

FINAL PROJECT REPORT



Effectiveness of Institutional versus domiciliary implementation of standard pulmonary Rehabilitation module in Bhopal gas exposed survivors having COPD.

(Duration: 19/01/2017 to 28/02/2019)

Principal Investigator: Dr.Ruma Galgalekar, Scientist-C (Med).

ABSTRACT

Pulmonary Rehabilitation (PR) is beneficial treatment to decrease symptoms, increase participation and to reduce health costs for COPD patients by helping to improve health quality. Our study compared the impact of pulmonary rehabilitation of gas exposed surviving COPD patients in ameliorating their health status in two operational settings i.e. supervised institutional and unsupervised home based.

The study sample used for PR was 180 gas exposed COPD subjects in age 40-75 yrs. of both gender, satisfying the inclusion (FEV_1 of less than 60% and with no active heart disease) and exclusion criteria which was randomized equally into two groups (institutional and domiciliary). Before starting PR program, a 6 minute Walk test, SGRQ score and PFT was done and the same was assessed every 6 months interval. PR program for 1hr consisted of breathing exercise, pursed lip breathing, huffing and coughing, diaphragmatic and incentive spirometry technique, active range of movements of all upper and lower limb joints and postural drainage.

Descriptive statistics of 6MWT with SPO₂, Pulse rate and distance walked by both groups after interval of 6months and 12 months of PR shows significant improvement in Institutional group as compared to domiciliary. There is no significant difference in the FEV_1 values at 6 months in both the groups but at 12th month follow up there is a significant reduction of 0.04 units in the FEV_1 values in the domiciliary group as compared to baseline. Analysis of quality of life assessment by SGRQ shows decrease in severity of symptoms score, marked improvement in activity score, impact scores and total scores in Institutional Group after 12 months of Pulmonary Rehabilitation. Improvement in Quality of life and functional exercise capacity is significantly higher in Institutional group as compared to domiciliary group.

Keywords: PR,6MWT,SGRQ, FEV_1 ,PFT.

SUMMARY

As pulmonary rehabilitation is a life - long process, special emphasis was given to develop community based pulmonary rehabilitation Centre near the residences of gas exposed COPD patients so that continuous exercise training, counseling, and educational program was conveniently provided to them to increase patients awareness and knowledge on their disease management. Pulmonary rehabilitation in cases of chronic obstructive pulmonary disease (COPD) helps to decrease symptoms, improve functional state, increase participation to reduce recurrent exacerbations and reduce health care costs. The study was carried out at Pulmonary Rehabilitation centre set up in Jawaharlal Lal Nehru, Gas Rahat Hospital located near severely gas exposed localities to facilitate easy accessibility and participation of COPD subjects for pulmonary rehabilitation. The proposed study has compared the impact of pulmonary rehabilitation to gas exposed surviving COPD patients in ameliorating their health status in two operational settings i.e supervised institutional and unsupervised home based. In this group study PR was given to participants and follow up of improvement was assessed by 6MWT,SGRQ Scoring and PFT at interval of 6months and 12 months.

The results of the study has shown that the Institutional Group showed better improvement as the participants were having better mobility by coming regularly to Pulmonary Rehabilitation Centre to participate in PR exercise schedule .Also group participation in exercise, personal discussion on their disease status and management by counseling helped to improve their physiological well being. There was great motivation to participants of coming together from community by slow walking or by other means of shared transport to attend Institutional Rehabilitation program. Whereas Domiciliary Group were feeling less enthusiastic as they were doing PR indoor at their respective residences and had no encouragement and support from their family to do their exercises regularly. Improvement in Quality of life and functional exercise capacity is significantly higher in Institutional group as compared to domiciliary group.

Annexure-1.

Title of the Research Project

Effectiveness of institutional versus domiciliary implementation of standard pulmonary rehabilitation module in Bhopal gas exposed survivors having COPD.

Background

A Cohort Study of ICMR on long term epidemiological studies on the health effects of toxic gas exposure at Bhopal which was initiated immediately after the disaster in Jan 1985 was aimed to investigate the epidemiological fallouts of the disaster. During this study regular field visits were conducted to collect data on socio economic profile, morbidities and mortality from Cohort. During these field visits the respiratory morbidity complaints by severe gas exposed population and the apprehension of the population regarding their disease lead to further clinical examination and investigation at NIREH. Initially the gas exposed individuals having respiratory symptoms were screened. The respiratory symptoms included for initial screening were cough, sputum production and dyspnoea. Such identified suspected cases of COPD were evaluated for detailed clinical history, smoking history, physical examination with blood pressure, height, weight. Following investigations were carried out for each subject viz. blood test that include total and differential cell counts, erythrocyte sedimentation rate and fasting blood sugar, electro cardiogram and ski grams chest PA view for diagnosing the cases of COPD. Sputum for acid fast bacilli was examined in suspected cases of tuberculosis. Pulmonary function test (FVC, FEV1, FEV1/FVC% and PEF 25-75%) was conducted for each subject before and after inhalation of short acting B₂ agonist as per the guidelines of American Thoracic Society. These subjects were examined by a pulmonologist to make final diagnosis of COPD and advised treatment and Pulmonary rehabilitation exercise by incentive spirometry. A trained physiotherapist was giving this PR program at community based mini unit -1 of BMHRC to COPD patients availing treatment at the centre. In a pilot study 19 identified COPD subjects (9 males, 10 females, age group 35-77 years) from the gas exposed population were given treatment and pulmonary rehabilitation at a community health centre for one hour for one month. Six minutes walk test before and after pulmonary rehabilitation was assessed which recorded improvement of 2.0-45.5 meters of distance walked after the pulmonary rehabilitation. Pulmonary rehabilitation might be an important

component of management of MIC exposed individuals presenting with chronic respiratory diseases and with evidence of air flow limitation.

Rationale

The proposed study would compare the impact of Pulmonary Rehabilitation to gas exposed surviving COPD patients in ameliorating their health status in two operational settings i.e supervised institutional and unsupervised home based.

Objectives

- 1) To compare the effectiveness of standard pulmonary rehabilitation module administered in institutional vis-à-vis domiciliary settings in managing COPD cases.
- 2) To recognize barriers preventing COPD cases undergoing pulmonary rehabilitation and realizing its clinical benefits.

Review of Literature

COPD is primarily a disease of the adults largely caused by smoking. COPD is characterized by progressive, partially reversible airway obstruction and lung hyper inflation with increasing frequency and severity of exacerbations^{6,7}. The global prevalence of COPD (GOLD Stage 2 or more) in adults age > 40 years is approximately 9-10%⁸. The prevalence of COPD in India based on study conducted by Wig et al in Delhi shows 3.36% prevalence in males and 2.54% in females⁹. COPD is fifth largest cause of morbidity and mortality world wise resulting in substantial economic and social burden.¹⁰ Individuals exposed to MIC in Bhopal have chronic persistent inflammatory changes in the lower respiratory tract¹¹. In addition, a proportion of subjects exposed to MIC have persisting airflow limitation that is indistinguishable from COPD¹².

Various randomized controlled trials have shown the effectiveness of pulmonary rehabilitation for COPD patients¹³⁻¹⁵. Ries and his colleagues studied 119 COPD patients comparing the effect of a comprehensive pulmonary rehabilitation program and education alone (control group) showed significant benefits of comprehensive pulmonary rehabilitation in improving exercise performance and important symptoms¹⁶. Cochrane Meta analysis examined the effect of 23 randomized trials¹⁷. It was seen that pulmonary rehabilitation for COPD improves dyspnoea and disease specific quality of life. Functional exercise capacity as assessed by 6 minute walk distance was also increased by 49m. The benefits were more in severe COPD as compared to

mild and moderate disease and effects were maintained for up to 6 months. A few other studies have found reduction in anxiety and depression after pulmonary rehabilitation in patients with COPD¹⁸⁻²⁰.

One clinical study using tiotropium has shown that a better outcome of pulmonary rehabilitation can be obtained using this therapy.²¹ An analysis of pooled data from number of trials demonstrated that pulmonary rehabilitation improved the endurance time during a constant work - rate by an average of 87%, peak work rate by an average of 18%, peak oxygen uptake by 11% compared with pre rehabilitation levels²². The American College of Physicians (ACP) guidelines²³ recommend that prescribing pulmonary rehabilitation in symptomatic individuals with COPD(FEV₁ less than 50% predicted) which contrasts with ATS/ERS guidelines suggesting pulmonary rehabilitation may be started from an earlier stage. Though the work is limited, yet rehabilitation may seem to be significant advantage for patients with many non - COPD disorders^{24,25}. Pulmonary Rehabilitation has been used in various different diseases such as asthma, cystic fibrosis, interstitial lung disease; obesity related respiratory disorders, pulmonary hypertension, neuro muscular and chest wall disorders²⁶. Studies have shown that pulmonary rehabilitation is important for patients with idiopathic pulmonary fibrosis and interstitial lung disease^{27,28}. An Indian study found 6 weeks of home based pulmonary rehabilitations program effective in increasing exercise endurance in patients with ILD²⁹. Another study of seven weeks of PR showed greater benefit as compared to 4weeks.⁵ Pulmonary rehabilitation might be an important component of management of MIC exposed individuals presenting with chronic respiratory diseases and with evidence of air flow limitation.

Sample Size

A total of 180 diagnosed COPD subjects among the toxic gas exposed cohort in Bhopal would be enrolled for rehabilitation program. This sample size is sufficient to have 99% confidence and 80% power of the study. The sample size is arrived at on the basis of significant difference ($p < 0.05$, paired t-test) found in the pulse rate before and after pulmonary physiotherapy in a pilot study on 19 COPD subjects.

Setting & Study subjects

The study was carried out at Pulmonary Rehabilitation centre set up in Jawaharlal Nehru, Gas Rahat Hospital, Bhopal which is located near severely gas exposed localities to facilitate easy accessibility and participation of COPD subjects for pulmonary rehabilitation. The

Rehabilitation Centre was equipped with nebulizers, oxygen, resuscitation equipment and trained staff to handle any event of an emergency to patients undergoing pulmonary rehabilitation. The study subjects were COPD cases in 40-75 years age group of both sexes selected from the gas exposed population satisfying the following inclusion and exclusion criteria.

Inclusion criteria

1. Confirmed diagnosis of COPD
2. Forced expiratory volume in 1 sec (FEV₁) of less than 60%
3. No active heart disease
4. Age group 40-75 years.

Exclusion criteria:-

1. Unstable Angina
2. Myocardial infarct within six weeks
3. Uncontrolled cardiac arrhythmias
4. Unstable hypertension
5. Severe cognitive impairment
6. Locomotor or other severe medical condition

Methodology

The study was carried out at Pulmonary Rehabilitation centre established in Jawaharlal Nehru, Gas Rahat Hospital, Bhopal, located near severely gas exposed localities to facilitate easy accessibility and participation of COPD subjects for pulmonary rehabilitation. The study subjects were confirmed COPD cases in 40-75 years of both sexes selected from the gas exposed population satisfying the inclusion and exclusion criteria. Inclusion criteria were confirmed diagnosis of COPD, Forced expiratory volume in 1 sec (FEV₁) of less than 60% and with no active heart disease. Ethical Committee approved the research project. The subjects included in the rehabilitation group were treated with the standard COPD medications as per GOLD criteria and given one week training of pulmonary rehabilitation at Institutional Centre. Before starting pulmonary rehabilitation a 6minute Walk test, SGRQ score and PFT was done. Written consent was obtained from participating subjects. Randomization of 180 gas exposed COPD subjects into

two groups Institutional and Domiciliary was completed. The rehabilitation program consisted of breathing exercise pursed lip breathing, huffing and coughing, diaphragmatic and incentive spirometry technique, active range of movements of all upper and lower limb joints and postural drainage. Subjects in the Institutional group underwent pulmonary rehabilitation daily for one hour duration at pulmonary rehabilitation centre under the supervision of qualified Physiotherapist and criteria of attendance (85-90%) was fixed for successful completion of pulmonary rehabilitation. Domiciliary group undertook same exercises for a hour duration at their residences. Follow up at interval of 6 months and 12 months was done.

Six –minute walking test (6MWT)

The 6MWT was administered to study subjects as per procedure recommended by American Thoracic Society (ATS) guidelines in an enclosed corridor.³

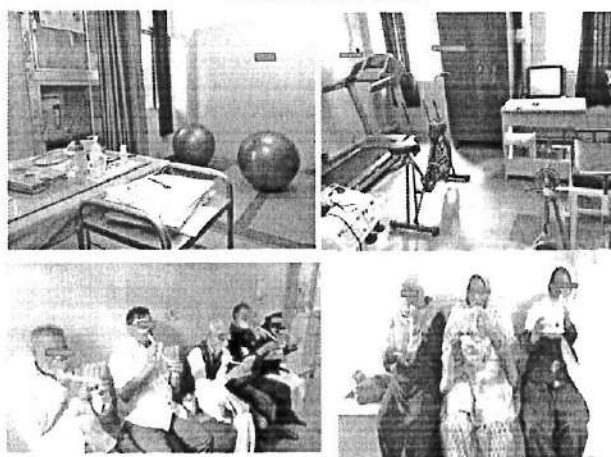
Pulmonary function testing

Spirometry and flow volumes were measured by Jaegers master screen unit.

St.George Respiratory Questionnaire (SGRQ)

The SGRQ Questionnaire is designed to measure health impairment in COPD patients. Three component scores were calculated;Symptoms,Activity,Impact .One total score is also calculated⁴.The questionnaire is designed for supervised self administration by patients. It is to elicit patient’s opinion of his/her health. Assessment and evaluation of any subjective symptom is difficult task and it typically relies on self reported by patients

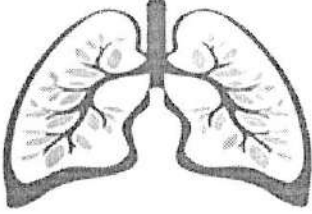
Rehabilitation Centre



Pamphlets to generate Awareness in Community

रैम पीडिन मरीज कृपया ध्यान दे

यदि इनमे से कोई भी लक्षण है तो संपर्क करें



- लगातार खाँसी के साथ बलगम का आना।
- खाँसी की अचानक दवाओं से आराम न मिलना।
- सोमस बदलने पर खाँसी बुरा काम बुरा बुरा होना हो।
- छाती में सीटी जैसी आवाज आनी हो।
- व्यायाम करने समय या भागने में सोंस फूलनी हो।
- रात को खाँसी की वजह से सोने में असुविधा होनी हो।

- यदि आप गिछने कुछ मामलों में धूमपान कर रहे हैं। और इसकी वजह से आपकी सोंस लेने में परेशानी है

नोट : मरीजों की जाँचों एवं उपचार की फोल्डर फाइल बनायी और मरीजों को दी जाएगी।

संपर्क करें : 8109147421।

8224942553

Result

The first two rounds of six monthly follow up of both the study groups (Institutional and domiciliary) has been completed.

Table 1: Descriptive statistics:6 MWT

	Group	Baseline			6 month			12 month		
		N	Pre 6MWT	Post 6MWT	N	Pre 6MWT	Post 6MWT	N	Pre 6MWT	Post 6MWT
SPO ₂ (%)	Institutional	90	93.38 (1.16)	92.48 (1.59)	86	94.29 (2.12)	93.30 (2.18)	86	94.93 (0.89)	94.43 (0.99)
	Domiciliary	90	93.16 (1.36)	92.14 (1.80)	84	94.21 (1.12)	93.36 (1.34)	84	94.43 (0.88)	93.69 (1.14)
PR (BPM)	Institutional	90	87.81 (8.24)	100.02 (9.67)	86	85.51 (7.62)	95.26 (8.01)	86	82.01 (5.17)	94.98 (5.89)
	Domiciliary	90	87.62 (8.69)	99.40 (9.66)	84	85.29 (7.76)	95.62 (8.55)	84	81.63 (4.80)	93.92 (5.74)
Distance(MTR)	Institutional	90	139.4651		86	151.7558		86	217.2442	

			(18.54324)		(19.64625)		(28.57351)
	Domiciliary	90	138.8721 (20.48632)	84	151.1667 (20.44377)	84	167.2857 (20.41)
Age	Institutional	90	58.03 (8.14)				
	Domiciliary	90	59.57 (7.40)				
Gender (Male): n(%)	Institutional	90	53 (61.63%)				
	Domiciliary	90	48 (55.81%)				

Provided mean(SD)

Descriptive statistics of 6 Minute Walk Test of variable oxygen saturation level (SPO₂).

Pulse rate (PR) , Distance, Age & Gender of COPD subjects follow up at 6 months & 12 months interval for pulmonary rehabilitation of Institutional & Domiciliary group after Pulmonary rehabilitation.

Table 2: Descriptive Statistics:SGRQ

SGRQ Score Type	Institutional			Domiciliary		
	Baseline	6 month	12 month	Baseline	6 month	12 month
Symptom	89.48 (2.87)	76.03 (12.19)	17.16 (6.40)	89.13 (2.79)	75.52 (12.10)	76.93 (12.74)
Activity	98.53 (3.18)	74.21 (14.62)	3.83 (5.41)	98.17 (3.24)	71.91 (15.40)	72.95 (15.67)
Impact	99.74 (1.01)	70.39 (14.10)	0.90 (1.13)	99.72 (0.53)	70.36 (15.20)	69.65 (16.45)
Total	97.67 (1.86)	72.49 (11.54)	4.49 (2.49)	97.49 (1.67)	71.69 (11.70)	71.86 (12.75)

Provided Mean (SD)

Descriptive Statistics St. George respiratory Questionnaire (SGRQ) of COPD subjects of Institutional and Domiciliary group at interval of 6 & 12 months after Pulmonary rehabilitation.

Table 3 : Descriptive statistics:PFT

	Group	Baseline			6 month			12 month		
		N	Pre bronchodilation	Post Bronchodilation	N	Pre bronchodilation	Post Bronchodilation	N	Pre bronchodilation	Post Bronchodilation
			Mean (SD)	Mean (SD)		Mean (SD)	Mean (SD)			
FEV1	Institutional	86	0.91 (0.34)	1.05 (0.36)	86	0.92 (0.33)	1.05 (0.36)	86	0.91 (0.33)	1.04 (0.36)
	Domiciliary	86	0.93 (0.35)	1.03 (0.35)	84	0.94 (0.34)	1.05 (0.35)	84	0.95 (0.37)	1.01 (0.35)

Provided mean(SD)

Spirometry of COPD subjects after undergoing pulmonary rehabilitation at interval of 6 and 12 months of Institutional and Domiciliary group.

Table 4 :FEV₁

Variable	Coefficient	SE	P value	95% CI
Age	-0.002	0.001	0.206	(-0.004, 0.0008)
Sex: Female	-0.05	0.02	0.009	(-0.09, -0.01)
BMI	0.003	0.002	0.166	(-0.001, 0.006)
FEV ₁ : Pre bronchodilation	0.83	0.03	0.000	(0.78, 0.88)
Group: Domiciliary	-0.02	0.02	0.245	(-0.07, 0.02)
Time*Group:				
6 month* Institutional	-0.001	0.01	0.923	(-0.03, 0.02)
6 month* Domiciliary	0.02	0.01	0.224	(-0.01, 0.04)
12 month* Institutional	-0.01	0.01	0.471	(-0.03, 0.02)
12 month*Domiciliary	-0.04	0.01	0.001	(-0.07, -0.02)

Comparison of Age, Sex, BMI and Forced expiratory vol. in 1 sec. (FEV₁) of Institutional and Domiciliary groups at interval of 6 and 12 months after pulmonary rehabilitation.

Statistical methods

To summarize the continuous variables we used mean and standard deviation and frequency with percentage was used to summarize the categorical variables. As pulmonary rehabilitation is a longitudinal study observes subjects over time, we used Generalized Estimating Equation (GEE) for studying the change in FEV₁, SPO₂, PR, Distance walked, SGRQ score (Symptom score, Activity score, Impact score and Total score) between Institutional vs Domiciliary group in the population over time after adjusting for other confounding variables such as age, gender and BMI. P value <0.05 was considered for statistical significance.

Discussion

The participants were assessed at baseline, after interval of 6months and 12 months of pulmonary rehabilitation program. The variables considered for statistical analysis included functional exercise capacity by six minute walk test (6MWT), quality of life assessment by SGRQ and spirometry values. Variables were compared between the Institutional and Domiciliary group after Pulmonary Rehabilitation. Descriptive statistics of 6MWT with SPO₂, PR, Distance as variables of COPD subjects undergoing pulmonary rehabilitation of both groups at baseline, 6 months 12months interval period shows improvement of distance walked in both the groups but significant improvement in Institutional versus Domiciliary group (Table-1). Analysis of quality of life assessment by SGRQ shows decrease in severity of symptoms score, marked improvement in activity score, impact scores and total scores in Institutional Group after 12 months of Pulmonary Rehabilitation. (Table-2). There is no significant difference in the FEV₁ values at 6months in both the groups as compared to baseline. (Table-3). The progressive decline in pulmonary function found in COPD patients is considered a major prognostic factor of the course of the disease. After 12 months follow up after Pulmonary Rehabilitation there is a significant reduction of 0.04 units in the FEV₁ values in the domiciliary group as compared to baseline after adjusting all other confounding variables in the model (p value = 0.001). (Table-4) While the Institutional group has maintained the baseline value of FEV₁. Improvement in Quality of life and functional exercise capacity is significantly higher in Institutional group as compared to domiciliary group.

References

1. Ries AL, Bauldoff GS, Carlin BW, Casaburi R, Emery CF, Mahler DA, Make B, Rochester CL, ZuWallack R, Herrerias C. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. *Chest*. 2007 May 1;131(5):4S-2S.
2. Goldstein RS, Gort EH, Avendano MA, Stubbing D, Guyatt GH. Randomized controlled trial of respiratory rehabilitation. *The Lancet*. 1994 Nov 19;344(8934):1394-7.
3. ATS statement: guidelines for the six-minute walk test. ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. *Am J Respir Crit Care Med*. 2002; 166(1):111-7.
4. Jones PW, Quirk FH, Baveystock CM. The St George's respiratory questionnaire. *Respiratory medicine*. 1991 Sep 1; 85:25-31.
5. Green RH, Singh SJ, Williams J, Morgan MD. A randomized controlled trial of four weeks versus seven weeks of pulmonary rehabilitation in chronic obstructive pulmonary disease. *Thorax*. 2001 Feb 1;56 (2):143-5.
6. O'donnell DE, Aaron S, Bourbeau J, Hernandez P, Marciniuk DD, Balter M, Ford G, Gervais A, Goldstein R, Hodder R, Kaplan A. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease–2007 update. *Canadian Respiratory Journal*. 2007;14(Suppl B):5B-32B.
7. O'donnell DE, Hernandez P, Kaplan A, Aaron S, Bourbeau J, Marciniuk D, Balter M, Ford G, Gervais A, Lacasse Y, Maltais F. Canadian Thoracic Society recommendations for management of chronic obstructive pulmonary disease–2008 update–highlights for primary care. *Canadian Respiratory Journal*. 2008;15(Suppl A):1A-8A.
8. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *European Respiratory Journal*. 2006 Sep 1;28(3):523-32.

9. Wig KL, Guleria JS, Bhasin RC, Holmes E, Vasudeva YL, Singh H. Certain clinical and epidemiological patterns of chronic obstructive lung disease as seen in Northern India. *Indian J chest Dis* 1964; 6: 183-194.
10. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *American journal of respiratory and critical care medicine*. 2001 Apr 1;163(5):1256-76.
11. Vijayan VK, Sankaran K. Relationship between lung inflammation, changes in lung function and severity of exposure in victims of the Bhopal tragedy. *European Respiratory Journal*. 1996 Oct 1;9(10):1977-82.
12. Cullinan P, Acquilla S, Dhara VR. Respiratory morbidity 10 years after the Union Carbide gas leak at Bhopal: a cross sectional survey. *Bmj*. 1997 Feb 1;314(7077):338.
13. Ries AL, Bauldoff GS, Carlin BW, Casaburi R, Emery CF, Mahler DA, Make B, Rochester CL, ZuWallack R, Herrerias C. Pulmonary rehabilitation: joint ACCP/AACVPR evidence-based clinical practice guidelines. *Chest*. 2007 May 1;131(5):4S-2S.
14. Goldstein RS, Gort EH, Avendano MA, Stubbing D, Guyatt GH. Randomised controlled trial of respiratory rehabilitation. *The Lancet*. 1994 Nov 19;344(8934):1394-7.
15. Griffiths TL, Phillips CJ, Davies S, Burr ML, Campbell IA. Cost effectiveness of an outpatient multidisciplinary pulmonary rehabilitation programme. *Thorax*. 2001 Oct 1;56(10):779-84.
16. Wedzicha JA, Bestall JC, Garrod R, Garnham R, Paul EA, Jones PW. Randomized controlled trial of pulmonary rehabilitation in severe chronic obstructive pulmonary disease patients, stratified with the MRC dyspnoea scale. *European respiratory journal*. 1998 Aug 1;12(2):363-9.
17. Güell R, Casan P, Belda J, Sangenis M, Morante F, Guyatt GH, Sanchis J. Long-term effects of outpatient rehabilitation of COPD: a randomized trial. *Chest*. 2000 Apr 1;117(4):976-83.

18. Troosters T, Gosselink R, Decramer M. Short-and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *The American journal of medicine*. 2000 Aug 15;109(3):207-12.
19. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Annals of internal medicine*. 1995 Jun 1;122(11):823-32.
20. McCarthy B, Casey D, Devane D, Murphy K, Murphy E, Lacasse Y. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane database of systematic reviews*. 2015(2).
21. Hill NS. Pulmonary rehabilitation. *Proceedings of the American Thoracic Society*. 2006 Mar;3(1):66-74.
22. Güell R, Resqueti V, Sangenis M, Morante F, Martorell B, Casan P, Guyatt GH. Impact of pulmonary rehabilitation on psychosocial morbidity in patients with severe COPD. *Chest*. 2006 Apr 1;129(4):899-904.
23. Godoy RF, Teixeira PJ, Becker Júnior B, Michelli M, Godoy DV. Long-term repercussions of a pulmonary rehabilitation program on the indices of anxiety, depression, quality of life and physical performance in patients with COPD. *Jornal Brasileiro de Pneumologia*. 2009 Feb;35(2):129-36.
24. Casaburi R, Kukafka D, Cooper CB, Witek Jr TJ, Kesten S. Improvement in exercise tolerance with the combination of tiotropium and pulmonary rehabilitation in patients with COPD. *Chest*. 2005 Mar 1;127(3):809-17.
25. Troosters T, Casaburi R, Gosselink R, Decramer M et al. Pulmonary rehabilitation in Copd. *Am J Respir Crit Care Med* 2005;172:19-38
26. Qaseem A, Snow V, Shekelle P, Sherif K, Wilt TJ, Weinberger S, Owens DK. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline from the American College of Physicians. *Annals of internal medicine*. 2007 Nov 6;147(9):633-8.

27. Swigris JJ, Fairclough DL, Morrison M, Make B, Kozora E, Brown KK, Wamboldt FS. Benefits of pulmonary rehabilitation in idiopathic pulmonary fibrosis. *Respiratory care*. 2011 Jun 1;56(6):783-9.
28. Markovitz GH, Cooper CB. Review series: Rehabilitation in non COPD: Mechanisms of exercise limitation and pulmonary rehabilitation for patients with pulmonary fibrosis/restrictive lung disease. *Chronic respiratory disease*. 2010 Feb;7(1):47-60.
29. Nici L, Donner C, Wouters E, Zuwallack R, Ambrosino N, Bourbeau J, Carone M, Celli B, Engelen M, Fahy B, Garvey C. American thoracic society/European respiratory society statement on pulmonary rehabilitation. *American journal of respiratory and critical care medicine*. 2006 Jun 15;173(12):1390-413.