■			■	2	0.2	97.9
	■		■	■	■			2	0.2	98.0
	■			■	■	■	■	2	0.2	98.2
				■	■		■	2	0.2	98.4
	■			■			■	2	0.2	98.5
	■		■	■	■	■		1	0.1	98.6
	■		■	■		■		1	0.1	98.7
■				■				1	0.1	98.8
				■	■	■	■	1	0.1	98.9
	■	■		■	■			1	0.1	99.0
	■			■	■	■		1	0.1	99.1
		■					■	1	0.1	99.1
	■		■		■			1	0.1	99.2
	■		■	■	■		■	1	0.1	99.3
	■			■	■		■	1	0.1	99.4
	■		■			■		1	0.1	99.5
	■	■			■			1	0.1	99.6
						■	■	1	0.1	99.7
				■		■	■	1	0.1	99.7
		■		■	■			1	0.1	99.8
	■		■	■	■	■	■	1	0.1	99.9
■	■			■				1	0.1	100.0

Supplementary Table E6. Number of patients with at least a certain average symptom frequency (recording dates/year) in the period of up to 12 years before IPF diagnosis.

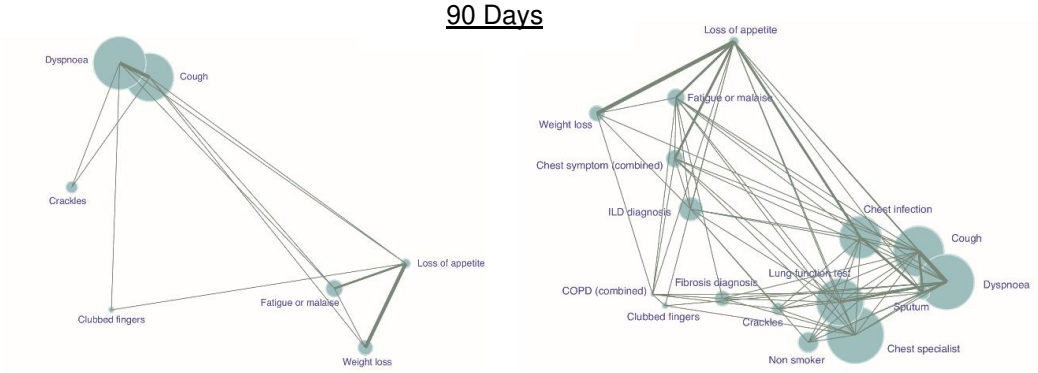
	N (%)			
Symptom frequency (recoding dates/year)	≥1	≥0.5	≥0.33	≥0.25
Cough	43 (9.3)	118 (25.6)	168 (36.4)	198 (43.0)
Dyspnoea	35 (7.6)	83 (18.0)	130 (28.2)	157 (34.1)
Fatigue/malaise	5 (1.1)	9 (2.0)	22 (4.8)	36 (7.8)
Weight loss recorded	2 (0.4)	4 (0.9)	9 (2.0)	13 (2.8)
Chest infection	1 (0.2)	5 (1.1)	7 (1.5)	11 (2.4)
Dry cough	0 (0.0)	3 (0.7)	7 (1.5)	10 (2.2)
Lung function test	2 (0.4)	2 (0.4)	6 (1.3)	9 (2.0)
Chest exam	1 (0.2)	1 (0.2)	2 (0.4)	4 (0.9)
Crackles	0 (0.0)	1 (0.2)	2 (0.4)	3 (0.7)
Loss of appetite	0 (0.0)	0 (0.0)	0 (0.0)	3 (0.7)
Specialist referral	1 (0.2)	1 (0.2)	3 (0.7)	3 (0.7)
Chest X-ray	2 (0.4)	2 (0.4)	2 (0.4)	2 (0.4)
Chest symptoms	0 (0.0)	1 (0.2)	1 (0.2)	2 (0.4)
Sputum	0 (0.0)	0 (0.0)	1 (0.2)	1 (0.2)

Supplementary Table E7. Life table for cumulative probability of IPF diagnosis since the first symptom of cough or dyspnoea.

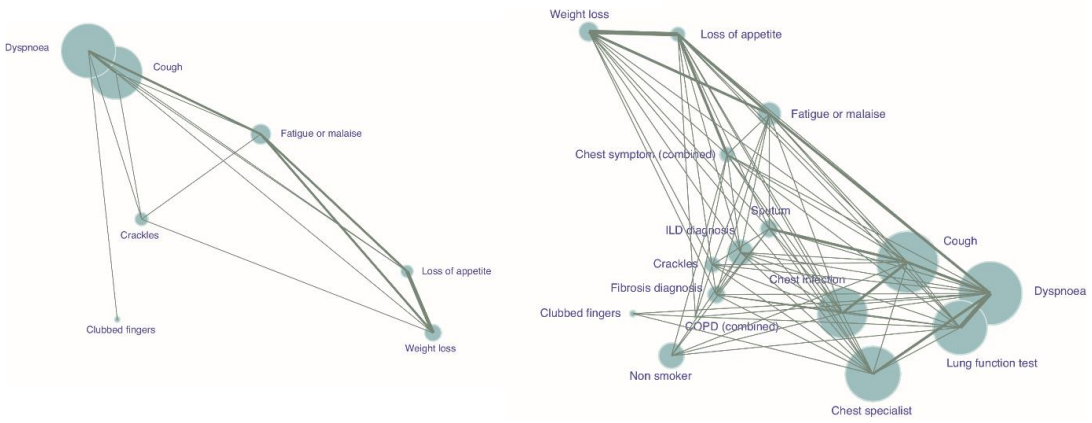
Year	Time since first cough			Time since first dyspnoea		
	At risk	Diagnosed	Cumulative probability	At risk	Diagnosed	Cumulative probability
1	322	56	0.17 (0.14-0.22)	293	86	0.29 (0.24-0.35)
2	266	30	0.27 (0.22-0.32)	207	35	0.41 (0.36-0.47)
3	236	20	0.33 (0.28-0.38)	172	23	0.49 (0.44-0.55)
4	216	27	0.41 (0.36-0.47)	149	26	0.58 (0.52-0.64)
5	189	28	0.50 (0.45-0.56)	123	18	0.64 (0.59-0.70)
6	161	20	0.56 (0.51-0.62)	105	14	0.69 (0.64-0.74)
7	141	27	0.65 (0.59-0.70)	91	16	0.74 (0.69-0.79)
8	114	14	0.69 (0.64-0.74)	75	13	0.79 (0.74-0.83)
9	100	19	0.75 (0.70-0.79)	62	14	0.84 (0.79-0.88)
10	81	15	0.80 (0.75-0.84)	48	19	0.90 (0.86-0.93)
11	66	12	0.83 (0.79-0.87)	29	6	0.92 (0.89-0.95)
12	54	8	0.86 (0.82-0.89)	23	4	0.94 (0.90-0.96)
13	46	10	0.89 (0.85-0.92)	19	7	0.96 (0.93-0.98)
14	36	6	0.91 (0.87-0.94)	12	5	0.98 (0.95-0.99)
15	30	4	0.92 (0.89-0.95)	12	0	0.98 (0.95-0.99)
16	26	3	0.93 (0.90-0.95)	12	0	0.98 (0.95-0.99)
17	23	3	0.94 (0.91-0.96)	7	2	0.98 (0.96-0.99)
18	20	3	0.95 (0.92-0.97)	5	2	0.99 (0.97-1.00)
19	17	4	0.96 (0.93-0.98)	5	0	0.99 (0.97-1.00)
20	13	5	0.98 (0.95-0.99)	3	1	0.99 (0.98-1.00)
21	8	1	0.98 (0.96-0.99)	2	2	1.00 (1.00-1.00)
22	7	2	0.98 (0.97-0.99)			
23	5	1	0.99 (0.97-1.00)			
24	4	1	0.99 (0.97-1.00)			
25	3	2	1.00 (0.98-1.00)			
30	1	1	1.00 (1.00-1.00)			

Supplementary Figure E1. Principal component analysis (PCA) based network chart for the association between signs & symptoms Read Code within 90 and within 365 days prior IPF diagnosis in overall IPF patients (n=1,116). Bubble size indicates prevalence, and thickness of lines indicate the degree of association between signs & symptoms.

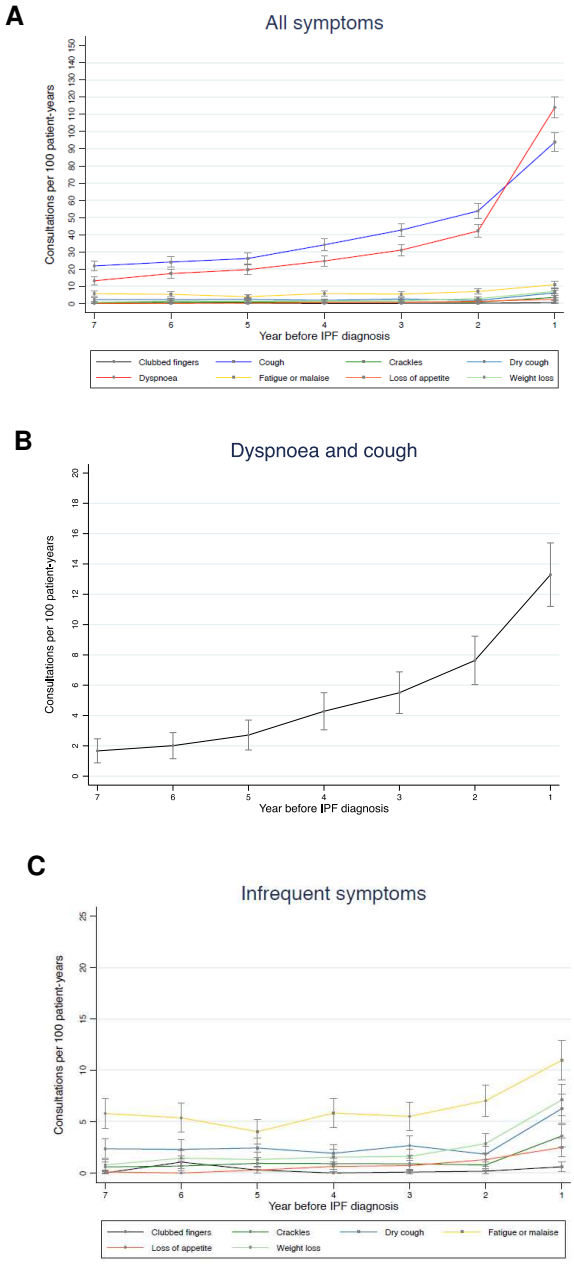
<u>90 Days</u>



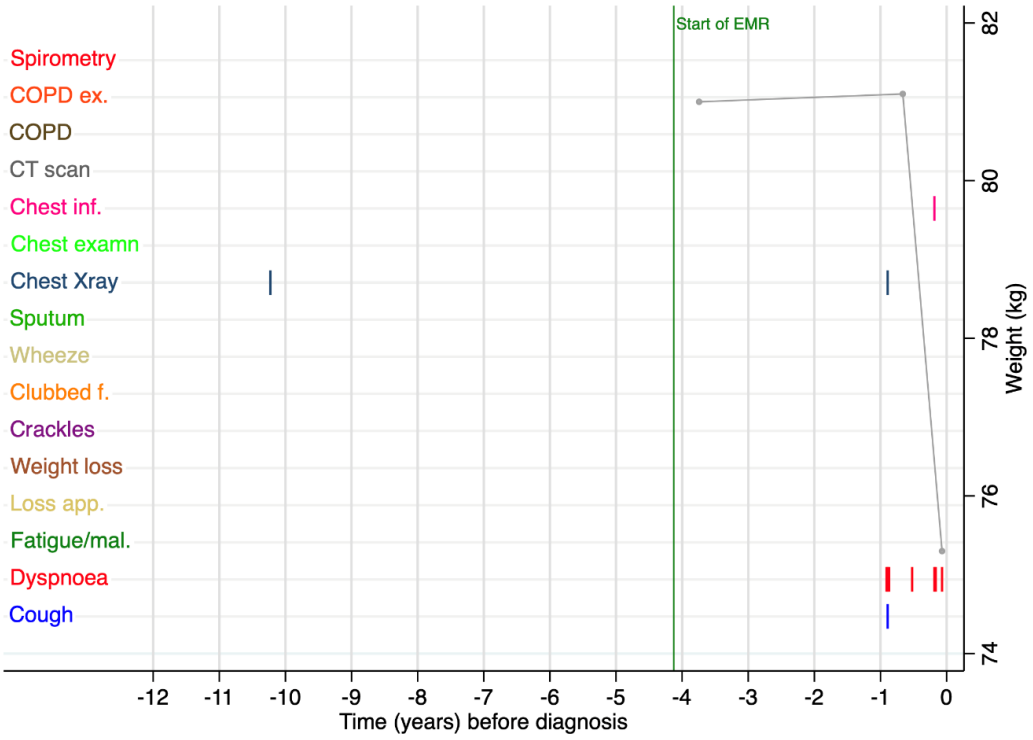
<u>365 Days</u>



Supplementary Figure E2. Frequency of codes for signs and symptoms from 7 years prior IPF diagnosis or medication – Overall IPF patients (n=1,116). A: All symptoms, B: Dyspnoea and Cough, C: Infrequent symptoms

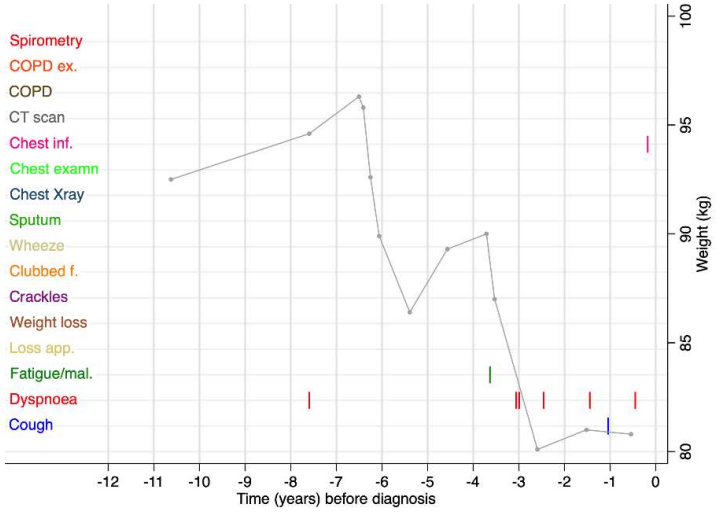


Supplementary Figure E3. Time course of respiratory symptoms and weight prior to the diagnosis of IPF showing rapid weight loss and early diagnosis.

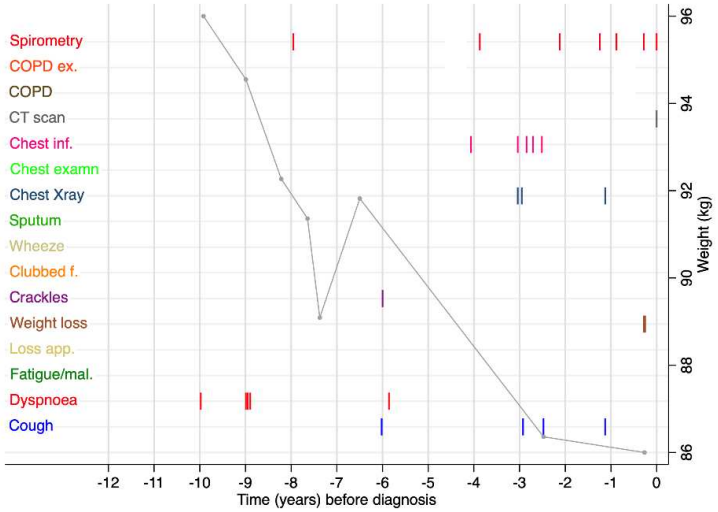


Supplementary Figure E4. Other time course of respiratory symptoms and weight patterns prior to diagnosis of IPF

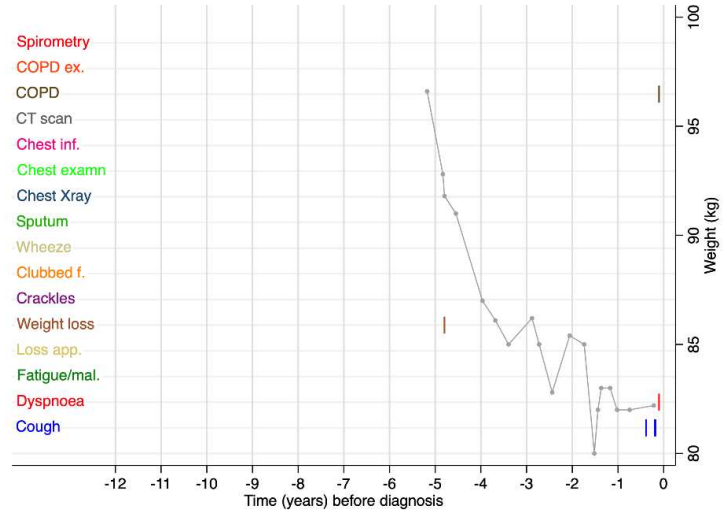
Late symptoms onset, mainly dyspnoea with catastrophic weight loss



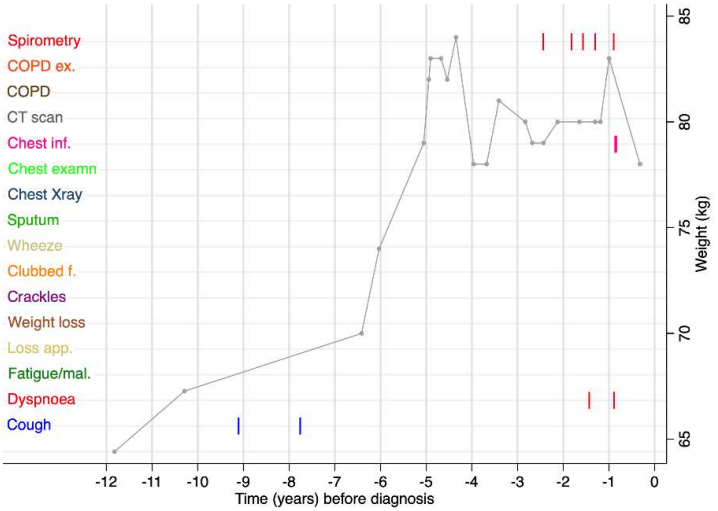
Long period of symptoms



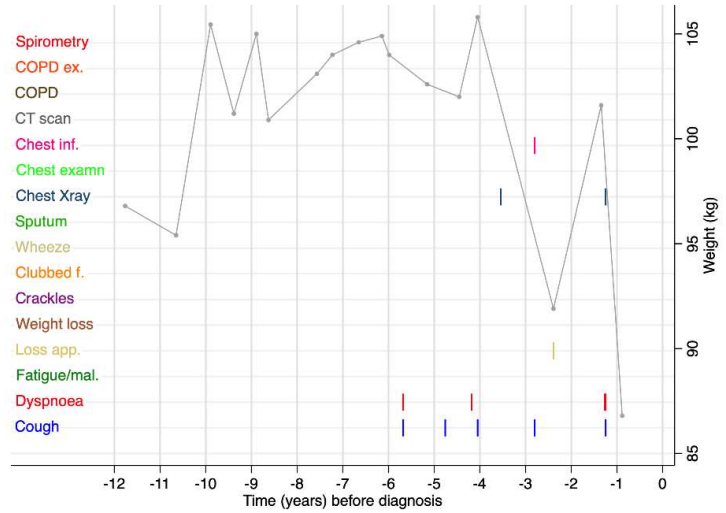
Weight loss as presenting symptom



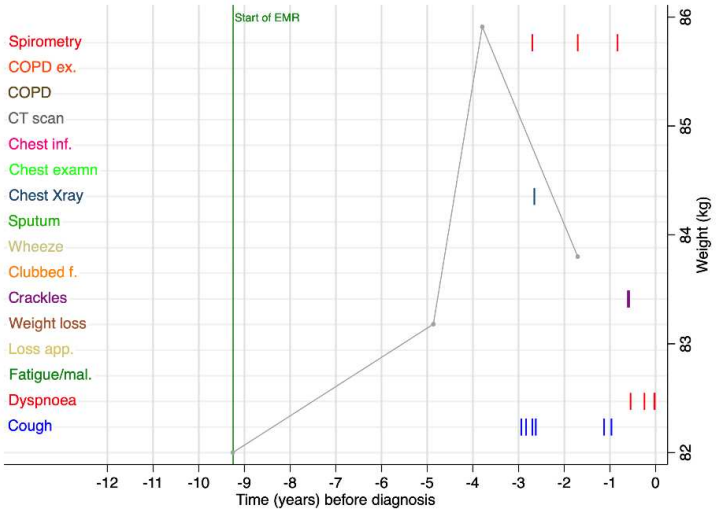
No obvious weight loss; dyspnoea as presenting symptom



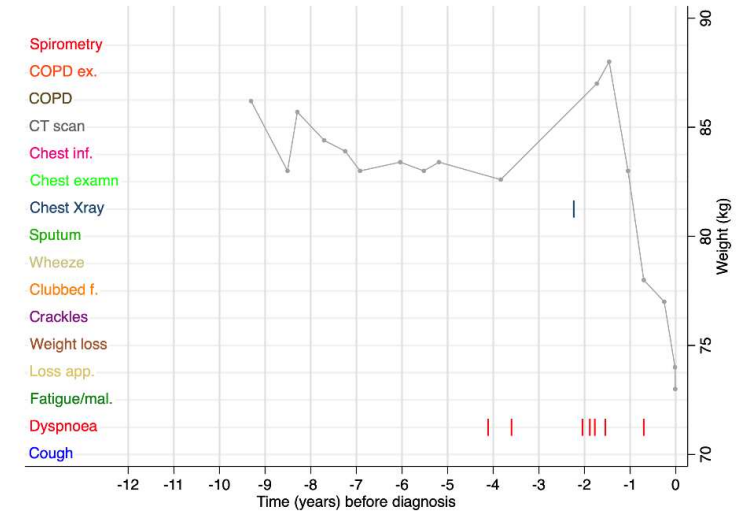
Long period of cough and dyspnoea



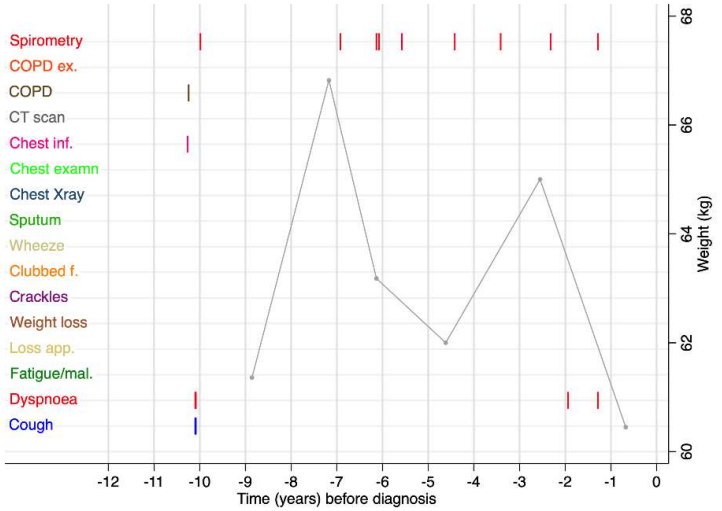
3 years of symptoms without weight loss



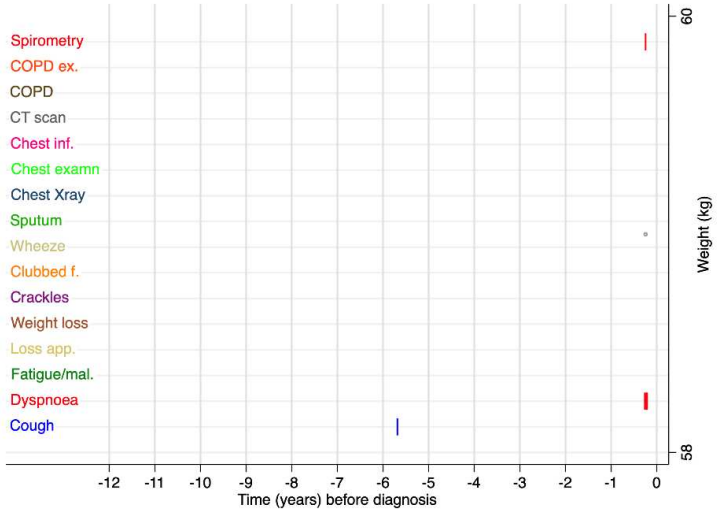
4 years of symptoms; late weight loss; likely treated as COPD



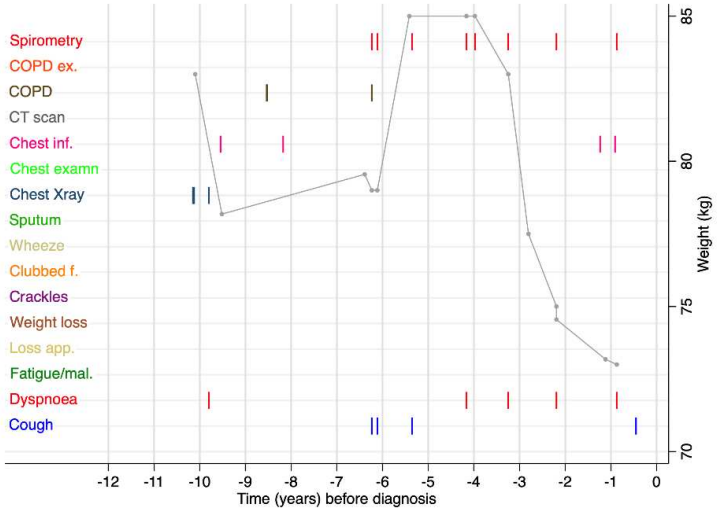
Likely treated as COPD for 10 years with ICS/LABA



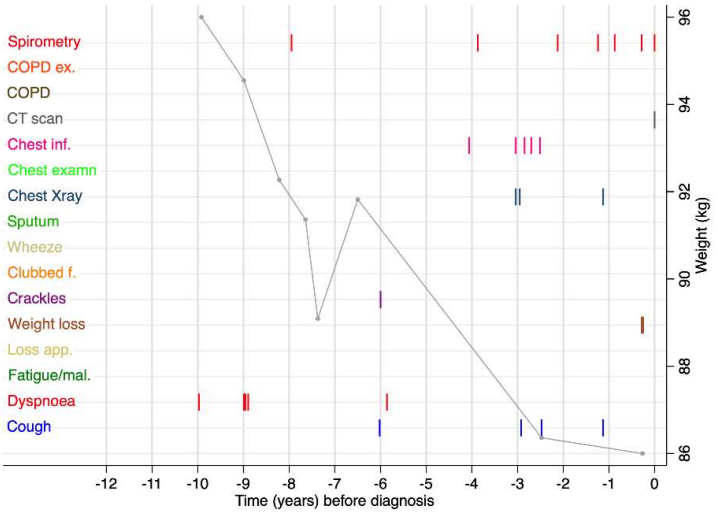
Rapid diagnosis



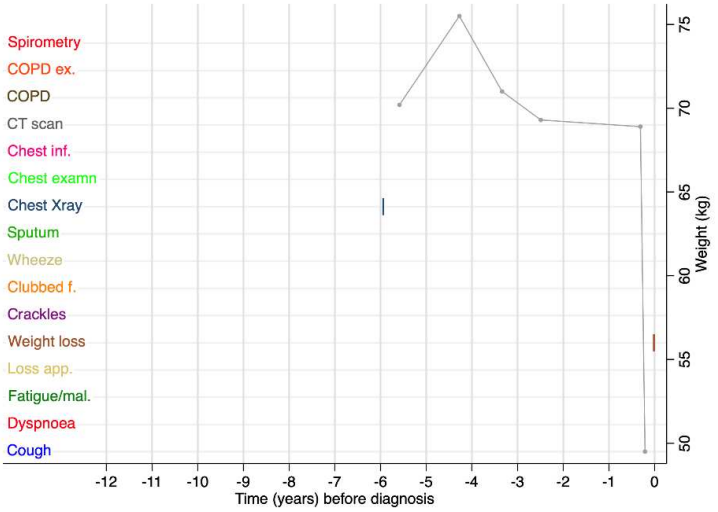
4 years of weight loss before diagnosis; Previously diagnosed with COPD



Long, slow weight decline; late diagnosis



Early diagnosis; no respiratory symptom recorded; investigated for weight loss



Supplementary Figure E5. Kaplan-Meier plot for cumulative probability of IPF diagnosis over time since first symptom of cough or dyspnoea.