Clinical routine rehabilitation of patients with chronic obstructive pulmonary disease at regional hospital

PhD dissertation

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Preface

The thesis is based on studies carried out during my employment at Horsens Regional Hospital and Centre for Public Health Central Denmark Region from September 2007 to April 2011.

I wish to thank the patients involved in the study, the hospital management and the pulmonary team at Horsens Regional Hospital. Specifically I wish to thank nurse Mette Elander Kristensen for coordinating the patient enrolment and for taking part in data collection and physician Tina Brandt Sørensen for supervising the management of COPD.

Thanks to my supervisors: Claus Vinther Nielsen and Jens Korsgaard, who have supported me from my very first pilot project on COPD rehabilitation at Silkeborg hospital in 2000, for their optimistic feedback and encouragement throughout in all phases in the project. I also want to thank Chris Jensen for rewarding discussions.

Thanks to datamanagement at the Centre of Public Health Jakob Hjort, Anne Marie Jensen and Elinborg Thorsteinsson and to biostatistician Niels Trolle Andersen; Aarhus University for advice and assistance with the data analyses. Thanks to Morten Pilegaard for his assistance and guidance in English.

I wish to thank my colleagues at Centre for Public Health Marselisborg Centret for creating a inspiring atmosphere and to my PhD student peers for discussions and for sharing experiences.

Finally, my most sincere thanks go to Egon Noe for his support and positive encouragement at all times.

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This PhD dissertation is based on the following three papers

I: Bjoernshave B, Korsgaard J, Vinther Nielsen C,
Title: Does pulmonary rehabilitation work in clinical practice?
A review on selection and dropout in randomized controlled trials on pulmonary rehabilitation.
Published in Clinical Epidemiology 2010:2 73-83

II: Bjoernshave B, Korsgaard J, Jensen C, Vinther Nielsen C
Title: Participation in Pulmonary Rehabilitation in routine clinical Practice
Accepted for future issue of Clinical Respiratory Journal January 2011

III: Bjoernshave B, Korsgaard J, Jensen C, Vinther Nielsen C
Title: Pulmonary rehabilitation in Clinical Routine
A follow-up study of completers, dropout and those with no rehabilitation offer
Submitted for Journal of Cardiopulmonary Rehabilitation and Prevention March 2011
**Outline of the Thesis**

**Chapter 1** summarizes the literature on rehabilitation of COPD patients, the effects and outcome measurements. To support the hypothesis raised the challenges in selecting participants for rehabilitation is addressed together with issues of completion and dropout.

**Chapter 2** describes methods and materials for the literature review in paper I as well as methods and materials used for the cohort study (paper II) and the follow-up study (paper III).

**Chapter 3** describes the results from the three papers.

**Chapter 4** focuses on methodological considerations: the study design, sampling, loss to follow-up, misclassification, validity of measurements and confounding.

**Chapter 5** discusses the study findings in relation to the hypothesis raised and the perspectives of the study.

The appendices contain the three papers and our previously published paper on rehabilitation besides the questionnaires used.
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<th>Description</th>
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<tr>
<td>COPD</td>
<td>Chronic Obstructive Pulmonary Disease</td>
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<tr>
<td>CRR</td>
<td>Clinical Routine Rehabilitation</td>
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<tr>
<td>RCT</td>
<td>Randomized Controlled Trials</td>
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<td>FEV1</td>
<td>Forced Expiratory Volume in First Second</td>
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<td>MRC</td>
<td>Medical Research Council dyspnea scale</td>
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<tr>
<td>6MWD</td>
<td>Six Minutes Walk Distance</td>
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<tr>
<td>QoL</td>
<td>Health related Quality of Life</td>
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<tr>
<td>SF36</td>
<td>Short Form 36 Health Related Quality of Life Questionnaire</td>
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<tr>
<td>MCS</td>
<td>Mental Component Summary Score SF36</td>
</tr>
<tr>
<td>PMC</td>
<td>Physical Component Summary Score SF36</td>
</tr>
<tr>
<td>ICF COPD</td>
<td>Questionnaire inspired of the International Classification of Functioning and Participation Core-Set for patients with chronic pulmonary disease</td>
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Chapter 1: Introduction
Since 2003, Horsens Regional Hospital in Denmark has been offering a rehabilitation program to patients suffering from the consequences of chronic obstructive pulmonary disease (COPD). The present study evaluate this clinical routine rehabilitation program, by characterizing a cohort of COPD patients treated at the hospital in order to identify predictors of rehabilitation completion. Furthermore outcomes and patients' subjective experience in relation to clinical routine rehabilitation are investigated in a follow-up study.

In Denmark, approximately 25% of 65-79-year-old citizens are diagnosed with COPD (1). With an increasing life expectancy, the number of people who will need treatment and rehabilitation is hence a serious challenge for the health care system now and in the future.

As a consequence, Danish COPD Disease Management Programs including rehabilitation have been developed following the guidelines of Global Initiative for Chronic Obstructive Lung Disease (GOLD) (2). As a multidisciplinary and comprehensive intervention, the effects of rehabilitation have been documented in a large number of randomized controlled trials (RCTs). A Cochrane review and international guidelines recommend rehabilitation as an important part of the care for COPD patients in order to improve their functional capacity, health related quality of life (QoL), and symptoms (3-5).

Horsens Regional Hospital has implemented a Disease Management Program in which the health care professionals emphasize a change of current practice and pioneer program development and implementation to ensure that treatment and rehabilitation of COPD patients be evidence-based (6).

Hospital management has requested an evaluation of the rehabilitation program to monitor its effect and evaluate its feasibility in clinical routine. This request initiated the present project, which has the overall purpose to form the basis for an optimal inclusion, completion and effect of clinical routine rehabilitation.
COPD rehabilitation: from best evidence to best practice

Definition of pulmonary rehabilitation
In 2006, the American Thoracic Society (ATS) and the European Respiratory Society (ERS) defined pulmonary rehabilitation as “an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic and often have decreased daily life activities. Integrated into the individualized treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease. Pulmonary rehabilitation programs involve patient assessment, exercise training, education, nutritional intervention and psychosocial support” (4).

In the following, the term rehabilitation will be used for the rehabilitation of COPD patients covered by this definition, while clinical routine rehabilitation (CRR) refers to rehabilitation program implemented in practice.

Before rehabilitation was known to be an essential part of the treatment of COPD, common knowledge was that since dyspnea was a major symptom, avoiding dyspnea constituted appropriate disease management. Patients were advised to avoid activities that led to dyspnea (7). Today rehabilitation is a part of an integrated care process defined by The World Health Organization as “a concept bringing together inputs, delivery, managements and organization of services related to diagnosis, treatment, care, rehabilitation and health promotion” (8). Rehabilitation includes self-management support, aiming to achieve a shift from management by the health care provider to management by the patients themselves (9). Integrated care of COPD is a major challenge for the health care systems and the professionals who must ensure that COPD patients achieve an interdisciplinary and coordinated effort across sectors that involves the patient’s resources and different needs at different times because the patient’s health status can improve, stabilize, or worsen over time (6).

COPD and criteria for diagnosing and selection participants for rehabilitation
Based on current knowledge, the GOLD guideline defines COPD as “a preventable and treatable disease with some significant extra pulmonary effects that may contribute to the severity in individual patients. Its pulmonary component is characterized by airflow limitation that is not fully reversible. The airflow limitation is usually progressive and is associated with an abnormal inflammatory response of the lungs to noxious particles or gases” (2).
COPD is diagnosed by spirometry which measures post-bronchodilator forced expiratory volume in one second (FEV1). Spirometry is used to classify COPD severity and COPD is divided into four stages according to severity of airflow limitation described in Table 1.

Table 1 The GOLD stages of COPD

| Spirometric Classification of COPD Severity Based on Post-Bronchodilator FEV1 |
|-----------------|-----------------|
| Stage I: Mild   | FEV1 ≥ 80% predicted |
| Stage II: Moderate | 50% ≤ FEV1 < 80% predicted |
| Stage III: Severe  | 30% ≤ FEV1 < 50% predicted |
| Stage IV: Very Severe | FEV1 < 30% predicted |

Global Initiative for Chronic Obstructive Lung Disease (GOLD) (2)

This classification forms the basis for the Disease Management Program in Denmark as the patients are stratified for treatment and rehabilitation according to their disease severity (6). The degree of airflow limitation and the symptoms reflect the disease severity, but the relationship between symptoms and the degree of airflow limitation is not clear. The spirometric classification is therefore a pragmatic approach that offers a general indication that may guide the initial approach to management (10).

COPD is often diagnosed late in its course because it is often ignored in early stages, maybe because the patients can avoid symptoms of dyspnea by gradually restricting their activity level. COPD patients are typically diagnosed when symptoms are undeniable, which is the case when more than half of the initial lung function has been lost, that is, typically in the patient’s mid-60s. (11). At this stage, secondary and tertiary prevention are in focus, e.g. modification of risk factor exposure, relevant pharmacological therapy, as well as prevention of complications and strategies minimizing e.g. cough, dyspnea, sleep disturbance, weight loss, and de-conditioning (10;12). At this stage, rehabilitation is therefore a core component in the integrated care for COPD patients with the aim of mitigating the consequences of COPD on the patient’s everyday life.

The population relevant for rehabilitation

Prevalence estimates form the epidemiological basis for rehabilitation policy programs. However, in general it is difficult to estimate the total number of COPD patients and to estimate the number of patients at different disease stages because different tools have been used to establish the current data pool. The observed prevalence is therefore dependent on factors other than the actual occurrence of COPD (13).

The overall Danish COPD prevalence among 45-84-year-olds has been estimated 12% in a population-based study (1). With a prevalence below 10% among people aged 35-49, the prevalence apparently rises with age, reaching 24% among people 65-79 years of age (1).
These estimates are based on data from 155 general practices. Another Danish study among those aged 65-79 years estimated the prevalence to be 13% for COPD at GOLD stage two and to be 4% for GOLD stage 3-4. These estimates are based on a study population of 4,908 persons resident in a neighborhood of Copenhagen (14). The prevalence of COPD patients divided by age groups is described in Table 2.

<table>
<thead>
<tr>
<th>Age</th>
<th>35-49 % (CI)</th>
<th>50-64 % (CI)</th>
<th>65-79 % (CI)</th>
<th>&gt;80 % (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD 1</td>
<td>3.6 (2.0;6.3)</td>
<td>5.3 (3.7;7.6)</td>
<td>7.1 (5.2;9.7)</td>
<td>12.0 (7.9;17.0)</td>
</tr>
<tr>
<td>GOLD 2</td>
<td>3.5 (2.0;6.2)</td>
<td>7.8 (5.9;10.4)</td>
<td>13.0 (10.4;16.2)</td>
<td>12.3 (8.1;18.2)</td>
</tr>
<tr>
<td>GOLD 3-4</td>
<td>0.1 (0.0;1.4)</td>
<td>1.1 (0.5;2.4)</td>
<td>4.0 (2.6;6.1)</td>
<td>2.3 (0.9;6.0)</td>
</tr>
</tbody>
</table>

The generalizability of these estimates depends on the representativeness of the study population. Thus, prevalence could be overestimated if the sampled persons were at increased risk. As the current Danish prevalence estimates vary, it is difficult to precisely estimate how many will need rehabilitation in the future.

The criteria for offering rehabilitation vary. According to a recent statement, rehabilitation is feasible for most stable COPD patients with a FEV1< 80% of their age-predicted value, although the patients who are typically referred for rehabilitation have GOLD stage 3-4 (9). The ATS/ERS statement (4) suggests that all patients who have reduced functional capacity or reduced health-related QoL are relevant for rehabilitation irrespective of their lung function. Candidates for rehabilitation are also defined as the COPD patients whose dyspnea is disproportionate to the severity of their disease (15). In addition to disease severity, participation in rehabilitation requires that the patient is motivated. Moreover, it has been suggested that demands should be made to the patient’s adherence to medication for a rehabilitation offer to be given (15). In general, pulmonary rehabilitation is not recommended for patients who are unable to walk or to those who suffer from unstable cardiac disease. Other contraindications include cognitive or psychiatric problems that would prevent the patient from comprehending or following the program (9). The 1997 ERS guidelines stated that smokers should not be allowed to participate in a pulmonary rehabilitation program (16). Conversely, the 2001 British Thoracic Society (17) and 2006 ATS/ERS guidelines (4) state that smokers should be offered rehabilitation including smoking cessation.
In summary, rehabilitation may benefit COPD patients at all disease severity stages although, the selection criteria are rather loose (17). In Denmark, the National Board of Health (18) suggests that the target population be patients with FEV1 below 50% of the predicted value, or equivalent to severe dyspnea (Medical Research Council dyspnea grade MRC ≥ 3). As the prevalence of patients with COPD varies the number of patients with COPD at various disease severity stages remains uncertain.

Effects and components of rehabilitation
The Cochrane Collaboration published a meta-analysis of RCTs on pulmonary rehabilitation in 2007 aiming to establish the influence and magnitude of the effect of rehabilitation on COPD patients’ health-related QoL and their functional and maximal exercise capacity (3). The meta-analysis showed that rehabilitation is effective in relieving dyspnea and fatigue, and in improving the patient’s emotional function and disease control. Furthermore, rehabilitation improves functional exercise capacity as measured by a timed walk test. The conclusion strongly supports the use of rehabilitation.

Several documents summarize current knowledge regarding the rehabilitation of COPD patients based on RCTs (4;5;15;17). All these documents conclude that rehabilitation has documented beneficial effect on three main outcomes in COPD patients: reducing dyspnea, improving functional capacity and improving QoL.

The question is therefore today no longer “should patients with chronic obstructive lung disease receive rehabilitation?”, but rather “how should rehabilitation be delivered to patients with COPD?” and “which components form the basis of the success of rehabilitation programs?” (15).

The recommended components are exercise training and patient education (4;5;15;17). Exercise training is a cornerstone because exercise intolerance resulting from dyspnea or fatigue is often the chief symptom reported by COPD patients. Inactivity is believed to be crucial to the development of the systemic consequences of COPD (4), such as skeletal muscle weakness, osteoporosis (19), and cardiovascular disease (20). The benefits from exercise training programs seems to accrue to patients with both mild, moderate, and severe COPD (21). The issues currently debated in the literature therefore center on the intensity, frequency, and duration of the training.
High-intensity programs are generally preferred, although lower-intensity exercise is also beneficial. It has been suggested that a rehabilitation program should feature at least two supervised sessions per week, each lasting three to four hours (22). In general, the suggested duration of a rehabilitation program ranges from 6-12 weeks to achieve substantial effect, but longer programs generally achieve more favorable results (4;5;15;17;22).

Griffiths et al studied one year of out-patient rehabilitation and found that an intensive rehabilitation program can have long-term benefits in terms of walk distance and health status (23). In the program investigated the patients attended the rehabilitation unit on 3 half days per week for 6 weeks for patient education and physical training. The training was intensive starting at 80% of the patients’ maximum walk speed on treadmill, and included also intensive step training. The patients were encouraged and supervised during each training session. After the 6 weeks the patients were instructed in home-exercises and invited for patient-run group that met weekly at a local leisure center.

Current debates discuss how relevant follow-up intervention may be provided after rehabilitation programs. An important aspect is the physical activity maintenance as the benefits of exercise capacity achieved in relation to rehabilitation tend to decline in the months after the intervention. Therefore, it is in general suggested that patients are encouraged to home exercise training after rehabilitation program (4;5;15).

A key goal of rehabilitation is to change the patient’s behavior from a sedentary one towards a more active lifestyle. The duration of the program may therefore be adapted to the time needed for this change to occur. Modern patient education aims to improve the patient’s self-management skills and self-health behaviors (9). Patient education traditionally addresses the patient’s understanding of the disease and its treatment, adherence to medication, early recognition of symptoms and access to early treatment in the event of exacerbations, breathing techniques, nutritional supervision, and smoking cessation (4;5).

**Outcome measurements in relation to COPD rehabilitation**

Rehabilitation outcome measures reflect the goals of rehabilitation. Measures therefore include the results of walk testing, assessments of health-related QoL, and evaluation of specific symptoms, viz. dyspnea. Walking distance is often measured by the 6-minute walk test (24-26). The above mentioned Cochrane meta-analysis estimated a pooled effect size of 49 m (CI:26;72 m), which was slightly below the threshold for the minimal, clinically important difference estimated to be 54 m (3). Health-related QoL is often measured by disease-specific questionnaires, e.g. the Chronic Respiratory Questionnaire (CRQ)(27) and the St. Georg...
Respiratory Questionnaire (SGRQ)(28;29). The Cochrane meta-analyses included RCTs comparing rehabilitation with usual care and investigated health related QoL changes in dimensions of CRQ. In all studies using this questionnaire, the weighted mean difference favors treatment. In studies using SCRQ, the weighted mean difference favors rehabilitation in two of six studies, although the pooled effect favors rehabilitation (3). Besides, the generic questionnaire the Short Form 36 questionnaire (SF36) is a valid instrument to measure health related QoL in patients with COPD (16;30-34).

The Medical Research Council dyspnea questionnaire (MRC) as a simple and valid method commonly used to measure the grade of dyspnea (2;35-37).

In brief, the implementation of COPD rehabilitation in clinical routine rests on well-documented components and effects. The criteria for selecting participants for rehabilitation in clinical routine and the definition of the relevant population seems less clear. The RCTs included in the Cochrane meta-analyses draw on homogeneous study samples and excluded patients with eg. co-morbidity to achieve high internal validity. This may implicate that those patients who are included in RCTs on rehabilitation may differ in certain respects from the population relevant for rehabilitation in clinical routine.

Experience of selection, completion and dropout of rehabilitation

Experience gained in practice shows that selection, completion, and dropout are persistent issues in the field of COPD rehabilitation. The health care professionals involved in the rehabilitation program at Horsens Regional Hospital argued that in order for the rehabilitation courses established to be used in a rational manner and resources spent for good value, the patients offered rehabilitation should be deemed capable of and motivated for completing the program. Although patients were accordingly selected in conformity with this assumption, some failed to attend and some dropped out for various reasons. We gained the experience on poor attendance and dropout in a RCT, which we carried out at Silkeborg Regional Hospital in Denmark in 2002 (Appendix IV). A total of 124 patient records were evaluated, 65 patients were invited for participation, 31 accepted, while only 20 patients completed the program. We used compliance check and evaluation of the performed exercise training so that the individual participant was encouraged, supervised, and given feedback in order to be able to cope with home training. Those who completed achieved a significant improvement in their functional capacity as measured by walk test; however, we found that only every third patient contacted completed the program. Our experience of poor attendance and dropout is supported by the literature which is addressed in the following.
Completion and dropout

Cote et al (38) found that compared with participants, those who declined to take part in rehabilitation were smokers and were more sick, measured by BODE index which integrates BMI, FEV1, dyspnea, and 6MWD (39). Young et al found that “non-adherent patients”, defined as dropouts and those who declined to participate, were likely to be divorced, live at rented accommodation, smoke, and also less likely to adhere to medication. There were no differences between adherent and non-adherent individuals in terms of FEV1, 6MWD, dyspnea, QoL, or depression (40). Sabit et al found that current smoking, more previous hospital admissions, higher MRC score, or enduring a long journey were risk factors for low attendance. Lower BMI and distance to rehabilitation center were of borderline importance (41). Garrod et al found that those who were most likely to dropout of rehabilitation were those with low muscle strength, higher pack-years of smoking and those depressed (42). Arnold et al did a qualitative study to explore non-adherence to rehabilitation and found that poor attendance was seen if either the time of the rehabilitation program, the day of the week, or time of the year was inconvenient (43). Another qualitative study explored patients’ beliefs about illness and treatment and found that divergence between the individual’s aims and the objective of the program led to dissatisfaction and poor adherence (44). From the rehabilitation of patients with ischemic heart disease in Denmark, it has been documented that males with short education who lived alone were more likely not to participate in rehabilitation than other participants (45). The same may be the case in COPD rehabilitation. The literature thus indicates that completion may be predicted by patient characteristics.

To conclude, the selection of participants for rehabilitation is an important issue in the context of RCTs and is an issue that is clearly recognized by the health care professionals involved in rehabilitation in clinical practice. Rehabilitation is already widely implemented in clinical routine in Denmark. The Danish National Board of Health devotes much attention to the implementation of the integrated care program for COPD patients including rehabilitation. At Horsens Regional Hospital, a particular interest in COPD management initiated the development of the CRR program, which has not yet been evaluated. Hospital management and the Hospital’s health care professional question if the rehabilitation program implemented hits its target in the sense that the patients who need rehabilitation are selected for participation, complete the program, and actually achieve improvements. The following hypotheses build on these questions.
Hypothesis

1. The RCTs on rehabilitation are not sufficiently explicit about their selection of participants and the ability to draw conclusion relevant for practice may therefore be impaired (Paper I).

2. Patients relevant for rehabilitation do get a rehabilitation offer.
   Patients’ characteristics predict completion as completers differ from dropout, and those who do not get a CRR offer (Paper II).

3. Completers in clinical routine rehabilitation achieve the improvements documented in RCTs measured by common outcome measures reflecting the goals of rehabilitation (Paper III).

Aims of the thesis

1. To examine the process through which COPD rehabilitation candidates are selected for participation in RCTs to inform a discussion about the generalizability of RCT findings to the clinical setting (Paper I).

2. To characterize a cohort of COPD patients treated at the Regional Hospital in Horsens with a view to identifying potential predictors of rehabilitation completion (Paper II).

3. In a follow-up study to examine changes in 6-minute walking distance (6MWD), quality-of-life and dyspnea during the course of a clinical routine rehabilitation program and to uncover the patients’ attitudes and subjective experience of rehabilitation outcomes (Paper III).
Chapter 2: Materials and methods

Materials and methods - paper I
A literature review of the RCTs originally included in a Cochrane meta-analysis (3) published in 2007. The Cochrane review included a total of 31 RCTs of which 26 full-text English language versions were examined. The 26 RCTs were analyzed with regard to their description of the sampling, their inclusion and exclusion criteria, as well as dropout. As such the analyses focused on three levels of the sampling process when selecting participants for rehabilitation illustrated in Figure 1.

Figure 1 Three levels of selecting participants for RCTs on rehabilitation
Methods and materials in paper II and III

**COPD rehabilitation at Horsens Regional Hospital**

The CRR program implemented at the Hospital was observed within its real-life context. The program "Disease Management Program for Chronic Obstructive Pulmonary Disease, Central Denmark Region” (6), is run by a group of health care professionals representing hospitals, communities, and general practitioner. It is hosted by the Health Administration of Central Denmark Region and published at their homepage. The program focuses on organization and coordination between hospital, community, and general practice. Stratification of patients according to disease severity is a central component.

The purpose of the program is to ensure the use of evidence-based recommendations, to focus on involving the patient’s own resources. According to the program patients with FEV1<50% of predicted value or dyspnea equivalent to an MRC-grade≥3 are offered rehabilitation as an integrated part of the specialist treatment regimen at the hospital. The content of the rehabilitation program was described as: course in self-management of COPD, physical training, managing daily activities, dietary guidance, psychosocial support, and medication guidance. This CRR program lasted for eight weeks with 90-minute sessions twice a week. The program is illustrated in Figure 2.

**Figure 2 COPD disease management program at Horsens Regional Hospital**
**Subjects and methods**
The present cohort consisted of COPD patients (ICD-10 DJ44X) treated as in- or out-patients at Horsens Regional Hospital from 1 September 2008 until 30 April 2009 (N=521).

In-patients were extracted from the hospital administrative system’s monthly list of patients diagnosed with COPD at discharge. Due to delay from discharge until the discharge summery was written every patient-list was re-evaluated after a three months period. At least 8 weeks after discharge the investigator invited the patients for baseline test by mail.

Out-patients were extracted from the out-patient clinic’s list of COPD patients attending routine visits. When listed the investigator invited the patients for test by mail.

The present study aimed to characterize the cohort at a baseline test and to follow all COPD patients treated at the hospital regardless of whether the patient attended CRR or not.

The investigator had no influence on the rehabilitation program or the participants attending, and did not interfere, but occasionally observed sessions of exercise training and patient education.

Excluded from the baseline test were patients (n=185) who had moved away, had the diagnosis of COPD withdrawn, had participated in a pilot-test for the present study, had participated in the rehabilitation program at the hospital within the preceding one year. The patients receiving long-term oxygen treatment were offered special treatment at home with rehabilitation and were therefore not included.

Those patients expected to be too ill to participate in the baseline test were not invited (n=71). The criteria for not inviting patients were severe cognitive impairment, e.g. dementia, severe stroke or psychiatric disease, severe drug or alcohol abuse; severe mobility impairment, e.g. users of wheel chairs, amputees, and patients with severe hip or knee disorders or very severe claudicatio; people living in rest homes, who were terminal ill, or who did not understand Danish.

At the end of the inclusion period, the patient-list from the outpatient clinic was compared with the list from the patient administrative system to ensure that all relevant COPD outpatients had been identified and referred to the baseline test. This quality assessment identified a group of patients with COPD (n=90), who were not identified at the out-patient in the prospective study-period. These patients were therefore not referred for the baseline test, although this would have been relevant.

Eligible patients (n=175) were invited for a baseline test and follow-up at 3, 6 and 12 month.
Paper I focuses on cohort characteristics and specifically the characteristics of the baseline test participants. Paper II focuses on changes in CRR outcomes from baseline to follow-up.

**Data collection**

Data were collected from clinical tests, structured interviews, and questionnaires.

The questionnaires were answered in face-to-face interviews and the questions were read for those patients who had reading difficulties (Appendix V).

At baseline, the patient characteristics and self-reported co-morbidity were registered. Also self-reported depression was obtained at baseline by the use of the case-finding questionnaire for common mental disorders: the CMDQ. A score above "0" indicated a positive test, meaning that depression should be considered (45;46).

At baseline and follow-up at 3, 6, and 12 months we measured: lung function (FEV1), dyspnea (MRC), walk distance (6MWD), Health related QoL (SF36) and functional capacity (ICF COPD questionnaire). The data collecting procedures are described in table 3

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Procedure</th>
</tr>
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<tbody>
<tr>
<td>FEV1</td>
<td>The lung function FEV1(%) of predicted value was measured by spirometry measure of FEV1 according to Danish guideline (47). Vitalograph 2120 nr 10122. The spirometry was measured without bronchodilator inhalation prior the measurements and the patients followed their medication prescription. The best of three measurements were registered.</td>
</tr>
<tr>
<td>MRC</td>
<td>The patients answered the Medical Research Council (MRC) dyspnea questionnaire by indicating the category which to the best expressed their dyspnea: 1: Not troubled with breathlessness except upon strenuous exercise. 2: Troubled by shortness of breath when hurrying or walking up a slight hill. 3: Walks slower than people of the same age due to breathlessness or has to stop for breath when walking at own pace on the level. 4: Stops for breath after walking about 100 m or after a few minutes on the level. 5: Too breathless to leave the house or breathless when dressing or undressing (2)</td>
</tr>
<tr>
<td>6MWD</td>
<td>Walking distance was measured by the 6-min walk distance test. The test was carried out according to ATS Guidelines, which has formed the Danish guideline(24;48). The test measures the distance that a patient can quickly walk over a period of 6 minutes. It is self-paced and assesses the sub-maximal level of functional capacity. The patients chose their own intensity and were allowed to stop and rest during the test. The investigator and the research nurse did the test and for practical reasons, the physiotherapist familiar with the test occasionally performed the test.</td>
</tr>
<tr>
<td>SF36</td>
<td>Health-related QoL was measured by the Medical Outcome Study Short Forms 36 Health Survey Questionnaire and analyzed due to Danish manual (49). SF-36 consists of 36 items forming eight subscales and two summary scores: Physical Component Score (PCS) and Mental Component Score (MCS) The minimal clinical important difference was set to 10 point (49) Each scale goes from 0 (poor health) to 100 (good health)</td>
</tr>
<tr>
<td>ICF-COPD Questionnaire</td>
<td>We used a questionnaire inspired by the International Classification of Functioning Core-Set for COPD patients (50). This questionnaire measures the proportion of patients feeling impaired in different aspect of activities and participation in everyday activities.</td>
</tr>
</tbody>
</table>
Patients’ attitudes towards CRR
Those who completed the rehabilitation program during the study period filled in a questionnaire at the end of the CRR concerning their attitudes towards the rehabilitation program and their subjective outcome (Appendix V).

Statistics
Characteristics of the patients were described using means with 95% confidence interval for normal distributed continuous variables and proportions for categorical variables. Analysis were performed comparing differences at baseline between groups.

Changes from baseline to follow-up at 3, 6 and 12 month within four groups were analyzed:
Patients who completed CRR during the study period (Completers)
Patients who dropped out of CRR during the study period (Dropout)
Patients with no CRR offer during the study period (NRO)
Patients who had previously completed CRR (PC)
The patients participating in the 12-month follow-up were analyzed separately from those lost to 12-month follow-up.

The MRC dyspnea scale was transformed into a three-point scale so that 1 and 2 were equivalent to mild, 3 was equivalent to moderate while 4 and 5 were equivalent to severe dyspnea.
The ICF-COPD Questionnaire had four categories: no impairment/feeling a little impaired/felling somewhat impaired/ feeling very much impaired. Proportions were calculated.
For the questionnaire used at the end of the rehabilitation program proportions were calculated.
Information on socio-economic factors and hospitalizations was obtained from national databases (Danmarks Statistik and E-sundhed).
The significance level was set at 5%. Statistical analysis was performed using Stata (version 11). Table 4 shows the outcome measured at baseline and follow-up.

Table 4 Statistical test of outcome

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Outcome</th>
<th>Between group</th>
<th>Within group</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1, 6MWD, SF36</td>
<td>Continuous, Normal</td>
<td>Unpaired t-test</td>
<td>Paired t-test</td>
</tr>
<tr>
<td></td>
<td>distributed</td>
<td>Oneway ANOVA</td>
<td></td>
</tr>
<tr>
<td>MRC</td>
<td>Categorical</td>
<td>Kruskal-Wallis equality of populations rank test</td>
<td>Wilcoxon Signed Rank Test</td>
</tr>
<tr>
<td>ICF-COPD questionnaire</td>
<td>Categorical</td>
<td>Kruskal-Wallis equality of populations rank test</td>
<td>Wilcoxon Signed Rank Test</td>
</tr>
</tbody>
</table>
Chapter 3: Results

Paper I

The review on selection and dropout in RCTs on pulmonary rehabilitation showed that among the 26 studies originally included in the Cochrane Meta-analysis from 2007 (3), only 3/26 (12%) of the studies described the number of patients contacted and from these studies 47% of the patients contacted were de-selected prior to randomization. The proportion of completers reflects the numerator used for calculating the number and it climbs when decreasing the numerator. The three mentioned studies are summarized in Table 5.

Table 5 Studies (3/26) originally included in the Cochrane meta-analyses with description of sampling

<table>
<thead>
<tr>
<th>Study/Aim</th>
<th>A Contacted</th>
<th>B Screened</th>
<th>C Left out (%)</th>
<th>D Randomized</th>
<th>E Left out (%)</th>
<th>F Dropout (%)</th>
<th>G Completers (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jones 1985 Inspiratory muscle training</td>
<td>52</td>
<td>38</td>
<td>14/52 (27)</td>
<td>30</td>
<td>8/38 (21)</td>
<td>9/30 (30)</td>
<td>a) 21/52 (40)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) 21/38 (55)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) 21/30 (70)</td>
</tr>
<tr>
<td>Bendstrup 1997 Out-patient rehabilitation</td>
<td>140</td>
<td>85</td>
<td>55/140 (39)</td>
<td>42</td>
<td>43/85 (51)</td>
<td>10/42 (24)</td>
<td>a) 32/140 (23)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) 32/85 (38)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) 32/42 (76)</td>
</tr>
<tr>
<td>Ringbaek 2000 Rehabilitation two sessions a week for 8 weeks</td>
<td>130</td>
<td>48</td>
<td>82/130 (63)</td>
<td>45</td>
<td>3/48 (6)</td>
<td>7/45 (16)</td>
<td>a) 38/130 (29)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) 38/48 (79)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) 38/45 (84)</td>
</tr>
<tr>
<td>Total N/(%)</td>
<td>322</td>
<td>171 (53)</td>
<td>151 (47)</td>
<td>117</td>
<td>54 (44)</td>
<td>26/117 (22)</td>
<td>a) 91/322 (28%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>b) 91/171 (53%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>c) 91/117 (78%)</td>
</tr>
</tbody>
</table>

Number of patients A: contacted; B: screened; C: left out from contacted to screened; D: randomized; E: left out from screening to randomization; F: Dropouts, G: Completers out of number contacted, screened, randomized

Table 5 is a short version of Table 1, Paper I.

The majority of the studies included in our review (18/26; 69%) contained information only on the number of patients randomized and for obvious reasons the number of patients randomized was used for calculation the proportion of completers. The proportion of completion reported ranged from approximately 60% to 100%.

The conclusion was that RCTs offer sparse information about the sampling procedure. Those patients who are included in RCTs on rehabilitation may differ in certain respects from the population relevant for rehabilitation in clinical routine. The risk may therefore exist that the results documenting the effects of rehabilitation suffer from selection bias. This may, in turn, imply that the results from RCTs on rehabilitation may be difficult to obtain in clinical routine.

The review raised the following question: What characterizes COPD patients in clinical routine. Do completers in CRR differ from non-completers and do they achieve the effects as documented in RCTs? This was investigated in a cohort study (paper II) and a follow-up study (paper III).
**Paper II**
The cohort consisted of 521 COPD patients treated as in- or out-patients at Horsens Regional Hospital in the specified time period. The study describes the characteristics of this COPD cohort from which completers of CRR were drawn. For practical reasons it was not possible to follow the whole cohort. Among those patients eligible for the baseline test their characteristics were registered to identify potential baseline differences between those who completed CRR and those who did not.

*From cohort to the study-population eligible for baseline test*
The process when sampling participants for the baseline is illustrated in Figure 3.

Figure 3 Sampling the participants for baseline test

![Diagram illustrating the process of sampling participants for baseline test.](image)

Excluded were 185 patients due to the criteria mentioned above, while 90 outpatients were not identified at the outpatient clinic at the beginning of this study. They were therefore not included although this would have been relevant and 71 patients were not invited for baseline test due to severe illness.

A total of 175 patients were invited for the baseline test. Among those, 27 did not want to participate. Among the 148 baseline participants we found that 46 patients completed CRR during the follow-up, 35 patients started CRR but dropped out. The patients who were not offered CRR counted 67 of those 33 patients had completed rehabilitation previously.

*Cohort characteristics*
As the 90 outpatients were not referred for the baseline test due to technical reasons, only their patient records were evaluated. The patients’ characteristics are shown in Table 6. The 90
outpatients were younger, had better lung function, and counted statistically significantly more non-smokers than the remaining patients referred for baseline test.

Table 6 Characteristics of COPD patients referred for baseline test versus outpatients not referred for technical reasons

<table>
<thead>
<tr>
<th></th>
<th>Referred for baseline test (n=246)</th>
<th>Out-patients not referred (n=90)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Female %</td>
<td>54</td>
<td>54</td>
<td>1.00</td>
</tr>
<tr>
<td>Age mean (95%CI)</td>
<td>70(69;71)</td>
<td>66(63;68)</td>
<td>0.001</td>
</tr>
<tr>
<td>Living alone %</td>
<td>48</td>
<td>64</td>
<td>0.013</td>
</tr>
<tr>
<td>FEV1 (%) mean (95%CI)</td>
<td>40(38;42)</td>
<td>47(44;50)</td>
<td>0.0003</td>
</tr>
<tr>
<td>MRC % mild, moderate, severe</td>
<td>50,30,20 (n=175)</td>
<td>43,43,14 (n=90)</td>
<td>0.71</td>
</tr>
<tr>
<td>Pack years of smoking mean(95%CI)</td>
<td>42 (40;45)(n=181)</td>
<td>39 (35;43)</td>
<td>0.18</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>57</td>
<td>40</td>
<td>0.007</td>
</tr>
<tr>
<td>Own their place of residence</td>
<td>51</td>
<td>64</td>
<td>0.03</td>
</tr>
<tr>
<td>7-10 years of primary school</td>
<td>95</td>
<td>98</td>
<td>0.12</td>
</tr>
<tr>
<td>Education short or less %</td>
<td>92</td>
<td>94</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 6 is a short version of Table 1 in Paper II (Proportion = %. FEV1 (%) = FEV1 % of predicted value, MRC% = Medical Research Council dyspnea questionnaire proportion with mild/ moderate/severe dyspnea)

A total of 71 patients were not invited due to severe or terminal illness as mentioned above. Table 7 shows their characteristics compared with the characteristics of those who were invited. Those not invited were older. FEV1 and MRC were missing for at large proportion, although it showed that the proportion of patients with a MRC score of severe dyspnea was higher.

Table 7 Characteristics of COPD patients invited for baseline test versus patients not invited

<table>
<thead>
<tr>
<th></th>
<th>Invited for baseline test (n=175)</th>
<th>Not invited for baseline test (n=71)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Female %</td>
<td>56</td>
<td>49</td>
<td>0.40</td>
</tr>
<tr>
<td>Age mean (95%CI)</td>
<td>68(67;70)</td>
<td>73(71;76)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Living alone %</td>
<td>51</td>
<td>40</td>
<td>0.12</td>
</tr>
<tr>
<td>FEV1(%) mean (95%CI)</td>
<td>40(38;42)</td>
<td>41(36;46)</td>
<td>0.82</td>
</tr>
<tr>
<td>MRC (% mild, moderate, severe)</td>
<td>54,30,17 (n=160)</td>
<td>13,33,54 (n=15)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Pack years of smoking mean(95%CI)</td>
<td>42 (40;45)(n=160)</td>
<td>42 (33;52)</td>
<td>0.1</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>53 (n=174)</td>
<td>60 (n=60)</td>
<td>0.37</td>
</tr>
</tbody>
</table>

This table 7 is a short version of table 2 in Paper II (Proportion = %. FEV1 (%) = FEV1 % of predicted value MRC% = Medical Research Council dyspnea questionnaire proportion with mild/ moderate/severe dyspnea)

Among the 175 patients invited for baseline test 27 patients did not want to participate. Their characteristics are compared with baseline participants in Table 8. Those who declined to participate were older and counted statistically significantly more patients with severe dyspnea and pack years of smoking.
### Table 8 Characteristics of COPD patients who participated in baseline test versus patients who did not want to participate

<table>
<thead>
<tr>
<th></th>
<th>Baseline participants (n=148)</th>
<th>Did not want to participate (n=27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Female %</td>
<td>55</td>
<td>60</td>
<td>0.83</td>
</tr>
<tr>
<td>Age mean (95%CI)</td>
<td>68(66;69)</td>
<td>72(68;77)</td>
<td>0.03</td>
</tr>
<tr>
<td>Living alone %</td>
<td>9</td>
<td>9</td>
<td>0.70</td>
</tr>
<tr>
<td>MRC (% mild, moderate, severe)</td>
<td>40(38;42) (n=146)</td>
<td>37(32;42) (n=14)</td>
<td>0.37</td>
</tr>
<tr>
<td>Pack years of smoking mean (95%CI)</td>
<td>41(38;44) (n=145)</td>
<td>53(39;67) (n=15)</td>
<td>0.03</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>50</td>
<td>69</td>
<td>0.09</td>
</tr>
</tbody>
</table>

This Table in not included in any of the papers (Proportion = %.  FEV1 (%) = FEV1 % of predicted value MRC%= Medical Research Council dyspnea questionnaire proportion with mild/ moderate/severe dyspnea)

The baseline participants

The 148 participants at baseline test had their 6MWD, FEV1 (%), MRC and QoL measured. In relation to baseline dyspnea, 6MWD, and QoL, we found that completers of CRR had the longest 6MWD despite a statistically significantly lower lung function and subjective perception of physical function. The results shown in Table 9 indicate that better physical performance characterized the completers at baseline.

The two summary scores: physical and mental component score (PCS and MCS) of the SF36 questionnaire showed no significant differences between the groups. Besides the difference in 6MWD and FEV1 at baseline, patient characteristics did not predict completion of CRR.

### Table 9 FEV1, MRC, 6MWD, SF36 for patients participating in baseline test

<table>
<thead>
<tr>
<th></th>
<th>Completers (n=46)</th>
<th>Dropout (n=35)</th>
<th>No CCR offer (n=67)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC % mild, moderate, severe</td>
<td>60,33,7</td>
<td>60,29,11</td>
<td>58,21,21</td>
<td>0.75</td>
</tr>
<tr>
<td>FEV1 (%) mean (95%CI)</td>
<td>37(32;41)</td>
<td>37(34;40)</td>
<td>44(40;48)</td>
<td>0.004</td>
</tr>
<tr>
<td>6 MWD(m) mean (95%CI)</td>
<td>413(379;447)</td>
<td>360(315;407)</td>
<td>350(322;379)</td>
<td>0.021</td>
</tr>
<tr>
<td>SF36 MCS mean (95%CI)</td>
<td>56(54;58) (n=40)</td>
<td>57(53;61)</td>
<td>55(52,57)</td>
<td>0.49</td>
</tr>
<tr>
<td>SF36 PCS mean (95%CI)</td>
<td>37(34;41) (n=40)</td>
<td>40(36;43)</td>
<td>39(37,41)</td>
<td>0.59</td>
</tr>
</tbody>
</table>

Table 9 is a short version of table 4 in Paper II (FEV1 (%) = FEV1 % of predicted value MRC%= Medical Research Council dyspnea questionnaire proportion with mild/ moderate/severe dyspnea)

MCS and PCS Mental and Physical Component score from the health related QoL SF36 questionnaire

The conclusion of paper II was that in terms of socio-demographic characteristics almost all the patients in the source-population had a school education of 7-10 years in primary school very few had high school or equivalent education. In general, the patients had no education or a short education.

Compared with the RCTs, our study of the CRR reveals a proportionately similar, large number of patients not selected for CRR. A mere of 9% completed rehabilitation within the study period, and 23% ever completed. The political ambition in Denmark is that 60% of COPD patients should be offered rehabilitation (51), although no target has been set for the
proportion of completion, seems to be a distant goal. In general our findings did not confirm the hypothesis that the patients’ characteristics predicted completion.
**Paper III**

This paper investigated the changes from baseline to follow-up a 3, 6 and 12 month in relation to rehabilitation outcomes: QoL, 6MWD, dyspnea, and the COPD ICF-Questionnaire.

**Follow-up study-population**

The 148 baseline participants extracted from the cohort formed the follow-up study population in paper III. They were divided into four groups: 46 completers, 35 dropouts, 34 previous completers (PC), and 33 with no CRR offer (NRO). The two latter groups were those labeled no rehabilitation offer in paper II. Figure 4 shows the number of participants at baseline and follow-up at 3, 6 and 12 month divided by group.

**Figure 4 Participants in follow-up**
**Baseline characteristics of the follow-up population**

Table 10 shows the baseline characteristics, co-morbidities and hospitalizations for the four groups. The proportions of patients with one or more co-morbidities ranged from 80-91% with the lowest proportion among completers. Depression was self-reported by approx. 20%, yet more than 50% tested positive in the questionnaire. The proportion of patients hospitalized before the follow-up study was in the range 18-79%; a difference that was statistically significant with the highest proportion among NRO (p=0.00).

<table>
<thead>
<tr>
<th></th>
<th>Completers (n=46)</th>
<th>Dropout (n=35)</th>
<th>NRO (n=33)</th>
<th>PC (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex Female %</td>
<td>54</td>
<td>54</td>
<td>67</td>
<td>47</td>
<td>0.45</td>
</tr>
<tr>
<td>Age mean (95%CI)</td>
<td>68(65;70)</td>
<td>67(64;70)</td>
<td>69(65;73)</td>
<td>68(65;71)</td>
<td>0.89</td>
</tr>
<tr>
<td>Pack years of smoking mean (95%CI)</td>
<td>42(37;48)</td>
<td>42(36;47)</td>
<td>38(31;45)</td>
<td>43(36;50)</td>
<td>0.67</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>50</td>
<td>54</td>
<td>55</td>
<td>41</td>
<td>0.66</td>
</tr>
<tr>
<td>Proportion with one or more co-morbidity</td>
<td>80</td>
<td>83</td>
<td>91</td>
<td>85</td>
<td>0.61</td>
</tr>
<tr>
<td>Self-reported Depression %</td>
<td>23</td>
<td>18</td>
<td>21</td>
<td>27</td>
<td>0.85</td>
</tr>
<tr>
<td>General Depression Scale positive %</td>
<td>55</td>
<td>54</td>
<td>50</td>
<td>53</td>
<td>0.97</td>
</tr>
<tr>
<td>Hospitalized 12 month from baseline %</td>
<td>26</td>
<td>34</td>
<td>24</td>
<td>27</td>
<td>0.80</td>
</tr>
<tr>
<td>More than one hospitalization 12 month from baseline %</td>
<td>58</td>
<td>58</td>
<td>63</td>
<td>11</td>
<td>0.09</td>
</tr>
<tr>
<td>Hospitalized prior for baseline %</td>
<td>33</td>
<td>46</td>
<td>79</td>
<td>18</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 10 is a short version of table 1 paper III (Proportion=%)
**Changes in CRR outcome**

Table 11 shows the changes within groups from baseline test to the 12-month follow-up. Completers declined 6MWD statistically significantly from baseline (mean 411 m) to the 12-month follow-up (mean 366 m), and the proportion of patients with moderate and severe dyspnea rose although the change was not statistically significant.

Among PC, the 6MWD fell statistically significantly from a mean of 385 m to 336 m ($p=0.05$) and the proportion of patients with moderate and severe dyspnea rose ($p=0.02$). Among dropouts and NRO, no changes in 6MWD from baseline to the 12-month follow-up were observed. No differences within groups were seen in QoL (MCS and PCS). The lowest PCS at the 12-month follow-up was seen among completers and PC.

**Table 11 FEV1, 6MWD, MCS PCS and MRC at baseline and 12-month follow-up by group**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>Number</th>
<th>Baseline test</th>
<th>12 month</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (%)</td>
<td>Completers</td>
<td>(n=35)</td>
<td>37(32;42)</td>
<td>37(33;42)</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>Dropout</td>
<td>(n=20)</td>
<td>35(32;39)</td>
<td>38(33;43)</td>
<td>0.2</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>(n=18)</td>
<td>56(52;60)</td>
<td>51(44;58)</td>
<td>0.15</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>(n=25)</td>
<td>36(31;42)</td>
<td>34(29;40)</td>
<td>0.1</td>
</tr>
<tr>
<td>6 MWD(m)</td>
<td>Completers</td>
<td>(n=34)</td>
<td>411(375;447)</td>
<td>336(269;403)</td>
<td>0.007</td>
</tr>
<tr>
<td></td>
<td>Dropout</td>
<td>(n=18)</td>
<td>401(358;444)</td>
<td>401(342;459)</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>(n=16)</td>
<td>362(310;415)</td>
<td>363(293;433)</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>(n=23)</td>
<td>385(351;419)</td>
<td>336(272;399)</td>
<td>0.05</td>
</tr>
<tr>
<td>MCS Mean (%)</td>
<td>Completers</td>
<td>(n=26)</td>
<td>55(52;59)</td>
<td>54(50;57)</td>
<td>0.32</td>
</tr>
<tr>
<td></td>
<td>Dropout</td>
<td>(n=19)</td>
<td>57(53;62)</td>
<td>57(53;60)</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>(n=11)</td>
<td>53(46;59)</td>
<td>50(41;58)</td>
<td>0.39</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>(n=22)</td>
<td>56(54;60)</td>
<td>58(53;61)</td>
<td>0.52</td>
</tr>
<tr>
<td>PCS Mean (%)</td>
<td>Completers</td>
<td>(n=26)</td>
<td>38(33;42)</td>
<td>37(33;42)</td>
<td>0.81</td>
</tr>
<tr>
<td></td>
<td>Dropout</td>
<td>(n=19)</td>
<td>41(36;42)</td>
<td>40(35;44)</td>
<td>0.55</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>(n=11)</td>
<td>37(31;42)</td>
<td>40(30;49)</td>
<td>0.45</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>(n=22)</td>
<td>38(34;42)</td>
<td>36(15;55)</td>
<td>0.31</td>
</tr>
<tr>
<td>MRC % Mild/Modera te/ Severe</td>
<td>Completers</td>
<td>(n=34)</td>
<td>68/29/3</td>
<td>54/34/12</td>
<td>0.18</td>
</tr>
<tr>
<td></td>
<td>Dropout</td>
<td>(n=20)</td>
<td>65/25/10</td>
<td>70/15/15</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>(n=18)</td>
<td>56/39/5</td>
<td>61/33/6</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>(n=25)</td>
<td>64/24/12</td>
<td>44/28/28</td>
<td>0.02</td>
</tr>
</tbody>
</table>

MCS and PCS Mental and Physical Component score from the health related QoL SF36 questionnaire
MRC Medical Research Council dyspnea questionnaire Proportion with mild/moderate/severe dyspnea
Table 11 is table 2 in paper III (Proportion=%)
The overall result of the ICF-COPD-Questionnaire showed no statistically significant difference between groups. Statistically significant differences within groups were seen for seven out of nine questions (Table 12).

Table 12 ICF COPD questionnaire at baseline and 12 month follow-up

<table>
<thead>
<tr>
<th>Proportions feeling not impaired/ little impaired/ some what impaired/ very much impaired</th>
<th>Group</th>
<th>Baseline</th>
<th>12 month follow-up</th>
<th>p-value Wilcoxon signed rank test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrying out daily routine</td>
<td>Completers</td>
<td>24/32/35/9</td>
<td>24/35/38/3</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>30/40/20/10</td>
<td>20/50/30/0</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>59/6/35/0</td>
<td>29/29/29/12</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>24/32/28/16</td>
<td>24/20/40/16</td>
<td>0.65</td>
</tr>
<tr>
<td>Handling stress and other psychological demands</td>
<td>Completers</td>
<td>20/26/37/17</td>
<td>26/43/26/6</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>45/30/10/15</td>
<td>35/40/20/5</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>12/47/35/6</td>
<td>24/41/24/12</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>40/20/32/8</td>
<td>28/24/28/20</td>
<td>0.09</td>
</tr>
<tr>
<td>Lifting and carrying objects</td>
<td>Completers</td>
<td>9/29/32/29</td>
<td>21/32/21/26</td>
<td>0.14</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>15/35/35/15</td>
<td>15/50/53/0</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>31/31/25/13</td>
<td>25/38/19/20</td>
<td>0.66</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>16/32/20/32</td>
<td>28/20/20/32</td>
<td>0.34</td>
</tr>
<tr>
<td>Walking</td>
<td>Completers</td>
<td>12/38/29/7</td>
<td>24/29/38/9</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>25/55/15/5</td>
<td>30/45/20/5</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>13/31/56/0</td>
<td>25/44/13/19</td>
<td>0.46</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>24/24/28/24</td>
<td>36/8/44/12</td>
<td>0.42</td>
</tr>
<tr>
<td>Doing housework</td>
<td>Completers</td>
<td>38/26/24/12</td>
<td>38/24/32/6</td>
<td>0.94</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>45/15/25/3</td>
<td>35/40/15/0</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>59/18/18/6</td>
<td>41/25/12/18</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>36/18/41/5</td>
<td>36/14/9/41</td>
<td>0.04</td>
</tr>
<tr>
<td>Looking after one health physically</td>
<td>Completers</td>
<td>23/34/31/11</td>
<td>26/37/29/9</td>
<td>0.47</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>30/40/20/10</td>
<td>35/20/35/10</td>
<td>0.56</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>38/25/31/6</td>
<td>13/50/25/13</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>20/32/32/16</td>
<td>20/36/28/36</td>
<td>0.71</td>
</tr>
<tr>
<td>Assisting others</td>
<td>Completers</td>
<td>47/29/15/8</td>
<td>38/27/29/7</td>
<td>0.24</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>50/35/5/10</td>
<td>35/40/15/13</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>44/31/13/13</td>
<td>44/31/13/13</td>
<td>1.0</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>50/4/29/17</td>
<td>25/21/21/33</td>
<td>0.01</td>
</tr>
<tr>
<td>Community life</td>
<td>Completers</td>
<td>55/23/16/6</td>
<td>68/19/13/0</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>68/26/0/5</td>
<td>68/16/11/5</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>56/25/13/6</td>
<td>44/13/29/5</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>46/29/17/8</td>
<td>42/21/25/13</td>
<td>0.16</td>
</tr>
<tr>
<td>Recreation and leisure</td>
<td>Completers</td>
<td>57/29/7/7</td>
<td>54/36/11/0</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>dropout</td>
<td>53/27/13/7</td>
<td>47/33/7/13</td>
<td>0.82</td>
</tr>
<tr>
<td></td>
<td>NRO</td>
<td>50/29/7/14</td>
<td>43/21/29/7</td>
<td>0.53</td>
</tr>
<tr>
<td></td>
<td>PC</td>
<td>53/11/16/21</td>
<td>32/21/15/32</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Table 12 is table 3 in paper III ICF COPD questionnaire is inspired by the ICF COPD Core-Set (50)

**Dropout from CRR**

Among those who dropped out of CRR 25 (71%) gave reasons for abandoning CRR. Seven had employment preventing their participation. Two had to undergo surgery, two mentioned exhausting transportation, one dropped out due to impaired vision and hearing, and one for the reason of back pain. Four did not feel comfortable with the set-up. Two felt the program
too exhausting. One was disappointed. Two preferred rehabilitation in the community. One had exacerbations. Two dropped out as CRR was inconvenient. Ten (29%) gave no reasons.

**Loss to follow-up**

The loss to the 12-month follow-up counted 50 patients (34%). Lost to follow-up among those who completed CRR during the follow-up period was 11/46 (24%). Among those who dropped out from CRR 15/35 (43%) were lost to follow-up. Among those who did not get a CRR offer in the study period 15/33 patients (45%) were lost to follow-up. Finally 9/34 (26%) among those who previously had completed CRR were lost to follow-up.

Reasons for loss to follow-up were: death (6), treatment with long term oxygen (6), hip fracture/fall (3), dementia (2), the diagnose of COPD withdrawn (4), did not have the strength/did not want to continue (18), did not show up at test although 2-3 appointments were made (11).

Baseline differences between follow-up patients and those lost to follow-up are not easily explained, but the latter tended to have shorter 6MWD and the proportion of patients in this group with severe dyspnea seemed to be larger.

**Completers objective outcome**

Completers of CRR were asked about their subjective outcome and their attitudes towards CRR (Table 13). A total of 75% of the completers answered that they felt very much better or somewhat better after rehabilitation compared with the time before.

Table 13 Questionnaire concerning attitudes toward rehabilitation and subjective outcomes answered by 41/46 (89%) among completers at the end of the CRR

<table>
<thead>
<tr>
<th>How did you experience the rehabilitation program...</th>
<th>percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>to have an influence on your mood</td>
<td>85/15</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to have an influence on your motivation for making changes in daily activities</td>
<td>90/10</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to give knowledge concerning COPD</td>
<td>95/5</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to influence your community life/participation in social life</td>
<td>61/39</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to influence your ability to cope with COPD in everyday life</td>
<td>85/15</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to increase your physical performance</td>
<td>86/14</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to influence your ability to cope with activities of daily living</td>
<td>66/34</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>to influence your ability to cope with breathlessness</td>
<td>93/7</td>
</tr>
<tr>
<td>Yes/Unchanged</td>
<td></td>
</tr>
<tr>
<td>Compared with the time before rehabilitation how do you feel now</td>
<td>34/42/24</td>
</tr>
<tr>
<td>Very much better /Somewhat better /The same</td>
<td></td>
</tr>
<tr>
<td>What are your overall opinion about the rehabilitation program</td>
<td>63/30/7/0</td>
</tr>
<tr>
<td>Excellent /Very good /Good/ Do not know</td>
<td></td>
</tr>
</tbody>
</table>

**The main results** were that completers of CRR did not improve in terms of 6MWD, QoL, or MRC despite a subjective feeling of improvement. Completers did sustain the walking distance
from baseline to the end of the rehabilitation program at the 3-month follow-up; yet, they experienced a statistically significant decline from baseline to the 12-month follow-up (Figure 5). The proportion of patients with moderate and severe dyspnea rose during follow-up while QoL sustained from baseline to follow-up (Figure 6, 7 and 8).

Figure 5  6MWD (m) mean (CI) by group at baseline and follow-up at 3, 6 and 12 month
Figure 6  MRC proportions of mild/moderate/severe dyspnea by group at baseline and follow-up at 3, 6 and 12 month

Figure 7 SF36 Physical Component score (PCS) mean (CI) by group at baseline and follow-up at 3, 6 and 12 month
The conclusion of paper III was that from the cohort of 521 COPD patients, 46 completed the CRR program during follow-up. Completers did not improve in terms of 6MWD, QoL, or MRC despite their subjective feeling of improvement. The 6MWD was sustained from baseline to 3 months of follow-up, but had fallen at the 12-month follow-up. The selection of participant for CRR followed no strict criteria. Despite convincing documentation, these CRR results at best show no improvements, at worst a decline.
Chapter 4: Methodological considerations

In order to interpret the findings of this study, an evaluation of the factors that impact on its validity are discussed.

Study design
We chose to perform an observational study of the CRR program already implemented in Horsens Regional Hospital, to investigate the inclusion, the completion and the outcome in relations to CRR. The observational approach was considered to provide us with the opportunity for systematically exploring events, collecting data, analyzing and reporting results within the real-life context of CRR, as it is well-known from practice and from the literature that the introduction of evidence-based guidelines in clinical practice may encounter resistance (52).

Selection problems

Sampling
The sampling of participants for baseline test and follow-up may have been influenced by selection issues. The aim of the detailed sampling process was to recruit a maximally representative subset of participants for follow-up. The characteristics of those not participating in follow-up therefore had to be as close as possible to those of the total cohort to avoid selection bias.

A total of 185 patients were excluded for obvious reasons, for example because the diagnosis of COPD had been withdrawn, the patients had died, or had moved away.

A total of 90 outpatients not included for technical reasons were younger and had better lung function. Furthermore, those 71 patients who were too ill to participate in the follow-up were older and at a more severe disease stage.

The fraction that actually participated in the follow-up is small 148/521 (28%), which might introduce selection problems. As a substantial number of subjects did not participate in the follow-up study which might raise doubts about the internal validity. I relation to case-control studies it has been stated that follow-ups that trace less than about 60 % of subjects are generally regarded to be too low to provide sufficient assurance against bias (53). However, we do not know if those patients not participating in the follow-up study might have influenced the findings, in case they have been included.

Despite the small fraction of participants in the follow-up we succeeded to include all patients who began CRR during the study-period (n=81).
Loss from follow-up
Loss from follow-up can pose a threat to the internal validity of the study. A total of 148 patients participated in the baseline test. The loss to the 12-month follow-up counted 50 patients (34%) and the percentages ranged from 24-45% in the four study groups lowest among completers.

Those patients lost to follow-up were analyzed separately from those followed. We found in relation to 6MWD, that those lost to follow-up among dropouts and previously completers of CRR had a clinical relevant lower walk distance than those participating in follow-up. In all four groups, those lost to follow-up had higher proportions with severe dyspnea than those participating in follow-up. For the MCS and PCS the differences were between 1 and 6 point, which is below the clinical important difference.

These differences, although, they did not systematically show that completers differed from the other groups, might induce bias due to differential loss to follow-up. This might affect internal validity and the generalizability of conclusions made about the total cohort.

Information bias
Data collection procedures can induce information bias. Such bias, however, will only arise if information is obtained differentially in the study groups. The outcome measures were related to the goals of rehabilitation and measured functional capacity, health-related QoL, and symptom severity. We used standardized tests for the three main outcomes 6MWD, SF36, and MRC scale. Data were collected prospectively and systematically using the standardized questionnaires and procedures.

The interviews were performed face-to-face by a research nurse or the investigator. We were aware that this might imply that a conversation goes beyond the themes raised in the questionnaires. Our expectation was that this would not introduce information bias as all participants had the same opportunity for a conversation whether they completed CRR or not. The data collecting procedures were identical for the four groups which will have served to minimize the risk of information bias.

Validity of measurements
Functional capacity is traditionally measured by a 6-minute walk-distance (6MWD) test or the shuttle walk test. We chose the 6MWD as it provides valid information relevant for activities in daily living (24-26). The 6MWD is used routinely at the Hospital and it is easy to administer because it requires neither exercise equipment nor advanced skills. The test was performed systematically using the technical guidelines. The validity of the test information can be affected by inter rater differences; however, we expect this risk to be negligent.
Health-related QoL was measured by the SF36, which is a validated generic questionnaire that focuses on broad aspects of QoL and health status (49). We chose the SF36 because this instrument is supposed to be used in future monitoring of chronic care programs across a wide range of disease conditions in our region.

Dyspnea as a specific, highly important symptom in COPD patients is not included in the SF36 and the present study therefore assessed dyspnea by means of the MRC dyspnea scale (54). This questionnaire is commonly used in RCTs on pulmonary rehabilitation and it is used in clinical routine at the Hospital. The validity of these questionnaires minimized the risk of weakened finding due to information bias.

Activities of daily living were measured by a questionnaire inspired by the International Classification of Functioning Core-Set for COPD patients (50). The face validity of the ICF-inspired questionnaire was pilot-tested among six randomly selected COPD patients admitted to the Hospital. The use of this questionnaire is the very first step in using the core set of questions developed for COPD patients based on the ICF. This questionnaire has not been validated; however, it built on a valid number of aspects relevant to activities in everyday life. We used simple summarizing methods in the analysis because a sum-score measure required systematical validation of the questionnaire, which is beyond the scope of this thesis. The use of the questionnaire did not differ between groups.

**Misclassification**

Information bias can be introduced by misclassification which occurs when patients with \( \text{FEV1} \geq 50\% \) of predicted value were offered rehabilitation although the formal criterion was that only patients with \( \text{FEV1} < 50\% \) should be offered rehabilitation. On the other hand, patients with \( \text{FEV1} < 50\% \) did not all receive an offer although they did meet the formal criteria. The changes in 6MWD, QoL, and dyspnea in relation to CRR can be biased due to this misclassification. However, as the FEV1 do not precise predict walk distance, health related QoL or dyspnea (10;55;56), we can not be sure in which direction the misclassification might affect the findings.

**Confounding**

The follow-up study design without randomization raises the question if the outcome in relation to CRR can be influenced by confounding. In relation to 6MWD, QoL, dyspnea, and the COPD-ICF-Questionnaire, the patients’ characteristics, co-morbidities, and exacerbations can introduce a difference between the groups and affect the changes within groups. The ATA/ERS guideline on rehabilitation stated that cardiac dysfunction, weight loss, and musculoskeletal dysfunction contribute to exercise intolerance (4), which might confound
6MWD and QoL. Barnes and Celli summarized the evidence of systemic manifestations and co-morbidities in COPD (57) and Mannino et al found that COPD is associated a higher prevalence of diabetes, hypertension, and cardiovascular disease than non-COPD patients (58). Our patients’ characteristics support this. However, we did not find that these known confounders were distributed differentially between the four groups. Unknown potential confounders cannot be prevented in a non-experimental study.

**Conclusion on methodological issues**
The follow-up study design is relevant in a study that tests hypotheses in relation to an exposure and its outcome. The internal validity of the study was enhanced by the use of valid, well-established measures and identical standard routine procedures for data collection across the study groups. However, the internal validity was influence by selection as only a small fraction of the source-population participated in follow-up. As a consequence the external validity might be threatened by a possible weakened internal validity. In contrast we succeeded to include all CRR participants.
The CRR program implemented at the Hospital in Horsens “became a case”, meaning that we believed that the findings made there would be similar to those that we could find for CRR at other regional hospitals (59). In this respect, the results of the present study can form the basis for optimizing inclusion and completion of CRR candidates, and for optimizing the effects of CRR itself, despite, the possibility that the internal validity might be affected.
Chapter 5: Discussion of study findings
The discussion is organized into three sections to address the hypotheses raised.

Selection in RCTs and generalizability to CRR
Paper I raised the hypothesis that the findings in RCTs of effects of rehabilitation interventions might be biased, if participants selected for rehabilitation were primarily those who were deemed to have the ability to complete and achieve improvement. In the affirmative, this would imply that the ability to generalize the RCT results to practice would be impaired. Our re-examination of the studies included in the Cochrane meta-analysis in many cases revealed a poorly documented sampling process. As discussed in Paper I details regarding the circumstances under which participants in RCTs were selected revealed e.g. that they were chosen among regular attendees at clinics or chosen among patient-records. Besides, patients were recruited by the means of announcements. However, the total number of relevant patients and their characteristics were not described. Furthermore, in RCTs patients were de-selected if they e.g. lived too far away or had social circumstance, which might affect their ability to cope with the intervention. This suggests that the effects of rehabilitation could be explained by a – possibly unconscious – selection of those patients who would most likely complete and, hence, benefit from the rehabilitation program.

Although, the rationale of RCTs can hardly be questioned as they are considered to represent the most scientifically rigorous method of hypothesis testing on the basis of the best possible evidence. There is therefore little reason to doubt the effect of rehabilitation as an effective intervention towards subgroups of COPD patients.

After all, the RCTs gave sparse information on the patient characteristics of those who were de-selected. Only three of the studies accounted for the number of patients deselected before randomization, which reached 47% in all three studies. We therefore do not know if completers of rehabilitation in RCTs differ from those who were de-selected. Our review supports that participants could have been selected owing to their ability to complete and to respond to the particular rehabilitation offered.

In conclusion, the re-examination of the RCTs included in the Cochrane meta-analysis did not allow us to refute the hypothesis of a possible systematic preferential selection, whether conscious or subconscious, of study subjects who were deemed able to complete the intervention and benefit from it. Most of the studies simply contained too little information about deselected subjects. Given that such selection had, indeed, taken place, we cannot
easily extrapolate from these findings to clinical practice; nor did the RCTs allow us to examine why their results may not be replicable in the context of clinical practice.

**Prediction of completion and dropout**

Given that the patients who were most likely to participate and benefit from the rehabilitation interventions were selected for the RCTs, we expected to find a similar selection of participants for the CRR program in Horsens. If so, the completion might be predicted by the patients’ characteristics. This was examined in Paper II.

From the cohort of 521 COPD patients in Horsens, 81 patients started the CRR program during the follow-up study period (the 46 patients who completed and 35 who dropped out). As discussed in Paper II, we identified various reasons for not participating and for dropping out of the CRR program. Compared with the RCTs, our study of the CRR reveals a proportionately similar, large number of patients not selected for CRR. Our findings thus did not confirm the hypothesis that the patients’ characteristics predicted completion.

The basic characteristics of those 46 patients (9%) who completed the CRR program did not differ systematically from those of the other groups. This suggests that the completion rate might be low not because the program was (deliberately) targeted at specific COPD subgroup, but rather because the program as such might not be adequately tailored to the COPD patients’ particular physical and social characteristics. Besides, the hospital had a limit of approximately four courses of CRR per year, which add to the explanation of the relatively small number of CRR participants.

We found that the study population was homogeneous in a number of respects as they, relatively speaking, lacked education and almost all have had a long mainly blue collar working life. This is consistent with the evidence that those with e.g. low education suffer a heavier burden of illness than their better-off counterparts (60-62). During their childhood and adolescence, many of the subjects may have been exposed to COPD risk factors such as smoking, poor nutrition, and they may repeatedly have suffered from airway infection and maybe untreated asthma (11;56;63). The Danish study on socioeconomic status and COPD found that socioeconomic factors operating from early in life affect the adult risk of developing COPD (64;65). COPD and social economic status also parallels smoking estimates and educations level in Denmark. The proportion of smokers and heavy smokers in different education levels show that 38% among blue collar workers smoke and 23% are heavy smokers. Among those with high education 15% smoke and 4% are heavy smokers (66). The homogeneity found in our study stresses the inequality in health and may also indicate that
participation and completion cannot be explained by any of the socio economic indicators normally applied in analysis of social inequality in health (60-62;67).

The low percentage of participants indicates, that the program is neither particularly well-targeted the group of COPD patients as a whole, nor is it targeted at a specific subgroup of COPD patients e.g. the well-educated, or those with the best physical performance. Therefore, it was of interest to examine whether the patients who completed the CRR achieved the expected improvements. This topic was explored in Paper III.

**Changes in main outcomes in relation to CRR**

Based on the evidence from the RCTs, we hypothesized that completers of CRR would improve in terms of functional capacity, health-related QoL, and dyspnea. Our findings could not document such improvements, even if the program implemented was based on current evidence and even if the Hospital had made a dire effort to change practice according to guidelines.

The documented effect of rehabilitation in the RCTs might be ascribed to the selection of patients that seemingly took place in the RCTs. In these studies, rehabilitation measures were thus studied in participants whom we must expect a priori to understand the rationale of the intervention better than those who were de-selected, and to have a better understanding of the benefit of following exercise instructions and other forms of guidance. Such superior understanding and insight will allow these participants to take more active part, simply because they have the resources that enable them to do what is recommended. Furthermore, it is very likely that the emphasis and attention given to the individual participant in the RCTs (23;68;69) were much stronger that what we will find in practice, even if the guidelines for rehabilitation are followed.

The patient characteristics observed in the present clinical study seems to differ markedly from those of the RCT participants, and interventions tested in RCTs e.g. with detailed exercise instructions, seem inadequately tailored to the particular, less resourceful patient groups encountered in clinical practice.

We a priori assumed that selection of patients for clinical routine rehabilitation would mirror selection practices in the RCTs so that CRR would be offered to the best “rehabilitation candidates” who would therefore achieve results matching those obtained in RCTs. However, our results showed differently: only a minor fraction completed rehabilitation which may suggest the presence of a motivation-based selection also in clinical routine rehabilitation. In spite of such non-explicit selection, we found no improvement in traditional effect measures. This would seem to indicate that the rehabilitation program itself, i.e. its contents and
methods, did not take into sufficient consideration the physical, psychological, and social characteristics of its target population. The immediate consequences of this are that for clinical routine intervention to improve physical functioning and health-related QoL of the individual patient undergoing clinical routine rehabilitation, it must be much more closely tailored to that individual’s needs and capabilities as also suggested by Bourbeau (9).

To conclude, there may be two overriding explanations why completers did not improve in terms of 6MWD, health-related QoL, and dyspnea following CRR. First, they differ from the study populations in RCTs. We therefore cannot take for granted that rehabilitation interventions designed for RCTs will work at all in CRR for patient groups who probably differ fundamentally from RCT population groups in terms of their ability to change life style and follow instructions. Second, the CRR offered in Horsens did not match the RCTs in terms of the quality of its contents and the methods used to monitor and ascertain improvement in a non-experimental, clinical practice setting. The Hospital has guideline based on international recommendations, but there is no guarantee that such guidelines will work in CRR in clinical practice. Furthermore, we have no documentation that the guideline was followed in a strict way.
Main conclusions

The selection of participants for rehabilitation takes place in the context of RCTs and in clinical routine rehabilitation. The RCTs on rehabilitation are not sufficiently explicit about their selection of participants and the ability to draw conclusion relevant for practice is therefore impaired. Compared with the RCTs, our study of the CRR implemented at Horsens Regional Hospital reveals a proportionately similar, large number of patients not selected for CRR. Only few are offered CRR due to existing formal selection criteria even if such criteria are not always followed stringently. A minority of 9% completed the program in the study period and 23% when previously completed are included.

The patients’ characteristics did not predict completion; however, we found that almost all COPD patients in the cohort had no or only short education and the group was homogeneous, representing a lower, hard-working social class. As such we have reason to believe that they differ from those included in RCTs on rehabilitation and socio-economic differences between completers and non-completers are expected to be small due to the homogeneity of the study-population.

In general completers in clinical routine rehabilitation did not differ from the other groups and did not achieve the improvements documented in RCTs measured by common outcome measures reflecting the goals of rehabilitation.

This present study shows that the goals set for the CRR program implemented in Horsens were not met in terms of improved functional capacity health related QoL and dyspnea, although the patients subjective attitudes towards rehabilitation were positive.
Perspectives
The findings in Horsens increase the understanding of CRR and identified important areas for further scrutiny in future research or in the context of clinical quality improvement. It is necessary to more precisely define which COPD patient groups are relevant for CRR, as the criteria of FEV1 criteria due to disease severity stages seems to be inadequate. Besides, these criteria might not meet the current prevalence of COPD at different disease stages. Furthermore, it is necessary to decide on adequate contents and feasible effect measures. As such there is a need for a redefinition of the rehabilitation intervention in the context of clinical routine as the effects seen in the RCTs are not easily obtained in clinical routine. The rehabilitation interventions in RCTs are designed to reduce symptoms, optimize functional capacity and health related QoL. However, our findings imply, that CRR is facing a huge challenge in gaining the expected effects in practice. It takes a stronger and more intensive program than has so far been offered and it may require a much stronger coaching and monitoring approach and support towards patients e.g. in relation to physical training. Moreover, patient education traditionally has focused on teaching addressing e.g. the patient’s understanding of the disease and its treatment. Modern patient education aims to improve the patient’s self-management skills and self-health behaviors indicating a shift from teaching to coaching. There might be a need to change patient education in that direction.

The way forward is not to sophisticate the methods for finding explanatory factors, but instead to strive for program heterogeneity in order to optimize rehabilitation completion and effects. The implementation of CRR is already widespread and a large number of health care professionals are involved in its implementation. Therefore, the changes needed have to be discussed in the near future.

Our findings are interesting in the context of the current initiatives concerning the monitoring of clinical routine rehabilitation of COPD patients. In Central Denmark Region is has been decided to make an intensive effort towards a documentation of the effects of disease management program for COPD patients. As such tools for monitoring, relevant databases are to be developed in the near future. For such monitoring to be effective, it is necessary, to define new success indicators relevant for clinical routine and to perform regular audit of the program implemented.

The question to be answered is how rehabilitation should be delivered to patients with COPD taking into account their characteristics to ensure that relevant patients are offered appropriate rehabilitation in clinical routine.
Dansk resume

Effekten af rehabilitering af patienter med kronisk obstruktiv lungesygdom (KOL) er dokumenteret i et stort antal klinisk kontrollerede studier (RCT’er). Der er på baggrund af den foreliggende evidens udarbejdet patientforløbsprogrammer og kliniske retningslinier i Danmark. Sundhedsstyrelsen og regionerne har stor opmærksomhed på implementeringen af disse programmer. På Regionshospitalet i Horsens er der implementeret et rehabiliteringsprogram, som forventes at kunne forbedre patienternes livskvalitet, funktionsevne og symptomer. Hospitalets ledelse har ønsket en undersøgelse heraf. Dette ønske gav anledning til dette projekt, hvis overordnede formål er at forbedre grundlaget for optimal inclusion og effekt af KOL-rehabilitering.

Der var tre formål med ph.d.-projektet:

1. At undersøge den udvælgelsesproces, der foregår i RCT’er vedrørende KOL-rehabilitering, for at diskutere generaliserbarheden af resultater opnået i RCT’er.

2. At karakterisere en kohorte af KOL-patienter behandlet på Regionshospitalet med henblik på at identificere prædiktorer for gennemførelse af rehabilitering.

3. At undersøge ændringer fra baseline til followup i 6 minutters gangdistance (6MWD), livskvalitet og åndenød i relation til rehabiliteringsforløb i klinisk rutine, samt at afdække patienternes holdning og subjektive resultater i relation til rehabilitering.

Hypotesen var, at KOL-patienter, der gennemførte rehabilitering i klinisk rutine, ville opnå forbedringer, og at de ville adskille sig fra dem, der ikke gennemførte mht. livskvalitet, funktionsevne og symptomer, og at deres basiskarakteristika kunne prædiktere gennemførelsen.


I forbindelse med et review af 26 RCT’er vedrørende KOL-rehabilitering, der oprindeligt var inkluderet i en Cochrane metaanalyse fra 2007, fandt vi, at kun 3 af de 26 studier beskrev en detaljeret udvælgelsesproces. Konklusionen var, at RCT’er gav begrænset information om udvælgelsesproceduren. Reviewet rejste spørgsmålet, om de effekter af rehabilitering, der er
dokumenteret i RCT’er, kan opnås, når rehabilitering implementeres i klinisk rutine. Dette blev undersøgt i followup studiet.

Her deltog 148 patienter af en samlet population på 521 patienter behandlet i tidsperioden. 46 patienter gennemførte rehabilitering i followup-perioden, mens 35 faldt ud, 34 havde tidligere gennemført, mens 33 ikke blev tilbudt rehabilitering. Resultatet var, at de patienter, der gennemførte, havde længere 6MWD ved baseline end de øvrige grupper på trods af en signifikant lavere subjektiv oplevelse af fysisk funktion. Patientkarakteristika kunne ikke prædiktere gennemførelsen af rehabiliteringen. Vi fandt ingen forbedringer fra baseline til 12 måneders followup mht. 6MWD, livskvalitet eller åndenød blandt dem, der gennemførte rehabiliteringen. Hovedparten (89%) at de patienter, der gennemførte rehabiliteringen, vurderede, at rehabiliteringen var fremragende, meget god eller god, mens 85 procent følte, at deres fysiske formåen var forbedret.

Resultaterne fra followup-undersøgelsen understreger de vanskeligheder, der er med at overføre interventioner undersøgt i RCT’er til klinisk rutine. Det er vigtige resultater, da KOL-forløbsprogrammer er implementeret over hele landet, mens evalueringen og kvalitetssikringen kun i sparsomt omfang er medtænkt.

Forklaringer på undersøgelsens resultater fokuserer på selektion i klinisk praksis og på kvaliteten af rehabiliteringsinterventionen. Der er behov for mere viden om, hvordan man kan kvalitetssikre rehabilitering i klinisk rutine mhp. at optimere inklusion og effekt.
Summary
The effect of pulmonary rehabilitation in patients with chronic obstructive pulmonary disease (COPD) is richly documented in many randomized clinical trials (RCTs). Current evidence is the bedrock of Danish rehabilitation programs and clinical guidelines. The implementation of these programs is closely monitored by The Danish National Board of Health and the Danish regions. The Regional Hospital of Horsens has introduced a rehabilitation program with a view to improving patients’ quality of life, functional capacity and symptoms. Launched in response to the Hospital management’s request for an evaluation of this program, the present Ph.D. was launched with the main aim of optimizing the selection of rehabilitation candidates and improving the effect of the COPD rehabilitation program.

The Ph.D. project served the following three specific purposes:

1. To examine the process through which COPD rehabilitation candidates are selected for participation in RCTs to inform a discussion about the generalizability of RCT findings to the clinical setting.

2. To characterize a cohort of COPD patients treated at the Regional Hospital in Horsens with a view to identifying predictors of rehabilitation completion.

3. In a follow-up to examine changes in 6-minute walking distance (6MWD), quality-of-life and dyspnea during the course of a clinical routine rehabilitation program and to uncover the patients’ attitudes and subjective experience of rehabilitation outcomes.

We hypothesized that COPD patients completing clinical routine rehabilitation would feel better, that they would differ from non-completers in terms of quality-of-life, functional capacity and symptoms, and that their basic characteristics would predict completion.

The study was designed as a cohort study with follow-up of hospitalized or ambulatory COPD patients treated at the Regional Hospital of Horsens during the period from 1 September 2008 to 30 April 2009. The follow-up consisted of a test at baseline and after 3, 6, and 12 months.

A review of 26 RCTs on COPD rehabilitation originally included in a 2007 Cochrane meta-analysis disclosed that only three of 26 RCTs detailed how their rehabilitation candidates had been selected. We therefore concluded that the information provided by the RCTs on the principles and practices of their selection process was hardly sufficient to safely allow their
results to be extrapolated to the clinical setting. We further explored the premises and implications of this conclusion in the follow-up study.

The follow-up study included 148 of 521 patients who had been treated during the study period. Forty-six completed the rehabilitation, 35 dropped out, 34 had previously participated in the program, and 33 were not offered rehabilitation. In spite of reporting a significantly lower subjective physical functioning level, completers performed better in the 6MWD test at baseline than any of the other groups. Patient characteristics did not predict rehabilitation completion: thus, completers did not perform better than non-completers at the 12-month examination of 6MWD, quality-of-life, or dyspnea. Still, the majority (89%) of completers evaluated the rehabilitation program as excellent, very good or good, and 85% reported subjective physical improvement.

The results of the follow-up highlight the inherent problem in extrapolating the results of interventions performed in an RCT setting to a clinical routine setting. The importance of this observation should be considered in light of the nationwide spree of COPD rehabilitation programs and the scarcity of attention devoted to the evaluation and quality assurance of such programs. The results of the follow-up study are explained in terms of the principles and practices that govern selection of candidates for clinical routine rehabilitation and in terms of the quality of the rehabilitation offer. Research addressing quality assurance of inclusion and effect monitoring in clinical routine rehabilitation is needed.
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Appendices Papers (I- III), Paper published 2005 (IV) and Questionnaires (V)
Does pulmonary rehabilitation work in clinical practice? A review on selection and dropout in randomized controlled trials on pulmonary rehabilitation

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Aim: To analyze randomized controlled trials (RCTs) on pulmonary rehabilitation (PR) to determine whether the patients who complete PR form a representative subset of the chronic obstructive pulmonary disease (COPD) target population and to discuss what impact this may have for the generalizability and implementation of PR in practice.

Material and methods: A review of 26 RCTs included in a Cochrane Review 2007. We analyzed the selection at three different levels: 1) sampling; 2) inclusion and exclusion; 3) and dropout.

Results: Of 26 studies only 3 (12%) described the sampling as the number of patients contacted. In these studies 28% completed PR. In all we found, that 75% of the patients suitable for PR programs were omitted due to sampling exclusion and dropout. Most of the study populations are not representative of the target population.

Conclusion: The RCTs selected for the Cochrane review gave sparse information about the sampling procedure. The demand for high internal validity in studies on PR reduced their external validity. The patients completing PR programs in RCTs were not drawn from a representative subset of the target population. The ability to draw conclusions relevant to clinical practice from the results of the RCTs on PR is impaired.

Keywords: COPD, rehabilitation, selection, dropout, external validity

Introduction

The primary goal of pulmonary rehabilitation (PR) is to restore the patients to the highest possible level of independent function, and the target population are patients with stable chronic obstructive pulmonary disease (COPD).1–6 PR evidently seems to benefit the patients in terms of quality of life, functional capacity, symptom relief, and reductions in exacerbation of the condition and in the number of days in hospital. PR is therefore recommended in all influential guidelines based on grade A.2,3,6,7

The concept of PR rests on a large number of randomized controlled trials (RCTs) and is defined as “an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases who are symptomatic, and often have decreased daily life activities. Integrated into the individualized treatment of the patient, pulmonary rehabilitation is designed to reduce symptoms, optimize functional status, increase participation, and reduce health care costs through stabilizing or reversing systemic manifestations of the disease”.4 Patients must accordingly exercise with a certain intensity, duration and frequency, and they must be well-informed about their disease through interventions such as patient education, together with being taught...
self-help and coping strategies. In addition, the patients must perform medication and breathing techniques correctly, and they must stop smoking.

Since the 1980s, at least 600 controlled trials on COPD and rehabilitation have been published. During this period, the PR concept has expanded, specific components have been developed, and techniques have steadily become more comprehensive and sophisticated.8–10

PR is recommended in Denmark and it has therefore been suggested that any COPD patient who is registered with severe dyspnea measured with Medical Research Council Dyspnea Scale MRC grade ≥3 should be offered PR.12 However, a report from the Danish National Indicator Project13 documents that approximately only 60% (CI:59–62) of patients registered with MRC grade ≥3 are offered rehabilitation. Also there is no documentation of number of patients that complete a program or the effects of the rehabilitation. This shows that we do not know who actually completes PR nor who will benefit from it, when it is to be implemented in clinical practice.12

In general, COPD patients have extensive rehabilitation needs because their disease imposes major restrictions on their everyday life;2,4,6 however, poor adherence is common in daily practice as some patients fail to attend programs and others drop out.3,4,6,7,14–18 Our experience is that in order to optimize the resources used on PR, patients are selected so that those who are deemed to have the ability and motivation to complete a PR program are more likely to be chosen for participation than patients with poor motivation. This may entail understandable, but ethically inappropriate inequality in access to health care.

The effect of PR is well documented in RCTs and its rationale can therefore hardly be questioned as RCTs are considered to represent the most scientifically rigorous method of hypothesis testing in order to provide the best evidence.7,19 RCTs must satisfy strict quality criteria and explicit standards regarding patient selection. However, RCTs on PR often fail to adequately discuss their external validity, ie, the ability to “produce unbiased inferences regarding the target population”.19 We may therefore justifiably question whether the reported effects can indeed be generalized to the target population.

Selection in RCTs may take place at three different levels: 1) sampling; 2) inclusion and exclusion; and 3) dropout. At the sampling level, a number of COPD patients are selected among all subjects within a particular population.19 The selection criteria used prior to randomization, ie, when some patients are contacted for screening, and others are not, need to be explicit. At the inclusion/exclusion level, criteria are defined to establish the study population and to homogenize the intervention group and the control group. This level faces the risk that the patients included differ in certain aspects from those who are not included.

At these first two levels, selection is a matter of the investigator’s choice and ideally, information about all patients who are not included must be registered in order to optimize the external validity.

At the third and final level, dropout may contribute to a weakening of the internal validity; ie, dropout may cause, that the observed differences between the compared groups, may not be attributed only to the hypothesized effect under investigation.19

The challenges involved in achieving high internal and external validity makes selection of patients for PR a pertinent issue. Patients, clinicians and decision-makers need clear messages about the evidence of PR to accept its widespread application and to ensure that scarce resources can be used to good effect. Dropout is usually well-described in RCTs on PR, but information on selection performed during sampling, ie, before randomization, remains sparse. There would therefore seem to be some room for strengthening the discussion of the validity of RCTs in general, and of their external validity in particular by examining pre-randomization selection issues at greater depth.

The aim of the present study is to analyze RCTs on PR to determine whether the patients who complete PR form a representative subset of the COPD target population and to discuss what impact this may have for the generalizability and implementation of PR in practice.

Material and methods
A literature review of the RCTs originally included in the Cochrane review20 published in 2007 endeavoured “to establish the influence and the effect size of pulmonary rehabilitation on health related quality of life, functional capacity in patients with COPD”. The review stated that “Rehabilitation relieves dyspnea and fatigue, improves emotional function and enhances patients’ sense of control over their condition”. This review was chosen for this present analysis because it strived to comprehensively identify and synthesize all the literature on PR, and it is in general, well-reputed and often cited.

The Cochrane review included a total of 31 RCTs of which 26 full-text English language versions were examined. Five studies were not examined; three studies were only available as English abstracts as the articles were published in Spanish,21 French,21 and Chinese.22 Boxall23 was not used in the form, ie, congress abstract, in which it was used in the
Cochrane review, it was instead published as an article in 2006. Chlumsky 2001 was not found. Casaburi was not included in this analysis as its focus on testosterone supplementation was deemed irrelevant to the present purpose.

The 26 RCTs were analyzed with regard to their description of sampling, inclusion and exclusion criteria, and dropout illustrated in Figure 1.

Correlation analyses were performed to examine possible associations between selection criteria, disease events, the rehabilitation program, and the number of patients left out.

**Results**

The results of the analysis are described in three sections corresponding to the three levels: 1. sampling, 2. inclusion and exclusion, and 3. dropout.

1. **Sampling**

Only three (12%) out of 26 studies described the number of patients contacted (Table 1). In these studies, a total of 322 patients were contacted and out of those 151 (47%) were left out without being screened.

These three studies did not differ from the other 23 studies in relation to the number of patients randomized, inclusion or exclusion criteria, dropout, or lung function.

Details regarding the circumstances under which the studies were carried out revealed that Jones and colleagues searched computerized records to identify regular attenders at their clinic. Bendstrup and colleagues invited patients who were chosen from hospital records, however, the total number of relevant records was not described. Ringbaek and colleagues contacted the patients with moderate COPD, who were recruited from an outpatient clinic during a six-month period, however, the total number of relevant records was not described.

In brief, the size of the total COPD population, which is relevant for the external validity of the studies reviewed, is largely unknown and only a few studies were explicit about the characteristics of the populations from which the study populations were drawn. Nearly half of the patients contacted were not offered screening, and only one third of the patients contacted actually completed the PR program.

![Figure 1](image-url) The different levels of selection.
<table>
<thead>
<tr>
<th>Ref number</th>
<th>Study/aim</th>
<th>Number of patients contacted</th>
<th>Number of patients screened</th>
<th>Left out from number of patients contacted to number of patients screened (%)</th>
<th>Number of patients left out from number of patients screened to number of patients randomized (%)</th>
<th>Number of dropouts after randomization (%)</th>
<th>Patients completed (%) out of number of patients a) contacted b) screened c) randomized</th>
<th>Number of exclusion criteria a) disease-specific b) others</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>Jones 1985</td>
<td>Examine the effectiveness of inspiratory muscle training</td>
<td>52</td>
<td>38</td>
<td>14/52 (27)</td>
<td>30</td>
<td>8/38 (21)</td>
<td>9/30 (30) (5: illness, 1: lack of time, 1: social breakdown, 1: stroke, 1: lost interest)</td>
</tr>
<tr>
<td>27</td>
<td>Bendstrup 1997</td>
<td>Investigate the effects on activities of daily living QoL and exercise tolerance of an out-patient rehabilitation</td>
<td>140</td>
<td>85</td>
<td>55/140 (39)</td>
<td>42</td>
<td>43/85 (51)</td>
<td>10/42 (24) (1: died, 1: acute abdominal surgery, 1: AMI, 7: did not want to participate)</td>
</tr>
<tr>
<td>29</td>
<td>Ringbaek 2000</td>
<td>Investigate feasibility, effect and economic aspects of a rehabilitation programme consisting of two sessions a week for 8 weeks</td>
<td>130</td>
<td>48</td>
<td>82/130 (63)</td>
<td>45</td>
<td>3/48 (6)</td>
<td>7/45 (16) (3: exacerbation, 2: joint or back pain, 1: lack of time, 1: failed to appear)</td>
</tr>
<tr>
<td>Total N/ (%)</td>
<td>322</td>
<td>171 (53%)</td>
<td>151 (47%)</td>
<td>117</td>
<td>54 (44%)</td>
<td>26/117 (22%)</td>
<td>a) 91/322 (28%) b) 91/171 (53%) c) 91/117 (78%)</td>
<td>4/4</td>
</tr>
</tbody>
</table>
2. Inclusion and exclusion

Information regarding the number of patients screened and the number of patients de-selected is mainly due to inclusion and exclusion criteria, which was stated in the three above-mentioned studies (Table 1) and in five other studies (Table 2).\textsuperscript{18,33,36,39,40}

In all, eight studies screened a total of 1,040 patients of whom 406 (39\%) were de-selected before randomization, and the de-selection percentage ranged from 8\%–64\%.

Reasons for leaving out some patients were, eg, those who lived too far away or whose social circumstances affected their ability to complete the program.\textsuperscript{18} Only patients who had the ability to travel independently to a physiotherapy practice and the motivation to improve self-care were chosen for participation.\textsuperscript{33}

A study recruited patients by means of announcements and some were screened over the telephone, however, neither the exact number of responders nor the number of telephone screenings were reported.\textsuperscript{36}

In general only stable patients were randomized. The majority of the studies (18 out of 26) were not explicit regarding the number of patients deselected due to exclusion criteria.

The correlation between the proportion of patients left out from screening to randomization and the total number of patients screened showed a correlation, the Spearman’s correlation coefficient (0.643) tended to be significant ($P = 0.086$).

This indicates that the higher the number of patients screened the stricter the screening procedures were. There was no statistically significant correlation between the number of patients left out from screening to randomization and the number of diagnosis-specific inclusion and exclusion criteria ($P = 0.9$) nor the number of non-disease-specific inclusion and exclusion criteria ($P = 0.3$).

The exclusion criteria varied. Up to 6 pulmonary disease-specific exclusion criteria were used in the studies, eg, lung function, dyspnea, arterial blood gases, oxygen saturation, and smoking. One to seven non-pulmonary disease-specific criteria were used in the studies, eg, ischemic heart disease, cognitive impairment, musculoskeletal disorders, social circumstances, transport difficulties, or language barriers.\textsuperscript{18,33}

To summarize, the wide range (6\%–64\%) of patients left out from screening to randomization could not be explained by the number of explicit exclusion criteria. The analysis showed that a total of 8 (31\%)\textsuperscript{18,27–29,33,36,39,40} of the 26 articles documented the sampling procedure from screening to randomization. The rate of patients completing a PR program out of the total number of patients screened ranged from 32\% to 100\%.

3. Dropout

Dropout was described in all 26 studies (Table 3).\textsuperscript{18,24,27–34,36–46,48–52} Dropout ranged from 0\% to 36\% in the intervention groups (mean = 17 [CI: 12–22]) and from 0\% to 54\% in the control groups (mean = 15 [CI:9–22]). We found no differences in dropout between the intervention groups and the control groups ($P = 0.4$), and the correlation analysis showed a statistically significant, positive correlation (Spearman 0.72, $P = 0.00$).

The reasons for dropout can roughly be divided into two categories: “disease-related reasons,” eg, exacerbations, illness and death, and “other reasons,” eg, lack of time, motivation or cooperation (ie, patients did not want to participate, travelling difficulties, the PR-programme was too hard). In 17 out of 26 studies, “other reasons” for dropout were described.

None of the studies discussed the possibility that dropout may cause misclassification,\textsuperscript{33} or the direction of possibly biased estimates.

Altogether we found, when the size of the unknown total population was ignored, that on average, three quarters of the patients most likely suitable for PR seemed to have been de-selected, probably in a biased way, due to sampling, exclusion criteria, and dropout. None of the studies discussed generalizability and applicability.

Discussion

The present study aimed to determine whether the patients who complete PR form a representative subset of the target population. This study details aspects of patient selection for RCTs based on the sampling procedures described in the RCTs on PR included in a Cochrane review. The main result of the study is that most RCT study populations are not sufficiently representative of the COPD target population. This seriously affects the external validity of these studies and may inhibit the implementation and effects of PR in clinical practice.

The discussion is divided into four parts. The first part concerns the target population and the following three parts discuss the different levels of selection as illustrated in Figure 1.

The target population

For the sake of generalizability the study population must be drawn from a representative subset of the target population,\textsuperscript{53} which, for PR, would comprise patients diagnosed with stable COPD. However, the target population is not easily determined as the COPD prevalence is generally difficult to estimate.\textsuperscript{54–56} Firstly, population-based estimates
<table>
<thead>
<tr>
<th>Ref number</th>
<th>Study/aim</th>
<th>Number of patients screened</th>
<th>Number of patients randomized</th>
<th>Number (%) left out from screening to randomization</th>
<th>Dropout/ randomized (%)</th>
<th>Dropout reasons</th>
<th>Dropout % intervention/ control</th>
<th>Patients completed/ Number exclusion criteria disease-specific/others</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Goldstein 1994 Evaluate Respiratory rehabilitation on exercise tolerance and QoL</td>
<td>244</td>
<td>89</td>
<td>155/244 (64)</td>
<td>11/89 (12)</td>
<td>Inconvenience of travelling (1), anger (1), anxiety (2), exacerbation (3), heart disease (1), arthritis (1), smoking (2)</td>
<td>16/9</td>
<td>a) 78/244 (32) b) 78/89 (88) 4/7</td>
</tr>
<tr>
<td>33</td>
<td>Cambach 1997 Evaluate the differences in efficacy in a 3 month rehabilitation programme including drug and a program with drug alone</td>
<td>130</td>
<td>89</td>
<td>41/130 (32)</td>
<td>23/89 (26)</td>
<td>Intensity of programme too high (9), illness (5), moved away (1), refused to take part (1), full-time job (3), could not be tested within three weeks (2), did not complete final test (1), broke arm (1)</td>
<td>20/33</td>
<td>a) 66/130 (51) b) 66/89 (74) 6/5</td>
</tr>
<tr>
<td>36</td>
<td>Emery 1998 Examine the effect of exercise and education</td>
<td>92</td>
<td>79</td>
<td>13/92 (14)</td>
<td>6/79 (8)</td>
<td>Illness (4), transport difficulties (2)</td>
<td>13/4</td>
<td>a) 73/92 (79) b) 73/79 (92) 3/5</td>
</tr>
<tr>
<td>40</td>
<td>Güell 1998 To translate Chronic Respiratory Questionnaire (CRQ) and measure properties</td>
<td>65</td>
<td>60</td>
<td>5/60 (8)</td>
<td>none</td>
<td>none</td>
<td>0/0</td>
<td>a) 60/65 (92) b) 60/60 (100) 4/2</td>
</tr>
<tr>
<td>39</td>
<td>Griffiths 2000 Assess the effect of outpatient PR on use on health care and patients wellbeing</td>
<td>338</td>
<td>200</td>
<td>138/338 (41)</td>
<td>16/200 (8)</td>
<td>Death (4), missing data (12)</td>
<td>10/6</td>
<td>a) 184/338 (54) b) 184/200 (92) 3/4</td>
</tr>
<tr>
<td>Total table 2</td>
<td></td>
<td>869</td>
<td>517</td>
<td>352/869 (41)</td>
<td>56/517 (11)</td>
<td></td>
<td></td>
<td>a) 461/869 (53) b) 461/517 (89) 3/4</td>
</tr>
<tr>
<td>Total table 1 + 2</td>
<td></td>
<td>1040</td>
<td>634</td>
<td>406/1040 (39)</td>
<td>82/634 (13)</td>
<td></td>
<td></td>
<td>a) 552/1040 (53) b) 552/634 (87)</td>
</tr>
</tbody>
</table>
Table 3  Studies were only the number of patients randomized were described, number of exclusions criteria and dropout (17/26 studies)

<table>
<thead>
<tr>
<th>Ref number</th>
<th>Study/aim</th>
<th>Randomized/completed (%)</th>
<th>Exclusion disease-specific/others</th>
<th>Dropout (%) (Intervention/control %)</th>
<th>Reasons dropout</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
<td>McGavin 1977 Evaluate a training scheme carried out by the patients unsupervised at home</td>
<td>28/24 (86)</td>
<td>3/4</td>
<td>4/28 (14) (29/0)</td>
<td>lack of enthusiasm (2), depressive (1), death (1)</td>
</tr>
<tr>
<td>35</td>
<td>Cockcroft 1981 Evaluate the effects of exercise training in men with chronic respiratory disability</td>
<td>39/34 (87)</td>
<td>1/2</td>
<td>5/39 (13) (5/20)</td>
<td>deterioration in condition (2) stroke (1) abroad (1) domestic problems (1)</td>
</tr>
<tr>
<td>31</td>
<td>Booker 1984 Longterm RCT to investigate the subjective and objective effects of progressive exercise training in patients with chronic airflow limitation</td>
<td>128/102 (80)</td>
<td>1/1</td>
<td>26/128 (20) (23/15)</td>
<td>no reasons described</td>
</tr>
<tr>
<td>32</td>
<td>Busch 1988 Effects of a 18 weeks home exercise program on physical work capacity and dyspnea</td>
<td>20/14 (70)</td>
<td>1/3</td>
<td>6/20 (30) (30/30)</td>
<td>death (1), exercising of own volition (2), did not perform exercise regularly (3)</td>
</tr>
<tr>
<td>42</td>
<td>Lake 1990 Evaluate the benefit of upper-limb exercise training alone and in combination with walking training</td>
<td>28/26 (93)</td>
<td>4/7</td>
<td>2/28 (7) (7/7)</td>
<td>infection (1) cerebral attack (1)</td>
</tr>
<tr>
<td>45</td>
<td>Simpson 1992 Determine whether specific muscle training techniques are helpful</td>
<td>34/28 (82)</td>
<td>2/3</td>
<td>6/34 (18) (18/17)</td>
<td>infection (1), change in treatment (2) unknown reasons (3)</td>
</tr>
<tr>
<td>49</td>
<td>Weiner 1992 Effect of specific inspiratory muscle training combined with exercise reconditioning for six months</td>
<td>36/36 (100)</td>
<td>1/3</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>44</td>
<td>Reardon 1994 Evaluate the effect of outpatient pulmonary rehabilitation on dyspnea</td>
<td>20/20 (100)</td>
<td>3/1</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>Wijkstra 1994 Investigate the effect of home rehabilitation programme on QoL and exercise tolerance</td>
<td>45/43 (96)</td>
<td>4/4</td>
<td>2/45 (4) (7/0)</td>
<td>cerebral tumor (1), arthrosis (1)</td>
</tr>
<tr>
<td>34</td>
<td>Clark 1996 Investigate physiological effects of a 12 week programme of conditioning of peripheral muscle</td>
<td>48/48 (100)</td>
<td>1/0</td>
<td>none</td>
<td></td>
</tr>
</tbody>
</table>

(Continued)
Table 3 (Continued)

<table>
<thead>
<tr>
<th>Ref number</th>
<th>Study/aim</th>
<th>Randomized/ completed (%)</th>
<th>Exclusion disease-specific/others</th>
<th>Dropout (%) (Intervention/ Control %)</th>
<th>Reasons dropout</th>
</tr>
</thead>
<tbody>
<tr>
<td>52</td>
<td>Strijbos 1996 Effects of a 12 weeks outpatient pulmonary rehabilitation compared with home-based program</td>
<td>50/45 (90)</td>
<td>6/3</td>
<td>5/50 (10) (20/7)</td>
<td>lack of motivation (2), death (2), cancer (1)</td>
</tr>
<tr>
<td>37</td>
<td>Engstrøm 1999 To examine long-term effects of outpatients rehabilitation</td>
<td>55/50 (91)</td>
<td>5/3</td>
<td>5/55 (9) (7/11)</td>
<td>death (3), heart disease (1), did not complete (1)</td>
</tr>
<tr>
<td>30</td>
<td>Behnke 2000 Examine home-based walking training</td>
<td>46/30 (65)</td>
<td>2/3</td>
<td>16/46 (35) (34/34)</td>
<td>death (2), exacerbation (4), lack of motivation (6), unrelated diseases (4)</td>
</tr>
<tr>
<td>48</td>
<td>Troosters 2000 Investigate short- and long-term effects of 6 months programme</td>
<td>62/100 (62)</td>
<td>2/5</td>
<td>38/100 (38) (32/44)</td>
<td>refused follow-up (33), death (5)</td>
</tr>
<tr>
<td>41</td>
<td>Hernandez 2000 Investigate the effectiveness of a home-based program of exercise training</td>
<td>60/37 (62)</td>
<td>4/6</td>
<td>23/6 (38) (33/43)</td>
<td>(lack of cooperation (13), exacerbation (8), cerebral accident (1) cancer (1))</td>
</tr>
<tr>
<td>38</td>
<td>Finnity 2001 Assess the effectiveness of outpatient-based PR</td>
<td>100/55 (65)</td>
<td>3/7</td>
<td>45/100 (45) (36/54)</td>
<td>failed to attend (27), failed to continue (18) reasons not described</td>
</tr>
<tr>
<td>46</td>
<td>Singh 2003 Evaluate the effect of domiciliary PR</td>
<td>40/40 (100)</td>
<td>6/4</td>
<td>none</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Boxall 2003/2005 Evaluate a 12 week home-based PR</td>
<td>60/46 (77)</td>
<td>2/3</td>
<td>14/60 (23) (23/23)</td>
<td>hip fracture (1), exacerbation (1), exercises to hard (3), cancer (1), death (1) reasons not described (7)</td>
</tr>
</tbody>
</table>

of COPD prevalence are complicated by the variety of tools and definitions used to describe COPD.56 Secondly, COPD terminology is inconsistent and widely accepted diagnostic standards are lacking, therefore COPD coding is insufficient and COPD data often inaccurate.54 Thirdly, the method by which prevalence is estimated (expert opinion, patient reporting, symptom reporting or measurement by spirometry) influences the reported prevalence estimates.55 Furthermore patients who participate in RCTs on PR are selected among patients already in clinical practice, eg, clinic, hospital or by GP, and not amongst patients identified from prevalence studies. For these reasons the exact target population in RCTs remains more or less unknown. None of the studies in the Cochrane review discussed whether the study population was a representative subset of the target population.

Pre-randomization selection
Most studies failed to describe which patient were selected and those who were not; so information is lacking on the number of patients left out and their characteristics. Only three (12%) of the included studies were explicit about who were contacted.25–29 We have estimated that almost half (47%) of the patients were left out before screening.

Of particular concern is that none of the studies were explicit about the selection of cases and the bias this may cause. We therefore cannot be sure that the study populations were representative subsets of the target populations studied in relation to the effect of PR. This obviously leaves some severe difficulties in generalizing the findings, both in terms of capability to complete, and on the effects of participating in PR.
Representativeness should be ensured by randomly selecting the study population so that, ideally, all patients relevant for a study would have the same chance of enrolment. This requires that the investigator controls the target population and pays attention to any difference between the patients who were selected and those who were not. During this selection process, patients who, eg, were deemed not to have the ability to complete the programs, who lived too far away, or who had difficult social circumstances would be at risk of being left out. Such left out patients would likely differ from those who were included in relation to important variables, eg, incriminating psychosocial situation.

**Inclusion and exclusion criteria**

Only in 8 of the 26 studies was number of patients deselected during screening explicit (Tables 1 and 2). Approximately one third of the patients were left out. No correlation was found between the number of patients lost from screening to randomization and the number of inclusion and exclusion criteria; therefore the number of patients left out cannot be directly explained with reference to these criteria. The study populations must be pathophysiologically uniform to optimize study power and therefore strict exclusions criteria must be used. This premise is obvious but there might still be a risk that nonexplicit criteria are responsible for the number of patients left out. This complicates the implementation of PR, as it is not known whether the findings can be applied to the population which is to benefit from PR.

We assume that the reviewed RCTs a priori recruited the most motivated patients to maximize completion and compliance with the intervention. Our analysis revealed that those who declined the intervention stated a variety of reasons, eg, skepticism as to their ability to attend and to adhere to study requirements, problems of transportation. Including smokers in PR programs is often conditional on their participation in a smoking cessation program, and smokers are therefore less likely to participate.

In summary there is a risk that patients selected for participation differed from the deselected patients in relation to social factors, co-morbidity and their general health status. The selection may not have been truly random, and therefore skewed by explicit as well as non-explicit choices. Implicit criteria hinder the possibility that effects, as documented in RCTs, are to be reached, when PR is implemented in the target population.

**Dropout**

In accordance with the Helsinki declaration, dropout was described in all 26 studies. Some dropout should be expected in PR due to the natural history of COPD and therefore selection is usually carried out to reduce dropout.

Our analyses showed huge variation in dropout rates (ranging from 0% to approximately 50%). Moreover, a strong positive correlation was observed between dropout in the intervention groups and in the control groups, which means that only a small part of the dropout can be explained by the intervention. Contrary to expectation, the number of explicit exclusion criteria and the duration of the intervention did not explain the wide variation in dropout.

The patients’ own views and experiences may influence dropout, (eg, if the patients think that the programs are either, too hard, too demanding, too difficult or too easy, unlikely to be helpful, and a waste of time), in which case they will be more likely to drop out. If the patients do not feel comfortable or unsafe and not at ease with the health professionals, or with the other patients, they may also tend to drop out. Whereas the support of family and peers may enhance patient adherence. Besides, the patients’ perception of their illness and its management may have an influence. If the rehabilitation program makes common sense, in relation to the patients’ personal beliefs about their illness, completion may be more likely to be achieved. Empathic understanding and the practitioner relationship may also have some impact.

In general, the differences between completers and dropouts are unknown and it is difficult to determine, how dropout has affected the results.

**In summary**

The question raised in this study is whether the findings of the RCTs and the recommendations that emanate from the Cochrane review apply to the entire PR target population. Our analyses show uncertainty regarding the representativeness of the COPD patients who completed the PR programs.

If PR, based on RCTs, is only applicable to a limited subset of the target population, it may lead to social inequality. Patients with severe disease may be too physically impaired to actively participate in and benefit from a program. Patients with a mild disease and minimal limitations may not benefit from the program because of a lack in perceived need and motivation. Patients at different stages of COPD have different needs, as the management of mild and moderate COPD involves the avoidance of risk factors in order to prevent the progression of the disease and pharmacotherapy.
to control symptoms. Severe and very severe COPD require integration of several different disciplines, a variety of treatment approaches, and continued patient support.\(^1\)

PR is a recommended standard of care that encourages patients to undertake their own health care and to become less dependent on health professionals and expensive medical resources. PR focuses on reducing disability from the disease despite the severity. For these reasons, it is problematic that the evidence for PR rests on studies where the study population is not representative, eg, that COPD patients with co-morbidity and different social circumstances are excluded.

**Conclusion**

In conclusion, the RCTs selected for the Cochrane review comprised information about the included patients and drop-outs, though not about the sampling procedure. The internal validity was assessed in order to examine the relationship between the intervention and the treatment effect. The demand for high internal validity in studies of the effect of PR reduced their external validity, which was not assessed.

The patients completing PR programs in RCTs were not drawn from a representative subset of the target population. A number of criteria which were not explicit were used during the sampling. The studies did not meet the ideal demands for representativeness, which should be obtained by random sampling, and for equality of opportunity to participate for all patients. This impairs our ability to draw general conclusions relevant to clinical practice from the results of the RCTs on PR.

To strengthen the external validity from studies on PR, there is an extensive need for explicitness in all levels of patient selection. Studies on PR in nonselected target populations drawn from prevalence studies are needed in order to determine the number of completers and the effects gained. In addition, studies focusing on potential differences between COPD patients who complete, drop out or de-select rehabilitation are relevant when discussing how PR can be implemented to a larger proportion of the target population.

**Disclosures**

The authors have no conflicts of interest relevant to the outcome of this work.

**References**

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Participation in pulmonary rehabilitation in routine clinical practice

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3 Centre for Public Health, Aarhus, Central Denmark Region, Denmark
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Abstract

Background and Aims: Denmark offers COPD rehabilitation to enable patients to tackle the consequences of COPD, but only a minority of the patients complete these programs. To increase the completion rate, a follow-up study was performed, to characterize COPD patients and to identify potential differences between those who complete and those who do not complete rehabilitation or do not even get a rehabilitation offer in daily clinical routine.

Methods: In- and out COPD-patients who participated in baseline tests were compared in terms of completion of rehabilitation, drop-out, and no rehabilitation offer. We obtained data on basic characteristics, co-morbidity, lung-function (FEV1), dyspnea (MRC), six-minute walk-distance (6MWD), and quality of life (SF36).

Results: The source population counted 521 COPD patients of whom 256 were excluded (diagnosis withdrawn, death, moved away, long-term oxygen, severe illness). Patients who completed rehabilitation had a 15% longer 6MWD than patients not offered rehabilitation and a 10% longer 6MWD than drop-outs despite a significant lower subjective perception of physical function among completers than in the two other groups. Patients not offered rehabilitation had a slightly better lung function than the other two groups. This suggests that lower physical performance with the same (drop-outs) or even higher (not offered) lung function indicates a lower chance of completion.

Conclusion: COPD patients who could potentially benefit most from completing rehabilitation seem to be deselected. A mere 9% completed rehabilitation within the study period and 23% ever completed. This demonstrates that the political target that 60% of COPD patients should be offered rehabilitation is still far away.


Introduction

Denmark has an estimated 24% chronic obstructive pulmonary disease (COPD) prevalence among people 65–79 years of age (1), while the overall COPD prevalence among Danes 45–84 years of age is estimated to be 9% (2). Hence, the number of patients who will need treatment and rehabilitation is a serious challenge for the health-care system now and in the future. COPD management programs are being implemented in Denmark on the demand of the National Board of Health (3–5) based on international guidelines (6–11). Danish health-care services, therefore, devote much attention to the implementation of these
programs (12), although they are rarely evaluated. Many studies have documented high dropout rates, which means that only few of those for whom it is relevant complete rehabilitation (8). In randomized controlled trials (RCTs), only a minority of patients complete pulmonary rehabilitation (PR). In order to optimize participation in PR, it is interesting to characterize patients selected for PR, as well as patients deselected and patients not wanting PR (13).

A follow-up study was, therefore, designed at Horsens Regional Hospital to characterize COPD patients and to identify potential differences between those who complete and those who do not complete rehabilitation or do not even get a rehabilitation offer in daily clinical routine.

We hypothesized that all COPD patients eligible for rehabilitation according to the disease management program would be offered rehabilitation and that their basic characteristics would predict completion.

Materials and methods

The study was designed as a prospective follow-up study of a population of COPD patients (ICD-10 DJ44X) treated as inpatients or outpatients from 1 September 2008 to 30 April 2009. A baseline test was performed to characterize the patients. They were followed from baseline until completion of the rehabilitation program within the study period or until they dropped out of rehabilitation. Not all patients received an offer of rehabilitation. According to the rehabilitation program implemented at the hospital, COPD patients with a forced expiratory volume in one second (FEV1) below 50% of the predicted value or equivalent to a MRC score ≥ 3 (Medical Research Council Dyspnea Scale) were to be offered an 8-week rehabilitation program with sessions twice a week.

Every patient’s record was evaluated, and all the patients identified were consecutively invited for a baseline test from October 2008 to August 2009.

Baseline test participants

Baseline test patients were recruited from the medical ward and from the outpatient clinic. The former were extracted from the hospital administrative system’s monthly list of patients diagnosed with COPD at discharge. The latter were extracted from the outpatient clinic’s list of COPD patients attending routine visits. Patients were invited for a test by mail.

Excluded from the baseline test were patients who had moved away, had the diagnosis of COPD withdrawn, had participated in a pilot test for the present study and those who had participated in the rehabilitation program at the hospital within the preceding 1 year. The patients receiving long-term oxygen treatment were offered special treatment at home with rehabilitation and were, therefore, not included in this study population.

Those who were expected to be too ill to complete the baseline test were not invited. The criteria for not inviting patients were severe cognitive impairment, e.g. dementia, severe stroke or psychiatric disease, severe drug or alcohol abuse; severe mobility impairment, e.g. users of wheel chairs, amputees and patients with severe hip or knee disorders or very severe claudication; people living in rest homes, who were terminal ill or who did not understand Danish.

At the end of the inclusion period, the patient list from the outpatient clinic was compared with the list from the patient administrative system to ensure that all relevant COPD outpatients had been identified and referred to the baseline test. This quality assessment identified a group of 90 patients with COPD, who were not identified in the prospective study period. These patients were, therefore, not referred for the baseline test, although they were relevant.

Data collection

Data concerning the total source population were collected from patient records. Data from baseline test participants were obtained at the test and from a structured interview.

Baseline test data were obtained for FEV1 (14, 15), dyspnea as assessed from the Medical Research Council Dyspnea Scale (16, 17), walk-distance by a 6-min walk distance test (6MWD) (18) and health-related quality of life using the Short-Form 36 questionnaire (SF-36) (19). Socioeconomic data and data on hospitalizations were obtained from two national databases (Danmarks Statistik and E-Sundhed).

Statistic

The SF-36 was analyzed as normally distributed variables using raw sum scales for the eight subscales and the two summary scores. Every scale goes from 0 (poor health) to 100 (good health) (19). In the Depression Screening Questionnaire, a score above ‘0’ indicates a positive test, meaning that depression should be considered (20). The 5-point MRC dyspnea scale was transformed into a 3-point scale, so that 1 and 2 were equivalent to mild, 3 was equivalent to moderate while 4 and 5 were equivalent to severe dyspnea (21). When comparing groups, the significance level was set at 5%. Statistical analysis was performed using Stata version 11 (StataCorp LP., College Station, Texas, USA).
Results

Study population

A total of 521 COPD patients treated at the hospital during the study period were defined as the source population (Fig. 1). Excluded were 185 patients: 65 had their COPD diagnosis withdrawn, 33 patients had died and 13 patients had moved away. Another 22 patients had participated in the rehabilitation program within the preceding year and four had participated in the pilot test preceding this study. Finally, 48 patients were

Source population \((n = 521)\)

Patients diagnosed with COPD at discharge or as outpatient

Patients not relevant for baseline test \((n = 185)\)
- COPD diagnosis withdrawn \((n = 65)\)
- Death \((n = 33)\)
- Long-term oxygen \((n = 48)\)
- Moved away \((n = 13)\)
- Pilot test \((n = 4)\)
- Rehabilitation within 1 year \((n = 22)\)

The intended population of COPD patients relevant for baseline test \((n = 336)\)

Outpatients not referred for baseline test although they were relevant \((n = 90)\)

Referred and relevant for baseline test \((n = 246)\)

NOT invited for baseline test due to severe illness \((n = 71)\)

Invited for baseline test \((n = 175)\)

Did not want to participate in baseline test \((n = 27)\)

Patients in baseline test \((n = 148)\)

Patients who completed rehabilitation in the study period \((n = 46)\)

Patients who were not offered rehabilitation in the study period \((n = 67)\)

Patients who dropped out of rehabilitation in the study period \((n = 35)\)

Figure. 1. Selection of study population from source population. COPD, chronic obstructive pulmonary disease.
in long-term treatment with oxygen. The remaining 336 patients formed the intended population. Among these, 90 outpatients were not identified at the outpatient clinic and, therefore, not referred for the baseline test. This left 246 patients for the baseline test, 71 of whom were not invited for testing because of severe illness, as previously described.

A total of 175 patients were invited for the baseline test (Fig. 1). Of these, 27 did not want to participate, leaving 148 for the baseline test. These 148 patients were divided into completers \((n=46)\), dropout \((n=35)\), and patients who were not offered rehabilitation \((n=67)\).

First level of analysis

Ninety outpatients belonging to the population intended for baseline test were not referred, although this would have been relevant. For 31 patients, the patient records showed that they did not want to participate. Table 1 shows the differences between those who were not referred \((n=90)\) and those who were \((n=246)\). The patients not referred were younger [mean age 66 years vs 70 \((P=0.001)\) ], had better lung function [mean FEV1 47% vs 40% \((P=0.003)\) ] and counted statistically more nonsmokers than the patients referred for baseline test. There were statistically significantly \((P=0.034)\) more patients not referred who owned their place of residence, and a statistically significantly higher number were living alone \((P=0.013)\).

More than 90% of the 336 patients had primary school as their highest school level and had a short education or no education at all. There was no difference in this respect between the groups.

Second level of analysis

The 246 patients for whom the baseline test was relevant were divided into patients who were invited for the test and patients who were not invited because of severe illness (Table 2). Those patients not invited were older, and the MRC scores of severe dyspnea were statistically significantly higher \((P=0.0004)\). The reasons for not inviting the 71 COPD patients were that, according to their patient records, they had severe illness or were in a terminal stage of their disease. Twenty four patients had very severe mobility disorders, so that the walking test was virtually impossible (knee or hip replacements, very severe claudication, wheelchair, amputees). Thirty eight had very severe ischemic heart disease, complications due to stroke and severe psychiatric disorders (schizophrenia and dementia), so that they were not able to cope with questionnaires or the walk test. Seven patients lived in rest homes and were terminally ill, while two did not understand Danish. They differed from those invited in these respects. Data on relevant measures like FEV1 were missing for more than half of these patients. There was no difference between the groups with regard to smoking, primary school or education.

Third level of analysis

The 148 COPD patients who participated in the baseline test were divided into completers, dropouts and those who were not offered rehabilitation. The three groups were compared in relation to final rehabilitation outcome.

Table 1. Characteristics of COPD patients who were referred for baseline testing vs the patients who were not referred

<table>
<thead>
<tr>
<th></th>
<th>Referred for test ((n=246))</th>
<th>Not referred for test ((n=90))</th>
<th>(P) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex F %</td>
<td>54</td>
<td>54</td>
<td>1.00</td>
</tr>
<tr>
<td>Age mean (95% confidence interval) ((\text{range}))</td>
<td>70 (69;71) ((31–97))</td>
<td>66 (63;68) ((38–90))</td>
<td>0.001</td>
</tr>
<tr>
<td>Marital status Alone %</td>
<td>48</td>
<td>64</td>
<td>0.013</td>
</tr>
<tr>
<td>FEV1 % mean (95%CI) ((\text{range}))</td>
<td>40 (38;42) ((16–105)) ((n=208))</td>
<td>47 (44;50) ((17–77)) ((n=87))</td>
<td>0.0003</td>
</tr>
<tr>
<td>MRC % mild, moderate, severe ((\text{n}))</td>
<td>50, 30, 20 ((n=175))</td>
<td>43, 43, 14 ((n=90))</td>
<td>0.71</td>
</tr>
<tr>
<td>Body mass index mean (95%CI) ((\text{range}))</td>
<td>25 (24,25) ((13–42)) ((n=231))</td>
<td>26 (24,27) ((16–41)) ((n=89))</td>
<td>0.15</td>
</tr>
<tr>
<td>Pack years of smoking</td>
<td>42 (40;45) ((3–120)) ((n=181))</td>
<td>39 (35,43) ((9–125)) ((n=76))</td>
<td>0.18</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>57</td>
<td>40</td>
<td>0.007*</td>
</tr>
<tr>
<td>Own their place of residence %</td>
<td>51</td>
<td>64</td>
<td>0.03</td>
</tr>
<tr>
<td>Primary school or less %</td>
<td>95</td>
<td>98</td>
<td>0.12</td>
</tr>
<tr>
<td>Education short or less %</td>
<td>92</td>
<td>94</td>
<td>0.63</td>
</tr>
</tbody>
</table>

*Smoking data were missing for 36/90 among patients not referred for test. Data available on 54/90 who were nonsmokers. Calculation made on the assumption that missing data indicated current smoking.

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; MRC, Medical Research Council Dyspnea Scale.
Patient characteristics and comorbidity

No statistically significant differences were observed between the three groups in relation to age, sex, marital status, educational level or comorbidities. The patients were asked if they had depression or were being treated for depression, and a range from 18% to 24% answered in the affirmative. When using the depression screening questionnaire, a range from 54% to 66% was tested positive. No significant differences between the groups were observed. In all three groups, approximately half of the patients were current smokers with an average of about 40 pack-years of smoking.

Table 2. Characteristics of COPD patients invited for baseline test vs patients not invited

<table>
<thead>
<tr>
<th></th>
<th>Invited for test (n = 175)</th>
<th>Not invited for test (n = 71)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex F %</td>
<td>56</td>
<td>49</td>
<td>0.40</td>
</tr>
<tr>
<td>Age mean [95% confidence interval (CI)] (range)</td>
<td>68 (67,70) (31–89)</td>
<td>73 (71;76) (36–97)</td>
<td>0.0008</td>
</tr>
<tr>
<td>Marital status Alone %</td>
<td>51</td>
<td>40</td>
<td>0.12</td>
</tr>
<tr>
<td>FEV1% mean (95%CI) (range)</td>
<td>40 (38,42) (16–105) (n = 174)</td>
<td>41 (36,46) (16–74) (n = 34)</td>
<td>0.82</td>
</tr>
<tr>
<td>MRC (% mild, moderate, severe)</td>
<td>54, 30, 17 (n = 160)</td>
<td>13, 33, 54 (n = 15)</td>
<td>0.0004</td>
</tr>
<tr>
<td>Body mass index mean (95%CI) (range)</td>
<td>25 (24,25) (13–42) (n = 174)</td>
<td>24 (23,26) (13–39) (n = 57)</td>
<td>0.96</td>
</tr>
<tr>
<td>Pack years of smoking</td>
<td>42 (40,45) (10–120) (n = 160)</td>
<td>42 (33,52) (3–100) (n = 21)</td>
<td>0.10</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>53 (n = 174)</td>
<td>60 (n = 60)</td>
<td>0.37</td>
</tr>
<tr>
<td>School primary or less</td>
<td>94</td>
<td>97</td>
<td>0.52</td>
</tr>
<tr>
<td>Own their place of residence %</td>
<td>56</td>
<td>38</td>
<td>0.02</td>
</tr>
<tr>
<td>Education short or less</td>
<td>91</td>
<td>97</td>
<td>0.17</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; MRC, Medical Research Council Dyspnea Scale.

Table 3. Characteristics and comorbidities of COPD patients participating in baseline test

<table>
<thead>
<tr>
<th>Patients characteristics</th>
<th>1 Completers (n = 46)</th>
<th>2 Dropout (35)</th>
<th>3 No rehabilitation offer (67)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean [95% confidence interval (CI)] (range)</td>
<td>68 (65,70) (50–84)</td>
<td>67 (64,70) (45–83)</td>
<td>67 (66,71) (31–89)</td>
<td>0.78</td>
</tr>
<tr>
<td>Sex F %</td>
<td>54</td>
<td>54</td>
<td>57</td>
<td>0.96</td>
</tr>
<tr>
<td>Marital status Alone %</td>
<td>65</td>
<td>49</td>
<td>54</td>
<td>0.29</td>
</tr>
<tr>
<td>Own their place of residence (%)</td>
<td>69</td>
<td>51</td>
<td>53</td>
<td>0.17</td>
</tr>
<tr>
<td>School primary or less</td>
<td>89</td>
<td>97</td>
<td>94</td>
<td>0.34</td>
</tr>
<tr>
<td>Education level short or none (%)</td>
<td>84</td>
<td>97</td>
<td>91</td>
<td>0.16</td>
</tr>
<tr>
<td>Current smoker %</td>
<td>50</td>
<td>54</td>
<td>48</td>
<td>0.82</td>
</tr>
<tr>
<td>Pack years of smoking mean (95%CI) (range)</td>
<td>42 (37,48) (15–100)</td>
<td>42 (36,47) (15–90)</td>
<td>41 (36,45) (10–120)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

Comorbidity

| Non-comorbidity (%)                           | 20                    | 17              | 12                            | 0.50    |
| Diabetes (%)                                 | 7                     | 9               | 12                            | 0.63    |
| Osteoporosis (%)                             | 37                    | 41              | 33                            | 0.74    |
| Arthritis (%)                                | 34                    | 20              | 36                            | 0.24    |
| Back pain (%)                                | 32                    | 44              | 34                            | 0.50    |
| Hypertension (%)                             | 39                    | 35              | 42                            | 0.81    |
| Angina pectoris (%)                          | 14                    | 21              | 15                            | 0.68    |
| Stroke (%)                                   | 14                    | 3               | 8                             | 0.23    |
| AMI (%)                                      | 12                    | 12              | 6                             | 0.52    |
| Self-reported depression %                   | 23                    | 18              | 24                            | 0.77    |
| Depression questionnaire subscale positive test % | 30                    | 44              | 42                            | 0.89    |
| Depression questionnaire general scale positive test % | 66                    | 54              | 54                            | 0.66    |

COPD, chronic obstructive pulmonary disease; AMI, acute myocardial infarct.
Lung function, dyspnea, walk distance, body mass index and health-related quality of life (Table 4)

As expected, given the decision not to refer patients with a FEV1 above 50% to rehabilitation, such patients had a statistically significantly better lung function, but a statistically significant 15% shorter 6MWD [mean difference 63 m (Bjørnsøe et al. 2011) CI (range) 18; 107] than completers. The 35 patients who dropped out of rehabilitation had a 10% shorter 6MWD with a lung function equal to completers. Even with this well-defined exclusion criteria of FEV1 > 50% predicted, in this study of PR in clinical practice, 15 were offered and 5 actually completed PR with an FEV1 above 50%.

The groups did not differ in terms of body mass index (BMI), which ranged from extreme underweight to obesity. The proportion of severely overweight (BMI > 35) patients was approximately 6% among those who were not offered rehabilitation and among dropouts, while there were no obese patients among completers (P = 0.06).

One subscale in the health-related quality of life questionnaire, 'Role Physical Score', was statistically significantly (P = 0.025) lower among completers than among the others, which implies that this group felt physically more impaired than dropouts and patients not offered rehabilitation.

In general, the SF-36 questionnaire showed no significant differences between the groups.

Among dropouts, 25 (71%) gave reasons to abandon the rehabilitation program. Seven had employment under special conditions, e.g. modified working hours and did not want to take more time off. Two had to undergo surgery, two mentioned exhausting transportation, one dropped out for impaired vision and hearing reasons and one because of back pain. Four did not feel the need for rehabilitation and did not feel comfortable with the setup. Two felt that the program was too exhausting, in combination with other demands in their daily life situation. One was disappointed and did not want to continue. Two preferred a rehabilitation offer from the community. One did not want to continue because of exacerbations. Two dropped out as the time of the program was inconvenient. Ten (29%) did not give any reasons for not wanting to continue the rehabilitation program.

Among those not offered rehabilitation at the hospital during the study period (n = 67), 33 (49%) had previously completed rehabilitation and four was not offered rehabilitation as they already were physically active in community-based training. Twenty three (34%) had FEV1 ≥ 50% of the predicted value, and according to the stratification criteria used, they were expected to be offered community-based rehabilitation program. However, none had gotten an offer when

<table>
<thead>
<tr>
<th>Variable</th>
<th>1 Completers (n = 46)</th>
<th>2 Dropout (35)</th>
<th>3 Not offered rehabilitation (67)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC (% mild, moderate, severe)</td>
<td>(60, 33, 7)</td>
<td>(60, 29, 11)</td>
<td>(58, 21, 21)</td>
<td>0.75</td>
</tr>
<tr>
<td>FEV1% of predicted mean [95% confidence interval (CI)] (range)</td>
<td>37 (32;41) (16–83)</td>
<td>37 (34;40) (18–60)</td>
<td>44 (40;48) (17–75)</td>
<td>0.004</td>
</tr>
<tr>
<td>6MWD (m) mean 95% CI (range)</td>
<td>413 (379;447) (193–635)</td>
<td>360 (315;407) (0–540)</td>
<td>350 (322;379) (50–632)</td>
<td>0.021</td>
</tr>
<tr>
<td>Body mass index mean (95% CI) (range)</td>
<td>24 (22;25) (13–35)</td>
<td>24 (22;26) (15–39)</td>
<td>26 (24;27) (16–42)</td>
<td>0.79</td>
</tr>
<tr>
<td>Mental component score</td>
<td>56 (54;58) (32–67)</td>
<td>57 (53;61) (26–72)</td>
<td>55 (52;57) (22–67)</td>
<td>0.49</td>
</tr>
<tr>
<td>Physical component score</td>
<td>37 (34;41) (17–56)</td>
<td>40 (36;43) (16–53)</td>
<td>39 (37;41) (17–62)</td>
<td>0.59</td>
</tr>
<tr>
<td>Physical function</td>
<td>54 (46–61) (10–95)</td>
<td>53 (45;62) (10–83)</td>
<td>54 (48;60) (5–100)</td>
<td>0.99</td>
</tr>
<tr>
<td>Role physical</td>
<td>46 (34;58) (0–100)</td>
<td>65 (51;78) (0–100)</td>
<td>66 (57;76) (0–100)</td>
<td>0.03</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>74 (65;83) (22–100)</td>
<td>78 (68;88) (10–100)</td>
<td>73 (66;79) (12–100)</td>
<td>0.68</td>
</tr>
<tr>
<td>General health</td>
<td>48 (42;54) (15–92)</td>
<td>51 (43;59) (0–100)</td>
<td>50 (44;55) (0–95)</td>
<td>0.83</td>
</tr>
<tr>
<td>Vitality scale</td>
<td>58 (51;65) (10–100)</td>
<td>62 (55;79) (10–95)</td>
<td>57 (52;63) (0–100)</td>
<td>0.56</td>
</tr>
<tr>
<td>Social functioning</td>
<td>88 (82;93) (38–100)</td>
<td>86 (77;94) (13–100)</td>
<td>89 (84;93) (13–100)</td>
<td>0.79</td>
</tr>
<tr>
<td>Role emotional</td>
<td>71 (60;82) (0–100)</td>
<td>81 (71;93) (0–100)</td>
<td>78 (70;87) (0–100)</td>
<td>0.35</td>
</tr>
<tr>
<td>Mental health</td>
<td>80 (76;85) (36–100)</td>
<td>80 (72;88) (20–100)</td>
<td>78 (73;84) (0–100)</td>
<td>0.86</td>
</tr>
</tbody>
</table>

COPD, chronic obstructive pulmonary disease; FEV1, forced expiratory volume in one second; MRC, Medical Research Council Dyspnea Scale; 6MWD, 6-min walk distance test; SF-36, short-form 36 questionnaire.
asked at the follow-up test. Alternatively, they should be offered community-based exercise training, but were not. One was not offered rehabilitation because of old age. The rest were not offered rehabilitation for unknown reasons.

**Discussion**

The ideal study design for investigating both the clinical effect of PR and the various aspects of completion and dropouts would initially imply a prevalence study of well-defined COPD patients in a geographically well-defined population. Patients should be selected for rehabilitation among the prevalent cases. Such a study has not yet been performed. Clinical studies on PR have been performed on patients selected from different clinical populations (8), and the few studies actually discussing completion of rehabilitation all quote small completion percentages (22–26).

The present study is the first to investigate selection and completion in detail in a prospective explorative design. Compared with existing RCTs in rehabilitation, this study goes one step backward to explore the selection process prior to rehabilitation and characterize the total source population from which completers were drawn. We aimed to invite every single COPD patient treated at the hospital for a baseline test irrespective of his or her rehabilitation outcome. The investigator observed who and how many actually completed rehabilitation and had no influence on who attended the rehabilitation program and who did not. We found that rehabilitation was completed by a mere 16% of the source population. This proportion is smaller than reported in most other rehabilitation studies. In a previous article, we found that 16% of the source population completed a rehabilitation program (27). Thus, only three studies (22, 24, 25) included in the Cochrane review from 2007 on PR (8) described the number of patients contacted, reporting rehabilitation completion proportions in the range of 23%–40% (13); however, as opposed to the present study, these percentages were not calculated on the basis of well-described original source populations.

Figure 1 shows the selection process for the baseline test, and it seems clinically justified to have excluded a number of patients from the source population due to, e.g. diagnostic misclassification. Ignoring these patients evidently reduces the study population and increases the proportion of completers. The completion rate would go up to 14% (46/336) if the rate was calculated based on the number of patients who were initially intended to be included in the study population; and it would reach 17% (46/265) if we ignored the 71 patients with severe illness. Whichever denominator is used, the proportion of completers remains surprisingly low.

A total of 76/521 (15%) of the source population had completed the rehabilitation program at some time during the period preceding the present study period, i.e. from 2004 to August 2008. A total of 122/521 (23%) had completed the rehabilitation program at the hospital either previously or during the present study period. The target set in the Danish National Indicator Project is that 60% of the Danish COPD population with an MRC ≥ 3 should be offered rehabilitation (28). No targets are set for the proportion of completers. Taking into account that dropout rates documented in RCTs reach 50%, we must expect the proportion of completers to be small (13).

We were surprised to learn that 90 outpatients with COPD were not registered in our patient list, but showed up when secondary data quality control systems were used to identify patients. This group of COPD patients not identified in the routine clinical setting differed from the patients identified by being younger and having better lung function. This may indicate that the clinical identification system in clinical routine misses COPD patients with less serious diseases. However, other factors may also shape this bias in patient selection; deselected patients more often lived alone and more often owned their place of residence. This suggests that social factors also influence the deselection of patients in the clinical routine. For obvious reasons, this group has not been studied in detail in any previous clinical studies.

It is hardly surprising that patients who were identified, but not invited for the baseline test, were more diseased and impaired than those invited. Comparison showed that the excluded patients were older and more dyspnoeic than invited patients. In this case, the deselection of participants seems well justified as it was rooted in obvious severe physical impairment.

We analyzed clinical data in relation to outcome of PR in the 148 baseline test participants. The analysis showed few differences between the completers, dropouts and patients not offered rehabilitation, and it seems difficult to precisely predict rehabilitation completion based on patient characteristics alone.

**Completers vs dropouts**

The most obvious difference between completers and those who dropped out of rehabilitation was a shorter 6MWD among dropouts, while there was no difference in lung function or other physical conditions between...
the groups. This suggests that lower physical performance despite having the same lung function indicates a lower chance of completion.

Depression has been reported as predictor for poor adherence to training program (29). In that respect, the result from this present study is in contrast. Among completers, the proportion reporting depression was 23% compared with 18% among dropouts. However, the difference was not statistically significant ($P = 0.80$). Instead, there is a chance that completers with depression are more likely to accept rehabilitation as improved depression is an expected (30) outcome, which might be motivating.

Concerning smoking, the proportion was 50% among completers and 54% among dropouts, and this difference was not statistically significant ($P = 0.70$). In that respect, this result cannot support an expectation that smokers might be more likely to dropout.

Exacerbations have been reported to be more frequent among dropouts (31). We found that 34% among dropouts were hospitalized during follow-up compared with 26% among completers, but this difference was not statistically significant ($P = 0.50$).

**Completers vs those who were not offered rehabilitation**

Those who were not offered rehabilitation in the clinical routine had a better lung function (mean FEV1 44%) than patients who completed rehabilitation (mean FEV1 37%). Despite their better basic lung function, their mean 6MWD was 63 m (15%) shorter than the completers. This difference is clinically relevant as a minimal important clinical difference has been estimated to be 54 min (11).

Approximately 20% of the patients who were not offered rehabilitation scored themselves having severe dyspnea compared with 7% among completers. This is consistent with Schlecht et al. (32) who concluded that dyspnea did not correlate with FEV1 and, therefore, dyspnea is an important clinical indicator.

The group of completers had the poorest subscale score on physical limitations, indicating that they were encountering problems in coping with daily activities as also recently reported by Brataas et al. (33).

The poorer physical performance seen among those who were not offered rehabilitation may also be explained by their tendency to have a higher BMI. Even if the differences between the groups with a BMI above 35 fell short of reaching statistical significance ($P = 0.06$), there was a trend for obese patients not to be offered rehabilitation.

Our observation of no positive correlation between lung function and 6MWD is consistent with Spruit et al. (34). They recently concluded that determinants of walking distance are complex and depend on physical as well as psychological factors and that 6MWD can not be predicted by conventional measures of lung function. This is interesting for various reasons.

Lung function, walking distance, BMI and dyspnea are common and widely accepted as relevant functional markers in COPD (32, 35–41), e.g. survival, hospitalizations (42), severity and number of exacerbations (39). However, they might be insufficient when assessing rehabilitation completion (43). Van den Bemt et al. have recently argued that there is an insufficient documentation of better management of COPD patients when these commonly used markers are deployed (44).

This present study explored in terms of socio-demographic characteristics that almost all the patients in the source population had a school education of 7–10 years in primary school; very few had high school or equivalent education. In general, the patients had no education or a short education. Trained workmen represented a very small proportion together with people with medium-term and long-term educations. The existence of a social gradient has been documented previously in terms of respiratory mortality and COPD in a Danish study (45). The use of tiotropium also depends on education so that there was less use with lower socioeconomic status (46). In addition, hospital admissions increase (47) and mobility decrease with low education (48).

In conclusion, the results suggest that better physical performance despite lower lung function characterizes patients who completed rehabilitation. There seems to be a tendency to deselect COPD patients who could benefit the most from actually completing rehabilitation. A mere 9% completed rehabilitation within the study period and 23% ever completed. This demonstrates that the political ambition that 60% of COPD patients should be offered rehabilitation (28) is still a distant goal.

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Central Denmark Region for supervising the data management. Mette Elander Kristensen, RN, Medical Department Horsens Regional Hospital, Denmark for data collection.

References

Pulmonary Rehabilitation in Clinical Routine
- A follow-up study of completers, dropouts and those with no rehabilitation offer

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Study-design, data analysis and revision of the paper
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Data-analysis and revision of the paper
Claus Vinther Nielsen⁴
Study-design, data analysis, and revision of the paper

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Jakob Hjort, Anne-Marie Jensen, Elinborg Thorsteinsson Department of Data-management, Centre for Public Health, Central Denmark Region for supervising data management.
Mette Elander Kristensen, RN, Medical Department Horsens Regional Hospital, Denmark for data collection.

Ethics
Permission was granted by the Danish Data Protection Agency. CVR-nr 11-88-37-29 Journal number 2008-41-2294.
Abstract

The effect of pulmonary rehabilitation has been amply documented in randomized controlled trials (RCTs). Knowledge of completion rates and effects of pulmonary rehabilitation are important before its introduction in clinical routine.

The aim of the present investigation was to study changes in walk-distance (6MWD), quality of life (QoL), and dyspnoea (MRC score) in relation to clinical routine rehabilitation (CRR). We hypothesized that completers would improve 6MWD, QoL, and MRC and that their basic characteristics would predict completion.

Materials and methods: Participants in follow-up were in- and outpatients with chronic obstructive pulmonary disease (COPD). CRR completers were compared with drop-outs, those who had previously completed CRR, and those with no CRR offer. We compared changes in MRC, 6MWD, and QoL (SF36) from baseline to follow-up at 3, 6, and 12 months.

Result:
From the cohort of 521 COPD patients, 148 participated in follow-up. 6MWD was sustained from baseline to the end of rehabilitation in completers, but had declined at the 12-month follow-up. MRC and QoL did not improve. The patients’ subjective attitudes toward rehabilitation were positive: 75% felt better or much better after rehabilitation. Basic characteristics did not predict completion.

Conclusion
CRR participants were not recruited in conformity with strict criteria. CRR completers did not improve 6MWD, QoL, or MRC despite a subjective feeling of improvement. More knowledge is needed on the effects of rehabilitation in relation to individual monitoring and quality control during rehabilitation in contexts where CRR targets broad COPD populations.

Keywords: COPD; completing; dropout; outcome; rehabilitation; selection;
**Introduction**

The effect of pulmonary rehabilitation (PR) is well documented in randomized controlled trials (RCTs) and rehabilitation intervention for COPD has been investigated in Denmark (1-3). RCT evidence of PR was summarized in a meta-analysis in 1996 and in an up-date by the Cochrane Collaboration in 2007 (4;5). Rehabilitation is an important component of COPD management (6-9) and evidence-based guidelines are integrated in Danish disease management programmes (10-12).

Aiming “to reduce symptoms, improve quality of life, and increase physical and emotional participation in everyday life activities” (7), PR targets a broad population with a range of problems associated with both moderate, severe, and very severe COPD (6-8;13). The GOLD guideline states that COPD patients benefit from exercise training irrespective of disease stage (7) and suggests rehabilitation for patients with an FEV1 below 80% of the predicted value for those who activities of daily living are impaired (13). Rehabilitation addresses various aspects and consequences of COPD (6-8) and physical training, patient education, and optimized medication form therapeutic cornerstones (13).

This present study focuses on the COPD clinical routine rehabilitation (CRR) implemented at Horsens Regional Hospital in Denmark in 2003 (12) to improve quality of life (QoL) and functional capacity of COPD patients. It describes changes in six minutes walk-distance (6MWD), QoL and dyspnea and compares those who complete CRR with dropouts, those with no CRR offer, and those who previously completed CRR.

We hypothesized that completers would improve 6MWD, QoL, and MRC and that their basic characteristics would predict completion.

**Materials and Methods**

The study was a follow-up study of a population of COPD patients (ICD-10 DJ44X) treated as in– or out-patients from 1 September 2008 until 30 April 2009. The patients were followed from baseline to follow-up at 3, 6, and 12 months. During this period, they either completed a CRR programme at the hospital, dropped out, or got no CRR offer. Some had already completed the programme. The investigator was blinded to attendance. Rehabilitation was offered by hospital health professionals according to the disease management programme.
Hospital rehabilitation programme
COPD patients with a forced expiratory volume in one second (FEV1) below 50% of the predicted value or a Medical Research Council dyspnea score (MRC) equivalent to MRC≥3 were to be offered an eight-week CRR with two weekly sessions (12). Participant selection rested partly on the patient's motivation and ability to leave home. Patients with an FEV1 above 50% of the predicted value were to be offered a community-based rehabilitation programme. Each session lasted 90 min with approximately 45 min of physical training. Patients were encouraged to remain physically active at home. No target was set for the intensity of each training session or precisely defined completion.

Follow-up study participants
Patients were recruited from the medical ward and the outpatient clinic: Every month a list of the patients diagnosed with COPD upon medical ward discharge were drawn from the hospital’s administrative system. COPD patients were listed by the health care professionals at the outpatient clinic when performing routine visit. Listed patients were invited into the study by mail.

Excluded from the baseline test were patients who had moved away, whose COPD diagnosis was withdrawn, had participated in a pilot-test for the present study, or had participated in the Hospital’s rehabilitation programme the preceding year. Patients receiving long-term oxygen treatment were excluded. Patients expected to be too ill to complete the test or who were in their terminal stages were not invited. Other exclusion criteria were severe cognitive impairment, severe mobility impairment, stay at rest homes, and failure to understand Danish. Outpatient clinic patients were compared to the Hospital’s patient administrative system to ensure that every relevant COPD outpatient was listed and referred to follow-up.
We identified 90 COPD patients who had not been identified in the prospective study period. Although eligible candidates, they were not referred to follow-up.

Data collection
At baseline, patient characteristics were registered and patients answered questions concerning depression and co-morbidity. At the follow-up tests, data were obtained on FEV1, MRC (14), 6MWD (15), QoL by use of the Short-Form 36 questionnaire (SF36) (16) and a questionnaire inspired by the ICF COPD Core-Set (17).
Additional data on socio-economic factors and hospitalization were obtained from two national databases (Danmarks Statistik and E-sundhed). Rehabilitation programme completers filled in a questionnaire at the end of the eight-week programme concerning their attitudes towards the programme and their subjective outcome.
Statistics
Patients’ characteristics were described using means with 95% confidence interval for normal distributed continuous variables and proportions for categorical variables.
We compared differences at baseline and follow-up within and between the following four groups:
Patients who completed the rehabilitation programme during the study period (Completers)
Patients who dropped out of rehabilitation programme during the study period (Dropouts)
Patients with no rehabilitation offer in the study period (NRO)
Patients who had previously completed the rehabilitation programme (PC)
When calculating inter-group differences in FEV1, 6MWD, MRC, SF36, and ICF-COPD from baseline to the 12-month follow-up, patients with 12 months of follow-up were analysed separately from those lost to the 12-month follow-up.
SF-36 questionnaire was analyzed as normally distributed variables due to the Danish manual. The questionnaire has eight sub-scales and two summary scores Physical and Mental Component Score (PCS and MCS). Each scale goes from 0 (poor health) to 100 (good health). A clinically important change was set to 10 point (16).
The proportion of patients tested positive on the Depression Screening Questionnaire was calculated so that a score above “0” indicated a positive test, meaning that depression should be considered (18).
The five-point MRC dyspnea scale was transformed into three categories: 1 and 2 equivalent to mild, 3 equivalent to moderate, and 4 and 5 equivalent to severe dyspnea. Differences were tested by between group using Kruskal-Wallis equality of populations rank test and within analysis using Wilcoxon Signed Rank Test.
The ICF-inspired questionnaire, measuring the proportion of patients feeling impaired in activities of daily living (ADL), was analyzed as categorical variables with four categories: no impairment/feeling a little impaired/felling somewhat impaired/ feeling very much impaired. Chi-square was used when calculating differences between groups at baseline and Wilcoxon Signed rank test used for within group analysis from baseline to follow-up a 12 month.
For the questionnaire used at the end of the rehabilitation program proportions were calculated.
The significance level was set at 5%. Statistical analysis was performed using Stata (version 11).
Results

The follow-up study-population

A total of 521 COPD patients formed the cohort (Figure 1). Their characteristics and selection of participants for follow-up study have been detailed in a previous paper (19). Excluded were 185 patients and 90 eligible out-patients not identified at the out-patient clinic. Seventy-one patients were not invited due to very severe illness. Among the 175 patients invited for follow-up, 27 declined the invitation.

Among 148 baseline participants, 125 attended a 3-month follow-up, 110 a 6-month follow-up, and 98 were included in the final analysis at 12 months.

Figure 1 Sampling the participants for baseline test
Table 1 shows the baseline characteristics, co-morbidities and hospitalizations. A statistically significant difference in FEV1 (p=0.015) was seen between completers (mean 37 (CI 32;41)) and NRO (mean 55 (CI 49;61)). The difference in 6MWD was statistically significant (p=0.053): the longest distance was seen among completers (mean 413(CI 379;447)); the shortest among NRO (mean 350(CI 301;398)).

The proportions of patients with one or more co-morbidities ranged from 80-91% with the lowest proportion among completers. Depression was self-reported by approx. 20%, yet more than 50% tested positive in the questionnaire.

The proportion of patients hospitalized before the follow-up study was in the range 18-79%; a difference that was statistically significant with the highest proportion among NRO (p=0.00). Most treatment documentation was seen for completers.
<table>
<thead>
<tr>
<th></th>
<th>Completers (n=46)</th>
<th>Dropout (n=35)</th>
<th>NRO (n=33)</th>
<th>PC (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female (%)</td>
<td>54</td>
<td>54</td>
<td>67</td>
<td>47</td>
<td>0.45</td>
</tr>
<tr>
<td>Age mean (95%CI)</td>
<td>68(65;70)</td>
<td>67(64;70)</td>
<td>69(65;73)</td>
<td>68(65;71)</td>
<td>0.89</td>
</tr>
<tr>
<td>MRC mild/ moderate/ severe (%)</td>
<td>60/33/7</td>
<td>60/29/11</td>
<td>63/25/12</td>
<td>53/18/29</td>
<td>0.64</td>
</tr>
<tr>
<td>FEV1% of predicted mean (95%CI)</td>
<td>37(32;41)</td>
<td>37(34;40)</td>
<td>55(49;61)</td>
<td>36(31;40)</td>
<td>0.02</td>
</tr>
<tr>
<td>6 MWD (m) mean (95%CI)</td>
<td>413(379;447)</td>
<td>360(315;407)</td>
<td>350(301;398)</td>
<td>351(316;387)</td>
<td>0.05</td>
</tr>
<tr>
<td>Body Mass Index mean (95%CI)</td>
<td>24 (22;25)</td>
<td>24(22;26)</td>
<td>26(24;28)</td>
<td>26(23;28)</td>
<td>0.16</td>
</tr>
<tr>
<td>Pack years of smoking mean (95%CI)</td>
<td>42 (37;48)</td>
<td>42(36;47)</td>
<td>38(31;45)</td>
<td>43(36;50)</td>
<td>0.67</td>
</tr>
<tr>
<td>Current smoker (%)</td>
<td>50</td>
<td>54</td>
<td>55</td>
<td>41</td>
<td>0.66</td>
</tr>
<tr>
<td>Self-reported living alone %</td>
<td>13</td>
<td>3</td>
<td>15</td>
<td>3</td>
<td>0.13</td>
</tr>
<tr>
<td>Own their place of residence (%)</td>
<td>31</td>
<td>49</td>
<td>52</td>
<td>44</td>
<td>0.27</td>
</tr>
<tr>
<td>School primary or less (%)</td>
<td>89</td>
<td>97</td>
<td>97</td>
<td>91</td>
<td>0.39</td>
</tr>
<tr>
<td>Education level short or none (%)</td>
<td>84</td>
<td>97</td>
<td>94</td>
<td>88</td>
<td>0.24</td>
</tr>
<tr>
<td>Vaccination yes (%)</td>
<td>74</td>
<td>83</td>
<td>76</td>
<td>88</td>
<td>0.39</td>
</tr>
<tr>
<td>Proportion one or more co-morbidity (%)</td>
<td>80</td>
<td>83</td>
<td>91</td>
<td>85</td>
<td>0.61</td>
</tr>
<tr>
<td>Ischemic heart disease (IHD) (%)</td>
<td>55</td>
<td>50</td>
<td>70</td>
<td>41</td>
<td>0.13</td>
</tr>
<tr>
<td>Musculoskeletal problems (%)</td>
<td>64</td>
<td>74</td>
<td>61</td>
<td>72</td>
<td>0.64</td>
</tr>
<tr>
<td>Diabetes (%)</td>
<td>7</td>
<td>9</td>
<td>9</td>
<td>15</td>
<td>0.70</td>
</tr>
<tr>
<td>Self-reported depression (%)</td>
<td>23</td>
<td>18</td>
<td>21</td>
<td>27</td>
<td>0.85</td>
</tr>
<tr>
<td>General Depression Scale positive (%)</td>
<td>55</td>
<td>54</td>
<td>50</td>
<td>53</td>
<td>0.97</td>
</tr>
<tr>
<td>Proportion hospitalized within 12 month from baseline (%)</td>
<td>26</td>
<td>34</td>
<td>24</td>
<td>27</td>
<td>0.80</td>
</tr>
<tr>
<td>Proportion with more than one hospitalization within 12 months from baseline (%)</td>
<td>58</td>
<td>58</td>
<td>63</td>
<td>11</td>
<td>0.09</td>
</tr>
<tr>
<td>Proportion hospitalized prior to baseline test (%)</td>
<td>33</td>
<td>46</td>
<td>79</td>
<td>18</td>
<td>0.00</td>
</tr>
<tr>
<td>Distance to hospital less than 15 km (%)</td>
<td>65</td>
<td>60</td>
<td>72</td>
<td>64</td>
<td>0.67</td>
</tr>
<tr>
<td>Proportion hospitalized who got an exercise plan at discharge (%)</td>
<td>85</td>
<td>75</td>
<td>62</td>
<td>33</td>
<td>0.17</td>
</tr>
<tr>
<td>Proportion hospitalized who had a functional capacity measures by COPM* (%)</td>
<td>80</td>
<td>69</td>
<td>62</td>
<td>17</td>
<td>0.05</td>
</tr>
<tr>
<td>Proportion hospitalized with inhalation technique controlled before discharge (%)</td>
<td>60</td>
<td>56</td>
<td>27</td>
<td>17</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Proportion = %
6 MWD = 6 Minute Walk Distance, MRC%= Medical Research Council dyspnea questionnaire proportion with mild/moderate/severe dyspnea
COPM = Canadian Occupational Performance Measure
Table 2 shows the changes within groups from baseline test to the 12-month follow-up. Among completers 6MWD declined statistically significantly from baseline (mean 411 m) to the 12-month follow-up (mean 366 m) (p=0.007). Among PC, the 6MWD fell statistically significantly from a mean of 385 m to 336 m (p=0.05). Among dropouts and NRO, no changes in 6MWD from baseline to the 12-month follow-up were observed. In relation to FEV1, MCS and PCS there were no statistical significant changes within groups from baseline to follow-up at 12 month. In relation to MRC to proportion with severe dyspnea rose.

### Table 2

FEV1, 6MWD, MCS and PCS and MRC at baseline and 12-month follow-up

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Group</th>
<th>Number</th>
<th>Baseline test</th>
<th>12 month follow-up</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV1 (%)</td>
<td>Completers (n=35)</td>
<td>37(32;42)</td>
<td>37(33;42)</td>
<td>0.87</td>
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<tr>
<td></td>
<td>Dropout (n=20)</td>
<td>35(32;39)</td>
<td>38(33;43)</td>
<td>0.2</td>
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<tr>
<td></td>
<td>NRO (n=18)</td>
<td>56(52;60)</td>
<td>51(44;58)</td>
<td>0.15</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>36(31;42)</td>
<td>34(29;40)</td>
<td>0.1</td>
<td></td>
</tr>
<tr>
<td>6 MWD(m)</td>
<td>Completers (n=34)</td>
<td>411(375;447)</td>
<td>336/269/403</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Mean(CI)</td>
<td>Dropout (n=18)</td>
<td>401(358;444)</td>
<td>401/342/459</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NRO (n=16)</td>
<td>362(310;415)</td>
<td>363/293/433</td>
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</tr>
<tr>
<td></td>
<td>PC (n=23)</td>
<td>385(351;419)</td>
<td>336/272/399</td>
<td>0.05</td>
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</tr>
<tr>
<td>MCS</td>
<td>Completers (n=26)</td>
<td>55(52;59)</td>
<td>54(50;57)</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td>Mean(CI)</td>
<td>Dropout (n=19)</td>
<td>57(53;62)</td>
<td>57(53;60)</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NRO (n=11)</td>
<td>53(46;59)</td>
<td>50(41;58)</td>
<td>0.39</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC (n=22)</td>
<td>56(54;60)</td>
<td>58(53;61)</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>PCS</td>
<td>Completers (n=26)</td>
<td>38(33;42)</td>
<td>37(33;42)</td>
<td>0.81</td>
<td></td>
</tr>
<tr>
<td>Mean(CI)</td>
<td>Dropout (n=19)</td>
<td>41(36;42)</td>
<td>40(35;44)</td>
<td>0.55</td>
<td></td>
</tr>
<tr>
<td></td>
<td>NRO (n=11)</td>
<td>37(31;42)</td>
<td>40(30;49)</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC (n=22)</td>
<td>38(34;42)</td>
<td>36(15;55)</td>
<td>0.31</td>
<td></td>
</tr>
<tr>
<td>MRC</td>
<td>Completers (n=34)</td>
<td>68/29/3</td>
<td>54/34/12</td>
<td>0.18</td>
<td></td>
</tr>
<tr>
<td>Mild/Modera</td>
<td>Dropout (n=20)</td>
<td>65/25/10</td>
<td>70/15/15</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>te/ Severe (%)</td>
<td>NRO (n=18)</td>
<td>56/39/5</td>
<td>61/33/6</td>
<td>0.56</td>
<td></td>
</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>64/24/12</td>
<td>44/28/28</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

*Paired t-test (FEV1, 6MWD, MCS, PCS) Wilcoxon signed rank test (MRC proportions). FEV1 (%) = FEV1 % of predicted value 6MWD = 6 Minute Walk Distance MCS and PCS Mental and Physical Component score from the health related QoL SF36 questionnaire MRC%= Medical Research Council dyspnea questionnaire proportion with mild/ moderate/severe dyspnea

Figure 2 shows changes in 6MWD by group from baseline to follow-up at 3, 6 and 12 month. Completers sustained 6MWD from baseline to the end of CRR at the 3-month follow-up. (Figure 2).
Figure 2  6MWD (m) mean (CI) by group at baseline and follow-up at 3, 6 and 12 month

![6MWD graph](image)

Figure 3 shows MRC by group. Among completers, the proportion of patients with moderate and severe dyspnea rose although the change was not statistically significant (Figure 3).

Figure 3  MRC proportion with mild/moderate/severe dyspnea by group at baseline and follow-up at 3, 6 and 12 month

Completers=Compl.  NRO=NO Rehabilitation Offer, PC=Previously Completers

![MRC graph](image)
No differences within groups were seen in QoL (MCS and PCS). The lowest PCS at the 12-month follow-up was seen among completers and PC (Figures 4 and 5).

Differences between follow-up patients and those lost to follow-up are not easily explained, but the latter tended to have shorter 6MWD and the proportion of patients in this group with severe dyspnea seemed to be larger.
The overall result of the ICF-COPD-Questionnaire showed no statistically significant difference between groups. Statistically significant differences within groups were seen for seven out of nine questions (Table 3).

Table 3 ICF COPD questionnaire at baseline and 12 month follow-up

<table>
<thead>
<tr>
<th>Proportions feeling not impaired/ little impaired/ somewhat impaired</th>
<th>Follow-up</th>
<th>Baseline</th>
<th>12-month follow-up</th>
<th>p-value Wilcoxon signed rank test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carrying out daily routine</td>
<td>Completers (n=34)</td>
<td>24/32/35/9</td>
<td>24/35/38/3</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>dropout (n=20)</td>
<td>30/40/20/10</td>
<td>20/50/30/0</td>
<td>0.91</td>
</tr>
<tr>
<td></td>
<td>NRO (n=17)</td>
<td>59/6/35/0</td>
<td>29/29/29/12</td>
<td>0.02</td>
</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>24/32/28/16</td>
<td>24/20/40/16</td>
<td>0.65</td>
</tr>
<tr>
<td>Handling stress and other psychological demands</td>
<td>Completers (n=35)</td>
<td>20/26/37/17</td>
<td>26/43/26/6</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>dropout (n=20)</td>
<td>45/30/10/5</td>
<td>35/40/20/5</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>NRO (n=17)</td>
<td>12/47/35/6</td>
<td>24/41/24/12</td>
<td>0.67</td>
</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>40/20/32/8</td>
<td>28/24/28/20</td>
<td>0.09</td>
</tr>
<tr>
<td>Lifting and carrying objects</td>
<td>completers (n=34)</td>
<td>12/38/29/7</td>
<td>24/29/38/9</td>
<td>0.05</td>
</tr>
<tr>
<td></td>
<td>dropout (n=20)</td>
<td>25/55/15/5</td>
<td>30/45/20/5</td>
<td>0.89</td>
</tr>
<tr>
<td></td>
<td>NRO (n=16)</td>
<td>13/31/56/0</td>
<td>25/44/13/19</td>
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<tr>
<td>Walking</td>
<td>PC (n=25)</td>
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<td>36/8/44/12</td>
<td>0.42</td>
</tr>
<tr>
<td>Doing housework</td>
<td>completers (n=35)</td>
<td>38/26/24/12</td>
<td>38/24/32/6</td>
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<td></td>
<td>dropout (n=20)</td>
<td>45/15/25/3</td>
<td>35/40/15/10</td>
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<tr>
<td></td>
<td>NRO (n=17)</td>
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<td>41/29/12/18</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>PC (n=22)</td>
<td>36/18/41/5</td>
<td>36/14/9/41</td>
<td>0.04</td>
</tr>
<tr>
<td>Looking after one health physically</td>
<td>completers (n=35)</td>
<td>23/34/31/11</td>
<td>26/37/29/9</td>
<td>0.47</td>
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<tr>
<td></td>
<td>dropout (n=20)</td>
<td>30/40/20/10</td>
<td>35/20/35/10</td>
<td>0.56</td>
</tr>
<tr>
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<td>NRO (n=16)</td>
<td>38/25/31/6</td>
<td>13/50/25/13</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>20/32/32/6</td>
<td>20/36/28/36</td>
<td>0.71</td>
</tr>
<tr>
<td>Assisting others</td>
<td>completers (n=34)</td>
<td>47/29/15/8</td>
<td>38/27/27/9</td>
<td>0.24</td>
</tr>
<tr>
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<td>dropout (n=20)</td>
<td>50/35/5/10</td>
<td>35/40/15/13</td>
<td>0.19</td>
</tr>
<tr>
<td></td>
<td>NRO (n=16)</td>
<td>44/31/13/3</td>
<td>44/31/13/3</td>
<td>1.0</td>
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<tr>
<td></td>
<td>PC (n=24)</td>
<td>50/4/29/17</td>
<td>25/21/21/33</td>
<td>0.01</td>
</tr>
<tr>
<td>Community life</td>
<td>completers (n=31)</td>
<td>55/23/16/6</td>
<td>68/19/13/0</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>dropout (n=20)</td>
<td>68/26/0/5</td>
<td>68/16/11/5</td>
<td>0.58</td>
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<tr>
<td></td>
<td>NRO (n=17)</td>
<td>56/25/13/6</td>
<td>44/13/19/25</td>
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</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>46/29/17/8</td>
<td>42/21/25/13</td>
<td>0.16</td>
</tr>
<tr>
<td>Recreation and leisure</td>
<td>completers (n=35)</td>
<td>57/29/7/7</td>
<td>54/36/11/0</td>
<td>0.18</td>
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<tr>
<td></td>
<td>dropout (n=19)</td>
<td>53/27/13/7</td>
<td>47/33/7/13</td>
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<tr>
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<td>NRO (n=17)</td>
<td>50/29/7/14</td>
<td>43/21/29/7</td>
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</tr>
<tr>
<td></td>
<td>PC (n=25)</td>
<td>53/11/16/21</td>
<td>32/21/15/32</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Among completers, the proportion of patients feeling impaired in handling stress and other psychological demands decreased statistically significant (p=0.05) while the proportion of completers who felt impaired walking increased.

The questionnaire concerning attitudes towards CRR was answered by 41 (89%) completers (Table 4). More than 85% answered that CRR had a positive influence on their mood,
motivation for making changes in their everyday life, and their COPD coping. A total of 86% answered that their physical performance had improved. Almost everyone was satisfied with the CRR programme. Almost 75% answered that they felt somewhat or very much better.

Table 4
Questionnaire concerning attitudes toward rehabilitation and subjective outcomes answered by 41/46 (89%) among completers at the end of the rehabilitation

<table>
<thead>
<tr>
<th>How did you experience the rehabilitation program....</th>
<th>percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>to have an influence on your mood</td>
<td>Yes/ Unchanged 85/15</td>
</tr>
<tr>
<td>to have an influence on your motivation for making changes in daily activities</td>
<td>Yes/Unchanged 90/10</td>
</tr>
<tr>
<td>to give knowledge concerning COPD</td>
<td>Yes /Unchanged 95/5</td>
</tr>
<tr>
<td>to influence your community life/participation in social life</td>
<td>Yes/Unchanged 61/39</td>
</tr>
<tr>
<td>to influence your ability to cope with COPD in everyday life</td>
<td>Yes/Unchanged 85/15</td>
</tr>
<tr>
<td>to increase your physical performance</td>
<td>Yes/ Unchanged 86/14</td>
</tr>
<tr>
<td>to influence your ability to cope with activities of daily living</td>
<td>Yes /Unchanged 66/34</td>
</tr>
<tr>
<td>to influence your ability to cope with breathlessness</td>
<td>Yes/Unchanged 93/7</td>
</tr>
<tr>
<td>Compared with the time before rehabilitation how do you feel now</td>
<td>Very much better /Somewhat better /The same 34/42/24</td>
</tr>
<tr>
<td>What are your overall opinion about the rehabilitation program</td>
<td>Excellent /Very good /Good/ Do not know 63/30/7/0</td>
</tr>
</tbody>
</table>

Among dropouts 25 (71%) gave reasons for abandoning CRR. Seven had employment preventing their participation. Two had to undergo surgery, two mentioned exhausting transportation, one dropped out due to impaired vision and hearing, and one for the reason of back pain. Four did not feel comfortable with the set-up. Two felt the programme too exhausting. One was disappointed. Two preferred rehabilitation in the community. One had exacerbations. Two dropped out as CRR was inconvenient. Ten (29%) gave no reasons.

The loss to 12-month follow-up counted 50 patients (34%). Lost to follow-up among those who completed CRR during the follow-up period was 11/46 (24%). Among those who dropped out from CRR 15/35 (43%) were lost to follow-up. Among those who did not get a CRR offer in the study period 15/33 patients (45%) were lost to follow-up. Finally 9/34 (26%) among those who previously had completed CRR were lost to follow-up.

Reasons for loss to follow-up were: death (6 patients), treatment with long term oxygen (6 patients), hip fracture/fall (3 patients), dementia (2 patients), the diagnose of COPD withdrawn (4 patients), did not have the strength/did not want to continue (18 patients), did not show up at test although 2-3 appointments were made (11 patients).
**Discussion**

Surprisingly, rehabilitation completers experienced no improvement in 6MWD, QoL, and dyspnea. Although their 6MWD was sustained from baseline to follow-up at 3-month, they experienced a statistically significant 75-m decrease from baseline to the 12-month follow-up. This contrasts with the expected 48-m improvement reportedly achievable in rehabilitation (7) (13). QoL is considered the primary outcome in rehabilitation (7). A one-point decrease in SF36 PCS as seen in the present study among completers is of little clinical relevance as a 10 point increase has been set as the clinically relevant change. Recently, a 6.5 point increase in the SF36 physical component has been reported (16). Moreover a 26-point increase in one SF36 subscale (physical function) was reported (20) as was a 7.7-point increase in singing teaching as a COPD therapy (21). Improvements in SF36 for COPD patients should therefore be expected. Still, our result tally with the gradual decline recently reported in a Danish rehabilitation study (22).

The MRC dyspnea score did not improve among completers; instead, the proportion of patients with moderate and severe dyspnea rose gradually. This runs counter to expectation and other studies (5;23).

This study details the patient sampling process and characterizes follow-up participants and non-participants.

Many completers felt subjective improvement. However, the fraction that actually completed rehabilitation was small and the fraction that answered the questionnaire even smaller. The result is therefore biased. This is interesting and could imply that patients have achieved improvements in their ADL that are relevant to them but remain uncaptured by existing instruments and it has been suggested that individual goal setting could be a subjective outcome measure (24).

The large number of non-participants highlights the difficulties in COPD management. From the cohort of 521 patients only 148 (44%) joined baseline test. Non-participants were, on the one hand, the oldest and those with very severe COPD and, on the other hand, the youngest and those with mild stage COPD.

The failure of completers to improve in 6MWD, QoL, or MRC is discussed below.

**Selection of rehabilitation participants**

The target population is COPD patients with an FEV1 below 80% (13;23) irrespective of their disease severity stage because COPD patients have been shown to benefit from rehabilitation irrespective of stage (5;23;25;26). However, in the present study the rehabilitation offer had limited resources and a criterion of FEV1 <50%. Although hospital exclusion criteria were well-
defined, 15 patients were offered and five actually completed rehabilitation with an FEV1 above 50%. This bears testimony to inconsistency and shows that strict criteria are difficult to use.

FEV1 is not the sole selection criterion (23;25;26). In clinical routine, health care professionals decide who should be offered rehabilitation on the basis of FEV1 and the patient’s motivation. But as attendance is also determined by the availability of resources only four courses per year were offered. This explains why only 81 (16%) from the total number of patients (N=521) treated at the hospital in the specified time period started rehabilitation. Some patients deselected rehabilitation themselves, among others for lack of motivation. Finally, selection criteria are less tight and stringent in clinical routine than in RCTs, wherefore improvement rates documented in RCTs may not be achieved in clinical routine.

In the present study, approx. 80% had at least one additional disease: half had ischemic heart disease, almost 70% had musculoskeletal difficulties, and approx. 20% were being treated for depression. Such patients would not have been included in RCTs and the clinical effects documented in RCTs might therefore not be achieved in clinical routine where co-morbidity strongly shapes the patient’s ability to improve (25;27).

Surprisingly, completers had the longest 6MWD at baseline and the shortest 6MWD of all groups at the 12-month follow-up. They may have been dedicated and motivated at baseline and have forced themselves to do their best, but may have fallen back due to exacerbation; viz. 26% of completers had a least one exacerbation during the follow-up.

**The quality of the rehabilitation intervention**

CRR might be applied less stringently than rehabilitation in RCTs where subjects are closely followed and encouraged and the investigator assumed to have sufficient resources earmarked for the intervention. The present hospital rehabilitation program ran for eight weeks. Besides hospital training, patients were encouraged to train at home as recommended (13;28;29). Physical exercise is the cornerstone in rehabilitation and endurance improvement reportedly grows with higher training intensity among COPD patients (9;13;28-31). The lack of improvement among completers reported here could therefore be blamed on the intervention. There seem to be room for improving monitoring of training intensity and support of home training and for introduction of modern, up-to-date equipment like easily applicable heart rate monitors and pedometers in the training class as quality control (13;32). Exercise training where the intensity or duration is “increased as tolerated” is difficult to implement. Imprecisely prescribed exercise regimes may cause patients to complete training sessions at suboptimal activity levels. Monitoring exercise intensity using dyspnea rating at a 10-point dyspnea rating scale also reportedly supports intensity monitoring (33). To optimize home-based training, each patients must be equipped with a heart rate monitor and encouraged, e.g. by cell phone,
wiis, or any electronic training support. Besides monitoring heart rate and dyspnea, training must be supervised closely for the intensity to remain high (13). Health care professionals’ competences in general and their dedication to the programme in all part of the health care system in particular must be improved to ensure effective widespread implementation of CRR for COPD patients (28).

**Methods used in clinical routine rehabilitation**
In this study, the main outcome measurements express the rehabilitation goals, e.g. to optimize the functional capacity measured by 6MWD and QoL and to decrease COPD symptoms, e.g. dyspnea, measured by MRC. Our results showed that most completers reported subjective benefits which could reflect individual successful rehabilitation, meaning that the failure to respond in terms of physiological benefits does not necessarily imply unsuccessful CRR (13). This supports the implementation of individual goals as mentioned above.

**Conclusion**
Among a source population of 521 COPD patients, 46 completed a CRR programme during follow-up. Completers did not improve in terms of 6MWD, QoL, or MRC despite their subjective feeling of improvement. The 6MWD was sustained from baseline to 3 months of follow-up, but had fallen at the 12-month follow-up. The selection of participants for CRR followed no strict criteria. Despite convincing documentation, these CRR results at best show no improvements, at worst a decline. These results are valuable because of the widespread nature of COPD CRR. More knowledge is needed on monitoring and continuous quality improvement of the rehabilitation intervention applied to a broad COPD population in clinical routine.
Reference List


Comparison of Two Different Levels of Physical Training in Patients with Moderate to Severe COPD

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Abstract. Our objective was to compare the effect of a 4–week homebased low and middle intensity and frequency training program in patients with moderate to severe chronic obstructive pulmonary disease. From 124 patients hospitalized with chronic obstructive lung disease (COPD) in an 18-month period 65 fulfilled the inclusion criteria and were invited to participate. Only 31 (48%) accepted and among these only 20 patients (31% of invited) completed the 4-week study period. The walking time in seconds in a standardized treadmill walking test was unchanged after 4 weeks of low intensity training 60 minutes per week for two weekly training sessions. In contrast, the walking time in seconds increased 55% \( (p < 0.001) \) from 321 seconds to 499 seconds in 9 patients who completed 4 weeks of middle intensity training which comprised 2½ hours of training per week for 5 weekly training sessions. There was no change in lung function over the 4 weeks but the combined score for physical quality of life (physical component summary) measured by SF-36 increased \( (p < 0.05) \) with both low intensity and middle intensity physical training. In conclusion, homebased physical training, which aims at improvements in patient performance and quality of life as part of pulmonary rehabilitation programs, is only accepted by about one-third of unselected patients with moderate to severe COPD. The minimum training time necessary to improve physical performance is 2–3 hours per week of middle intensity training.

Key words: Chronic obstructive lung disease—Pulmonary rehabilitation—Physical training—Quality of life.

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Introduction

It is estimated that at least 150,000 Danish people from a total population of just above 5 million suffers from chronic obstructive pulmonary disease (COPD) [1], which corresponds to an overall prevalence among smokers of 15% [2]. More detailed age-related studies [3] find a rising prevalence with increasing age where 50% of all smokers who reach 75 years of age will suffer from COPD. The disease is characterized by irreversible reduction in lung function and progresses over years with deterioration of lung function and increasing symptoms.

As a supplement to regular drug therapy treatment, multidisciplinary rehabilitation programs, including systematic exercise training, patient education and/or psychosocial support have been introduced. Although different programs in different locations often vary widely in content and amount of scheduled training time, it is well documented [4] that rehabilitation programs overall improve exercise capacity and health-related quality of life (HRQL). Nevertheless there is a need to better define the types and intensity of training programs to achieve the best effect of exercise training [5]. The purpose of the present study was to estimate more precisely the effect of outpatient systematic training in patients with moderate to severe COPD by comparing the individual effect of two training programs with different training times and intensities.

Materials and Methods

All 124 adult patients below 70 years of age discharged with a diagnosis of COPD from the department of internal medicine, Silkeborg County Hospital from June 1st 2000 and until November 30, 2001 were evaluated for inclusion in the study. Being the only hospital in the area, the Department of Internal Medicine receives unselected patients from a mixed rural and urban population of 96,000 people. Patients invited to participate had a clinical diagnosis of COPD with varying degrees of chronic bronchitis and emphysema. They were between 40 and 70 years of age and all had a FEV₁ in stable condition of less than 60% and above 20% of predicted FEV₁. No patients were treated with home oxygen treatment and only those able to understand given information were invited to participate. Patients with reversible obstructive lung disease, with a documented reversibility of 15% or more of predicted FEV₁, and those with a known chronic disease other than lung disease that would limit their ability to perform physical training were excluded. Also patients with a known diagnosis of malignant disease were excluded. No patients were treated with oral steroids. Among the 31 patients included, a total of 20 patients completed the investigation and completed the training program. The investigation was performed as a prospective, randomized, nonblinded parallel group investigation.

Methods

Tests

The FEV₁ was measured with a vitalograph (Vitalograph Compact II) and the best of three measurements was used. A standardized walking test was performed on a treadmill (Siemens Cardio Exercise Treadmill Model 18–54). It was structured with three different levels of increasing performance. At the first level the patient walked 2 min at a speed of 2 km/h and an elevation of 5°. At the second level the speed was increased to 4 km/h at an elevation of 5°. There was a 5 minute break
between the first and second level and between the second and third level. In the third level the speed was further increased to 5 km/h (elevation 5°) and the time was extended to last until exhaustion or a maximum duration of 20 minutes. The primary variable was the walking time in seconds (0 – 24 min or 0 – 1440 sec). During the test, pulse and oxygen saturation were monitored (Novametrix Model 511 M). The patients were not allowed to take short-acting beta-2-agonists 6 h before testing.

**Questionnaire**

Quality of life was measured with the Danish version of the generic questionnaire Short Form Health Survey (SF-36) which measures quality of life in eight specific dimensions. These can be combined in two more general expressions of quality of life as physical component summary and mental component summary. Written permission for the test was obtained from The Collaborating Centre of Mental Health.

**Diary**

During the investigation all patients were requested to keep a diary with information on the frequency, duration and intensity of training just as they measured morning and evening peak flow (Mini Wright peak flow meter) where they noted the highest of three measurements. Lastly, they graded their experience of each of the two symptoms of dyspnea and coughing in an arbitrary 1 to 4 point scale.

**Intervention**

The intervention was planned as a four week home-based training program. After inclusion the patients were randomized to undergo either low intensity or middle intensity home-based training. In both groups of low or middle intensity the training was performed with sessions of graded stair-climbing exercises with a standard 18 cm high footstool and by instruction in outdoor walking trips. For stairs the frequency of climbing was defined by music where the patients either followed a step frequency of 30 steps per min (middle intensity) or 15 steps per min (low intensity). Patients randomized to middle intensity training [7] were instructed to train 5 days a week and in each training session to perform stair-climbing with a frequency of 30 steps/min for a duration of 15 min and an outdoor walking tour for 15 min with as high an intensity as possible for a total training time of 2½ h per week.

Patients randomized to low intensity training [7] were instructed to train only 2 days a week by stair-climbing with a frequency of 15 steps/min for 15 min and thereafter an outdoor walking tour for 15 min in a quiet pace. The total training time per week was 1 hour. Both groups were evaluated at days 1 and 28 for walking tests, lung function and SF-36. At day 14 they were seen as outpatients at the hospital for a compliance check and evaluation of the performed training.

**Data**

The collected data were processed in SPSS 10.0 The primary variables were walking time in seconds, quality of life and lung function while the secondary variables was the experience of symptoms and compliance. The data were analyzed with parametric tests where appropriate, otherwise the data were analyzed non-parametric.

The study was performed according to the Declaration of Helsinki II and the investigation was approved by the local ethical committee. All participating patients gave written consent.
A total of 31 were included along with 16 patients randomized to middle intensity training and 15 were randomized to low-intensity training. Only 20 patients (65%) completed the 4-week training period, 9 of whom completed middle intensity training and 11 completed low intensity training (p = 0.337). From the 65 patients invited, only 31% were included and completed the scheduled training sessions. There was a slightly higher drop-out rate (Pearson chi-square = 0.99, p = 0.32) in the middle intensity group (7/16 = 44%) than in the low intensity group (4/15 = 27%). From the basic demographic data (Table 1) there was no difference in age, body mass index, lung function or sex between patients allocated to middle intensity or those allocated to low intensity training. Patients in both groups had moderate to severe obstructive lung disease with a mean FEV1 predicted of 29% (low intensity) to 42% (middle intensity) (p = 0.059).

The measured walking time in seconds, between individual patients, as a measure of patient endurance, on the three-level treadmill walking test varied widely from below 100 sec to above 800 sec (Fig. 1). When mean walking time was compared before and after low or middle intensity training, all 9 patients who completed 4 weeks of middle intensity training increased their walking time from a mean of 321 seconds in the first test to 499 sec in the second test, an increase of 55% (p < 0.001). In comparison, the increase walking time with low intensity before and after training was only 14% (p = 0.141). Also when analyzed as changes in the two groups, the differences in both absolute (p < 0.001) and relative (p = 0.007) walking times were higher in the middle intensity group as compared to the low intensity training group. Regression analysis further showed no significant influence of sex and baseline lung function on walking time. With adjustment for sex and baseline lung function there was still significant (p < 0.001) difference in walking time between the two groups.

The increase in walking time in the middle intensity training group of 55%, expressing a larger working capacity in watt, was obtained with a similar mean pulse at the end of the walking test before and after 4 weeks of homebased training (Table 2) and thus reflects an improvement in the physical condition of

### Table 1. Mean and 95% confidence interval (CI) of basic demographic and clinical characteristics for 20 patients with COPD and randomized to either middle intensity physical training (9 patients) or low intensity physical training (11 patients) for 4-weeks

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Middle intensity training (n = 9)</th>
<th>Low intensity training (n = 11)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 (60–65)</td>
<td>63 (59–66)</td>
<td>0.858</td>
</tr>
<tr>
<td>Body mass index</td>
<td>24 (20–28)</td>
<td>25 (21–30)</td>
<td>0.592</td>
</tr>
<tr>
<td>FEV1 % predicted</td>
<td>42 (31–53)</td>
<td>29 (22–38)</td>
<td>0.059</td>
</tr>
<tr>
<td>Female (%)</td>
<td>67</td>
<td>36</td>
<td>0.370</td>
</tr>
</tbody>
</table>
the 9 patients in the middle intensity training group. Also oxygen saturation was unchanged at the end of the walking test in the middle and low intensity training groups (Table 2).

The FEV₁-predicted was unchanged in both training groups after 4 weeks of physical training (Table 2) just as peak flow measurements and patient symptom score on dyspnea and coughing (data not shown) were unchanged before and after training.

Among the 8 specific dimensions in SF-36 there was a tendency (p < 0.10) to improvement in three dimensions in the middle intensity training group but no difference before and after training in the low intensity group (Table 3). For the combined measure of questions on physical quality of life (physical component summary), both the middle and low intensity groups improved during the 4-week training period, with no difference in the mental component summary (Table 3) in either training groups.
Patient compliance with regard to training frequency was 89% of sessions completed in the group with middle intensity training and 92% completed in the group with low intensity training. As to training intensity, calculated as the total number of steps completed over the 4-week training period in percentage of calculated scheduled number of steps in the stair-climbing sessions, the middle intensity group completed 65% of number of scheduled steps while the low intensity group completed 84% of the total number of steps over the 4-week period. The reported outdoor walking distance in the middle intensity training group increased 61% over 4 weeks, while the reported distance in the low intensity group decreased slightly by 4% ($p = 0.091$).

**Discussion**

Those patients included in the present investigation were chosen from a group of patients with chronic obstructive pulmonary disease who had been hospitalized with exacerbation of their disease in a period of 18 months preceding entry into the study. The 65 patients fulfilling the inclusion criteria were thus unselected patients with COPD from a well-defined geographical area. The percentage of patients who completed the study from the number contacted 20/65 (31%) and

<table>
<thead>
<tr>
<th>SF-36 dimension</th>
<th>Middle intensity training ($n = 9$)</th>
<th>Low intensity training ($n = 11$)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 1</td>
<td>Day 28</td>
</tr>
<tr>
<td>Physical function</td>
<td>65 (40–70)</td>
<td>70 (45–85)</td>
</tr>
<tr>
<td>Role function physical</td>
<td>25 (0–100)</td>
<td>75 (0–100)</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>74 (41–100)</td>
<td>100 (41–100)</td>
</tr>
<tr>
<td>General health perceptions</td>
<td>52 (15–72)</td>
<td>57 (15–72)</td>
</tr>
<tr>
<td>Vitality</td>
<td>50 (15–85)</td>
<td>60 (20–75)</td>
</tr>
<tr>
<td>Social function</td>
<td>100 (50–100)</td>
<td>100 (50–100)</td>
</tr>
<tr>
<td>Role limitations due to emotional problems</td>
<td>66.7 (0–100)</td>
<td>66.7 (0–100)</td>
</tr>
<tr>
<td>General mental health</td>
<td>84 (48–100)</td>
<td>76 (36–88)</td>
</tr>
<tr>
<td>Physical component summary</td>
<td>36 (29–42)</td>
<td>45 (40–50)</td>
</tr>
<tr>
<td>Mental component summary</td>
<td>50 (43–57)</td>
<td>50 (42–57)</td>
</tr>
</tbody>
</table>
from the number included 20/31 (65%) were disappointingly low and illustrates that systematic physical training in patients with moderate to severe COPD only seems feasible in about one-third of patients. Previous studies on patient dropout rate most often do not report [8, 9] the exact dropout rate in relation to number of patients contacted or the basic population is ill defined [10]. In studies where the basic population is well defined and information is given on rates of completion, comparable frequencies of 29% [11], 32% [12] and 34% [13] were obtained. Likewise, the dropout rate among patients included in programs of physical training is 12–32% [11–13]. We observed a slightly (nonsignificant) higher drop-out rate with middle intensity compared to low intensity training which could suggest an increasing drop-out rate with increasing training intensity.

The present results clearly demonstrate that a program of middle intensity and frequency physical training is superior in effect to a program of low intensity training as the patients who completed the middle intensity training gained a 55% increase in walking time with an unchanged end pulse rate at testing, while the patients in the low intensity training group did not improve significantly in walking time over the 4-week training period. The best estimate of a minimum training duration and intensity from the present results is a total weekly training duration of 2–3 hours with an achievement of 50–60% of maximum pulse.

In the literature both duration of training per week and in part training intensity seems to reflect the gain in exercise capacity, as studies with a weekly training of 360 minutes show a 102% improvement in the study group [9] and a weekly training of 180 min [13] show a 25% improvement in the study group compared to control patients. Likewise has been reported [10] a 52% increase in working capacity with only 90 minutes training per week but to a level of 80% maximum pulse. On the other hand, studies with comparable lower training time with a total of 50-minute training sessions per week [14], 60 minutes per week [15] and 120 minutes per week [11] show increase in working capacity of 8%, 27% and 7%, respectively, compared to control patients.

There was no change in lung function or peak flow with physical training and this supports previous findings [8, 12, 14] of no change in FEV1 with physical training in COPD. Likewise, we found no difference in symptoms of disease, but this seems in contrast to previous findings [9, 10, 12, 14] of a decreased report of dyspnea with physical training. This could be due to the relatively low number of patients who completed the present study or to the use of the relative crude measure of dyspnea with an arbitrary 1 to 4 point scale.

Both the low and middle intensity training groups improved in SF-36 reported component summary measure on physical quality of health. This could not be explained by improvement in physical performance as the low intensity group remained unchanged, but could possibly relate to the close observation of patients by the participating health care personnel.

In this short-term controlled trial on the value of homebased physical exercise in patients with COPD we have shown that low intensity training for 60 minutes per week does not change the physical working capacity. On the other hand, much can be achieved by increasing the training amount to 2–3 hours weekly with middle intensity training for only 4 weeks. Only a minority of relevant patients
could be included and future studies could focus on increasing the participation rate in middle intensity, homebased COPD physical training programs.

References

1. Danish Institute of Clinical Epidemiology. Sundhed og sygelighed i Danmark (1987) Danish Institute of Clinical Epidemiology

Accepted for publication: 27 September 2004
Questionnaires (V)

No. 1: SF-36

No. 2: ICF-COPD questionnaire

No. 3: Depression

No. 4: Questionnaire at the end of clinical routine rehabilitation
No. 1: SF-36

Regions hospitalet i Horsens

Spørgeskema til Lungepatienter om Helbredstilstand

**VEJLEDNING:** Dette spørgeskema handler om din opfattelse af dit helbred. Oplysningerne vil give et overblik over, hvordan du har det, og hvor godt du er i stand til at udføre dine daglige gøremål.

Besvar hvert spørgsmål ved at sætte ring om det svar, der passer bedst på dig. Hvis du er i tvivl om, hvordan du skal svare, svar da venligst så godt du kan.

1. Hvordan synes du dit helbred er alt i alt? (Sæt kun én ring)
   - Fremragende 1
   - Vældig godt 2
   - Godt 3
   - Mindre godt 4
   - Dårligt 5

2. Sammenlignet med for ét år siden, hvordan er dit helbred alt i alt nu? (Sæt kun én ring)
   - Meget bedre nu end for ét år siden 1
   - Noget bedre nu end for ét år siden 2
   - Nogenlunde det samme 3
   - Noget dårligere nu end for ét år siden 4
   - Meget dårligere nu end for ét år siden 5
3. De følgende spørgsmål handler om aktiviteter i dagligdagen. Er du på grund af dit helbred begrænset i disse aktiviteter? I så fald, hvor meget? (sæt ring om ét tal for hver linie)

<table>
<thead>
<tr>
<th></th>
<th>Ja, meget begrænset</th>
<th>Ja, Lidt begrænset</th>
<th>Nej, Slet ikke begrænset</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a. Kræver aktiviteter</strong>, som fx at løbe, løfte tunge ting, deltage i anstrengende sport</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>b. Lettere aktiviteter</strong>, såsom at flytte et bord, støvsuge eller cykle</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>c. At løfte eller bære dagligvarer</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>d. At gå flere etager op ad trapper</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>e. At gå én etage op ad trapper</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>f. At bøje sig ned eller gå ned i knæ</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>g. Gå mere end én kilometer</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>h. Gå nogle hundrede meter</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>i. Gå 100 meter</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td><strong>j. Gå i bad eller tage tøj på</strong></td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
</tbody>
</table>

4. Har du inden for de sidste 4 uger, haft nogen af følgende problemer med dit arbejde eller andre daglige aktiviteter på grund af dit fysiske helbred? (sæt ring om ét tal for hver linie)

<table>
<thead>
<tr>
<th></th>
<th>JA</th>
<th>Nej</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>a. Jeg har skåret ned på den tid, jeg bruger på arbejde eller andre aktiviteter</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>b. Jeg har nået mindre, end jeg gerne ville</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>c. Jeg har været begrænset i hvilken slags arbejde eller andre aktiviteter jeg har kunnet udgøre</strong></td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>d. Jeg har haft besvær med at udføre mit arbejde eller andre aktiviteter (fx krævende det en ekstra indsats)</strong></td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>
5. Har du inden for de sidste 4 uger haft nogen af følgende problemer med dit arbejde eller andre daglige aktiviteter på grund af følelsesmæssige problemer?

(sæt ring om ét tal for hver linie)

<table>
<thead>
<tr>
<th>a. Jeg har skåret ned på den tid, jeg bruger på arbejde eller andre aktiviteter</th>
<th>JA</th>
<th>NEJ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>b. Jeg har nået mindre, end jeg gerne ville</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>c. Jeg har udført mit arbejde eller andre aktiviteter mindre omhyggeligt, end jeg plejer</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

6. Inden for de sidste 4 uger, hvor meget har dit fysiske helbred eller følelsesmæssige problemer vanskeliggjort din kontakt med familie, venner, naboer eller andre?

(sæt kun én ring)

- Slet ikke: 1
- Lidt: 2
- Noget: 3
- En hel del: 4
- Virkelig meget: 5

7. Hvor stærke fysiske smerter har du haft i de sidst 4 uger?

(sæt kun én ring)

- Ingen smerter: 1
- Meget lette smerter: 2
- Lette smerter: 3
- Middelstærke smerter: 4
- Stærke smerter: 5
- Meget stærke smerter: 6
8. Inden for de sidste 4 uger hvor meget har fysisk smerter vanskeliggjort dit daglige arbejde (både arbejde udenfor hjemmet og husarbejde)?
   (sæt kun én ring)
   - Slet ikke: 1
   - Lidt: 2
   - Noget: 3
   - En hel del: 4
   - Virkelig meget: 5

9. Disse spørgsmål handler om, hvordan du har haft det i de sidste 4 uger. Hvor stor en del af tiden i de sidste 4 uger –

   (sæt ring om ét tal for hver linie)

<table>
<thead>
<tr>
<th></th>
<th>Hele tiden</th>
<th>Det meste af tiden</th>
<th>En hel del af tiden</th>
<th>Noget af tiden</th>
<th>Lidt af tiden</th>
<th>På intet tidspunkt</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Har du følt dig veloplagt og fuld af liv?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>b. Har du været meget nervøs?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>c. Har du været så lang nede, at intet kunne opmuntre dig?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>d. Har du følt dig rolig og afslappet?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>e. Har du været fuld af energi?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>f. Har du følt dig trist til mode?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>g. Har du følt dig udslidt?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>h. Har du været glad og tilfreds?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
<tr>
<td>i. Har du følt dig træt?</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>
10. Inden for de sidste 4 uger, hvor stor en del af tiden har dit fysiske helbred eller følgesmæssige problemer gjort det vanskeligt at se andre mennesker (f.eks. besøge venner, slægtninge osv.)?

(sæt kun en ring)

<table>
<thead>
<tr>
<th></th>
<th>Hele tiden</th>
<th>Det meste af tiden</th>
<th>Noget af tiden</th>
<th>Lidt af tiden</th>
<th>På intet tidspunkt</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

11. Hvor rigtige eller forkerte er de følgende udsagn for dit vedkommende?

(sæt ring om ét tal for hver linie)

<table>
<thead>
<tr>
<th></th>
<th>Helt rigtigt</th>
<th>Overvejende Rigtigt</th>
<th>Ved ikke</th>
<th>Overvejende forkert</th>
<th>Helt forkert</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Jeg bliver nok lidt lettere syg end andre</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>b. Jeg er lige så rask som enhver anden, jeg kender</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>c. Jeg forventer, at mit helbred bliver dårligere</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>d. Mit helbred er fremragende</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>
No. 2: ICF-COPD questionnaire

Spørgeskema til patienter med kronisk lungesygdom

Indledning
På lungeafsnittet, Regionshospitalet i Horsens vil vi gerne løbende forbedre den behandling, vi giver.
Vi vil derfor gerne vide mere om, hvordan KOL påvirker din dagligdag og dine muligheder for at leve så godt med sygdommen som muligt.
Vi vil bruge svarere til at forbedre den behandling og pleje, vi tilbyder.
Vi vil derfor bede dig svare på følgende spørgsmål ved at sætte ét kryds for hvert spørgsmål.

1. De følgende spørgsmål handler om din dagligdag og almindelige opgaver

Føler du dig begrænset i at overskue daglige gøremål?
- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at klare pressede situationer?
- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at føre en længere samtale?
- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at rejse dig op fra siddende stilling?
- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
Føler du dig begrænset i at løfte og bære ting?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at gå?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at færdes udenfor hjemmet?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

2. De følgende spørgsmål handler om dine muligheder for at drage omsorg for dig selv

Føler du dig begrænset i at vaske og tørre dig?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at klare af- og påklædning?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
Føler du dig begrænset i at klare købe ind?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
- Ikke relevant

Føler du dig begrænset i at klare huslige opgaver?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
- Ikke relevant

Føler du dig begrænset i at spise varieret kost?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at holde dig i fysisk form?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

Føler du dig begrænset i at hjælpe andre?

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
3. De følgende spørgsmål handler om dine muligheder for samspil og kontakt med andre mennesker

**Føler du dig begrænset i at opreholde tæt relation til nærtstående?**

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset

**Føler du dig begrænset i at deltage i sociale arrangementer?**

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
- Ikke relevant

**Føler du dig begrænset i at dyrke din hobby?**

- Nej, jeg er ikke begrænset
- Lidt begrænset
- Noget begrænset
- Meget begrænset
- Ikke relevant

Med venlig hilsen

Overlæge Tina Brandt Sørensen
Lungesygeplejerske Mette Elander Kristensen
Ph.d. stud. Bodil Bjørnshave
Lungeafsnittet medicinsk afdeling
Regions hospitalet i Horsens
No. 3: Depression

**Regionshospital i Horsens**
**Spørgeskema om angst og depression**

**I de sidste 4 uger, hvor meget har du været generet af:**
(sæt ét kryds i hver linje)

<table>
<thead>
<tr>
<th></th>
<th>Slet</th>
<th>Ikke</th>
<th>Lidt</th>
<th>Noget</th>
<th>En heltel</th>
<th>Virkelig meget</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nervøsitet eller indre uro?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>At bekymre dig for meget?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>At føle dig ængstelig</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>At føle dig uden håb for fremtiden?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>En følelse af, at alting er anstrengende?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>Anfald af rædsel eller panik?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>At føle dig nedtrykt?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>En følelse af ingenting at være værd?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>Tanker om at gøre en ende på dit liv?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>En følelse af at være fanget i en fælde?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>At føle dig ensom?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
<tr>
<td>Selvbebrejdelser?</td>
<td>☐ 1</td>
<td>☐ 2</td>
<td>☐ 3</td>
<td>☐ 4</td>
<td>☐ 5</td>
<td></td>
</tr>
</tbody>
</table>
No. 4:
Questionnaire at the end of clinical routine rehabilitation

Spørgeskema til KOL-patienter
der har gennemført lungeskole

Hvor lang tid gik der fra du blev tilbudt lungeskole til du begyndte?

- mindre end 2 måneder
- mellem 2 og 4 måneder
- mellem 4 og 6 måneder
- mere end 6 måneder

I hvilken grad har du oplevet at lungeskolen har haft indflydelse på dit humør?

- Det har haft en særdeles positiv indflydelse på mit humør
- Det har haft en nogenlunde positiv indflydelse på mit humør
- Mit humør er uændret
- Det har haft en negativ indflydelse på mit humør
- Det har haft en særdeles negativ indflydelse på mit humør

I hvilken grad oplever du, at lungeskolen har motiveret dig til at foretage ændringer i din hverdag?

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke

I hvilken grad oplever du, at lungeskolen har givet dig mere viden om din lungesygdom?

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke
I hvilken grad oplever du, at lungeskolen har haft indflydelse på dit overskud til at deltage sociale aktiviteter?

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke

I hvilken grad oplever du, at lungeskolen har været en hjælp til at klare hverdagen med din sygdom?

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke

I hvilken grad oplever du, at lungeskolen har forbedret din fysiske udhdenhed? (at gå, gå på trapper, komme omkring)

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke

I hvilken grad oplever du, at lungeskolen har været en hjælp til at klare dine daglige gøremål? (f.eks. indkøb, madlavning, personlig pleje)

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke
I hvilken grad oplever du, at lungeskolen har været en hjælp til at håndtere åndenød?

- I høj grad
- I nogen grad
- Det er uændret
- I ringe grad
- Slet ikke

Det følgende handler i hvordan du har oplevet at deltage på Lungeskolen

I hvilken grad følte du dig tryg ved at skulle deltage?

- I høj grad
- I nogen grad
- I ringe grad
- Slet ikke
- Ved ikke

I hvilken grad følte du, at du kunne overskue det, der skulle ske?

- I høj grad
- I nogen grad
- I ringe grad
- Slet ikke
- Ved ikke

I hvilken grad følte du dig velkommen?

- I høj grad
- I nogen grad
- I ringe grad
- Slet ikke
- Ved ikke
I hvilken grad følte du, at du fik tingene fortalt på en god og overskuelig måde

- I høj grad
- I nogen grad
- I ringe grad
- Slet ikke
- Ved ikke

I hvilken grad har du kunnet gennemføre den fysiske træning, som du er instrueret i?

- I høj grad
- I nogen grad
- I ringe grad
- Slet ikke
- Ved ikke

I hvilken grad har du været forpustet mens du gennemførte træningen?

- Ja hele tiden
- Det meste af tiden
- En del af tiden
- Noget af tiden
- Lidt af tiden
- På intet tidspunkt

Hvordan synes du lungeskolens har været alt i alt?

- Fremragende
- Vældig god
- God
- Mindre god
- Dårlig
Sammenlignet med tiden før lungeskolen, hvordan har du alt i alt nu?

- Meget bedre end før
- Noget bedre end før
- Nogenlunde det samme
- Noget dårligere end før
- Meget dårligere end før

Hvad synes du, at du har fået mest ud af ved at deltage på lungeskolen?

________________________________________________________________________

________________________________________________________________________

Hvad har du fået mindst ud af ved at deltage på lungeskolen?

________________________________________________________________________

________________________________________________________________________

Hvad kunne du tænke dig anderledes ved på lungeskolen?

________________________________________________________________________

________________________________________________________________________

Hvis du har kommentarer er du meget velkommen til at skrive dem her.

________________________________________________________________________

________________________________________________________________________

________________________________________________________________________

Med venlig hilsen

Tina Brandt Sørensen overlæge
Mette E. Kristensen lungesygeplejerske
Bodil Bjørnshave sygeplejerske ph.d. studerende