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Effectiveness of the Assessment of Burden of COPD (ABC) tool on health-related quality of life in COPD patients: A cluster randomised controlled trial in primary and hospital care

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ABSTRACT

Objective Assessing the effectiveness of the Assessment of Burden of COPD (ABC) tool on disease-specific quality of life in patients with chronic obstructive pulmonary disease (COPD) measured with the St. George's Respiratory Questionnaire (SGRQ), compared with usual care.

Methods A pragmatic cluster-randomised controlled trial, in 39 Dutch primary care practices and 17 hospitals, with 357 COPD (post-bronchodilator FEV1/FVC ratio<0.7) patients ≥40 years of age, who could understand and read the Dutch language. Healthcare providers were randomly assigned to the intervention or control group. The intervention group applied the ABC tool, which consists of a short validated questionnaire assessing the experienced burden of COPD, objective COPD parameter (e.g., lung function), and a treatment algorithm including a visual display and treatment advice. The control group provided usual care. Researchers were blinded to group allocation during analyses. Primary outcome was the number of patients with a clinically relevant improvement in SGRQ-score between baseline and 18-month follow-up. Secondary outcomes were the COPD Assessment Test (CAT) and the Patient Assessment of Chronic Illness Care (PACIC; a measurement of perceived quality of care).

Results At 18 months follow-up 34% of the 146 patients from 27 healthcare providers in the intervention group showed a clinically relevant improvement in the SGRQ, compared with 22% of the 148 patients from 29 healthcare providers in the control group (OR 1.85, 95% CI 1.08 to 3.16). No difference was found on the CAT (-0.26 points (scores ranging from 0 to 40); 95% CI -1.52 to 0.99). The PACIC showed a higher improvement in the intervention group (0.32 points (scores ranging from 1 to 5): 95% CI, 0.14 to 0.50).

Conclusions This study showed that use of the ABC tool may increase quality of life and perceived quality of care.

Trial registration: Netherlands Trial Register, NTR3788

Keywords: COPD, shared decision-making, patient-centred care, quality of life, communication tool, disease-management

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study was a pragmatic study, which makes the results more applicable to daily care.
- The study was executed nationwide in both primary and hospital care.
- Due to the design of the study, no blinding and allocation concealment was possible.
- Due to the pragmatic design, not all data was reported that was necessary to perform all analyses.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic disease with millions of sufferers worldwide. This number is expected to increase, mainly due to an aging population and an increase in smoke exposure in women.[1-3]

COPD has a major impact on daily life and quality of life that goes beyond airway limitation.[4-8] The Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guideline recommends a combined assessment of COPD using the so-called "ABCD" classification model, which, apart from spirometry, assesses both future risk (exacerbations) and current burden/impact of disease using questionnaire data.[3] However, tools advocated to assess the burden of COPD only measure a limited number of aspects, and do not provide a visual display to educate and involve patients in their treatment. Perhaps even more importantly, the way in which to make use of the patient-reported outcomes or the impact of assessing the burden of disease in this way on outcomes of care have not been tested at all. Therefore the Assessment of Burden of COPD (ABC) tool was developed[9], an innovative tool measuring and visualising integrated health status. An important part of the tool is the ABC scale (see Appendix A), which is largely based on the Clinical COPD Questionnaire (CCQ),[10] and which measures the experienced burden of COPD. The CCQ was adapted by adding four questions to the existing ten questions, to comply with the definition of burden of COPD, which was formulated by an expert team and confirmed by patients and healthcare providers.[9] The ABC scale consists of five domains (i.e., symptoms, functional state, mental state, emotions, and fatigue),[9] and shows excellent reliability and validity.[11] This scale is combined with other parameters (i.e., lung function, exacerbations, body mass index, co-morbidity, smoking status, and self-reported level of physical activity) to assess the integrated health status of a COPD patient. The ABC tool visualises the outcome (using balloons, see Figure 1) and therewith promotes awareness for patient and healthcare provider, and offers a treatment algorithm. Moreover, it provides the opportunity to support personalised care planning including a personal treatment goal. When a balloon is selected, an evidence-based treatment advice is shown, which the patient and healthcare provider can discuss. They can then decide on a treatment plan together through shared decision-making (see Box 1).

The majority of treatment options includes lifestyle changes, such as smoking cessation and increasing physical activity, which requires commitment, engagement and self-management skills of patients.[12,13] The ABC tool can be used as a communication tool in both primary and hospital care (i.e., both in mild/moderate and severe/very severe COPD patients), and it also provides the opportunity to monitor progression or deterioration by displaying the balloons of previous visits in grey (see Figure 1). We hypothesised that giving patients the possibility and the responsibility in setting personal treatment goals and making their own treatment plan will influence self-management, facilitate and stimulate behavioural change, and eventually lead to an improved quality of life.

The primary aim of this study was to assess the effectiveness of using the ABC tool in COPD patients on disease-specific quality of life based on the Saint George's Respiratory Questionnaire (SGRQ),[14] over a period of 18 months compared with a control group receiving usual care.

Secondary outcomes were quality of life based on the COPD Assessment Test (CAT)[15] and the patients' perceived quality of care as assessed with the Patient Assessment of Chronic Illness Care (PACIC).[16]

METHODS

Study design, setting and patients

The current study was a pragmatic, two-armed, cluster randomised controlled trial, conducted in 56 healthcare centres (39 primary care, 17 hospital care) across the Netherlands from March 2013 to May 2015 (Netherlands Trial Register, NTR3788). Ethics approval was obtained from the Medical Ethics Committee of Zuyderland Hospital, Heerlen, the Netherlands. A detailed protocol of this study has been published elsewhere.[17] Informed consent was signed by patients prior to enrolment.

Healthcare providers were recruited by the researchers, with no specific criteria or prerequisites. These healthcare providers recruited patients, who were eligible to participate if they had a spirometry-confirmed diagnosis of COPD (post-bronchodilator Forced Expiratory Volume in 1 second (FEV1)/Forced Vital Capacity (FVC)< 0.7), were 40 years of age or over, and could understand and read the Dutch language. Exclusion criteria were: exacerbation less than six weeks before initiation of the study, an addiction to hard drugs, a life-threatening co-morbid condition, or pregnancy at the start of the study.[17] Eligibility criteria were checked by the healthcare providers.

Randomisation and masking

We randomised at the level of healthcare providers to prevent contamination. Block randomisation of healthcare centres (random blocks of 2, 4 and 6), stratified by health care setting (i.e., primary vs. hospital care) was performed by the researchers using a computer program developed by the Maastricht University Centre for Data and Information Management (MEMIC). Blinding of healthcare professionals and patients was not possible due to the nature of the intervention, but the study team was blind to the nature of the treatment arms in the dataset. Unblinding was performed after unanimous agreement on data cleaning, handling of missing data, statistical analyses, and conclusions drawn for the primary outcome.

Intervention

Healthcare providers (i.e., GPs, practice nurses, pulmonologists and nurse specialists) were instructed to use the ABC tool during their routine consultations. In each consultation, patients were asked to fill out the ABC scale[9], report their dyspnoea using the Medical Research Council (MRC) dyspnoea scale[18] and self-report their level of physical activity. Healthcare providers were instructed to obtain some additional parameters (i.e., lung function, exacerbations, body mass index, co-morbidity, and smoking status) and enter these into the computer program. The program displayed the results as balloons (see Figure 1 for an example). The colours and altitude of the balloons and corresponding implications could then be discussed, and consequently, patients and healthcare providers could decide on a treatment plan together. Patients were encouraged to formulate a personal treatment goal, in their own words, and a specific treatment plan in accordance with this goal (Box 1 provides an example). It was possible to print out an overview of the balloons, the personal goal, and treatment plan at the end of the consultation. The ABC tool is also meant to be used to monitor patients' health status: previous results are displayed using grey balloons, resulting in the possibility to discuss progress and deterioration of different parameters and to evaluate treatment success.

Box 1 Example of a patient's personal goal and treatment plan

Patient Ms A:
This patient completed the ABC scale, the MRC-scale and reported her level of physical activity. Additional parameters were reported by the healthcare provider. The ABC tool is shown in Figure 1. The patient decides, together with the GP, to increase her level of physical activity.
Treatment plan:
Patient will raise her level of physical activity. Evaluation in three months.
Personal goal:
Walking my dog, three times a day, every day, for at least 15 minutes each time.

Control
Healthcare providers in the control group were instructed to provide care as usual to their patients, as described in the Dutch COPD healthcare guidelines.[19,20] These guidelines are in line with guidelines from the European Respiratory Society, the American Thoracic Society,[4] and with the GOLD[3] guideline. The ABC scale and tool were not used in the control group.

Measurements
Health-related quality of life data were collected at four different points in time: at baseline and at 6, 12, and 18-month follow-up. A set of questionnaires, i.e., SGRQ, CAT, and PACIC, was sent by the researchers and completed by patients at home without supervision, either on paper or online (as preferred by the patient). Patients received reminders if they had not returned the questionnaires within three weeks.

The SGRQ,[21,22] is a disease-specific measure of health status with scores that range from 0 to 100 (=maximum impairment). Missing data were handled as described in the SGRQ-Manual.[23]
The CAT is another disease-specific questionnaire with scores ranging from 0 to 40, where higher scores indicate greater impairment of health-related quality of life. Scores were calculated if no more than two items were missing.[15]
The PACIC is a validated questionnaire that assesses patients' perceptions of the quality of care they have received in the past six months. Scores range from 1 to 5, with higher scores representing higher perceived quality of care.[16] As no specific missing data rules are provided for the PACIC, it was decided to only include patients in the analyses if at least 50% of the questions were completed.[24]

Objective parameters (i.e., lung function and exacerbations) were entered by the healthcare providers into the registration system developed for this trial. Reminders to report the outcomes were sent twice during the 18-month follow-up.

Outcomes

The primary outcome measure was a clinically relevant improvement on the SGRQ,[14] defined as a decrease of at least 4 points on the total score of the SGRQ between baseline and the 18-month follow-up.

Secondary outcomes:

1. Clinically relevant improvement on the SGRQ between baseline and six months, and between baseline and 12 months.
2. Clinically relevant deterioration on the SGRQ between baseline and six-months, baseline and 12-months, and baseline and 18-months.
3. Change in SGRQ total score between baseline and 18-months.
4. Change in CAT score between baseline and 18-months.
5. Change in perceived quality of care based on the PACIC between baseline and 12-months, and baseline and 18-months.

According to our research protocol[17] two other clinical outcomes were to be used, i.e., lung function and exacerbation rate. Data for these analyses had to be reported by healthcare providers. However, in the control group these data were reported for only one third of the patients, a problem encountered because of the pragmatic design of the study. Because of this large amount of missing data it was decided not to address these two outcomes.

Sample size

The sample size calculation[17] indicated that a total of 360 patients (180 patients per arm) was required to detect a difference in the response rate on the primary outcome between the intervention and control group (i.e., 50% vs. 30% patients with a clinically relevant improvement of at least 4 points in the intervention group and control group, respectively[14]), with an attrition rate of 25%, a power of 80% to detect this difference, and a two-tailed alpha of 5%. We estimated that 40 GPs (average of 5 patients per GP) and 20 pulmonologists (average of 8 patients per pulmonologist) were required. A detailed description of the sample size calculation can be found in Appendix B.

Statistical analyses

Data were analysed according to the intention to treat principle, that is, all available data of all randomised healthcare providers and patients were included in the analysis, using maximum likelihood inference with mixed regression for repeated measures. To address the primary outcome and the first two secondary outcomes (see above), change scores in the SGRQ were calculated by subtracting the baseline score from the scores at the six, 12, and 18-month follow-up. These change scores were then dichotomised into improved (i.e., a decrease of four points or more on the SGRQ total score[14]) vs. not improved, and into deteriorated (i.e., an increase of four points or more on the SGRQ total score[14]) vs. not deteriorated. The relationship between treatment and SGRQ improvement (yes or no) was then analysed with mixed logistic regression, taking into account that the times of measurement (change after six, 12 and 18 months) were nested within patients, and patients were nested within healthcare providers (three levels). Treatment arm (i.e., intervention group vs. control group), time, treatment by time interaction, and covariates were incorporated into the model as predictors. Covariates included in

the analyses were age, sex, smoking status at baseline and healthcare setting (i.e., primary care vs. hospital care). This analysis was repeated three times for the outcome clinically relevant SGRQ improvement yes/no, with 18 months (primary outcome) and six and 12 months (secondary outcomes) as reference time-points respectively, in order to estimate and test the treatment effect in a simple way for each time point (primary: 18 months, secondary: six and 12 months).
The same analyses were repeated for the outcome clinically relevant SGRQ deterioration yes/no.

To address the other secondary outcomes - i.e., the mean change in SGRQ total score, CAT total score, and PACIC total score - analyses were performed with mixed linear regression, with cluster, patient, and measurements as three levels. Predictors used in the model were time using dummy coding with baseline as the reference category, and dummy indicators for the 12 and 18-month follow-up, and for SGRQ and CAT also a dummy indicator for the six-month follow-up, treatment by time interaction, and the same covariates as mentioned above.

The primary treatment effect and the effect on improvement after six and 12 months were tested using $\alpha = 0.05$ (two-tailed) following the protocol. However, in view of multiple testing, treatment effects on the other secondary outcomes were required to be significant at $\alpha = 0.01$. All analyses were performed using IBM SPSS statistics for Windows, version 21.0.

Sensitivity analyses

For the purpose of sensitivity analysis for the primary outcome, a mixed logistic regression analysis was also performed on only those patients for whom an SGRQ score at baseline and at 18 months had been recorded, allowing computation of change without borrowing information from other patients or other points in time in case of a missing value at 18 months. So, patients were nested in clusters and the dependent variable was a dichotomous change score at 18 months (i.e., improved vs. not improved). The results of this analysis were compared with those of the intention to treat analysis including all available measurements of all patients.

RESULTS

Sixty two healthcare providers were randomised into the two treatment groups: 42 from primary care and 20 from hospital care. Three healthcare providers from primary care, and three from hospital care did not include any patients. Figure 2 shows the study flowchart with the number of healthcare providers and patients included in the study and randomised in the intervention or control group. In the intervention group the average age of the healthcare providers was 50.4 years (SD=8.3) and in the control group it was 50.3 years (SD=7.5). The average years of work experience with COPD patients in the intervention group was 15.1 years (SD=8.9), and in the control group 11.6 years (SD=7.5). In the intervention group and control group the numbers of male healthcare providers were six and nine, respectively.

Thirteen patients dropped out before the baseline measurement and were excluded from the analyses. A total of 357 patients completed at least one set of questionnaires. At 18 months, 305 patients, from 56 clusters, completed the study (of these 305 patients 11 patients did not complete the SGRQ at baseline).

The baseline characteristics of the 357 patients included in the intervention group and control group are shown in Table 1. Patients from the intervention group showed a somewhat lower FEV_1/FVC ratio, and FEV_1 %.

Intervention compliance

To check for intervention compliance, we looked at the number of times the ABC scale was completed, the number of times a treatment plan was made, and the number of times a personal goal was formulated per patient according to the registration system of the ABC tool (example in Figure 1 and Box 1). On average, in 18 months patients completed the ABC scale 2.7 times (SD=1.3). Furthermore, on average, a treatment plan was recorded 2.4 times (SD=1.3), and a personal goal was formulated 2.3 times (SD=1.3).

Table 1 *Patients' baseline characteristics*

	Intervention group (n=175)	Control group (n=182)
Age, years, mean (SD)	64.8 (8.7)	65.8 (8.8)
Sex, male, % (n)	52.6 (92)	60.4 (110)
Recruiting healthcare provider		
Primary care, % (n)	54.9 (96)	63.7 (116)
Hospital care, % (n)	45.1 (79)	36.3 (66)
FEV_1/FVC ratio, mean (SD)	48.5 (12.8)	52.1 (11.8)
FEV_1, % predicted, mean (SD)	56.6 (17.8)	62.3 (19.8)
GOLD stage, % (n)		
1 (FEV1 >80% predicted)	8.6 (15)	17.0 (31)
2 (FEV1 50-80% predicted)	48.6 (85)	46.7 (85)
3 (FEV1 30-50% predicted)	30.9 (54)	24.2 (44)
4 (FEV1 <30% predicted)	5.1 (9)	2.7 (5)
Missing	6.9 (12)	9.3 (17)
Diagnosed with COPD since, % (n)		
1-3 year(s)	33.1 (58)	26.4 (48)
>3 years	62.3 (109)	67.0 (122)
Unknown	4.6 (8)	6.6 (12)
Number of exacerbations in last year, % (n)		
0	44.0 (77)	49.5 (90)
1	26.3 (46)	24.7 (45)
2	12.0 (21)	10.4 (19)
>2	13.7 (24)	7.7 (14)
Missing	4.0 (7)	7.7 (14)
Smoking status, % (n)		
Current smoker	32.6 (57)	24.7 (45)
Ex-smoker	60.0 (105)	60.4 (110)
Never smoked	5.1 (9)	4.4 (8)
Missing	2.3 (4)	10.4 (19)
Pack-years smoking, mean (SD)	33.2 (28.3)	30.8 (23.7)
Baseline SGRQ, mean (SD)		
Symptoms	49.9 (22.2)	44.2 (25.5)
Activity	44.6 (23.8)	41.4 (24.3)
Impact	24.6 (14.7)	22.8 (15.1)
Total	39.7 (17.8)	36.2 (19.3)

Primary outcome: Improvement after 18 months

In the intervention group 49 (33.6%) patients showed a clinically relevant improvement on the SGRQ after 18 months, compared with 33 (22.3%) patients in the control group. The adjusted odds of a clinically relevant improvement as defined by an improvement of at least 4 points on the SGRQ after 18 months was 1.85 times as high (95% CI 1.08 to 3.16, p=0.02) in the intervention group as in the control group (Figure 3). The outcome variation between care providers was 0.035 (p=0.75), giving an intraclass correlation (ICC) of 0.01 according to the ICC definition for binary outcomes in Hedeker.[25]

As sensitivity analysis a mixed logistic regression analysis was subsequently performed with the 294 cases with complete data on the SGRQ at baseline and after 18 months, disregarding the measurements after six and 12 months, so that clinical improvement was solely based on SGRQ at baseline and after 18 months, without borrowing information from other points in time or patients. This analysis yielded similar results as the previously mentioned mixed logistic repeated measures analysis of the primary analysis (adjusted OR, 1.78: 95% CI 1.02 to 3.10, p=0.04).

Furthermore, since there seemed to be an imbalance between groups at baseline with respect to FEV1% and the FEV1/FVC ratio, we repeated the primary intention to treat analysis with FEV1% predicted and FEV1/FVC ratio added to the model as covariates. This analysis also resulted in significantly higher odds of improvement for the intervention group (adjusted OR 1.90, 95%CI 1.07 to 3.38, p=0.03).

Secondary outcomes

Improvement in SGRQ

After six months, there was no statistically significant difference in the number of patients with a clinically relevant improvement in SGRQ between groups (adjusted OR = 1.30, 95%CI 0.79 to 2.13, p=0.30). After 12 months, the adjusted odds of a minimal clinically relevant improvement in SGRQ was 2.03 times as high (95% CI 1.20 to 3.41, p<0.01) in the intervention group as in the control group (see Figure 3).

Deterioration in SGRQ

The adjusted odds ratio of the outcome clinically relevant deterioration in SGRQ was 0.96 after six months (95%CI 0.59 to 1.58, p=0.87). After 12 months the adjusted odds of a deterioration in the intervention group was 0.60 times as small as in the control group (95%CI 0.36 to 1.00, p=0.04). After 18 months the difference between the intervention group and the control group was in the same direction as the difference after 12 months (adjusted OR = 0.64, 95%CI 0.39 to 1.04, p=0.07) (see Figure 3).

SGRQ (continuous score)

Table 2 shows the associations between treatment and SGRQ total score and domain scores at six, 12 and 18-month follow-up. There was no significant association between treatment and the total score after six months (-0.90 points: 95% CI -2.85 to 1.05, p=0.37), but there was a significant association with improvement after 12 months (-2.96 points: 95% CI -4.99 to -0.93, p<0.01) and after 18 months (-3.08 points: 95% CI -5.36 to -0.80, p<0.01). There was no outcome variation between healthcare providers giving an ICC of 0.00. These results indicate that treatment according to the ABC tool was associated with better quality of life.

Additional analyses of the subdomains of the SGRQ showed that, after 18 months, treatment was associated with an improvement in the symptom domain (-4.52 points: 95% CI -8.15 to -0.89, p=0.015). However, this was just short of significance when taking the more stringent significance level of 1% into account. There was a significant asssociation with the subdomain impact (-2.59 points: 95% CI -4.66 to -0.52, p=0.01), but not with the activity domain (-2.34 points: 95% CI -5.52 to 0.83, p=0.15).

Table 2 Effect of treatment (ABC tool) on the total score and subdomains of the SGRQ at different points in time, as established with mixed linear regression correcting for age, gender, healthcare setting, and smoking status, N=334

	Score in intervention group, mean (SD)	Score in control group, mean (SD)	β*	95% CI		P value
				Lower	Upper	
SGRQ symptoms						
6 months	48.81 (22.83)	43.15 (26.19)	-0.83	-3.95	2.30	0.602
12 months	44.65 (21.58)	45.63 (26.27)	-5.50	-8.92	-2.07	0.002
18 months	46.16 (23.69)	45.33 (26.46)	-4.52	-8.15	-0.89	0.015
SGRQ activity						
6 months	45.35 (24.54)	43.36 (25.96)	-0.86	-3.74	2.02	0.557
12 months	44.66 (24.92)	43.62 (26.86)	-1.12	-4.00	1.77	0.447
18 months	44.23 (26.59)	43.72 (27.45)	-2.34	-5.52	0.83	0.147
SGRQ impact						
6 months	25.45 (16.24)	23.14 (15.92)	0.23	-1.82	2.29	0.822
12 months	24.43 (15.94)	24.51 (15.59)	-1.46	-3.42	0.50	0.144
18 months	23.86 (15.58)	24.68 (17.36)	-2.59	-4.66	-0.52	0.014
SGRQ total score						
6 months	39.88 (20.29)	36.79 (20.29)	-0.90	-2.85	1.05	0.365
12 months	37.91 (18.33)	38.10 (20.80)	-2.96	-4.99	-0.93	0.004
18 months	38.39 (19.26)	37.84 (21.92)	-3.08	-5.36	-0.80	0.008

* β = mixed linear regression weight for treatment at that point in time. β < 0 indicates a lower score in the intervention group. Lower scores or negative change scores indicate a higher quality of life based on the SGRQ

CAT

The total CAT scores of the treatment groups after 18 months did not differ significantly from each other (-0.26 points: 95% CI -1.52 to 0.99, p=0.68). There was no outcome variation between healthcare providers, thus yielding an ICC of 0.00.

PACIC

The analyses of the PACIC total score showed that treatment had a significant effect after 18 months on the total score of 0.32 points (95% CI 0.14 to 0.50, p<0.01; see table 3). The outcome variation between healthcare providers was 0.886 (p=0.08), yielding an ICC of 0.05.

Analyses of the subdomains showed that treatment was significantly associated with improvement after 18 months in all domains (p<0.01), except for the 'follow-up/coordination' domain (see table 3). These results indicate that treatment according to the ABC tool was associated with better perceived quality of care. Table 3 also displays the results after 12 months.

Table 3 Effect of treatment (ABC tool) on the total score and subdomains of the PACIC at different points in time, as established with mixed linear regression correcting for age, gender, healthcare setting, and smoking status, N=331

	Score in intervention group, mean (SD)	Score in control group, mean (SD)	β*	95% CI		P value
				Lower	Upper	
Activation						
12 months	3.26 (1.26)	2.97 (1.22)	0.15	-0.11	0.41	0.267
18 months	3.45 (1.21)	2.90 (1.24)	0.39	0.14	0.65	0.003
Delivery system design						
12 months	3.55 (1.07)	3.26 (1.08)	0.19	-0.04	0.43	0.100
18 months	3.73 (1.03)	3.11 (1.10)	0.52	0.30	0.75	<0.001
Goal setting						
12 months	3.21 (1.12)	2.57 (1.00)	0.40	0.18	0.61	<0.001
18 months	3.24 (1.05)	2.53 (.97)	0.50	0.29	0.71	<0.001
Problem-solving						
12 months	3.26 (1.18)	2.88 (1.16)	0.22	0.02	0.46	0.068
18 months	3.29 (1.22)	2.76 (1.14)	0.38	0.14	0.62	0.002
Follow-up/ Coordination						
12 months	2.29 (1.13)	2.05 (0.99)	0.12	-0.07	0.31	0.215
18 months	2.29 (1.09)	2.14 (1.08)	0.04	-0.16	0.23	0.708
Total score						
12 months	3.09 (1.00)	2.71 (.91)	0.20	0.02	0.38	0.032
18 months	3.11 (.95)	2.62 (.97)	0.32	0.14	0.50	0.001

* β = mixed linear regression weight for treatment at that point in time. β > 0 indicates a higher score in the intervention group. Higher scores or positive change scores indicate a higher perceived quality of care based on the PACIC

DISCUSSION

The use of the ABC tool in daily care resulted in more patients experiencing an improved disease-specific quality of life as measured by the SGRQ after a period of 18 months, compared to usual care. This result was also found after 12 months, but not after six months. The latter might be explained by the fact that the collaboration between patient and healthcare provider using the ABC tool requires time and experience to work optimally and that interventions often also require a behavioural change of the patient. The additional analyses of the different domains of the SGRQ showed that there was mainly an improvement in the symptom domain and the impact domain, but these associations are just short of significance when taking the more stringent significance level of 1% to correct for multiple testing of secondary outcomes.

In evaluating the effect of the ABC tool on patients' perceived quality of care (using the PACIC), a significantly better response was found in the ABC-guided group compared to the control group. Positive effects on quality of care were perceived in patient activation, decision support, goal setting, and problem-solving, which could be expected from the person-centred COPD approach with the ABC tool.

This research in the context of other research

In 2013 Agusti and MacNee advocated more personalised medicine for COPD patients,[26] by suggesting that healthcare providers need a 'control panel' for the assessment and management of COPD. To our knowledge, apart from the ABC tool, only one other instrument has been developed for this purpose,[27] although this tool has not yet been evaluated in a randomised trial.

In the management of COPD, interventions are necessary to reduce its burden and prevent its progression.[28,29] Although no interventions like the ABC tool were found in literature,[9] many studies have been described evaluating the effect of behavioural interventions in COPD patients on disease-specific quality of life. These studies show varying results, due to different populations, methods and interventions.[30-38] In many cases, no clinically relevant or statistically significant effect on the SGRQ was found.[34,37-39] Interventions that did result in significant effects on the SGRQ were often much more demanding and intensive, such as pulmonary rehabilitation programs,[30,31] integrated disease-management programs,[32] thorough pro-active self-management education,[33] or weekly home-visits by health professionals.[34] The ABC tool however, is a much more simple and easy to use visual approach that can be deployed as a communication tool in routine COPD care, facilitating shared decision-making.[40-42]

We expected to find results on the CAT comparable to the SGRQ since both questionnaires are strongly correlated[43-45] and in previous studies the CAT and the SGRQ usually showed similar results.[46-48] Additionally, a systematic review about the CAT[43] found that the CAT is a reliable, valid, and responsive instrument. However, most studies evaluating the responsiveness of the CAT focused on patients with acute exacerbations and on patients receiving pulmonary rehabilitation interventions.[49-52] In our study, the ABC tool was used in stable patients from both primary and hospital care. This might indicate that the CAT is less sensitive to change in more stable situations than the SGRQ.

Strengths and limitations

A strength of the study was the fact that it was executed in almost every province of the Netherlands, in both primary and hospital care, providing information about the effects of the intervention in different settings and disease severities. This has positive consequences for the generalisability of the results and potential implementation of the ABC tool. Usual care was based on national guidelines which are in line with international guidelines. However, different usual care in other countries cannot be excluded, which might affect the generalisability to some extent of our results towards other countries.

An additional strength was the pragmatic design to test the effectiveness of the ABC tool in real-life routine practice, which makes the results more applicable to daily primary and hospital care. However, the pragmatic approach also presented challenges. First, the use of the ABC tool was not actively promoted during the study, which meant that four percent of the patients did not receive the intervention. Second, healthcare providers were not actively stimulated to practice using the tool (if they requested the opportunity to practice, a dummy-account was provided), since we believed using the tool would be a self-explanatory. It is conceivable that with more training with the ABC tool, the effect might have been even greater, and more training might be warranted when implementing the tool with less motivated/experienced healthcare providers.

Due to an error in data collection, smoking status was not recorded in all patients in the control group at baseline. However, at the 15 and 18-month follow-up, smoking status was recorded and these data were used to impute the baseline status in patients with missing smoking status at baseline. To validate this imputed baseline smoking status, Cohen's kappa measure of agreement was calculated between the observed and the imputed smoking status in patients with available baseline data. Kappa was 0.86, indicating good agreement, and it was therefore concluded that missing smoking status at baseline could be replaced with data at the 15 or 18-month follow-up.

Perhaps due to randomisation at cluster level instead of individual patient-level, there was some imbalance between both groups at baseline. The intervention group showed a lower initial lung function. In order to detect any possible confounding from this imbalance, we repeated the primary analysis with FEV1% predicted and FER as covariates in the model. This analysis yielded similar results. Additionally, on the symptom domain of the SGRQ the intervention group seemed to score worse at baseline. However, this difference was not significant and we corrected for this difference by calculating change scores. Therefore, we conclude that the results remain unchanged, despite these imbalances.

Furthermore, no blinding and allocation concealment was possible due to the nature of the intervention. However, the researchers performed the analyses on a blinded dataset and were therefore unaware of the coding of treatment arm until unanimous conclusions had been drawn about the results by all authors.

Implications

This study showed a promising development towards person-centred care. Visualisation of the integrated health status seems to be a valid contribution to efforts to place patients in the driver seat of care planning, together with their healthcare provider. Future research should focus on replication of this trial, in other settings and perhaps for other diseases as well, to investigate the underlying mechanisms of the effect of the ABC tool and especially the visually facilitated shared decision making.

Conclusion

Our trial results indicate that the ABC tool has an added value for patients with COPD. Patients treated with the ABC were more likely to report clinically relevant improvement in quality of life, as measured by the SGRQ, compared with patients treated with usual care. Patients also perceived quality of care as better when the ABC tool was applied. Further research is necessary to replicate the results and further investigate the added value of the ABC tool in different settings.

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Conflicts of interest.
All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and AS, DK, MT, SH, PLS, GvB, MPMHRvM, LMAG, NHC, TvdM, GMA, PNRD, and JCCMitV declare that they have not had relationships with any company that might have an interest in the submitted work in the previous 3 years and no non-financial interests that may be relevant to the submitted work. HAMK's institution has recieved grants and fees for consultancies from Boehringer Ingelheim, Pfizer, Almirall, AstraZeneca, Chiesi, GlaxoSmithKline, Novartis, and Takeda, all not related to this submitted work. OCPvS received personal and institutional grants of Pfizer and Boehringer Ingelheim, not related to this submitted work.

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Authors contributions
AHMS, NHC, MPMHRvM, HAMK, TvdM, GMA, PNRD, SH, PLS, JCCMitV, and OCPvS conceived and designed this study, and developed the ABC tool. AHMS and MT gathered the data. AHMS, DK, OCPvS and MT analysed and interpreted the data. GvB and LMAG provided statistical expertise on this paper and analysed and interpreted the data. AHMS drafted the manuscript. DK, OCPvS, JCCMitV, and NHC advised on the preparation of the manuscript. All authors read, edited, and approved the final version of the manuscript. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing
We are planning on producing further publications using this dataset. Afterwards, patient level data and full dataset will be available from the corresponding author. Consent for sharing was not obtained from patients but the presented data are anonymised and risk of identification is low.

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Figure 1 Visualisation of the integrated health status of a COPD patient
The green balloons towards the top of the figure indicate a satisfactory score in that domain, whereas the red balloons signify a low score, and orange balloons an intermediate score. Grey balloons are the balloons of previous visits which provide the opportunity to monitor over time. The five domains of experienced burden of COPD, as measured with the ABC scale, are represented by the last five balloons, symptoms, functional status, mental status, fatigue and emotions. Dyspnoea (evaluated by the MRC scale[18]) and level of physical activity are also reported by the patients. Smoking status, exacerbations, body mass index (BMI) and lung function are reported by the healthcare providers.

Figure 2 Flowchart of patients in the study

Figure 3 Comparison of clinical relevant improvement and deterioration on the SGRQ, after 6, 12 and 18 months between the intervention and control group.

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252x162mm (300 x 300 DPI)

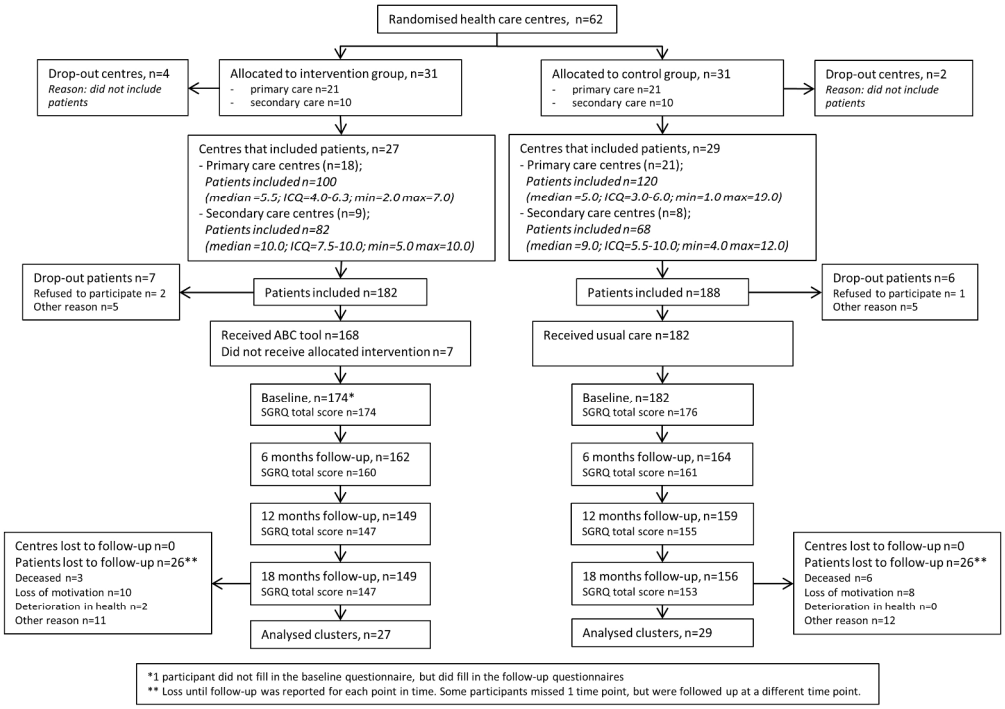

Figure 2 Flowchart of patients in the study
234x167mm (300 x 300 DPI)

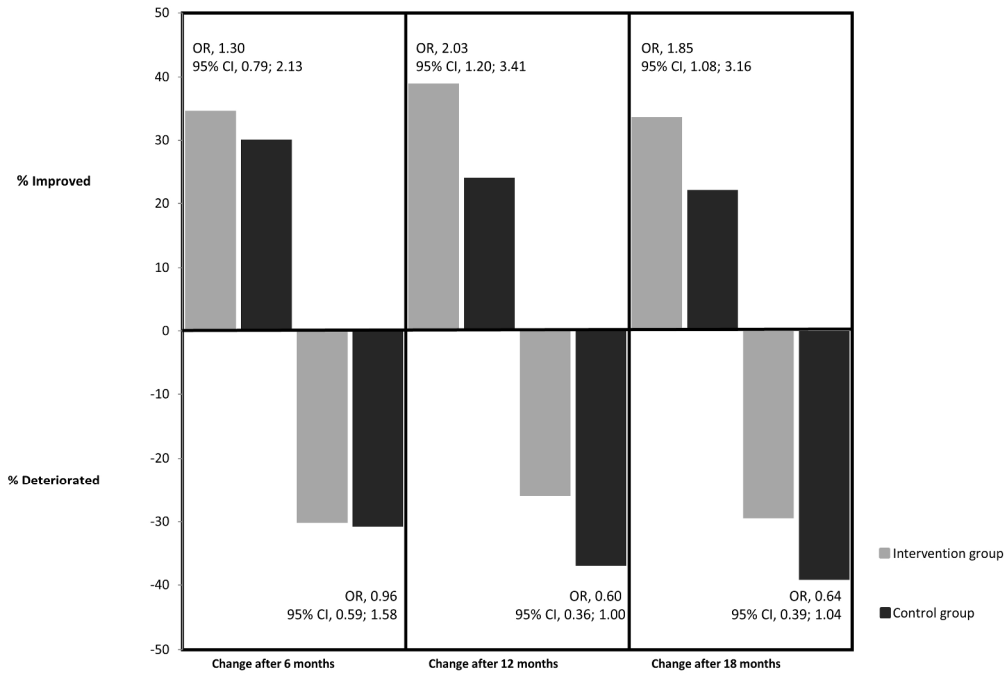

Figure 3 Comparison of clinical relevant improvement and deterioration on the SGRQ, after 6, 12 and 18 months between the intervention and control group.
244x163mm (300 x 300 DPI)

Appendix A The Assessment Of Burden Of COPD (ABC) Scale

Supplemental files

On average, during the past week, how often did you feel:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
1 Short of breath at rest?	☐	☐	☐	☐	☐	☐	☐
2 Short of breath doing physical activities?	☐	☐	☐	☐	☐	☐	☐
3 Concerned about getting a cold or your breathing getting worse?	☐	☐	☐	☐	☐	☐	☐
4 Depressed (down) because of your breathing problems?	☐	☐	☐	☐	☐	☐	☐
In general, during the past week, how much of the time:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
5 Did you cough?	☐	☐	☐	☐	☐	☐	☐
6 Did you produce phlegm?	☐	☐	☐	☐	☐	☐	☐
On average, during the past week, how limited were you in these activities because of your breathing problems:							
	Not limited at all	Very slightly limited	Slightly limited	Moderately limited	Very limited	Extremely limited	Totally limited/ or unable to do
7 Strenuous physical activities (such as climbing stairs, hurrying, doing sports)?	☐	☐	☐	☐	☐	☐	☐
8 Moderate physical activities (such as walking, house work, carrying things)?	☐	☐	☐	☐	☐	☐	☐
9 Daily activities at home (such as dressing, washing yourself)?	☐	☐	☐	☐	☐	☐	☐
10 Social activities (such as talking, being with children, visiting friends/relatives)?	☐	☐	☐	☐	☐	☐	☐
How often in the past week did you suffer from:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
11 Worry?	☐	☐	☐	☐	☐	☐	☐
12 Listlessness?	☐	☐	☐	☐	☐	☐	☐
13 A tense feeling?	☐	☐	☐	☐	☐	☐	☐
14 Fatigue?	☐	☐	☐	☐	☐	☐	☐

Appendix B *Sample size calculation*

The required sample size of 360 patients (180 patients per group) was based on the following assumptions:

1) A clinical response (a clinically relevant improvement of at least 4 points [20]) of 50% in the intervention group versus 30% in the control group [57 58] (implying an effect size *d* = 0.42 for the clinical response), and a power of 80% to detect a difference of the primary outcome between the intervention and control group with a two-tailed alpha of 5%. This assumption gave a sample size of 180 patients in total (90 patients per group), ignoring at first the design effect due to clustering of patients within physicians.
2) The number of participating GPs was about twice as large as the number of pulmonologists.
3) An estimated availability of 5 patients per GP and 8 patients per pulmonologist on average. This, together with assumptions 1 and 2, gave a total of 20 GPs and 10 pulmonologists. However, the following three steps (4-6) resulted in a sample size which was twice as large, that is 40 GPs and 20 pulmonologists.
4) An intraclass correlation coefficient (ICC) of 0.05, meaning that about 5% of the total outcome variation within each group is between GPs and between pulmonologists, instead of between patients of the same physician. Literature suggested that an ICC of 0.05 was a good default value for trials in primary care [59-61]. Combined with assumptions 2 and 3, and allowing for 10% more clusters (healthcare providers) to compensate the power loss due to variation in cluster size, that is, in number of patients included per healthcare provider, this ICC of 0.05 implied a design effect of 1.38 [62]. The number of clusters was thus multiplied with 1.38.
5) A dropout rate of 25% of patients and/or clusters, was compensated by multiplying the number of clusters to be included by 1.33 (since 75% of 1.33 is 1). Dropouts were included into the analyses (intention to treat), but contributed less to the power due to missing data, hence the present correction.
6) Data analysis of the primary outcome with the recommended PQL2 (penalized quasi-likelihood) estimation method which required a further multiplication of the number of clusters with a factor of 1.10 [63].

Combining assumptions 4, 5 and 6 gave a multiplication factor of 1.38 * 1.33 * 1.10 = 2 for the number of GPs and pulmonologists as computed in steps 1 to 3, leading to the planned sample size of 40 GPs, 20 pulmonologists and 360 patients in total [21].

Supplementary file: Participating healthcare providers

Primary care centres	Healthcare providers
Huisartsenpraktijk Wedde	J.D. Berg
Huisartsenpraktijk van Vliet	V. van Vliet / N. Schumacher
Huisartsenpraktijk Smink	S. de Vries
Huisartsenpraktijk Rauws	J. Rauws
Huisartsenpraktijk Zandweg-Oostwaard	R. Wennekes
Huisartsenpraktijk Wijlre	S. Koopmans / P. Schijns
Huisartsenpraktijk Het Heelhuis	R. van der Putten/ E. Zeegers
Huisartsenpraktijk Renswoude	J. Dirven / A. van Hamersveld
Huisartsenpraktijk Gezondheidshuis	F. Oldenhof
Groepspraktijk Huizen	N. IJkelenstam
Gezondheidscentrum Samen beter	G. van Roekel /R. Kockx
Huisartsenpraktijk Noorderhaven	W. de Vreeze / F.A. van Gemert
Huisartsenpraktijk Appel en Hutter	T. Lootsma
Huisartsenpraktijk Korvel	P. Dingemans
Gezondheidscentrum de Haak	A. Veldman
Huisartsen Stellendam	P. de Vries / I. Eigenraam
Huisartsenpraktijk DOC werk	F. Buys
Huisartsenpraktijk Oosting en Flenter	I. Steenkamp
Huisartsenpraktijk Mijnsheerenland	K. Aulbers
Huisartsenpraktijk de Kade	L. Kool
Huisartsen Hoge Hond	M. Vrolijk
Huisartsenpraktijk 't Hart	L. Rorije
Huisartsenpraktijk Hoogh Teylingen	M. de Winde
Huisartsenpraktijk Balkbrug	B. Tigelaar
Huisartsenpraktijk Schuttevaer	Z. Oostwoud
Huisartsenpraktijk de Latyrus	J. Bakker
Huisartsenpraktijk Warnaars	M. Cousin
Gezondheidscentrum Hoensbroek	R. Fornaro / A. Coenen
Huisartsen Moolenburgh	C. Moolenburgh
Huisartsenpraktijk Copenhaege	Y. Holstein / M. Pruijt
Huisartsenpraktijk Timmers	J. Keijser
Huisasrtsenpraktijk Twekkelerveld	B. Gierkink
Huisartsenpraktijk 't Rak	M. van Gend
Van de Vijver & Fesevur huisartsen	E. Moerman
Huisartsenpraktijk de Goudenregen hof	M. van der Zon
Huisartsenpraktijk Jan Hendrik	N. Wiggers
Huisartsenpraktijk de Watertoren	L. van Tiel
Huisartspraktijk Schravenhoff	R. Schravenhoff
Zaaijer & Zaaijer Huisartsen	G. Zaaijer
Hospitals	**Healthcare providers**
Orbis MC	B. Maesen
Wilhelminaziekenhuis Assen	S. de Hosson / T. Meints
Diakonessenhuis	R. van Snippenburg
ZiekenhuisGroep Twente	H. Timmer
Ziekenhuis Gelderse Vallei	J. Verheul / M. van Nieuw-Amerongen

Rijnstate ziekenhuis	F.J.J. Van den Elshout / A. van der Pouw
TweeSteden ziekenhuis	J. Retera
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Catharina ziekenhuis Eindhoven	W. van Litsenburg
Deventer Ziekenhuis	K. Groenewegen
Meander medisch centrum	P. Dalinghaus / G. van Essen
Ommelander Ziekenhuis Groep	J.W. de Jong
MC Zuiderzee	N. Kinket
Ziekenhuis Bethesda	R. van Heerde
Elkerliek	W. Pieters

CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Reported yes/no	Page No *
Title and abstract					
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	**Yes**	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	**Yes**	3
Introduction					
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	**Yes** **Yes**	4 5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the cluster level, the individual participant level or both	**Yes**	4 4
Methods					
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	**Yes**	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		**n.a.**	
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	**Yes** **Yes**	5 5
	4b	Settings and locations where the data were collected		**Yes**	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	**Yes**	5-6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	**Yes**	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons		**Yes**	7
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	**Yes**	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines		**n.a.**	
Randomisation:					

Sequence generation	8a	Method used to generate the random allocation sequence		**Yes**	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	**Yes**	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	**Yes**	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c		
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	**Yes**	5
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	**Yes**	5
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	**Yes**	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		**Yes**	5
	11b	If relevant, description of the similarity of interventions		**n.a.**	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	**Yes**	7-8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		**Yes**	7-8
Results					
Participant flow (a diagram is strongly	13a	For each group, the numbers of participants who were randomly assigned, received intended	For each group, the numbers of clusters that were randomly assigned, received intended	**Yes**	9 Figure 2

recommended)		treatment, and were analysed for the primary outcome	treatment, and were analysed for the primary outcome		
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	**Yes**	9 Figure 2
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**Yes**	5
	14b	Why the trial ended or was stopped		**n.a.**	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	**Yes**	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	**Yes** **Yes**	Tables
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	**Yes**	10-11
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		**Yes**	9-10
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		**Yes**	11
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		**n.a.**	
Discussion					
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		**Yes**	13
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	**Yes**	12-13
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		**Yes**	12/14
Other information					

Registration	23	Registration number and name of trial registry		**Yes**	3
Protocol	24	Where the full trial protocol can be accessed, if available		**Yes**	16 Reference list Supplementary file
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		**Yes**	3, 15

** Note: page numbers optional depending on journal requirements*

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Effectiveness of the Assessment of Burden of COPD (ABC) tool on health-related quality of life in COPD patients: A cluster randomised controlled trial in primary and hospital care

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Effectiveness of the Assessment of Burden of COPD (ABC) tool on health-related quality of life in COPD patients: A cluster randomised controlled trial in primary and hospital care

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ABSTRACT

Objective Assessing the effectiveness of the Assessment of Burden of COPD (ABC) tool on disease-specific quality of life in patients with chronic obstructive pulmonary disease (COPD) measured with the St. George's Respiratory Questionnaire (SGRQ), compared with usual care.

Methods A pragmatic cluster-randomised controlled trial, in 39 Dutch primary care practices and 17 hospitals, with 357 COPD (post-bronchodilator FEV1/FVC ratio<0.7) patients ≥40 years of age, who could understand and read the Dutch language. Healthcare providers were randomly assigned to the intervention or control group. The intervention group applied the ABC tool, which consists of a short validated questionnaire assessing the experienced burden of COPD, objective COPD parameter (e.g., lung function), and a treatment algorithm including a visual display and treatment advice. The control group provided usual care. Researchers were blinded to group allocation during analyses. Primary outcome was the number of patients with a clinically relevant improvement in SGRQ-score between baseline and 18-month follow-up. Secondary outcomes were the COPD Assessment Test (CAT) and the Patient Assessment of Chronic Illness Care (PACIC; a measurement of perceived quality of care).

Results At 18 months follow-up 34% of the 146 patients from 27 healthcare providers in the intervention group showed a clinically relevant improvement in the SGRQ, compared with 22% of the 148 patients from 29 healthcare providers in the control group (OR 1.85, 95% CI 1.08 to 3.16). No difference was found on the CAT (-0.26 points (scores ranging from 0 to 40); 95% CI -1.52 to 0.99). The PACIC showed a higher improvement in the intervention group (0.32 points (scores ranging from 1 to 5): 95% CI, 0.14 to 0.50).

Conclusions This study showed that use of the ABC tool may increase quality of life and perceived quality of care.

Trial registration: Netherlands Trial Register, NTR3788

Keywords: COPD, shared decision-making, patient-centred care, quality of life, communication tool, disease-management

STRENGTHS AND LIMITATIONS OF THIS STUDY

- This study was a pragmatic study, which makes the results more applicable to daily care.
- The study was executed nationwide in both primary and hospital care.
- Due to the design of the study, no blinding and allocation concealment was possible.
- Due to the pragmatic design, not all data was reported that was necessary to perform all analyses.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a chronic disease with millions of sufferers worldwide. This number is expected to increase, mainly due to an aging population and an increase in smoke exposure in women.[1-3]

COPD has a major impact on daily life and quality of life that goes beyond airway limitation.[4-8] The Global Initiative for Chronic Obstructive Pulmonary Disease (GOLD) guideline recommends a combined assessment of COPD using the so-called "ABCD" classification model, which, apart from spirometry, assesses both future risk (exacerbations) and current burden/impact of disease using questionnaire data.[3] However, tools advocated to assess the burden of COPD only measure a limited number of aspects, and do not provide a visual display to educate and involve patients in their treatment. Perhaps even more importantly, the way in which to make use of the patient-reported outcomes or the impact of assessing the burden of disease in this way on outcomes of care have not been tested at all. Therefore the Assessment of Burden of COPD (ABC) tool was developed[9], an innovative tool measuring and visualising integrated health status. An important part of the tool is the ABC scale (see Appendix A), which is largely based on the Clinical COPD Questionnaire (CCQ),[10] and which measures the experienced burden of COPD. The CCQ was adapted by adding four questions to the existing ten questions, to comply with the definition of burden of COPD, which was formulated by an expert team and confirmed by patients and healthcare providers.[9] The ABC scale consists of five domains (i.e., symptoms, functional state, mental state, emotions, and fatigue),[9] and shows excellent reliability and validity.[11] This scale is combined with other parameters (i.e., lung function, exacerbations, body mass index, co-morbidity, smoking status, and self-reported level of physical activity) to assess the integrated health status of a COPD patient. The ABC tool visualises the outcome (using balloons, see Figure 1) and therewith promotes awareness for patient and healthcare provider, and offers a treatment algorithm. Moreover, it provides the opportunity to support personalised care planning including a personal treatment goal. When a balloon is selected, an evidence-based treatment advice is shown, which the patient and healthcare provider can discuss. They can then decide on a treatment plan together through shared decision-making (see Box 1).

The majority of treatment options includes lifestyle changes, such as smoking cessation and increasing physical activity, which requires commitment, engagement and self-management skills of patients.[12,13] The ABC tool can be used as a communication tool in both primary and hospital care (i.e., both in mild/moderate and severe/very severe COPD patients), and it also provides the opportunity to monitor progression or deterioration by displaying the balloons of previous visits in grey (see Figure 1). We hypothesised that giving patients the possibility and the responsibility in setting personal treatment goals and making their own treatment plan will influence self-management, facilitate and stimulate behavioural change, and eventually lead to an improved quality of life.

The primary aim of this study was to assess the effectiveness of using the ABC tool in COPD patients on disease-specific quality of life based on the Saint George's Respiratory Questionnaire (SGRQ),[14] over a period of 18 months compared with a control group receiving usual care.

Secondary outcomes were quality of life based on the COPD Assessment Test (CAT)[15] and the patients' perceived quality of care as assessed with the Patient Assessment of Chronic Illness Care (PACIC).[16]

METHODS

Study design, setting and patients

The current study was a pragmatic, two-armed, cluster randomised controlled trial, conducted in 56 healthcare centres (39 primary care, 17 hospital care) across the Netherlands from March 2013 to May 2015 (Netherlands Trial Register, NTR3788). Ethics approval was obtained from the Medical Ethics Committee of Zuyderland Hospital, Heerlen, the Netherlands. A detailed protocol of this study has been published elsewhere.[17] Informed consent was signed by patients prior to enrolment.

Healthcare providers were recruited by the researchers, with no specific criteria or prerequisites. These healthcare providers recruited patients, who were eligible to participate if they had a spirometry-confirmed diagnosis of COPD (post-bronchodilator Forced Expiratory Volume in 1 second (FEV1)/Forced Vital Capacity (FVC)< 0.7), were 40 years of age or over, and could understand and read the Dutch language. Exclusion criteria were: exacerbation less than six weeks before initiation of the study, an addiction to hard drugs, a life-threatening co-morbid condition, or pregnancy at the start of the study.[17] Eligibility criteria were checked by the healthcare providers.

Randomisation and masking

We randomised at the level of healthcare providers to prevent contamination. Block randomisation of healthcare centres (random blocks of 2, 4 and 6), stratified by health care setting (i.e., primary vs. hospital care) was performed by the researchers using a computer program developed by the Maastricht University Centre for Data and Information Management (MEMIC). Blinding of healthcare professionals and patients was not possible due to the nature of the intervention, but the study team was blind to the nature of the treatment arms in the dataset. Unblinding was performed after unanimous agreement on data cleaning, handling of missing data, statistical analyses, and conclusions drawn for the primary outcome.

Intervention

Healthcare providers (i.e., GPs, practice nurses, pulmonologists and nurse specialists) were instructed to use the ABC tool during their routine consultations. As described in the study protocol patients should visit their healthcare providers at least four times during the 18 months follow-up.[17] Therefore healthcare providers were instructed to invite patients for consultation at least once every six months. In each consultation, patients were asked to fill out the ABC scale[9], report their dyspnoea using the Medical Research Council (MRC) dyspnoea scale[18] and self-report their level of physical activity. Healthcare providers were instructed to obtain some additional parameters (i.e., lung function, exacerbations, body mass index, co-morbidity, and smoking status) and enter these into the computer program. The program displayed the results as balloons (see Figure 1 for an example). The colours and altitude of the balloons and corresponding implications could then be discussed, and consequently, patients and healthcare providers could decide on a treatment plan together. Patients were encouraged to formulate a personal treatment goal, in their own words, and a specific treatment plan in accordance with this goal (Box 1 provides an example). It was possible to print out an overview of the balloons, the personal goal, and treatment plan at the end of the consultation. The ABC tool is also meant to be used to monitor patients' health status: previous results are displayed using grey balloons, resulting in the

possibility to discuss progress and deterioration of different parameters and to evaluate treatment success.

Box 1 Example of a patient's personal goal and treatment plan

Patient Ms A:
This patient completed the ABC scale, the MRC-scale and reported her level of physical activity. Additional parameters were reported by the healthcare provider. The ABC tool is shown in Figure 1. The patient decides, together with the GP, to increase her level of physical activity.
Treatment plan:
Patient will raise her level of physical activity. Evaluation in three months.
Personal goal:
Walking my dog, three times a day, every day, for at least 15 minutes each time.

Control

Healthcare providers in the control group were instructed to provide care as usual to their patients, as described in the Dutch COPD healthcare guidelines.[19,20] These guidelines are in line with guidelines from the European Respiratory Society, the American Thoracic Society,[4] and with the GOLD[3] guideline. The ABC scale and tool were not used in the control group.

Measurements

Health-related quality of life data were collected at four different points in time: at baseline and at 6, 12, and 18-month follow-up. A set of questionnaires, i.e., SGRQ, CAT, and PACIC, was sent by the researchers and completed by patients at home without supervision, either on paper or online (as preferred by the patient). Patients received reminders if they had not returned the questionnaires within three weeks.

The SGRQ,[21,22] is a disease-specific measure of health status with scores that range from 0 to 100 (=maximum impairment). Missing data were handled as described in the SGRQ-Manual.[23]
The CAT is another disease-specific questionnaire with scores ranging from 0 to 40, where higher scores indicate greater impairment of health-related quality of life. Scores were calculated if no more than two items were missing.[15]
The PACIC is a validated questionnaire that assesses patients' perceptions of the quality of care they have received in the past six months. Scores range from 1 to 5, with higher scores representing higher perceived quality of care.[16] As no specific missing data rules are provided for the PACIC, it was decided to only include patients in the analyses if at least 50% of the questions were completed.[24]

Objective parameters (i.e., lung function and exacerbations) were entered by the healthcare providers into the registration system developed for this trial. Reminders to report the outcomes were sent twice during the 18-month follow-up.

Outcomes

The primary outcome measure was a clinically relevant improvement on the SGRQ,[14] defined as a decrease of at least 4 points on the total score of the SGRQ between baseline and the 18-month follow-up.

Secondary outcomes:

1. Clinically relevant improvement on the SGRQ between baseline and six months, and between baseline and 12 months.
2. Clinically relevant deterioration on the SGRQ between baseline and six-months, baseline and 12-months, and baseline and 18-months.
3. SGRQ total score at 18-months.
4. CAT score at 18-months.
5. PACIC score at 12-months, and at 18-months.

According to our research protocol[17] two other clinical outcomes were to be used, i.e., lung function and exacerbation rate. Data for these analyses had to be reported by healthcare providers. However, in the control group these data were reported for only one third of the patients, a problem encountered because of the pragmatic design of the study. Because of this large amount of missing data it was decided not to address these two outcomes.

Sample size

The sample size calculation[17] indicated that a total of 360 patients (180 patients per arm) was required to detect a difference in the response rate on the primary outcome between the intervention and control group (i.e., 50% vs. 30% patients with a clinically relevant improvement of at least 4 points in the intervention group and control group, respectively[14]), with an attrition rate of 25%, a power of 80% to detect this difference, and a two-tailed alpha of 5%. We estimated that 40 GPs (average of 5 patients per GP) and 20 pulmonologists (average of 8 patients per pulmonologist) were required. A detailed description of the sample size calculation can be found in Appendix B.

Statistical analyses

Data were analysed according to the intention to treat principle, that is, all available data of all randomised healthcare providers and patients were included in the analysis, using maximum likelihood inference with mixed regression for repeated measures. To address the primary outcome and the first two secondary outcomes (see above), change scores in the SGRQ were calculated by subtracting the baseline score from the scores at the six, 12, and 18-month follow-up. These change scores were then dichotomised into improved (i.e., a decrease of four points or more on the SGRQ total score[14]) vs. not improved, and into deteriorated (i.e., an increase of four points or more on the SGRQ total score[14]) vs. not deteriorated. The relationship between treatment and SGRQ improvement (yes or no) was then analysed with mixed logistic regression, taking into account that the times of measurement (change after six, 12 and 18 months) were nested within patients, and patients were nested within healthcare providers (three levels). Treatment arm (i.e., intervention group vs. control group), time, treatment by time interaction, and covariates were incorporated into the model as predictors. Covariates included in the analyses were age, sex, smoking status at baseline and healthcare setting (i.e., primary care vs.

hospital care). This analysis was repeated three times for the outcome clinically relevant SGRQ improvement yes/no, with 18 months (primary outcome) and six and 12 months (secondary outcomes) as reference time-points respectively, in order to estimate and test the treatment effect in a simple way for each time point (primary: 18 months, secondary: six and 12 months).
The same analyses were repeated for the outcome clinically relevant SGRQ deterioration yes/no.

To address the other secondary outcomes - i.e., the SGRQ total score, CAT total score, and PACIC total score - analyses were performed with mixed linear regression, with cluster, patient, and measurements as three levels. Predictors used in the model were time using dummy coding with baseline as the reference category, and dummy indicators for the 12 and 18-month follow-up, and for SGRQ and CAT also a dummy indicator for the six-month follow-up, treatment by time interaction, and the same covariates as mentioned above. The interaction effect of treatment with the dummy indicator for 18 months represents the group difference in change from baseline to 18 months, and likewise for the other two treatment by time dummy interaction terms. Further, given that baseline is the reference time point, the treatment effect itself is the group difference at baseline (0 months), which can be expected to be zero due to the randomised treatment assignment. If this treatment effect was indeed not significant, then it was removed from the mixed model. The treatment by time interaction effect then became equivalent to the treatment effect at follow-up adjusted for the baseline as a covariate.[25-27]

The primary treatment effect and the effect on improvement after six and 12 months were tested using $\alpha = 0.05$ (two-tailed) following the protocol. However, in view of multiple testing, treatment effects on the other secondary outcomes were required to be significant at $\alpha = 0.01$. All analyses were performed using IBM SPSS statistics for Windows, version 21.0.

Sensitivity analyses

For the purpose of sensitivity analysis for the primary outcome, a mixed logistic regression analysis was also performed on only those patients for whom an SGRQ score at baseline and at 18 months had been recorded, allowing computation of change without borrowing information from other patients or other points in time in case of a missing value at 18 months. So, patients were nested in clusters and the dependent variable was a dichotomous change score at 18 months (i.e., improved vs. not improved). The results of this analysis were compared with those of the intention to treat analysis including all available measurements of all patients.

RESULTS

Sixty two healthcare providers were randomised into the two treatment groups: 42 from primary care and 20 from hospital care. Three healthcare providers from primary care, and three from hospital care did not include any patients. Figure 2 shows the study flowchart with the number of healthcare providers and patients included in the study and randomised in the intervention or control group. In the intervention group the average age of the healthcare providers was 50.4 years (SD=8.3) and in the control group it was 50.3 years (SD=7.5). The average years of work experience with COPD patients in the intervention group was 15.1 years (SD=8.9), and in the control group 11.6 years (SD=7.5). In the intervention group and control group the numbers of male healthcare providers were six and nine, respectively.

Thirteen patients dropped out before the baseline measurement and were excluded from the analyses. A total of 357 patients completed at least one set of questionnaires. At 18 months, 305 patients, from 56 clusters, completed the study (of these 305 patients 11 patients did not complete the SGRQ at baseline).

The baseline characteristics of the 357 patients included in the intervention group and control group are shown in Table 1. Patients from the intervention group showed a somewhat lower FEV_1/FVC ratio, and FEV_1 %.

Intervention compliance

To check for intervention compliance, we looked at the number of times the ABC scale was completed, the number of times a treatment plan was made, and the number of times a personal goal was formulated per patient according to the registration system of the ABC tool (example in Figure 1 and Box 1). On average, in 18 months patients completed the ABC scale 2.7 times (SD=1.3). Furthermore, on average, a treatment plan was recorded 2.4 times (SD=1.3), and a personal goal was formulated 2.3 times (SD=1.3).

Table 1 *Patients' baseline characteristics*

	Intervention group (n=175)	Control group (n=182)
Age, years, mean (SD)	64.8 (8.7)	65.8 (8.8)
Sex, male, % (n)	52.6 (92)	60.4 (110)
Recruiting healthcare provider		
Primary care, % (n)	54.9 (96)	63.7 (116)
Hospital care, % (n)	45.1 (79)	36.3 (66)
FEV_1/FVC ratio, mean (SD)	48.5 (12.8)	52.1 (11.8)
FEV_1, % predicted, mean (SD)	56.6 (17.8)	62.3 (19.8)
GOLD stage, % (n)		
1 (FEV1 >80% predicted)	8.6 (15)	17.0 (31)
2 (FEV1 50-80% predicted)	48.6 (85)	46.7 (85)
3 (FEV1 30-50% predicted)	30.9 (54)	24.2 (44)
4 (FEV1 <30% predicted)	5.1 (9)	2.7 (5)
Missing	6.9 (12)	9.3 (17)
Diagnosed with COPD since, % (n)		
1-3 year(s)	33.1 (58)	26.4 (48)
>3 years	62.3 (109)	67.0 (122)
Unknown	4.6 (8)	6.6 (12)
Number of exacerbations in last year, % (n)		
0	44.0 (77)	49.5 (90)
1	26.3 (46)	24.7 (45)
2	12.0 (21)	10.4 (19)
>2	13.7 (24)	7.7 (14)
Missing	4.0 (7)	7.7 (14)
Smoking status, % (n)		
Current smoker	32.6 (57)	24.7 (45)
Ex-smoker	60.0 (105)	60.4 (110)
Never smoked	5.1 (9)	4.4 (8)
Missing	2.3 (4)	10.4 (19)
Pack-years smoking, mean (SD)	33.2 (28.3)	30.8 (23.7)
Baseline SGRQ, mean (SD)		
Symptoms	49.9 (22.2)	44.2 (25.5)
Activity	44.6 (23.8)	41.4 (24.3)
Impact	24.6 (14.7)	22.8 (15.1)
Total	39.7 (17.8)	36.2 (19.3)

Primary outcome: Improvement after 18 months

In the intervention group 49 (33.6%) patients showed a clinically relevant improvement, as defined by an improvement of at least 4 points, on the SGRQ after 18 months, compared with 33 (22.3%) patients in the control group. The adjusted odds of a clinically relevant improvement after 18 months was 1.85 times as high (95% CI 1.08 to 3.16, p=0.02) in the intervention group as in the control group (Figure 3). The outcome variation between care providers was 0.035 (p=0.75), giving an intraclass correlation (ICC) of 0.01 according to the ICC definition for binary outcomes in Hedeker.[28]

As sensitivity analysis a mixed logistic regression analysis was subsequently performed with the 294 cases with complete data on the SGRQ at baseline and after 18 months, disregarding the measurements after six and 12 months, so that clinical improvement was solely based on SGRQ at baseline and after 18 months, without borrowing information from other points in time or patients. This analysis yielded similar results as the previously mentioned mixed logistic repeated measures analysis of the primary analysis (adjusted OR, 1.78: 95% CI 1.02 to 3.10, p=0.04).

Furthermore, since there seemed to be an imbalance between groups at baseline with respect to FEV1% and the FEV1/FVC ratio, we repeated the primary intention to treat analysis with FEV1% predicted and FEV1/FVC ratio added to the model as covariates. This analysis also resulted in significantly higher odds of improvement for the intervention group (adjusted OR 1.90, 95%CI 1.07 to 3.38, p=0.03).

Secondary outcomes

Improvement in SGRQ

After six months, there was no statistically significant difference between groups with respect to the proportion of patients with a clinically relevant improvement in SGRQ (adjusted OR = 1.30, 95%CI 0.79 to 2.13, p=0.30). After 12 months, the adjusted odds of a minimal clinically relevant improvement in SGRQ was 2.03 times as high (95% CI 1.20 to 3.41, p<0.01) in the intervention group as in the control group (see Figure 3).

Deterioration in SGRQ

The adjusted odds ratio of the outcome clinically relevant deterioration in SGRQ was 0.96 after six months (95%CI 0.59 to 1.58, p=0.87). After 12 months the adjusted odds of a deterioration in the intervention group was 0.60 times as small as in the control group (95%CI 0.36 to 1.00, p=0.04). After 18 months the difference between the intervention group and the control group was in the same direction as the difference after 12 months (adjusted OR = 0.64, 95%CI 0.39 to 1.04, p=0.07) (see Figure 3).

SGRQ (continuous score)

Table 2 shows the difference between treatment arms with respect to SGRQ total score and domain scores at six, 12 and 18-month follow-up, based on the final mixed model, that is, after deleting the group effect at baseline, which was not significant (p = 0.195, for details see the Statistical Analyses paragraph in the Methods section). There was no significant difference between treatment arms on the total score after six months (-0.90 points: 95% CI -2.85 to 1.05, p=0.37), but there was a significant difference after 12 months (-2.96 points: 95% CI -4.99 to -0.93, p<0.01) and after 18 months (-3.08 points: 95% CI -5.36 to -0.80, p<0.01). There was no outcome variation between healthcare providers

giving an ICC of 0.00. These results indicate that treatment according to the ABC tool was associated with better quality of life. For completeness, we mention that the mixed regression analysis with the treatment effect at baseline still in the model gave very similar effect sizes and the same conclusions about the significance of each effect. Figure 4a shows the change of the observed means in SGRQ total score after six, 12 and 18 months follow-up compared to baseline measurement, for both groups. Since observed means can be biased due to drop-out, Figure 4b shows the change in predicted values based on the mixed regression model, which is much less prone to selection bias. The two plots showed almost the same pattern, that is an increase in group difference in favour of intervention up to month 12 and maintenance of that difference till 18 months.

Additional analyses of the subdomains of the SGRQ showed that, after 18 months, the intervention group had a better score on the symptom domain (-4.52 points: 95% CI -8.15 to -0.89, p=0.015). However, this was just short of significance when taking the more stringent significance level of 1% into account. There was a significant difference in favour of the intervention group on the subdomain impact (-2.59 points: 95% CI -4.66 to -0.52, p=0.01), but not on the activity domain (-2.34 points: 95% CI -5.52 to 0.83, p=0.15).

Table 2 Effect of treatment (ABC tool) on the total score and subdomains of the SGRQ at different points in time, as established with mixed linear regression correcting for age, gender, healthcare setting, and smoking status, N=334

	Observed score, mean (SD)		β*	95% CI		P
	Intervention group	Control group		Lower	Upper	value
SGRQ symptoms						
6 months	48.81 (22.83)	43.15 (26.19)	-0.83	-3.95	2.30	0.602
12 months	44.65 (21.58)	45.63 (26.27)	-5.50	-8.92	-2.07	0.002
18 months	46.16 (23.69)	45.33 (26.46)	-4.52	-8.15	-0.89	0.015
SGRQ activity						
6 months	45.35 (24.54)	43.36 (25.96)	-0.86	-3.74	2.02	0.557
12 months	44.66 (24.92)	43.62 (26.86)	-1.12	-4.00	1.77	0.447
18 months	44.23 (26.59)	43.72 (27.45)	-2.34	-5.52	0.83	0.147
SGRQ impact						
6 months	25.45 (16.24)	23.14 (15.92)	0.23	-1.82	2.29	0.822
12 months	24.43 (15.94)	24.51 (15.59)	-1.46	-3.42	0.50	0.144
18 months	23.86 (15.58)	24.68 (17.36)	-2.59	-4.66	-0.52	0.014
SGRQ total score						
6 months	39.88 (19.09)	36.79 (20.29)	-0.90	-2.85	1.05	0.365
12 months	37.91 (18.33)	38.10 (20.80)	-2.96	-4.99	-0.93	0.004
18 months	38.39 (19.26)	37.84 (21.92)	-3.08	-5.36	-0.80	0.008

* β = mixed linear regression weight for treatment at that point in time. β < 0 indicates a lower score in the intervention group. Lower scores or negative change scores indicate a higher quality of life based on the SGRQ. Effects in this table are based on the mixed model after deleting the treatment effect at baseline, which was never significant. Effects before deleting the treatment effect were very similar and agreed with the present table in terms of significance yes/no.

CAT

The total CAT scores of the treatment groups after 18 months did not differ significantly from each other (-0.26 points: 95% CI -1.52 to 0.99, p=0.68). There was no outcome variation between healthcare providers, thus yielding an ICC of 0.00.

PACIC

The analyses of the PACIC total score showed that treatment had a significant effect after 18 months on the total score of 0.32 points (95% CI 0.14 to 0.50, p<0.01; see table 3). The outcome variation between healthcare providers was 0.886 (p=0.08), yielding an ICC of 0.05.

Analyses of the subdomains showed a significant difference between treatment arms at 18 months in all domains (p<0.01), except for the 'follow-up/coordination' domain (see table 3). These results indicate that treatment according to the ABC tool increased perceived quality of care as compared to the control group. Table 3 also displays the results after 12 months.

Table 3 Effect of treatment (ABC tool) on the total score and subdomains of the PACIC at different points in time, as established with mixed linear regression correcting for age, gender, healthcare setting, and smoking status, N=331

	Score in intervention group, mean (SD)	Score in control group, mean (SD)	β*	95% CI		P value
				Lower	Upper	
Activation						
12 months	3.26 (1.26)	2.97 (1.22)	0.15	-0.11	0.41	0.267
18 months	3.45 (1.21)	2.90 (1.24)	0.39	0.14	0.65	0.003
Delivery system design						
12 months	3.55 (1.07)	3.26 (1.08)	0.19	-0.04	0.43	0.100
18 months	3.73 (1.03)	3.11 (1.10)	0.52	0.30	0.75	<0.001
Goal setting						
12 months	3.21 (1.12)	2.57 (1.00)	0.40	0.18	0.61	<0.001
18 months	3.24 (1.05)	2.53 (.97)	0.50	0.29	0.71	<0.001
Problem-solving						
12 months	3.26 (1.18)	2.88 (1.16)	0.22	0.02	0.46	0.068
18 months	3.29 (1.22)	2.76 (1.14)	0.38	0.14	0.62	0.002
Follow-up/ Coordination						
12 months	2.29 (1.13)	2.05 (0.99)	0.12	-0.07	0.31	0.215
18 months	2.29 (1.09)	2.14 (1.08)	0.04	-0.16	0.23	0.708
Total score						
12 months	3.09 (1.00)	2.71 (.91)	0.20	0.02	0.38	0.032
18 months	3.11 (.95)	2.62 (.97)	0.32	0.14	0.50	0.001

* β = mixed linear regression weight for treatment at that point in time. β > 0 indicates a higher score in the intervention group. Higher scores or positive change scores indicate a higher perceived quality of care based on the PACIC. Effects in this table are based on the mixed model after deleting the treatment effect at baseline, which was never significant (see Methods section). Effects before deleting the treatment effect were very similar and agreed with the present table in terms of significance yes/no.

DISCUSSION

Main findings

We were able to analyse three different outcome measures related to disease-specific quality of life and perceived quality of care. We found significant differences between intervention and control arm on the SGRQ and the PACIC, but not on the CAT.

SGRQ

The use of the ABC tool in daily care resulted in more patients experiencing an improved disease-specific quality of life as measured by the SGRQ after a period of 18 months, compared to usual care. This result was also found after 12 months, but not after six months. The latter might be explained by the fact that the collaboration between patient and healthcare provider using the ABC tool requires time and experience to work optimally and that interventions often also require a behavioural change of the patient. The additional analyses of the different domains of the SGRQ showed that there was mainly an improvement in the symptom domain and the impact domain, but these associations are just short of significance when taking the more stringent significance level of 1% to correct for multiple testing of secondary outcomes.

CAT

We expected to find results on the CAT comparable to the SGRQ since both questionnaires are strongly correlated[29-31] and in previous studies the CAT and the SGRQ usually showed similar results.[32-34] Additionally, a systematic review about the CAT[29] found that the CAT is a reliable, valid, and responsive instrument. Our study however did not indicate any differences between the treatment arms, which might relate to the fact that most studies evaluating the responsiveness of the CAT focused on patients with acute exacerbations and on patients receiving pulmonary rehabilitation interventions.[35-38] In our study, the ABC tool was used in stable patients from both primary and hospital care. This might indicate that the CAT, compared to the SGRQ, is less sensitive to change in more stable situations than the SGRQ.

PACIC

In evaluating the effect of the ABC tool on patients' perceived quality of care (using the PACIC), a significantly better response was found in the ABC-guided group compared to the control group. Positive effects on quality of care were perceived in patient activation, decision support, goal setting, and problem-solving, which could be expected from the person-centred COPD approach with the ABC tool. When developing the ABC tool the main goal was to make a tool that measures burden of COPD, and additionally visualises the integrated health status and provides a treatment algorithm. Furthermore, the tool had to provide room for writing down a treatment plan including a personal treatment goal. All of these components are considered to be important in order to involve the patient in the decision making process and help them take control of the disease, eventually leading to improved self-management and a better quality of life.[39-41]

This research in the context of other research

In 2013 Agusti and MacNee advocated more personalised medicine for COPD patients,[42] by suggesting that healthcare providers need a 'control panel' for the assessment and management of COPD. To our knowledge, apart from the ABC tool, only one other instrument has been developed for this purpose,[43] although this tool has not yet been evaluated in a randomised trial.

In the management of COPD, interventions are necessary to reduce its burden and prevent its progression.[44,45] Although no interventions like the ABC tool were found in literature,[9] many studies have been described evaluating the effect of behavioural interventions in COPD patients on disease-specific quality of life. These studies show varying results, due to different populations, methods and interventions.[46-54] In many cases, no clinically relevant or statistically significant effect on the SGRQ was found.[50,53-55] Interventions that did result in significant effects on the SGRQ were often much more demanding and intensive, such as pulmonary rehabilitation programs,[46,47] integrated disease-management programs,[48] thorough pro-active self-management education,[49] or weekly home-visits by health professionals.[50] The ABC tool however, is a much more simple and easy to use visual approach that can be deployed as a communication tool in routine COPD care, facilitating shared decision-making.[56-58]

Strengths and limitations

A strength of the study was the fact that it was executed in almost every province of the Netherlands, in both primary and hospital care, providing information about the effects of the intervention in different settings and disease severities. This has positive consequences for the generalisability of the results and potential implementation of the ABC tool. Usual care was based on national guidelines which are in line with international guidelines. However, different usual care in other countries cannot be excluded, which might affect the generalisability to some extent of our results towards other countries.

An additional strength was the pragmatic design to test the effectiveness of the ABC tool in real-life routine practice, which makes the results more applicable to daily primary and hospital care. However, the pragmatic approach also presented challenges. First, the use of the ABC tool was not actively promoted during the study, which meant that four percent of the patients did not receive the intervention. Second, healthcare providers were not actively stimulated to practice using the tool (if they requested the opportunity to practice, a dummy-account was provided), since we believed using the tool would be a self-explanatory. It is conceivable that with more training with the ABC tool, the effect might have been even greater, and more training might be warranted when implementing the tool with less motivated/experienced healthcare providers.

Due to an error in data collection, smoking status was not recorded in all patients in the control group at baseline. However, at the 15 and 18-month follow-up, smoking status was recorded and these data were used to impute the baseline status in patients with missing smoking status at baseline. To validate this imputed baseline smoking status, Cohen's kappa measure of agreement was calculated between the observed and the imputed smoking status in patients with available baseline data. Kappa was 0.86,

indicating good agreement, and it was therefore concluded that missing smoking status at baseline could be replaced with data at the 15 or 18-month follow-up.

Perhaps due to randomisation at cluster level instead of individual patient-level, there was some imbalance between both groups at baseline. The intervention group showed a lower initial lung function. In order to detect any possible confounding from this imbalance, we repeated the primary analysis with FEV1% predicted and FER as covariates in the model. This analysis yielded similar results. Additionally, on the symptom domain of the SGRQ the intervention group seemed to score worse at baseline. However, this difference was not significant and we corrected for this difference by calculating change scores. Therefore, we conclude that the results remain unchanged, despite these imbalances.

When calculating the required sample size, the expected proportions of patients improved were difficult to estimate, since little evidence was available on the effect of disease-management interventions on disease specific quality of life as measured by the SGRQ.[59] Therefore, the expected proportions of patients improved were solely based on results of previous drug trials.[60,61] The results from our trial showed that the proportion of patients improved by four points - our primary outcome - was 33.6% in the intervention group compared to 22.3% in the control group. Although this difference was smaller than estimated for the sample size calculation, it was a statistically significant difference. This is at least partly due to the fact that both the actual drop-out rate and the intraclass correlation coefficient (ICC (18% and 0.01, respectively) were lower than expected in the study planning stage (25% and 0.05, respectively). The smaller than expected difference in the proportion of patients improved (11.3% observed vs. 20% expected) may partly be due to the fact that, instead of for example a single drug intervention, a high variety of interventions was possible in this trial, which might dilute the effect. Another possible explanation is the fact that the group COPD patients included in the study was a stable group with better quality of life and therefore lower baseline SGRQ total scores than in other studies, leaving less room for improvement.[62-65]

Furthermore, no blinding and allocation concealment was possible due to the nature of the intervention. However, the researchers performed the analyses on a blinded dataset and were therefore unaware of the coding of treatment arm until unanimous conclusions had been drawn about the results by all authors.

Implications

This study showed a promising development towards person-centred care. Visualisation of the integrated health status seems to be a valid contribution to efforts to place patients in the driver seat of care planning, together with their healthcare provider. Future research should focus on replication of this trial, in other settings and perhaps for other diseases as well, to investigate the underlying mechanisms of the effect of the ABC tool and especially the visually facilitated shared decision making.

Conclusion

Our trial results indicate that the ABC tool has an added value for patients with COPD. Patients treated with the ABC were more likely to report clinically relevant improvement in quality of life, as measured

by the SGRQ, compared with patients treated with usual care. Patients also perceived quality of care as better when the ABC tool was applied. Further research is necessary to replicate the results and further investigate the added value of the ABC tool in different settings.

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Conflicts of interest.
All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and AS, DK, MT, SH, PLS, GvB, MPMHRvM, LMAG, NHC, TvdM, GMA, PNRD, and JCCMitV declare that they have not had relationships with any company that might have an interest in the submitted work in the previous 3 years and no non-financial interests that may be relevant to the submitted work. HAMK's institution has recieved grants and fees for consultancies from Boehringer Ingelheim, Pfizer, Almirall, AstraZeneca, Chiesi, GlaxoSmithKline, Novartis, and Takeda, all not related to this submitted work. OCPvS received personal and institutional grants of Pfizer and Boehringer Ingelheim, not related to this submitted work.

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Authors contributions
AHMS, NHC, MPMHRvM, HAMK, TvdM, GMA, PNRD, SH, PLS, JCCMitV, and OCPvS conceived and designed this study, and developed the ABC tool. AHMS and MT gathered the data. AHMS, DK, OCPvS and MT analysed and interpreted the data. GvB and LMAG provided statistical expertise on this paper and analysed and interpreted the data. AHMS drafted the manuscript. DK, OCPvS, JCCMitV, and NHC advised on the preparation of the manuscript. All authors read, edited, and approved the final version of the manuscript. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Data sharing
We are planning on producing further publications using this dataset. Afterwards, patient level data and full dataset will be available from the corresponding author. Consent for sharing was not obtained from patients but the presented data are anonymised and risk of identification is low.

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Figure 1 Visualisation of the integrated health status of a COPD patient
The green balloons towards the top of the figure indicate a satisfactory score in that domain, whereas the red balloons signify a low score, and orange balloons an intermediate score. Grey balloons are the balloons of previous visits which provide the opportunity to monitor over time. The five domains of experienced burden of COPD, as measured with the ABC scale, are represented by the last five balloons, symptoms, functional status, mental status, fatigue and emotions. Dyspnoea (evaluated by the MRC scale[18]) and level of physical activity are also reported by the patients. Smoking status, exacerbations, body mass index (BMI) and lung function are reported by the healthcare providers.

Figure 2 Flowchart of patients in the study

Figure 3 Comparison of clinical relevant improvement and deterioration on the SGRQ, after 6, 12 and 18 months between the intervention and control group, including percentages of patients at different time points with no clinically relevant change.

Figure 4a Mean change in observed SGRQ total scores at six months, 12 months and 18 months follow-up compared to baseline, with a higher score indicating worse quality of life.

Figure 4b Mean change in predicted SGRQ total scores at six months, 12 months and 18 months follow-up compared to baseline, with a higher score indicating worse quality of life.

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252x162mm (300 x 300 DPI)

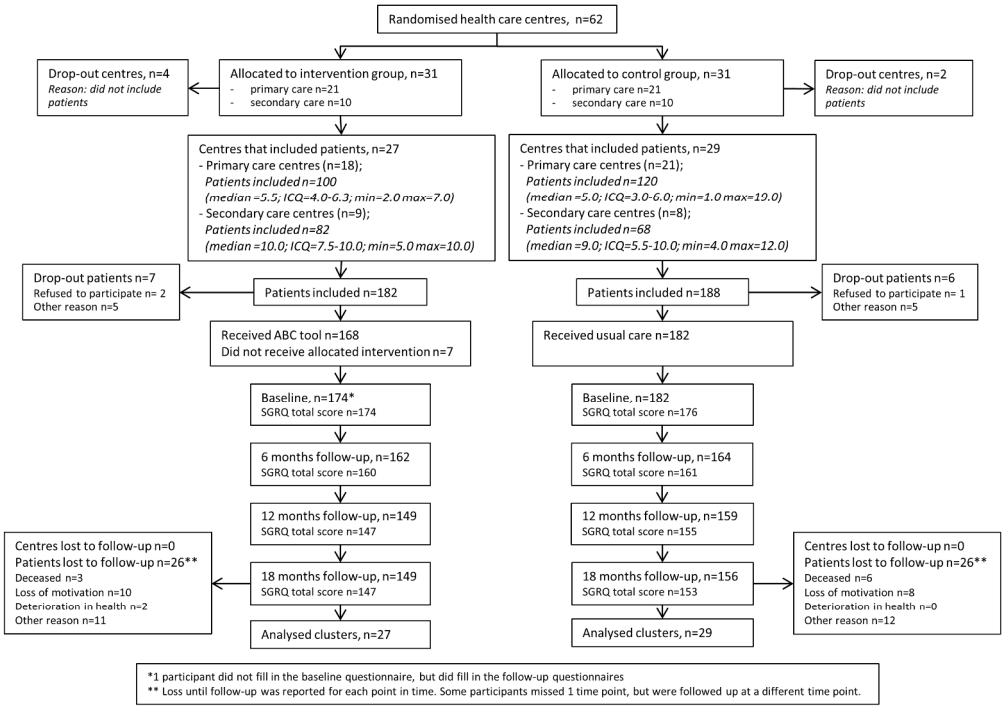

Figure 2 Flowchart of patients in the study
234x167mm (300 x 300 DPI)

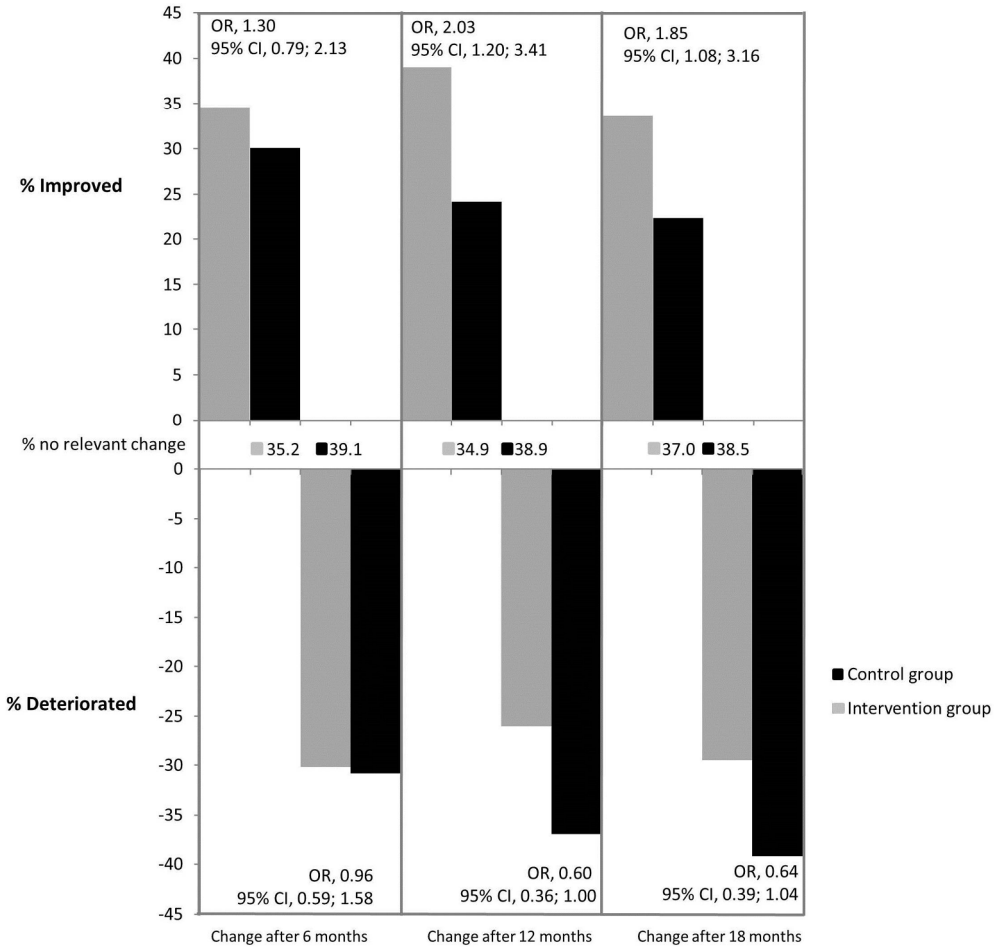

Figure 3 Comparison of clinical relevant improvement and deterioration on the SGRQ, after 6, 12 and 18 months between the intervention and control group, including percentages of patients at different time points with no clinically relevant change.
188x177mm (300 x 300 DPI)

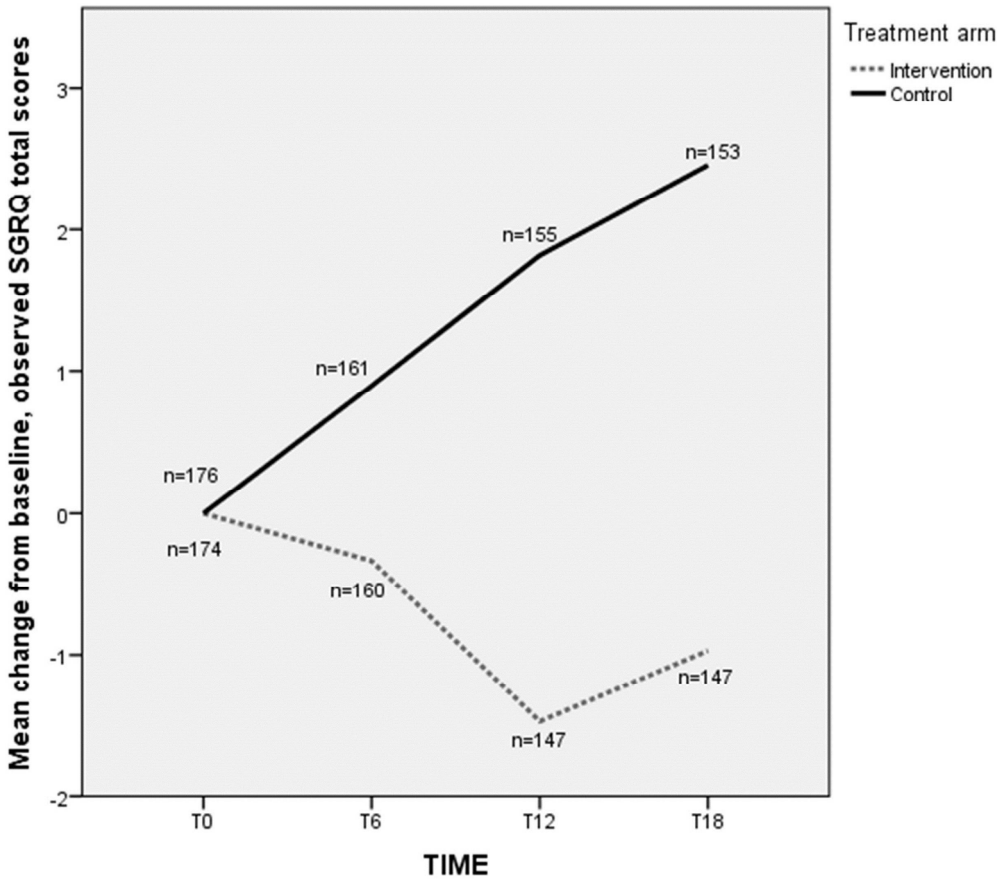

Figure 4a Mean change in observed SGRQ total scores at six months, 12 months and 18 months follow-up compared to baseline, with a higher score indicating worse quality of life.
207x181mm (300 x 300 DPI)

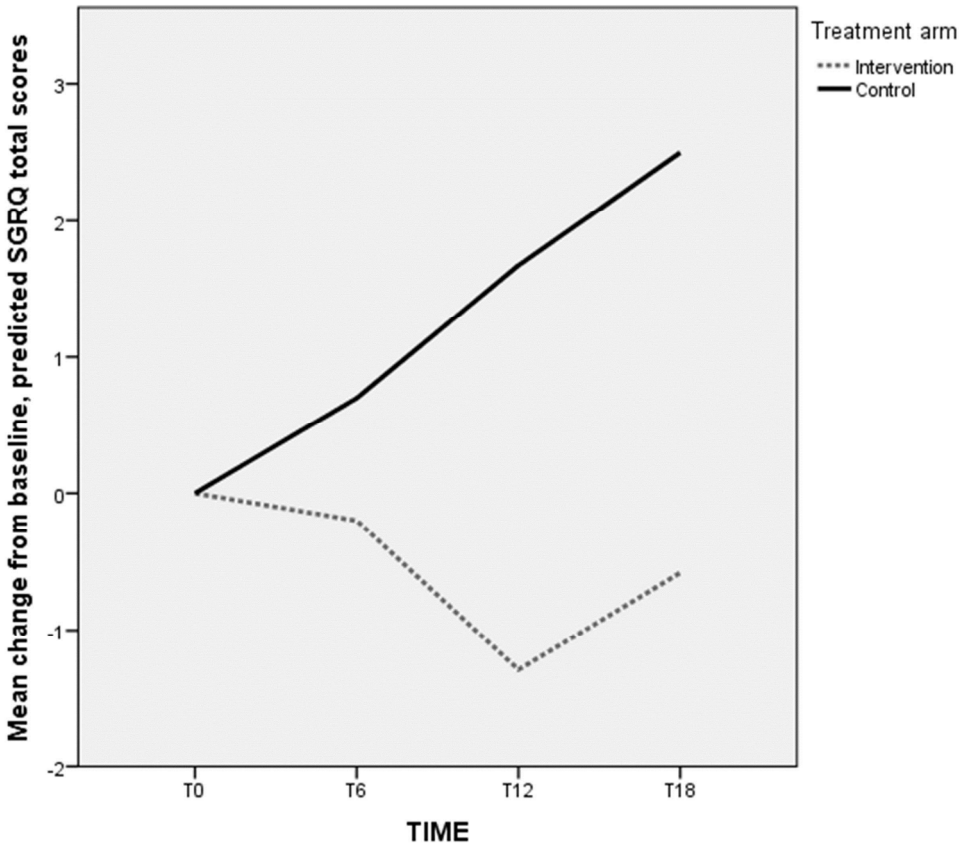

Figure 4b Mean change in predicted SGRQ total scores at six months, 12 months and 18 months follow-up compared to baseline, with a higher score indicating worse quality of life.
211x179mm (300 x 300 DPI)

Appendix A The Assessment Of Burden Of COPD (ABC) Scale
Supplemental files

On average, during the past week, how often did you feel:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
1 Short of breath at rest?	☐	☐	☐	☐	☐	☐	☐
2 Short of breath doing physical activities?	☐	☐	☐	☐	☐	☐	☐
3 Concerned about getting a cold or your breathing getting worse?	☐	☐	☐	☐	☐	☐	☐
4 Depressed (down) because of your breathing problems?	☐	☐	☐	☐	☐	☐	☐
In general, during the past week, how much of the time:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
5 Did you cough?	☐	☐	☐	☐	☐	☐	☐
6 Did you produce phlegm?	☐	☐	☐	☐	☐	☐	☐
On average, during the past week, how limited were you in these activities because of your breathing problems:							
	Not limited at all	Very slightly limited	Slightly limited	Moderately limited	Very limited	Extremely limited	Totally limited/ or unable to do
7 Strenuous physical activities (such as climbing stairs, hurrying, doing sports)?	☐	☐	☐	☐	☐	☐	☐
8 Moderate physical activities (such as walking, house work, carrying things)?	☐	☐	☐	☐	☐	☐	☐
9 Daily activities at home (such as dressing, washing yourself)?	☐	☐	☐	☐	☐	☐	☐
10 Social activities (such as talking, being with children, visiting friends/relatives)?	☐	☐	☐	☐	☐	☐	☐
How often in the past week did you suffer from:							
	Never	Hardly ever	A few times	Several times	Many times	A great many times	Almost all the time
11 Worry?	☐	☐	☐	☐	☐	☐	☐
12 Listlessness?	☐	☐	☐	☐	☐	☐	☐
13 A tense feeling?	☐	☐	☐	☐	☐	☐	☐
14 Fatigue?	☐	☐	☐	☐	☐	☐	☐

Appendix B *Sample size calculation*

The required sample size of 360 patients (180 patients per group) was based on the following assumptions:

1) A clinical response (a clinically relevant improvement of at least 4 points [20]) of 50% in the intervention group versus 30% in the control group [57 58] (implying an effect size *d* = 0.42 for the clinical response), and a power of 80% to detect a difference of the primary outcome between the intervention and control group with a two-tailed alpha of 5%. This assumption gave a sample size of 180 patients in total (90 patients per group), ignoring at first the design effect due to clustering of patients within physicians.
2) The number of participating GPs was about twice as large as the number of pulmonologists.
3) An estimated availability of 5 patients per GP and 8 patients per pulmonologist on average. This, together with assumptions 1 and 2, gave a total of 20 GPs and 10 pulmonologists. However, the following three steps (4-6) resulted in a sample size which was twice as large, that is 40 GPs and 20 pulmonologists.
4) An intraclass correlation coefficient (ICC) of 0.05, meaning that about 5% of the total outcome variation within each group is between GPs and between pulmonologists, instead of between patients of the same physician. Literature suggested that an ICC of 0.05 was a good default value for trials in primary care [59-61]. Combined with assumptions 2 and 3, and allowing for 10% more clusters (healthcare providers) to compensate the power loss due to variation in cluster size, that is, in number of patients included per healthcare provider, this ICC of 0.05 implied a design effect of 1.38 [62]. The number of clusters was thus multiplied with 1.38.
5) A dropout rate of 25% of patients and/or clusters, was compensated by multiplying the number of clusters to be included by 1.33 (since 75% of 1.33 is 1). Dropouts were included into the analyses (intention to treat), but contributed less to the power due to missing data, hence the present correction.
6) Data analysis of the primary outcome with the recommended PQL2 (penalized quasi-likelihood) estimation method which required a further multiplication of the number of clusters with a factor of 1.10 [63].

Combining assumptions 4, 5 and 6 gave a multiplication factor of 1.38 * 1.33 * 1.10 = 2 for the number of GPs and pulmonologists as computed in steps 1 to 3, leading to the planned sample size of 40 GPs, 20 pulmonologists and 360 patients in total [21].

Supplementary file: Participating healthcare providers

Primary care centres	Healthcare providers
Huisartsenpraktijk Wedde	J.D. Berg
Huisartsenpraktijk van Vliet	V. van Vliet / N. Schumacher
Huisartsenpraktijk Smink	S. de Vries
Huisartsenpraktijk Rauws	J. Rauws
Huisartsenpraktijk Zandweg-Oostwaard	R. Wennekes
Huisartsenpraktijk Wijlre	S. Koopmans / P. Schijns
Huisartsenpraktijk Het Heelhuis	R. van der Putten/ E. Zeegers
Huisartsenpraktijk Renswoude	J. Dirven / A. van Hamersveld
Huisartsenpraktijk Gezondheidshuis	F. Oldenhof
Groepspraktijk Huizen	N. IJkelenstam
Gezondheidscentrum Samen beter	G. van Roekel /R. Kockx
Huisartsenpraktijk Noorderhaven	W. de Vreeze / F.A. van Gemert
Huisartsenpraktijk Appel en Hutter	T. Lootsma
Huisartsenpraktijk Korvel	P. Dingemans
Gezondheidscentrum de Haak	A. Veldman
Huisartsen Stellendam	P. de Vries / I. Eigenraam
Huisartsenpraktijk DOC werk	F. Buys
Huisartsenpraktijk Oosting en Flenter	I. Steenkamp
Huisartsenpraktijk Mijnsheerenland	K. Aulbers
Huisartsenpraktijk de Kade	L. Kool
Huisartsen Hoge Hond	M. Vrolijk
Huisartsenpraktijk 't Hart	L. Rorije
Huisartsenpraktijk Hoogh Teylingen	M. de Winde
Huisartsenpraktijk Balkbrug	B. Tigelaar
Huisartsenpraktijk Schuttevaer	Z. Oostwoud
Huisartsenpraktijk de Latyrus	J. Bakker
Huisartsenpraktijk Warnaars	M. Cousin
Gezondheidscentrum Hoensbroek	R. Fornaro / A. Coenen
Huisartsen Moolenburgh	C. Moolenburgh
Huisartsenpraktijk Copenhaege	Y. Holstein / M. Pruijt
Huisartsenpraktijk Timmers	J. Keijser
Huisasrtsenpraktijk Twekkelerveld	B. Gierkink
Huisartsenpraktijk 't Rak	M. van Gend
Van de Vijver & Fesevur huisartsen	E. Moerman
Huisartsenpraktijk de Goudenregen hof	M. van der Zon
Huisartsenpraktijk Jan Hendrik	N. Wiggers
Huisartsenpraktijk de Watertoren	L. van Tiel
Huisartspraktijk Schravenhoff	R. Schravenhoff
Zaaijer & Zaaijer Huisartsen	G. Zaaijer
Hospitals	**Healthcare providers**
Orbis MC	B. Maesen
Wilhelminaziekenhuis Assen	S. de Hosson / T. Meints
Diakonessenhuis	R. van Snippenburg
ZiekenhuisGroep Twente	H. Timmer
Ziekenhuis Gelderse Vallei	J. Verheul / M. van Nieuw-Amerongen

Rijnstate ziekenhuis	F.J.J. Van den Elshout / A. van der Pouw
TweeSteden ziekenhuis	J. Retera
Maasstadziekenhuis	G. Verhoeven
Isala	Vd Berg / M. Joxhorst
Medisch Centrum Leeuwarden	R. Koppers / A. Goosensen
Catharina ziekenhuis Eindhoven	W. van Litsenburg
Deventer Ziekenhuis	K. Groenewegen
Meander medisch centrum	P. Dalinghaus / G. van Essen
Ommelander Ziekenhuis Groep	J.W. de Jong
MC Zuiderzee	N. Kinket
Ziekenhuis Bethesda	R. van Heerde
Elkerliek	W. Pieters

CONSORT 2010 checklist of information to include when reporting a cluster randomised trial

Section/Topic	Item No	Standard Checklist item	Extension for cluster designs	Reported yes/no	Page No *
Title and abstract					
	1a	Identification as a randomised trial in the title	Identification as a cluster randomised trial in the title	**Yes**	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)[1,2]	See table 2	**Yes**	3
Introduction					
Background and objectives	2a	Scientific background and explanation of rationale	Rationale for using a cluster design	**Yes** **Yes**	4 5
	2b	Specific objectives or hypotheses	Whether objectives pertain to the cluster level, the individual participant level or both	**Yes**	4 4
Methods					
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	Definition of cluster and description of how the design features apply to the clusters	**Yes**	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons		**n.a.**	
Participants	4a	Eligibility criteria for participants	Eligibility criteria for clusters	**Yes** **Yes**	5 5
	4b	Settings and locations where the data were collected		**Yes**	6
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	Whether interventions pertain to the cluster level, the individual participant level or both	**Yes**	5-6
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	Whether outcome measures pertain to the cluster level, the individual participant level or both	**Yes**	7
	6b	Any changes to trial outcomes after the trial commenced, with reasons		**Yes**	7
Sample size	7a	How sample size was determined	Method of calculation, number of clusters(s) (and whether equal or unequal cluster sizes are assumed), cluster size, a coefficient of intracluster correlation (ICC or *k*), and an indication of its uncertainty	**Yes**	7
	7b	When applicable, explanation of any interim analyses and stopping guidelines		**n.a.**	
Randomisation:					

Sequence generation	8a	Method used to generate the random allocation sequence		**Yes**	5
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	Details of stratification or matching if used	**Yes**	5
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	Specification that allocation was based on clusters rather than individuals and whether allocation concealment (if any) was at the cluster level, the individual participant level or both	**Yes**	5
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	Replace by 10a, 10b and 10c		
	10a		Who generated the random allocation sequence, who enrolled clusters, and who assigned clusters to interventions	**Yes**	5
	10b		Mechanism by which individual participants were included in clusters for the purposes of the trial (such as complete enumeration, random sampling)	**Yes**	5
	10c		From whom consent was sought (representatives of the cluster, or individual cluster members, or both), and whether consent was sought before or after randomisation	**Yes**	5
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how		**Yes**	5
	11b	If relevant, description of the similarity of interventions		**n.a.**	
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	How clustering was taken into account	**Yes**	7-8
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses		**Yes**	7-8
Results					
Participant flow (a diagram is strongly	13a	For each group, the numbers of participants who were randomly assigned, received intended	For each group, the numbers of clusters that were randomly assigned, received intended	**Yes**	9 Figure 2

recommended)		treatment, and were analysed for the primary outcome	treatment, and were analysed for the primary outcome		
	13b	For each group, losses and exclusions after randomisation, together with reasons	For each group, losses and exclusions for both clusters and individual cluster members	**Yes**	9 Figure 2
Recruitment	14a	Dates defining the periods of recruitment and follow-up		**Yes**	5
	14b	Why the trial ended or was stopped		**n.a.**	
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Baseline characteristics for the individual and cluster levels as applicable for each group	**Yes**	Table 1
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	For each group, number of clusters included in each analysis	**Yes** **Yes**	Tables
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	Results at the individual or cluster level as applicable and a coefficient of intracluster correlation (ICC or k) for each primary outcome	**Yes**	10-11
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended		**Yes**	9-10
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory		**Yes**	11
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms[3])		**n.a.**	
Discussion					
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses		**Yes**	13
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	Generalisability to clusters and/or individual participants (as relevant)	**Yes**	12-13
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence		**Yes**	12/14
Other information					

Registration	23	Registration number and name of trial registry		**Yes**	3
Protocol	24	Where the full trial protocol can be accessed, if available		**Yes**	16 Reference list Supplementary file
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders		**Yes**	3, 15

** Note: page numbers optional depending on journal requirements*

REFERENCES

1 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG, et al. CONSORT for reporting randomised trials in journal and conference abstracts. *Lancet* 2008, 371:281-283

2 Hopewell S, Clarke M, Moher D, Wager E, Middleton P, Altman DG at al (2008) CONSORT for reporting randomized controlled trials in journal and conference abstracts: explanation and elaboration. *PLoS Med* 5(1): e20

3 Ioannidis JP, Evans SJ, Gotzsche PC, O'Neill RT, Altman DG, Schulz K, Moher D. Better reporting of harms in randomized trials: an extension of the CONSORT statement. *Ann Intern Med* 2004; 141(10):781-788.