

# Long-Term Efficacy of Pulmonary Rehabilitation in Patients with Occupational Respiratory Diseases

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### Key Words

Pulmonary rehabilitation · Occupational respiratory disease · Physical performance · Psychosocial factors · Dyspnea

### Abstract

**Background:** Pulmonary rehabilitation is a well-recognized treatment option in chronic obstructive lung disease improving exercise performance, respiratory symptoms and quality of life. In occupational respiratory diseases, which can be rather cost-intensive due to the compensation needs, very little information is available. **Objectives:** This study aims at the evaluation of the usefulness of pulmonary rehabilitation in patients with occupational respiratory diseases, partly involving complex alterations of lung function and of the sustainability of effects. **Methods:** We studied 263 patients with occupational respiratory diseases (asthma, silicosis, asbestosis, chronic obstructive pulmonary disease) using a 4-week inpatient rehabilitation program and follow-up examinations 3 and 12 months later. The outcomes evaluated were lung function, 6-min walking distance (6MWD), maximum exercise capacity (Wmax), skeletal muscle strength, respiratory symptoms, exacerbations and associated medical consultations, quality of life (SF-36, SGRQ), anxiety/depression (HADS) and Medical Research Council and Baseline and Transition Dyspnea Index scores. **Results:** Compared to baseline, there were significant ( $p < 0.05$ ) improvements in 6MWD, Wmax and muscle strength immediately after rehabilitation, and these were maintained over 12 months ( $p < 0.05$ ). Effects were less pronounced in asbestosis. Overall, a significant reduction in the rate of exacerbations by 35%, antibiotic therapy by 27% and use of health care services by 17% occurred within 12 months after rehabilitation. No changes were seen in the questionnaire outcomes. **Conclusions:** Pulmonary rehabilitation is effective even in the complex settings of occupational respiratory diseases, providing sustained improvement of functional capacity and reducing health care utilization.

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sion (HADS) and Medical Research Council and Baseline and Transition Dyspnea Index scores. **Results:** Compared to baseline, there were significant ( $p < 0.05$ ) improvements in 6MWD, Wmax and muscle strength immediately after rehabilitation, and these were maintained over 12 months ( $p < 0.05$ ). Effects were less pronounced in asbestosis. Overall, a significant reduction in the rate of exacerbations by 35%, antibiotic therapy by 27% and use of health care services by 17% occurred within 12 months after rehabilitation. No changes were seen in the questionnaire outcomes. **Conclusions:** Pulmonary rehabilitation is effective even in the complex settings of occupational respiratory diseases, providing sustained improvement of functional capacity and reducing health care utilization.

### Introduction

Pulmonary rehabilitation is an established component in the therapy of patients with chronic obstructive pulmonary disease (COPD) [1]. The main goals are improvement of exercise capacity, maintenance of independent function in daily life and reduction of respiratory symptoms. While the efficacy has been demonstrated in

COPD, the effects are less clear in other respiratory diseases such as fibrosis or asthma [2–6].

In Germany, the most frequent occupational respiratory diseases are asthma induced by allergens or toxic substances, pneumoconiosis due to inhalation of asbestos or silicate dust, and COPD in coal miners. The underlying functional impairments are reversible or irreversible airway obstruction, restrictive lung disorders, or a complex combination. As a part of their duties the social accident insurances enforce tertiary prevention using all appropriate means including rehabilitation.

This longitudinal study evaluated short- and long-term effects of a pulmonary rehabilitation program performed in two specialized German rehabilitation clinics, Falkenstein and Bad Reichenhall, both operated by social accident insurances.

## Methods

### Study Design and Subjects

The study was a longitudinal prospective clinical trial with pre-to-post comparisons. Inpatient rehabilitation lasted 4 weeks. Baseline evaluation was performed during the first 2 days of admission (abbreviated as T1/T2), and final examination on the last day (T3). Subjects were encouraged to maintain their physical activity after discharge, without being offered a maintenance program. Two follow-up examinations, after 3 (T4) and 12 months (T5), were conducted in the same clinic in which the patients had undergone rehabilitation.

The recruiting criteria were: (a) recognized occupational respiratory disease diagnosed as asthma, asbestosis, silicosis or COPD in coal miners, (b) reduction in earning capacity by 20–50%, (c) age  $\leq 70$  years, (d) no rehabilitation in the previous 2 years, (e) maximum exercise capacity of at least 40 W and (f) no progressive malignant diseases.

This study was approved by DGUV according to official ethic regulations (Project No. FFFB0094). Patients gave their informed consents.

### Rehabilitation Program

Duration, type of training and minimum number of training sessions were pre-defined in order to standardize the rehabilitation program. Subjects were excluded if they did not complete the minimum numbers:

Session-type	Number of sessions
Endurance-training (treadmill or ergometer)	17
Gymnastics	15
Skeletal muscle strength training	10
Nordic walking	9
Breathing exercises	8
Relaxing techniques	7
Nutritional education	2

The program was individually tailored. Training workload started at 60% of baseline ergometer maximum load. The training was supervised and duration and workload were adapted to progression. Peripheral muscles of the upper and lower extremities were trained to the same degree on fitness devices.

### Assessments

On all study days the same data were collected; the assessments are listed in table 1. The prevalence of exacerbations and use of health care services within the 12 months before and after rehabilitation were assessed at T1/T2 and T5.

### Statistical Analysis

For data description, absolute and relative frequencies as well as mean values and standard deviations (SD), ranges or standard errors of mean (SEM) were computed. At baseline, subgroups were compared with each other using one-way analysis of variance (ANOVA) and  $\chi^2$  tests of contingency tables.

To evaluate intraindividual changes over time, values of continuous variables were compared using repeated measures analysis of variance (ANOVA). If overall differences were statistically significant, appropriate post hoc multiple comparisons were made using the Student-Newman-Keuls multiple range test. The total group and the individual groups (asthma, asbestosis, silicosis, COPD) were analyzed. The adequacy and admissibility of ANOVA was checked by standard procedures regarding data distributions and residuals.

The Wilcoxon signed rank matched-pairs test was used to compare the rates of secondary outcomes within the 12-month periods before and after rehabilitation.

Statistical significance was defined as  $p < 0.05$ . All analyses were performed with SAS software (version 9.2; SAS Institute Inc., Cary, N.C., USA).

## Results

Between 2007 and 2010, 263 patients completed a 4-week inpatient pulmonary rehabilitation program as well as two follow-up evaluations up to 1 year after intervention. The characteristics of the patient groups are shown in table 2. There were significantly fewer females in all subgroups ( $p < 0.05$  for each); 80% of the ever-smokers had quit smoking at least 1 year before intervention.

In tables 3a–d, baseline data (T1/T2) describing exercise capacity, quality of life and dyspnea are presented, as well as data at the end of rehabilitation (T3) and the follow-up evaluations after 3 (T4) and 12 months (T5). At baseline the percent predicted forced vital capacity (FVC%pred) was significantly ( $p < 0.05$ ) lower in asbestosis, while the percent predicted forced expiratory volume in 1 second (FEV<sub>1</sub>%pred) was similar in all groups. Six-minute walking distance (6MWD) was shorter in COPD and silicosis patients compared to the two other groups ( $p < 0.05$  for each). Overall, the participants exhibited mild to moderate impairment of lung function and

**Table 1.** Tests, questionnaires and other measures used to determine the effects of rehabilitation in the study

Type of test	Measures assessed
Spirometry (Master Screen Body, Care Fusion, Germany)	FEV <sub>1</sub> , FVC, VC, Tiffeneau index; using standard quality criteria
Respiratory muscle force (Master Screen Body, Care Fusion, Germany)	P <sub>i</sub> <sub>max</sub> , P <sub>0,1</sub> ; as indices of potential limitation in respiratory muscle function and load
6-minute walking test according to ATS-guidelines, 30 m oval parcour (Pulsoximeter, Konica/Minolta, Japan)	6MWD, Borg-scale, heart rate, O <sub>2</sub> -saturation before and after test
Ergometer (Master Screen CPX, Care Fusion, Germany; e-Bike Basic PC Plus-Ctrl, ergoline GmbH, Germany) starting at 30 W, increased by 20 W every 2 min until symptom limitation	Wmax, heart rate and blood pressure continuously; arterial blood gases and lactate before and at maximum workload
Handgrip force by hydraulic hand dynamometer (Jamar, Sammons Preston Inc., Ont., Canada)	Best of 3 tests, results in kilograms
Quadriceps force (DigiMax Muskelfunktionstest, Mechatronic, Germany)	Maximum isometric knee extension, hip and knee in 90° flexion, best of 3 tests, results in kilograms
Health-related quality of life	SF-36 SGRQ HADS
Dyspnea	MRC BDI, TDI
Respiratory infections/exacerbations Doctors consultations Antibiotic courses Hospital admissions	Self-reported number of incidents in the 12 months before and after rehabilitation

FEV<sub>1</sub> = Forced expiratory volume in 1 second; FVC = forced vital capacity; Tiffeneau index = ratio of FEV<sub>1</sub> to FVC; P<sub>i</sub><sub>max</sub> = maximum inspiratory pressure; P<sub>0,1</sub> = pressure 1,200 ms after normal inspiration; 6MWD = 6-minute walking distance Wmax = maximum work load; SF-36 = 36-Item Short Form Health Survey; SGRQ = St. George's Respiratory Questionnaire; HADS = Hospital Anxiety and Depression Scale; MRC = Medical Research Council Dyspnea Scale; BDI, TDI = Baseline and Transition Dyspnea Index.

**Table 2.** Baseline characteristics of patients

Patient characteristics	Value
Total, n	263
Gender (female/male), n	22/241
Age, years	64 (35–77)
Asthma, n	121
Asbestosis, n	66
Silicosis, n	42
COPD, n	34
MdE	27.9 (20–50)
Non-smoker, n	85
Ex-smoker <20 PY, n	57
Ex-smoker ≥20 PY, n	71
Current smoker (mean 33 PY), n	44
BMI	29.1 (19.2–56.9)

Absolute numbers or mean values and ranges (in parentheses) are given. MdE = Reduction of earning capacity; PY = pack years.

physical performance, while psychological well-being was markedly reduced.

#### Acute Effects

Immediately after rehabilitation (T3 vs. T1/T2) all disease groups showed statistically significant ( $p < 0.05$ , ANOVA) improvements in maximum exercise capacity (Wmax), quadriceps and handgrip force (table 3a–d). The absolute magnitudes of improvement were similar in all groups, but the relative gains were greater in silicosis and COPD due to the lower baseline values. 6MWD increased significantly in all groups except asbestosis ( $p < 0.05$  for each). The changes in lung function measures and respiratory muscle function were not statistically significant.

The hospital anxiety and depression scale (HADS) questionnaire showed a significant reduction in anxiety immediately after rehabilitation (T3) in all groups (table 3a–d). Both subscales of the 36-Item Short Form Health Survey (SF-36) questionnaire improved only in asthma patients ( $p < 0.05$ ; table 3a). The scores of the following three questionnaires did not change significantly: St. Georges Respiratory Questionnaire (SGRQ), Medical Research Council dyspnea scale (MRC) and Baseline and Transition Dyspnea Index (BDI/TDI).

#### Long-Term Effects

Patients with asthma and COPD (table 3a, d) showed significant long-lasting improvements of peripheral mus-

**Table 3.** Acute and long-term results of rehabilitation in the four patient groups**a** Results in asthma patients

	Asthma (n = 121)			
	T1/T2	T3	T4	T5
FEV <sub>1</sub> %pred	82.0 (22.1)	80.8 (21.6)	80.0 (22.9)	79.7 (22.6)
FVC%pred	96.2 (19.8)	96.0 (19.5)	96.8 (20.4)	95.7 (20.1)
Tiffeneau, %pred	85.4 (14.0)	85.7 (14.4)	84.7 (15.1)	85.6 (14.6)
P <sub>i</sub> <sub>max</sub>	7.5 (3.0)	7.2 (3.0)	7.6 (2.9)	7.5 (3.0)
P <sub>0,1</sub> /P <sub>i</sub> <sub>max</sub>	0.03 (0.02)	0.04 (0.02)	0.04 (0.02)	0.04 (0.03)
6MWD, m	511.3 (90.7)	534.6 (81.7)**	532.1 (80.9)**	522.1 (82.2)**
Borg 6MWD	3.9 (2.0)	3.9 (1.9)	4.0 (2.1)	4.5 (1.9)**
Wmax, W	117.0 (38.9)	128.3 (40.8)**	127.6 (41.4)**	124.9 (43.1)**
Quadriceps force, kg	64.4 (24.7)	77.2 (28.2)**	78.3 (29.0)**	74.0 (28.9)**
Handgrip force, kg	70.2 (19.9)	80.0 (21.1)**	79.4 (19.8)**	78.1 (19.9)**
HADS anxiety	11.8 (3.1)	9.6 (1.9)**	11.7 (2.5)	11.5 (2.7)
HADS depression	9.7 (1.8)	9.7 (1.6)	10.0 (2.0)	10.0 (1.8)
SF-36 physical	36.5 (10.6)	39.0 (10.2)**	39.0 (10.4)**	37.5 (10.0)
SF-36 psychomental	46.8 (12.0)	49.9 (10.4)**	46.7 (11.4)	46.2 (11.3)
SGRQ-total score	60.2 (11.6)	60.4 (12.0)	61.1 (10.8)	60.3 (11.3)
MRC	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)	1.8 (1.0)
BDI/TDI	6.75 (2.46)	6.34 (3.44)	5.83 (4.62)	5.09 (5.44)

**b** Results in silicosis patients

	Silicosis (n = 42)			
	T1/T2	T3	T4	T5
FEV <sub>1</sub> %pred	79.9 (16.8)	79.2 (19.2)	79.4 (17.9)	78.7 (19.9)
FVC%pred	92.2 (16.5)	91.4 (18.0)	94.0 (15.2)	93.3 (18.0)
Tiffeneau, %pred	88.7 (13.4)	89.3 (13.9)	88.7 (16.2)	88.8 (15.9)
P <sub>i</sub> <sub>max</sub>	6.4 (2.4)	6.1 (2.5)	6.4 (2.6)	6.0 (2.6)
P <sub>0,1</sub> /P <sub>i</sub> <sub>max</sub>	0.03 (0.02)	0.04 (0.02)	0.03 (0.02)	0.04 (0.02)
6MWD, m	457.8 (75.1)	477.4 (68.7)**	471.9 (66.3)**	461.1 (70.3)
Borg 6MWD	4.2 (1.8)	4.6 (2.3)	4.5 (2.1)	5.2 (2.3)*
Wmax, W	108.3 (30.2)	117.6 (27.7)**	117.6 (27.6)**	118.3 (26.7)**
Quadriceps force, kg	57.8 (20.9)	73.4 (25.4)**	74.1 (25.5)**	71.0 (24.1)**
Handgrip force, kg	71.9 (19.0)	80.4 (17.4)**	80.8 (18.5)**	76.5 (19.1)**
HADS anxiety	11.8 (3.5)	8.9 (2.2)**	11.5 (2.6)	10.8 (2.5)
HADS depression	9.8 (1.8)	9.9 (1.7)	9.9 (1.8)	10.3 (2.0)
SF-36 physical	36.7 (8.9)	36.9 (8.1)	36.2 (8.6)	35.6 (9.5)
SF-36 psychomental	47.4 (11.5)	48.5 (11.8)	44.8 (11.4)	45.7 (11.3)
SGRQ-total score	57.5 (10.9)	57.7 (10.0)	56.2 (11.1)	55.1 (11.1)
MRC	2.0 (1.0)	1.7 (0.9)	1.9 (0.8)	2.1 (0.8)
BDI/TDI	6.93 (2.30)	6.34 (3.08)	4.98 (3.99)	3.78 (4.67)

Mean values and SD (in parentheses) are given. \* p < 0.05 for improvement compared to pre-PR values, \*\* p < 0.01. PR = Pulmonary rehabilitation; for other abbreviations see table 1.

cle force, Wmax and 6MWD over the follow-up period of 12 months (T5 vs. T1/2). The effects for patients with asbestosis (table 3c) were smaller: muscle force was enhanced over 12 months (T5 vs. T1/2, p < 0.05), improvements of Wmax lasted only until the first follow-up at 3 months (T4 vs. T1/2, p < 0.05) and 6MWD did not change

significantly. The results for patients with silicosis (table 3b) varied, revealing responses similar to asthma and COPD regarding muscle force and Wmax, but the improvement in 6MWD lasted only until the first follow-up (p < 0.05). Lung function measures and respiratory muscle function did not significantly change over time.

**c** Results in asbestosis patients

	Asbestosis (n = 66)			
	T1/T2	T3	T4	T5
FEV <sub>1</sub> %pred	76.6 (20.0)	74.7 (21.5)*	74.1 (22.3)*	73.8 (21.9)*
FVC%pred	81.2 (17.9)	80.9 (17.8)	80.6 (18.6)	80.6 (18.1)
Tiffeneau, %pred	94.6 (12.6)	94.0 (14.0)	93.4 (16.0)	92.8 (15.0)
P <sub>i</sub> <sub>max</sub>	6.8 (2.8)	6.3 (2.8)	6.7 (2.7)	6.7 (2.5)
P <sub>0.1</sub> /P <sub>i</sub> <sub>max</sub>	0.04 (0.02)	0.05 (0.03)	0.04 (0.03)	0.04 (0.03)
6MWD, m	504.7 (88.7)	507.6 (83.7)	497.0 (71.6)	483.5 (74.6)**
Borg 6MWD	3.8 (2.1)	3.8 (1.9)	4.3 (2.0)	4.7 (1.9)**
W <sub>max</sub> , W	107.7 (23.7)	115.2 (23.9)**	112.2 (24.4)**	111.7 (28.1)
Quadriceps force, kg	61.5 (19.9)	71.6 (22.0)**	72.9 (20.7)**	69.5 (21.1)**
Handgrip force, kg	69.9 (18.3)	77.3 (17.0)**	76.4 (16.4)**	75.6 (19.1)**
HADS anxiety	11.2 (3.5)	9.1 (2.0)**	11.1 (2.2)	11.2 (2.6)
HADS depression	9.9 (1.9)	10.0 (1.6)	10.0 (1.5)	10.0 (1.5)
SF-36 physical	35.8 (9.6)	36.4 (8.6)	38.8 (9.3)*	36.7 (9.3)
SF-36 psychomental	46.9 (12.8)	48.8 (11.9)	46.6 (10.6)	48.3 (10.5)
SGRQ-total score	56.8 (12.0)	55.7 (10.5)	56.1 (11.9)	55.6 (11.6)
MRC	1.8 (1.0)	1.8 (0.8)	1.8 (0.8)	2.0 (0.9)
BDI/TDI	7.01 (2.41)	6.21 (3.30)	5.43 (4.10)	3.99 (4.78)

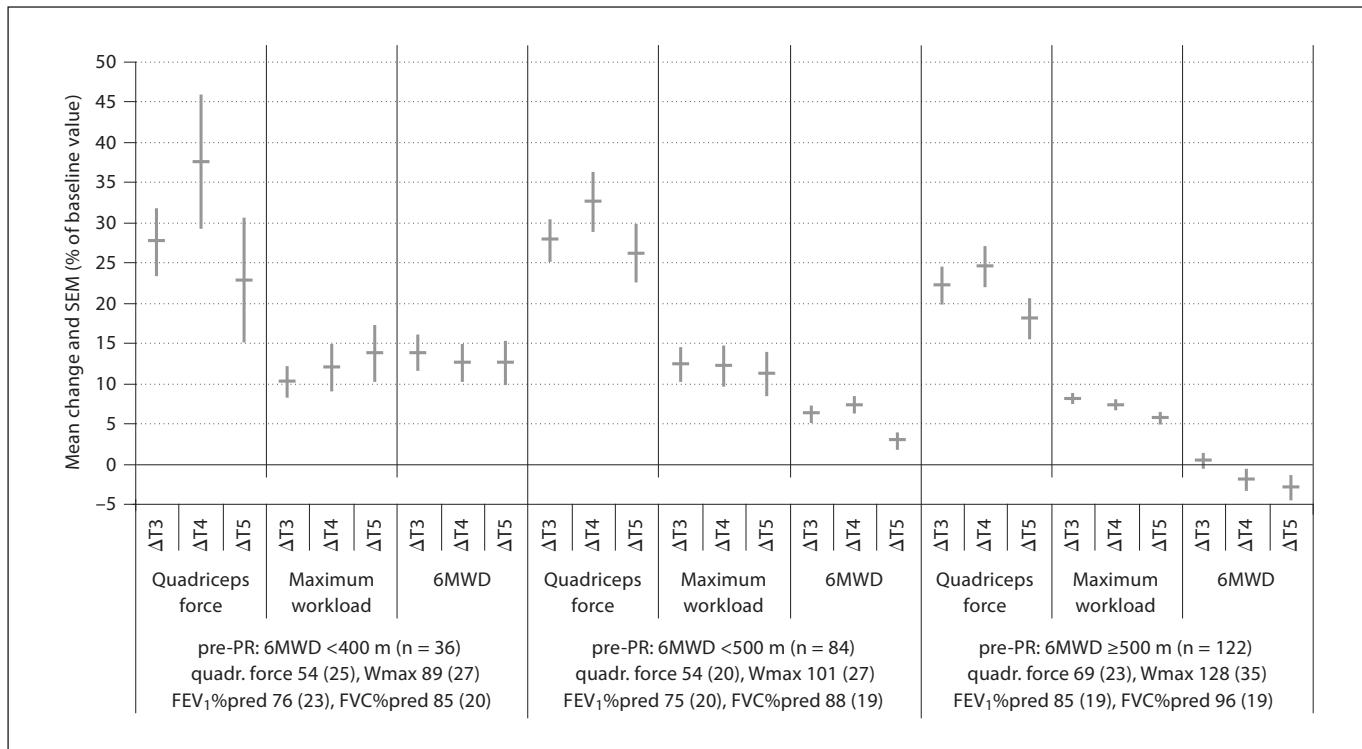
**d** Results in COPD patients

	COPD (n = 34)			
	T1/T2	T3	T4	T5
FEV <sub>1</sub> %pred	77.9 (19.2)	79.8 (17.6)	77.0 (20.0)	77.9 (19.9)
FVC%pred	92.1 (20.2)	93.8 (20.0)	92.6 (18.4)	91.8 (18.7)
Tiffeneau, %pred	84.2 (11.7)	86.2 (12.3)	84.9 (12.6)	87.0 (12.8)
P <sub>i</sub> <sub>max</sub>	6.2 (1.6)	6.0 (1.9)	6.2 (1.9)	6.2 (2.3)
P <sub>0.1</sub> /P <sub>i</sub> <sub>max</sub>	0.03 (0.02)	0.03 (0.02)	0.03 (0.02)	0.04 (0.05)
6MWD, m	435.8 (82.2)	468.6 (72.4)**	459.3 (75.3)**	452.0 (66.9)**
Borg 6MWD	4.0 (1.6)	4.4 (2.0)	3.9 (2.1)	5.3 (2.3)**
W <sub>max</sub> , W	108.8 (35.6)	115.6 (35.9)**	115.0 (31.9)**	115.9 (28.4)**
Quadriceps force, kg	54.9 (24.9)	68.7 (25.0)**	70.4 (25.0)**	64.9 (23.0)**
Handgrip force, kg	68.5 (15.2)	77.0 (14.6)**	78.1 (13.5)**	74.4 (14.4)**
HADS anxiety	11.2 (3.2)	8.7 (1.7)**	11.1 (2.3)	11.4 (1.9)
HADS depression	9.1 (1.8)	9.2 (1.6)	9.8 (1.8)	9.6 (1.5)
SF-36 physical	35.1 (9.2)	36.4 (11.1)	37.2 (10.4)	32.9 (7.9)
SF-36 psychomental	44.8 (11.9)	45.6 (10.4)	44.8 (11.1)	44.9 (10.3)
SGRQ-total score	53.4 (14.6)	54.8 (13.8)	55.9 (13.1)	52.4 (14.1)
MRC	1.9 (1.2)	1.8 (2.0)	1.9 (0.9)	1.9 (0.9)
BDI/TDI	7.35 (2.47)	6.12 (3.48)	5.41 (4.49)	4.24 (5.22)

Mean values and SD (in parentheses) are given. \* p < 0.05 for improvement compared to pre-PR values,  
\*\* p < 0.01. PR = Pulmonary rehabilitation; for other abbreviations see table 1.

The improvements in the physical SF-36 subscale in asthma patients (table 3a) were maintained over 3 months (T4; p < 0.05) but not 12 months. Scores of all other questionnaires or questionnaire scores in other disease groups did not change significantly from baseline.

The number of exacerbations and the use of the health care system for treatment of respiratory problems, i.e. hospital admissions, doctors consultations and need for antibiotic courses, are displayed in table 4. Reductions in these parameters occurred in all disease groups. The changes were statistically significant in the overall group



**Fig. 1.** Changes in physical performance after rehabilitation and at follow-up after 3 and 12 months as a function of the 6MWD prior to rehabilitation (pre-PR). pre-PR = Baseline values before pulmonary rehabilitation (T1/T2); ΔT3, ΔT4, ΔT5 = respective differences in relation to baseline values (T1/T2). For other abbreviations see table 1 and 3.

**Table 4.** Respiratory infections and utilization of health care services, the number of incidents per person before and after pulmonary rehabilitation

	Total		Asthma		Silicosis		Asbestosis		COPD	
	pre	post	pre	post	pre	post	pre	post	pre	post
Respiratory infections	1.53	0.99*	1.77	1.26*	1.33	0.80	1.14	0.78	1.68	0.71*
Physician consultations	1.35	1.12*	1.99	1.62	0.83	0.55	0.70	0.83	1.06	0.65
Antibiotic courses	0.66	0.48*	0.82	0.66	0.43	0.23	0.44	0.40	0.81	0.31*
Hospital admissions	0.13	0.06*	0.16	0.10	0.10	0.03	0.08	0.03	0.15	0

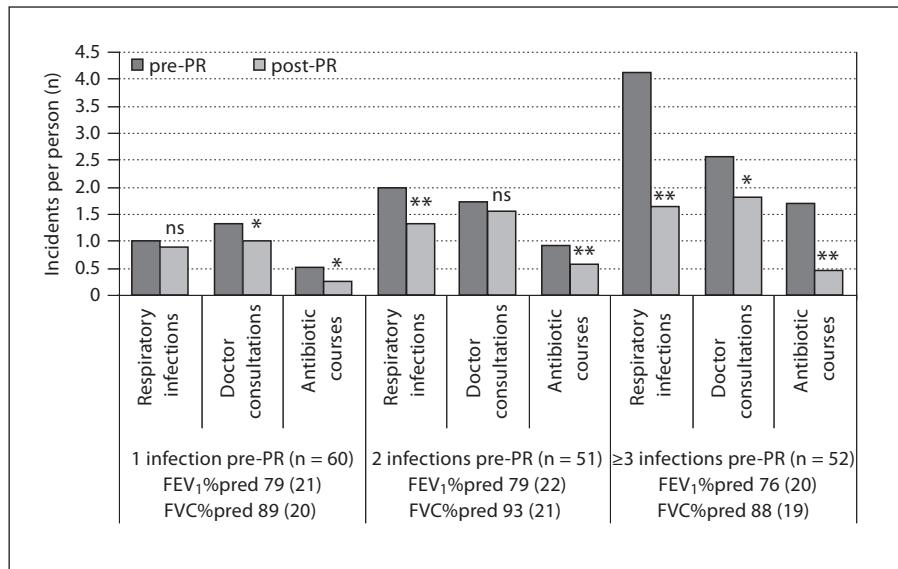
\* p < 0.05 for improvement compared to pre-PR values, \*\* p < 0.01. pre = Values in the 12 months before pulmonary rehabilitation; post = values in the 12 months after pulmonary rehabilitation.

(p < 0.05), showing a 35% reduction in exacerbations, 27% for antibiotic courses and 17% for physician consultations due to respiratory problems.

#### Analysis Stratified according to Baseline Values

When patients were stratified according to their baseline 6MWD, which was used as an indicator of function-

al capacity prior to rehabilitation, the relative changes of 6MWD, quadriceps force and Wmax were higher in patients with greater impairment at baseline (fig. 1). Patients with a baseline 6MWD exceeding 500 m demonstrated higher baseline values of FEV<sub>1</sub>%pred and FVC%pred, quadriceps force and Wmax (p < 0.05 for each, ANOVA) compared to those with lower baseline 6MWD. Whereas



**Fig. 2.** Reduction of respiratory infections and use of health care services as a function of the rate of respiratory infections prior to rehabilitation (pre-PR). pre-PR = Baseline values before pulmonary rehabilitation; post-PR = values 12 months after pulmonary rehabilitation. FEV<sub>1</sub>%pred and FVC%pred values are mean (SD). \* p < 0.05 for reduction compared to pre-PR values, \*\* p < 0.01, ns = non-significant.

muscle force and Wmax increased in these patients, no improvement was seen in 6MWD.

Of the 99 patients who did not report any exacerbations in the 12 months prior to rehabilitation, 55 remained without, 35 experienced one, and 9 experienced two or more exacerbations afterwards. Figure 2 shows a stratified analysis of patients having reported  $\geq 1$  exacerbation in the 12 months before rehabilitation. Baseline lung function and 6MWD did not differ between the categories. There was a significant reduction in the number of respiratory infections, doctors consultations and courses of antibiotics in nearly all exacerbation categories (p < 0.05). In patients previously reporting  $\geq 3$  exacerbations, the effect on respiratory exacerbation rate was most pronounced.

## Discussion

This prospective study demonstrated substantial short- and long-term effects of a 4-week inpatient pulmonary rehabilitation program in a large group of patients with different occupational respiratory diseases. While acute improvements were relatively similar between diseases, the persistence of effects over a period of 12 months after rehabilitation differed. The secondary outcomes (number of respiratory infections, antibiotic courses, visits to a doctor due to the underlying lung disease) were also significantly reduced, indicating an overall improvement of the health status.

There is strong evidence that pulmonary rehabilitation improves physical performance, psychosocial situation and dyspnea [1]. These domains interact with each other – physical impairment affects self-reliance, quality of life and dyspnea. Depression, anxiety and dyspnea favor inactivity, and dyspnea increases anxiety. To cover as many of these changes as possible we chose a broad panel of functional and psychosocial measures.

Due to the underlying pathophysiology, a persistent improvement in lung function is unlikely to occur after rehabilitation. However, optimized medication, better compliance and daily physical activity may have a long-term impact. Thus, clinically important effects such as reductions in exacerbation rates and reduced use of health care resources were included.

### Short-Term Effects

Impaired exercise tolerance is common in chronic lung diseases. Beyond airflow limitations and reductions in lung volume and gas exchange, skeletal muscle weakness is recognized as a causal factor [7–9]. Improvement of physical performance can break the vicious circle induced by inactivity leading to deconditioning, loss of functional capacity in daily life and indirectly to depression and poor quality of life. Regarding physical performance, our results confirm that intensified endurance and resistance training in combination with therapeutic and educational sessions over 4 weeks is capable of improving exercise capacity and muscle strength, irrespective of the underlying pulmonary disease. Peripheral

muscle strength as well as 6MWD improved. As the absolute improvement of muscle strength was independent of baseline values, patients displaying lower strength at baseline had greater relative gain.

Endurance and resistance training act synergistically on exercise tolerance, and 6MWD is known to improve after resistance training [10, 11]. Besides dyspnea, the dominant symptom limiting exercise capacity appears to be leg effort, as indicated by its correlation with dyspnea, muscle strength and exercise tolerance [12]. Correspondingly, a 2-fold increase in muscle strength was associated with a decrease of dyspnea and the sensation of intolerable leg effort and a 1.5-fold increase in work capacity [9].

Both 6MWD and maximum workload by ergometer testing address exercise tolerance. There was a negative correlation between baseline values and change in 6MWD, which is consistent with previous data [13]. While 6MWD is sensitive in patients with advanced pulmonary impairment, its informative value is lower in less impaired patients due to a ceiling effect, which is different to maximum workload. This suggests that both methods should be used in populations with varying severity of disease.

COPD [14, 15] as well as asthma [16] are associated with anxiety and depression. In our study the HADS questionnaire [17] revealed unexpectedly high scores. About 90% of patients displayed a depressive mood at baseline according to threshold values from the literature [18–20]. The score for depression remained unchanged, contrary to previous observations [15]. Concerning anxiety, there was a short benefit of rehabilitation reflected by an average improvement of 2.5 points, which exceeded the previously reported 1.3 and 0.8 points [18, 19].

Both the SGRQ and SF-36 questionnaires indicated a lower quality of life at baseline than expected from lung function, age and disease [21–24]. No clinically relevant changes were observed after rehabilitation. The explanation might be the specific psychosocial situation in occupational diseases. Subjects are often forced to give up their occupation, with the risk of unemployment and loss of social standing. A reduced quality of life has already been reported in patients with occupational asthma compared to asthma of nonoccupational etiology [25–27]. Overall, the high level of depression may be responsible for the reduced quality of life and the lack of change in our study population.

According to the MRC and BDI/TDI values, we did not observe an improvement in dyspnea, in contrast to the literature [1]. Dyspnea is known to be a complex sensation that is affected by the discrepancy between an in-

creased respiratory drive during exercise and the inability to appropriately increase tidal volume. Chronic bronchoconstriction and a long duration of disease may lead to desensitization concerning the perceived information. For example, in asthma the perception of dyspnea has been found to be negatively correlated to disease severity and depression status [28]. No plausible associations were found between functional measures and dyspnea scores in our study. This suggests that in our specific population, psychosocial factors played an important role, underlining the importance of objective measures to quantify the effects of rehabilitation.

#### *Long-Term Effects*

One aim of pulmonary rehabilitation is to sustain the acute effects. The improvement in peripheral muscle strength was maintained over 1 year in almost all patients, independent of baseline levels and disease. In obstructive diseases, i.e. asthma and COPD, and in combined ventilatory disorders due to silicosis, the improvements in Wmax and 6MWD were comparable and long-lasting. Patients with restrictive impairment due to asbestosis showed minor benefits; 6MWD did not improve at all, and the gain in Wmax lasted only 3 months, corresponding to other results for the rehabilitation of patients with interstitial lung disease [4, 5].

The study by van Wetering et al. [29] seems to be most similar to our study; however, these authors compared their intervention group with a control group. When evaluating their data versus baseline, the increase of cycling endurance time was maintained during follow-up. Both SGRQ total score and MRC score improved immediately after intervention but the first had decreased to baseline by 8 months and the second by 20 months. 6MWD never exceeded baseline and worsened over the follow-up.

Concerning pulmonary rehabilitation in occupational respiratory diseases, only patients with asbestosis have been previously evaluated [30, 31] using a 3-week intensified outpatient program followed by a 3-month maintenance program. This improved quadriceps muscle strength and 6MWD; ergometer testing was not conducted. During follow-up, only patients continuing physical activity maintained the effects of rehabilitation, while the others returned to baseline within 6 months. These results correspond with our findings.

Besides the maintenance of acute effects, the secondary long-term outcomes, i.e. the rate of exacerbations and the use of health care resources, are also important [29, 32–36]. About half of the rehabilitation studies revealed

statistically significant improvements in these measures [6]. Patients with pulmonary diseases are particularly susceptible to respiratory infections, leading to exacerbations as reflected by a worsening of lung function, additional medications and absence from the workplace. In COPD, the frequency of exacerbations correlates with disease severity, lung function decline and mortality [37], and self-reported exacerbations predict future exacerbations [38, 39]. As a minimal clinically important difference, a 20% reduction in incidents per year has been suggested for clinical trials [40]. Moreover, in COPD a medication-induced reduction of annual exacerbations by 11% was recently considered as clinically relevant [32].

We determined the self-reported rates of acute exacerbations, respiratory problems requiring physician visits, prescribed antibiotic courses, as well as the number and duration of hospital stays within 12 months before and after rehabilitation, showing a statistically significant reduction in the total group. The annual rate of exacerbations was reduced by 35% and this was especially apparent in patients with a higher baseline rate. In our study collective with less advanced impairment, hospital admissions due to respiratory illness were rare but even these showed a reduction.

Pulmonary rehabilitation has been discussed as a factor in reducing exacerbation rates in COPD [37, 41]. This positive effect has not been reported previously in asthma or interstitial lung disease. Regarding structural changes of the bronchial system, silicosis bears similarities to COPD, thus a reduction of the exacerbation rate should be of comparable relevance. In asthma, severe acute exacerbations are responsible for the major part of the disease-related health burden [42], showing a strong association with respiratory infections [43]. The role of respiratory infections in asbestosis is not clear. In our population, the rate at baseline was significantly lower in comparison with the other groups, suggesting a lower relevance.

#### *Limitations of the Study*

Due to ethical and legal considerations, the rehabilitation of patients entitled to receive rehabilitation could not be postponed for more than 1 year. In Germany, rehabilitation is an enforceable claim as part of compensation in occupational diseases. This prevented us from creating a matched control group without rehabilitation. Our goal of studying whether improvements are sustained and how effects compare between diseases did not seem to require a randomized, control-group design. The longitudinal analysis with two follow-up visits also provided

the greatest statistical power to detect long-term benefits and their minimum duration.

Enrollment was organized by 15 social accident insurance companies, which were asked to search their database according to the inclusion criteria. The investigators did not have an influence on the recruitment and do not have information regarding the total numbers of patients fulfilling the criteria or asked to or refusing to participate. However, the study population does not obviously differ from the occupational compensation cases seen in our outpatient clinic and the rehabilitation clinics.

The rather small proportion of females can be attributed to the prevalence of male-dominated occupations associated with the evaluated occupational diseases. The group sizes also differed, mainly because the age of patients with silicosis and of coal miners often exceeds 70 years and a considerable number of these patients undergo annual rehabilitation.

#### *Conclusion and Perspective*

Our results indicate that in occupational respiratory diseases, an inpatient pulmonary rehabilitation program is capable of improving physical capacity and exacerbation rates over at least 1 year. Probably a subsequent maintenance program, e.g. as provided by sport groups, could support maintaining these functional effects. It could also have an impact on exacerbation rates and the use of health care resources, with the potential to influence the course of the disease. This should be evaluated in future studies on pulmonary rehabilitation in occupational diseases.

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