

**ORIGINAL RESEARCH**

# Integrated disease management improves one-year quality of life in primary care COPD patients: a controlled clinical trial

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## Abstract

**Aim:** To assess the long-term effectiveness of an integrated disease management (IDM) program (consisting of optimal medication, reactivation, education, and exacerbation management) in primary care patients with chronic obstructive pulmonary disease (COPD).

**Method:** Controlled trial comparing the effects of IDM on quality of life – assessed by the St. George's Respiratory Questionnaire (SGRQ) – in primary care COPD patients. The minimal clinically important change on the SGRQ was accepted as being -4 points. Baseline and one-year differences were compared using paired sample T-tests. The differential effects of an FEV<sub>1</sub>/FVC ratio <0.7 and dyspnoea as assessed by the Medical Research Council (MRC) Dyspnoea scale were investigated.

**Results:** The average age of subjects was 63 years, with an average post-bronchodilator FEV<sub>1</sub> of 67% predicted, average FEV<sub>1</sub>/FVC ratio of 0.65, a mean of 35 pack-years smoking, and 63% were male. No significant differences existed between groups at baseline. After one year of IDM, SGRQ had improved by -4.6 points (95% CI, -7.2 to -2.0; p=0.001) in the intervention group, versus -0.7 points (95% CI, -3.0 to 1.6; p=0.6) in the usual care group. In patients with an FEV<sub>1</sub>/FVC ratio <0.7, SGRQ improved by -5.9 points (95% CI, -9.6 to -2.2; p=0.002) in the IDM group, while in the usual care group SGRQ improved by -0.8 points (95% CI, -4.1 to 2.4; p=0.6). In patients with an MRC Dyspnoea score >2 and FEV<sub>1</sub>/FVC <0.7, SGRQ improved by -13.4 points (95% CI, -20.8 to -6.1; p=0.002) in the IDM group, versus -0.3 points (95% CI, -5.5 to 4.9; p=0.9) in the usual care group.

**Conclusion:** In this study, IDM improved one-year quality of life in primary care COPD patients, compared to usual care. The improvement in SGRQ was both clinically relevant and statistically significant, and was greatest in patients with FEV<sub>1</sub>/FVC <0.7 and MRC Dyspnoea score >2.

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## Background

Since the concept of COPD as a treatable disease was introduced in the 2004 ATS/ERS COPD position paper,<sup>1</sup> several studies have shown beneficial effects of medication on exercise tolerance,<sup>2</sup> quality of life,<sup>3</sup> and exacerbations.<sup>4</sup> The size of the effect, however, was usually modest, and the study populations often consisted of selected moderate to very

severe patients, considerably reducing the external validity for primary care patients.<sup>5</sup>

The importance of non-medical interventions such as smoking cessation and physical activity enhancement was underscored recently, when 20-year follow-up data were published<sup>6,7</sup> showing that daily exercise reduces lung function decline (and consequently the risk of developing COPD),

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hospitalisation and even respiratory mortality by 30 to 40% – a protective effect which until now remained reserved for smoking cessation alone,<sup>8</sup> since medical interventions have failed to show significant effects on mortality.<sup>4</sup> Self-management programmes can also reduce hospitalisations by 40%, but this has until now only been demonstrated in patients with severe COPD.<sup>9</sup>

In daily practice, the majority of patients are treated in primary care, where most suffer from mild to moderate COPD.<sup>10</sup> Therefore, pragmatic primary care studies in which optimal medical and non-medical treatments are combined into an integrated disease management (IDM) intervention are needed, but to our knowledge have been lacking to this date.

From longstanding clinical observations during the development of disease management programmes in primary care COPD patients, we deduced a hypothesis: the potential for improvement in quality of life (QoL) seems greatest when lung function is relatively intact, while symptoms of dyspnoea are already considerable. We have therefore performed a controlled clinical trial in primary care COPD patients to assess the effects of an IDM programme on long term disease-specific QoL.

## Method

Two primary health care centres serving two separate villages in the southern part of the Netherlands were recruited for epidemiological reasons: both had very similar patient populations with comparable regional living conditions, but these were traditionally self-sufficient communities with little risk of intervention contamination.

Due to pre-existing national primary care guidelines for the diagnosis and treatment of COPD, health care providers in the two centres were working in a comparable fashion before commencing the study; this changed, however, when the IDM model was introduced in the intervention setting during which time usual care was maintained in the control health centre. The control health centre, lying on the other side of a hill separating the two villages, was kept strictly unaware of the new treatment strategies, on the condition that swift and facilitated implementation would occur after the study was completed successfully. The IDM programme was based largely on recommendations from the ATS/ERS COPD Standards,<sup>10</sup> with additions from earlier work on disease management,<sup>11</sup> and included optimal medication prescribing and adherence monitoring, rapid action plans for exacerbations, personalised physical activity training programmes (at least three sessions of at least 40 minutes of physical activity per week over three months) and continuous self-management education including personal goal-setting by motivational interviewing techniques.

An integrated COPD management team was created, comprising two specialised physiotherapists, a respiratory nurse, a physician assistant, a dietician, a pharmacist, a supervising primary care physician, and a logistical manager, who took charge of the monthly team meetings. A standardised treatment protocol was written by all team members, each taking responsibility for their respective areas of expertise, which could be optimally tailored to individual patient needs.

Patients were recruited on the basis of an existing diagnosis of COPD, with chronic respiratory complaints in the absence of a prior history of asthma or atopy, and had to fulfil former national guideline lung function criteria with a post-bronchodilator FEV<sub>1</sub> <80% predicted and/or a post-bronchodilator FEV<sub>1</sub>/FVC ratio <0.7. Since the latter requirement was not a diagnostic criterion in the earlier national guideline, it was decided beforehand to investigate the differential effects of both the FEV<sub>1</sub>/FVC ratio <0.7 and the patients' Medical Research Council (MRC) Dyspnoea scores. Exclusion criteria were limited, and consisted of rapidly progressing or terminal disease, immobility, substance abuse, or inability to fill in questionnaires.

Power calculation (power of 80% with  $\alpha = 0.05$ ) indicated that 2x75 patients were needed to detect a clinically relevant change in QoL on the St George's Respiratory Questionnaire (SGRQ),<sup>12</sup> including 20% lost to follow-up. We used the Dutch self-administered version of the SGRQ, and considered a -4 unit change as the minimum clinically important difference (MCID) for within-group comparison.<sup>13</sup> As a second disease-specific measure of QoL we used the Dutch diary version of the Clinical COPD Questionnaire (CCQ),<sup>14</sup> which is especially useful in the primary care setting and which shows an MCID of -0.4 points.<sup>15</sup> The MRC Dyspnoea score was used to assess dyspnoea, using the original 5-point scale.<sup>16</sup> By simply naming daily physical activities like walking or cycling, we obtained an impression of inactive lifestyle at baseline. Current and past smoking was assessed by asking systematically for smoking history and calculating pack-years. We did not use biochemical methods to validate smoking status as the primary outcome was not smoking cessation.

Data were analysed with SPSS version 13, using independent T-tests and chi-square tests for baseline characteristics comparison. We only used paired sample T-tests for prospective within-group comparisons, since this pragmatic controlled clinical trial was not randomised and thus head-to-head comparison was not deemed statistically sound. The regional Medical Ethics Committee of the Atrium Medical Centre Heerlen approved of the study protocol, while all participating patients gave their written informed consent.

**Table 1. Baseline characteristics of intervention versus control group\***

	Intervention (n=79)	Control (n=73)	p-value#
Age (yrs)	64 (11)	63 (11)	0.53
Gender (% male)	59	67	0.32
Pack-years (n)	37 (24)	33 (17)	0.33
Current smoking (%)	38	45	0.42
Body Mass Index	27 (5)	27 (5)	0.98
Inactive lifestyle (%)	45	47	0.87
FEV <sub>1</sub> pre-BD (%)	62 (19)	66 (16)	0.15
FEV <sub>1</sub> post-BD (%)	66 (20)	68 (17)	0.59
FEV <sub>1</sub> /FVC post-BD	0.65 (.14)	0.65 (.13)	0.83
SGRQ –Total	29.6 (20)	34.5 (19)	0.12
CCQ	1.3 (.9)	1.6 (1)	0.10
MRC>2 (%)	36	32	0.61

\*all values are means (SD) except when stated otherwise; #no significant differences between groups existed at baseline

## Results

We recruited 162 primary care COPD patients, of whom 152 had analysable data – 79 in the intervention group and 73 in the control group. Table 1 shows the study baseline characteristics. There were no significant differences in demographic variables – including smoking behaviour, physical activity, QoL measures, or respiratory symptoms – between the intervention and control group. The population consisted of middle-aged patients with largely mild to moderate COPD; 10% (11/106) had GOLD stage I disease, 61% (65/106) stage II, 25% (27/106) stage III, and 3% (3/106) had stage IV disease (data not shown). Subjects had an average smoking history of about 35 pack-years. The proportion of patients with dyspnoea on little exertion or worse, expressed by an MRC score >2, was about a third of the study population, while the proportion of patients with an FEV<sub>1</sub>/FVC ratio <0.7 was 70% (106/152).

During the first year of the study, 24 patients (15%) were lost to follow-up: 11 patients in the intervention group, and 13 in the control group. Most withdrawals (80%) were due to an unwillingness to fill in questionnaires repeatedly or to

attend annually for lung function measurements. No COPD-attributable deaths were recorded in either group (data not shown).

Table 2 shows the changes in MRC Dyspnoea scores. After one year, the proportion of patients in the intervention group with MRC >2 had decreased from 36% to 13% (relative change -64%), whereas the number increased in the control group from 32% to 44% (relative increase +38%).

Table 3 shows the one-year changes in SGRQ and CCQ scores in the two groups. There were statistically significant large to moderate improvements of -4.61 and -0.28, respectively, in the intervention group, while the control group showed non-significant changes of -0.67 and +0.06, respectively. In patients with an FEV<sub>1</sub>/FVC ratio < 0.7, (Table 4), the effect on SGRQ and CCQ in the intervention group was a large and statistically significant improvement of -5.9 and -0.39, respectively, while the control group maintained non-significant changes of -0.83 and +0.01, respectively. In patients with both FEV<sub>1</sub>/FVC <0.7 and MRC scores >2, (Table 5), the effect on SGRQ and CCQ in the intervention group was a very substantial, statistically significant and clinically relevant

**Table 2. MRC Dyspnoea Scale; relative changes for the intervention versus control group at 1 year**

	Intervention group baseline / after 1 year		Relative change	Control group baseline / after 1 year		Relative change
MRC 1-2	64%	87%	+36%	68%	56%	-18%
MRC 3-5	36%	13%	-64%	32%	44%	+38%

**Table 3. Effect of integrated disease management on quality of life at 1 year\***

	Intervention group 1 yr difference / 95% CI		p-value	Control group 1 yr difference / 95% CI		p-value
SGRQ	-4.61	[-7.2, -2.0]	0.001	-0.67	[-3.0, 1.6]	0.56
CCQ	-0.28	[-.44, -.12]	0.001	+0.06	[-.07, 0.2]	0.36

\*paired samples T-test; p is considered significant at values <0.05; MCID SGRQ = -4<sup>13</sup>; MCID CCQ = -0.4<sup>15</sup>

**Table 4. Effect of integrated disease management on quality of life in patients with FEV<sub>1</sub>/FVC <0.7 at 1 year\***

	Intervention group 1 yr difference / 95% CI		p-value	Control group 1 yr difference / 95% CI		p-value
SGRQ	-5.91	[-9.6, -2.2]	0.002	-0.83	[-4.1, 2.4]	0.61
CCQ	-0.39	[-.62, -.17]	0.001	+0.01	[-.17, 0.2]	0.88

\*paired samples T-test; p is considered significant at values <0.05; MCID SGRQ = -4<sup>13</sup>; MCID CCQ = -0.4<sup>15</sup>

**Table 5. Effect of integrated disease management on quality of life in patients with FEV<sub>1</sub>/FVC <0.7 and MRC >2 at 1 year\***

	Intervention group 1 yr difference / 95% CI		p-value	Control group 1 yr difference / 95% CI		p-value
SGRQ	-13.42	[-20.8, -6.1]	0.002	-0.29	[-5.5, 4.9]	0.91
CCQ	-0.92	[-1.4, -.41]	0.002	+0.01	[-.29, 0.29]	1.0

\*paired samples T-test; p is considered significant at values <0.05; MCID SGRQ = -4<sup>13</sup>; MCID CCQ = -0.4<sup>15</sup>

improvement of -13.42 and -0.92, respectively, while the control group patients remained showed non-significant changes of -0.29 and +0.01 respectively.

## Discussion

This pragmatic controlled clinical trial shows that, contrary to common belief, primary care COPD patients can be successfully treated, provided a dedicated multidisciplinary team is in place.

As hypothesised beforehand, the greatest room for improvement seems to be present in patients with mild to moderate disease with an FEV<sub>1</sub>/FVC <0.7 but with considerable dyspnoea (MRC score >2). An important notion seems to be that lung function is still relatively well maintained at that stage, the situation is far from hopeless, and thus physical condition training is of benefit. Possibly, the actual room for improvement is much larger than in patients with (very) severe disease. The physically perceptible change in dyspnoea which occurs within 4-6 weeks of training could be crucial for COPD patients' motivation, as they start to feel that finally there is something that can be done for their disease.

Furthermore, our intervention served different areas of disease expression: personal goals for each individual patient

were explicitly formulated and registered on a time-contingent and adjustable basis; exacerbations were tackled at an early stage, since patients were encouraged to seek help within three days of increasing symptoms; group training sessions often led to increased social contacts, as participants were encouraged to start up sporting groups with their peers; and through tailor-made education, patients learned about their disease in-depth and about effective therapies and self-management possibilities, which they were often not aware of during years of slowly progressing disease.

All these factors must have contributed to a surprising sense of regaining control, which was reflected in the clinically relevant and statistically significant improvements in QoL measurements. Interestingly, the SGRQ showed the most dramatic improvements across all group comparisons, while the CCQ seemed somewhat less clear. This could possibly be a result of measurements taking place after a year; the most tangible improvements were likely to occur 6-12 weeks after inclusion, and this possibly reflects the sensitive but slightly more volatile character of the CCQ as compared to the SGRQ.

The study setting in two comparable but separate villages that traditionally hardly interact has shown to be effective, since there were no significant baseline differences and very few

instances of possible contamination were reported. The study team actively looked for intervention contamination during the whole study period, and especially monitored prescription and referral behaviour from the control health centre. Before the study, the control GPs were promised swift and facilitated implementation once the study had ended – if the results turned out to be favourable – but only if the study was completely finished and no attempt was made to interfere with the intervention. It is due to the collective determination of the study team members and a prevailing attitude where these promises were kept, that meant that the contrast between the intervention and control groups was maintained throughout the study.

A favourable factor (for this study) was the low availability and accessibility of rehabilitation facilities in the surrounding areas of the two villages; a bus connection with several stopovers, or a costly taxi journey are required to reach the nearest rehabilitation centre. This certainly meant that our population was in need of our community-based intervention. Nevertheless, this lamentable situation is not unique in the Netherlands (and other countries as well), where insufficient availability and accessibility of nearby rehabilitation facilities is a common and increasing problem at the same time as COPD prevalence is on the rise worldwide.

This study was not designed to optimise smoking cessation, although all smoking participants in both settings were offered guidance according to national COPD guidelines. A non-significant cessation difference of 4% versus 1% at one year (data not shown) was observed in favour of the intervention group, although this could not explain the significant and clinically relevant change in QoL outcomes. It suggests however, that integrated disease management offers a favourable environment for smoking cessation.

The GOLD definition of obstruction as a fixed ratio of FEV<sub>1</sub>/FVC below 0.7 has only recently been recommended in the revised Dutch national COPD guidelines of 2007. At the time of study commencement, the guideline still recommended an FEV<sub>1</sub> of below 80% predicted for labelling COPD. In our study we applied both criteria, since we aimed to be inclusive rather than exclusive, in order to increase external validity.<sup>5</sup> Interestingly, downsizing the study group by using the fixed ratio did not dilute the effect on QoL, as could have been expected, but rather the contrary occurred. Probably the content of the programme had a distinct effect on patients with fixed obstruction and a tangible burden of respiratory symptoms, who likely are in greatest need of integrated disease management.

The further applicability of IDM programmes such as this needs further cost-benefit studies. We tried solely to demonstrate an optimally achievable result in primary care COPD patients. Developing the study protocol and designing the treatment plans were time-consuming elements. However, since

all health care workers wrote their own part of the protocol (supervised by the study coordinator), deploying the treatment plans was less of a burden, and quickly became an integrated part of daily work. Nevertheless, overall costs of the program have likely been a fraction of formal rehabilitation costs, since all patients continued to live in their own habitat, trained twice a week under supervision and once at home, while contacts with the respiratory nurse were usually every 3-6 months, depending on disease severity. Team meetings were kept at a monthly one-hour session with intermittent one-to-one interdisciplinary consultations if needed (usually ten minutes once a week).

Furthermore, all health care workers reported that, contrary to common belief, it became a pleasure to work with these COPD patients, since they improved so clearly and quickly. In addition, the patients' personal goals were central to regaining a sense of control after many years of gradually losing it. Disease education and exacerbation management were excellent tools to understand the process and to remain in control for the future. Finally, the newly-found social contacts and consequent peer pressure to take control through an active lifestyle, probably are essential to make a lasting change.

Many studies have demonstrated the beneficial effects of formal COPD rehabilitation programmes in severe to very severe patients, but have also shown the difficulty in maintaining initial results in the longer term. Self-management in severe COPD patients reduced hospitalisations in Canada by almost 40%,<sup>9</sup> but in milder patients hospitalisations are considerably less common, and depend strongly on health care systems. By providing simpler rehabilitation programmes for less severe patients in primary care, people learn how to manage COPD in their own habitat, and health care providers are trained to coach this process directly. The negative spiral of dyspnoea and de-conditioning has earlier been recognised as a central mechanism for COPD development;<sup>17</sup> we now propose that integrated disease management can counteract this mechanism. It is likely that costs will be lower while patients are helped at an earlier stage, possibly reducing decline and disease progression in the long term. We recommend that future studies address these issues in a larger primary care population, taking into account feasibility in different health care organisations.

## Conclusion

In this study, integrated disease management (IDM) improves one-year quality of life in primary care COPD patients, compared to usual care. The improvement in SGRQ was both clinically relevant and statistically significant, and was greatest in patients with an FEV<sub>1</sub>/FVC ratio <0.7 and an MRC Dyspnoea score >2.

## Conflicts of interest

All authors declare that they have no conflict of interest with regard to this study.

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