

A pulmonary rehabilitation program reduces hospitalizations in chronic obstructive pulmonary disease patients: A cost-effectiveness study

Maria Elena Toubes-Navarro¹, Francisco Gude-Sampedro², José Manuel Álvarez-Dobaño^{3,4}, Francisco Reyes-Santías⁵, Carlos Rábade-Castedo¹, Carlota Rodríguez-García¹, Óscar Lado-Baleato^{6,7}, Raquel Lago-Fidalgo^{2,8}, Noelia Sánchez-Martínez^{2,8}, Jorge Ricoy-Gabaldón¹, Ana Casal-Mouriño¹, Romina Abelleira-Paris¹, Vanessa Riveiro-Blanco¹, Carlos Zamarrón-Sanz¹, Nuria Rodríguez-Núñez¹, Adriana Lama-López¹, Lucía Ferreiro-Fernández^{1,3}, Luis Valdés-Cuadrado^{1,3,9}

¹Department of Pulmonology, University Clinical Hospital of Santiago de Compostela, ²Department of Clinical Epidemiology, University Clinical Hospital of Santiago de Compostela, ³Interdisciplinary Group of research in Pulmonology, Institute of Sanitary research from Compostela, ⁴University Clinical Hospital of Santiago de Compostela, ⁵Department of Human Resources and General Services, University Clinical Hospital of Santiago de Compostela, ⁶Research Methods Group, Health Research Institute of Santiago de Compostela, ⁷ISCIII Support Platforms for Clinical Research, Health Research Institute of Santiago de Compostela, ⁸Mathematics University of Santiago de Compostela, ⁹Medicine University of Santiago de Compostela, Spain

Address for correspondence:

Dr. Ana Casal-Mouriño,
Department of
Pulmonology, University
Clinical Hospital of
Santiago de Compostela,
Spain.
E-mail: ana.casal.mourino@sergas.es

Submission: 08-03-2023
Revised: 06-07-2023
Accepted: 23-08-2023
Published: 17-10-2023

Access this article online

Quick Response Code:



Website:

www.thoracicmedicine.org

DOI:

10.4103/atm.atm_70_23

Abstract:

BACKGROUND: Although pulmonary rehabilitation (PR) is recommended in patients with chronic obstructive pulmonary disease (COPD), there is a scarcity of data demonstrating the cost-effectiveness and effectiveness of PR in reducing exacerbations.

METHODS: A quasi-experimental study in 200 patients with COPD was conducted to determine the number of exacerbations 1 year before and after their participation in a PR program. Quality of life was measured using the COPD assessment test and EuroQoL-5D. The costs of the program and exacerbations were assessed the year before and after participation in the PR program. The incremental cost-effectiveness ratio (ICER) was estimated in terms of quality-adjusted life years (QALYs).

RESULTS: The number of admissions, length of hospital stay, and admissions to the emergency department decreased after participation in the PR program by 48.2%, 46.6%, and 42.5%, respectively ($P < 0.001$ for all). Results on quality of life tests improved significantly ($P < 0.001$ for the two tests). The cost of PR per patient and the cost of pre-PR and post-PR exacerbations were €1867.7 and €7895.2 and €4201.9, respectively. The PR resulted in a cost saving of €1826 (total, €365,200) per patient/year, and the gain in QALYs was +0.107. ICER was -€17,056. The total cost was <€20,000/QALY in 78% of patients.

CONCLUSIONS: PR contributes to reducing the number of exacerbations in patients with COPD, thereby slowing clinical deterioration. In addition, it is cost-effective in terms of QALYs.

Keywords:

Chronic obstructive pulmonary disease, cost-effectiveness study, exacerbations, pulmonary rehabilitation

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Toubes-Navarro ME, Gude -Sampedro F, Álvarez-Dobaño JM, Reyes-Santías F, Rábade- Castedo C, Rodríguez-García C, *et al.* A pulmonary rehabilitation program reduces hospitalizations in chronic obstructive pulmonary disease patients: A cost-effectiveness study. *Ann Thorac Med* 2023;18:190-8.

Key Findings

Key findings

PR contributes to reducing the number of exacerbations in patients with COPD, thereby slowing clinical deterioration. In addition, it is cost-effective in terms of quality-adjusted life years.

What is known and what is new?

- PR is a therapeutic procedure that helps reduce the number of exacerbations in patients with COPD and slows clinical deterioration
- It is a cost-effective intervention in terms of quality-adjusted life years gained, ultimately resulting in health cost savings.

What is the implication, and what should change now?

The data obtained should encourage public health systems allocate resources to these services.

Chronic obstructive pulmonary disease (COPD) is one of the world's three most frequent causes of death. More than three million died of this disease in 2017, with an increase in the number of deaths between 2007 and 2017 of 17.5%.^[1] It is a challenge for public health systems to prevent and treat this disease. However, the course of the disease may take years and cause early death directly or indirectly.

At present, there is cumulative evidence to suggest the benefits of pulmonary rehabilitation (PR) in terms of physical exercise tolerance; peripheral muscle function; dyspnea; health-related quality of life; physical activity; use of health-care resources;^[2] and possibly on survival^[3] in COPD patients. These programs, however, are scarcely available in Spain, as only 35% of hospitals have a specific PR unit, of which 53% are dependent on rehabilitation services and not on pulmonology services.^[4]

Patients with COPD are frequent users of health-care services. Exacerbations, whether they require ambulatory care or hospitalization, influence the course of the disease and are associated with deterioration of lung function^[5] and increased mortality.^[6] There is little evidence on the influence and role of PR in reducing exacerbations. A review of the benefits of RP on readmissions is heterogeneous, explained due to the variety of rehabilitation programs and the methodological quality of the included studies.^[7] Although there is limited data on the cost-effectiveness of PR, some studies suggest that it may provide benefits to the health-care system,^[8-10] while in others, the cost-effectiveness is uncertain or depends on the willingness to pay.^[11]

The purposes of this study included (i) Determining whether PR contributes to reducing the number of exacerbations in COPD patients, slow clinical deterioration, and improve quality of life; and (ii) determine whether PR is a cost-effective intervention.

We present the following article in accordance with the CHEERS reporting checklist.

Methods

A quasi-experimental pre- and postintervention study in 200 patients with COPD was conducted in a tertiary 1000-bed hospital in Spain serving a population of 450,000 inhabitants between the years 2015 and 2021, both inclusive.

Diagnosis of COPD was established in accordance with widely accepted guidelines and recommendations from scientific societies.^[12] Exacerbation was defined as an acute episode of clinical instability occurring during the course of the disease, characterized by a sustained worsening of respiratory symptoms beyond daily variability.^[12] Exacerbation was considered mild-moderate if hospital admission was not required and severe if the patient was hospitalized.^[13]

A comparison was performed of the number of exacerbations the year before and after the implementation of the PR program. The number of emergency department (ED) admissions, hospital admissions, and length of hospital stay were analyzed pre- and postintervention. ED admissions were defined as a visit to the ED that did not required hospital admission. Data were collected from the electronic medical record of each patient.

Quality of life was measured using the COPD assessment test (CAT)^[14] and EuroQol-5D (EQ-5D)^[15] 1 year before and after the implementation of the PR program. Quality of life was considered to have improved if post-PR CAT score decreased by at least 2 points with respect to baseline CAT^[14] and EQ-5D increased by a minimum of 0.051.^[15]

The sample included COPD patients with dyspnea ≥ 2 on the adjusted *Medical Research Council* scale (mMRC)^[16,17] who agreed to participate in the study and were recruited from the pulmonology outpatient clinic or during hospitalization for COPD exacerbation. Exclusion criteria were a short life expectancy (<3 months); mobility impairment; mental illness; or acute heart disease. The PR program was incorporated to local routine practice and consisted of 24–28 sessions (3/week) for a period of 8–9 weeks, with a duration of 75–90 min each. The exercises performed in each session were aerobic/

resistance training of the lower extremities (continuous or in intervals according to tolerance) with progressive increase for 20–40 min (on a treadmill and on a bicycle), strength training of the upper extremities performed with dumbbells (progressively increasing the number of series and/or repetitions), breathing exercises and manual techniques for the drainage of bronchial secretions.

Cost assessment

An estimation was performed of the costs of the PR program and exacerbations the year before and after the intervention. The cost of the PR program was calculated as a function of: (i) number of consultations needed; (ii) cost of the program [equipment (straight-line amortization over 5 years); hiring a full-time physiotherapist (€33,693.3); and maintenance, cleaning service, supplies, security, and communications;^[18] (iii) travel costs from patient’s home to the hospital (0.19 €/km);^[19] (iv) cost of the loss of productivity due to the time spent travelling to the hospital (mean weighted time devoted to travelling, parking, moving to the consultation area, and moving to the consultation office: 79 min) depending on whether the population was active (based on patient average gross income [€20,288.1] and unemployment rate [7.9%]),^[20] or retired (mean retirement pension €11,097.6€) (2.3% of subjects >65 were engaged in volunteer work^[21] and 22.6% performed activities that contributed to the gross domestic product);^[22] and costs related to leisure time (47% of labor cost);^[23] and (v) CO₂ emissions per private car travel (volume of CO₂ emitted per kilometer and cost of each CO₂ gram).^[24,25] The mean number of PR sessions/patient was 25.5.

The cost of exacerbations was estimated on the basis of the fees of the *Servizo Galego de Saúde*^[26] (emergency care, complementary studies, pharmacy costs, length of hospital stay, length of intensive care unit (ICU) stay, where appropriate, and follow-up visits); Added to travel costs and loss of productivity during exacerbations [Supplementary Table 1].

Quality-adjusted life years (QALYs) were estimated based on EQ-5D score. Thus, EQ-5D score along with

every life year yields the QALYs of each patient. To determine whether the PR program is cost-effective in patients with COPD, the incremental cost-effectiveness ratio (ICER) was used as the economic value of QALYs, in accordance with the following formula:

$$R = (C_T - C_B) / (U_T - U_B) = \otimes C / \otimes U$$

Where R is the ICER; C_T , the mean cost after the intervention (post-PR); U_T , the mean utility after the intervention (post-PR EQ-5D); C_B , the mean baseline cost (pre-PR); U_B , the mean baseline utility (pre-PR EQ-5D); $\otimes C$, the incremental cost and $\otimes U$, the incremental utility. The British National Health System established a cutoff value of £20,000/QALY to determine whether PR is cost-effective (NICE).^[27]

The scheme of action is shown in Figure 1. The study was approved by the Ethics Committee of the hospital (2019/551).

Statistical analysis

Continuous variables are expressed as median values (25th–75th percentiles) that is the interquartile range. Given that most of the variable distributions were nonnormal distributed, for the sake of simplicity, we have considered to express all continuous variables as median (P25, P75). Imputation of missing follow-up data was performed using multiple imputations by chained equations. A total of 1000 random imputations were performed and, based on replicates, the presence of pre-and postintervention differences in quality of life scores and hospital admissions was verified using Wilcoxon test for paired data. Cost-effectiveness planes were presented through imputed data pairs of cost-effectiveness. $P = 0.05$ was used for significance testing. Statistical analyses were performed using the mice and hesim^[28] packages, freely available from CRAN-R.

Results

Figure 2 displays the patient flow chart. Of the

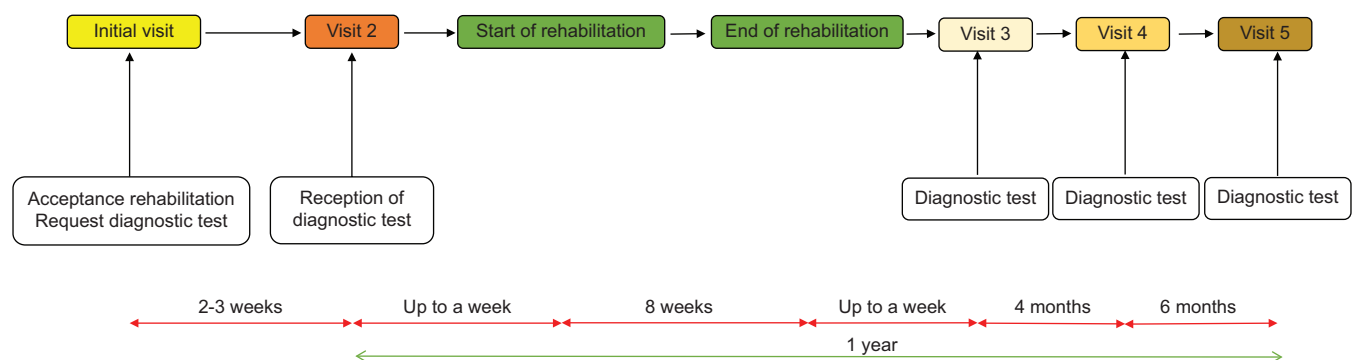


Figure 1: Scheme of action

645 patients who were invited to take part in the PR program, only 219 (34%) agreed to participate, of whom 200 completed the study (31%). Table 1 describes the baseline characteristics of the 200 patients that completed the PR program.

Table 2 compares the number of exacerbations the year before and after the participation in the PR program. The number of hospital admissions, length of stay, and ED admissions were 48.2%, 46.6%, and 42.5%, respectively [Figure 3a and b]. In total, 53% of patients (106/200) experienced a reduction in the number of exacerbations (ED admissions [104; 52%] and number of hospital admissions [92; 46%]). Conversely, the number of exacerbations remained the same in 66 patients (33%) and increased in 28 (14%).

Table 3 shows the median CAT and EQ-5D scores at baseline and at 1 year following the initiation of the PR program. The two tests demonstrated a significant improvement in quality of life ($P < 0.001$). CAT improved in 61.5% of patients (123/200) (≥ 2 points) and EQ-5D improved in 61% (122/200) (≥ 0.051).

The overall cost of the PR program was €373,540. The pre-and post-PR cost of exacerbations was €1,579,060 and €840,320, respectively. Table 4 shows the mean cost/patient of the PR program (€1867.7) (left side of the table) and the mean cost of exacerbation/patient pre-PR (€7895.2) and post-PR (€4201.9) (right side of the table). The total cost of the PR program was €6069.6/patient, which is calculated by the sum of €1867.7 of the program itself and €4201.9/patient for post-PR exacerbations. The total saving was €365.200,

which represents €1826/patient/year. Pre-and post-PR exacerbations had a different cost since pharmacy costs and mean cost of hospital and ICU stay differed across periods.

The mean pre-PR EQ-5D score was 0.617 versus 0.724 at 1 year. The mean gain of the PR program for 1-year survival was 0.107 QALYs. ICER was –€17,056.

Table 1: Baseline characteristics of study patients

Characteristics	Overall
Demographics	
Patients (n)	200
Sex (male/female)	159 (79.5)/41 (20.5)
Age (years)	65 (59–70)
BMI (kg/m ²)	27.3 (23.4–30.1)
Smoking habit	
Never-smokers/former smokers/active smoker	17 (8.5)/169 (84.5)/14 (7)
Packs/year index	40 (30–60)
Other associated diseases	
OSA	20 (10)
Bronchiectasis	47 (23.5)
Cardiovascular disease	75 (37.5)
Anxiety/depression	15 (7.5)
Neoplasm	12 (6)
Diabetes mellitus	21 (10.5)
Alpha-1-antitrypsin deficiency	13 (6.5)
Other diseases	29 (14.5)
Charlson's index	
1	126 (63)
2	24 (12)
3	31 (15.5)
4	10 (5)
5	4 (2)
6	2 (1)
7	3 (1.5)
Home respiratory therapies	
Oxygen	60 (30)
CPAP	14 (7)
BiPAP	5 (2.5)
Respiratory function test	
FVC (%)	77.6 (65.7–96)
FEV ₁ (%)	44.9 (33.7–60)
FEV ₁ /FVC ratio	46 (39–56.4)
Inspiratory capacity (%)	78 (61–96)
DLCOSb (%)	44 (30.7–59.4)
DLCO/VA (%)	59 (40.4–75)
6' walk test (m)	385.5 (315–449.8)
Dyspnea scale (mMRC)	3 (2–3)
BODE index	4 (2–5.25)

Data are expressed as absolute frequencies (%) and medians (25th–75th percentile). BiPAP=Bilevel positive airway pressure, BODE=Body mass index, airflow Obstruction, dyspnea and exercise capacity index, CPAP=Continuous positive airway pressure, DLCOSb=Carbon monoxide diffusion (single breath), DLCO/AV=Diffusing capacity for carbon monoxide/alveolar volume ratio, FEV₁=Forced expiratory volume in the 1 s, FVC=Forced vital capacity, mMRC=Modified Medical Research Council, BMI=Body mass index, OSA=Obstructive sleep apnea

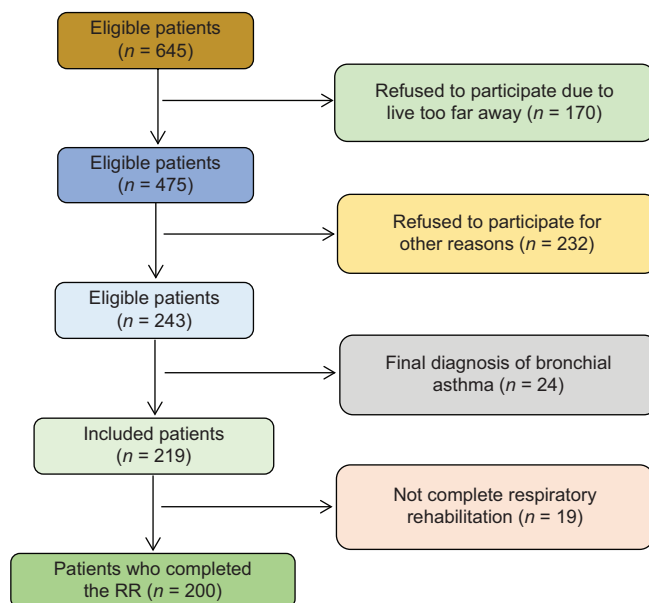


Figure 2: Flow chart of study patients with chronic obstructive pulmonary disease

Figure 4 shows the results of the cost-benefit analysis in relation to the PR program. Figure 4a demonstrates how the PR program resulted in cost savings for 47% of patients. As shown in Figure 4b, quality of life improved in 61% of patients ($EQ-5D \geq 0.051$). Bivariate analysis [Figure 4c] displays the distribution of costs and changes in quality of life. Most data (68%) are located within the two quadrants corresponding to improved quality of life (right side). In total, the cost was $<€20,000/QALY$ in 78% of patients. One in three

patients (32%) experienced an improvement in their quality of life and reduced costs (right side lower quadrant), whereas the quality of life worsened and costs increased (left-hand upper quadrant) in only 18% of patients, with respect to the year before the PR.

Discussion

The results of this study demonstrate that PR reduces the number of exacerbations in COPD patients and

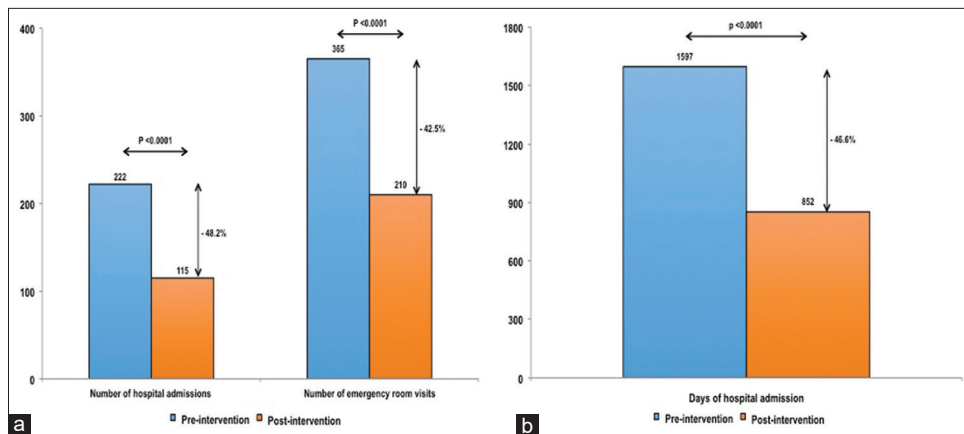


Figure 3: Progression of the number of hospital admissions, EuroQol visits (a) days of hospital stay (b), before and after the participation in pulmonary rehabilitation

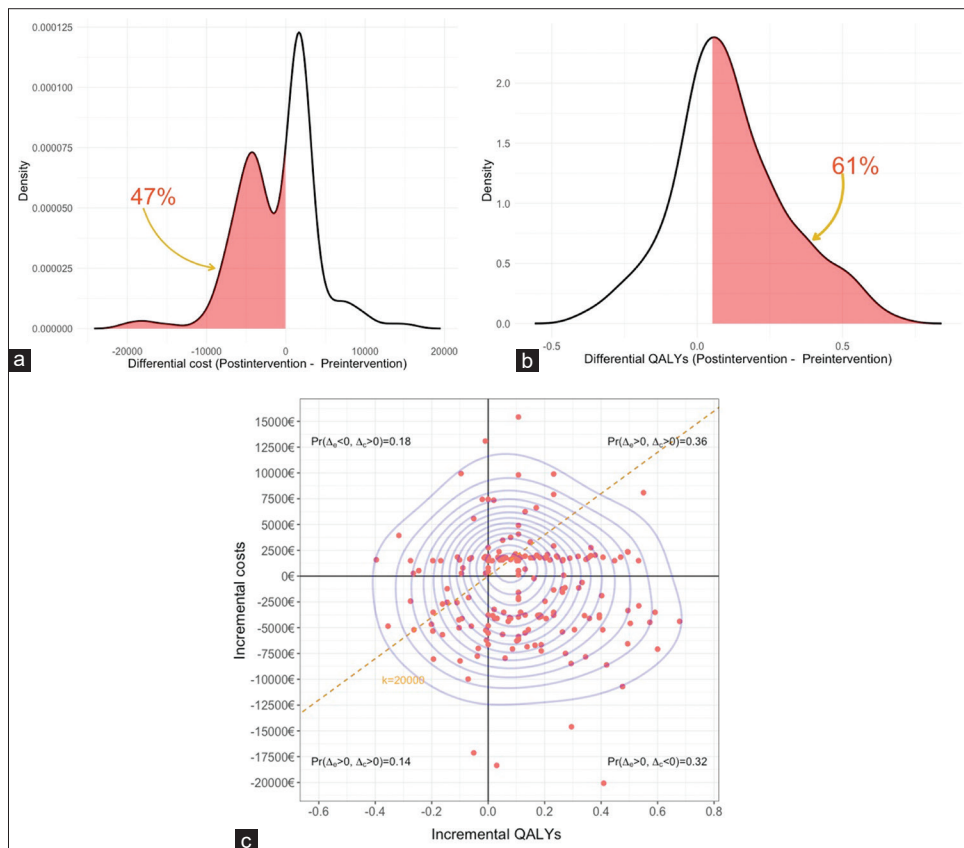


Figure 4: Cost-benefit analysis of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease. (a) Probability density function of cost difference between the PR program and standard care over a year; (b) Probability density function of change in quality of life (measured based on EuroQol-5D questionnaire score) for patients engaged in the program; (c) Bivariate density plot of change in quality of life against cost difference before and after pulmonary rehabilitation. QALY: Quality-adjusted life year

Table 2: Comparative analysis of the parameters used to assess exacerbations a year before and after engagement in pulmonary rehabilitation

Variable	Year before	Year after	P	Reduction in exacerbations
Number of admissions, n (%)	222 87 (43.5)	115 141 (52.5)	<0.001	Worse: 14 Sustained: 33 Improved: 53
Admissions/patient/year ratio	1.1	0.6		
Days of hospital stay (ICU excluded)	1,597	852	<0.001	
Days of ICU stay	20*	2*	0.25	
ED visits (not hospitalized)	365	210	<0.001	
ED visits/patient/year ratio	1.8	1.1		
Total rate of exacerbations/patient/year	2.9	1.6		
Mean stay (days)	7.2	7.4		

*It corresponds to a single patient in each case. Data are expressed as absolute frequencies (%). ED=Emergency department, ICU=Intensive care unit

Table 3: Median chronic pulmonary obstructive disease assessment test score at baseline and at 1 year, statistical significance, and number of patients responsive to treatment

Parameter	Baseline		Year		P	Improvement (reduction in CAT ≥ 2 points; increase in EQ-5D ≥ 0.051)
	n	Global	n	Global		
CAT	200	18 (14.00–24.00)	200	16.37 (9.03–21.73)	<0.001	CAT: 123/200 (61.5)
EQ-5D	200	0.617 (0.493–0.737)	200	0.724 (0.645–0.794)	<0.001	EQ-5D: 122/200 (61)

Data are expressed as medians (25th–75th percentiles). COPD=Chronic pulmonary obstructive disease, CAT=COPD assessment test, EQ-5D=EuroQoL-5D

Table 4: Mean cost/patient of a pulmonary rehabilitation program (left side) and mean cost of exacerbation/patient before and after the pulmonary rehabilitation program (right side)

Cost of the rehabilitation program	Costs	Prerehabilitation	Postrehabilitation
PR cost (€) - 1414.9	Mean hospital travel cost (€)	30.3	24.6
Travel costs related to PR (€) - 267.4	Mean cost of loss of productivity (€)	391.3	195.3
Costs related to loss of productivity associated with PR (€) - 161.2	Mean cost of pollution (€)	5.5	4.4
Cost of pollution (€) - 24.2	Mean cost of moderate exacerbation (€)	1,804.3	1,038.1
	Mean cost of severe exacerbation (€)	5,549.6	2,937.1
	Cost of ICU admission (€)	114.2	11.4
Total cost/patient (€) - 1867.7	Total cost/patient (€)	7,895.2	4,201.9

PR=Pulmonary rehabilitation, ICU=Intensive care unit

contributes to slowing clinical deterioration and improving quality of life, which ultimately results in a reduction of healthcare costs.

One of the most relevant challenges facing participation in PR programs is the high rate of declinations to participate in the program,^[29] which reached 66% in our study. There is not clear reason that explains this phenomenon. Contributing factors may include unawareness of the benefits of the program; the time required; the high percentage of rural population living far away from the hospital and, occasionally, the need for assistance to travel to the hospital, with the difficulties involved.^[30] However, the results of the PR program should be interpreted with caution. Thus, the program design (number of weekly sessions, duration, etc.),^[31] type of study,^[32] or number of comorbidities of study patients^[33] may influence results, which hinders cross-comparison. We chose a conservative PR program, with a quasi-experimental design (each patient was compared against himself/herself), as it was considered unethical to deprive half of the patients from the probable

benefits of the PR program, as it has shown benefits in other disease domains.^[2] As all types of patients with COPD with all types of comorbidities were included (in our case, low: median Charlson 1 index [1–2.25]), we assumed that the population would be heterogeneous. The only limitation established was the baseline dyspnea had to be ≥ 2 on the mMRC scale.

Several studies have evaluated the influence of PR on exacerbations and hospital admissions. Griffiths *et al.* implemented an 18-session program with a duration of 6 weeks, which failed to reduce the number of hospital admissions but was effective in reducing hospital stays, as compared to controls.^[34] Another study conducted in only 61 patients revealed a reduction of admissions over a 2-year period.^[35] Bourbeau *et al.* observed a decrease in hospital admissions (39.8%), length of hospital stay (42.4%), and ED admissions (41%) in patients who engaged in a PR program, as compared to the control group.^[36] A small pre- and post-intervention study in 28 patients showed that the rate of admissions/patient/year at 1 postintervention year decreased from 1.2 to

0.6 ($P < 0.005$), and the mean length of hospital stay was reduced from 7.4 to 3.3 days ($P < 0.01$).^[37] In a systematic review of 18 studies, although randomized controlled studies (10 in number) demonstrated that PR reduced hospital admissions, pooled results did not confirm these results. This may be due to the heterogeneity of the samples and variability across PR programs.^[32] A systematic review of eight studies (810 participants) showed moderate-quality evidence that PR reduces hospital readmissions (overall odds ratio 0.44, 95% confidence interval: 0.21–0.91), but the results were heterogeneous, possibly explained by the extension of the PR programs and the risk of bias of the included studies.^[7]

Another case series of 187 patients comparing outcomes before and after an 8-week PR program documented a reduction of 46% and 62% in the number of hospital admissions and length of hospital stay, respectively.^[38] Finally, in a study in 72 patients who completed a PR program, the number of hospital admissions and stays 1 year after the program decreased from 63% to 55%, respectively.^[39] The results of our study are consistent with previous studies (48.2%, 46.6%, and 42.5% reduction in the number and length of hospital admissions and in the number of visits to the ED, respectively). Therefore, the evidence available supports the hypothesis that PR contributes to reducing exacerbations in patients with COPD. These results are supported by the study by Garcia-Aymerich *et al.* in 2386 patients based on data from the *Copenhagen City Heart Study*. This study confirms that COPD patients who engage in regular physical activity have a lower risk of admission and lower mortality.^[40]

A year after the participation in the PR program, the median scores on quality of life tests (CAT and EQ-5D) improved significantly with respect to baseline scores ($P < 0.001$ in all cases). These results are in agreement with the evidence available.^[41] Whereas CAT is widely used to assess quality of life in COPD patients, experience with EQ-5D is more limited. According to Ringbaek *et al.*, the Saint George Respiratory Questionnaire has higher sensitivity than EQ-5D. This may be probably due to the fact that a high proportion of the patients evaluated using the EQ-5D test had maximum baseline values (authors named it “the ceiling effect”).^[42] However, we decided to use this test to perform a health economic assessment in these patients.

Several studies have analyzed the cost/utility of PR in patients with COPD. The Irish Department of Health estimates a mean cost per patient who completes the PR program of near €1950,^[43] which is consistent with our estimations (€1867.7). In addition, in a case series study conducted in UK, Ramos *et al.* compared two populations of COPD patients: patients who

engaged in physical activity and a sedentary group. As compared to sedentary patients, physical activity was associated with a cost savings of –£2568 as a result of a reduction in mortality (–6%) and a lower number of hospital admissions (–2%). In addition, patients gained more years of life (+0.82) and more QALYs (+0.66). Therefore, physical activity generates long-term economic benefits.^[44] Leemans *et al.* investigated whether PR was cost-effective in patients with COPD through a systematic review of 11 studies (3261 participants). Although the methods used to measure costs, effectiveness, and utility differed across case series, four studies were interpreted as cost-effective; two were not cost-effective; and cost-effectiveness was uncertain in five studies.^[45] This inconsistency of results may be explained by differences in the content and intensity of the type of interventions, the methods used for measurement and comparison, and the different exacerbation rates in each case series. Only two of the studies included in this systematic review analyzed the cost-effectiveness of PR in relation to exacerbations.^[46,47] The intervention was not found to be cost-effective in the first study, conducted in primary care.^[46] In contrast, a significant improvement was observed in quality of life but not in the number of exacerbations in the second study, with a moderate cost per QALY ratio, within the range of what is considered acceptable.^[47] In contrast, our study revealed a significant reduction in the number of exacerbations, which certainly contributed to the cost-effectiveness of the PR program. The difference in these results could be explained by the fact that, in previous studies, the rate of exacerbations before the PR was low (0.36 moderate exacerbations and 0.02 severe exacerbations^[46] and 1.2^[47]), where this rate was high in our study (2.9). These results suggest that PR is more likely to be cost-effective in patients who frequently experience exacerbations, as it may be difficult to reduce them when they are infrequent. A systematic review carried out in different settings shows that PR can be potentially cost-effective,^[9] and in a recent study conducted in the USA, a country with a health system totally different from ours, PR performed after COPD hospitalization appears to be cost-effective with cost savings and improved quality of life.^[10]

The study has some limitations that may have influenced the results obtained: This is a quasi-experimental study, not a clinical trial; the sample of patients is not high; collection of data on pre-PR exacerbations was retrospective; the group of patients with COPD was very heterogeneous (only selected by the level of dyspnea); it is a single-center study and results were not validated on a case series. In addition, a high rate of patients declined to participate, probably due to them living a long distance from the hospital, needing assistance to travel to the hospital, or from fear of the COVID-19 pandemic.

Article Info Item	Prof. Dr. Nanshan Zhong	
	Question	Authors' response (place "-" if not applicable)
1	Would you like to share data collected for your study to others?	No
2	If not, would you like to share the reason for your decision?	The database contains information from the patients of our hospital and its collection has required a lot of time and effort
3	What data in particular will be shared?	Other documents of the study
4	Any other documents will be share? Such as study protocol, statistical analysis plan, informed consent form, clinical study report, analytic code	Yes
5	When will data availability begin?	When requested
6	When will data availability end?	The necessary time
7	To whom will you share the data?	To other clinical investigators
8	For what type of analysis or purpose?	Similar studies
9	How or where can the data/documents be obtained?	On request
10	Any other restrictions?	No

Conclusions

In summary, PR is a therapeutic procedure that helps reduce the number of exacerbations in patients with COPD and slows clinical deterioration. In addition, PR emerges as a cost-effective intervention in terms of QALYs gained, ultimately resulting in health cost savings. The data obtained should encourage public health systems allocate resources to these services.

Acknowledgments

O.L.B. is supported by ISCIII Support Platforms for Clinical Research (ISCIII/PT20/00043/Cofunded by European Union).

Reporting checklist

The authors have completed the STROBE statement checklist.

Data sharing statement

Ethical statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. GBD 2017 Causes of Death Collaborators. Global, regional, and national age-sex-specific mortality for 282 causes of death in 195 countries and territories, 1980-2017: A systematic analysis for the Global Burden of Disease Study 2017. *Lancet* 2018;392:1736-88.
2. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y.

3. Ryrso CK, Godtfredsen NS, Kofod LM, Lavesen M, Mogensen L, Tobberup R, *et al.* Lower mortality after early supervised pulmonary rehabilitation following COPD-exacerbations: A systematic review and meta-analysis. *BMC Pulm Med* 2018;18:154.
4. Breath Spanish Lung Foundation SEPAR. White Paper: Pulmonology in Spain. Barcelona: Breath Spanish Foundation Lung SEPAR; 2016. p. 90.
5. Donaldson GC, Seemungal TA, Bhowmik A, Wedzicha JA. Relationship between exacerbation frequency and lung function decline in chronic obstructive pulmonary disease. *Thorax* 2002;57:847-52.
6. Soler-Cataluña JJ, Martínez-García MA, Román Sánchez P, Salcedo E, Navarro M, Ochando R. Severe acute exacerbations and mortality in patients with chronic obstructive pulmonary disease. *Thorax* 2005;60:925-31.
7. Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T. Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2016;12:CD005305.
8. Griffiths TL, Phillips CJ, Davies S, Burr ML, Campbell IA. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax* 2001;56:779-84.
9. Liu S, Zhao Q, Li W, Zhao X, Li K. The cost-effectiveness of pulmonary rehabilitation for COPD in different settings: A systematic review. *Appl Health Econ Health Policy* 2021;19:313-24.
10. Mosher CL, Nanna MG, Jawitz OK, Raman V, Farrow NE, Aleem S, *et al.* Cost-effectiveness of pulmonary rehabilitation among US adults with chronic obstructive pulmonary disease. *JAMA Netw Open* 2022;5:e2218189.
11. Gillespie P, O'Shea E, Casey D, Murphy K, Devane D, Cooney A, *et al.* The cost-effectiveness of a structured education pulmonary rehabilitation programme for chronic obstructive pulmonary disease in primary care: The PRINCE cluster randomised trial. *BMJ Open* 2013;3:e003479.
12. Global Initiative for Chronic Obstructive Lung Disease. 2021 Global Strategy for Prevention, Diagnosis and Management of COPD. GOLD; 2021. Available from: <https://goldcopd.org/2021-gold-reports/>. [Last accessed on 2021 Apr 06].
13. Soler-Cataluña JJ, Piñera P, Trigueros JA, Calle M, Casanova C, Cosío BG, *et al.* Spanish COPD guidelines (GesEPOC) 2021 update diagnosis and treatment of COPD exacerbation syndrome. *Arch Bronconeumol* 2022;58:159-70.
14. Dodd JW, Hogg L, Nolan J, Jefford H, Grant A, Lord VM, *et al.* The COPD assessment test (CAT): Response to pulmonary rehabilitation. A multicentre, prospective study. *Thorax*

- 2011;66:425-9.
15. Nolan CM, Longworth L, Lord J, Canavan JL, Jones SE, Kon SS, *et al.* The EQ-5D-5L health status questionnaire in COPD: Validity, responsiveness and minimum important difference. *Thorax* 2016;71:493-500.
 16. Mahler DA, Wells CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988;93:580-6.
 17. Bolton CE, Bevan-Smith EF, Blakey JD, Crowe P, Elkin SL, Garrod R, *et al.* British Thoracic Society guideline on pulmonary rehabilitation in adults. *Thorax* 2013;68 Suppl 2:i1-30.
 18. Sicras A, Huerta A, Navarro R, Ibañez J. Use of resources and associated costs of chronic obstructive pulmonary disease exacerbations: A population based retrospective study. *Semergen* 2014;40:189-97.
 19. State official newsletter, n 266; 2009. Available from: <https://www.boe.es/boe/dias/2009/11/04/pdfs/BOE-A-2009-17495.pdf>. [Last accessed on 2019 Sep 11].
 20. Robusté F, Campos Cacheda JM. Transport accounts of Travelers in the Metropolitan Region of Barcelona; Authority of Metropolitan Transport: Barcelona, Spain; 2000.
 21. CIS-IMSERO. Survey on Older People; 2010. Available from: https://www.imserso.es/imserso_01/espaciomayores/eprec/enc_ppmm/index.htm. [Last accessed on 2021 Sep 02].
 22. Center for Sociological Research. Study "Conditions of Life of the Elderly". Available from: https://www.cis.es/cis/openem/ES/1_encuestas/estudios/ver.jsp?estudio=7740&cuestionario=8954&muestra=14085. [Last accessed on 2021 Sep 02].
 23. Cabañés Argudo ML. Income-work-leisure implications in the north-south context. *Cuad Econ* 2002;25:185-204.
 24. Chester M, Horvath A. Environmental Life-Cycle Assessment Of Passenger Transportation: Detailed Methodology for Energy, Greenhouse Gas and Criteria Pollutant Inventories of Automobiles, Buses, Light Rail, Heavy Rail and Air, UC Berkeley Center for Future Urban Transport; 2008. Available from: https://repositories.cdlib.org/its/future_urban_transport/vwp-2008-2. [Last accessed on 2021 Sep 02].
 25. Litman T. Air Pollution Costs Spreadsheet; 2006. Available from: <https://www.vtpi.org/airpollution.xls>. [Last accessed on 2021 Sep 02].
 26. Rates for Health Services in Dependent Centers of the Galician Health Service. DOG n° 96; 2014. Available from: https://www.xunta.gal/dog/Publicados/2014/20140521/AnuncioC3K1-140514-0001_es.html. [Last accessed on 2019 Sep 10].
 27. Claxton K, Briggs A, Buxton MJ, Culyer AJ, McCabe C, Walker S, *et al.* Value based pricing for NHS drugs: An opportunity not to be missed? *BMJ* 2008;336:251-4.
 28. van Buuren S, Groothuis-Oudshoorn K. Mice: Multivariate imputation by chained equations in R. *J Stat Softw* 2011;45:1-67.
 29. Boutou AK, Tanner RJ, Lord VM, Hogg L, Nolan J, Jefford H, *et al.* An evaluation of factors associated with completion and benefit from pulmonary rehabilitation in COPD. *BMJ Open Respir Res* 2014;1:e000051.
 30. Garrod R, Marshall J, Barley E, Jones PW. Predictors of success and failure in pulmonary rehabilitation. *Eur Respir J* 2006;27:788-94.
 31. Garrod R, Ford K, Daly C, Hoareau C, Howard M, Simmonds C. Pulmonary rehabilitation: Analysis of a clinical service. *Physiother Res Int* 2004;9:111-20.
 32. Moore E, Palmer T, Newson R, Majeed A, Quint JK, Soljak MA. Pulmonary rehabilitation as a mechanism to reduce hospitalizations for acute exacerbations of COPD: A systematic review and meta-analysis. *Chest* 2016;150:837-59.
 33. Crisafulli E, Costi S, Luppi F, Cirelli G, Cilione C, Coletti O, *et al.* Role of comorbidities in a cohort of patients with COPD undergoing pulmonary rehabilitation. *Thorax* 2008;63:487-92.
 34. Griffiths TL, Burr ML, Campbell IA, Lewis-Jenkins V, Mullins J, Shiels K, *et al.* Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: A randomised controlled trial. *Lancet* 2000;355:362-8.
 35. Foglio K, Bianchi L, Ambrosino N. Is it really useful to repeat outpatient pulmonary rehabilitation programs in patients with chronic airway obstruction? A 2-year controlled study. *Chest* 2001;119:1696-704.
 36. Bourbeau J, Julien M, Maltais F, Rouleau M, Beupré A, Bégin R, *et al.* Reduction of hospital utilization in patients with chronic obstructive pulmonary disease: A disease-specific self-management intervention. *Arch Intern Med* 2003;163:585-91.
 37. Hui KP, Hewitt AB. A simple pulmonary rehabilitation program improves health outcomes and reduces hospital utilization in patients with COPD. *Chest* 2003;124:94-7.
 38. Cecins N, Geelhoed E, Jenkins SC. Reduction in hospitalisation following pulmonary rehabilitation in patients with COPD. *Aust Health Rev* 2008;32:415-22.
 39. Rubí M, Renom F, Ramis F, Medinas M, Centeno MJ, Górriz M, *et al.* Effectiveness of pulmonary rehabilitation in reducing health resources use in chronic obstructive pulmonary disease. *Arch Phys Med Rehabil* 2010;91:364-8.
 40. Garcia-Aymerich J, Lange P, Benet M, Schnohr P, Antó JM. Regular physical activity reduces hospital admission and mortality in chronic obstructive pulmonary disease: A population based cohort study. *Thorax* 2006;61:772-8.
 41. Dodd JW, Marns PL, Clark AL, Ingram KA, Fowler RP, Canavan JL, *et al.* The COPD assessment test (CAT): Short- and medium-term response to pulmonary rehabilitation. *COPD* 2012;9:390-4.
 42. Ringbaek T, Brøndum E, Martinez G, Lange P. EuroQoL in assessment of the effect of pulmonary rehabilitation COPD patients. *Respir Med* 2008;102:1563-7.
 43. Management of Chronic Obstructive Pulmonary Disease (COPD) National Clinical Guideline No. 27. Annex D: COPD Budget Impact Analysis. Management of Chronic Obstructive Pulmonary Disease in adults; 2021.
 44. Ramos M, Lamotte M, Gerlier L, Svangren P, Miquel-Cases A, Haughney J. Cost-effectiveness of physical activity in the management of COPD patients in the UK. *Int J Chron Obstruct Pulmon Dis* 2019;14:227-39.
 45. Leemans G, Taeymans J, Van Royen P, Vissers D. Respiratory physiotherapy interventions focused on exercise training and enhancing physical activity levels in people with chronic obstructive pulmonary disease are likely to be cost-effective: A systematic review. *J Physiother* 2021;67:271-83.
 46. Kruis AL, Boland MR, Schoonvelde CH, Assendelft WJ, Rutten-van Mölken MP, Gussekloo J, *et al.* RECODE: Design and baseline results of a cluster randomized trial on cost-effectiveness of integrated COPD management in primary care. *BMC Pulm Med* 2013;13:17.
 47. Hoogendoorn M, van Wetering CR, Schols AM, Rutten-van Mölken MP. Is INTERdisciplinary COMMunity-based COPD management (INTERCOM) cost-effective? *Eur Respir J* 2010;35:79-87.

**Supplementary Table 1: Servizo Galego de Saúde^[19]
 fees in relation to emergency care and hospital
 admissions due to exacerbation of chronic
 obstructive pulmonary disease**

Test	Cost (€)
Emergency care	361.59
Emergency care (with admission)	528.95
Blood test, arterial blood gas test included	180
Chest X-ray	40,35
Electrocardiogram	181
Sputum culture	161.84
Pharmacy cost of moderate exacerbation	58.87
Pharmacy cost of moderate exacerbation before PR (mean stay, 7.2 days)	94.09
Pharmacy cost of moderate exacerbation after PR (mean stay, 7.4 days)	96.07
Follow-up consultations	58.37
Daily cost of hospital stay	528.95
Daily cost of ICU stay	1142.47

ICU=Intensive care unit, PR=Pulmonary rehabilitation