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# Epidemiology of idiopathic pulmonary fibrosis in Europe - an update

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**Abstract.** Idiopathic pulmonary fibrosis (IPF) is a non-neoplastic pulmonary disease that is characterised by the formation of scar tissue within the lungs in the absence of any known cause. IPF is the most common of the idiopathic interstitial pneumonias and is an important cause of respiratory mortality. IPF is a relatively rare disease with an estimated prevalence ranging from two to 29 cases per 100,000 and slightly higher in men (20.2/100,000) than in women (13.2/100,000). The mean age at presentation is 66 years. Little recent epidemiological data on the prevalence, incidence, risk factors, and mortality related to the disease are available or are limited by methodological weaknesses. Outstanding questions remain, including the causes of IPF, why the incidence is on the rise, and how best to manage this disease. New comparable epidemiological data on IPF are needed. *(Sarcoidosis Vasc Diffuse Lung Dis 2013; 30 Suppl 1: 6-12)*

**Key words:** epidemiology, Europe, idiopathic pulmonary fibrosis, incidence, mortality, prevalence

## Introduction

Idiopathic pulmonary fibrosis (IPF) belongs to a family of lung disorders known as diffuse interstitial (or parenchymal) lung diseases (ILDs) that represent a large group of more than 200 different entities, many of which are rare or 'orphan' diseases (1). Within this broad category, IPF belongs to the subgroup differentiated by specific clinical features and pathological patterns known as idiopathic interstitial pneumonia (IIP) (2). IPF is associated with the pathological pattern known as usual interstitial pneumonia (UIP) and is the most common and deleterious form of the seven distinct IIPs (3-5).

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IPF is a chronic, progressive, life-threatening disease that manifests over several years and is characterised anatomically by scarring of the lungs and symptomatically by exertional dyspnoea and chronic dry cough (4, 6). IPF is usually fatal, with an estimated 5-year survival rate approaching 20% (6, 7), worse than several types of cancer (7). Respiratory failure is the most frequent cause of death, and has been reported to account for over 80% of all fatalities; heart failure, bronchogenic carcinoma, ischaemic heart disease, infection, and pulmonary embolism are also common causes of mortality (8-10). IPF aetiology is unknown, and the pathogenic mechanisms involved in its initiation and progression are poorly understood (11). Potential risk factors for the development of IPF include cigarette smoking, wood, mineral and metal dust exposure, past viral infection, and chronic gastro-oesophageal reflux with micro-aspiration (12, 13). Collection of

existing epidemiological data and new comparable data on IPF are needed to better understand the disease.

## IPF distribution

Despite being the most pernicious and frequent of the ILDs accounting for 55% of IIPs (14, 15), there is a paucity of precise data of the incidence and prevalence of IPF and its associated mortality (16). IPF is a rare disease with an incidence of approximately 10.7/100,000 in men and 7.4/100,000 in women (17). Prevalence estimates for IPF have varied from two to 29 cases per 100,000 and are also slightly greater in men (20.2/100,000) than in women (13.2/100,000) (17-21). Worldwide data suggest that IPF favours no particular race, ethnic group or social environment. IPF has no distinct geographical distribution. However, the age-adjusted mortality rates appear higher among whites and lower among blacks (22). IPF most commonly appears between the fifth and seventh decades of life, with two-thirds of all cases arising in patients over 60 years of age. The mean age at presentation is 66 years but the incidence increases with age (12). It also appears that the incidence of IPF has been increasing steadily over the last two to three decades (23, 24).

## IPF in Europe

There are an estimated 80-85,000 patients living with IPF in the 27 European Union (EU) countries (25). The estimated prevalence of IPF in the EU ranges from 1.25 to 23.4/100,000, and is rising with an estimated 40,000 new cases diagnosed each year (26-29). More recent estimates of disease prevalence (range, 1-24 cases per 100,000) are available from several European Studies (Table 1) (20, 27-29).

### *United Kingdom*

There are currently few data available on the incidence of ILD in the United Kingdom (UK) with most estimates coming either from disease registries or, in the case of IPF, from death certificate registrations. One study in the UK reported an overall incidence rate of IPF of 7.44 per 100,000 person-years from a longitudinal computerised general practice database. Moreover, the incidence increased by 35% from 2000 to 2008 with annual death certificate recordings for IPF rising six-fold from 0.92/100,000 in the 1968-1972 calendar periods to 5.10/100,000 in the 2006-2008 calendar period (Table 2) (23). Another study from the UK reported an overall incidence rate of IPF at 4.6/100,000 person-years and also observed a progressive increase in the incidence of 11% annually between 1991 and 2003 (30). This increase was not felt to be attributable to the aging of the population or increased ascertainment of milder cases. A further study from the UK showed that the annual number of hospital admissions from IPF-CS for all National Health Service (NHS) hospital trusts in England increased at a rate of approximately 5% between 1998 and 2010 and was highest in men and the older population (31). These data contrast with those from Minnesota, USA that do

**Table 1.** Prevalence and incidence of IPF in Europe (20, 21, 23, 27-30)

| | Prevalence/100000 | | Incidence/100000 |
|---|---|---|---|
| | Age (years) | IPF | IPF |
| Belgium (Thoomer, 2001) | All | 1.25 | 0.22 |
| Czech Republic (Kolek, 1995) | All | 12.1 | 0.94 |
| Finland (Hodgson, 2002) | All | 16-18 | |
| Greece (Karakatsani, 2009) | All | 3.38 | 0.93 |
| Norway (von Plessen, 2003) | ≥16 | 23 | 4 |
| | | 17-31* | 4-5* |
| UK (Gribbin, 2006) | ≥40 | - | 5 |
| | | | 6-3* |
| UK (Navaratnam, 2011) | ≥40 | - | 7 |
| | | | 9-5* |
| **France** | ONGOING | | |
| **Italy** | ONGOING | | |

*cryptogenic fibrosing alveolitis

**Table 2.** The rising incidence of IPF in the UK (23)

| | Cases | Crude incidence rates (95% CI) per 100 000 person-years | Rate ratios (95% CI) |
|---|---|---|---|
| Year | | | |
| 2000 | 160 | 5.77 (4.95-6.74) | 1.0 |
| 2001 | 179 | 6.12 (5.28-7.08) | 1.08 (0.87-1.33) |
| 2002 | 203 | 6.69 (5.83-7.68) | 1.20 (0.98-1.48) |
| 2003 | 221 | 7.14 (6.26-8.15) | 1.30 (1.06-1.60) |
| 2004 | 253 | 8.08 (7.14-9.14) | 1.41 (1.16-1.72) |
| 2005 | 260 | 8.14 (7.21-9.19) | 1.45 (1.19-1.77) |
| 2006 | 243 | 7.54 (6.65-8.55) | 1.35 (1.11-1.65) |
| 2007 | 294 | 9.05 (8.07-10.15) | 1.63 (1.34-1.98) |
| 2008 | 261 | 8.04 (7.12-9.08) | 1.37 (1.12-1.67) |
| | | | P for trend < 0.0001 |
| Sex | | | |
| Male | 1307 | 9.46 (8.96-9.98) | 1.0 |
| Female | 767 | 5.46 (5.07-5.86) | 0.44 (0.40-0.48) |
| | | | P for trend < 0.0001 |
| Age group (years) | | | |
| ≤54 | 187 | 0.86 (0.75-1.00) | 0.02 (0.02-0.03) |
| 55-59 | 180 | 10.48 (9.06-12.13) | 0.28 (0.23-0.33) |
| 60-64 | 250 | 20.76 (18.34-23.50) | 0.56 (0.47-0.65) |
| 65-69 | 386 | 36.45 (32.99-40.27) | 1.0 |
| 70-74 | 425 | 47.57 (43.26-52.32) | 1.35 (1.18-1.55) |
| 75-79 | 365 | 47.38 (42.76-52.49) | 1.359 (1.21-1.61) |
| 80-84 | 211 | 60.05 (52.47-68.73) | 1.89 (1.59-2.23) |
| ≥84 | 70 | 34.82 (27.55-44.01) | 1.18 (0.92-1.53) |
| | | | P for trend < 0.0001 |

not show any increase (Fernandez-Perez). However, these data were based uniquely on healthcare providers' records.

*Italy*

One epidemiology study of IPF in Italy has been undertaken in the Lazio Region using linked data from the regional population, hospital and mortality registries. The study included patients discharged from hospital between January 1, 2005 and December 31, 2009, who were classified into either 'broad' or 'narrow' cases according to ICD9 criteria. Preliminary results indicate an incidence ranging from 4.9 to 7.5, according to reporting criteria. This is similar to that registered in the UK study, with incidence increasing with male gender and older age (32).

*France*

In the first epidemiologic study conducted in France since previous studies of sarcoidosis and farmer's lung, data were obtained from three different sources from November 2011 to November 2012: hospital respiratory medicine departments, primary care, and from National Health Insurance medical records (33). Preliminary results after eight months of investigation among patients from hospitals and primary care showed that a diagnosis was determined in 90% of the 453 cases according to international guidelines, with 10% of cases undetermined but often with possible UIP based on high resolution computed tomography (HRCT) scans. Sarcoidosis was most frequent (51%), followed by secondary ILDs (31%), and interstitial idiopathic pneumonia (16%). The average age of patients was 54.5±15.8 years with a gender ratio of 1.29 for females. Each case was reviewed by an expert panel. The results showed an incidence of 6.7/100,000 and a prevalence of 35/100,000 over a period of 8 months (Figures 1-3). (33)

## Methodological issues

Available epidemiological data are limited by methodological weaknesses.

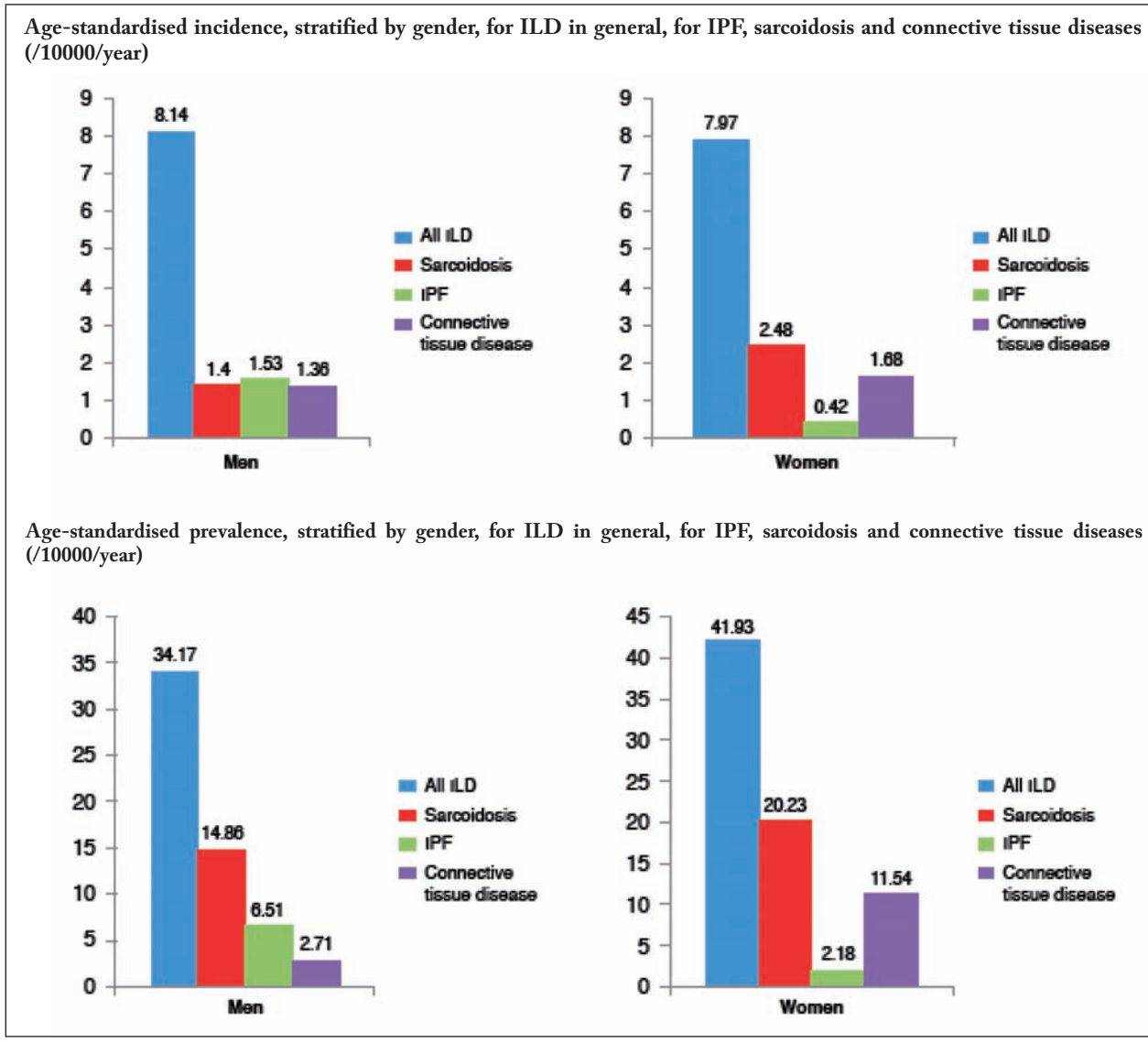



**Fig. 1.**

This lack of reliable epidemiological data represents a distinct barrier to the optimal management of these patients (30). In particular, most of the available data have been obtained from studies performed before the current uniform standardised definition used in identifying cases of IPF was adopted (34). Population studies utilised historical information relating to vital statistics, diagnostic coding data, and death certificates to identify cases. Thus, differences in study designs and populations have made it difficult to establish a truly accurate estimate of the incidence and prevalence of IPF (12). The lack of exhaustivity in the recruitment has constituted another weakness so far.

Furthermore, with the introduction of HRCT in the early 1990s, it is difficult to verify whether the apparent rapid increase in the incidence of IPF over time reflects a true increase in disease incidence or whether other factors, such as an increase in case ascertainment or changes in disease recording, play a role. Ascertainment is a particularly important point to consider because of the important impact it has

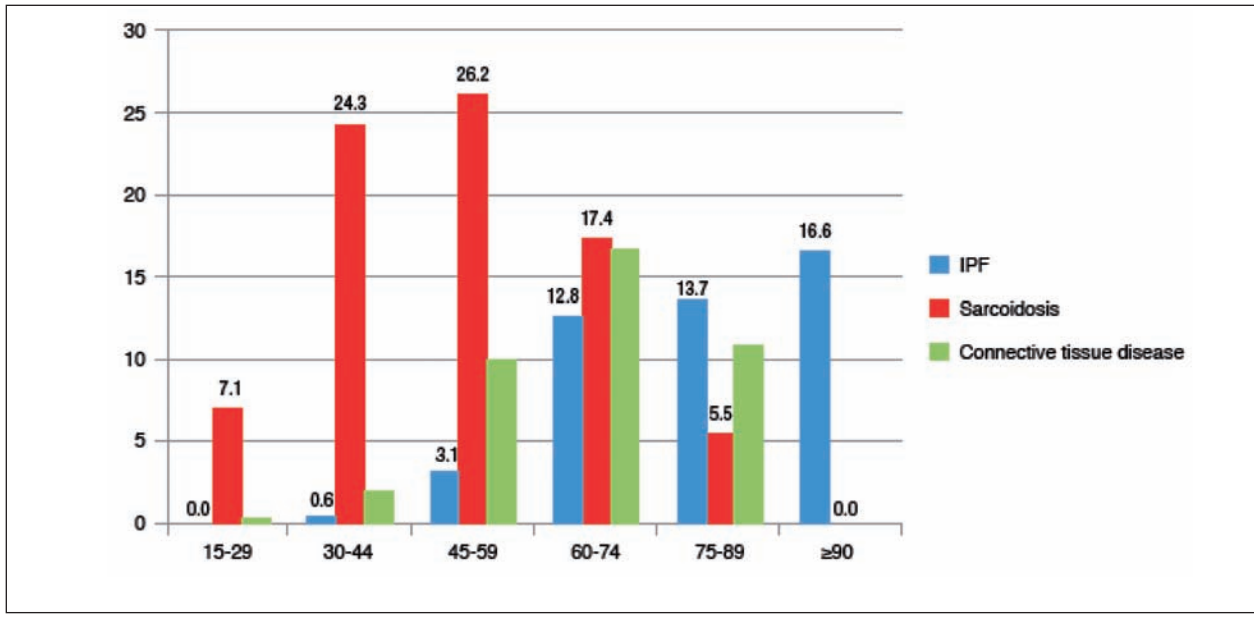
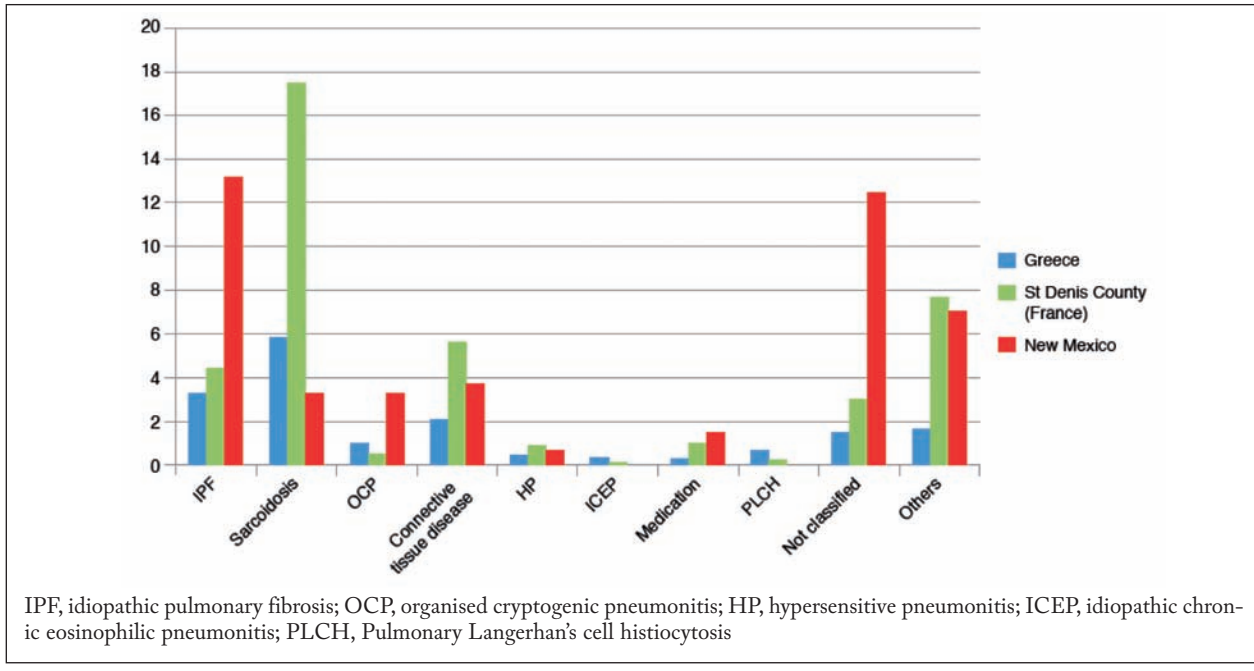



**Fig. 2.** Prevalence of IPF, sarcoidosis and connective tissue diseases according to age (/10,000)




IPF, idiopathic pulmonary fibrosis; OCP, organised cryptogenic pneumonitis; HP, hypersensitive pneumonitis; ICEP, idiopathic chronic eosinophilic pneumonitis; PLCH, Pulmonary Langerhan's cell histiocytosis

**Fig. 3.** Prevalence by pathology (/10000): comparison with literature

had on the investigation and diagnosis of ILD, especially IPF. In general, as ascertainment of a disease increases, severity decreases because the additional cases tend to have milder disease and because patients are treated.

Another potential weakness is that some cases may actually be prevalent rather than incident; this may overestimate survival time, since prevalent cases are, by definition, survivors and have a longer median survival length than incident cases (35). In addi-

tion, estimates of disease incidence from registry datasets may be overinflated because of the problem of accurately defining the denominator population, while estimates from death registrations are usually underestimates because the diagnosis is not included on the death certificate (34).

## Conclusions

It is apparent that the incidence of IPF in primary and secondary care (hospital admissions) and registered death will continue to rise. This will obviously result in escalating costs of in-patient care, a significant financial burden on healthcare resources. Clearly, new comparable epidemiological data from patients with IPF, using standardised and harmonised methods for collecting baseline and trend data, with mandatory clinical IPF registries are required.

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