Pulmonary Rehabilitation Where We've Succeeded and Where We've Failed

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Disclosures: Consultant, Grants, Speakers Bureau

for Boehringer-Ingelheim, Novartis, Astra Zeneca,

GSK, Astellas

Pulmonary Rehabilitation - outline -

- Where we've succeeded
 - —Establishing a firm scientific basis of patient-relevant benefits
- Where we've failed
 - Poor availability for patients who would benefit
- ...And a path forward

The Accumulated Evidence

Pulmonary rehabilitation:

- improves exercise tolerance
- improves the symptom of dyspnea
- improves health-related quality of life

These benefits are generally of greater magnitude than for any other COPD therapy

High profile publications document the effectiveness of pulmonary rehabilitation

State of the Art

Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease

Thierry Troosters, Richard Casaburi, Rik Gosselink, and Marc Decramer

Respiratory Rehabilitation and Respiratory Division, University Hospital; Department of Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Katholieke Universiteit Leuven; and Respiratory Rehabilitation, Universitaire Ziekenhuizen Gasthuisberg, Leuven, Belgium; and Rehabilitation Clinical Trials Center, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California

AJRCCM 172:19–38, 2005



CHEST

Supplement

PULMONARY REHABILITATION: JOINT ACCP/AACVPR EVIDENCE-BASED CLINICAL PRACTICE GUIDELINES

Pulmonary Rehabilitation*

Joint ACCP/AACVPR Evidence-Based Clinical Practice Guidelines

Andrew L. Ries, MD, MPH, FCCP (Chair); Gerene S. Bauldoff, RN, PhD, FCCP; Brian W. Carlin, MD, FCCP; Richard Casaburi, PhD, MD, FCCP; Charles F. Emery, PhD; Donald A. Mahler, MD, FCCP; Barry Make, MD, FCCP; Carolyn L. Rochester, MD; Richard ZuWallack, MD, FCCP; and Carla Herrerias, MPH

Chest 2007,131:4S-42S

The NEW ENGLAND JOURNAL of MEDICINE

CLINICAL THERAPEUTICS

Pulmonary Rehabilitation for Management of Chronic Obstructive Pulmonary Disease

Richard Casaburi, Ph.D., M.D., and Richard ZuWallack, M.D.

N ENGL J M ED 360;13 NEJM.ORG MARCH 26, 2009

American Thoracic Society Documents

An Official American Thoracic Society/European Respiratory Society Statement: Key Concepts and Advances in Pulmonary Rehabilitation

Martijn A. Spruit, Sally J. Singh, Chris Garvey, Richard ZuWallack, Linda Nici, Carolyn Rochester, Kylie Hill, Anne E. Holland, Suzanne C. Lareau, William D.-C. Man, Fabio Pitta, Louise Sewell, Jonathan Raskin, Jean Bourbeau, Rebecca Crouch, Frits M. E. Franssen, Richard Casaburi, Jan H. Vercoulen, Ioannis Vogiatzis, Rik Gosselink, Enrico M. Clini, Tanja W. Effing, François Maltais, Job van der Palen, Thierry Troosters, Daisy J. A. Janssen, Eileen Collins, Judith Garcia-Aymerich, Dina Brooks, Bonnie F. Fahy, Milo A. Puhan, Martine Hoogendoorn, Rachel Garrod, Annemie M. W. J. Schols, Brian Carlin, Roberto Benzo, Paula Meek, Mike Morgan, Maureen P. M. H. Rutten-van Mölken, Andrew L. Ries, Barry Make, Roger S. Goldstein, Claire A. Dowson, Jan L. Brozek, Claudio F. Donner, and Emiel F. M. Wouters; on behalf of the ATS/ERS Task Force on Pulmonary Rehabilitation

This official statement of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) was approved by the ATS Board of Directors, June 2013, and by the ERS Scientific and Executive Committees in January 2013 and February 2013, respectively

AJRCCM 188:1011-1027,2013

Targets for Improving Exercise Tolerance

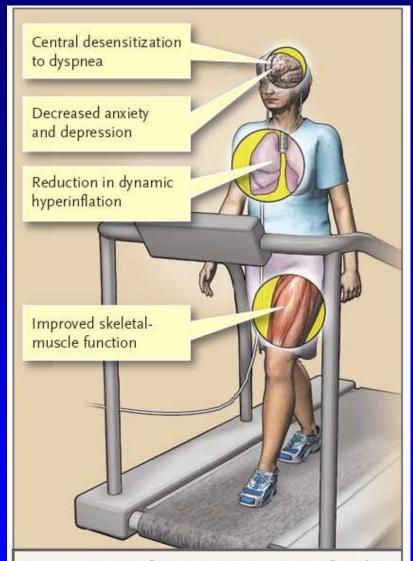


Figure 1. Targets of Exercise Training as Part of a Pulmonary Rehabilitation Program for Patients with COPD.

Targets for Improving Exercise Tolerance

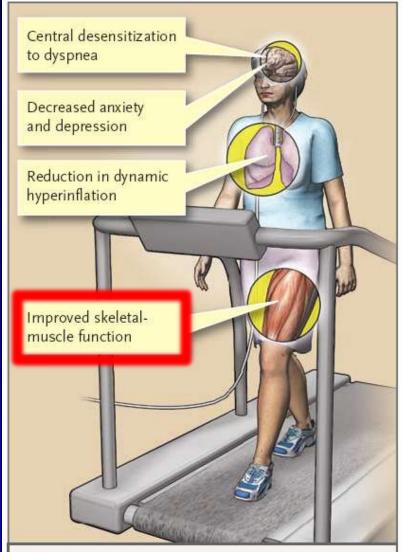


Figure 1. Targets of Exercise Training as Part of a Pulmonary Rehabilitation Program for Patients with COPD.

Physiologic Benefits of Exercise Training in Rehabilitation of Patients with Severe Chronic Obstructive Pulmonary Disease

RICHARD CASABURI, JANOS PORSZASZ, MARY R. BURNS, EVE R. CARITHERS, ROBERT S. Y. CHANG, and CHRISTOPHER B. COOPER

Division of Respiratory and Critical Care Physiology and Medicine, Harbor-UCLA Medical Center; Pulmonary Rehabilitation Program,
Little Company of Mary Hospital, Torrance, California

1997 Am J Respir Crit Care Med

486 Citations!

American Thoracic Society/European Respiratory Society

Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease

A Statement of the American Thoracic Society and European Respiratory Society

1999

AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society/European Respiratory Society Statement: Update on Limb Muscle Dysfunction in Chronic Obstructive Pulmonary Disease

François Maltais, Marc Decramer, Richard Casaburi, Esther Barreiro, Yan Burelle, Richard Debigaré, P. N. Richard Dekhuijzen, Frits Franssen, Ghislaine Gayan-Ramirez, Joaquim Gea, Harry R. Gosker, Rik Gosselink, Maurice Hayot, Sabah N. A. Hussain, Wim Janssens, Micheal I. Polkey, Josep Roca, Didier Saey, Annemie M. W. J. Schols, Martijn A. Spruit, Michael Steiner, Tanja Taivassalo, Thierry Troosters, Ioannis Vogiatzis, and Peter D. Wagner; on behalf of the ATS/ERS Ad Hoc Committee on Limb Muscle Dysfunction in COPD

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) AND THE EUROPEAN RESPIRATORY SOCIETY (ERS) WAS APPROVED BY THE A DIRECTORS, NOVEMBER 2013, AND BY THE ERS EXECUTIVE COMMITTEE, SEPTEMBER 2013

2014

Five Most Effective Interventions to Improve COPD Limb Muscle Function

- 1. Exercise training
- 2. Exercise training
- 3. Exercise training
- 4. Exercise training
- 5. Exercise training

Strategies to Improve the Effectiveness of Pulmonary Rehabilitative Programs in COPD

- Bronchodilators
- Anabolic drugs
- Oxygen breathing
- Heliox breathing
- Pressure support ventilation
- Interval training
- Electrical muscle stimulation

Global Initiative for Chronic Obstructive Lung

"The benefits to COPD patients from pulmonary rehabilitation are considerable and rehabilitation has been shown to be the most effective therapeutic strategy to improve shortness of breath, health status and exercise tolerance. Pulmonary rehabilitation is appropriate for most patients with COPD; improved functional exercise capacity and health related quality of life have been demonstrated across all grades of COPD severity"

2018 Update

GLOBAL STRATEGY FOR THE DIAGNOSIS,
MANAGEMENT, AND PREVENTION OF
CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Pulmonary Rehabilitation -outline -

- Where we've succeeded
 - -Establishing a firm scientific basis of patient-relevant benefits
- Where we've failed
 - Poor availability for patients who would benefit
- ...And a path forward

Three Major COPD Therapies

- Bronchodilators
- Supplemental Oxygen
- Pulmonary Rehabilitation

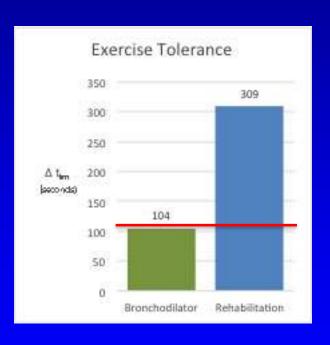
Bronchodilator Oxygen Rehabilitation

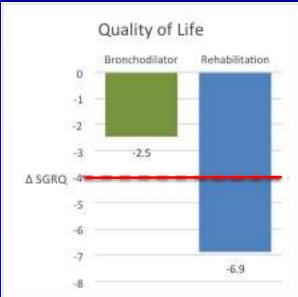
	Bronchodilator	Oxygen	Rehabilitation
Exercise Tolerance	^	^	个个个

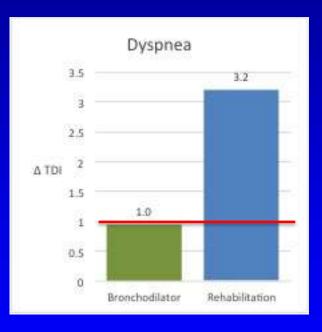
	Bronchodilator	Oxygen	Rehabilitation
Exercise Tolerance	^	^	^ ^^
Dyspnea	^	^	^

	Bronchodilator	Oxygen	Rehabilitation
Exercise Tolerance	1	^	^ ^^
Dyspnea	^	↑ ↑	^ ^^
Quality of Life	^	^	^ ^^

Magnitude of Benefit Bronchodilator vs. Rehabilitation







Data from literature meta-analyses Red line = MCID Bronchodilator = LABA or LAMA

	Bronchodilator	Oxygen	Rehabilitation
Exercise Tolerance	1	^	^ ^^
Dyspnea	^	^	^
Quality of Life	^	^	^
Duration of Benefit after Withdrawal	Hours- Days	Minutes	Months- Years

- Bronchodilators
- Supplemental Oxygen
- Pulmonary Rehabilitation

- Bronchodilators
 - -Near universal use in diagnosed disease

- Supplemental Oxygen
 - -Near universal availability to qualifying patients
 - -Over ~\$3 billion spent annually for ~1 million patients

- Pulmonary Rehabilitation
 - Available to roughly 1.2% of COPD patients who would benefit

ORIGINAL RESEARCH

An International Comparison of Pulmonary Rehabilitation: A Systematic Review

Laura Desveaux,^{1,2} Tania Janaudis-Ferreira,^{2,3} Roger Goldstein,^{1,2,4,5} and Dina Brooks^{1,2,4,5} J COPD, 2014

"The annual national capacity for pulmonary rehabilitation...consistently translated to ≤1.2% of the estimated COPD population for each respective country." No US data available for inclusion.



Pulmonary Rehabilitation Utilization in Older Adults With Chronic Obstructive Pulmonary Disease, 2003 to 2012

J Cardiopulm Rehabil, 2016

Shawn P. E. Nishi, MD; Wei Zhang, MS; Yong-Fang Kuo, PhD; Gulshan Sharma, MD

- The only published US based utilization data
- Only relates to Medicare-eligible patients
- Medicare claims data reviewed based on a 5% sampling of beneficiaries
- Spans period before and after pulmonary rehabilitation becoming a Medicare benefit (circa 2010)
- Found pulmonary rehabilitation participation rate increased from **2.6%** in 2003 to **3.7%** in 2012
- May well be an overestimate of general COPD population

AMERICAN THORACIC SOCIETY DOCUMENTS

An Official American Thoracic Society/European Respiratory Society Policy Statement: Enhancing Implementation, Use, and Delivery of Pulmonary Rehabilitation

Carolyn L. Rochester, Ioannis Vogiatzis, Anne E. Holland, Suzanne C. Lareau, Darcy D. Marciniuk, Milo A. Puhan, Martijn A. Spruit, Sarah Masefield, Richard Casaburi, Enrico M. Clini, Rebecca Crouch, Judith Garcia-Aymerich, Chris Garvey, Roger S. Goldstein, Kylie Hill, Michael Morgan, Linda Nici, Fabio Pitta, Andrew L. Ries, Sally J. Singh, Thierry Troosters, Peter J. Wijkstra, Barbara P. Yawn, and Richard L. ZuWallack; on behalf of the ATS/ERS Task Force on Policy in Pulmonary Rehabilitation

This Official Policy Statement of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) was approved by the ATS BOARD OF DIRECTORS, OCTOBER 2015, AND BY THE ERS SCIENCE COUNCIL, SEPTEMBER 2015

AJRCCM, 2015

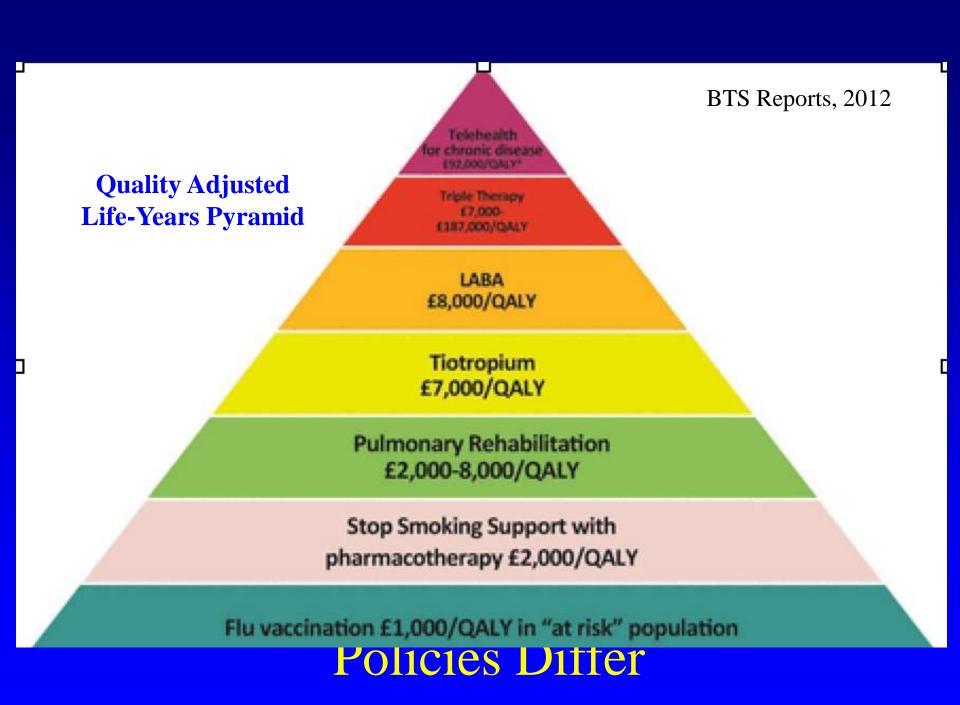
Conclusions: "The ATS and ERS commit to undertake actions that will improve access to and delivery of PR services for suitable patients. They call on their members and other health professional societies, payers, patients, and patient advocacy groups to join in this commitment."



- Bronchodilators
- Supplemental Oxygen
- Pulmonary Rehabilitation

Similar Guidelines Approval

All Considered Standard of Care

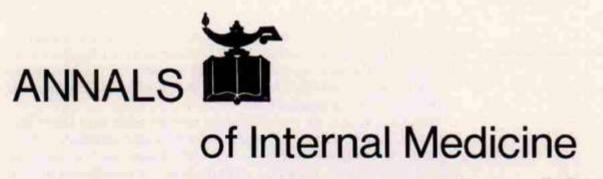


Bronchodilators have

• Bronchodilators have marketing

- Bronchodilators have marketing
- Supplemental oxygen

- Bronchodilators have marketing
- Supplemental oxygen *improves* survival





Dr. Thomas L. Petty

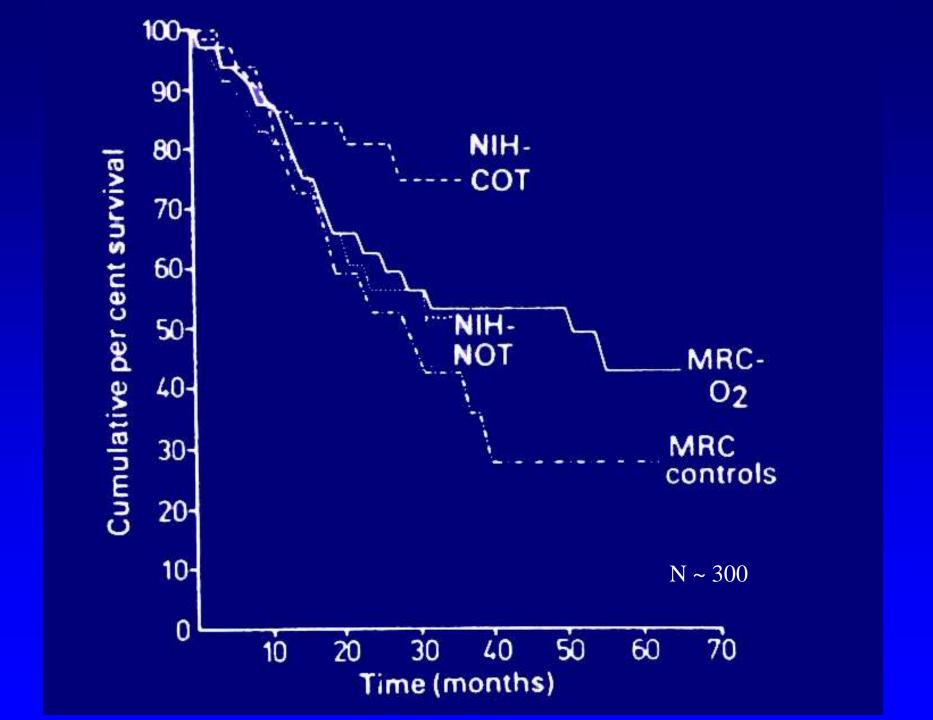
SEPTEMBER 1980 · VOLUME 93 · NUMBER 3

Published Monthly by the American College of Physicians

Continuous or Nocturnal Oxygen Therapy in Hypoxemic Chronic Obstructive

Lung Disease

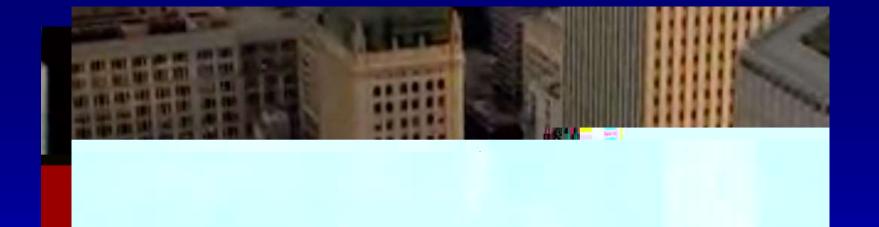
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What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

- Bronchodilators have marketing
- Supplemental oxygen *improves* survival

Therapies that improve survival have a high priority...for patients, their physicians and for health care systems



The Powerful
Attraction of LifeExtending
Therapies

What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

- Bronchodilators have marketing
- Supplemental oxygen *improves* survival

Rehabilitation will never have marketing Does it improve survival?

State of the Art

Pulmonary Rehabilitation in Chronic Obstructive Pulmonary Disease

Thierry Troosters, Richard Casaburi, Rik Gosselink, and Marc Decramer

Respiratory Rehabilitation and Respiratory Division, University Hospital; Department of Rehabilitation Sciences, Faculty of Physical Education and Physiotherapy, Katholieke Universiteit Leuven; and Respiratory Rehabilitation, Universitaire Ziekenhuizen Gasthuisberg, Leuven, Belgium; and Rehabilitation Clinical Trials Center, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California

So far no study has convincingly shown evidence of improved survival after pulmonary rehabilitation...Because patients who enroll in pulmonary rehabilitation are generally in a relatively stable state, their likelihood of dying in the short term is rather low. Hence the absolute reduction in mortality is likely to be relatively modest. Studies investigating patients with higher mortality risk (e.g., after discharge from the hospital for an acute exacerbation) may be more successful in finding effects on survival."



Cochrane Database of Systematic Reviews

2016

Pulmonary rehabilitation following exacerbations of chronic obstructive pulmonary disease (Review)

Puhan MA, Gimeno-Santos E, Cates CJ, Troosters T

Figure 3. Forest plot of comparison: I Rehabilitation versus control, outcome: I.I Hospital readmission (to end of follow-up).

	Pulmonary rehab		Control		Odds Ratio		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% CI	M-H, Random, 95% CI
Behnke 2000	3	14	9	12	8.8%	0.09 [0.01, 0.56]	
Eaton 2009	11	47	15	50	14.8%	0.71 [0.29, 1.77]	-
Greening 2014	108	169	84	151	17.8%	1.41 [0.90, 2.21]	 -
Ko 2011	16	30	13	30	14.0%	1.49 [0.54, 4.14]	
Ko 2016	44	90	63	90	16.8%	0.41 [0.22, 0.76]	
Man 2004	2	20	12	21	9.5%	0.08 [0.02, 0.45]	
Murphy 2005	2	13	5	13	8.5%	0.29 [0.04, 1.90]	
Seymour 2010	2	30	10	30	9.9%	0.14 [0.03, 0.72]	
Total (95% CI)		413		397	100.0%	0.44 [0.21, 0.91]	•
Total events	188		211				
Heterogeneity: Tau2:	0.74; Chi ² = 3	29.80, df	= 7 (P =	0.0001); P= 779	6	0.002 0.1 1 10 500
Test for overall effect				and Art A	***************************************		0.002 0.1 1 10 500 Favours rehabilitation Favours control

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The Dream

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Pulmonary Rehabilitation Improves Survival in COPD

The Pulmonary Rehabilitation Investigator Group

Hypothesis: A convincing demonstration that pulmonary rehabilitation improves survival would yield a reformulation of health policy, resulting in improved access and uptake of this therapy.



The Long and Winding Road
To a Rehabilitation Survival Trial

COPD Town Hall Meeting Hosted by NHLBI

Improving Access to Pulmonary Rehabilitation Cited as a Major Priority

NHLBI Approaches Rehabilitation Community for Suggestions for Research to Address this Priority

Pulmonary Rehabilitation After Hospitalization for COPD: The PROPEL Study





28 Investigators
Recruited
9 Committees Formed



-preliminary design features-

- Recruit ~2000 patients during a hospitalization for a COPD exacerbation
- Randomize within 2-4 weeks after discharge to rehabilitation vs. usual care at ~30 <u>US sites</u>
- Follow for ~2 years with re-hospitalization or mortality and primary outcome
- Assess other mediators and modulators of primary outcome prominently including physical activity in everyday life and frailty
- Determine cost-effectiveness

-preliminary design features-

Components of the Next-Generation Pulmonary Rehabilitation

- Physiologically Based Exercise Training
- Activity Promotion
- Behavior Modification
- Maintenance Program

-preliminary design features-

Components of the Next-Generation Pulmonary Rehabilitation

- Physiologically Based Exercise Training
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- Behavior Modification
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BMJ Open Behaviour-change intervention in a multicentre, randomised, placebo-controlled COPD study: methodological considerations and implementation

Jean Bourbeau, ¹ Kim L Lavoie, ^{2,3} Maria Sedeno, ¹ Dorothy De Sousa, ⁴ Damijan Erzen, ⁵ Alan Hamilton, ⁴ François Maltais, ⁶ Thierry Troosters, ⁷

Nancy Leidy⁸

Aim: Modify patient behaviors, enhance adherence to healthenhancing patient behaviors and increase activity level in everyday life

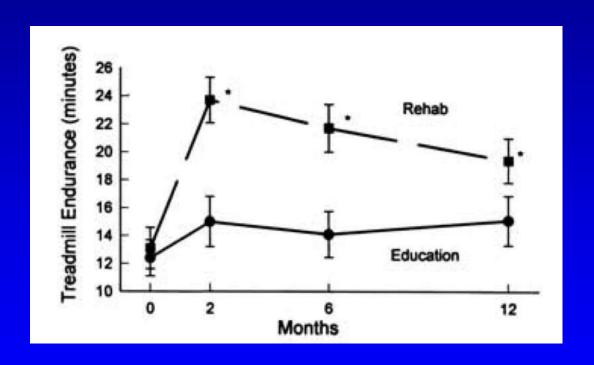
-preliminary design features-

Components of the Next-Generation Pulmonary Rehabilitation

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Effects of Pulmonary Rehabilitation on Physiologic and Psychosocial Outcomes in Patients with Chronic Obstructive Pulmonary Disease

Andrew L. Ries, MD, MPH; Robert M. Kaplan, PhD; Trina M. Limberg, BS; and Lela M. Prewitt





Ann Int Med, 1995

Pulmonary Rehabilitation After Hospitalization for COPD: The PROPEL Study



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Barry Make, MD • National Jewish Health

Richard Casaburi, MD, PhD • Los Angeles Biomed Research Inst

Jerry Krishnan, MD, PhD • University of Illinois at Chicago

Stephen Wisniewski, PhD • DCC, University of Pittsburgh

Maria Brooks, PhD • DCC, University of Pittsburgh

Frank Sciurba, MD • DCC, University of Pittsburgh

Third submission to NHLBI February, 2018

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Rehabilitation Clinical Trials Center