Cough in pulmonary rehabilitation: a retrospective analysis of responders and nonresponders

Ana Sofia Grave[1,2,3], Cátia Paixão[1,2,4,5], Diogo Tecelão[3], Alda Marques[1,2] and Ana Oliveira[1,2,6]

[1]Respiratory Research and Rehabilitation Laboratory (Lab3R), School of Health Sciences (ESSUA), University of Aveiro, Aveiro, Portugal. [2]iBiMED – Institute of Biomedicine, Department of Medical Sciences, University of Aveiro, Aveiro, Portugal. [3]C-mo Medical Solutions, Lisbon, Portugal. [4]Coimbra Health School, Polytechnic of Coimbra, Coimbra, Portugal. [5]Jean Piaget Higher School of Health, Viseu, Portugal. [6]School of Rehabilitation Science, McMaster University, Hamilton, ON, Canada.

Corresponding author: Ana Oliveira (alao@ua.pt)

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People with low cough-related quality of life and medium–high disease impact at baseline are 4–11 times more likely to respond to pulmonary rehabilitation https://bit.ly/3TDvxcM

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Abstract

Background Pulmonary rehabilitation (PR) is essential for people with chronic respiratory diseases (CRDs), yet its impact on cough-related quality of life (CR-QoL) remains unexplored. We assessed the effects of PR on CR-QoL, described the characteristics of responders and nonresponders to PR, and explored determinants of responsiveness in this health domain in individuals with CRDs.

Methods A retrospective study was conducted. We assessed CR-QoL using the Leicester Cough Questionnaire (LCQ) and the impact of the disease with the COPD Assessment Test (CAT), before and after PR. Cut-offs of <17.05 in LCQ total score and ⩾10 in CAT were used to detect low CR-QoL and medium impact of the disease. Responders were defined as achieving a minimal clinically important difference (MCID) of ⩾1.3 on the LCQ total score. Pre- *versus* post-PR analysis involved the t-test, Wilcoxon test or McNemar test and comparisons between groups included the independent t-test, Mann–Whitney U-test or Fisher's exact test. Logistic regression was employed to investigate factors influencing MCID achievement.

Results 135 participants with CRDs (39% females; age 68±10 years; 61% COPD; forced expiratory volume in 1 s (FEV_1) % pred 62.6±23.0%) were included. After PR, significant improvements were observed in all LCQ domains and CAT. 31% of participants were identified as responders in the LCQ (36% females; age 66±10 years; 62% COPD; FEV_1 % pred 60.0±22.3%), showcasing significant differences in the LCQ and CAT compared to nonresponders. People with low CR-QoL and medium/high impact of the disease at baseline were 11 and 4 times more likely to respond to PR in CR-QoL, respectively.

Conclusion PR enhances CR-QoL. Identification of CR-QoL and disease impact traits at baseline offers insights to optimise this outcome responsiveness to PR.

Introduction

Cough is prevalent in people with chronic respiratory diseases (CRDs), impacting up to 90% of this population [1]. Urinary incontinence, social embarrassment, as well as disruption in speaking and sleep are common features presented by people with cough [2]. Furthermore, presenting cough can predict mortality in some CRD populations, *i.e.* idiopathic pulmonary fibrosis [3]. Thus, identifying and managing cough in people with CRDs is a priority.

Pharmacological treatments for cough control include anti-acids (*e.g.* esomeprazole) and neuromodulators (*e.g.* gabapentin) [2]. However, these drugs usually cause adverse events, such as dry mouth, constipation, dizziness and fatigue [2]. Nonpharmacological approaches to cough control that include education strategies to reduce cough, laryngeal hygiene, hydration strategies and breathing exercises have been demonstrated to be effective [4]. However, robust evidence on those effects is lacking [4, 5].

Pulmonary rehabilitation (PR) is a nonpharmacological evidence-based approach strongly recommended for people with CRDs [6]. PR has been shown to improve symptoms (*e.g.* dyspnoea) [7], health-related quality of life (HR-QoL), functional status and exercise capacity in CRDs [7, 8]. Previous research has shown that half of PR attendees present with cough [9]. However, the effects of PR on cough-related outcomes, *i.e.* cough-related QoL (CR-QoL), have not been explored.

International guidelines [2] recommend that CR-QoL should be assessed in individuals with cough through the Leicester Cough Questionnaire (LCQ) [10]. Nevertheless, the LCQ is rarely used as an outcome measure in PR [11]. Moreover, previous studies on functional status [12], dyspnoea, exercise performance and other measures [13] are often used to categorise participants with CRD as responders and nonresponders. However, this classification has not been explored in CR-QoL nor the determinants of that response.

Thus, this study aims to: 1) explore the effects of PR on CR-QoL, 2) characterise responders and nonresponders to PR on CR-QoL, and 3) investigate the determinants of response in this domain in people with CRDs.

Material and methods

Study design

This retrospective study is a secondary analysis from three randomised controlled trials (3R (ClinicalTrials.gov: NCT03799666), iLiFE (ClinicalTrials.gov: NCT04224233) and CENTR(AR) (ClinicalTrials.gov: NCT04711057)) with data collected between January 2019 and December 2023. This study followed the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for observational studies [14]. Ethical approval was obtained from the following ethics committees: the Regional Health Administration of Centro (73/2016; 16/2020), Centro Hospitalar do Baixo Vouga (15-04-2019; 15-05-2019), Centro Hospitalar de Entre Douro e Vouga (CA-0036/2022-0t_MP/CC), Hospital Distrital da Figueira da Foz (CiC2Fs – OBS_CIC.04|2022; 18JUL'2017), the Health Sciences Research Unit: Nursing from the Nursing School of Coimbra (P/N°P619-10/2019; P620-10/2019; P/N°P620-10/2019). The study also followed the European Union General Data Protection Regulation (EU 2016/679).

Participants

Adults (⩾18 years old) with stable CRD who enrolled in a community-based PR programme were included. Participants were recruited through clinicians at the Centro Hospitalar Baixo Vouga (Aveiro, Portugal), Centro Hospitalar Entre-o-Douro e Vouga (Santa Maria da Feira, Portugal) and Hospital da Figueira da Foz (Figueira da Foz, Portugal). People with missing data on the LCQ were excluded.

Data collection

Sociodemographic (*i.e.* sex and age), anthropometric (*i.e.* height and weight to compute body mass index (BMI)) and clinical (*i.e.* long-term oxygen therapy (LTOT) and lung function) data were collected prior to the start of the intervention to characterise the sample. The most recent spirometry records, *i.e.* forced expiratory volume in 1 s (FEV_1), forced vital capacity (FVC) and FEV_1/FVC (Tiffeneau–Pinelli index), were obtained by consulting participants' medical records.

CR-QoL was measured with the LCQ [10]. The LCQ compiles 21 questions about cough impact on physical, psychological and social levels [10]. Additionally, this questionnaire includes a total score (the sum of the levels described previously), with lower scores representing lower CR-QoL [10]. The LCQ has been reported to be valid, reliable [15–17] and responsive to PR in people with CRDs [16–18]. A cut-off of <17.05 on LCQ total score was used for detecting low CR-QoL [19].

The impact of the disease was measured with the COPD Assessment Test (CAT) [1]. The CAT compiles eight questions covering cough, phlegm, chest tightness, breathlessness going uphill/stairs, limitations at home, confidence leaving home, sleep and energy [20]. The CAT is validated for COPD [16, 21], asthma [21], bronchiectasis [22], asthma–COPD overlap [21] and interstitial lung disease [23, 24], and has been widely used to assess the symptoms of people with coronavirus disease 2019 and lung cancer [24–28].

Dyspnoea (measured with the modified Medical Research Council (mMRC) Dyspnoea scale), functional exercise capacity (assessed using the 1-min sit-to-stand (1MSTS) and 6-min walk test (6MWT)), HR-QoL (measured with the St George's Respiratory Questionnaire (SGRQ)), lower limb muscle function (quadriceps muscle voluntary contraction (QMVC) measured with handheld dynamometry), and symptoms of anxiety and depression (assessed with the Hospital Anxiety and Depression Scale (HADS)) were also collected [29].

All outcome measures were collected within 2 weeks before and within 1 week after the intervention.

Intervention

All participants completed a 12-week community-based PR programme. The PR programme was conducted in seven locations: six primary healthcare centres and at a university centre (Respiratory Research and Rehabilitation Laboratory (Lab3R), School of Health Sciences, University of Aveiro, Aveiro, Portugal). Prior to the start of the PR programme, healthcare professionals from each centre received two sessions of training, each lasting ∼5 h. These sessions covered elements to be addressed in the assessments, and exercise, educational and psychosocial components of the programme. The education and psychosocial sessions were standardised across all programmes, and no specific session on managing cough was provided [30].

PR was conducted twice per week with a duration of ∼60 min per session including warm-up, aerobic and strength exercises, and cool-down. Every 2 weeks, education and psychosocial sessions were provided by a multidisciplinary team (physiotherapists, physicians, nurses, dieticians psychologists and social workers) about the following topics: information about the CRD, management of respiratory symptoms, including airway clearance techniques, management of anxiety, medication including inhaler techniques, exacerbations control, healthy lifestyles and community resources. To further ensure the standardisation of the education and psychosocial sessions, thematic flyers were distributed to the multidisciplinary team to guide the sessions. Further details on the multidisciplinary team training and the intervention can be found in Marques *et al.* [30].

Data analysis

Descriptive statistics were performed for sample characterisation. Continuous variables are presented as mean with standard deviation or as median (interquartile range (IQR)), depending on the data distribution which was assessed with the Shapiro–Wilk test. Categorical variables are presented as frequency (percentage).

Comparisons between baseline and post-intervention for continuous variables were analysed using the related-samples t-test or Wilcoxon signed-ranked test according to data distribution. Differences between pre- and post-intervention for categorical variables were analysed using the McNemar test.

A minimal clinically important difference (MCID) of ⩾1.3 points on LCQ total score [18, 31] was considered a clinically positive significant response to PR. Comparisons between responders (change in LCQ total score ⩾1.3 points) and nonresponders (change in LCQ total score <1.3 points) were analysed using the independent t-test, Mann–Whitney U-test or Fisher's exact test according to the nature of the data and its distribution.

A logistic regression analysis was performed to explore the determinants of reaching the MCID on CR-QoL after PR. We included the following variables in the model: sex, age, diagnosis, use of LTOT, presenting affective conditions [32], such as anxiety/depression symptoms (score ⩾8 on the HADS defined "more anxiety/depression symptoms" [33]), medium or high impact of the disease (⩾10 on the CAT identified "medium or high disease impact" [34]), lower CR-QoL and PR attendance. Potential determinants of reaching the MCID on the LCQ were chosen based on the literature [7, 8, 29, 32, 35, 36] and following discussion among the research team.

All analyses were performed using SPSS Statistics version 28.0 (IBM, Armonk, NY, USA). A p-value <0.05 was considered statistically significant.

Results

Sample characterisation

357 individuals were identified among the three studies; however, 17 (5%) were excluded, mainly due to not having a CRD (n=8) or having unstable cardiovascular disease (n=3), and 50 dropped out (14%) from the studies before initiating PR. From those who enrolled in the PR programme (n=290), 155 were excluded due to presenting missing data on the LCQ (53%). Thus, 135 participants were included in this study (figure 1).

Our sample included 52 (39%) females with an average age of 68±10 years diagnosed with COPD (61%) and other CRDs (39%). The values of FEV_1 % pred, FVC % pred and FEV/FVC were 58.0% (43.8–79.0%), 79.0% (67.0–92.0%) and 63.0% (48.4–75.7%), respectively. At baseline, 36% of the participants presented low CR-QoL (table 1).

Participants with COPD were mainly males, older and presented poorer lung function compared to those with other CRDs, as indicated by lower FEV_1 % pred (53.9±18.1% *versus* 79.6±22.0%; p<0.001) and FEV_1/FVC (55.0% (43.9–64.5%) *versus* 78.0% (68.5–83.3%); p<0.001). Additionally, they used fewer

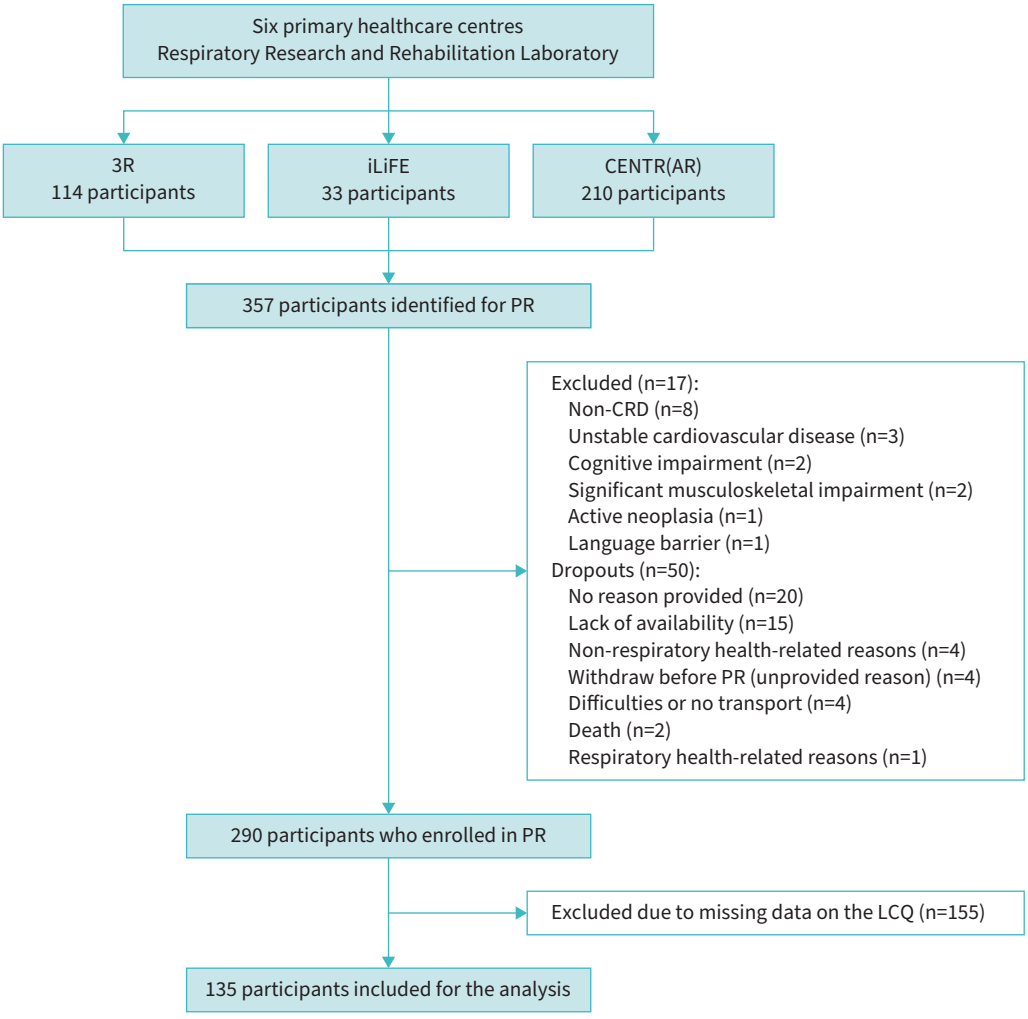

FIGURE 1 Flow diagram of people with chronic respiratory diseases (CRDs) recruited and included in the study. PR: pulmonary rehabilitation; LCQ: Leicester Cough Questionnaire.

oral corticosteroids (p=0.010) and immunosuppressors (p<0.001). A higher proportion of people with COPD were current/former smokers (p<0.001). Furthermore, people with COPD presented with higher quadriceps muscle strength. Regarding CR-QoL, significant differences were observed in the LCQ social domain (p=0.035) and the percentage of individuals scoring below the lower limit of normal (<17.05) on the LCQ (p=0.043) between those with COPD and those with other CRDs.

Effects of PR

Participants attended an average of 20 of the 24 PR sessions (83.3% (71.0–96.0%) attendance). After PR, significant improvements were observed in LCQ total score (18.7 (15.5–20.6) *versus* 20.0 (16.6–21.0); p=0.005) and across the LCQ physical (6.0 (4.6–7.0) *versus* 6.4 (5.2–7.0); p=0.010) and psychological domains (6.2 (5.1–7.0) *versus* 6.7 (5.4–7.0); p=0.003) but not the social domain (6.8 (5.8–7.0) *versus* 7.0 (6.0–7.0); p=0.073). No significant differences (p=0.281) were observed in the proportion of people scoring below the lower limit of normal (<17.05) on LCQ total score after PR (figure 2 and table 2).

Significant decreases in the mMRC Dyspnoea scale proportion (p=0.017), SGRQ total score (43.9±19.0 *versus* 36.9±19.0; p<0.001), CAT (15.0 (10.0–22.0) *versus* 11.0 (6.0–17.0); p<0.001) and HADS scores (anxiety: 6.0 (4.0–8.0) *versus* 5.0 (2.0–8.0); p<0.001 and depression: 6.0 (3.0–9.0) *versus* 5.0 (2.0–8.0); p=0.002), and increases in 1MSTS (22.0 (16.0–27.5) *versus* 25.0 (20.0–30.0) repetitions; p<0.001), 6MWT (431.0 (355.7–498.0) *versus* 466.0 (385.7–528.0) m; p<0.001) and lower limb muscle function (QMVC 27.1±8.9 *versus* 30.2±9.4 kgF; p<0.001) were observed, confirming the comprehensive efficacy of the PR programme (table 2).

TABLE 1 Baseline characteristics of people with chronic respiratory diseases (n=135)

	All sample (n=135)	COPD (n=82)	Non-COPD (n=53)	p-value
Female	52 (38.5)	19 (23.2)	33 (62.3)	<0.001*
Age, years	69.0 (62.5–76.0)	69.8±8.9	66.0±10.7	0.015*
BMI, kg·m^{-2}	26.8 (23.0–30.8)	26.6 (22.6–30.3)	27.2 (24.9–31.1)	0.117
Diagnosis				<0.001*
COPD	82 (60.7)	82 (100.0)	0 (0.0)	
ILD	16 (11.9)	0 (0.0)	16 (30.2)	
Asthma	19 (14.1)	0 (0.0)	19 (35.8)	
ACO	10 (7.4)	0 (0.0)	10 (18.9)	
Bronchiectasis	6 (4.4)	0 (0.0)	6 (11.3)	
Lung cancer	1 (0.7)	0 (0.0)	1 (1.9)	
Long COVID	1 (0.7)	0 (0.0)	1 (1.9)	
Comorbidities (n=131)				
Arterial hypertension	73 (54.1)	43 (53.1)	30 (60.0)	0.473
Dyslipidaemia	53 (39.3)	28 (34.6)	25 (50.0)	0.100
Diabetes	24 (17.8)	12 (24.0)	12 (14.8)	0.245
Arrhythmia	15 (11.1)	7 (8.6)	8 (16.0)	0.260
Depression	10 (7.4)	4 (4.9)	6 (12.0)	0.178
OSA	7 (5.2)	3 (6.0)	4 (8.0)	1.000
Heart failure	6 (4.4)	2 (2.5)	4 (8.0)	0.201
Anxiety	5 (3.7)	2 (2.5)	3 (6.0)	0.369
Sinusitis	5 (3.7)	2 (2.5)	3 (6.0)	0.369
Rhinitis	2 (1.5)	1 (1.2)	1 (2.0)	1.000
Respiratory medication				
LABA/ICS combination (n=109)	44 (32.6)	28 (39.4)	16 (42.1)	0.839
LABA/LAMA combination (n=109)	29 (21.5)	23 (32.4)	6 (15.8)	0.072
Oral corticosteroids (n=122)	25 (18.5)	10 (13.0)	15 (33.3)	0.010*
LAMA (n=109)	27 (20.0)	22 (31.0)	5 (13.2)	0.061
Immunosuppressors (n=122)	20 (14.8)	4 (5.3)	16 (34.8)	<0.001*
ICS (n=109)	12 (8.9)	8 (11.3)	4 (10.5)	1.000
SABA (n=109)	10 (7.4)	8 (11.3)	2 (5.3)	0.489
SAMA (n=109)	10 (7.4)	5 (7.0)	5 (13.2)	0.313
LABA (n=109)	14 (10.4)	10 (14.1)	4 (10.5)	0.767
Triple combination (n=109)	10 (7.4)	7 (9.9)	3 (7.9)	1.000
LTRA (n=108)	9 (6.7)	7 (10.0)	2 (5.3)	0.489
Antifibrotics (n=124)	4 (3.0)	1 (1.3)	3 (6.5)	0.144
Opioids (n=121)	1 (0.7)	1 (1.3)	0 (0.0)	1.000
Smoking status				<0.001*
Former	65 (48.1)	48 (58.5)	17 (32.1)	
Never	53 (39.3)	21 (25.6)	32 (60.4)	
Current	17 (12.6)	13 (15.9)	4 (7.5)	
Lung function				
FEV_1, % pred (n=115)	58.0 (43.8–79.0)	53.9±18.1	79.6±22.0	<0.001*
FVC, % pred (n=118)	79.0 (67.0–92.0)	77.5 (62.5–88.5)	81.3 (68.0–96.0)	0.106
FEV_1/FVC, % (n=115)	63.0 (48.4–75.7)	55.0 (43.9–64.5)	78.0 (68.5–83.3)	<0.001*
LTOT use	22 (16.3)	13 (15.9)	9 (17.0)	1.000
mMRC Dyspnoea scale (n=124)				
0–2	95 (70.4)	55 (71.4)	40 (85.1)	0.125
⩾3	29 (21.5)	22 (28.6)	7 (14.9)	
1MSTS, repetitions (n=127)	22.0 (16.0–27.5)	22.0 (15.5–26.5)	22.0 (15.0–27.0)	0.288
6MWT, m (n=114)	435.4 (360.0–498.3)	418.0 (333.0–494.8)	453.0 (389.0–510.0)	0.207
SGRQ total score (n=117)	43.6±19.0	43.5±20.3	43.8±16.7	0.930
QMVC, kgF (n=134)	27.2±8.5	29.0±8.7	24.0±7.5	0.001*
CAT score	15.4±8.3	16.4±8.5	13.9±7.7	0.088
⩾10	102 (75.6)	63 (76.8)	39 (73.6)	0.686
HADS: Anxiety score (n=130)	6.0 (4.0–8.0)	6.0 (3.0–8.0)	6.0 (4.0–8.5)	0.288
⩾8	43 (31.9)	26 (33.3)	17 (32.7)	1.000
HADS: Depression score (n=130)	6.0 (3.0–9.0)	6.0 (3.0–9.0)	6.0 (2.0–9.0)	0.888
⩾8	47 (35.3)	27 (33.8)	20 (37.7)	0.712

Continued

TABLE 1 Continued

	All sample (n=135)	COPD (n=82)	Non-COPD (n=53)	p-value
LCQ score				
Physical domain	6.0 (4.7–6.8)	6.0 (4.5–6.8)	5.9 (5.0–6.9)	0.394
Psychological domain	6.1 (5.1–7.0)	5.9 (4.9–7.0)	6.4 (5.4–7.0)	0.055
Social domain	6.8 (5.8–7.0)	6.5 (5.0–7.0)	7.0 (6.3–7.0)	0.035*
Total score	18.7 (15.5–20.6)	18.6 (14.7–20.6)	19.8 (17.1–20.9)	0.066
<17.05	48 (35.6)	35 (42.7)	13 (24.5)	0.043*

Data are presented as n (%), median (interquartile range) or mean±SD, unless other stated. BMI: body mass index; ILD: interstitial lung disease; ACO: asthma–COPD overlap; OSA: obstructive sleep apnoea; LABA: long-acting β_2-agonist; ICS: inhaled corticosteroid; LAMA: long-acting muscarinic antagonist; SABA: short-acting β_2-agonist; SAMA: short-acting muscarinic antagonist; LTRA: leukotriene receptor antagonist; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; LTOT: long-term oxygen therapy; mMRC: modified Medical Research Council; 1MSTS: 1-min sit-to-stand; 6MWT: 6-min walk test; SGRQ: St George's Respiratory Questionnaire; QMVC: quadriceps muscle voluntary contraction; CAT: COPD Assessment Test; HADS: Hospital Anxiety and Depression Scale; LCQ: Leicester Cough Questionnaire. *: p<0.05.

Characteristics of responders and nonresponders, and predictors of response

After PR, 42 (31%) participants were identified as responders (38% females; age 66±10 years; 61% COPD; FEV_1 % pred 57.0% (42.0–77.0%); FVC % pred 78.6% (67.5–88.0%); FEV_1/FVC 57.0% (47.0–77.4%)) and 93 (69%) as nonresponders (40% females; 69±9 years old; 60% COPD; FEV_1 % pred 60.0% (44.0–79.0%); FVC % pred 79.0% (66.0–92.1%); FEV_1/FVC 63.8% (49.4–74.6%)) on the LCQ.

At baseline, responders presented a significantly higher score on the CAT (17.5 (14.0–23.0) *versus* 13.0 (7.0–18.0); p=0.002) and a lower total score on the LCQ than nonresponders (15.3 (11.5–17.2) *versus* 20.2 (17.9–20.9); p<0.001). Additionally, the physical (4.6 (3.9–5.5) *versus* 6.5 (5.5–6.9); p<0.001), psychological (5.1 (4.0–5.7) *versus* 6.9 (5.6–7.0); p<0.001) and social (5.6 (4.0–6.3) *versus* 7.0 (6.5–7.0); p<0.001) LCQ domain subscores were decreased in responders compared to nonresponders (figure 3).

Supplementary table S1 provides an in-depth description of the baseline characteristics of responders and nonresponders.

People with low CR-QoL (LCQ <17.05; p<0.001) and those with medium or high impact of the disease (CAT ⩾10; p=0.030) at baseline were 11 and 4 times, respectively, more likely to be a responder in CR-QoL after PR (table 3).

Discussion

This study showed that PR is effective in improving CR-QoL in some patients with CRD, especially those presenting low CR-QoL and medium or high impact of the disease. Predictors of response included scoring ⩾10 on the CAT and scoring below the lower limit of normal (<17.05) on LCQ total score.

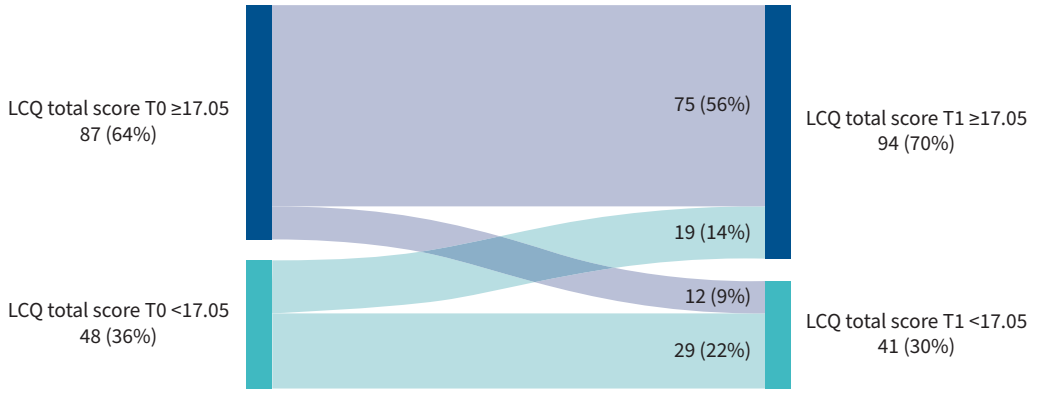

FIGURE 2 Sankey diagram depicting the flow and distribution of participants according to their total score on the Leicester Cough Questionnaire (LCQ) at baseline (T0) and post-pulmonary rehabilitation (T1) (n=135). Scores <17.05 on the LCQ indicate low cough-related quality of life.

TABLE 2 Baseline and post-pulmonary rehabilitation (PR) characteristics and comparisons in people with chronic respiratory diseases (n=135)

	Baseline	Post-PR	p-value
BMI, kg·m^{-2} (n=134)	26.8 (22.9–30.8)	26.7 (23.7–30.5)	0.349
mMRC Dyspnoea scale (n=124)			0.017*
0–2	95 (70.4)	107 (79.3)	
⩾3	29 (21.5)	17 (12.6)	
1MSTS, repetitions (n=126)	22.0 (16.0–27.5)	25.0 (20.0–30.0)	<0.001*
6MWT, m (n=113)	431.0 (355.7–498.0)	466.0 (385.7–528.0)	<0.001*
SGRQ total score (n=115)	43.9±19.0	36.9±19.0	<0.001*
QMVC, kgF (n=132)	27.1±8.9	30.2±9.4	<0.001*
CAT score (n=134)	15.0 (10.0–22.0)	11.0 (6.0–17.0)	<0.001*
⩾10	102 (75.6)	77 (57.0)	<0.001*
HADS: Anxiety score (n=130)	6.0 (4.0–8.0)	5.0 (2.0–8.0)	<0.001*
⩾8	43 (31.9)	38 (29.2)	0.167
HADS: Depression score (n=130)	6.0 (3.0–9.0)	5.0 (2.0–8.0)	0.002*
⩾8	47 (35.3)	38 (29.0)	0.169
LCQ score			
Physical domain	6.0 (4.6–7.0)	6.4 (5.2–7.0)	0.010*
Psychological domain	6.1 (5.1–7.0)	6.7 (5.4–7.0)	0.003*
Social domain	6.8 (5.8–7.0)	7.0 (6.0–7.0)	0.073
Total score	18.7 (15.5–20.6)	20.0 (16.6–21.0)	0.005*
<17.05	48 (35.6)	41 (30.4)	0.281

Data are presented as median (interquartile range), n (%) or mean±SD, unless other stated. BMI: body mass index; mMRC: modified Medical Research Council; 1MSTS: 1-min sit-to-stand; 6MWT: 6-min walk test; SGRQ: St George's Respiratory Questionnaire; QMVC: quadriceps muscle voluntary contraction; CAT: COPD Assessment Test; HADS: Hospital Anxiety and Depression Scale; LCQ: Leicester Cough Questionnaire. *: p<0.05.

International respiratory organisations identify PR as a crucial intervention to manage symptoms in people with CRDs [6, 34], yet there has been minimal attention for cough [37, 38]. To the best of our knowledge, this is the first study to explore the effects of PR on CR-QoL. A systematic review and meta-analysis conducted with people with bronchiectasis did not find significant differences in LCQ total score after PR [39]. The authors reported that the included studies used airway clearance techniques in both the control and experimental groups [39]. In our study, we also included airway clearance techniques in the education and psychosocial sessions of the PR programme, yet our results differed from that study. However, it is important to note that our sample comprised individuals with a range of CRDs, not exclusively bronchiectasis. Additionally, our dropout rate was lower than the median/mean dropout rates reported in the studies included in the referenced systematic review (19%) [39] and the rates observed in other PR studies (39%) [40]. The differences in sample composition and retention rates may account for the discrepancies observed between our findings and those of other studies.

Despite the statistically significant results on CR-QoL after PR, it should be noted that two-thirds of the participants did not show improvements and that the proportion of people with low CR-QoL (LCQ total score <17.05) remained similar after PR. This result might be caused by a lack of knowledge of the healthcare professionals on how to manage cough [9] or lack of specificity of the intervention, as it was not targeted to address cough. Another explanation for this result might be the differences in cough phenotypes (such as respiratory-related cough, refractory chronic cough or iatrogenic cough) across participants [41].

Responders and nonresponders in our study presented different characteristics. Responders showed higher disease severity and low CR-QoL compared to nonresponders. Additionally, there was a high proportion of participants who scored <17.05 on LCQ total score in the responders group. Previous studies on PR effects on other outcomes (*i.e.* dyspnoea, HR-QoL, anxiety and depression symptoms, and functional status) found similar trends, where individuals with more severe symptoms and greater physical impairment tend to show more significant improvement than those with milder symptoms [12, 13, 42]. This pattern may be attributed to individuals with higher symptoms having more room for improvement [42]. To further investigate this point, we conducted an exploratory subanalysis comparing participants whose CR-QoL deteriorated below the 17.05 threshold after PR to those who met or exceeded the 17.05 threshold after the intervention (supplementary table S2). We found that individuals who deteriorated on the LCQ were older

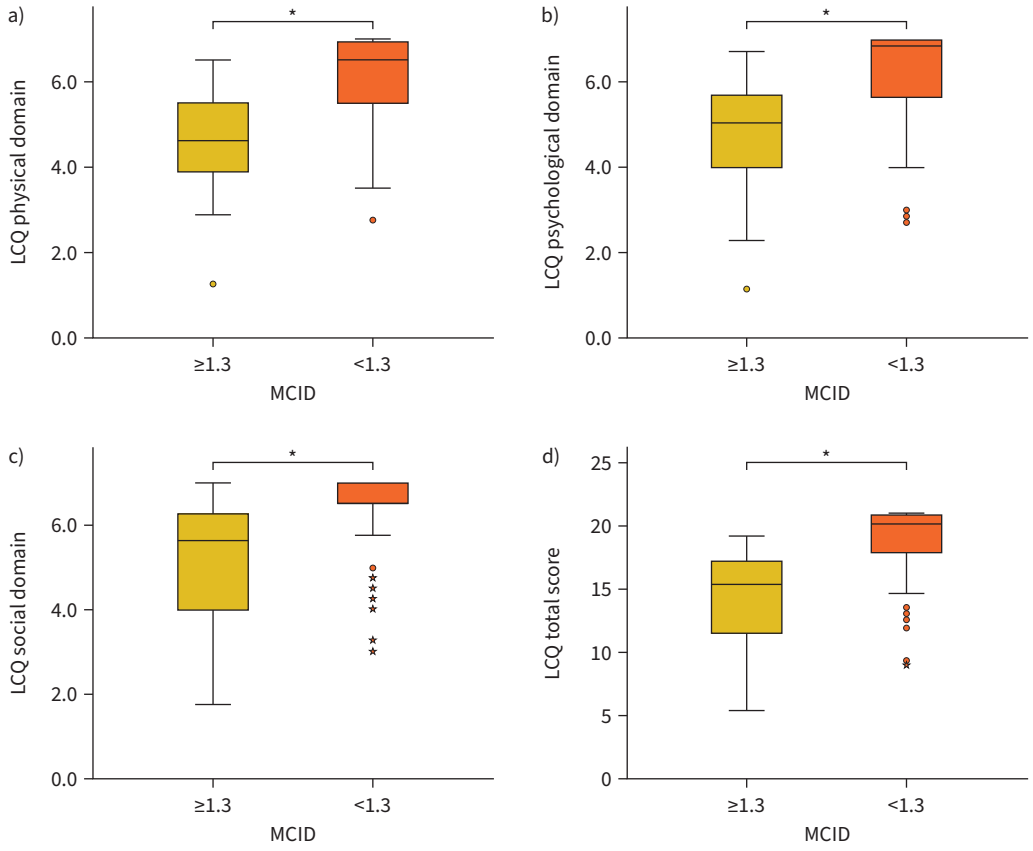

FIGURE 3 Median and interquartile range between baseline values of responders (minimal clinically important difference (MCID) of ⩾1.30 points on Leicester Cough Questionnaire (LCQ) total score) and nonresponders (MCID of <1.30 points on LCQ total score) (n=135): a) physical domain, b) psychological domain, c) social domain and d) total score. Circles and stars indicate mild and extreme outliers, respectively. *: p<0.05.

than those who improved, which could be due to the general decline in health status associated with ageing [43]. Also, all domains of the LCQ were lower in those who improved, reinforcing the conclusion from our responder and nonresponder analysis. Our study also found that low CR-QoL and medium to high disease impact were considered determinants for the PR response on CR-QoL, which also

TABLE 3 Logistic regression analysis of determinants for reaching the minimal clinically important difference on the Leicester Cough Questionnaire in people with chronic respiratory diseases after pulmonary rehabilitation (PR)

	OR (95% CI)	p-value
Female (sex)	1.273 (0.422–3.837)	0.668
Age	1.017 (0.963–1.075)	0.545
COPD	0.492 (0.172–1.404)	0.185
LTOT user	1.059 (0.312–3.592)	0.927
CAT score ⩾10	4.297 (1.152–16.034)	0.030*
HADS: Anxiety score ⩾8	1.115 (0.359–3.461)	0.851
HADS: Depression score ⩾8	0.326 (0.105–1.012)	0.053
LCQ total score <17.05	10.578 (3.511–31.871)	<0.001*
PR sessions attended	1.006 (0.979–1.034)	0.647

LTOT: long-term oxygen therapy; CAT: COPD Assessment Test; HADS: Hospital Anxiety and Depression Scale; LCQ: Leicester Cough Questionnaire. *: p<0.05.

corroborates those findings [12, 13, 39]. This highlights the importance of targeting individuals with more severe symptoms and higher disease impact to maximise the benefits of PR.

Finally, it is noteworthy that anxiety approached significance as a determinant of cough improvement following PR. While this finding did not reach statistical significance, it suggests a potential role of anxiety in cough-related outcomes. Future prospective studies with powered sample sizes are necessary to confirm this hypothesis.

Several limitations need to be acknowledged. We did not collect information on participants' chronic cough or their cough characteristics (*e.g.* dry or productive cough, cough duration, or cough triggers). To address this gap, we consulted participants' individual responses on patient-reported outcome measures that included cough-related questions, such as the CAT and the LCQ, for an indication of participants who might have chronic cough. Interestingly, we found that some participants (n=8) who reported "I never cough" on the CAT had a higher impact on their CR-QoL (LCQ <17.05). This discrepancy may be due to differences in the timing of cough assessment between the CAT, which evaluates the present moment, and the LCQ, which reflects the previous 2 weeks. Additionally, the LCQ provides a more comprehensive assessment of cough, capturing aspects and constructs not addressed by the CAT. Consequently, we were unable to reliably identify participants with chronic cough, possibly leading to the inclusion of some participants for whom cough was not the primary problem. Similarly, we did not consider extrapulmonary causes of cough, such as upper airway obstruction or posterior nasal drip. Future research should focus on the effects of PR considering cough characteristics. The MCID on the LCQ considered was only validated for the COPD population [18], which corresponds to most of the participants included. Finally, the participants included in the analysis were mainly older adults (sample age: 68±10 years), which might limit the generalisation of our results for younger/middle-aged adults with CRD. Future research is required in younger people with CRDs to explore the effects of PR on CR-QoL outcomes [13].

In conclusion, our study showed that PR is effective when targeting CR-QoL. We observed that people with CRDs, low CR-QoL and medium or higher disease impact are 11 and 4 times more likely to be responders in the LCQ after PR, respectively. Future research should focus on tailored interventions for people with CRDs who remained below the lower levels of normal on CR-QoL and on exploring possible reasons that could explain why some individuals do not respond to PR on CR-QoL outcomes [13].

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