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
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
Pulmonary Rehabilitation for Management of Chronic Obstructive Pulmonary Disease

Richard Casaburi, Ph.D., M.D., and Richard ZuWallack, M.D.
An Official American Thoracic Society/European Respiratory Society Statement: Key Concepts and Advances in 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.
Targets for Improving Exercise Tolerance

- Central desensitization to dyspnea
- Decreased anxiety and depression
- Reduction in dynamic hyperinflation
- Improved skeletal-muscle function

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

Central desensitization to dyspnea
Decreased anxiety and depression
Reduction in dynamic hyperinflation
Improved skeletal-muscle function

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

486 Citations!

1997 Am J Respir Crit Care Med
Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease
A Statement of the American Thoracic Society and European Respiratory Society


François Maltais, Marc Decramer, Richard Casaburi, Esther Barreiro, Yan Burelle, Richard Debigré, 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 ATS Directors, November 2013, and by the ERS Executive Committee, September 2013
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
“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
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
**Comparison of Benefits**

<table>
<thead>
<tr>
<th>Bronchodilator</th>
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- ↑ indicates a slight increase.
- ↑↑ indicates a moderate increase.
- ↑↑↑ indicates a significant increase.
- ↑↑↑↑ indicates a substantial increase.
### Comparison of Benefits

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<td>↑</td>
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Magnitude of Benefit
Bronchodilator vs. Rehabilitation

Data from literature meta-analyses
Red line = MCID
Bronchodilator = LABA or LAMA
## Comparison of Benefits

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<td>↑</td>
<td>↑↑↑↑↑</td>
<td>↑↑↑↑↑</td>
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<tr>
<td>Duration of Benefit after Withdrawal</td>
<td>Hours-Days</td>
<td>Minutes</td>
<td>Months-Years</td>
</tr>
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Three Major COPD Therapies
-Comparing Availability-

- Bronchodilators
- Supplemental Oxygen
- Pulmonary Rehabilitation
Three Major COPD Therapies
-Comparing Availability-

• Bronchodilators
  – Near universal use in diagnosed disease
Three Major COPD Therapies - Comparing Availability -

• Supplemental Oxygen
  – Near universal availability to qualifying patients
  – Over ~$3 billion spent annually for ~1 million patients
Three Major COPD Therapies
- Comparing Availability-

- Pulmonary Rehabilitation
  - Available to roughly 1.2% of COPD patients who would benefit
"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.
• 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
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.”
Three Major COPD Therapies - Comparing Availability -

• Bronchodilators
• Supplemental Oxygen
• Pulmonary Rehabilitation

Similar Guidelines Approval

All Considered Standard of Care
Three Major COPD Therapies
- Bronchodilators
- Supplemental Oxygen
- Pulmonary Rehabilitation

Annual Costs Roughly Similar Though Third Party Payment Policies Differ

BTS Reports, 2012

Quality Adjusted Life-Years Pyramid

Telehealth for chronic disease £92,000/QALY

Triple Therapy £7,000-£187,000/QALY

LABA £8,000/QALY

Tiotropium £7,000/QALY

Pulmonary Rehabilitation £2,000-8,000/QALY

Stop Smoking Support with pharmacotherapy £2,000/QALY

Flu vaccination £1,000/QALY in “at risk” population

Policies Differ
What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

• Bronchodilators have
What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

- Bronchodilators have *marketing*
What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

- Bronchodilators have *marketing*
- Supplemental oxygen
What do bronchodilators and supplemental oxygen have that rehabilitation lacks?

• Bronchodilators have *marketing*
• Supplemental oxygen *improves survival*
Continuous or Nocturnal Oxygen Therapy in Hypoxemic Chronic Obstructive Lung Disease
N ~ 300
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 Life-Extending 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?
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.”
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: 1 Rehabilitation versus control, outcome: 1.1 Hospital readmission (to end of follow-up).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Pulmonary rehab</th>
<th>Control</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Behnke 2000</td>
<td>3</td>
<td>14</td>
<td>9</td>
<td>12</td>
<td>0.09 [0.01, 0.56]</td>
</tr>
<tr>
<td>Eaton 2009</td>
<td>11</td>
<td>47</td>
<td>15</td>
<td>50</td>
<td>0.71 [0.29, 1.77]</td>
</tr>
<tr>
<td>Greening 2014</td>
<td>108</td>
<td>169</td>
<td>84</td>
<td>151</td>
<td>1.41 [0.90, 2.21]</td>
</tr>
<tr>
<td>Ko 2011</td>
<td>16</td>
<td>30</td>
<td>13</td>
<td>30</td>
<td>1.49 [0.54, 4.14]</td>
</tr>
<tr>
<td>Ko 2016</td>
<td>44</td>
<td>90</td>
<td>63</td>
<td>90</td>
<td>0.41 [0.22, 0.76]</td>
</tr>
<tr>
<td>Man 2004</td>
<td>2</td>
<td>20</td>
<td>12</td>
<td>21</td>
<td>0.08 [0.02, 0.45]</td>
</tr>
<tr>
<td>Murphy 2005</td>
<td>2</td>
<td>13</td>
<td>5</td>
<td>13</td>
<td>0.29 [0.04, 1.90]</td>
</tr>
<tr>
<td>Seymour 2010</td>
<td>2</td>
<td>30</td>
<td>10</td>
<td>30</td>
<td>0.14 [0.03, 0.72]</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>413</td>
<td>397</td>
<td>100%</td>
<td>0.44 [0.21, 0.91]</td>
<td></td>
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<tr>
<td>Total events</td>
<td>188</td>
<td>211</td>
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</table>

Heterogeneity: Tau² = 0.74; Chi² = 29.80, df = 7 (P = 0.0001); I² = 77%
Test for overall effect: Z = 2.20 (P = 0.03)
Pulmonary Rehabilitation
- outline -

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• Where we’ve failed
  – Poor availability for patients who would benefit

• And a path forward
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

National Institutes of Health on February 29 - March 1

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
The PROPEL Study -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 US sites
• 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
The PROPEL Study
-preliminary design features-

Components of the Next-Generation Pulmonary Rehabilitation

• Physiologically Based Exercise Training
• Activity Promotion
• Behavior Modification
• Maintenance Program
The PROPEL Study
-preliminary design features-

Components of the Next-Generation Pulmonary Rehabilitation

- Physiologically Based Exercise Training
- Activity Promotion
- Behavior Modification
- Maintenance Program
Aim: Modify patient behaviors, enhance adherence to health-enhancing patient behaviors and increase activity level in everyday life
The PROPEL Study
-preliminary design features-
Components of the Next-Generation Pulmonary Rehabilitation

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

Wish Us Luck!

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