Changes in the physical and affective dimensions of dyspnoea after a home-based pulmonary rehabilitation in fibrotic idiopathic interstitial pneumonias

Cécile Chenivesse[1,5], Sarah Gephine[2,3,5], Martin Dornbierer[4], Victor Valentin [1], Olivier Le Rouzic[1], Lidwine Wémeau[1] and Jean-Marie Grosbois[2]

[1]University of Lille, CHU Lille, Inserm, CNRS, Institut Pasteur de Lille, U1019, UMR 9017, Center for Infection and Immunity of Lille (CIIL), Lille, France. [2]FormAction Santé, Pérenchies, France. [3]University of Lille, University of Artois, University of Littoral Côte d'Opale, ULR 7369 – URePSSS – Unité de Recherche Pluridisciplinaire Sport Santé Société, Lille, France. [4]University of Lille, CHU, Lille, France. [5]These two authors contributed equally to the work.

Corresponding author: Sarah Gephine (sgephine@formactionsante.com)

Shareable abstract (@ERSpublications)
An 8-week individualised home-based pulmonary rehabilitation programme was associated with short-, medium- and long-term improvements in both physical and affective components of dyspnoea https://bit.ly/3RBUmnL

Cite this article as: Chenivesse C, Gephine S, Dornbierer M, *et al*. Changes in the physical and affective dimensions of dyspnoea after a home-based pulmonary rehabilitation in fibrotic idiopathic interstitial pneumonias. *ERJ Open Res* 2024; 10: 00722-2023 [DOI: 10.1183/23120541.00722-2023].

Received: 29 Sept 2023
Accepted: 16 Dec 2023

Abstract

Background Our objective was to evaluate the short-, medium- and long-term benefits of home-based pulmonary rehabilitation (PR) on the physical and affective components of dyspnoea in people with fibrotic idiopathic interstitial pneumonias (f-IIPs). Anxiety and depressive symptoms, fatigue, health-related quality of life and exercise tolerance were also assessed.

Methods Data on 166 individuals with f-IIPs who enrolled in an 8-week home-based PR programme (weekly supervised 90-min session) were retrospectively analysed. Assessments included the Dyspnoea-12 (D-12) questionnaire, Hospital Anxiety and Depression Scale, Fatigue Assessment Scale, Visual Simplified Respiratory Questionnaire and 6-min stepper test, and were performed at home at short, medium (6 months) and long (12 months) term.

Results Among the 166 individuals with f-IIPs who enrolled in PR, 75 (45%) and 91 (55%) participants had a diagnosis of idiopathic pulmonary fibrosis and fibrosing non-specific interstitial pneumonia, respectively, and 87 (52%) participants concluded a full year of follow-up. In the total group, both physical and affective components of dyspnoea were improved, at short, medium and long term, after PR. Overall, half of the participants reached the minimally important difference of 3 points of the D-12 questionnaire at the end of PR, and at the 6- and 12-month follow-ups. Anxiety and depressive symptoms, fatigue and health-related quality of life were also improved, while the short-term benefits in exercise tolerance were not maintained 1 year after PR.

Conclusion An individualised home-based PR programme resulted in short-, medium- and long-term improvements in both physical and affective components of dyspnoea assessed by the D-12 questionnaire.

Introduction

Fibrotic idiopathic interstitial pneumonias (f-IIPs), including idiopathic pulmonary fibrosis (IPF) and fibrosing non-specific interstitial pneumonia (f-NSIP), belong to the family of rare interstitial lung diseases (ILDs) with a worldwide prevalence estimated between 6.3 and 71 per 100 000 people [1]. While IPF, the most prevalent ILD, mainly affects men about 60 years old with a history of smoking and has a survival between 3 and 5 years, NSIP mainly affects non-smoking women with a better prognosis [1].

By affecting 68–98% of the individuals, dyspnoea is the most reported symptom in f-IIPs [2]. Dyspnoea has been associated with impaired health-related quality of life (HRQoL) [3], exercise tolerance [4, 5] and physical activity [6], and it represents the main cause of suffering at the end stage of the disease [7]. A

pooled data analysis of multinational phase 3 trials conducted in IPF showed that pirfenidone (an antifibrotic agent) had no effect on dyspnoea increase over time [8]. Therefore, dyspnoea represents a primary cause of suffering in people with f-IIPs that may not be relieved by current drug therapies.

Pulmonary rehabilitation (PR) is a comprehensive intervention including education, physical training and self-management and motivational strategies that is offered to individuals with chronic respiratory diseases to improve HRQoL and exercise tolerance [9, 10]. In heterogeneous populations of ILDs, PR has been effective for improving HRQoL, exercise tolerance and exercise-related dyspnoea [11–15], but these benefits are not always maintained 6 months following the intervention, especially in people with IPF [13]. Strategies such as repeated PR [16] or long-term motivational sessions using tele-rehabilitation could be a solution to overcome the loss of benefits. In f-IIPs, we previously reported short- and long-term positive benefits of a home-based PR programme on exercise tolerance, HRQoL and anxiety symptoms [5]. Evaluating the long-term changes following PR in f-IIPs is important since the progressive nature of the disease and exercise-induced hypoxaemia may limit the PR benefits over time. The effectiveness of PR for reducing dyspnoea in f-IIPs is more controversial, in which the variability of tools used to assess dyspnoea, their unidimensional evaluation and their low sensitivity to PR are often mentioned as limitations [17]. Although dyspnoea is defined as a subjective experience of breathing discomfort including sensory, physical and affective dimensions [18], studies mainly assess dyspnoea with unidimensional tools, such as the Baseline Dyspnoea Index or the modified Medical Research Council (mMRC) dyspnoea scale [13, 17]. Multidimensional tools have been developed to address this issue, such as the Dyspnoea-12 (D-12) questionnaire, which is a validated self-reported questionnaire [19] that provides an evaluation of both physical and affective components of dyspnoea during daily life activities [20].

Therefore, the aim of the study was to evaluate the short-, medium- and long-term benefits of a home-based PR programme on the physical and affective components of dyspnoea assessed by the D-12 questionnaire in people with f-IIPs. The secondary outcomes were the changes in anxiety and depressive symptoms, HRQoL and exercise tolerance.

Methods

Study design and participants

This was a single-centre retrospective study conducted on prospectively collected data, from September 2014 to June 2018. Eligible individuals, aged ⩾18 years, were referred to the home-based PR programme by their respiratory specialist who was responsible for providing the clinical assessment, certifying the diagnosis of f-IIPs [21] and validating that the participants were absent of cardiovascular contraindications to exercise training. Depending on the respiratory specialist, the majority of the patients had the choice between home-based and centre-based PR, while a minority, often the frailest ones, were offered home-based PR only. Exclusion criteria were dementia or poorly controlled psychiatric illness, neurological sequelae or bone and joint diseases preventing physical activity. The study was approved by the Observational Research Protocol Evaluation Committee of the Société de Pneumologie de Langue Française (CEPRO; number 2021-054). All participants were informed and gave their written consent to use the collected data for research purposes.

PR programme

All participants performed an 8-week home-based PR programme, consisting of a weekly supervised 90-min home session, during which education, self-management strategies and physical training were implemented as previously described [22]. The intervention was designed according to an initial evaluation of the individual's needs and expectations, and then implemented throughout the programme through a collaborative process between the PR team, the patient and his/her caregiver. The healthcare team received the same standardised therapeutic education training from a licensed instructor. Apart from the weekly visit of the team member who supervised the sessions, participants were expected to perform, on their own, personalised physical training (at least four additional non-supervised sessions per week) and self-management plan the rest of the week. To implement the personalised self-management plan, interactive presentations, card games and an illustrated folder were used and left at the patient's home. The main objective of the negotiated weekly plan was to implement realistic and positive health behaviour changes in the patient's daily life, at short term (during PR) but especially at long term, during which there was no visit by the PR team members apart from those mandated to complete the evaluation at 6 and 12 months after PR. The personalised self-management plan was also re-assessed during these two follow-up sessions.

The core education topics included pathophysiology of f-IIPs, medication and its use, prevention and recognition of exacerbations, physical exercise and exercise-induced hypoxaemia, breathing strategies,

stress management and emotional responses related to the disease and dyspnoea, management of oxygen therapy and end of life [23]. According to individual needs, other interventions could be added: nutritional counselling, smoking cessation strategies, airway clearance techniques, relaxation techniques such as yoga, cardiac coherence, mindfulness meditation and hypnosis.

Each participant received a cycle ergometer (Domyos 120; Decathlon, Villeneuve-d'Ascq, France) and/or a stepper (Go Sport, Grenoble, France), and other muscle strengthening equipment such as dumbbells, elastic bands, Swiss ball or foam balls, for the duration of the 8-week intervention. Loaned equipment was collected at the end of the 8-week exercise training, with an exception for the elastic bands and foam balls that were given to patients. Regarding the cardiorespiratory training, the goal was to achieve a total of 30–45 min of daily exercise (performed by 10-min sequences or shorter according to their respective physical capacity) at least five sessions per week (including the weekly supervised session). Exercise intensity was progressively adjusted to reach a dyspnoea score between 3 and 4 on the Borg 0–10 scale or 11–13 on the Borg 6–20 scale [24]. Exercise training could be performed with oxygen supply according to the individual's medical prescription. When exercise oxygen saturation was <85% despite the prescribed oxygen supply, oxygen flow was increased to ensure an exercise peripheral oxygen saturation >85%. In this case, a 24-h oximetry test was performed at the patient's home and a report was sent to the prescribing physician for adjusting oxygen flow, if needed.

Assessments

Lung function [25], medication and comorbidity data were collected from the individual's medical record provided by the respiratory specialist. The EPICES multidimensional questionnaire was used to assess social deprivation [26]. Participants were evaluated at home, at the beginning (M0), at the end of PR (M2, short term) and at 6 months (M8, medium term) and 12 months (M14, long term) after the end of PR, to conclude a full year of follow-up post-PR.

Dyspnoea was assessed with the French validated version of the D-12 questionnaire [27]. Each 12-item (seven items for the physical component and five items for the affective component) score ranges from 0 ("none") to 3 ("severe") with a total score ranging from 0 to 36 (lower is better), a physical score ranging from 0 to 21 and an affective score ranging from 0 to 15 [19]. A minimal clinically important difference (MCID) of −4 to −6 points in the D-12 total score was reported after PR in people with severe COPD [28]. In individuals with chronic cardiorespiratory diseases a minimally important difference (MID) of −3 points has been reported (2 points for the physical component and 1 point for the affective component) [29]. The mMRC dyspnoea scale was also used to evaluate the physical dimension of dyspnoea.

The Hospital Anxiety and Depression Scale (HADS) (14 items: seven each for anxiety and depression with minimum and maximum subscores of 0 and 21; lower is better) [30] and the Fatigue Assessment Scale (FAS) (10 items: five reflecting physical fatigue and five reflecting mental fatigue with a test score ranging from 10 to 50; lower is better) [31] were assessed. A HADS anxiety or depressive symptom score >11 indicates a probable clinical diagnosis of anxiety or depression and a change of 1.5 units is considered as the MCID in people with COPD, while a FAS score ⩾22 suggests abnormal fatigue and a change of 4 points is considered as the MCID in people with sarcoidosis [32].

HRQoL was evaluated with the Visual Simplified Respiratory Questionnaire (VSRQ) (eight questions on a scale from 0 to 10 with a total score ranging from 0 to 80; higher is better) [33].

The 6-min stepper test (6MST) was used to evaluate exercise tolerance at home [34]. The MCID of the 6MST is considered to be a change of 40 steps in people with COPD [35].

Statistical analysis

Statistical analyses were performed using SPSS version 28.0 (IBM, Armonk, NY, USA) and the significance threshold was considered at 0.05. Continuous variables are expressed as mean with standard deviation or median with standard error (interquartile range (IQR) for non-normal distribution). Normality of distribution was assessed using histograms and Shapiro–Wilk tests. At baseline, comparison between groups (IPF *versus* f-NSIP) was performed using the t-test or Wilcoxon test in case of non-normality for quantitative variables and the Chi-squared or Fisher's exact tests in case of non-normality for qualitative variables.

Linear mixed models with a random intercept to account for the correlation between samples obtained within the same individuals were used to evaluate the changes in study outcomes over time (M2, M8 and M14). Normality of the model residuals was checked for each outcome using graphs of conditional

residuals. The missing data (participants who dropped out at M2, M8 and M14) were imputed using a regression-switching approach [36]. Estimates obtained in the different imputed datasets were combined using Rubin's rules. A sensitivity analysis was performed on the participants who completed the 12-month follow-up (n=87).

Results

Baseline characteristics

We retrospectively analysed data on 166 individuals with f-IIPs who enrolled in PR, of which 87 (52%) participants concluded a full year of follow-up (figure 1). Compared with the participants who concluded a full year of follow-up, participants who dropped out of the study (n=79 (48%)) were characterised at baseline by older age (71.2±10.6 *versus* 66.2±10.2 years; p=0.003), a lower diffusing capacity of the lung for carbon monoxide (D_{LCO}) (31.9±14.0% predicted *versus* 39.0±13.3% predicted; p=0.008), higher dyspnoea (affective component) (7.2±5.3 *versus* 5.2±4.6 points; p<0.015), depressive symptoms (8.6±4.5 *versus* 6.0±4.0 points; p<0.001) and fatigue (28.7±7.9 *versus* 24.3±7.9 points; p<0.001) and poorer HRQoL (27.9±14.6 *versus* 38.5±15.6 points; p<0.001) and exercise tolerance (262±178 *versus* 393 ±183 steps; p<0.001) (supplementary table A1). Overall, 20 (27%) individuals with IPF and 15 (17%) individuals with f-NSIP died between the beginning of PR and the 1-year follow-up.

The majority of the enrolled participants were males (65%), overweight, aged 69±11 years old, with a mean forced vital capacity (FVC) of 70±21% predicted and a mean D_{LCO} of 36±14% predicted (table 1). 83% of the participants had long-term oxygen therapy (LTOT) and/or ambulatory oxygen at baseline; among them, 70 (51%) participants did not complete the 1-year follow-up (39% died and 3% received

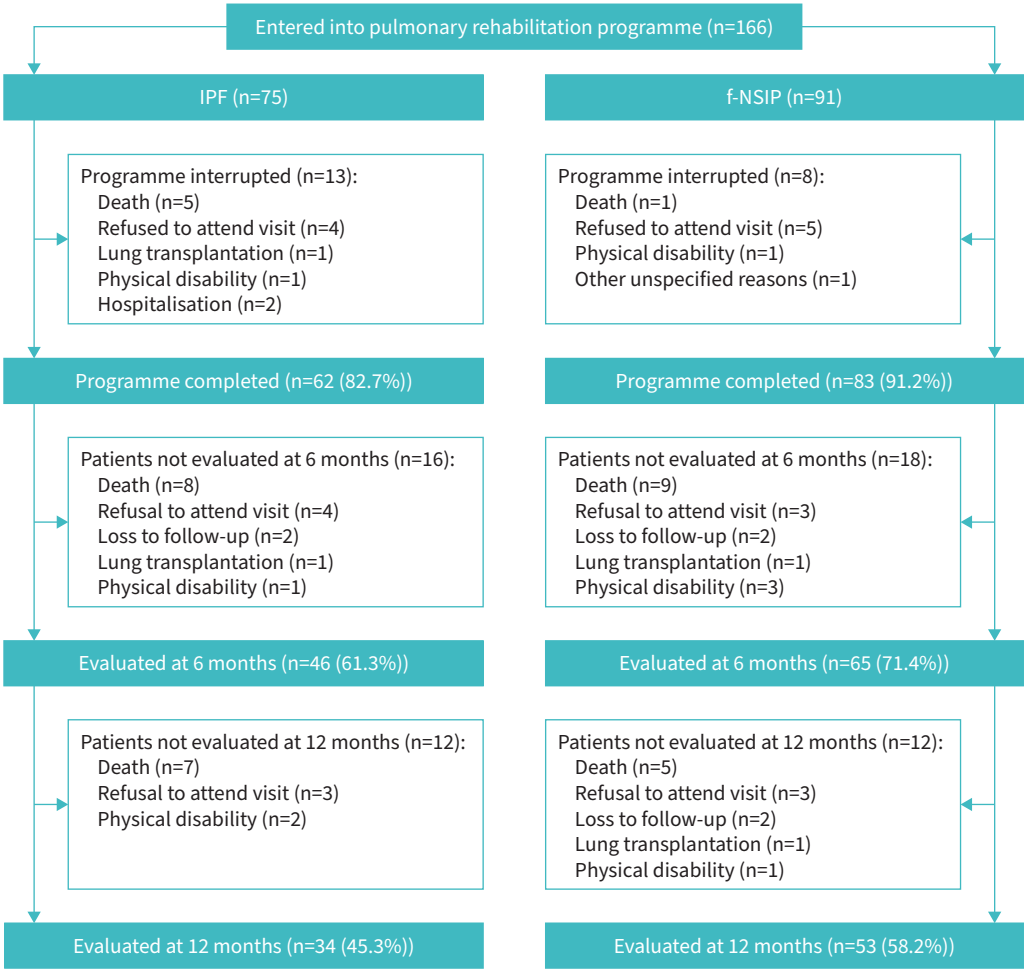

FIGURE 1 Flowchart of the follow-up of study participants. IPF: idiopathic pulmonary fibrosis; f-NSIP: fibrosing non-specific interstitial pneumonia.

TABLE 1 Baseline characteristics of the participants according to fibrotic idiopathic interstitial pneumonia disease status

	Total (n=166)	IPF (n=75)	f-NSIP (n=91)	p-value
Age, years	68.6±10.7	69.7±9.7	67.7±11.4	0.22
Male	108 (65)	64 (85)	44 (48)	<0.001
BMI, kg·m^{-2}	29±8.6	27.7±7.6	30.2±10.4	0.054
Social deprivation	55 (35)	22 (29)	33 (38)	0.059
Smoking status				0.016
Current smoker	4 (2)	3 (4)	1 (1)	
Ex-smoker	82 (50)	49 (65)	33 (37)	
Never-smoker	78 (48)	23 (31)	55 (62)	
Pulmonary function test[#]				
FEV_1 % pred	66.4±19.2	75.4±19.0	65.1±21.2	0.001
FVC % pred	69.6±20.8	70.6±18.1	63.1±19.5	0.011
D_{LCO} % pred	35.8±14.0	34.9±14.0	36.5±14.0	0.559
LTOT and/or ambulatory oxygen	138 (83)	62 (83)	76 (84)	0.885
Antifibrotic agents	54 (33)	49 (65)	5 (6)	<0.001
Oral corticosteroids	103 (62)	33 (44)	70 (77)	<0.001
Immunosuppressants	44 (27)	4 (5)	40 (44)	<0.001
Comorbidities[#]				
Ischaemic heart disease	32 (19)	18 (24)	14 (15)	0.158
Hypertension	86 (52)	40 (53)	46 (51)	0.723
Diabetes	46 (28)	22 (29)	24 (26)	0.674
Anxiety	60 (36)	22 (29)	38 (42)	0.010
Depression	31 (19)	11 (15)	20 (22)	0.224

Data are presented as mean±SD or n (%), unless otherwise stated. IPF: idiopathic pulmonary fibrosis; f-NSIP: fibrosing non-specific interstitial pneumonia; BMI: body mass index; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; D_{LCO}: diffusing capacity of the lung for carbon monoxide; LTOT: long-term oxygen therapy. [#]: collected from the medical record provided by the respiratory specialist.

lung transplantation). Among the 166 included participants, 75 (45%) and 91 (55%) participants had a diagnosis of IPF and f-NSIP, respectively. Participants with f-NSIP were more often females (52% *versus* 15%), who never smoked (62% *versus* 31%), with a more severe lung volume restriction (FVC 63% predicted *versus* 71% predicted) and were more often treated with anxiolytics for anxiety symptoms (42% *versus* 29%) and oral corticosteroids (77% *versus* 44%) compared with individuals with IPF (table 1).

The study baseline assessments are presented in table 2. Results were not statistically or clinically different between groups (table 2). Among the total group, 40 (24%) and 30 (18%) participants reported anxiety and

TABLE 2 Baseline assessment scores according to fibrotic idiopathic interstitial pneumonia disease status

	Total	IPF	f-NSIP	p-value
Dyspnoea-12				
Physical (0–21)	11.4±4.9	11.1±4.3	11.6±5.4	0.760
Affective (0–15)	6.3±4.2	6.0±4.0	6.5±4.4	0.362
Total (0–36)	17.7±8.4	17.2±7.6	18.2±9.0	0.527
mMRC dyspnoea (0–4)	2.7±0.9	2.5±1.2	2.8±0.8	0.180
HADS Anxiety (0–21)	8.1±3.8	7.7±3.5	8.5±4.0	0.211
HADS Depression (0–21)	7.2±3.5	7.1±2.9	7.4±4.0	0.472
FAS (10–50)	26.6±6.8	26.8±6.4	26.4±7.1	0.701
VSRQ (0–80)	34.5±11.7	36.4±9.7	33.1±13.2	0.173
6MST, steps	366±129	372±115	360±139	0.666

Data are presented as mean±SD, unless otherwise stated. IPF: idiopathic pulmonary fibrosis; f-NSIP: fibrosing non-specific interstitial pneumonia; mMRC: modified Medical Research Council; HADS: Hospital Anxiety and Depression Scale; FAS: Fatigue Assessment Scale; VSRQ: Visual Simplified Respiratory Questionnaire; 6MST: 6-min stepper test.

depression subscores >11 points, respectively (IPF: 15 (20%) and 10 (13%); p=0.260, respectively; f-NSIP: 25 (27%) and 20 (22%); p=0.197, respectively). Regarding baseline abnormal fatigue, this was reported by 75% of the patients with IPF and by 65% of the patients with f-NSIP (p=0.174).

Changes at short, medium and long term after PR

In the total group, both physical and affective components of dyspnoea (figure 2) and all the other assessments were improved after PR (M2) (table 3). Only mMRC score and 6MST performance were not significantly improved at medium and long term, respectively (table 3). Results of the sensitivity analysis are presented in supplementary table A2. Changes in participants with f-NSIP were similar to those reported in the total group (supplementary table A3). In participants with IPF, the affective component of dyspnoea, mMRC score, VSRQ score and 6MST performance were no longer improved at the 1-year follow-up after PR (supplementary table A4). According to the linear mixed models, the changes in the study outcomes thorough time were similar between the f-NSIP group and the IPF group. The number of individuals reaching the D-12 questionnaire total score and subscores MID [29] is presented in table 4. Overall, the number of participants reaching the MID or the MCID of the D-12 questionnaire total score at the end of PR and at the 6- and 12-month follow-ups was higher in participants with f-NSIP than in participants with IPF.

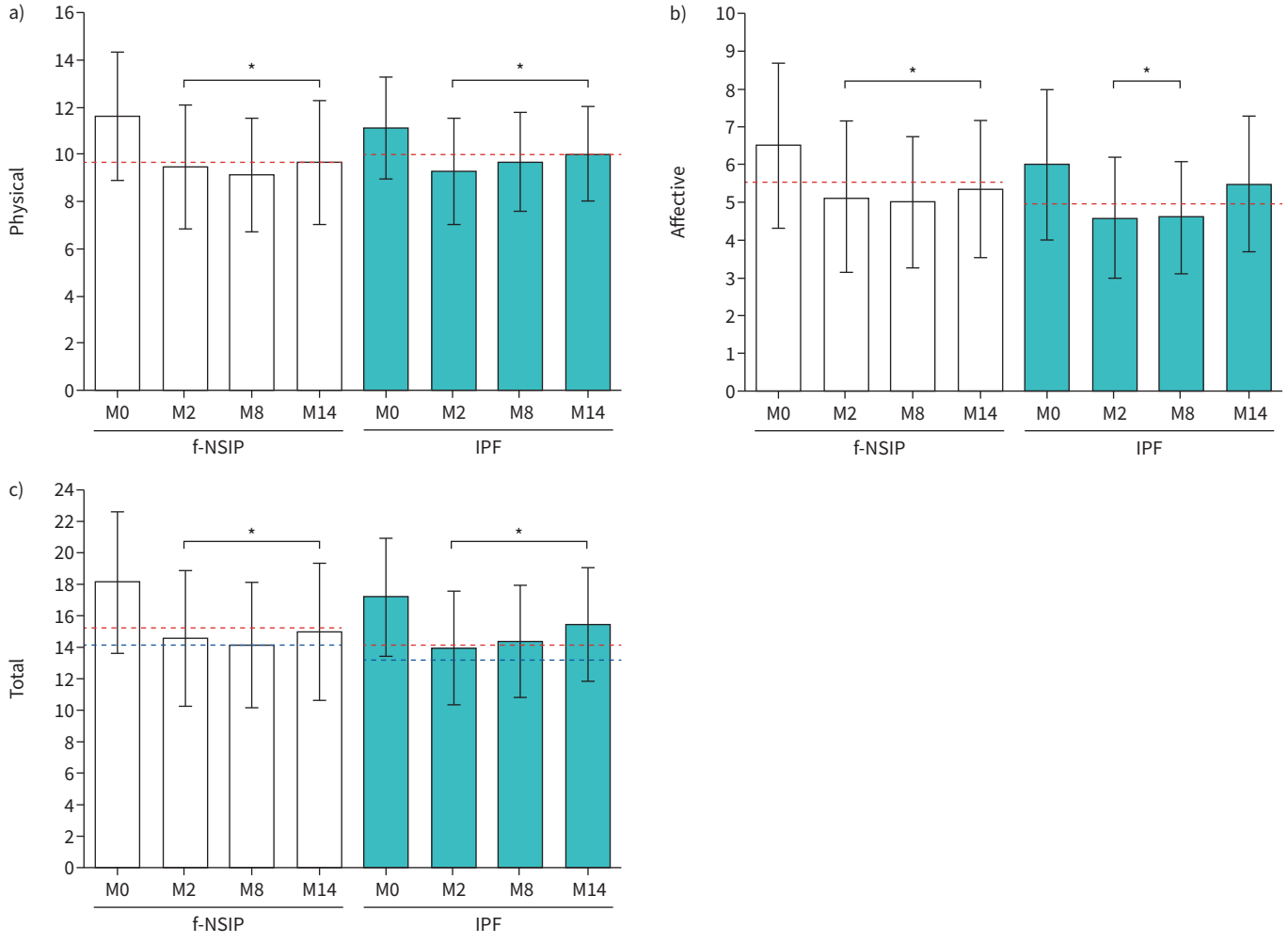

FIGURE 2 Dyspnoea-12 questionnaire a) physical subscore, b) affective subscore and c) total score at the beginning of the programme (M0) and at short (M2), medium (M8) and long term (M14) after pulmonary rehabilitation in people with fibrosing non-specific interstitial pneumonia (f-NSIP) and idiopathic pulmonary fibrosis (IPF). The red dashed lines in a), b) and c) indicate the expected minimal important difference of −2 points in the physical component score, −1 point in the affective component score and −3 points in the total score, respectively. The blue dashed lines in c) indicate the expected minimal clinically important difference of −4 points in the total score. *: p<0.05.

TABLE 3 Changes in outcomes at short (M2), medium (M8) and long term (M14) after pulmonary rehabilitation in the total group

	M2			M8			M14		
	Score	ΔM2–M0	p-value	Score	ΔM8–M0	p-value	Score	ΔM14–M0	p-value
Dyspnoea-12									
Physical (0–21)	9.4±4.9	−2.0±3.8	<0.001	9.4±4.5	−2.0±4.3	<0.001	9.8±4.6	−1.6±3.8	<0.001
Affective (0–15)	4.9±3.7	−1.4±2.6	<0.001	4.8±3.3	−1.5±2.9	<0.001	5.4±3.7	−0.9±2.5	<0.001
Total (0–36)	14.3±8.0	−3.4±5.7	<0.001	14.3±7.5	−3.5±6.2	<0.001	15.2±8.0	−2.5±5.5	<0.001
mMRC dyspnoea (0–4)	2.5±1.0	−0.2±0.6	0.013	2.7±0.9	0.0±0.7	0.472	2.5±1.0	−0.2±0.9	0.014
HADS Anxiety (0–21)	7.4±3.2	−0.8±2.3	0.001	6.6±2.8	−1.6±2.7	<0.001	7.7±3.3	−1.6±2.7	<0.001
HADS Depression (0–21)	6.6±3.1	−0.6±2.1	0.002	6.1±3.2	−1.1±2.4	<0.001	6.1±3.0	−1.1±2.2	<0.001
FAS (10–50)	24.5±5.8	−2.1±4.1	<0.001	24.4±6.0	−2.2±5.2	<0.001	24.8±6.0	−1.8±5.1	<0.001
VSRQ (0–80)	40.5±12.0	6.0±7.7	<0.001	40.2±11.9	5.7±8.5	<0.001	36.4±12.7	1.9±9.7	0.033
6MST, steps	420±135	48±80	<0.001	392±160	19±97	0.044	357±178	12±99	0.104

Data are presented as mean±SD, unless otherwise stated. mMRC: modified Medical Research Council; HADS: Hospital Anxiety and Depression Scale; FAS: Fatigue Assessment Scale; VSRQ: Visual Simplified Respiratory Questionnaire; 6MST: 6-min stepper test.

Discussion

This real-life study conducted in patients with severe f-IIPs, in whom 83% required LTOT and/or ambulatory oxygen, showed that an 8-week individualised home-based PR programme was associated with short-, medium- and long-term improvements in both physical and affective components of dyspnoea assessed by the D-12 questionnaire. These changes were also clinically significant, although the benefits on affective and physical dyspnoea seemed to fade over the long term. Anxiety and depressive symptoms, fatigue and HRQoL were also improved at short, medium and long term. Only the short- and medium-term improvements in exercise tolerance were not maintained at the 1-year follow-up. Both dyspnoea due to the progression of the disease and/or exacerbation and/or the lack of motivation to engage and maintain regular physical activity over the long term could partly explain this result. Baseline dyspnoea, anxiety and depressive symptoms, fatigue, HRQoL and exercise tolerance were similar between people with IPF and people with f-NSIP. However, improvements were more difficult to maintain at long term for the former. The poorer prognosis and faster decline in IPF leading to a higher number of dropouts and deaths in the present study (55% in IPF *versus* 43% in f-NSIP) may partly explain this result.

In a recent meta-analysis reporting the effects of PR in ILD [13, 17], dyspnoea was assessed using specific tools like the mMRC scale or the Borg index, and non-specific tools like the Chronic Respiratory Disease Questionnaire or the St George's Respiratory Questionnaire. These tools do not cover the affective dimension of dyspnoea, which may be more associated with the aforementioned comorbidities. Moreover, neither the mMRC scale nor the Borg index are recommended as patient-reported outcome measures [37], unlike the D-12 questionnaire which was specifically developed and validated in individuals with ILD [19, 20]. A previous randomised controlled trial conducted by Wadell *et al.* [38] in patients with COPD considered multidimensional tools for assessing dyspnoea and reported improvements in the affective domain of dyspnoea following an 8-week outpatient PR programme, while the sensory-perceptual domain

TABLE 4 Number of individuals reaching the Dyspnoea-12 questionnaire minimally important difference (MID) and minimal clinically important difference (MCID) according to fibrotic idiopathic interstitial pneumonia disease status at short (M2), medium (M8) and long term (M14)

	IPF			f-NSIP		
	M2	M8	M14	M2	M8	M14
MID responders [29]						
Physical: change ⩾ −2 points	37 (49)	35 (47)	32 (43)	47 (52)	51 (56)	46 (51)
Affective: change ⩾ −1 point	39 (52)	40 (53)	35 (47)	48 (53)	54 (59)	49 (54)
Total: change ⩾ −3 points	39 (52)	38 (51)	36 (48)	50 (55)	50 (55)	47 (52)
MCID responders [28]						
Total: change ⩾ −4 points	35 (47)	34 (45)	27 (36)	42 (46)	45 (49)	44 (48)

Data are presented as n (%). IPF: idiopathic pulmonary fibrosis; f-NSIP: fibrosing non-specific interstitial pneumonia.

of dyspnoea was not improved. Although they did not use the D-12 questionnaire, our results support that the affective domain of dyspnoea is sensitive to PR.

The MID of the D-12 questionnaire has not been yet specifically reported in patient with f-IIPS. Ekström *et al*. [29] reported a MID total score of −3 points in individuals with various chronic respiratory disease (among them 19% of the cohort had IPF), which should not be confused with the MCID of −4 to −6 points reported by Beaumont *et al*. [28] in individuals with COPD who had performed PR. By taking the lowest range value reported by Beaumont *et al*. [28], the number of individuals with f-NSIP reaching the MCID ranged between 46% and 50% over the 1-year follow-up, while 47% of the individuals with IPF reached the MCID at short and medium term and only 36% at long term. Despite that missing data have been imputed to avoid overestimating the benefits of PR, the faster negative course of IPF and/or the high number of disease exacerbations that we did not record, leading to greater anxiety and dyspnoea, might have influenced this long-term result. Moreover, it is not clear whether D-12 questionnaire subscores can be used and interpreted independently. Beaumont *et al*. [28] did not consider it appropriate to determine a specific MCID for the affective and physical subscores. Studies are still needed to clarify the clinical interpretation and sensitivity of the subdomains of the D-12 questionnaire. Regarding the mMRC changes, the absence of significant or clinical improvements in both groups relaunched the usefulness of the mMRC scale and its sensitivity to PR [13, 17].

Anxiety and depressive symptoms were also significantly improved at short, medium and long term in the total group. The clinical improvement is questionable as only the f-NSIP group was able to achieve a change >1.5 points at 6 and 12 months after PR. However, in both groups anxiety and depressive symptoms scores were <11 points, which is lower than the scores reported in patients with COPD [39], but consistent with the literature in people with ILD [5, 40, 41]. Despite that anxiety and depressive symptoms affect 15–60% of people with ILD [41], none of the meta-analyses [13, 17] report the benefits of PR on these comorbidities. Managing anxiety, depression and panic has been determined as a core educational topic by health professionals and people with ILD [42], therefore evaluating anxiety and depressive symptoms should be considered alongside dyspnoea assessment in PR. Finally, the short-term clinical benefit (MCID of 40 steps) observed for exercise tolerance was not maintained at 6 and 12 months after PR. Holland *et al.* [11] reported similar results with the 6-min walk test after an 8-week outpatient PR, while Ryerson *et al.* [14] demonstrated that benefits were maintained with a mean improvement of 49.8 m after 6–9 weeks of PR. The proportion of patients with IPF between the two studies (60% for the former and 41% for the latter) may explain the medium-term improvement difference. Using the 6MST, Wallaert *et al*. [5] reported long-term clinical improvements that were just above the MCID (42 steps). However, when looking at the more severe participants who completed the study, it seems that clinical benefits were not maintained 12 months after PR [5]. Moreover, Wallaert *et al*. [5] did not impute their missing data (45% dropout 1 year after the end of PR), which could also explain the differences with the present study.

Strengths and limitations

Despite that we included 166 individuals with f-IIPS, the monocentric, non-randomised nature of the study and the absence of a control group may limit the scope of the results, which should be confirmed by robustly designed randomised and controlled studies. However, data were collected systematically and consistently as an integral part of the home-based PR programme which was conducted by the same trained team. Because of the retrospective nature of the study, details regarding the number of participants using LTOT and those only using ambulatory oxygen cannot be provided. Another limitation is the high number of dropouts 12 months after the end of PR, especially in individuals with IPF. Two studies have reported 6-month dropouts of 17% [11] and 28% [14] in patients with ILD, which is lower than in the present study (39% in IPF and 29% in f-NSIP). However, in the present study participants had a greater impairment of gas exchange (mean D_{LCO} 36% predicted *versus* 49% predicted [11] and 47% predicted [14]). Finally, for each patient, the team member who supervised the home-based sessions also performed all the home assessments. To avoid any human influence on the results, team members received the same training to perform the exercise tolerance test (standardised instructions and no encouragement) and to complete the questionnaires (at the beginning and at the end of PR, questionnaires were patient self-administrated).

Conclusions

Both physical and affective components of dyspnoea were reduced, at short, medium and long term, by 8 weeks of individualised real-life home-based PR in people with f-IIPs. Changes in anxiety and depressive symptoms, fatigue and HRQoL were also positive, while the short-term benefits in exercise tolerance were not maintained 1-year after PR.

Provenance: Submitted article, peer reviewed.

Acknowledgements: We thank the members of the rehabilitation team: Sophie Duriez, Mathieu Grosbois, Marjorie Lambinet, Maite Masson, Valentine Opsomer, Camille Paluch, Lucas Sion, Aurore Taccoen, Florence Urbain, Sandrine Vanexem and Virginie Wauquier.

Author contributions: C. Chenivesse, S. Gephine and J-M. Grosbois: conceptualisation, execution, acquisition of data, formal analysis and interpretation, writing the original draft. M. Dornbierer: formal analysis and interpretation, writing the original draft. L. Wémeau, V. Valentin, O. Le Rouzic: writing: review and editing. All authors gave final approval of the version to be published.

Conflict of interest: C. Chenivesse reports personal fees and non-financial support unrelated to the submitted work from ALK-Abello, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, MEDA Pharma, Medexact, Novartis, Pierre Fabre, Pfizer, Roche, Sanofi, Santélys and Teva. S. Gephine, M. Dornbierer, L. Wémeau and V. Valentin have nothing to disclose. J-M. Grosbois reports personal fees and non-financial support unrelated to the submitted work from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GlaxoSmithKline. O. Le Rouzic reports personal fees and non-financial support unrelated to the submitted work from AstraZeneca, Boehringer Ingelheim, Chiesi, CSL Behring, GlaxoSmithKline, MSD France, Vertex and VitalAire, and is a principal investigator in studies for Vertex and CSL Behring.

Ethics approval: The study was approved by the Observational Research Protocol Evaluation Committee of the Société de Pneumologie de Langue Française (CEPRO; number 2021-054). All participants were informed and gave their written consent to use the collected data for research purposes.

Support statement: The delivery of home-based PR was financially supported by Adair, Aeris Santé, Bastide, Elivie, France Oxygène, Homeperf, LVL, Médopale, NorOx, Santélys, Santéo, SOS Oxygène, Sysmed, VentilHome, VitalAire and ARS Hauts-de-France. The funders played no role in the design, conduct or reporting of this study. Funding information for this article has been deposited with the Crossref Funder Registry.

References

1 Kaul B, Cottin V, Collard HR, *et al.* Variability in global prevalence of interstitial lung disease. *Front Med* 2021; 8: 751181.
2 Carvajalino S, Reigada C, Johnson MJ, *et al.* Symptom prevalence of patients with fibrotic interstitial lung disease: a systematic literature review. *BMC Pulm Med* 2018; 18: 78.
3 Swigris JJ, Kuschner WG, Jacobs SS, *et al.* Health-related quality of life in patients with idiopathic pulmonary fibrosis: a systematic review. *Thorax* 2005; 60: 588–594.
4 Eaton T, Young P, Milne D, *et al.* Six-minute walk, maximal exercise tests: reproducibility in fibrotic interstitial pneumonia. *Am J Respir Crit Care Med* 2005; 171: 1150–1157.
5 Wallaert B, Duthoit L, Drumez E, *et al.* Long-term evaluation of home-based pulmonary rehabilitation in patients with fibrotic idiopathic interstitial pneumonias. *ERJ Open Res* 2019; 5: 00045-2019.
6 Wallaert B, Monge E, Le Rouzic O, *et al.* Physical activity in daily life of patients with fibrotic idiopathic interstitial pneumonia. *Chest* 2013; 144: 1652–1658.
7 Bajwah S, Higginson IJ, Ross JR, *et al.* Specialist palliative care is more than drugs: a retrospective study of ILD patients. *Lung* 2012; 190: 215–220.
8 Noble PW, Albera C, Bradford WZ, *et al.* Pirfenidone for idiopathic pulmonary fibrosis: analysis of pooled data from three multinational phase 3 trials. *Eur Respir J* 2016; 47: 243–253.
9 Rochester CL, Vogiatzis I, Holland AE, *et al.* An official American Thoracic Society/European Respiratory Society policy statement: enhancing implementation, use, and delivery of pulmonary rehabilitation. *Am J Respir Crit Care Med* 2015; 192: 1373–1386.
10 McCarthy B, Casey D, Devane D, *et al.* Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2015; 2: CD003793.
11 Holland AE, Hill CJ, Conron M, *et al.* Short term improvement in exercise capacity and symptoms following exercise training in interstitial lung disease. *Thorax* 2008; 63: 549–554.
12 Dowman LM, McDonald CF, Hill CJ, *et al.* The evidence of benefits of exercise training in interstitial lung disease: a randomised controlled trial. *Thorax* 2017; 72: 610–619.
13 Dowman L, Hill CJ, May A, *et al.* Pulmonary rehabilitation for interstitial lung disease. *Cochrane Database Syst Rev* 2021; 2: CD006322.
14 Ryerson CJ, Cayou C, Topp F, *et al.* Pulmonary rehabilitation improves long-term outcomes in interstitial lung disease: a prospective cohort study. *Respir Med* 2014; 108: 203–210.

15 Sciriha A, Lungaro-Mifsud S, Fsadni P, *et al.* Pulmonary rehabilitation in patients with interstitial lung disease: the effects of a 12-week programme. *Respir Med* 2019; 146: 49–56.
16 Al Chikhanie Y, Bailly S, Amroussia I, *et al.* Trajectories of COPD patients' response to repeated pulmonary rehabilitation programs. *Respir Med* 2021; 190: 106678.
17 Reina-Gutierrez S, Torres-Costoso A, Martinez-Vizcaino V, *et al.* Effectiveness of pulmonary rehabilitation in interstitial lung disease, including coronavirus diseases: a systematic review and meta-analysis. *Arch Phys Med Rehabil* 2021; 102: 1989–1997.
18 Parshall MB, Schwartzstein RM, Adams L, *et al.* An official American Thoracic Society statement: update on the mechanisms, assessment, and management of dyspnea. *Am J Respir Crit Care Med* 2012; 185: 435–452.
19 Yorke J, Swigris J, Russell AM, *et al.* Dyspnea-12 is a valid and reliable measure of breathlessness in patients with interstitial lung disease. *Chest* 2011; 139: 159–164.
20 Yorke J, Moosavi SH, Shuldham C, *et al.* Quantification of dyspnoea using descriptors: development and initial testing of the Dyspnoea-12. *Thorax* 2010; 65: 21–26.
21 Raghu G, Remy-Jardin M, Myers JL, *et al.* Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/JRS/ALAT clinical practice guideline. *Am J Respir Crit Care Med* 2018; 198: e44–e68.
22 Grosbois JM, Gicquello A, Langlois C, *et al.* Long-term evaluation of home-based pulmonary rehabilitation in patients with COPD. *Int J Chron Obstruct Pulmon Dis* 2015; 10: 2037–2044.
23 Holland AE, Fiore JF, Goh N, *et al.* Be honest and help me prepare for the future: what people with interstitial lung disease want from education in pulmonary rehabilitation. *Chron Respir Dis* 2015; 12: 93–101.
24 Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc* 1982; 14: 377–381.
25 Miller MR, Hankinson J, Brusasco V, *et al.* Standardisation of spirometry. *Eur Respir J* 2005; 26: 319–338.
26 Sass C, Gueguen R, Moulin JJ, *et al.* Comparaison du score individuel de précarité des centres d'examens de santé, EPICES, à la définition socio-administrative de la précarité. [Comparison of the individual deprivation index of the French Health Examination Centres and the administrative definition of deprivation.] *Sante Publique* 2006; 18: 513–522.
27 Beaumont M, Couturaud F, Jego F, *et al.* Validation of the French version of the London Chest Activity of Daily Living scale and the Dyspnea-12 questionnaire. *Int J Chron Obstruct Pulmon Dis* 2018; 13: 1399–1405.
28 Beaumont M, Le Garrec M, Peran L, *et al.* Determination of the minimal important difference for Dyspnoea-12 questionnaire in patients with COPD, after pulmonary rehabilitation. *Clin Respir J* 2021; 15: 413–419.
29 Ekström M, Bornefalk H, Sköld CM, *et al.* Minimal clinically important differences for Dyspnea-12 and MDP scores are similar at 2 weeks and 6 months: follow-up of a longitudinal clinical study. *Eur Respir J* 2021; 57: 2002823.
30 Lepine JP, Godchau M, Brun P. Anxiety and depression in inpatients. *Lancet* 1985; 2: 1425–1426.
31 Michielsen HJ, De Vries J, Van Heck GL. Psychometric qualities of a brief self-rated fatigue measure: the Fatigue Assessment Scale. *J Psychosom Res* 2003; 54: 345–352.
32 de Kleijn WP, De Vries J, Wijnen PA, *et al.* Minimal (clinically) important differences for the Fatigue Assessment Scale in sarcoidosis. *Respir Med* 2011; 105: 1388–1395.
33 Perez T, Arnould B, Grosbois JM, *et al.* Validity, reliability, and responsiveness of a new short Visual Simplified Respiratory Questionnaire (VSRQ) for health-related quality of life assessment in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2009; 4: 9–18.
34 Grosbois JM, Riquier C, Chehere B, *et al.* Six-minute stepper test: a valid clinical exercise tolerance test for COPD patients. *Int J Chron Obstruct Pulmon Dis* 2016; 11: 657–663.
35 Pichon R, Couturaud F, Mialon P, *et al.* Responsiveness and minimally important difference of the 6-minute stepper test in patients with chronic obstructive pulmonary disease. *Respiration* 2016; 91: 367–373.
36 Van Buuren S, Groothuis-Oudshoom K. mice: multivariate imputation by chained equations. *J Stat Softw* 2011; 45: 1–67.
37 Lemmers JMJ, Vonk MC, van den Ende CHM. Patient-reported outcomes to assess dyspnoea in interstitial lung disease and pulmonary hypertension: a systematic literature review of measurement properties. *Eur Respir Rev* 2022; 31: 220091.
38 Wadell K, Webb KA, Preston ME, *et al.* Impact of pulmonary rehabilitation on the major dimensions of dyspnea in COPD. *COPD* 2013; 10: 425.
39 Grosbois JM, Gephine S, Kyheng M, *et al.* Physical and affective components of dyspnoea are improved by pulmonary rehabilitation in COPD. *BMJ Open Respir Res* 2022; 9: e001160.
40 Deniz S, Sahin H, Yalniz E. Does the severity of interstitial lung disease affect the gains from pulmonary rehabilitation? *Clin Respir J* 2018; 12: 2141–2150.
41 Yohannes AM. Depression and anxiety in patients with interstitial lung disease. *Expert Rev Respir Med* 2020; 14: 859–862.
42 Holland AE, Watson A, Glaspole I. Comprehensive pulmonary rehabilitation for interstitial lung disease: a consensus approach to identify core education topics. *Patient Educ Couns* 2019; 102: 1125–1130.