Exploring responsiveness of the Living with Pulmonary Fibrosis questionnaire in patients with pulmonary fibrosis – insights from the IFILE registry

D.E. Hofman[1], M. Oude Voshaar[2], C.C. Moor[3], G. Nakshbandi[3], R.L.M. Mostard[3], W. Wuyts[4], V. Cottin[5], M. Kreuter[6], M. Polke[7], K. Buschulte[7], P. Saunders[8], K. Antoniou[9], A. Froidure[10], H. Slabbynck[11], A.M. Hoffman-Vold[12], M.T. Durheim[13], A. van Veen[14], H.J. Bjørkekjær[15], M.C. Vonk[16], Z. Daniil[17], L.G. Spencer[18], P. Bonniaud[19], G. Prévot[20], L. Blok[1], P. Molyneaux[21], M.S. Wijsenbeek[1]

[1]Erasmus Rare Lung Diseases Center and Netherlands, Department of Pulmonary Medicine, Erasmus MC, [2]Department of Public Health, Erasmus Medical Center, [3]Department of Pulmonary Medicine, Zuyderland Medical Centre, [4]Department of Respiratory Medicine, Leuven Interstitial Lung Diseases, University Hospitals Leuven, [5]Reference Center for Rare Pulmonary Diseases, Louis Pradel Hospital, Claude Bernard University Lyon, [6]Mainz Center for Pulmonary Medicine, Mainz University Medical Center and Department of Pulmonary, Mainz Lung Clinic, [7]Center for Interstitial and Rare Lung Diseases, University of Heidelberg, [8]Oxford University Hospitals NHS Foundation Trust, [9]Pulmonology Department, Groningen University Medical Center, [10]Department of Pneumology, Zeta Medical Institute, [11]Department of Respiratory Medicine, Ghent University Hospital, [12]Department of Rheumatology, University of Oslo, [13]Department of Rheumatology, Hospital of Southern Norway, University of Oslo, [14]Department of Respiratory Medicine, Canisius Wilhelmina Ziekenhuis, [15]Department of Rheumatology, Hospital of Southern Norway, [16]Department of Respiratory Medicine, University of Texas, [17]Liverpool Interstitial Lung Disease Service, Liverpool University Hospitals NHS, [18]Interstitial Lung Disease Service, Liverpool University Hospitals NHS, [19]Rare Pulmonary Reference Center for Rare Pulmonary Diseases, Department of Pulmonary Medicine and Intensive Care Unit, Bocage University Hospital, [20]Service de Pneumologie, Poitiers Centre, [21]NIHR Respiratory Clinical Research Facility, Royal Brompton Hospital

Introduction

- The **Living with Pulmonary Fibrosis questionnaire (L-PF)** is a patient-reported outcome (PROM)
- L-PF measures **symptoms** and their impact on quality of life (**QoL**) with scores ranging from 0-100 (higher scores represent worse health status).[1]
- Data on **responsiveness to change** of the L-PF are scarce, stem from clinical trials, and only available for L-PF dyspnea and cough.[2]
- **Aim** To explore responsiveness to change of different L-PF modules to support utility of the L-PF in real-world populations.

Ref: [1]Swigris et al. 2021, PMID: 34046493, [2]Swigris et al. 2022, PMID: 35241434.

I-FILE study

Prospective multicentre patient-led registry (n=395)

Patients with a fibrotic ILD diagnosis established in an MDT

Patients participate in a home monitoring program, consisting of home spirometry and PROM completion

Study visits at baseline, 6-, 12-, 18-, and 24 months

Methods

- PROMs & lung function data at baseline, 6-, & 12 months follow up on incidental (< 3 months) and prevalent patients was used.
- Preliminary analyses on **adjusted mean scores** of the L-PF domains were derived using linear mixed models with random intercepts and antifibrotic use as fixed effect. Subsequently, scores were plotted for each timepoint.
- To analyze **responsiveness**, mean change scores were calculated across groups that deteriorated and improved based on predefined thresholds in Forced Vital Capacity (FVC), K-BILD, EQ5D-5L, LCQ, and General Rating of Change (GRoC).

Results

Table 1: Baseline characteristics

	(n=395)
Female	103 (26%)
Age (years)	68 (10)
IPF diagnosis	195 (49%)
FVC % of predicted	82.1 (18.9)
DLCO % of predicted	56.2 (18.3)

Data are presented as n (%) or mean (±SD).

Figure 1: Adjusted mean scores of L-PF domain scores at baseline, 6 months, and 12 months

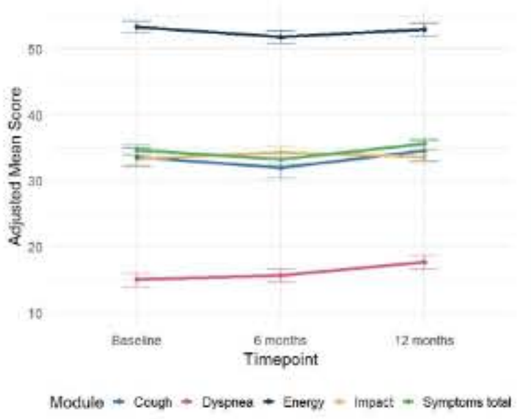

Table 2. Difference in adjusted mean scores from baseline to 12 months on L-PF domains

	Δ Adjusted mean score (SE)
L-PF symptoms total	+1.0 (0.8)
L-PF dyspnea	+2.7 (0.7)**
L-PF cough	+1.0 (1.6)
L-PF energy	0.4 (1.0)
L-PF impacts	+0.3 (0.9)

Data is presented as mean scores adjusted for baseline L-PF score and antifibrotic use. Frequencies at baseline, 6, and 12 months for L-PF impacts: n=310, 224, 207 and L-PF symptoms n=219, 174, 165.
SE, standard error.

Table 3: Mean L-PF change scores from baseline to 12 months in a patient group who deteriorate vs improve based on predefined thresholds

	Deterioration	Improvement
L-PF symptoms total		
FVC	8.4 (12.4)	-0.8 (10.3)
L-PF dyspnea		
FVC	8.4 (12.6)	0.5 (11.1)
*K-BILD breathlessness and activities***	6.8 (12.7)	-1.8 (8.5)
*EQ5D index**	7.7 (14.8)	1.0 (9.0)
GRoC	7.5 (14.8)	-0.8 (8.0)
L-PF cough		
*FVC**	13.5 (19.6)	-7.1 (21.8)
*LCQ***	14.1 (18.2)	-3.4 (16.7)
L-PF impacts		
*FVC**	5.1 (16.5)	-6.1 (13.9)
*K-BILD total****	10.6 (16.6)	-6.5 (11.6)
*K-BILD psychological****	9.6 (16.9)	-5.6 (11.1)
*EQ5D VAS**	3.9 (14.3)	-5.5 (15.1)
*GRoC***	7.1 (17.4)	-3.0 (9.6)

*Data is presented as difference scores in L-PF scores of different modules from baseline to 12 months. Anchors were selected if there was a r>0.3 (Pearson). Pairwise comparisons were tested to examine whether scores differed significantly between groups using Games-Howell analyses. *p<0.05, **p<0.01, ***p<0.001.*
SD, standard deviation. Mean change scores for L-PF energy could not be derived due to lack of significant correlations.

Conclusions

Over 12 months, dyspnea measured with L-PF significantly worsened in a real-world PF population.

Mean change scores support the responsiveness to change of L-PF symptoms total, dyspnea, cough, and impacts.

The I-FILE study is supported by an unrestricted research grant from Boehringer Ingelheim

ERS CONGRESS | 2025
27 September – 1 October | Amsterdam, Netherlands

Exploring responsiveness and minimal important changes of the Living with Pulmonary Fibrosis questionnaire in patients with pulmonary fibrosis

D. Hofman (Rotterdam, Netherlands), M. Oude Voshaar (Rotterdam, Netherlands), C. Moor (Rotterdam, Netherlands), G. Nakshbandi (Rotterdam, Netherlands), R. Mostard (Heerlen, Netherlands), W. Wuyts (Leuven, Belgium), V. Cottin (Lyon, France), M. Kreuter (Mainz, Germany), M. Polke (Heidelberg, Germany), K. Buschulte (Heidelberg, Germany), P. Saunders (Oxford, United Kingdom), K. Antoniou (Heraklion, Greece), A. Froidure (Bruxelles, Belgium), H. Slabbynck (Antwerpen, Belgium), A. Hoffmann-Vold (Oslo, Norway), M. Durheim (Oslo, Norway), A. Van Veen (Nijmegen, Netherlands), H. Bjørkekjær (Kristiansand, Norway), M. Vonk (Nijmegen, Netherlands), Z. Daniil (Thessaly, Greece), L. Spencer (Liverpool, United Kingdom), P. Bonniaud (Dijon, France), G. Prévot (Toulouse, France), P. Molyneaux (London, United Kingdom), M. Wijsenbeek (Rotterdam, Netherlands)

Background The *Living with Pulmonary Fibrosis* (L-PF) questionnaire measures symptoms and their impact on quality of life (QoL) in patients with pulmonary fibrosis (PF). Data on responsiveness and available minimal important changes (MICs) are scarce, stem from clinical trials, and are only available for L-PF Dyspnea and Cough.

Aim To estimate MICs of different L-PF modules in a diverse real-life PF patient population to better understand the impact of interventions.

Methods Baseline and 6-month data of the I-FILE study [NCT04304898], a multicenter registry of patients with PF, were used. MICs were estimated using anchor-based methods by calculating mean change scores of those patients categorized as deteriorated or improved according to predefined thresholds for several anchors (table 1). Currently available complete data were used.

Results 395 patients from 7 European countries were included with a mean age of 71 years, 72% were male, and 46% had IPF. Except for L-PF Energy, all L-PF modules correlated with various anchors. L-PF Symptoms total, Cough, Dyspnea and Impacts were responsive to change over 6 months and MICs could be estimated (table 1).

Conclusion These results support the responsiveness of four L-PF modules as measures of symptom burden and impact on QoL in patients with PF but underline the need for further validation studies in larger patient populations.

Table 1. Minimal important change estimates for L-PF modules based on anchor change scores for deterioration and improvement

Anchor variables for each domain		Patients with deterioration		Patients with improvement	
	r	n	Mean change score for L-PF module	n	Mean change score for L-PF module
L-PF Symptoms total			**MIC estimate: 1 – 4**		**MIC estimate: -9 – -1**
Change in FVC %	-0.22#				
Change in DLCO %	-0.38*	12	0.8 (11.0)	6	-9.1 (9.8)
Change in K-BILD total	-0.30***	28	4.1 (10.5)	30	-1.2 (8.9)
L-PF Dyspnea			**MIC estimate: 5 – 6**		**MIC estimate: -2 – -0.5**
Change in FVC %	-0.12#				
Change in DLCO %	-0.36*	16	4.9 (14.9)	8	-0.5 (5.9)
Change in K-BILD Breathlessness and activities	-0.37***	47	5.9 (14.2)	51	-1.7 (7.3)
L-PF Cough			**MIC estimate: 13**		**MIC estimate: -9**
Change in FVC %	-0.32#				
Change in DLCO %	-0.30#				
Change in LCQ	-0.46***	28	13.1 (21.4)	29	-9.3 (18.5)
L-PF Energy			**MIC could not be calculated**		**MIC could not be calculated**
Change in FVC %	0.18#				
Change in DLCO %	0.14#				
Change in FAS	-0.15*				
L-PF Impacts			**MIC estimate: 4 – 7**		**MIC estimate: -5 – -2**
Change in FVC %	-0.38**	17	6.4 (14.1)	28	-2.3 (10.4)
Change in DLCO %	-0.38**	22	5.9 (12.6)	7	-4.8 (8.6)
Change in K-BILD total	-0.38***	51	7.3 (14.4)	54	-3.7 (10.5)
Change in EQ-5D VAS	-0.32***	75	4.4 (13.7)	36	-4.6 (12.3)
GRoC at 6 months	-0.22**				

L-PF Symptoms scores range from 0 to 100, with higher scores indicating greater impairment.
Pearson correlation coefficient (r) represents the strength of variable relationships. Significance levels: *p<0.05, **p<0.01, ***p<0.001, #not significant. MIC estimates are determined when p<0.05 where r<0.03, following COSMIN recommendations. Scores are mean (SD) changes from baseline, analysed using one-way analyses of variance.

Abbreviations: DLCO, Diffusing capacity of the lungs for carbon monoxide; EQ-5D VAS, EuroQoL-5D Visual Analogue Scale; FAS, Fatigue Assessment Scale; FVC, Forced Vital Capacity; GRoC, Global Rating of Change; K-BILD, King's Brief Interstitial Lung Disease; LCQ, Leicester Cough Questionnaire; L-PF, Living with Pulmonary Fibrosis; MIC, Minimal Important Change.