PCR245

Humanistic and Economic Burden Associated with Progressive Fibrosing Interstitial Lung Disease (PF-ILD): Summary of Evidence from Systematic Literature Reviews (SLRs)

Authors: Pratik Pimple[1], Ashish Pandey[2], Larisa Gofman[3]

Affiliation: [1]Boehringer Ingelheim, Germany; [2]ZS Associates, New Delhi, India; [3]ZS Associates, Princeton, NJ, USA

Background and Objectives

- Progressive fibrosing ILD (PF-ILD) refers to multiple subtypes of interstitial lung disease (ILD) with a similar progressive fibrosing phenotype as idiopathic pulmonary fibrosis (IPF)
- A number of ILDs other than IPF can manifest as PF-ILD and although they share common downstream mechanistic pathways and disease behaviour with IPF, PF-ILD often begins with an inflammatory phase triggered by either an endogenous autoantigen or an exogenous antigen (e.g. environmental trigger) (1)
- Patients with non-IPF ILD who are progressing despite management show similar trajectories to patients with untreated IPF, with a high risk of further clinical, functional, and/or radiological worsening, respiratory failure, and premature death (2)
- PF-ILD is associated with higher hospitalisations, high costs, and deterioration in health-related quality of life (HRQoL) (3)
- Two SLRs were conducted to assess the humanistic and economic burden associated with PF-ILD

Methods

- Database (MEDLINE®, Embase, PubMed®, Cochrane CENTRAL, EconLit) and supplementary searches (conference abstracts and HTA bodies) were conducted on September 26, 2023, to identify the evidence on the humanistic and economic burden associated with PF-ILD published between January 2014 and September 2023. The SLRs followed the Cochrane (4) and PRISMA (5) guidelines. The search included keywords and a combination of subject headings incorporating “progressing ILDs/ILDs“and study design terms (RCTs), combined with interventions of interest
- Key outcomes assessed were HRQoL, healthcare resource utilisation (HCRU) and the direct and indirect costs

Results

- The flow of study selection for the humanistic and economic burden SLRs is presented in Figure 1 and Figure 2, respectively:

Figure 1: PRISMA flow diagram of humanistic SLR

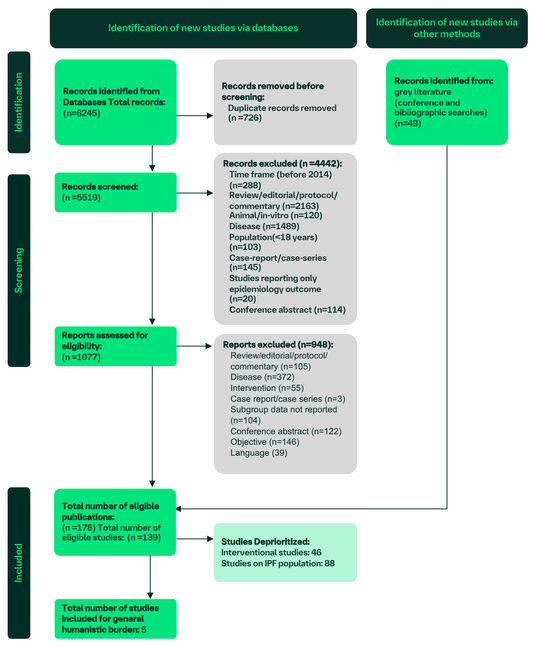
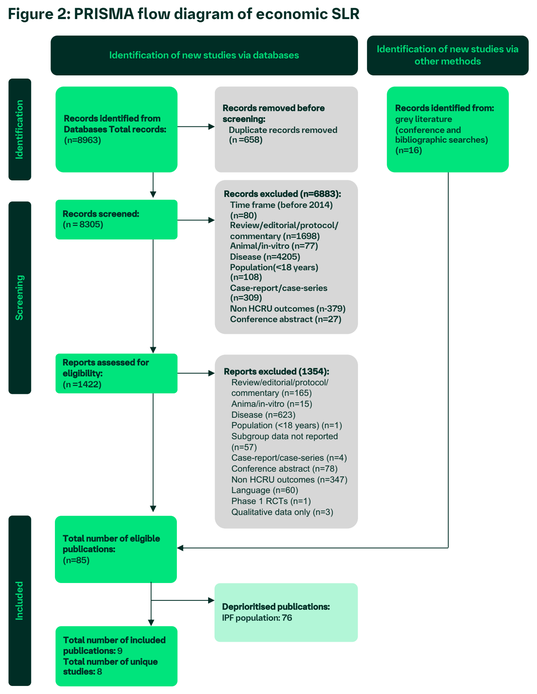


Figure 2: PRISMA flow diagram of economic SLR

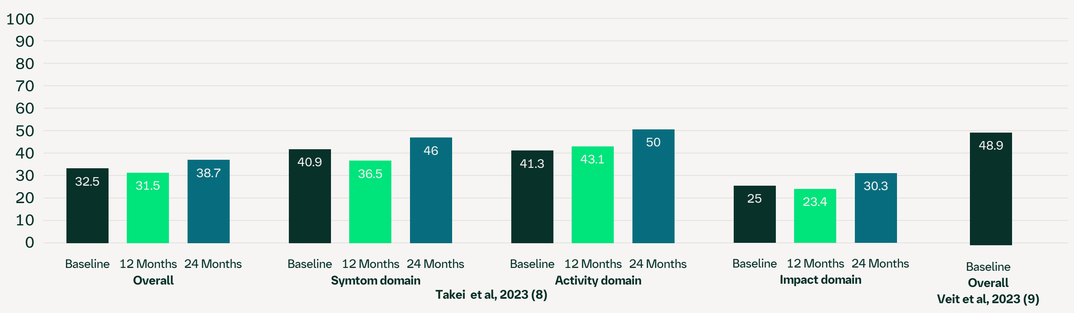


Key findings of the humanistic burden SLR

Five studies (including one conference abstract) assessed the humanistic burden of PF-ILD (Figure 1) (6-10), utilising HRQoL measures including:

- **St. George’s Respiratory Questionnaire (SGRQ)** which assesses overall health, daily life, and perceived well-being in patients in three domains (activity, symptom and impact domains), with scores ranging from 0-100 with higher scores indicating worse health and quality of life (8, 9)
- **King’s Brief Interstitial Lung Disease questionnaire (K-BILD)** which includes psychological, breathlessness and activities, and chest symptoms domains with a total score ranging from 0–100, where 100 represents best health status (6, 9)
- **Visual analogue scale cough (C-VAS)** for evaluation of cough severity in patients with chronic cough with higher values on VAS cough scale indicating a higher severity of cough (9)
- **COPD Assessment Test (CAT)** composed of eight items related to symptoms of respiratory disease and their impact including cough, phlegm, chest tightness, breathlessness, activity limitation, confidence, sleep, and energy, each assessed on a 0–5 response scale for a total score range from 0–40 where a score of 0 indicates no impairment (8)
- **Pittsburgh Sleep Quality Index (PSQI**) which is a 24-item scale that measures sleep disturbances along seven dimensions (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction), with a cumulative score ranging from 0–21, where lower scores denote a healthier sleep quality (6)
- **Delphi questionnaire** that utilised a modified Delphi method to assess HRQoL in patients with progressive fibrosing ILD by 40 European experts in ILD management (10)
- PF-ILD was associated with poor baseline (9) and further clinically important deterioration in SGRQ scores (odds ratio 5.04, 95%CI; 2.61, 9.76; p<0.01) across the three domains at 24 months (8) (**Figure 3**)

Figure 3: SGRQ scores at 24 months in patients with PF-ILD



- Declines in patients’ HRQoL from baseline have been observed as measured by K-BILD (−1.9 mean change at 12 months; p=0.28), PSQI (0.9 mean change at 12 months; p=0.36) (6), and CAT (2.0 mean change at 24 months; p-value not reported) with significantly higher CAT scores in patients with PF-ILD compared with those without (p<0.01) (8)
- Despite a decline in other HRQoL measures over time, a decrease in the mean VAS cough score and lower cough severity was observed as measured by C-VAS (−0.7 mean change over 6 months; p-value not reported) (9)
- The results of a Delphi questionnaire with a high level of agreement (85–90% of panellists) indicated that PF-ILD negatively impacts health, sleep, daily activities, emotional well-being, social life, and finances of unpaid caregivers (10)

Key findings of the economic burden SLR

- Eight studies (9 publications) met the inclusion criteria (**Figure 2**); four were conducted in Europe: Germany (11), Spain (12), France (13), and multinationally (Belgium, Denmark, Greece, the Netherlands, Portugal, Finland, Norway, and Sweden) (10); the rest were carried out in the US (14-18)

HCRU

- All studies suggested that PF-ILD was associated with high HCRU burden (10, 11, 13-16, 18) even prior to a definitive diagnosis (12)
- A high proportion of patients with PF-ILD reported hospitalisations for respiratory care across several European countries(10, 13) with a significant proportion of patients (75.2%) requiring hospitalisation due to acute events (13)
- Overall, significantly higher numbers of tests (laboratory and imaging; p<0.05) in patients with PF-ILD compared with those with non-/slow-progressing fibrosing ILD, and higher numbers of healthcare visits including frequency (4.4 vs 2.6 hospitalisations per patient), and mean duration of hospitalisation (5.9 days vs 3.9 days), were estimated by the Delphi panellists in the European based study (**Table 1**)(10)
- Compared with patients with non-PPF ILD, the HCRU was considerably higher for patients with PF-ILD across European countries (**Table 1**)(10), and the USA (14, 16, 18)

Table 1: Annual HCRU during follow-up of patients with non-/slow-progressive fibrosing ILD and patients with PF-ILD

HCRU		PF-ILD Mean [IQR]	Non/slow progressing ILD Mean [IQR]
Number of visits per patient per year	Total	7 [5–9]	4.7 [3-5]
Number of laboratory tests per patient per year	Total	13.6 [9–19]	4.7 [3-5]
Number of imaging or other tests per patient per year	Total	19* [15–23]	14.2* [9-22]
Number of hospitalisations per patient per year	Total	4.4 [2–5]	2.6 [0-4]
	Number of hospital admissions	1.9 [1–2]	1.5 [0-2]
	Number of admissions at the pulmonary department	2.2 [1–2]	1.1 [0-1.5]
	Number of hospital admissions at the intensive care unit	0.5 [0–1]	0.1 [0-0]
Length of hospital stay (days) per year	Mean duration of admission	5.9 [4–7]	3.9 [2-5]
	Mean duration of a pulmonary department hospitalisation	6.2 [4–7]	4.3 [3-5]
	Mean duration of intensive care unit hospitalisation	3.4 [2–5]	2.5 [2-3]

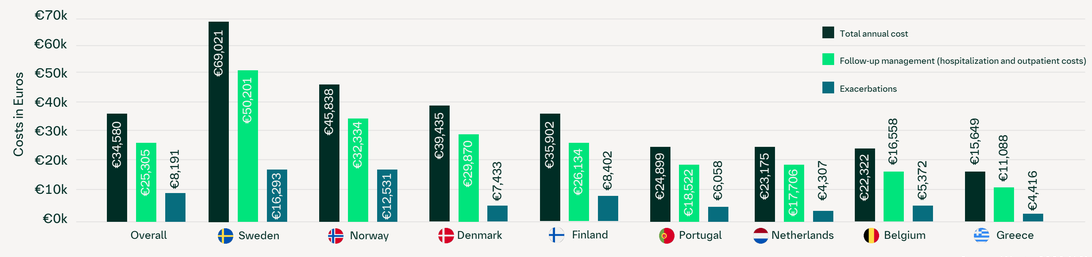
* p<0.05 Source: Wuyts et al, 2020 (10)

Direct costs

Europe

- The total annual costs for diagnosis, follow-up management (hospitalisation and outpatients costs) and treatment of exacerbations per patient with PF-ILD ranged between a median of €25,613 in France (13), a mean annual cost of €32,934 in Spain (12), and an average of €34,530 across several EU countries (10, 12) (Figure 4). Despite the decrease in the follow-up annual costs observed, the mean annual costs per PF-ILD patient (€34,530) were estimated. This cost was 1.8 times higher than the costs for patients with non- or slow-progressive ILD (€18,745 [2019]) in a European study using a modified Delphi approach, where cost estimates were based on resources used for diagnosis (visits, tests, treatments including mean doses and duration of treatment, and hospitalisations), annual number of follow-ups and adverse events management, management of exacerbations, and end-of-life care (10)
- In the Germany-based HILDA study, the adjusted ILD-specific mean medication costs increased from €46 at baseline to €1,215 at 12 months for patients with PF-ILD (recruited between November 2016 and April 2017) (11)
- Management costs of acute exacerbations (12) including hospitalisations (13) were the major cost drivers

Figure 4: Annual cost of PF-ILD per patient across several European countries.

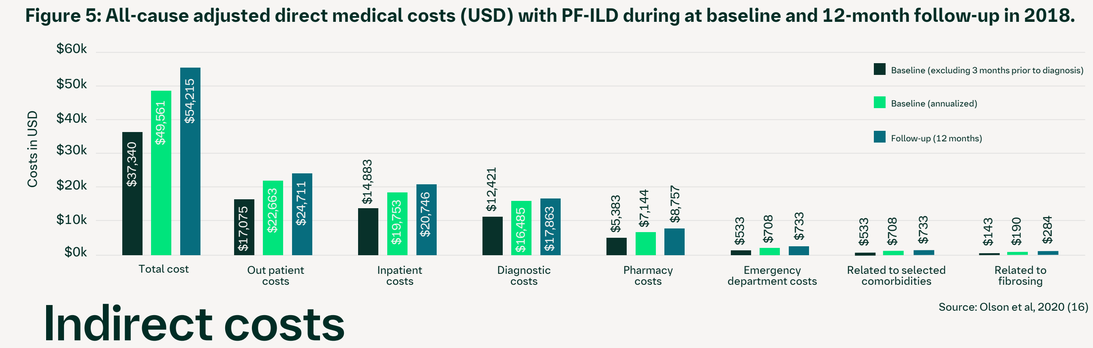


Source: Wuyts, 2020 (10)

USA

- The mean total direct per patient per year (PPPY) costs (varying types of direct costs) for managing PF-ILD ranged from $34,447 (2019 USD) to $77,666 (2016 USD) (17, 18)
- As per the US claims database (IBM MarketScan databases, 1 October 2011 to 30 September 2015), the baseline annual mean total cost was $49,561 in patients with PF-ILD, and increased to $54,215 at 12 months of follow-up (15) (**Figure 5**); for the period 2014–2016 the mean annual costs per patient with PF-ILD was higher than that of non-IPF ILD ($77,666 vs $68,085 for any medical claims, and $35,364 vs $20,211 for ILD-specific claims) (16)
- The analyses of the Optum Research Database data suggest that the costs were significantly higher for progressing non-IPF vs non-progressing patients (14, 18); for example, the total monthly healthcare costs per non-IPF patient with progressive phenotype vs non-progressive patients were significantly higher ($4,382±9,597 vs $2,243±4,162; p<0.001), including medical costs ($3,662±9,150 vs $1,627±3,524; p<0.001) and pharmacy costs ($720±2,097 vs $616 ±2,070; p=0.002), and were primarily driven by higher inpatient costs (18)

Figure 5: All-cause adjusted direct medical costs (USD) with PF-ILD during at baseline and 12-month follow-up in 2018.



Source: Olson et al, 2020 (16)

Indirect costs

- Compared with non-/slowly progressive ILD, a higher proportion of PF-ILD patients were estimated to have total permanent disability (19.6% vs 48.1%) and disability related job loss (8.8% vs 22.8%) (10)

Conclusions

- The limited evidence on the burden of PF-ILD suggests that disease progression is associated with increased exacerbations and worse patient and unpaid caregiver quality of life across all domains
- The per patient HCRU and costs are higher for patients with progressive fibrosing ILD than for the non- or slow progressing types and were mainly due to the longer and more frequent hospital stays for managing exacerbations
- Disease management approaches that reduce the need for hospitalisation and agents that prevent disease progression are needed to reduce the substantial humanistic burden of PF-ILD on patients and caregivers and the associated economic burden on healthcare systems

Abbreviations

IPF, idiopathic pulmonary fibrosis; SLR, systematic literature review. SGRQ, St. George’s Respiratory Questionnaire. HCRU, healthcare resource utilisation; IPF, idiopathic pulmonary fibrosis; RCT, randomised controlled trial; SLR, systematic literature review; ILD, interstitial lung disease; IQR, interquartile range; PF-ILD, progressive fibrosing ILD; PPPY, per patient per year. USD, United States Dollars.

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Disclosures

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