



Idiopathic pulmonary fibrosis: another step in understanding the burden of this disease



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Idiopathic pulmonary fibrosis: good-quality Canadian study with high incidence adds to the epidemiological jigsaw <http://ow.ly/gArO300hdSx>

The past 25 years have seen a steady increase in the number of studies examining the incidence of idiopathic pulmonary fibrosis (IPF) worldwide [1, 2]. In general, early studies tended to involve clinicians collating cases from their local area [3, 4] or asking interested colleagues to contribute to registries [5, 6], whereas later studies have made use of large databases collected for clinical care or administrative reasons [7–10]. These later studies boasted far greater numbers, though with some concern about the validity of the cases, the reliability of clinical coding and generalisability to the wider population. A recent systematic review estimated the incidence of IPF to be 3–9 cases per 100 000 in Europe and North America, although this included a heterogenous mix of studies with different case definitions and populations, and several less reliable estimates had to be excluded [2]. Therefore, identifying the true incidence of IPF remains a challenge [11].

In this issue of the *European Respiratory Journal*, HOPKINS *et al.* [12] add to the literature with their study of IPF in Canada. The authors used two data sources to identify cases: a mandatory nationwide database of hospital admissions, and a smaller database of emergency department and outpatient clinic attendances covering ~50% of the national population. Incident and prevalent cases were identified with both “broad” and “narrow” definitions of IPF, as with other studies [7, 9]: the latter more specific definition requiring the presence of a relevant diagnostic test (computed tomography, lung biopsy or bronchoscopy) prior to the record with the diagnostic code for IPF.

The key findings were an incidence of IPF of 18.7 cases per 100 000 for the broad definition, and 9.0 cases per 100 000 for the narrow definition. These findings are important for two reasons. First, the study has been conducted carefully: cases were well-defined, the study period was contemporaneous, there was a clear denominator population that was comprehensively sampled, and this was clearly representative of the entire country, with minimal extrapolation. Secondly, the estimates are amongst the highest reported in the literature. Although some recent studies have reported higher incidence figures, these have tended to be for a specified population over a certain age (*e.g.* those aged >50 years or >65 years) [10, 13], whereas the current study presents estimates applicable to the entire population, allowing easier comparison to the rest of the literature. The results place the incidence of IPF higher than other major studies from both Europe and North America [2, 7, 8].

How can we interpret this study? Do these estimates reflect the true incidence of IPF worldwide, or is it simply more common in Canada than elsewhere? The key to this lies in determining whether individual studies are likely to be over- or underestimating case numbers, which in turn reflects diagnostic processes

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and clinical coding. There is evidence from the USA that coding in insurance claims-based data may over-estimate cases of IPF [14], which raises some concerns about the widespread use of large datasets without additional clinical verification. However, it is also possible that precise codes in these datasets may not capture all cases of IPF. One study from Italy reported a higher incidence of IPF after review of additional case records than when using coding criteria alone [15], yielding a very similar result for the narrow case definition to that obtained by HOPKINS *et al.* [12] in the current study.

The current study used code J84.1 from the Canadian modification of ICD-10, defined as “other interstitial pulmonary diseases with fibrosis”. Although the most specific code available for IPF, it is possible this may include other idiopathic interstitial pneumonias such as nonspecific interstitial pneumonia, which are poorly accommodated by the ICD-10 coding system [16]. Future coding proposals, including the new US clinical modification of ICD-10 (ICD-10-CM) and the World Health Organisation’s proposed ICD-11 (due 2018) [17], offer more precise coding and may provide clarity; however, these will take time to become established, by which point history suggests that definitions used in clinical practice may have moved on. It is likely that some cases in the current study may not be “true” IPF, while others may be labelled differently and missed, although without clinical validation it is difficult to estimate the scale of any coding inaccuracies. What is certain is the need to try to understand the impact of potential miscoding, either under- or over-estimating disease incidence, to ensure accurate assessment of disease burden, and subsequently the appropriate distribution of healthcare resources. For example, access to pulmonary rehabilitation or palliative care may be less available if incidence is inappropriately underestimated.

Part of the challenge is how the diagnosis of IPF is applied in clinical practice. Although clinicians can be guided by excellent international consensus statements [18, 19], there will always be variation when there is no pathological “yes or no” answer to clinch a diagnosis, rather a mix of terms such as “probable” and “possible” put forward by variably experienced members of multidisciplinary teams. When a specific imaging pattern can mean IPF (and potential exciting new medications) or asbestosis (if the appropriate detailed history is elicited) or even connective tissue disease-related interstitial lung disease or interstitial pneumonia with autoimmune features (if the hospital has the appropriate panel of new autoimmune tests available) [20] then the reliability of diagnostic labels may clearly vary between centres, let alone countries. It is clear that radiologists may disagree with regards to identifying a usual interstitial pneumonia pattern on imaging [21]; an interesting proposal would be to share sample case histories and radiology between different specialist centres and assess the degree of diagnostic concordance that arises. Some physicians may pragmatically diagnose IPF while others spend time hunting a specific cause; others may prefer to diagnose unclassifiable disease unless the picture is clear-cut. The extent of this variation in practice may underlie some of the variation in disease incidence from studies.

Nevertheless, accepting potential variation in clinical practice and coding, the application of a specific ICD-10 code clearly suggests a fibrotic interstitial lung disease that may well be IPF or something very similar, and this was more common in the study by HOPKINS *et al.* [12] than many other studies. This may reflect missed cases elsewhere, but the fact that some studies have taken a similar approach and still yielded lower incidences [22, 23] suggests there may well be true differences in IPF incidence across regions. There are several possible reasons for this: the latter of two recent studies from Italy with varying estimates speculated about environmental differences such as concentration and sources of environmental pollution [15, 23], and studies from Japan have typically shown lower rates which may be due to genetic differences [24, 25]. This highlights why estimating IPF incidence is so important, not only to understand the volume of disease presenting each year, but also to explore variation in incidence across countries and regions, thereby shedding light on potential aetiological factors underlying this (currently) idiopathic disease.

The study by HOPKINS *et al.* [12] provides other insights. The authors estimated the prevalence of IPF, and found this to be 41.8 cases per 100 000 (broad definition) and 20.0 cases per 100 000 (narrow definition). While this gives a flavour of the population burden of disease, incidence remains the most useful measure in IPF epidemiology for two reasons. First, by better reflecting the impact of a disease that typically has low survival (where prevalence estimates may be biased by the minority of patients living longer), and secondly, by being a more dynamic marker that allows unexpected variation over time due to changing aetiological risk factors to be identified.

As well as incidence and prevalence, the authors were able to assess survival and quality of life. In both cases, patients with IPF did worse than those with chronic obstructive pulmonary disease, highlighting the clear burden of the disease on patients. This supports the work of the European IPF Patient Charter in highlighting unmet needs of people with IPF [26]. Overall, the study provides a further piece in the IPF epidemiology jigsaw, standing out as one of the few “national” database studies from a western country, and revealing a higher incidence of disease than elsewhere. It also highlights the importance of accurate clinical coding, consistent diagnostic approaches and the value of large databases in monitoring disease burden. Given the higher incidence of IPF shown in this study, and other evidence that mortality from

IPF is increasing [27], it is crucial that healthcare systems adapt to provide the care needed for patients newly diagnosed with this disease.

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References

- 1 Demedts M, Wells AU, Anto JM, *et al.* Interstitial lung diseases: an epidemiological overview. *Eur Respir J* 2001; 18: Suppl 32, 2s–16s.
- 2 Hutchinson J, Fogarty A, Hubbard R, *et al.* Global incidence and mortality of idiopathic pulmonary fibrosis: a systematic review. *Eur Respir J* 2015; 46: 795–806.
- 3 Coultas DB, Zumwalt RE, Black WC, *et al.* The epidemiology of interstitial lung diseases. *Am J Respir Crit Care Med* 1994; 150: 967–972.
- 4 Kolek V. Epidemiology of cryptogenic fibrosing alveolitis in Moravia and Silesia. *Acta Univ Palacki Olomuc Fac Med* 1994; 137: 49–50.
- 5 Thomeer M, Demedts M, Vandeurzen K. Registration of interstitial lung diseases by 20 centres of respiratory medicine in Flanders. *Acta Clinica Belgica* 2001; 56: 163–172.
- 6 Tinelli C, De Silvestri A, Richeldi L, *et al.* The Italian register for diffuse infiltrative lung disorders (RIPID): a four-year report. *Sarcoidosis Vasc Diffuse Lung Dis* 2005; 22: Suppl 1, S4–S8.
- 7 Raghu G, Weycker D, Edelsberg J, *et al.* Incidence and prevalence of idiopathic pulmonary fibrosis. *Am J Respir Crit Care Med* 2006; 174: 810–816.
- 8 Navaratnam V, Fleming KM, West J, *et al.* The rising incidence of idiopathic pulmonary fibrosis in the U.K. *Thorax* 2011; 66: 462–467.
- 9 Lai CC, Wang CY, Lu HM, *et al.* Idiopathic pulmonary fibrosis in Taiwan – a population-based study. *Respir Med* 2012; 106: 1566–1574.
- 10 Raghu G, Chen SY, Yeh WS, *et al.* Idiopathic pulmonary fibrosis in US Medicare beneficiaries aged 65 years and older: incidence, prevalence, and survival, 2001–11. *Lancet Respir Med* 2014; 27: 566–572.
- 11 Samet JM, Coultas D, Raghu G. Idiopathic pulmonary fibrosis: tracking the true occurrence is challenging. *Eur Respir J* 2015; 46: 604–606.
- 12 Hopkins RB, Burke N, Fell C, *et al.* Epidemiology and survival of idiopathic pulmonary fibrosis from national data in Canada. *Eur Respir J* 2016; 48: 187–195.
- 13 Perez ER, Daniels CE, Schroeder DR, *et al.* Incidence, prevalence, and clinical course of idiopathic pulmonary fibrosis: a population-based study. *Chest* 2010; 137: 129–137.
- 14 Esposito DB, Lanes S, Donneyong M, *et al.* Idiopathic pulmonary fibrosis in United States automated claims. Incidence, prevalence, and algorithm validation. *Am J Respir Crit Care Med* 2015; 192: 1200–1207.
- 15 Agabiti N, Porretta MA, Bauleo L, *et al.* Idiopathic pulmonary fibrosis (IPF) incidence and prevalence in Italy. *Sarcoidosis Vasc Diffuse Lung Dis* 2014; 31: 191–197.
- 16 World Health Organization. International Statistical Classification of Diseases and Related Health Problems, 10th Revision. 2016.
- 17 World Health Organization. The International Classification of Diseases 11th Revision is due by 2018. www.who.int/classifications/icd/revision/en/
- 18 Travis WD, Costabel U, Hansell DM, *et al.* An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. *Am J Respir Crit Care Med* 2013; 188: 733–748.
- 19 Raghu G, Collard HR, Egan JJ, *et al.* An official ATS/ERS/JRS/ALAT statement: idiopathic pulmonary fibrosis: evidence-based guidelines for diagnosis and management. *Am J Respir Crit Care Med* 2011; 183: 788–824.
- 20 Fischer A, Antoniou KM, Brown KK, *et al.* An official European Respiratory Society/American Thoracic Society research statement: interstitial pneumonia with autoimmune features. *Eur Respir J* 2015; 46: 976–987.
- 21 Walsh SL, Calandriello L, Sverzellati N, *et al.* Interobserver agreement for the ATS/ERS/JRS/ALAT criteria for a UIP pattern on CT. *Thorax* 2016; 71: 45–51.
- 22 Kornum JB, Christensen S, Grijota M, *et al.* The incidence of interstitial lung disease 1995–2005: a Danish nationwide population-based study. *BMC Pulm Med* 2008; 8: 24.
- 23 Harari S, Madotto F, Caminati A, *et al.* Epidemiology of idiopathic pulmonary fibrosis in Northern Italy. *PLoS One* 2016; 11: e0147072.
- 24 Ohno S, Nakaya T, Bando M, *et al.* Idiopathic pulmonary fibrosis – results from a Japanese nationwide epidemiological survey using individual clinical records. *Respirology* 2008; 13: 926–928.
- 25 Natsuizaka M, Chiba H, Kurohama K, *et al.* Epidemiologic survey of Japanese patients with idiopathic pulmonary fibrosis and investigation of ethnic differences. *Am J Respir Crit Care Med* 2014; 190: 773–779.
- 26 Bonella F, Wijssenbeek M, Molina-Molina M, *et al.* European IPF Patient Charter: unmet needs and a call to action for healthcare policymakers. *Eur Respir J* 2016; 47: 597–606.
- 27 Hutchinson JP, McKeever TM, Fogarty AW, *et al.* Increasing global mortality from idiopathic pulmonary fibrosis in the twenty-first century. *Ann Am Thorac Soc* 2014; 11: 1176–1185.