Unravelling the health and economic burden of interstitial lung diseases in adults in Australia

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Background
Interstitial lung diseases (ILD) are a heterogenous group of over 200 disorders affecting the pulmonary interstitium. Although there have been advances in knowledge on ILDs in Australia, the characterisation of the health and economic burden of disease remained largely undetermined until recently.

Objective
The main objective of this review is to provide a synopsis of health and economic burden of ILDs in Australia, based on recently completed research.

Discussion
Recent research has demonstrated that idiopathic pulmonary fibrosis (IPF) is the most frequent ILD in Australia. Incidence and prevalence of IPF have demonstrated an increasing trend over the past decades. Mortality has also increased over the past decades, but has shown a slight decreasing trend recently, since the introduction of antifibrotic medication. Health-related quality of life is poor in patients with IPF, and care is estimated to cost approximately AU$299 million per year in Australia. Early diagnosis and referral to tertiary care is crucial for favourable outcomes, and general practitioners are considerably important to this as the first interface to identify patients at risk and detect early symptoms of ILDs.

INTERSTITIAL LUNG DISEASES (ILDs) are a heterogenous group of over 200 disorders affecting the pulmonary interstitium, the oxygen-absorbing component of the lung, many of which are considered rare diseases.[1] Characterised by inflammation and/or fibrosis of the lung tissue, ILDs invariably lead to impaired gas exchange and declining lung function.[1] Clinically, ILDs are characterised by the cardinal symptoms of dyspnoea and dry cough in most instances. The disease course of ILDs is quite variable depending on the subtype, and can range from stable to rapidly progressive, irreversible lung tissue damage, respiratory failure and death in many cases where fibrosis is involved, unless lung transplantation is offered.[1,2]

Several risk factors for ILDs have been identified, including smoking, autoimmune conditions, occupational, environmental and drug exposures. Family history and genetic susceptibility to pulmonary fibrogenesis are additional important risk factors, which have been identified with increased understanding of the 'at risk' genetic profile for developing ILD.[3]

The establishment of registries, longitudinal cohorts and use of administrative health databases have improved the understanding of ILDs over the past decades. ILDs are considered a significant contributor to the global burden of chronic respiratory diseases and contribute to approximately 3.0% of all chronic respiratory disease deaths and 5.0% of disability-adjusted life years (DALYs).[4] Epidemiological data vary across geographic regions and countries partly due to differing methodology and coding systems used to identify ILDs, and differing diagnostic definitions for the ILD subtypes.[5,6] Prevalence estimates have demonstrated an increasing trend over the past decades and vary globally from 6.27 to 71.0 per 100,000, with idiopathic pulmonary fibrosis (IPF) being identified as the most frequent subtype in most countries.[6]

IPF is a progressive, irreversible fibrotic ILD with few treatment options and poor outcomes and a median survival of two to five years.[1,2] Mortality rates have generally demonstrated an increasing trend over the past decades; however, recent research has shown some promise with decreasing trends in mortality, which might be attributable to more effective and evidence-based treatment options in the last few years.[7–10] Evidenced-based treatment options and management guidelines are limited and depend on the underlying cause, diagnosis and expected disease course.[1] Antifibrotic medications (nintedanib and pirfenidone) have been shown to slow the decline in forced vital capacity (FVC) percent predicted in progressive IPF, and now also in non-IPF progressive pulmonary fibrosis.[1] Although immunosuppressive therapy has been proven beneficial in the treatment of ILDs resulting from connective tissue disorder associated with ILDs, they are detrimental in the treatment of other ILD forms including IPF.[1] Supportive measures to alleviate symptoms, supplemental oxygen therapy

and pulmonary rehabilitation are important interventions that can improve quality of life.[1] Lung transplantation is a realistic option for relatively few candidates given the usual later age of onset of ILDs, and the likelihood of multimorbidity.[2]

The Australian context

Although there have been advances in knowledge through clinical and basic science research on ILDs in Australia, the characterisation of the health and economic burden of disease remained largely undetermined until recently.[11,12] The availability of data through the establishment of multicentre, longitudinal registries, firstly the Australian IPF registry (AIPFR) in 2012–19 and the Australasian ILD Registry (AILDR) in 2016, presented ground-breaking opportunities for the health and economic burden of disease.[13,14] These two registries have been the foundation of our Australian National Health and Medical Research Council (NHMRC)-funded research through the Centre for Research Excellence in Pulmonary Fibrosis (CRE-PF) established in 2017, in collaboration with the Lung Foundation Australia, with continued funding for 2023–28.[12] Through these registries, their participants, data linkage and Australian Bureau of Statistics data, the first quantification of the burden of IPF in Australia was feasible, including the epidemiological burden, burden on patients' quality of life and cost burden.[15–18]

Data from the AILDR revealed that IPF is the most frequent ILD in registrants, and for this reason, our focus here will be on the burden of IPF for which most of the data are currently analysed.[13] Incidence and prevalence of IPF have demonstrated an increasing trend over the past decades, with crude incidence increasing from 7.5 per 100,000 in 1997, to 14.2 per 100,000 in 2018, and projections to increase to 16.3 per 100,000 by 2025.[15] Similarly, crude prevalence was 23.7 per 100,000 in 1997, 42.7 per 100,000 by 2018 and is projected to increase to 48.3 per 100,000 by 2025.[15] Mortality also increased between 1997 and 2016 from 5.2 to 6.8 per 100,000, but with new treatment regimens for IPF available from 2017, a slight decreasing trend was demonstrated, with estimates of 6.6 per 100,000 in 2022 and projected estimates in 2025 of 6.4 per 100,000.[15] All estimates were higher in males, and highest rates of disease were observed in persons aged ≥70 years, who accounted for approximately 82–83% of all IPF deaths, incident and prevalent cases (see the annual crude and age-standardised mortality, incidence and prevalence estimates for the period 1997–2015 and projected rates for 2016–25 in Cox et al 2022).[15]

Given the heavy symptom burden associated with IPF, health-related quality of life (HRQoL) is an important measure for clinical evaluation and patient care. How the disease impacts an individual's ability to live a fulfilling life is defined as health-related quality of life. HRQoL is determined by several factors, including the disease course, the individual's perceptions of their disease and their coping mechanisms. IPF has a significant negative impact on HRQoL, and this only increases with disease severity.[16,17] On average, there is a 1–5% decline in HRQoL of an individual with each 10-point decrease in the spirometric FVC percent predicted, mainly influenced by attributes measuring physical health as compared to psychosocial health.[16,17] This decline is further worsened by the addition of comorbidities. Having two or more comorbidities (multimorbidity) led to worsened HRQoL by a further 16–26%.[16,17] Musculoskeletal comorbidities such as arthritis, osteoporosis and heart disease were the biggest contributors to a decrease in HRQoL.[18] In general, people living with IPF had worse HRQoL than people living with angina, bronchiectasis, chronic kidney failure and even most individuals living with non-small cell lung cancer on treatment with no side effects, but similar to an individual living with a compensated stroke or chronic obstructive pulmonary disease (COPD).[19]

When compared to the annual national per capita expenditure on health in Australia for 2021 (AU$7927), annual costs related to IPF care were approximately four-fold greater, estimated at AU$31,655 per person per annum.[20] To put this into perspective, when we compare the national per capita expenditure to that for some other diseases experienced by this age group, for osteoarthritis, it was 0.1-fold the national average; for asthma, 1.7-fold; for diabetes, 1.1-fold; for COPD, 1.3-fold; for lung cancer 6.3-fold and for cardiovascular disease, it was 1.1-fold the national average.[21–23] Antifibrotic medication and hospitalisations accounted for approximately 74% of the IPF-related costs,[20] with disease severity and comorbidities having the greatest impacts on costs and similarly on hospitalisations.[20] With each 10-unit decrease in FVC percent predicted, annual per-patient costs and length of stay in hospital increased by 7–8% and 17% respectively.[20] To provide a broader context of the economic burden of IPF, extrapolating these estimates to the likely prevalence of IPF in Australia, total costs are projected to be approximately AU$299 million per year.[20]

Implications for general practice

ILDs are still considered rare diseases and consequently, might not always be considered in the differential diagnosis of patients with chronic respiratory symptoms. The symptoms are often insidious and non-specific in nature and might be attributed to ageing or other more frequent respiratory or cardiac conditions, resulting in a delay in diagnosis. Early diagnosis and early treatment are pivotal to improving patient outcomes, HRQoL, reduced number of acute exacerbations and resultant cost savings.

General practitioners (GPs) are uniquely placed to play an active part in detecting early signs/symptoms of ILDs. Timely consideration, investigation and referral to tertiary centres are crucial for an early confirmatory diagnosis by a multidisciplinary team and subsequent management. Careful consideration and evaluation of patients presenting with cardinal symptoms of ILDs (chronic dry cough, dyspnoea and weight loss) is paramount, especially in patients with a familial history of ILDs, smokers/ex-smokers, patients diagnosed with connective tissue/autoimmune disorders and patients who are at high risk to occupational or other exposures known to cause ILDs such as silica dust, asbestos, grain dust, bird and animal droppings, radiation therapy and chemotherapy medications.[1]

About one-quarter of the Australian population who attend general practices have two or more diagnosed chronic conditions, and in the IPF population we have studied, approximately 80% had one or more additional chronic diseases.[16,17,20,24] As mentioned earlier, multimorbidity was one of the main negative influential factors

on IPF patient outcomes, including having an effect on HRQoL, healthcare resource use and the associated costs.[16,17,20] Balancing care for patients with multimorbidity can be complex, especially in siloed health systems built to deal with individual conditions.[25] Continuity of care and its coordination are important pillars of the care of individuals with multimorbidity, ensuring that there is consistency between acute, specialist and community-based health services to achieve the best outcomes.[25] For the ILD patient, the GP's care coordination role is critical for: mitigating the risk of inappropriate treatment combinations or adverse events to medication interactions; establishing timely communication channels across speciality areas and other providers; and to assist patients in self-management and accessing community and disease-specific support services to improve their outcomes. Finally, the GP also plays an important role in ensuring early referral during acute episodes, securing optimal outcomes and follow-up care.

In conclusion, GPs continue to play an important role in early detection, diagnosis and continuity of care, which all lead to better health as well as economic outcomes.[26]

Future directions

Globally and in Australia, current clinical research and clinical trials continue to investigate options to reduce the morbidity and mortality associated with ILDs, providing much needed hope for patients. Genetics, multiomics and biomarker testing have created opportunities for risk detection and precision medicine, offering patients prospects for primary/secondary prevention, earlier diagnosis, and individualised care.[2] Insight into the pathogenesis of the gamut of ILDs has generated research into scope and timing of current therapies and in addition to novel therapies, which will hopefully increase the range of ILD treatment options available.[2] Symptom-based management, self-management and home-based care using technology (mobile apps) are also avenues for ongoing research.[2]

With the promise of novel diagnostics, treatments and precision medicine comes the challenge of costs; who pays for what and access to medications. Medicare and the Pharmaceutical Benefits Scheme (PBS) provide access to otherwise unaffordable health services in Australia. Resource allocations are evidenced-based and rely on clinical, epidemiological and health economic evidence. The health economic evidence serves as an integral tool to translate clinical research outputs into a language that influences policymakers and subsequent resource allocation for health services. The CRE-PF has premised its work on integrating epidemiological and health economic evidence as a critical part of the research platform, which provides the basis for rapid access to IPF diagnostic and therapeutic outputs from clinical research. Future work will focus on clearly defining the epidemiological burden of ILDs in Australia beyond IPF, defining the health burden with a broader investigation of HRQoL across all ILDs, and assessing the economic burden associated with ILDs. This will support the economic evaluation of the clinical research outputs from the CRE-PF and reduce delays to patients getting access to new interventions through Medicare and the PBS.

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