Appendix A: General Methodological Principles of Study Design

When making national coverage determinations, CMS evaluates relevant clinical evidence to determine whether or not the evidence is of sufficient quality to support a finding that an item or service falling within a benefit category is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member. The critical appraisal of the evidence enables us to determine whether: 1) the specific assessment questions can be answered conclusively; and 2) the intervention will improve health outcomes for patients. An improved health outcome is one of several considerations in determining whether an item or service is reasonable and necessary.

CMS divides the assessment of clinical evidence into three stages: 1) the quality of the individual studies; 2) the relevance of findings from individual studies to the Medicare population; and 3) overarching conclusions that can be drawn from the body of the evidence on the direction and magnitude of the intervention's risks and benefits.

The issues presented here represent a broad discussion of the issues we consider when reviewing clinical evidence. However, it should be noted that each coverage determination has unique methodological aspects.

1. Assessing Individual Studies

Methodologists have developed criteria to determine weaknesses and strengths of clinical research. Strength of evidence generally refers to: 1) the scientific validity underlying study findings regarding causal relationships between health care interventions and health outcomes; and 2) the reduction of bias. In general, some of the methodological attributes associated with stronger evidence include those listed below:

- Use of randomization (allocation of patients to either intervention or control group) in order to minimize bias.
- Use of contemporaneous control groups (rather than historical controls) in order to ensure comparability between the intervention and control groups.
- Prospective (rather than retrospective) studies to ensure a more thorough and systematical assessment of factors related to outcomes.
- Larger sample sizes in studies to help ensure adequate numbers of patients are enrolled to demonstrate both statistically significant as well as clinically significant outcomes that can be extrapolated to the Medicare population. Sample size should be large enough to make chance an unlikely explanation for what was found.
- Masking (blinding) to ensure patients and investigators do not know to which group patients were assigned (intervention or control). This is important especially in subjective outcomes, such as pain or quality of life, where enthusiasm and psychological factors may lead to an improved perceived outcome by either the patient or assessor.

Regardless of whether the design of a study is a randomized controlled trial, a non-randomized controlled trial, a cohort study or a case-control study, the primary criterion for methodological strength or quality is the extent to which differences between intervention and control groups can

be attributed to the intervention studied. This is known as internal validity. Various types of bias can undermine internal validity. These include:

- Different characteristics between patients participating and those theoretically eligible for study but not participating (selection bias)
- Co-interventions or provision of care apart from the intervention under evaluation (confounding)
- Differential assessment of outcome (detection bias)
- Occurrence and reporting of patients who do not complete the study (attrition bias)

In principle, rankings of research design have been based on the ability of each study design category to minimize these biases. A randomized controlled trial minimizes systematic bias (in theory) by selecting a sample of participants from a particular population and allocating them randomly to the intervention and control groups. Thus, randomized controlled studies have been typically assigned the greatest strength, followed by non-randomized clinical trials and controlled observational studies. The following is a representative list of study designs (some of which have alternative names) ranked from most to least methodologically rigorous in their potential ability to minimize systematic bias:

- Randomized controlled trials
- Non-randomized controlled trials
- Prospective cohort studies
- Retrospective case control studies
- Cross-sectional studies
- Surveillance studies (e.g., using registries or surveys)
- Consecutive case series
- Single case reports

When there are merely associations but not causal relationships between a study's variables and outcomes, it is important not to draw causal inferences. Confounding refers to independent variables that systematically vary with the causal variable. This distorts measurement of the outcome of interest because its effect size is mixed with the effects of other extraneous factors. For observational, and in some cases randomized controlled trials, the method in which confounding factors are handled (either through stratification or appropriate statistical modeling) are of particular concern. For example, in order to interpret and generalize conclusions to our population of Medicare patients, it may be necessary for studies to match or stratify their intervention and control groups by patient age or co-morbidities.

Methodological strength is, therefore, a multidimensional concept that relates to the design, implementation and analysis of a clinical study. In addition, thorough documentation of the conduct of the research, particularly study's selection criteria, rate of attrition and process for data collection, is essential for CMS to adequately assess the evidence.

2. Generalizability of Clinical Evidence to the Medicare Population

The applicability of the results of a study to other populations, settings, treatment regimens, and outcomes assessed is known as external validity. Even well-designed and well-conducted trials may not supply the evidence needed if the results of a study are not applicable to the Medicare population. Evidence that provides accurate information about a population or setting not well represented in the Medicare program would be considered but would suffer from limited generalizability.

The extent to which the results of a trial are applicable to other circumstances is often a matter of judgment that depends on specific study characteristics, primarily the patient population studied (age, sex, severity of disease, and presence of co-morbidities) and the care setting (primary to tertiary level of care, as well as the experience and specialization of the care provider). Additional relevant variables are treatment regimens (dosage, timing, and route of administration), co-interventions or concomitant therapies, and type of outcome and length of follow-up.

The level of care and the experience of the providers in the study are other crucial elements in assessing a study's external validity. Trial participants in an academic medical center may receive more or different attention than is typically available in non-tertiary settings. For example, an investigator's lengthy and detailed explanations of the potential benefits of the intervention and/or the use of new equipment provided to the academic center by the study sponsor may raise doubts about the applicability of study findings to community practice.

Given the evidence available in the research literature, some degree of generalization about an intervention's potential benefits and harms is invariably required in making coverage decisions for the Medicare population. Conditions that assist us in making reasonable generalizations are biologic plausibility, similarities between the populations studied and Medicare patients (age, sex, ethnicity and clinical presentation), and similarities of the intervention studied to those that would be routinely available in community practice.

A study's selected outcomes are an important consideration in generalizing available clinical evidence to Medicare coverage determinations because one of the goals of our determination process is to assess health outcomes. We are interested in the results of changed patient management not just altered management. These outcomes include resultant risks and benefits such as increased or decreased morbidity and mortality. In order to make this determination, it is often necessary to evaluate whether the strength of the evidence is adequate to draw conclusions about the direction and magnitude of each individual outcome relevant to the intervention under study. In addition, it is important that an intervention's benefits are clinically significant and durable, rather than marginal or short-lived.

If key health outcomes have not been studied or the direction of clinical effect is inconclusive, we may also evaluate the strength and adequacy of indirect evidence linking intermediate or surrogate outcomes to our outcomes of interest.

3. Assessing the Relative Magnitude of Risks and Benefits

Generally, an intervention is not reasonable and necessary if its risks outweigh its benefits. Health outcomes are one of several considerations in determining whether an item or service is reasonable and necessary. For most determinations, CMS evaluates whether reported benefits translate into improved health outcomes. CMS places greater emphasis on health outcomes actually experienced by patients, such as quality of life, functional status, duration of disability, morbidity and mortality, and less emphasis on outcomes that patients do not directly experience, such as intermediate outcomes, surrogate outcomes, and laboratory or radiographic responses. The direction, magnitude, and consistency of the risks and benefits across studies are also important considerations. Based on the analysis of the strength of the evidence, CMS assesses the relative magnitude of an intervention or technology's benefits and risk of harm to Medicare beneficiaries.

Author, Year and Title	Study Design	Demographics	Interventions (I) and Outcome Measures (O)	Results	Conclusions
				Intervention Group v Control Group	
					There is evidence favoring the efficacy of exercise-based PR among patients who are recovering from, or recently recovered from acute exacerbations of COPD. Exercise-based PR improves patients' quality of life, maximal and functional exercise capacity beyond what would be expected by chance. Mortality and hospital re-admissions appear to decrease with exercise-PR based interventions after acute COPD exacerbations Re:Safety of exercise-based pulmonary rehabilitation versus conventional care - Data on safety were very sparsely reported. This paucity of data should not be viewed as evidence of absence of adverse events

				Question 2: Assessment of specific components in exercise-based pulmonary rehabilitation interventions **Q2.1 Incremental efficacy and safety of exercise training** a. Exercise training +non-exercise PR component(s) versus the same non-exercise PR component(s) e.g., education, education + psychological intervention (stress management), and IMT training i. Dyspnea and disease-specific quality of life – Temporary improvement in QoL for less severe dyspnea. ii. Functional exercise capacity – Equivocal results in favor of exercise + IMT iii. Maximal exercise capacity –No significant difference iv. All cause mortality – Numbers too small. v. Safety – No data **Q2.2 Efficacy and safety of exercise training compared with other non-exercise PR component** a. Exercise training versus non-exercise PR component(s) i. Exercise training versus inspiratory muscle training.-No differences between arms. ii. Exercise training versus education. -No differences between arms iii. Exercise training versus breathing exercises- no difference re: dyspnea, questionable difference favoring PR for 12M timed walk iv. exercise training versus phone follow-up- Unclear data **Q2.3 Incremental efficacy and safety of non-exercise pulmonary rehabilitation components** COPD patients – Overall No significant differences for Qol, FEC, MEC a b. Patients with bronchiectasis – 1 RCT (Newall) - Generalizability to the Medicare population was good – no clinical significance some questionable improvement in group with IMT + exercise **Q2.4 Efficacy and safety of different modes of exercise training** Higher versus lower intensity training - No Data a b. Endurance versus strength training - Generalizable to the Medicare-pop – no significant differences testing for QoL and FEC, and NEC. c. continuous versus interval training – Outcome exercise training of ambulatory muscles. QoL tested non-significant	**Q2 Re: Relative value of different exercise training protocols and of different pulmonary rehabilitation component-**Did not assess the effects on non-exercise components versus no intervention – There is no formally significant difference between exercise protocols that are tailored to address each patient's specific weaknesses and exercise protocols that are common for all patient. Strength training was not consistently associated beyond chance with more favorable outcomes compared to endurance training. Compared with education alone, exercise and education confer additional benefits in health-related quality of life (total CRDQ) and functional exercise capacity in subjects with moderate functional limitation resulting from dyspnea. The authors did not find statistically significant differences when they assessed combined exercise training and non-exercise components (i.e., IMT, activity training and lecture series) versus exercise training alone

Bjornshave B, Korsgaard J. Comparison of two different levels of physical training in patients with moderate to sever COPD. Lung 2005 183:101-108	RCT-Setting Home	20 patients out of 124 with COPD who were selected and who accepted. 9 in 1 group and 11 in other. Aged 40-70 years –	I= low-frequency v middle-frequency exercise over 4 weeks. O= % increase in walk time on standardized treadmill test	Middle-frequency 55% improvements vs <20% in low-frequency.	Authors conclude middle-frequency is better. Low sample size and poor design
Boxall A, et al. A randomized controlled trial of home-based pulmonary rehabilitation for elderly housebound patients. Jrnl Cardiopulm Rehab 2005;25:378-385	RCT-Setting Home	23 patients in each of two groups completed – drop out due to death and illness. Age ≥60 years M=F in intervention, M:F 2:1 in control. –	I=individually tailored supervised walking and arm-exercise program plus patient education, v none. O= 6MWT, St. Georges Respiratory questionnaire and the Borg subjective breathlesness score	Statistically significant results were an improvement in the Borg score, the St. Georges score, and the 6MWT of the intervention group as compared to the control group. 6 months the intervention group demonstrated a shorter hospital length of stay (LOS) on readmission with exacerbation	The authors concluded that a 12 week home-based PR program is effective in improving exercise intolerance, subjective breathlessness, and QoL for housebound elderly COPD patients. Control and treatment groups were not wee-matched on sex and other variables, and severity of illness and co-morbidities not taken into account.

Carrier-Kohlman versus et al. Impact of brief or extended exercise training on the benefit of a dyspnea self-management program in COPD. Jrnl Cardiopulmon rehabil 2005;25:275-284	Setting Hospital: RCT-3 arms	103 patients (average age 66, F:M ratio=57:46)	Interventions: dyspnea self-management only (DM=individualized education and demonstration of dyspnea self-management strategies and bi-weekly nurse telephone calls), DM plus four supervised exercise sessions (DME) or DM plus 24 supervised exercise sessions (DMT) Outcomes were measured every 2 months for 1 year and consisted of dyspnea degree (Borg test) during incremental treadmill testing and on exercise performance on incremental and endurance treadmill tests at 6 and 12 months.	Dyspnea on ADL and self-reported physical functioning (CRQ, SF-36) improved for all groups with DMT better than DME or DM as time went on. This was attributed by the authors to continuing supervised exercise sessions. DME and DMT were not significantly different from DM or each other at the end of one year. The authors were missing data in 24 of 103 patients and an additional 12 patients dropped out before the first two-month period	The authors concluded that the greater the number of supervised exercise training sessions, the more improved ADLs and physical functioning would be for patients with COPD.

Coultas D, Frederick M, et al., A randomized trial of two types of nurse-assisted home care for patients with COPD. Chest 2005; 128:2017-2024.	RCT – Setting Home Care	The 3 arms were medical management (MM), nurse-assisted collaborative care (CM) and usual care (UC) with 51, 49, and 51 patients completing the study respectively. Patients all had ≥20 pack-year history and were ≥ 45 years of age- Setting Home	I= patient education, enhanced follow-up, and enhanced patient self-management skills over a 6-month period O= SF-36 and disease-specific (SGRQ) questionnaires	No significant differences when comparing the results of the various interventions three arms	interventions in patient education, enhanced follow-up, and enhanced patient self-management skills in patients with COPD do not result in clinically meaningful improvements in health-care status and self-reported health care utilization
De Blok et al., The effects of a lifestyle physical activity counseling program and feedback with a pedometer during PR in patients with COPD: A pilot study. Pt Educ and Counseling 2006: 61;48-55	RCT-Setting Output	N=21 (10 in intervention, 11). Age range 40-85 years. M:F not given. –t	I=counseling plus PR vs PR only. O=primary-Daily physical activity measured by pedometers. Secondary-HRQL, ADL depression, self-efficacy.	Intervention group increased 1430 steps/day(69% increase) vs 455 steps/day (19%) in control (PR only) group, not statistically significant. No differences in secondary outcomes.	Authors concluded that pedometer was feasible in combination with exercise counseling as an addition to PR program. Study showed small sample size and other design defects. Considered poor.

De Godoy DV et al. A randomized controlled trial of the effect of psychotherapy on anxiety and depression in COPD. Arch Phys Med Rehabil 2003;84:1154-1157	RCT-Setting Outpatient	The patients averaged 60+ years of age and demographic differences between groups were not significant, apparently due to the small sample size (TG 14, CG 16) –	I= Psychotherapy +PR in TG, CG = PR) O= measured at inception and 12 weeks of therapy Beck Anxiety Inventory (BAI) and the Beck Depression Inventory (BDI) and 6MWD	Both groups showed statistically significant improvement on the 6MWD, while only the TG had significant reduction in anxiety ($p<.001$) and depression ($p<0.02$) levels	The authors concluded that including psychotherapy in a PR program for patients with COPD reduced anxiety and depression levels but did not impact 6MWD performance. The potential confounders in this study were not able to be adjusted for, due to the small sample size.
Green RH et al. A randomized control trial of four weeks versus seven weeks of pulmonary rehabilitation in COPD. Thorax (2001);56:143-145	Setting: outpatient	Forgy four persons with COPD, 28 men and 16 women, average age 68	I= PR for 4 weeks versus 7 weeks. O= The subjects were measured before and after intervention on the CRQ (the primary outcome variable), the Breathing Problem Questionnaire (BPQ), the shuttle walking test (SWT) and the treadmill endurance test (TET).	Clinical and statistical significance was reached for the total CRQ score in favor of the 7-week group ($p<0.05$) and its domains for dyspnea ($p<0.05$), emotion ($P<0.005$) and mastery ($P<0.05$).	The authors concluded that a seven-week PR program provides greater benefits than a 4 week PR program in terms of health status.

Guell R, et al. The impact of PR on psychosocial morbidity in patients with severe COPD. Chest 2006;129,4:899-904.	RCT-Setting Outpatient	N=35 (not including 5 dropouts) 18 in PR group 17 in control group. (All male but they report 2 females in the study. Avg age 66-68. No significant demographic characteristics between groups –	I=4 months of intense PR program both arms were treated with salbutamol, ipatropium bromide, and inhaled budesonide (before admission to the trial), and one arm additional al intensive PR for 4 months (relaxation, various breathing exercises, chest abdominal wall exercise) O= Outcome measures were psychological assessment using the MHBI (Million Behavioral Health Inventory) , the Revised Symptom Checklist (SCL-90-R), the 6MWT, and the CRQ for HRQL.	In the results there were 2 females listed in the control group, none in the PR group. At 4 months the PR group showed statistically significant improvements relative to the control group, on the MBHI, in selected scales of personality (forceful, sensitive, introversive and chronic tension) and not others. At 4 months the PR group showed statistically significant improvements relative to the control group, on the SCL-90-R, in selected scales of somatization, depression, anxiety, hostility, total score and others, as well as in HQRL as measured by the CRQ. Domains of dyspnea and mastery. Finally, the PR group showed a statistically significant improvement in the 6MWT showing an increase of 63 meters as compared to 22 meters decrease in the control group	The authors concluded that PR may decrease psychosocial morbidity in COPD patients even when no specific psychological intervention is performed.. They also reiterated that PR has a positive impact on functional exercise capacity and HRQL. This study had small groups and measures many outcomes for each test, significance testing was questionable and there was no adjustment for the myriad significance tests.

LaCasse Y, Goldstein R, Lasserson TJ, Martin S. Pumonary rehabilitation for chronic obstructive pulmonary disease. Cochran Collaboration. John Wiley & Sons, Ltd. 2006	Metanalysis 31RCTs	*QoL*-13 RCT- Demographics not stated *MEC*-18 RCT 334 participants active PR-296 controls *FEC* 22RCT- 458 active PR with 432 controls Avg age-sex-etc not stated.-	1. I=PR 2. O= QoL 3. O= FEC 4. O= MEC	1. QoL-Statistical and Clinical significant improvement 2. FEC –not significant 3. MEC -- uncertain	Strong support for PR exercise training ≥ 4 wks for COPD and QoL(dyspnea, fatigue, emotional function and mastery). Indications of improvement in FEC
Miller JD et al (2005). A randomized clinical trial of LVRS versus best medical care for patients with advanced emphysema: a two-year study from Canada. Ann. Thoracic Surg 2006;81:314-21	RCT – Setting hospital	N=62 (30 and 32) . Mean age 63-64, M:F approx 2:1, smoker-years higher in LVRS arm, 6MWT not significant diff.	I=LVRS vs MT O= Mortality and pulmonary function, along with QoL	This RCT compared LVRS with optimal medical therapy, in sever emphysema. The trial included additional pulmonary rehab over standard in the control group. The trial did not permit crossover of the 62 patients in both arms. Mortality and pulmonary function wire compared at the end. Mortality was no different in both groups but pulmonary function had improved more in the LVRS arm.	The authors conclusion: LVRS was better re: improving pulmonary function, exercise activity and QoL in selected persons with advanced emphysema

Ries AL et al. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with COPD. Ann Intern Med. 1995 Jun 1;122(11):823-32	Setting: outpatient - RCT	352 patients with COPD were screened and 119 met the inclusion criteria and remained in the study (15 women and 42 men in the TG and 17 women and 45 men in the CG). The average age for the TG was 61 years and for the CG it was 63yrs.	*Intervention:* PR versus brief advice or education 8 weeks. Followed over an 18 month period All were on medical treatment. O=pulmonary function, maximum exercise tolerance (MET), endurance exercise and rest and exercise gas exchange. Psychosocial measures consisted of a self-efficacy questionnaire, a quality of well-being scale, the Centers for Epidemiologic Studies Depression Scale (CES-D) and the University of California SD shortness of breath (SOB) questionnaire	Results demonstrated that the 8 week PR program produced significantly greater improvement in exercise endurance, MET, symptoms of perceived breathlessness, reported SOB, and self-efficacy for walking (all $p<0.05$). These benefits persisted for between 6 and 24 months after the intervention. There were no significant differences between groups in pulmonary function, depression or general QoL.	The authors concluded that there were definite benefits of pulmonary rehabilitation with COPD in the areas of exercise endurance, MET, symptoms of perceived breathlessness, reported SOB, and self-efficacy for walking in a comprehensive PR program as compared to education only.

Sassi-Dambron DE et al. A controlled clinical trial of dyspnea management strategies. Chest 1995;107:724-729	RCT – Setting Outpatient	N=98 with 18 dropouts= 80 patients. M:F approx 5:4 No significant demographic differences	I=Shortness of breath education for 6 weeks versus or health education on topics not directly related to lung disease (CG) O=Outcome measures consisted of dyspnea measures and exercise tolerance (6MWD).	At 6 weeks there was no significant difference between the TG and the CG on any outcome measure.	The authors concluded that Dyspnea management without structured exercise training or other PR program components does not improve exercise tolerance, dyspnea, HQRL, anxiety or depression.

Steiner MC et al. Nutritional enhancement of exercise performance in COPD: a randomised control trial. Thorax 2003;58:745-751.	RCT Setting Outpatient	There was no statistically significant difference between groups on demographics at baseline with average age of 66-68 years and M:F ratio approximately 3.5:5 in both groups	I= **I**n this study 85 persons with COPD were randomized to receive a carbohydrate supplement or non-nutritive placebo daily during a 7-week outpatient PR program (endurance, low impact conditioning, education O= Peak and submaximal exercise performance as well as walk tests, health status, body composition, muscle strength and macronutrient intake were measured	The results showed that both groups increased walking and health status significantly, The placebo group lost weight while the treatment group gained weight	The authors concluded that exercise training results in negative energy balance that can be overcome by nutritional supplementation

TA: Pulmonary Rehabilitation for COPD and other lung diseases. Agency for Healthcare Research and Quality-HHS 2006	Systematic Review Metanalyses and RCTs	Avg age ≥59yrs males approx 71%	1. I=PR 2. O= QoL 3. O= FEC 4. O= MEC 5. O=Mortality 6. O=# exacerbations	**Q1-Efficacy and safety of exercise-based pulmonary rehabilitation** **a) COPD Stable** **1. Qol-clinically meaningful improvement for PR in CRDQ dyspnea, fatigue and mastery of breath domain** **2. FEC- The improvement is not greater than the minimal clinically significant difference in the 6MWT** **3. MEC a statistically significant increase in the maximum achieved workload was observed in favor of the PR arm** **4. no overall effect of exercise-based PR on mortality (odds ratio 1.03, 95% confidence interval: 0.54, 1.89)** **5. acute exacerbations of COPD –equivocal 2RCT reduction, 1 RCT no change** **6. Reductions in hospitalizations, ER visits and LOS were assessed in 1RCT (Bourbeau). They were significantly reduced in the intervention arm** **After acute exacerbation of COPD:** **7. PR v Conventional care For dyspnea, FEC, and QoL there was a significant improvement in favor of the PR arm** **8. All cause mortality and hospitalizations non significant difference between arms** **Patients with non-COPD lung disorders:** **9. Stable** a. Asthma-No data b. Bronchiectasis-comprehensive PR arm had statistically significantly better improvement in the total SGRQ at treatment and followup end. c. FEC-better at training end no followup **d.** MEC-FEC-better at training end no follow**up** **10. Weaning from mechanical ventilation-**sparse good data **Q1.1 Long term effects of pulmonary rehabilitation –**CDRQ-statistically significant in favor of PR, FEC and MEC not significant **Q1.2 Relationship between pulmonary rehabilitation-associated harms and comorbid conditions –** little or no data **Q1.3 Patient level features that modify the effect of pulmonary rehabilitation –**No clear evidence **Q1.4 Comparison of pulmonary rehabilitation with general versus individually targeted exercise-**1 good RCT –No differences between arms **Q1.5 Comparison of pulmonary rehabilitation in different settings and of supervised versus unsupervised pulmonary rehabilitation-** 3 RCTs poor methodological quality – data not used **Q1.6 Efficacy of repeated pulmonary rehabilitation programs-** 1 RCT - **i**ntervention arm had PR at baseline, one year, and two years while subjects in the control arm had PR at baseline and second year. -No difference in dyspnea and QoL between arms. **Q1.7 Efficacy and safety of long term maintenance interventions for pulmonary rehabilitation effects-** 4 RCTs evaluated efforts to maintain the effects of PR after the end of the PR interventions- Dyspnea-worsened but equal in both arms. QoL better if COPD was mild to start with otherwise were similar.	Overall, There is little evidence available on the efficacy and safety of PR on diseases other than COPD. Almost all trials were small and potentially underpowered to detect small change. Q1-Re:Efficacy of exercise-based pulmonary rehabilitation versus conventional care- Especially in the short term, the improvements in three domains of the CRDQ instrument (namely dyspnea, fatigue and mastery) and in the 6MWT were significantly greater than the minimal clinically significant differences in these outcomes. There is no evidence that the benefits of PR are translated into survival differences, at least among people with stable COPD. This is not surprising, given that few RCT extended follow-up beyond 12 months, and deaths are just too sparse in the short term to detect a statistically significant difference. However, exercise-based PR interventions may reduce hospitalizations and primary care consultations.

White RJ et al. Pulmonary rehabilitation compared with brief advice given for severe COPD. Jrnl Cardiopulm Rehabil 2002;22:338-344	Setting: outpatient- RCT	103 pts with COPD. Avg age 67. M:F=2:1	*Intervention:* PR (walking/educ/step strengthening) versus brief advice or education – PR2x week at hosp vs 1 advice session with education.	At 3 months they were reassessed on their original tests leading to before-after comparison. The TG (N=54) 6-minute walking distance increased significantly ($p<0.001$) by 43 meters as compared to 23 meters in the brief advice group (N=49), but there was no difference in the two groups re: HRQL as measured by the CRQ.	The authors concluded that even a short PR program was beneficial in terms of improved exercise tolerance as compared to brief advice