

Improved health status of severe COPD patients after being included in an integrated primary care service: A prospective cohort study

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KEY MESSAGES

- Severe COPD patients might benefit significantly from care provided by integrated primary care services at similar costs as standard GP care.
- Future studies with larger sample sizes should focus on characteristics of care and patients associated with benefits for severe COPD patients in primary care.

ABSTRACT

Background: Chronic obstructive pulmonary disease (COPD) is a prevalent lung disease. It is assumed that severe patients will receive better treatment in specialised care centres but the prevalence of severe COPD in primary care is high. Integrated primary care services combine input from several sources and advice from pulmonologists to provide general practitioners with support needed to improve diagnosis and treatment of patients with COPD.

Objectives: To evaluate patient-reported outcomes and costs of managing patients classified as GOLD D in an integrated primary care service over 12 months.

Methods: Patients were included in this 1-year prospective cohort study if they met the 2014 GOLD D criteria, were aged ≥ 40 years and gave written informed consent for this study. Recruitment took place through the patients' general practitioners. The primary outcome was health status, assessed with the Clinical COPD Questionnaire (CCQ) and COPD Assessment Test (CAT). Secondary outcomes included self-reported exacerbations, quality-adjusted life years and health(care)-related costs.

Results: Forty-nine patients were included. At baseline, the mean CAT score was 15.9 and the median CCQ score was 1.7. After 12 months, scores had improved by 2.3 (95% confidence interval, 0.8–3.7) and 0.4 (95% confidence interval, 0.2–0.7), respectively. Percentage of patients with ≥ 2 exacerbations in the past 12 months also decreased from baseline (77.6%) to 12 months (16.7%). Changes in mean quarterly costs were small.

Conclusion: An integrated service for COPD based in primary care may improve the health status of patients with a large burden of disease while not increasing health care costs.

ARTICLE HISTORY

Received 7 April 2021
Revised 11 March 2022
Accepted 17 March 2022

KEYWORDS

Asthma/COPD; Health care organisation and management; integrated care; longitudinal designs; non-experimental; treatment/intervention research; health care economics

Introduction

Chronic obstructive pulmonary disease (COPD), characterised by progressive non-reversible airway obstruction, is one of the most prevalent chronic lung diseases worldwide [1]. It results in a disabling symptom complex of breathlessness, reduced exercise capacity, fatigue, muscle wasting and sleep and

mood disturbances [2]. Although impaired lung function appears to result in reductions in daily functioning and quality of life, this relationship is only moderate [3], with management typically focussing on optimising symptomatology and functioning. Despite more advanced treatment options, deaths caused by COPD are expected to increase both

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worldwide and in Europe until the year 2030 at the earliest [4].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) has developed a classification system that incorporates both the severity of symptoms and the number of exacerbations. The GOLD classification allocates patients to groups A–D. This was based on two criteria: (1) risk, as measured by airflow limitation expressed as the forced expiratory volume in 1 s (FEV₁) and the number of admissions or exacerbations; and (2) symptom scores, using functional status questionnaires. The importance of symptoms has been further stressed in the GOLD reports from 2017 onwards and patient classification in groups A–D is currently based on health status and exacerbations alone, with data for spirometry now excluded [5].

Lifestyle factors, such as smoking habits or a sedentary lifestyle, affect prognosis and in addition to inhaler technique [6], adherence, and behavioural adaptation, must be addressed in the management of COPD [5]. Consequently, the assessment and treatment of patients with COPD demands integrated multidisciplinary care. It is assumed that more severe patients, such as those classified as GOLD group D, are better treated in specialised care centres. However, this conflicts with the reality that COPD group D comprises more than a quarter of all newly diagnosed COPD patients in primary care (range, 28%–36%) and that there is a need for patient care in the community [7]. Cooperation between general practitioners (GPs) and other caregivers in integrated care projects has proven effective for improving

the quality of life and health statuses of patients with COPD [8–10]. This can be seen with the success of the Asthma/COPD (AC) service in the north of the Netherlands, established in 2007 allowing GPs and pulmonologists to collaborate, giving GPs support when diagnosing and managing patients with COPD [11].

This study evaluated the outcomes and costs of managing patients classified as GOLD D in an integrated primary care AC service. We assessed the changes in the health statuses and health care costs of suitable patients who entered the AC service between baseline and 12 months. We also examined characteristics associated with changes in health status.

Methods

Design and setting

We conducted an observational 12-month follow-up study of patients diagnosed with COPD and classified as GOLD D by the AC service, which operates in the northern region of the Netherlands after GP referral for chronic lung disease. Patients were sampled between 1 August 2015 and 1 August 2017. Ethical approval was granted from the Medical Ethics Committee of the University Medical Centre Groningen, the Netherlands [12].

The AC service is an essential part of the integrated care system. In this service, a trained lung function technician takes the patient's history using a standardised form, including allergies, smoking status and medication use. The technician also performs lung function tests

Asthma/ COPD (AC) - service

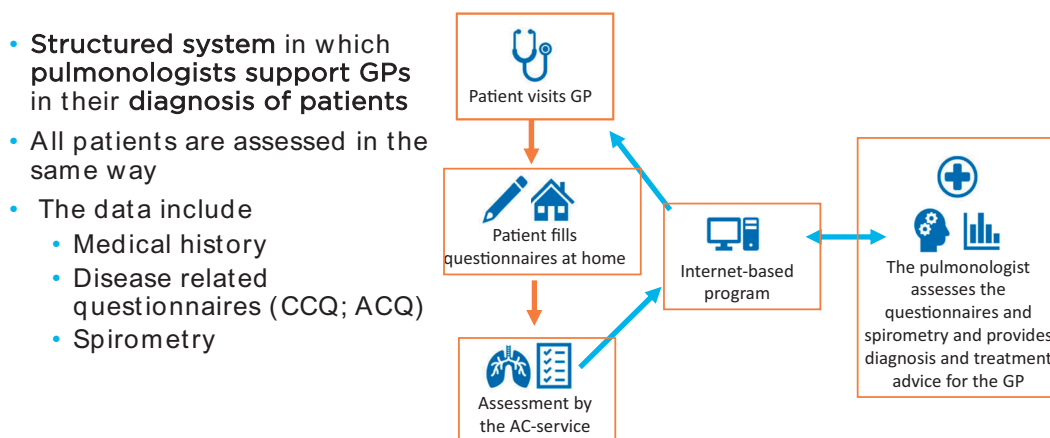


Figure 1. Graphical illustration of the collaboration between GPs, AC service and pulmonologists. Developed by and with permission of the General Practice Research Institute (GPRI).

and evaluates inhaler techniques. Data are made available to a pulmonologist responsible for making a diagnosis and providing treatment advice through a protected website. Advice is based on usual clinical care, for which the pulmonologists apply (inter)national guidelines. These data and advice are then returned to the GP, who decides whether to accept the diagnoses and follow the advice [11]. All these steps together, the AC service, the input from the pulmonologist and the GP, form the integrated care system (Figure 1).

Patients

Patients were eligible if they were newly diagnosed COPD patients aged ≥ 40 years and met the GOLD D classification criteria, as adapted from those outlined in the GOLD 2014 Report [13]. These criteria require that patients present with ≥ 2 reported exacerbations in the previous year or a FEV₁% predicted of $< 50\%$, including a score of ≥ 10 points on the CAT or a score of ≥ 1 on the CCQ. Patients had to give written informed consent. Patients were excluded if they had diagnoses of asthma, asthma/COPD overlap, or other respiratory illnesses, if they could not complete the questionnaires due to language or cognitive difficulties or if time between the initial AC service visit and response > 6 weeks. This time window was added to have enough time to observe outcomes of the integrated care system within the first 6 months follow-up. Response could be delayed because of time laps between assessment by the AC service and the advice of the pulmonologist and because of difficulties of attaining responses from the GP and the patient.

Procedures

All patients from GP practices in the northern region of the Netherlands could be included in the study.

Patients could enter the AC service through two routes. At some participating general practices, all patients with known or suspected COPD were screened by the AC service. At others, only patients who had consulted their GPs with lung complaints or who had previously been diagnosed with COPD were referred for (re)assessment. The AC Service research nurse then contacted the GPs of eligible patients to ask for their consent to include them in the study. After approval of their GPs, the patients themselves were contacted, informed about the study, and asked to provide written informed consent. Patients subsequently received the baseline questionnaire.

Measurements

Measurements were performed at baseline and at 3, 6, 9 and 12 months of follow-up (Table 1).

Primary outcome

The primary outcome was COPD-specific health status, as assessed by the CCQ and CAT questionnaires. The CCQ consists of 10 items distinguishing three domains: symptoms (4 items), functional state (4 items) and emotional state (2 items). The items concern the duration of complaints experienced over the last week and answering options range from 0 (never) to 6 (always). Total and domain scores are calculated by averaging item scores [14]. The CAT consists of eight items about the currently perceived impact of COPD on health status, each answered on 6-point scale from 0 (no impact at all) to 5 (severe impact). Items are summed giving a total score of 0–40 [15]. We defined minimally clinically important change levels as 2 points for CAT and 0.4 points for CCQ [16,17].

Table 1. Overview of measurements.

	Follow-up assessment				
	Baseline	3 months ^b	6 months	9 months ^b	12 months
Comorbidity	X				X
History (including smoking status)	X				
Spirometry (FEV ₁ predicted, %)	X				X
COPD-related health status					
CCQ	X		X		X
CAT	X		X		X
Current medication use (pulmonary and non-pulmonary)	X		X		X
Inhalation technique	X				X
Exacerbations ^a	X		X		X
Cost data including medication	X	X	X	X	X
Generic QOL (EQ-5D-3L)	X		X		X
Full blood count	X				

CAT: COPD assessment test; CCQ: clinical COPD questionnaire; COPD: chronic obstructive pulmonary disease; FEV₁: forced expiratory volume in 1 s; QOL (EQ-5D-3L): generic health-related quality of life.

^aN (%) Exacerbations in the last 12 months (at baseline), 6 months (at 6 and 12 months).

^bFollow-up was by phone interview.

Secondary outcomes

Secondary outcomes included the number of self-reported exacerbations, quality-adjusted life years (QALY), and health(care)-related costs. Patients reported the number of exacerbations over the past 6 months that indicated worsening of their symptoms beyond normal day-to-day variation and warranted additional treatment (either oral corticosteroids, antibiotics or hospital admission), which was converted to a 1-year estimate by multiplying this number by two. The EQ-5D-3L was used to assess generic health-related quality of life [18]. The answers were transformed to utilities using the Dutch tariff for the EQ-5D-3L, ranging from 0 (death) to 1 (perfect health) [19]. We also calculated the QALYs for the 12 months' follow-up. Health care costs were assessed from a societal perspective [20], using an adapted version of the Treatment Inventory of Costs in Psychiatric Patients questionnaire covering direct costs of primary and secondary health care usage and lung medication, and indirect costs related to productivity loss in the previous 3 months [21]. Medication costs were valued using Dutch GIP databank prices [22]. Other items were valued using the cost manual of The Dutch National Health Care Institute (ZIN) for 2014 [23].

Baseline characteristics and covariates

Age, gender, smoking history, height, weight and comorbidities were assessed by self-report at baseline. Pack-years were calculated by dividing the average number of cigarettes by 20, multiplied by the number of smoking years. Comorbidity was assessed with the adapted age-adjusted Charlson Comorbidity Index with scores ranging from 0 to 25 (higher scores reflect more severe comorbidity) [24]. We extracted the data on heart failure separately. Standard spirometry was performed at the AC service to calculate FEV1% predicted. A complete blood count was done at baseline to assess haemoglobin, leucocytes, neutrophils, lymphocytes, monocytes and eosinophils (dichotomised at $300 \text{ cells}/\mu\text{L}^5$).

Statistical analyses

Baseline characteristics, medication use and costs and utilities were described by means and SDs or medians and IQRs, and by frequencies and percentages. For costs, we compared the 3 months before baseline with the average quarterly costs during the 1-year follow-up period.

The change in CAT scores and CCQ total and domain scores over time were modelled using linear mixed-effects analyses, with positive change scores reflecting a deterioration in health status. The number of exacerbations was modelled by Poisson mixed-effects analyses. Models included time as a fixed factor and a random intercept variance on the individual level. Mixed model analyses provide valid estimates under the missing at random assumption. We performed univariable linear regression analysis to explore associations between baseline variables and changes in CCQ and CAT from baseline to 12 months. For the CCQ as outcome, CIs were based on repeated bootstraps and computed with the bias accelerated procedure. Descriptive and linear regression analyses were performed with IBM SPSS version 26 (IBM Corp., Armonk, NY, USA), and mixed model analyses were

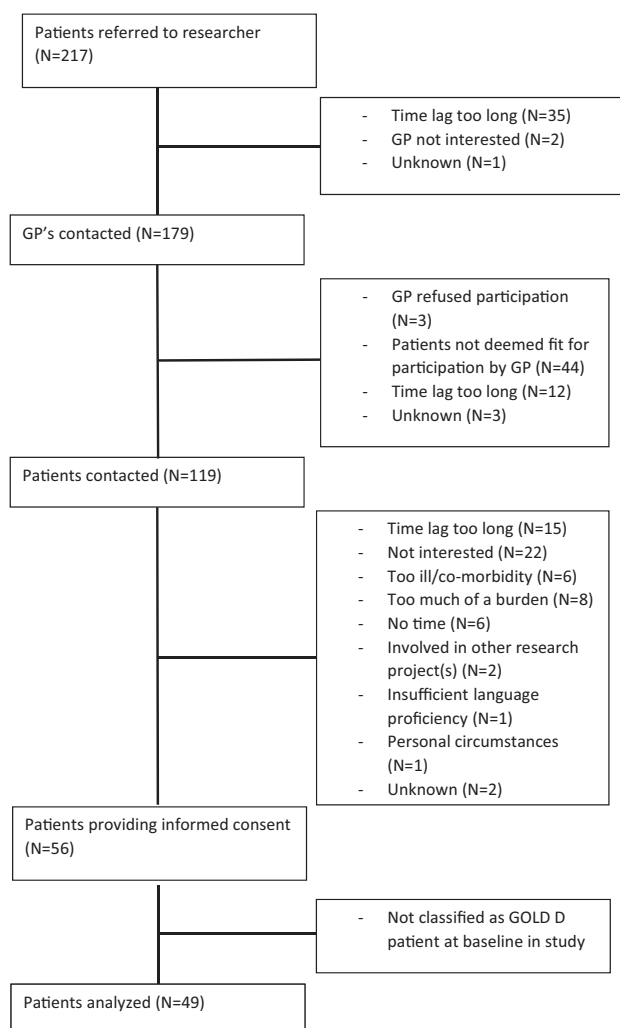


Figure 2. Flow chart of patient inclusion.

performed with STATA Statistical Software 16SE (StataCorp., College Station, TX, USA).

Results

Inclusion and classification of patients

Researchers at the AC service received 217 referrals for patients with COPD that could be classified as GOLD D during the inclusion period (Figure 2). Many patients could not be included in the study, mainly because time between referral and contact with GP and/or patients was too long or patients were (deemed) too ill. We ultimately received informed consent from 56 patients. Seven patients did not fulfil the GOLD D classification criteria at baseline, having both CAT scores < 10 and CCQ scores < 1, and were excluded from analyses.

Baseline characteristics

Forty-two patients could be classified as GOLD D by both CCQ (≥ 1) and CAT (≥ 10) criteria (Table 2). Mean age was 66.4 years (SD = 9.5), 57% was male and the median body mass index was 27.2 kg/m² (interquartile range [IQR]=25.3–30.1). In total, 38 (78%) had experienced ≥ 2 exacerbations over the previous year. Inhaler technique was assessed in 40 patients, of whom 20 (40.8%) required advice (e.g. inhaler preparation).

Trends in COPD-specific health status and GOLD status during follow-up

Between baseline and 6 months, the mean scores on the CAT and CCQ improved by -2.7 (95% confidence

Table 2. Baseline characteristics of sample and stratified for persons with CCQ ≥ 1 and CAT ≥ 10 .

	Total group (N = 49)	CCQ ≥ 1 (N = 48)	CAT ≥ 10 (N = 43)
Age, mean (SD)	66.4 (9.5)	66.5 (9.6)	66.1 (9.9)
Males, N (%)	28 (57)	28 (58)	23 (54)
BMI, median (IQR)	27.2 (25.3–30.1)	27.3 (25.6–30.1)	27.4 (25.6–30.1)
Comorbidity score ≥ 1 , N (%)	9 (18)	9 (19)	8 (19)
CAT score, mean (SD)	15.9 (5.4)	16.0 (5.4)	16.9 (4.8)
CCQ			
Total, median (IQR)	1.7 (1.4–2.3)	1.7 (1.4–2.3)	1.7 (1.6–2.3)
Symptoms, median (IQR)	2.3 (1.8–3.0)	2.3 (1.8–3.0)	2.3 (1.8–3.3)
Functional state, median (IQR)	1.8 (1.3–2.3)	1.9 (1.3–2.3)	2.0 (1.5–2.3)
Emotional state, median (IQR)	0.5 (0–1.3)	0.5 (0–1.4)	1.0 (0–1.5)
Exacerbations in 12 months, N (%)			
0	8 (16)	8 (17)	8 (19)
1	3 (6)	3 (6)	3 (7)
2	24 (49)	23 (48)	19 (44)
≥ 3	14 (29)	14 (29)	13 (30)
FEV1 % predicted, median (IQR)	55.0 (45.5–71.5)	55.5 (46.0–71.8)	50 (45–72)
Pack-years, median (IQR)	26.8 (14.5–40.8)	26.9 (14.3–42.4)	25.0 (14.0–35.3)
Blood counts ^a			
Haemoglobin, median (IQR)	9.1 (8.5–9.6)	9.1 (8.5–9.6)	9.1 (8.5–9.6)
Leucocytes, median (IQR)	8.1 (7.4–9.9)	8.1 (7.4–9.9)	8.1 (7.5–9.9)
Neutrophils, median (IQR)	5.0 (3.8–5.8)	5.0 (3.8–5.8)	5.0 (3.9–5.9)
Lymphocytes, median (IQR)	2.3 (2.0–2.9)	2.3 (2.0–2.9)	2.3 (2.0–3.0)
Monocytes, median (IQR)	0.7 (0.6–0.9)	0.7 (0.6–0.9)	0.7 (0.6–0.9)
Eosinophils, median (IQR)	0.2 (0.2–0.3)	0.2 (0.2–0.3)	0.2 (0.2–0.3)
≥ 300 cells/ μ L, N (%)	10 (22)	10 (22)	9 (22)
Utility, median (IQR) ^b	0.81 (0.72–0.90)	0.81 (0.72–0.90)	0.81 (0.71–0.90)

^aIn 10⁹ cells/L; three missing values.

^bOne missing value.

BMI: body mass index; CAT: COPD assessment test; CCQ: clinical COPD questionnaire; FEV1: forced expiratory volume in 1 s; IQR: interquartile range; N: number.

Table 3. Estimated mean changes in CAT and CCQ scores between baseline, 6, and 12 months.

	Baseline to 6 months	6 to 12 months	Baseline to 12 months
CAT ^a	-2.7 (-4.1 to -1.3)	0.4 (-1.0 to 1.9)	-2.3 (-3.7 to -0.8)
CCQ ^{b,c}			
Total	-0.50 (-0.73 to -0.30)	0.11 (-0.13 to 0.30)	-0.39 (-0.67 to -0.15)
Symptoms	-0.56 (-0.84 to -0.30)	0.18 (-0.10 to 0.42)	-0.37 (-0.72 to -0.10)
Functional state	-0.50 (-0.90 to -0.22)	0.07 (-0.21 to 0.30)	-0.43 (-0.81 to -0.11)
Emotional state	-0.33 (-0.55 to -0.13)	0.04 (-0.3 to 0.31)	-0.29 (-0.60 to -0.01)

Changes were calculated as scores for follow-up – baseline and 12 and 6 months; numbers in parentheses indicate 95% confidence intervals.

^aBaseline N = 49; 6 months N = 46; 12 months N = 46.

^bBaseline N = 49; 6 month N = 46; 12 month N = 44.

^cBias accelerated confidence intervals based on 2000 bootstrap samples.

CAT: COPD assessment test; CCQ: clinical COPD questionnaire; M: months.

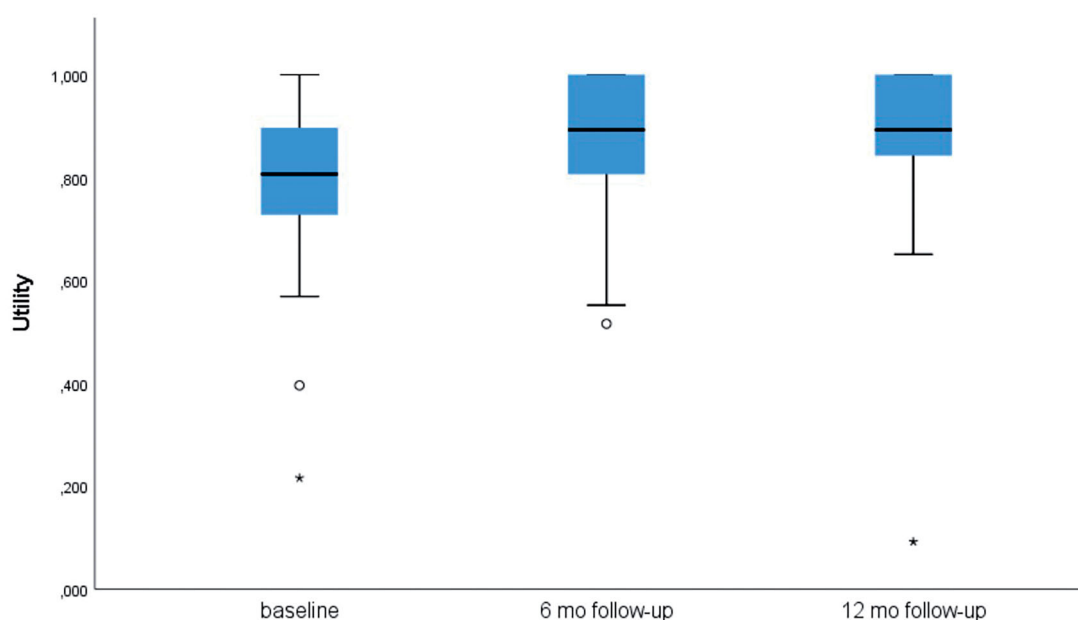


Figure 3. Utilities over time. Range from 0 (equals a state of death) to 1 (equals a state of perfect health).

Table 4. Medication use and number of exacerbations over time.

	Baseline (N = 49)		6 months (N = 46)		12 months (N = 42)	
	<2	≥2	<2	≥2	<2	≥2
Type of medication						
Short-acting ^a	0 (0%)	1 (3%)	1 (2%)	0 (0%)	0 (0%)	0 (0%)
Long-acting ^b	4 (36%)	15 (40%)	17 (41%)	1 (25%)	16 (46%)	0 (0%)
Short- and long-acting	2 (18%)	3 (8%)	5 (12%)	0 (0%)	3 (9%)	0 (0%)
ICS and long-acting agents	2 (18%)	9 (24%)	10 (24%)	2 (50%)	8 (23%)	4 (57%)
ICS and short- and long-acting ^c	1 (9%)	8 (21%)	6 (14%)	0 (0%)	5 (14%)	2 (29%)
No medication	2 (18%)	2 (5%)	3 (7%)	1 (25%)	3 (9%)	1 (14%)
Total	11	38	42	4	35	7

^aShort-acting beta-agonists or muscarinic antagonists only.

^bLong-acting beta-agonists or muscarinic antagonists only.

^cThis category includes one patient, who at baseline used ICS and short-acting beta-agonists. ICS: inhaled corticosteroids.

interval [CI]: -4.1 to -1.3) and -0.5 (95% CI: -0.7 to -0.3), respectively; they subsequently stabilised between 6 and 12 months (Table 3). The same trend was observed for the CCQ domain scores. Between baseline and 12 months, 3 patients (7%) changed to GOLD C, 25 (57%) to GOLD B, and 2 (5%) to GOLD A, while 14 (32%) remained classified as GOLD D.

Trends in exacerbations, utilities, costs and medication use during follow-up

Compared with baseline (Table 2), results from our analyses indicate an estimated five-fold decrease in exacerbations after 6 months (incidence rate ratio (IRR): 0.2; 95% CI: 0.1–0.3). Although the number of exacerbations increased somewhat between 6 and 12 months, this remained well below the baseline number (IRR: 0.3; 95% CI: 0.2–0.5).

The median number of QALYs throughout the 12-month follow-up period was 0.9 (IQR = 0.8–0.9). This implies that participants perceived the year they were followed-up as 0.9 years lived in perfect health. Median utilities increased from 0.8 at baseline to 0.9 at 6 and 12 months (Figure 3). Changes in mean quarterly costs from before baseline to 12 months were small. They declined for health care visits (35€; SD, 248€) and respiratory medication (5€; SD, 51€). For productivity loss, costs increased slightly (23€; SD 468€).

Table 4 summarises the medication used by patients with either ≥ 2 exacerbations or < 2 exacerbations. At baseline, 6 months and 12 months, inhaled corticosteroids (ICSs) were used by 40.8%, 39.1% and 45% of patients, respectively. Among patients with ≥ 2 exacerbations, 21 of the 38 (55.3%) at baseline did not use an ICS, compared with only 1 of 7 (14.3%) at 12 months.

Table 5. Results from univariable linear regression analyses relating changes in quality of life between baseline and 12-month follow-up to patient characteristics.

Characteristic	Delta CAT ^c		Delta CCQ ^{b,c}	
	B	95% BI	B	95% BI
Gender	1.89	−1.24 to 5.02	0.09	−0.40 to 0.59
≥ 2 exacerbations ^a	3.05	−0.82 to 6.91	0.54	0.07 to 1.05
FEV1pred change (0–12 months)	−0.05	−0.36 to 0.25	−0.02	−0.06 to 0.01
BMI ^a	−0.15	−0.51 to 0.22	0.00	−0.06 to 0.08
Blood counts				
Haemoglobin ^a	−0.24	−2.41 to 1.94	−0.47	−0.78 to 0.11
Leucocytes ^a	0.32	−0.55 to 1.19	0.08	−0.06 to 0.21
Neutrophils ^a	0.09	−0.98 to 1.16	−0.01	−0.19 to 0.22
Lymphocytes ^a	0.94	−0.76 to 2.63	0.35	0.08 to 0.55
Monocytes ^a	−2.32	−9.32 to 4.68	−0.39	−1.63 to 0.85
Eosinophils > 300 cells/ μ L ^a	0.29	−3.57 to 4.16	0.90	0.25 to 1.55
Pack-years ^a	0.05	−0.02 to 0.12	0.02	0.00 to 0.03
Comorbidity score $\geq 1^a$	−0.34	−4.50 to 3.82	−0.71	−1.27 to −0.16

^aAt baseline.^bBias accelerated confidence intervals based on 1000 bootstrap samples.^cHigher values indicate less beneficial changes. Positive change scores reflect deterioration.

Correlates of changes in CCQ and CAT

In general, less favourable baseline health (e.g. reporting two or more exacerbations) or health behaviour (e.g. pack-years smoked) were associated with less favourable changes in functioning, most clearly observable for the CCQ scores, except for a comorbidity score ≥ 1 , the lymphocyte count, and an eosinophil count > 300 cells/ μ L (Table 5).

Discussion

Main findings

In this prospective observational study, we showed that symptomatology and functioning of patients newly diagnosed with GOLD D class COPD improved, without increasing health care costs, by providing GPs standardised diagnostic support and advice from hospital-based pulmonologists. A previous study showed that almost one in five patients with COPD assessed in the AC service was classified as GOLD D [11]. Descriptive data in this study indicate that our incident cohort seems typical of patients with COPD in primary care both nationally and internationally [25]. As such, our results have the potential to impact patient outcomes significantly.

Patients experienced considerable improvements in COPD-related health status and dramatic reductions in exacerbation rates. Specifically, these changes occurred between baseline and 6 months of follow-up, after which health status and exacerbation rates remained more or less stable. Median utilities based on generic health-related quality of life measurements showed the same trend over time.

Exploratory analyses showed that baseline health and health behaviours at baseline were generally inversely associated with change in health status. For comorbidity, lymphocyte and eosinophil counts, we observed positive associations, however. These results appeared more prominent for the CCQ than the CAT, which might be related to the fact that the CCQ is somewhat more responsive to change than the CAT [26]. Further research with larger sample sizes is needed in this area.

GPs prescribed bronchodilator and ICS medications in combination to 40.8% of all patients classified as GOLD D at baseline. This overall proportion did not change over time. However, among patients with ≥ 2 exacerbations, where ICS is recommended, only one out of seven patients did not use ICS at 12 months follow-up.

Studies in several European countries have indicated that primary care physicians' poor adherence to treatment guidelines is widespread [25]. Several factors may contribute to this discrepancy between real-life practice and treatment recommendations. A critical barrier appears to be poor familiarity with the recommendations, which is associated with non-adherence to specific recommendations on ICS and long-acting bronchodilator prescribing [27]. Difficulty in differentiating between asthma and COPD in adults with airways disease or in establishing when these coexist also seems relevant [28]. The AC service provides diagnostic clarity and supplements it with treatment and lifestyle advice from pulmonologists. By offering a direct support system for the GP, we believe it helped improve the symptoms and functioning of patients with COPD classified as GOLD D.

Several methodological issues should be considered when interpreting the results of this study. First of all, we applied an observational design without comparison group. More robust evidence from randomised

controlled trials comparing integrated care to care as usual is needed before firm conclusions about the effectiveness of integrated care can be drawn. Our results indicate that average changes, especially between baseline and 6 months follow-up exceeded the a priori set minimally clinically important change levels of 2 points for CAT and 0.4 points for CCQ17 [16]. It should be noted though that a more recent study from our group has shown that a level of 3 points for the CAT should be used [29], which is a little larger than the average CAT score changes we found. Additionally, of the 217 patients enrolled in the AC service and classified into GOLD group D we could only include 49 in our analyses because many were deemed unfit for participation. As such, the final cohort was probably in better health than might be expected for the average patient in GOLD group D in primary care. Analyses suggested that patients in GOLD group D presenting with worse health or health behaviours experience less beneficial change in health status over a year. Therefore, the changes we observed in health status, may overestimate those in the entire GOLD D population in primary care. Overestimations may also result from regression to the mean. Furthermore, the small size of the sample hampers reliability of some results. Nonetheless, results concerning changes in quality of life and number of exacerbations all point in the same direction and seem robust. Results on characteristics associated with changes in health status from the regression analyses and the results from the cost analyses should be interpreted as exploratory at this stage.

Based on the findings from our observational 1-year follow-up study, we conclude that an integrated service for COPD patients based in primary care may improve the health status of patients with a large burden of disease while not increasing health care costs. Randomised controlled and sufficiently powered studies compared to care as usual are needed to substantiate our results.

Acknowledgements

The authors thank Dr Robert Sykes (www.doctored.org.uk) for providing editorial services, Ellen van de Heijst and Angela Bennink for providing data management at the AC service and all patients who participated in this study for their time.

Author contributions

All authors have made substantial contributions to the conception (JWHK, TvdM) or design of the work (CdJ; JWHK, JvB, TvdM); or the acquisition, analysis (CdJ, MRdB, MYB) or

interpretation of data (MdB, MYB, TvdM, JvB, JWH). All authors have contributed either to drafting of the work or substantively revised it. All authors have approved the submitted version and have agreed both to be personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved and the resolution documented in the literature.

Disclosure statement

Cd J, MRd B and MYB: have no conflict of interest. JWHK reports grants, personal fees and non-financial support from AstraZeneca, grants, personal fees and non-financial support from Boehringer Ingelheim, grants and personal fees from Chiesi Pharmaceuticals, grants, personal fees and non-financial support from GlaxoSmithKline, grants and personal fees from Novartis, grants from Mundipharma, grants from TEVA, outside the submitted work, all paid to his institution; and holds 72.5% of shares in the General Practitioners Research Institute (GPRI). JFMvB has received consultancy fees, honorarium and research funding from AstraZeneca, Boehringer Ingelheim, Chiesi, Menarini, Novartis, Nutricia, Pill Connect, TEVA and Trudell Medical to consult, give lectures, provide advice, and conduct independent research, all paid to his institution. TvdM was an employee of GSK from 2017 till June 2019.

Funding

This study was conducted with financial support from GlaxoSmithKline B.V.

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Data availability statement

Data that support the findings of this study will be made available by the corresponding author upon reasonable request.

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