International Journal of COPD

Dovepress
open access to scientific and medical research

Open Access Full Text Article

REVIEW

Sustained effects of integrated COPD management on health status and exercise capacity in primary care patients

This article was published in the following Dove Press journal:
International Journal of COPD
24 November 2010
Number of times this article has been viewed

Annemarije L Kruis[1]
Joan van Adrichem[2]
Magda R Erkelens[2]
Huub Scheepers[3]
Hans in 't Veen[4]
Jean WM Muris[5]
Niels H Chavannes[1]

[1]Department of Public Health and Primary Care, Leiden University Medical Center, Leiden, [2]Physiotherapy Center De Beweging, Rotterdam, [3]Well-being Medical Center, Bocholtz-Simpelveld, [4]Department of Pulmonary Diseases, Sint Franciscus Gasthuis, Rotterdam, [5]Department of General Practice, Maastricht University Medical Center, The Netherlands

Background: Chronic obstructive pulmonary disease (COPD) constitutes a growing health care problem worldwide. Integrated disease management (IDM) of mild to moderate COPD patients has been demonstrated to improve exercise capacity and health status after one year, but long-term results are currently lacking in primary care.

Methods: Long-term data from the Bocholtz study, a controlled clinical trial comparing the effects of IDM versus usual care on health status in 106 primary care COPD patients during 24 months of follow-up, were analyzed using the Clinical COPD Questionnaire (CCQ). In addition, the Kroonluchter IDM implementation program has treated 216 primary care patients with mild to moderate COPD since 2006. Longitudinal six-minute walking distance (6MWD) results for patients reaching 24 months of follow-up were analyzed using paired-sample *t*-tests. In prespecified subgroup analyses, the differential effects of baseline CCQ score, Medical Research Council (MRC) dyspnea score, and 6MWD were investigated.

Results: In the Bocholtz study, subjects were of mean age 64 years, with an average postbronchodilator forced expiratory volume in one second (FEV_1) of 63% predicted and an FEV_1/forced vital capacity (FVC) ratio of 0.56. No significant differences existed between groups at baseline. CCQ improved significantly and in a clinically relevant manner by 0.4 points over 24 months; effect sizes were doubled in patients with CCQ $>$ 1 at baseline and tripled in patients with MRC dyspnea score $>$2. In the Kroonluchter cohort, 56 subjects completed follow-up, were of mean age 69 years, with an FEV_1/FVC ratio of 0.59, while their postbronchodilator FEV_1 of 65% predicted was somewhat lower than in the total group. 6MWD improved significantly and in a clinically relevant manner up to 93 m at 12 months and was sustained at 83 m over 24 months; this effect occurred faster in patients with MRC dyspnea score $>$2. In patients with baseline 6MWD $<$ 400 m the improvement remained $>$100 m at 24 months.

Conclusion: In this study, IDM improved and sustained health status and exercise capacity in primary care COPD patients during two years of follow-up. Improvements in health status are consistently higher in patients with CCQ $>$ 1 at baseline, being strongest in patients with baseline MRC dyspnea score $>$2. Improvements in exercise capacity remain highest in patients with 6MWD $<$ 400 m at baseline and seem to occur earlier in patients with MRC dyspnea score $>$2.

Keywords: chronic obstructive pulmonary disease, disease management, integrated care, pulmonary rehabilitation, primary care

Correspondence: Niels H Chavannes, MD PhD Associate Professor, Department of Public Health and Primary Care, Leiden University Medical Center, PO Box 9600, Zone V0-P, 2300 RC Leiden, The Netherlands
Tel +31 071 526 8444
Fax +31 071 526 8259
Email n.h.chavannes@lumc.nl

Background

Chronic obstructive pulmonary disease (COPD) constitutes a major and progressive health care problem worldwide and is expected to be the third cause of death globally over the next 20 years.[1] Besides smoking cessation, pulmonary rehabilitation is the recommended treatment and has been proven to be effective across the whole

spectrum of COPD patients.[2–5] A recent meta-analysis shows that pulmonary rehabilitation relieves dyspnea and fatigue, improves mental status, and enhances patients' control over their disease.[6] However, despite proven efficacy, pulmonary rehabilitation is still only available for a small proportion of the worst patients, due to capacity problems and high costs.[7] It is expected that the rise in prevalence of COPD will progressively cause an even higher burden on rehabilitation programmers in the future.

At present, the majority of COPD patients are treated in primary care, and approximately 80% suffer from mild to moderate disease.[8] As a result, general practitioners often find themselves at a crossroads in the organization of care for COPD patients. Nevertheless, interdisciplinary cooperation between primary health care providers, as well as primary and secondary care, is often needed. In earlier reports[9,10] we hypothesized that if components of pulmonary rehabilitation were tailored into an integrated disease management (IDM) program available for primary care and carried out by a multidisciplinary, integrated care team, the benefits of pulmonary rehabilitation could be extended to a larger population of COPD patients in need. This would explicitly include those with milder stages of disease, given that they have sufficient symptom burden to justify an integrated intervention. Elements that can often be integrated include smoking cessation, exacerbation management, optimal medication, self-management, patient education, dietary intervention, and an exercise program.

In an earlier paper, we demonstrated that our IDM program in primary care improved health status in a clinically relevant way in patients with mild to moderate COPD at 12 months' follow-up. The greatest room for improvement was shown in COPD patients with a Medical Research Council (MRC) dyspnea score >2.[9] After we had demonstrated 12 months' efficacy of the IDM program in a controlled setting, a real-life implementation cohort was set up in the city of Rotterdam. In this pragmatic IDM program, we focused on improving exercise capacity because we believed this would be an important driver to sustain effectiveness. Currently, long-term results of pulmonary rehabilitation programs are mixed, and some authors report that most benefits of pulmonary rehabilitation dissipate over time.[11–13] Similarly, the longer-term effect of IDM in primary care is still unclear. The aim of the present study was to determine the long-term effects of IDM on health status and exercise capacity in primary care COPD patients.

Methods

We analyzed 24 months of follow-up data for primary care IDM programs in the Bocholtz controlled clinical trial and the Kroonluchter implementation cohort. Both study populations consisted of primary care patients with chronic respiratory symptoms and a postbronchodilator forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) < 0.7, in accordance with national and international guidelines.[3,8] Exclusion criteria were terminal illness, immobility, substance abuse, and inability to fill in questionnaires. In the Bocholtz clinical trial, the regional Medical Ethics Committee of the Atrium Medical Centre, Heerlen, approved the study protocol. All participating patients gave their written informed consent. In the Kroonluchter cohort, all patients gave their written informed consent for participation in the implementation program.

In the following section we provide a brief description of both study settings and designs. We refer to our previous publications for an extensive description of the clinical one-year results and methods for the Bocholtz study,[9] as well as the background and design of the Kroonluchter IDM program.[10]

Picasso Bocholtz study

The Picasso Bocholtz study was a controlled clinical trial assessing the effects of IDM on health status in COPD patients from two comparable primary health care centers in the south of The Netherlands. Patients were followed up for two years, during which time the intervention group received an IDM program and the control group received usual care. Patients were included based on chronic respiratory complaints, postbronchodilator lung function testing, and adequate workup in case of more complex disease by a local pulmonologist, on indication by the patients' primary care physician. In the intervention setting, an integrated COPD management team was formed, including two physiotherapists, a respiratory nurse, a physician assistant, a dietician, a pharmacist, a supervising primary care physician, and a logistics manager. All team members contributed in their area of expertise to a standardized written treatment protocol, which included different elements of IDM, based on the joint American Thoracic Society/European Respiratory Society COPD standards.[14] Examples included personalized physical activity training programmers, optimal medication prescribing and adherence monitoring, rapid action plans for exacerbations, and continuous self-management education.[9]

Kroonluchter cohort

Based on the encouraging results of the Bocholtz study, the Kroonluchter integrated disease management program was implemented in a low socioeconomic status borough in Rotterdam. Since 2006, a total of 216 primary care patients

with chronic respiratory complaints have been included after clinical assessment, including postbronchodilator lung function testing, confirmed eligibility according to GOLD (Global Initiative for Chronic Obstructive Lung Disease) criteria. A multidisciplinary dedicated team of primary care physicians, nurse specialists, and physiotherapists was formed and trained to establish a locally agreed collaborative protocol. Diagnostic workup in case of complex disease was provided by collaborating pulmonologists, after referral by the primary care physician. In cooperation with the patient, an individualized plan of action was designed, based on an explicitly formulated personal target, varying from "quitting smoking with guidance within six months" to "climbing a short flight of stairs without hindrance by feelings of dyspnea within six months". Based on disease burden and patient needs, an individual program was assembled, which could include self-management training and exacerbation management, an exercise training program, smoking cessation strategies, better medication use, and personalized disease education.

In case of obesity or muscular depletion, referral to a dietician for dietary intervention was possible. Because of good local collaboration and arrangements for additional workup, patients could be referred to pulmonary physicians at short notice. In addition, extra attention was given to follow-up of patients after an exacerbation. Patients with an MRC dyspnea score >2 or patients known by their primary care physician to be inactive were assigned to a six-month COPD-specific training program run by specialized physiotherapists. Physical exercise training consisted of one month of individual training, followed by five months of group training. Training was focused on strength as well as endurance exercises, and was tailored to the individual abilities and limitations of the patient. Patients trained for one hour twice per week under supervision and were instructed to train one hour per week at home. After six months, there was a follow-up of one hour per week in order to sustain any effects over time.[10]

Outcomes and measurements

Baseline measurements in both studies included age, gender, smoking habits, body mass index, lung function, and score on the MRC dyspnea scale (a short and valid questionnaire to quantify dyspnea).[15]

In the Bocholtz study, the Clinical COPD Questionnaire (CCQ) was used to assess health status, because it is well validated and easy to administer in primary care.[15] Primary outcome at 24 months in the Bocholtz study was the difference in CCQ at 24 months compared with baseline CCQ score in both the intervention and control groups.

In the Kroonluchter cohort, the six-minute walking distance (6MWD), a measure of functional capacity, was conducted according to international recommendations.[16] The 6MWD is a practical, self-paced test, measuring the maximum distance subjects can walk in six minutes. The primary outcome of this program was the difference in 6MWD at 24 months compared with baseline 6MWD score.

Power calculations

In the Bocholtz study, we calculated that a sample size of 2×45 patients was needed (with a power of 80% and $\alpha = 0.05$) to detect a minimum clinically important difference of −0.4 unit change in quality of life on the CCQ.[15]

Because the Kroonluchter project was designed as an ongoing implementation program, no formal group comparison or power calculation was conducted. On the basis of earlier studies and a minimum clinically important difference of 54 m, which represents the threshold value for a clinically significant change on the 6MWD,[16] a minimum group size of 50 patients was deemed necessary to analyze 24-month results. In this study, the first batch of consecutive COPD patients completing 6MWD measurements at baseline and months 3, 6, 12, and 24 were analyzed.

Statistical analysis

Data were analyzed using SPSS version 13, using independent *t*-tests and Chi-square tests for comparison of baseline characteristics. Baseline and annual differences in CCQ (Bocholtz) and 6MWD (Kroonluchter) were compared using paired-sample *t*-tests. In prespecified subgroup analyses, the differential effects of baseline CCQ score, MRC score, and 6MWD were investigated.

Results

Patients

In the Bocholtz study, 106 COPD patients diagnosed according to GOLD classification were analyzed for baseline measurements, comprising 59 patients in the intervention group and 47 patients in the control group. This initial COPD population is described in Table 1. Subjects were of mean age 64 years, with an average postbronchodilator FEV_1 of 63% predicted (standard deviation 19) and an FEV_1/FVC ratio of 0.56. There were no significant differences in demographic variables, smoking habits, or lung function between the intervention and control groups at baseline. Of the initial population of 106 patients, 86 patients (81%) completed a follow-up of two years (44 in the intervention group and 42 in the control group) and could be further analyzed.

Table 1 Baseline characteristics of intervention versus control group in primary care COPD patients of the Bocholtz study*

	Intervention (n = 59)	Control (n = 47)	*P* value#
Age (years)	64.7 (10)	62.3 (9)	0.99
Gender (% male)	66.4	64.3	0.12
Current smoking (%)	33.9	46.8	0.08
Body mass index	25.8 (5)	26.0 (5)	0.75
FEV_1 post-BD (%)	63.9 (21)	61.7 (17)	0.06
FEV_1/FVC post-BD	0.55 (.10)	0.57 (.10)	0.72
MRC > 2 (%)	38.6	33.3	0.32
CCQ	1.4 (1)	1.6 (1)	0.75

Notes: *All values are means (SD) except when stated otherwise; #no significant difference between groups at baseline.
Abbreviations: MRC, Medical Research Council dyspnea score; CCQ, Clinical COPD Questionnaire; SD, standard deviation; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; BD, bronchodilator.

Of the original group of 216 patients in the Kroonluchter cohort, 39 (18%) dropped out due to relocation, severe comorbidity, or unwillingness to fill out repeated questionnaires. Of the initial 216 patients, 104 (48%) were referred to a physiotherapy training program, based on MRC dyspnea score >2 or inactivity that necessitated an integrated approach. So far, 56 patients (54%) have completed the 24-month 6MWD test, and their data could be used for analysis. Table 2 shows the baseline characteristics of the initial cohort and the group that finished 24 months of follow-up. The mean age of the latter group was 69 years, with an FEV_1/FVC ratio of 0.59, while their postbronchodilator FEV_1 of 65% was somewhat lower than in the total group (71%).

Primary outcome in Bocholtz study

Table 3 shows the long-term changes in CCQ scores in COPD patients in the intervention and control groups of the Bocholtz study. Compared with baseline, a statistically significant change of −0.4 is sustained in the intervention group during 24 months, while the control group shows nonsignificant changes during 24 months. The prespecified subgroup analysis of patients with baseline CCQ > 1 shows a statistically significant and clinically relevant difference of −0.9, while the control group shows no significant improvement. In patients with MRC scores >2, the effect on CCQ score is tripled and shows a statistically significant and clinically relevant difference of −1.2, compared with a nonsignificant change of −0.02 in the control group.

Table 2 Baseline characteristics of total versus 6MWD group in primary care COPD patients of the Kroonluchter cohort*

	Total (n = 216)	6MWD (n = 56)	*P* value
Age (years)	67.1 (14)	69.2 (10)	0.11
Gender (% male)	42.1	37.3	0.38
Current smoking (%)	41.2	33.3	0.78
Body mass index	27.3 (6)	27.8 (5)	0.45
FEV_1 post-BD (%)	70.5 (18)	64.5 (17)	0.002#
FEV_1/FVC post-BD	0.61 (.12)	0.59 (.14)	0.098
MRC > 2 (%)	45.8	51.9	0.24
6MWD (m)	364.0 (128)	354.6 (126)	0.44

Notes: *All values are means (SD) except when stated otherwise; #significant difference between groups at baseline.
Abbreviations: COPD, chronic obstructive pulmonary disease; MRC, Medical Research Council dyspnea score; 6MWD, six-minute walking distance; SD, standard deviation; FEV_1, forced expiratory volume in one second; FVC, forced vital capacity; BD, bronchodilator.

Primary outcome in Kroonluchter cohort

Table 4 shows the long-term changes in 6MWD in the Kroonluchter cohort at months 3, 6, 12, and 24. The 6MWD improves significantly and in a clinically relevant manner up to 93 m at 12 months, and remains at 83 m over 24 months. In patients with MRC scores >2, 6MWD differences are comparable in significance and clinical relevance, but seem to occur somewhat earlier, ie, at three months. In patients with baseline 6MWD < 400 m, the 6MWD difference is 112 m at 12 months and remains statistically significant and clinically relevant at 24 months, with effect sizes over 100 m.

Discussion

Our studies demonstrate that IDM programs can be successfully implemented in real-life primary care populations. Even after two years, considerable proportions of the patients involved in the programs still show significant and clinically relevant improvements in health status and exercise tolerance. In patients with a baseline CCQ > 1 and in those with MRC dyspnea score >2, the long-term effect on CCQ score seems to be doubled and even tripled, respectively. In patients with baseline 6MWD < 400 m, the 6MWD difference remains substantially large over two years, with effect sizes exceeding 100 m.

A typical structured program of pulmonary rehabilitation in the secondary and tertiary care setting is usually of relatively short duration, ranging from 6 to 12 weeks.[17] Positive results up to three months have been widely published,[6,17–19] but several clinical trials have reported that initial benefits of the intervention tend to recede over time, and that effects above clinical relevance thresholds are lost again at six to 18 months' follow-up.[11–13,20,21]

As a result, recommendations regarding prolonged duration of pulmonary rehabilitation have been issued, and several studies have evaluated longer-term programs in more severe patients, with inconclusive results. Guell randomized

Table 3 Long-term effects of integrated disease management on health status in primary care COPD patients of the Bocholtz study*

		Intervention group		*P* value	Control group		*P* value
		CCQ difference*/95% CI			CCQ difference**/95% CI		
All patients							
	12 mo	–0.4	(–0.6, –0.2)	0.001	+0.01	(–0.2, 0.2)	0.9
	24 mo	–0.4	(–0.7, –0.1)	0.004	+0.02	(–0.4, 0.5)	0.9
Subgroup baseline CCQ > 1							
	12 mo	–0.8	(–1.1, –0.4)	0.001	–0.1	(–0.3, 0.08)	0.2
	24 mo	–0.9	(–1.2, –0.5)	0.001	–0.03	(–0.5, 0.5)	0.9
Subgroup baseline MRC > 2							
	12 mo	–0.9	(–1.4, –0.4)	0.002	+0.01	(–0.3, 0.3)	1.0
	24 mo	–1.2	(–1.8, –0.5)	0.004	–0.02	(–0.8, 0.8)	1.0

Notes: *Paired samples *t*-test; *P* is considered significant at values < 0.05; **minimum clinically important difference CCQ = –0.4.[15]
Abbreviations: CCQ, Clinical COPD Questionnaire; CI, confidence interval; MRC, Medical Research Council dyspnea score.

60 GOLD Stage III COPD patients to 12 months of intervention or standard care and followed them up for two years. Benefits on exercise tolerance, dyspnea, and quality of life were accrued, but diminished in the second year of follow-up.[22] In a randomized controlled study in moderate to very severe COPD patients, Berry et al concluded that an 18-month exercise program resulted in greater improvements in self-reported disability and physical functioning when compared with a three-month exercise program.[4] Wijkstra et al reported improvements in quality of life over 18 months in GOLD Stage III patients following rehabilitation at home for three months, followed by physiotherapy sessions once a month. However, the authors concluded that change in quality of life was not associated with a change in exercise tolerance.[23] Positive findings in selected patient groups in secondary and tertiary care, following a prolonged pulmonary rehabilitation program, were further confirmed by Troosters et al, Engstrom et al, and Bendstrup et al, suggesting that structured, supervised exercise participation should be continued for extended periods in patients undergoing pulmonary rehabilitation.[24–26]

Table 4 Long-term effects of integrated disease management on exercise tolerance in primary care chronic obstructive pulmonary disease patients of the Kroonluchter cohort*

		6MWD difference** compared with baseline (95% CI)		*P* value
All patients				
	3 mo	38.3	(27.2, 49.4)	<0.0001
	6 mo	62.5	(47.4, 77.7)	<0.0001
	12 mo	93.5	(71.4, 115.6)	<0.0001
	24 mo	83.3	(60.0, 106.6)	<0.0001
Subgroup baseline MRC > 2				
	3 mo	52.1	(37.1, 67.2)	<0.0001
	6 mo	59.2	(40.8, 77.7)	<0.0001
	9 mo	93.0	(62.9, 123.1)	<0.0001
	12 mo	80.0	(44.7, 115.3)	<0.0001
Subgroup baseline 6MWD < 400 m				
	3 mo	52.7	(38.9, 66.5)	<0.0001
	6 mo	78.2	(52.5, 103.9)	<0.0001
	9 mo	112.3	(77.9, 146.7)	<0.0001
	12 mo	101.4	(64.3, 138.6)	<0.0001

Notes: *Paired-samples t-test; *P* is considered significant at values <0.05; **6MWD = 54 m.[17]
Abbreviations: 6MWD, six-minute walking distance; CI, confidence interval; MRC, Medical Research Council dyspnea score.

To the best of our knowledge, this is the first study describing long-term follow-up results of IDM in primary care. Our positive results can be explained by two important differences, as compared with the mixed results summarized earlier. First, we studied the effect of IDM programs developed especially for primary care, which consist of an interdisciplinary approach involving different primary health care team members, aided by secondary care where needed. Furthermore, other pulmonary rehabilitation studies usually included more severe COPD patients, while our programs were directed at the whole range of COPD patients, including those with milder stages of disease, but with sufficient symptom burden to justify intervention.

Our results are probably more in line with the recent INTERCOM (Interdisciplinary Community-Based COPD Management Program) study that included secondary care COPD patients with less advanced airflow obstruction, but impaired exercise capacity. In this randomized controlled trial, the intervention group received exercise training, education, nutritional therapy, and smoking cessation counseling in a community-based, multidisciplinary setting. Quality of life, functional exercise capacity, and breathlessness remained significantly favorable in the intervention group versus usual care over the entire two-year intervention.[27]

It is well known that COPD patients have a less active lifestyle compared with healthy elderly persons.[28] One study by Pitta et al showed that significant improvements in time spent walking in daily life were only obtained after six months of rehabilitation, but were not present at three months.[29] These findings are mirrored in our Kroonluchter cohort results for the 6MWD, stressing the importance of implementing programs for at least six months to optimize the potential for improvement. It is likely that benefits achieved after following an exercise program tend to dissipate after the initial intervention and when the accompanying supervision terminates. Therefore, we successfully developed a training program which included extra follow-up training of one hour per week after the initial six months, intended to enhance social support in the training groups and sustain results in the long term. It is likely that our clinically relevant and statistically significant results on the 6MWD at 24 months of follow-up are the result of more prolonged supervision by physiotherapists and the peer support offered in the training groups.

Our studies had several methodologic limitations. The Bocholtz program was designed as a clinical controlled trial, but was not randomized, because it was primarily developed to measure a maximally achievable effect of an IDM program at a primary care practice level. Indeed, the study setting was chosen to include demographically comparable villages but with limited interaction in daily life, resulting in near absence of contamination between groups.[12] The Kroonluchter cohort was based on lessons learned from the Bocholtz study, and was primarily developed as an implementation program in a real-life setting. As a result, a power calculation was not done beforehand. Nevertheless, our significant 6MWD results at 24 months reached far beyond the minimum clinically important difference of 54 m, demonstrating an adequate sample size. The first adequate batch of consecutive COPD patients completing 6MWD measurements at 24 months analyzed in this study may represent selection of more motivated patients, although their baseline characteristics differed little from the total group (see Table 2). Indeed, we have observed that higher levels of intrinsic motivation usually come with a higher burden of symptoms at baseline. This may be part of the reason that indicators of disease burden (CCQ $>$ 1, MRC dyspnea score $>$2, 6MWD $<$ 400 m) do seem to increase the chances of achieving clinically relevant effects on health status in patients with mild to moderate COPD. These results suggest a potential usefulness of phenotypic profiling in a primary care COPD population, which we intend to study further, and we recommend that other research groups do so as well.

Regaining control over one's own disease state is probably a crucial factor in the success of both of our programs. During the IDM program, improved feelings of self-efficacy and independence became notable in participating patients. Overall, the greatest improvements were found in patients with a baseline MRC dyspnea score $>$2, and to a lesser extent in patients with CCQ $>$ 1. At this stage, lung function is still relatively well maintained and thus patients perceive a tangible change in symptom burden. When asked, they felt more capable of actually breaking through the vicious circle of inactivity, anxiety, and increasing dyspnea. This was prominently reflected in the patient group with a baseline 6MWD below 400 m, who have achieved the most dramatic improvements in exercise capacity. This cutoff was in fact more sensitive than the 350 m cutoff point used in the BODE (body mass index, obstruction, dyspnea, exercise) index, probably reflecting more room for improvement in primary care COPD patients.[30]

When COPD patients are treated with IDM at an earlier stage, it is likely that costs per patient will be lower, and that larger groups of eligible patients can benefit. Further disease progression in terms of health status and exercise capacity will be positively influenced and, if sustained, even long-term deterioration of lung function may be reduced. We have demonstrated that teams of general practitioners, physiotherapists, and nurse practitioners, supported by pulmonary physicians, can provide adequate IDM designed for primary care, because patients' health status and exercise capacity improved substantially, even after two years of follow-up. In the future, we therefore recommend pragmatic randomized controlled trials addressing the costs and long-term effectiveness of large-scale IDM programs in primary care.

Conclusion

In this study, IDM improved and sustained health status and exercise capacity in primary care COPD patients during two years of follow-up. Improvements in health status were consistently higher in patients with CCQ $>$ 1 at baseline, being strongest in patients with MRC dyspnea score $>$2. Improvements in exercise capacity remain highest in patients with 6MWD $<$ 400 m at baseline and seem to occur earlier in patients with MRC dyspnea score $>$2.

Acknowledgment

The authors would like to thank all participating patients, health centers, and coworkers for their efforts, which enabled the successful completion of this study.

Disclosure

The Bocholtz Study was funded by PICASSO for COPD, an initiative of Boehringer Ingelheim, Pfizer, and the Caphri Research Institute, Maastricht University, The Netherlands.

References

1. World Health Organization. World Health Statistics 2008. Geneva: World Health Organization; 2008.
2. Nici L, Donner C, Wouters E, et al. American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. *Am J Respir Crit Care Med*. 2006;173(12):1390–1413.
3. Rabe KF, Hurd S, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med*. 2007;176(6):532–535.
4. Berry MJ, Rejeski WJ, Adair NE, Ettinger WH Jr, Zaccaro DJ, Sevick MA. A randomized, controlled trial comparing long-term and short-term exercise in patients with chronic obstructive pulmonary disease. *J Cardiopulm Rehabil*. 2003;23(1):60–68.
5. Takigawa N, Tada A, Soda R, et al. Comprehensive pulmonary rehabilitation according to severity of COPD. *Respir Med*. 2007;101(2):326–332.
6. Lacasse Y, Martin S, Lasserson TJ, Goldstein RS. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane systematic review. *Eura Medicophys*. 2007;43(4):475–485.
7. Landry MD, Hamdan E, Al MS, Brooks D. The precarious balance between 'supply' and 'demand' for health care: The increasing global demand for rehabilitation service for individuals living with chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis*. 2008;3(3):393–396.
8. Smeele IJM, van Weel C, van Schayck CP, et al. Dutch College of General Practitioners Guideline for COPD. *Huisarts Wet*. 2007;50(8):362–379. Dutch.
9. Chavannes NH, Grijsen M, van den Akker M, et al. Integrated disease management improves one-year quality of life in primary care COPD patients: A controlled clinical trial. *Prim Care Respir J*. 2009;18(3):171–176.
10. Chavannes N. Integrated chronic obstructive pulmonary disease management in primary care. *Dis Manage Health Outcomes*. 2008;16(5):315–318.
11. Ries AL, Kaplan RM, Limberg TM, Prewitt LM. Effects of pulmonary rehabilitation on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease. *Ann Intern Med*. 1995;122(11):823–832.
12. Griffiths TL, Burr ML, Campbell IA, et al. Results at 1 year of outpatient multidisciplinary pulmonary rehabilitation: A randomised controlled trial. *Lancet*. 2000;355(9201):362–368.
13. Vale F, Reardon JZ, ZuWallack RL. The long-term benefits of outpatient pulmonary rehabilitation on exercise endurance and quality of life. *Chest*. 1993;103(1):42–45.
14. Celli BR, MacNee W. Standards for the diagnosis and treatment of patients with COPD: A summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23(6):932–946.
15. Bestall JC, Paul EA, Garrod R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 1999;54(7):581–586.
16. Redelmeier DA, Bayoumi AM, Goldstein RS, Guyatt GH. Interpreting small differences in functional status: The six minute walk test in chronic lung disease patients. *Am J Respir Crit Care Med*. 1997;155(4):1278–1282.
17. Nici L, Raskin J, Rochester CL, et al. Pulmonary rehabilitation: What we know and what we need to know. *J Cardiopulm Rehabil Prev*. 2009;29(3):141–151.
18. Maltais F, Bourbeau J, Shapiro S, et al. Effects of home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: A randomized trial. *Ann Intern Med*. 2008;149(12):869–878.
19. American Thoracic Society. Pulmonary Rehabilitation. *Am J Respir Crit Care Med*. 1999;159(5 Pt 1):1666–1682.
20. Guyatt GH, Berman LB, Townsend M. Long-term outcome after respiratory rehabilitation. *CMAJ*. 1987;137(12):1089–1095.
21. Strijbos JH, Postma DS, van Altena R, Gimeno F, Koeter GH. A comparison between an outpatient hospital-based pulmonary rehabilitation program and a home-care pulmonary rehabilitation program in patients with COPD. A follow-up of 18 months. *Chest*. 1996;109(2):366–372.
22. Guell R, Casan P, Belda J, et al. Long-term effects of outpatient rehabilitation of COPD: A randomized trial. *Chest*. 2000;117(4):976–983.
23. Wijkstra PJ, Ten Vergert EM, van Altena R, et al. Long term benefits of rehabilitation at home on quality of life and exercise tolerance in patients with chronic obstructive pulmonary disease. *Thorax*. 1995;50(8):824–828.
24. Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: A randomized trial. *Am J Med*. 2000;109(3):207–212.
25. Engstrom CP, Persson LO, Larsson S, Sullivan M. Long-term effects of a pulmonary rehabilitation programme in outpatients with chronic obstructive pulmonary disease: A randomized controlled study. *Scand J Rehabil Med*. 1999;31(4):207–213.
26. Bendstrup KE, Ingemann JJ, Holm S, Bengtsson B. Out-patient rehabilitation improves activities of daily living, quality of life and exercise tolerance in chronic obstructive pulmonary disease. *Eur Respir J*. 1997;10(12):2801–2806.
27. van Wetering CR, van Nooten FE, Mol SJ, Hoogendoorn M, Rutten-van Molken MP, Schols AM. Systemic impairment in relation to disease burden in patients with moderate COPD eligible for a lifestyle program. Findings from the INTERCOM trial. *Int J Chron Obstruct Pulmon Dis*. 2008;3(3):443–451.
28. Pitta F, Troosters T, Spruit MA, Probst VS, Decramer M, Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2005;171(9):972–977.
29. Pitta F, Troosters T, Probst VS, Langer D, Decramer M, Gosselink R. Are patients with COPD more active after pulmonary rehabilitation? *Chest*. 2008;134(2):273–280.
30. Celli BR, Cote CG, Marin JM, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. *N Engl J Med*. 2004;350(10):1005–1012.