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ORIGINAL ARTICLE

## What Predicts Change in Pulmonary Function and Quality of Life in Asthma or COPD?

A. E. HESSELINK, PH.D.,<sup>1,2,\*</sup> D. A. W. M. VAN DER WINDT, PH.D.,<sup>1,2</sup> B. W. J. H. PENNINX, PH.D.,<sup>1,3</sup>  
H. A. H. WIJNHOFEN, PH.D.,<sup>1</sup> J. W. R. TWISK, PH.D.,<sup>1</sup> L. M. BOUTER, PH.D.,<sup>1</sup> AND J. TH. M. VAN EIJK, PH.D.<sup>4</sup>

<sup>1</sup>EMGO Institute, VU University Medical Center, Amsterdam, The Netherlands

<sup>2</sup>Department of General Practice, VU University Medical Center, Amsterdam, The Netherlands

<sup>3</sup>Department of Psychiatry, VU University Medical Center, Amsterdam, The Netherlands

<sup>4</sup>Department of Medical Sociology, Maastricht University, Maastricht, The Netherlands

Information about predictors of decline in pulmonary function (forced expiratory volume in 1 second [FEV<sub>1</sub>]) or health-related quality of life (HRQoL) in patients with asthma or (chronic obstructive pulmonary disease [COPD]) might help to determine those who need additional care. A 2-year prospective cohort study was conducted among 380 asthma and 120 COPD patients. In both asthma and COPD patients, a 2-year change in FEV<sub>1</sub> was only weakly associated with a 2-year change in HRQoL ( $r = .0.19$  and  $0.24$ , respectively). In both groups, older age, living in an urban environment, and a lower peak expiratory flow rate (PEFR) at baseline were associated with a decline in FEV<sub>1</sub>. Additional predictors of FEV<sub>1</sub> decline were greater body weight, less chronic cough or sputum production, and less respiratory symptoms in asthma patients and current smoking in COPD patients. A decline in HRQoL was associated with older age, non-compliance with medication, more dyspnea, and a lower PEFR in asthma patients and with male gender, lower education, lower body weight, more dyspnea, and more respiratory symptoms in COPD patients. Our results show that FEV<sub>1</sub> and HRQoL appear to represent different disease aspects influenced by different predictors.

**Keywords** asthma, chronic obstructive pulmonary disease (COPD), health-related quality of life, pulmonary function, longitudinal study

### INTRODUCTION

Pulmonary function and health-related quality of life (HRQoL) are both independently of great importance in the management of asthma and chronic obstructive pulmonary disease (COPD) (1–4). Assessing the airway obstruction by measuring the forced expiratory volume in one second (FEV<sub>1</sub>) was, until recently, the most common way to assess disease severity, response to therapy, and (short-term) prognosis in asthma and COPD patients (4). Yet, the use of FEV<sub>1</sub> as the single best evaluation parameter has been questioned (5–9). Therefore, in the past decade, HRQoL has become an established parameter to assess a patient's subjective experience of the impact of disease (4, 10). Since there is no strong association between FEV<sub>1</sub> and HRQoL, both measures seem to highlight different aspects of the disease and therefore provide complementary information on the actual severity of the disease (1–4).

Until now, most studies on FEV<sub>1</sub> or HRQoL were based on cross-sectional research. Longitudinal research has mainly focused on evaluating the effectiveness of treatment. Consequently, information on the predictors of changes in FEV<sub>1</sub> or HRQoL evaluated in non-experimental settings is scarce. Information on the variables used in routine follow-up care, which may predict changes in FEV<sub>1</sub> or HRQoL, might help physicians to distinguish between patients who need additional attention (11). The objectives of this study were (1) to

study the course of FEV<sub>1</sub> and HRQoL over a period of 2 years and (2) to identify predictors of changes in FEV<sub>1</sub> and HRQoL over time. Chronic airway obstruction is a common characteristic of asthma and COPD. However, asthma and COPD are different diseases with a different clinical manifestation, and thus were analyzed separately (12).

### METHODS

#### Design and Study Population

Patients enrolled in a cohort study received three annual examinations, including a pulmonary function test, a face-to-face interview, and a written questionnaire. All examinations were performed between 1995 and 2000 by well-trained research assistants. A detailed description of patients and methods can be found elsewhere (1). Briefly, 31 general practitioners (GPs) from 25 practices in two rural regions in the east and northwest and one urban region in the west of the Netherlands selected all patients who met the following inclusion criteria: a clinical diagnosis of asthma, COPD, or mixed disease (asthma with persisting airway obstruction), age 16 to 75 years, primarily treated in the general practice and absence of other specific pulmonary or terminal diseases. The GPs selected 2,047 patients, of whom 1,325 (65%) participated. Non-responders were generally younger and more often male than responders ( $p < 0.01$ ). Of the responders only those who stated at their initial interview that they currently used asthma or COPD medication and experienced disease symptoms such as coughing and sputum production or dyspnea were included in the study ( $n = 867$ ). The final criterion was that they had attended at least one follow-up examination. Of the 1,325 responders, 539 (41%) met all inclusion

\*Corresponding author: Arlette E. Hesselink, Ph.D., GG&GD Amsterdam, Cluster EDG, P.O. Box 2200, 1000 CC Amsterdam, The Netherlands; E-mail: A.E.Hesselink@AMC.UVA.nl

criteria and were included in the present prospective cohort study.

### Outcome Measures

The outcome variables of FEV<sub>1</sub> and HRQoL were measured at baseline and after 1 and 2 years. All assessments took place during the same period each year. FEV<sub>1</sub> was measured according to the American Thorax Society (ATS) criteria using a handheld spirometer (SpiroSense; Tamarac Systems, Denver, CO, USA) in the west and east of the county, and a dry rolling seal spirometer (MasterScreen CS/FRC; Jaeger Toennies, Hoechberg, Germany) in the northwest (13). Patients were instructed not to use bronchodilators on the day that their pulmonary function was assessed. FEV<sub>1</sub> was expressed as a percentage of the predicted FEV<sub>1</sub> (FEV<sub>1</sub>%pred). The predicted FEV<sub>1</sub> was based on gender, height, and age using the predicted adult standards of European Community for Coal and Steel (14).

HRQoL was measured using the Quality of Life in Respiratory Illness Questionnaire, which was filled out at the respondent's home (15). This questionnaire was specifically developed and validated for patients with mild to moderate asthma or COPD and covers a broad range of aspects of daily life. It contains 55 items divided into 7 subscales: breathing problems, physical problems, emotions, general activity, situation triggers, daily and domestic activities, and social activities. Each item assesses, on a 7-point scale, the extent to which the patient is troubled due to pulmonary complaints: (1) "no trouble at all" to (7) "very much trouble." A score is calculated for each subscale separately, after which a total score is computed (possible range 7–49). Less than 50% missing items were allowed per subscale and were substituted, and one missing subscale was allowed for the calculation of the overall HRQoL score. At baseline, Cronbach's alpha varied from 0.84 to 0.92 for the subscales and was 0.96 for the overall scale, which confirms the internal consistency of this questionnaire. The scale was transformed in such a way that a low score indicated a poor HRQoL.

### Predictors

The GPs provided information about age (years) and gender. Information about the level of education (classified as low, medium, or high, depending on the duration of the education), co-morbidity (if a patient had one or more other chronic conditions), medication (categorized according to the step-care therapy rules) (16), duration of disease (years), and hyperreactivity (sensitive to more than four of eight triggers such as smoke, temperature changes, humidity, stress, and physical activity) were gathered during the face-to-face interview with the patient. In addition, patients were asked about their degree of dyspnea according to the Medical Research Council (MRC) questionnaire (scale from 0 = no dyspnea to 4 = dyspnea when standing still), wheezing (never, ever, or most days and nights), and chronic cough or sputum production (present, not present). A blood sample was taken for the assessment of allergy, which was defined as present if a patient had a positive Phadiathop test (Pharmacia AB, Uppsala, Sweden) (17). In a written questionnaire, information was gathered about compliance with anti-inflammatory agents using a three-item checklist and on smoking behavior

(never, former, current). In the 2 weeks after this baseline assessment the patients filled out a diary chart monitoring a morning and evening peakflow expiratory flow rate (PEFR) measured with a peak flow meter. Variability in PEFR was expressed as the lowest morning PEFR measured in one day, expressed as a percentage of the predicted PEFR (18). On the diary charts the patients also recorded the use of bronchodilators and whether the past day or night had been disturbed by respiratory symptoms. In case of missing data on PEFR, use of bronchodilators, or respiratory symptoms, data were extrapolated if valid data were provided for at least 10 days (1).

### Diagnosis of Asthma, COPD or Mixed Disease

The diagnosis of the disease was based on baseline pulmonary function, according to the guidelines issued by the Dutch College of General Practitioners (1, 19). Asthma was defined as: (1) pre (before use of a bronchodilator) FEV<sub>1</sub>%pred  $\geq$ 80% or (2) a combination of preFEV<sub>1</sub>%pred <80%, a reversible obstruction ( $\geq$ 9% increase of FEV<sub>1</sub> 10 minutes after admission of bronchodilator), and a post (after use of a bronchodilator) FEV<sub>1</sub>%pred  $\geq$ 80%. COPD was defined as: preFEV<sub>1</sub>%pred <80% combined with an irreversible obstruction (increase FEV<sub>1</sub> 10 minutes after admission of bronchodilator <9% of predicted). Mixed disease was defined as preFEV<sub>1</sub>%pred <80%, a reversible obstruction, and a postFEV<sub>1</sub>%pred <80%.

### Statistical Analyses

Data were analyzed using SPSS 9.0 software (Chicago, IL, USA) and MLwiN (Centre for Multilevel Modeling 2002, version 1.10.0007). Of the 539 patients who met all inclusion criteria, 39 patients were diagnosed as having mixed disease; since this number is too small for the analyses used in this study, these patients were excluded from further analyses. All analyses were performed for asthma and COPD separately. Descriptive statistics, including Chi-square tests, *t* tests, or Mann Whitney U-tests, were used to compare baseline characteristics between asthma and COPD patients. In the northwest region, an education program was provided for a subsample of patients, but this program had no effect on HRQoL or on any other variables included in this study (20). Nevertheless, the intervention was introduced in all analyses as a covariate.

To study change in FEV<sub>1</sub> and HRQoL over time, multiple linear multilevel regression analyses were applied, conducted with time as categorical predictor variable. Pearson's correlation coefficients (*r*) were calculated to predict the correlation between FEV<sub>1</sub> and HRQoL at baseline and between changes in FEV<sub>1</sub> and HRQoL over time. To investigate the predictive value of different baseline patient and disease characteristics on changes in FEV<sub>1</sub> and HRQoL over time, multivariate linear multilevel regression analyses were also applied, including the baseline value of FEV<sub>1</sub> or HRQoL as a covariate. Multilevel analyses were used to account for correlations within patients. Furthermore, patients were clustered within one general practice. Therefore, analyses were performed with a three-level structure (time, patient, and GP). First, for all potential predictors, the univariate association with the outcome measure was examined. Each variable with

an association of  $p < 0.20$  was entered in the multivariate model. Finally, the best predictive model was constructed, using a (manual) backward selection method, deleting those variables that had the weakest association with the outcome ( $p > 0.10$ ). Separate models were constructed for the two outcome measures FEV<sub>1</sub> and HRQoL and for asthma and COPD.

## RESULTS

In Table 1, patient characteristics are presented separately for asthma and COPD patients. As expected, compared to asthma, significantly more COPD, patients were male, were older, had a lower level of education, more often had comorbidities, were more often current or former smokers, were less often allergic or hyperreactive, and had more severe dyspnea, more frequent respiratory symptoms, and a lower PEFr. In addition, patients with more COPD often used medication,

were less compliant with treatment, had their disease longer, and used bronchodilators more often than patients with asthma. Furthermore, COPD patients had a poorer FEV<sub>1</sub> and a poorer HRQoL.

### Changes in FEV<sub>1</sub> and HRQoL During Follow-Up

Changes in FEV<sub>1</sub> and HRQoL after 1 and 2 years, compared to baseline, can be seen in Figures 1 and 2. In asthma patients, the mean change in FEV<sub>1</sub> after 1 year (mean change  $-0.07\%$ , 95%CI  $-1.04$  to  $0.91$ ) and after 2 years (mean change  $-0.01\%$ , 95%CI  $-1.05$  to  $1.03$ ) was small. The total score for HRQoL and all subscales improved slightly in the first year (mean change  $0.51$ , 95%CI  $0.03$  to  $0.98$ ) and decreased slightly in the second year (mean change  $0.37$ , 95%CI  $-0.14$  to  $0.89$ ). In patients with COPD a considerable decline in FEV<sub>1</sub> was noted after 1 year (mean change  $-2.96\%$ , 95%CI  $-4.48$  to  $-1.45$ ) and, after 2 years (mean change  $-3.17\%$ , 95%CI  $-4.82$  to  $-1.52$ ). For HRQoL, a mixture of positive and negative changes on the subscales was seen after 1 year in COPD patients, resulting in a small nonsignificant improvement in the total HRQoL scale (mean change  $0.19\%$ , 95%CI  $-0.59$  to  $0.97$ ). After 2 years the total HRQoL (mean change  $-0.89$ , 95%CI  $-1.74$  to  $-0.04$ ) and all subscales declined. Despite the small mean changes in FEV<sub>1</sub> and HRQoL, there was sufficient variation in change on both outcome measures across patients to continue with the analyses of predictors of change.

The correlation between FEV<sub>1</sub> and HRQoL at baseline was nonsignificant in both asthma ( $r = 0.07$ ) and COPD ( $r = 0.11$ ) patients. The correlation between the changes in FEV<sub>1</sub> and HRQoL over 2 years was statistically significant, but low in both asthma ( $r = 0.19$ ) and COPD ( $r = 0.24$ ) patients.

### Predictors of Changes in FEV<sub>1</sub> and HRQoL

The results of the longitudinal linear regression analyses, studying the influence of different predictors on changes in FEV<sub>1</sub> and HRQoL, can be seen in Table 2 (univariate analyses) and Table 3 (multivariate analyses). In asthma patients, age, comorbidity, respiratory symptoms, and PEFr at baseline were univariately associated ( $p < 0.20$ ) with changes in both FEV<sub>1</sub> and HRQoL. In addition, level of education, body weight, demographic region, chronic cough or sputum production, and HRQoL were associated with changes in FEV<sub>1</sub>, whereas gender, poor compliance with treatment, duration of disease, hyperreactivity, and dyspnea were associated with changes in HRQoL. The best predictive model (Table 3) showed that for asthma patients, older age and greater body weight were associated with a decline in FEV<sub>1</sub>. Living in a suburban region (east or northwest), chronic cough or sputum production, more frequent respiratory symptoms, and a higher PEFr at baseline were associated with an increase in FEV<sub>1</sub>. In asthma patients, older age, poor compliance with treatment, more dyspnea, and a lower PEFr were associated with a decline in HRQoL. For example, patients who were older showed a decline in FEV<sub>1</sub> of 0.10 and a decline in HRQoL of 0.87, compared with younger patients.

In patients with COPD, age, body weight, smoking, a positive allergy test, respiratory symptoms, and PEFr at baseline

TABLE 1.—Baseline characteristics of patients.

Characteristics	Asthma (n = 380)	COPD (n = 120)	p value
Gender (men)	130 (34%)	70 (58%)	<0.01
Age, years (SD)	45.0 (14.3)	57.5 (13.4)	<0.01
Educational level			
Low	188 (49%)	83 (69%)	<0.01
Medium	124 (33%)	25 (21%)	
High	68 (18%)	12 (10%)	
Body weight, kgs (SD)	78.1 (15.3)	75.7 (13.8)	0.13
Region of living			
West (urban)	172 (45%)	56 (47%)	0.09
East (suburban)	63 (17%)	29 (24%)	
North-west (suburban)	145 (38%)	35 (29%)	
Comorbidity	144 (38%)	58 (48.3%)	0.04
Smoking			
Never	169 (45%)	25 (21%)	<0.01
Former	115 (31%)	49 (42%)	
Current	89 (24%)	44 (37%)	
Medication <sup>1</sup>			
Step 1	87 (23%)	13 (11%)	<0.01
Step 2	229 (60%)	60 (50%)	
Step 3 and 4	64 (17%)	47 (39%)	
Compliance			
Compliant	141 (37%)	17 (14%)	0.01
Not compliant	130 (34%)	57 (48%)	
Missing	109 (29%)	46 (38%)	
Duration of disease (years)	19.9 (15)	25.8 (21)	<0.01
Allergy test			
Negative	152 (40%)	72 (60%)	<0.01
Positive	204 (54%)	41 (16%)	
Missing	24 (6%)	7 (6%)	
Hyperreactivity	259 (70%)	70 (60%)	0.05
Dyspnea-grade, <sup>2</sup> score 0 to 4 (SD)	1.1 (1.2)	1.5 (1.2)	0.01
Wheeze			
Never	28 (8%)	14 (12%)	0.24
Ever	284 (75%)	81 (68%)	
Most days and nights	67 (18%)	25 (21%)	
Chronic cough or sputum production present	192 (51%)	64 (53%)	0.59
Days or nights disturbed by respiratory complaints, <sup>3</sup> number (SD)	1.6 (2.6)	2.6 (3.7)	<0.01
Use of $\beta$ -agonists, <sup>3</sup> number (SD)	7.1 (7.1)	10.7 (5.4)	<0.01
PEFr (low [morning]% predicted), <sup>3</sup> (SD)	81.7 (17.8)	57.6 (17.1)	<0.01
FEV <sub>1</sub> %pred, <sup>4</sup> (SD)	95.1 (15.)	60.6 (16.)	<0.01
HRQoL, <sup>3</sup> (score 7 to 49 (SD)	40.6 (6.1)	39.2 (6.2)	0.02

<sup>1</sup> Stepped care therapy: step 1,  $\beta$ -agonists only; step 2, low or moderate dose corticosteroids or cromoglycine; step 3, moderate dose corticosteroids or cromoglycine and long-acting  $\beta$ -agonists; and step 4, high dose corticosteroids or cromoglycine with long-acting  $\beta$ -agonists.

<sup>2</sup> Higher score indicates more severe dyspnea.

<sup>3</sup> Measured by day chart over a period of 14 days.

<sup>4</sup> Higher score indicates better FEV<sub>1</sub>%pred and HRQoL.

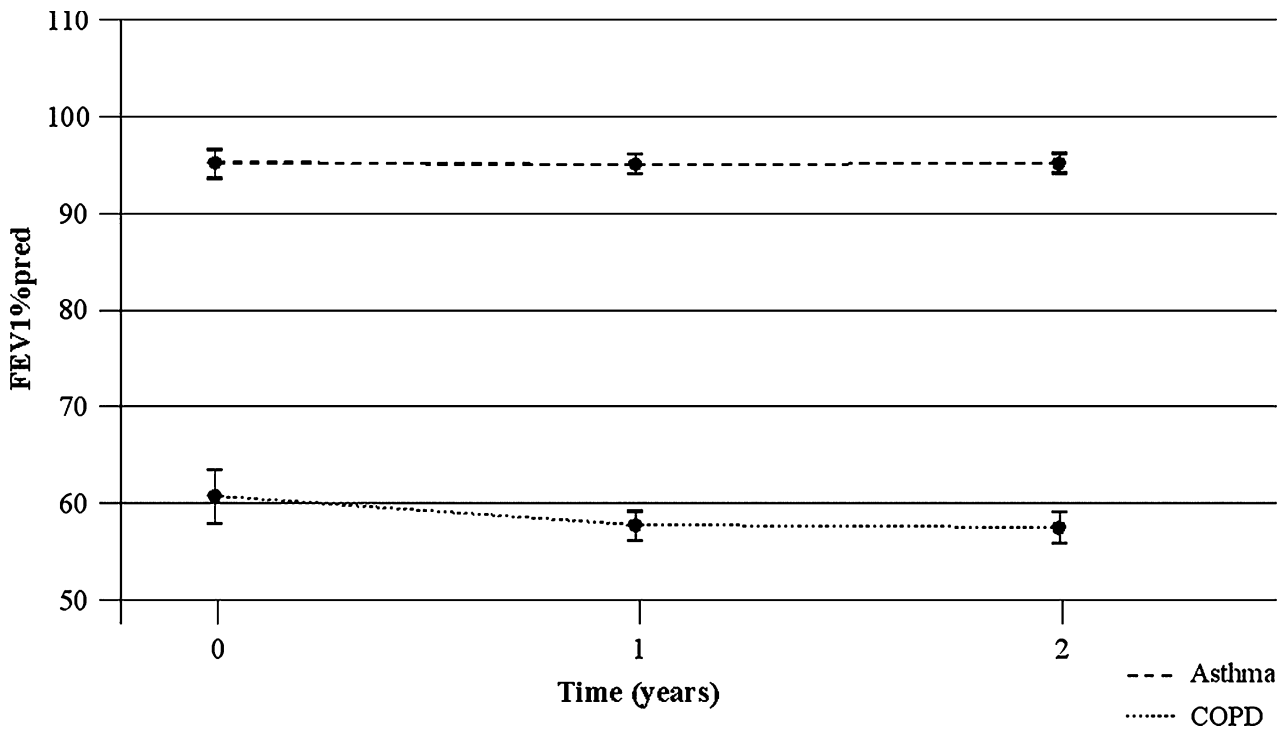


FIGURE 1.—FEV<sub>1</sub> at baseline, after one and after two years.

were univariately associated ( $p < 0.20$ ) with changes in both FEV<sub>1</sub> and HRQoL (Table 2). In addition, demographic region, wheezing, and bronchodilator use were associated with a change in FEV<sub>1</sub>. Gender, level of educational, comorbidity,

medication use, dyspnea and FEV<sub>1</sub> were associated with changes in HRQoL. The best predictive model (Table 3) showed that older age, living in an urban region (west), current smoking, and low PEF<sub>R</sub> predicted a decline in

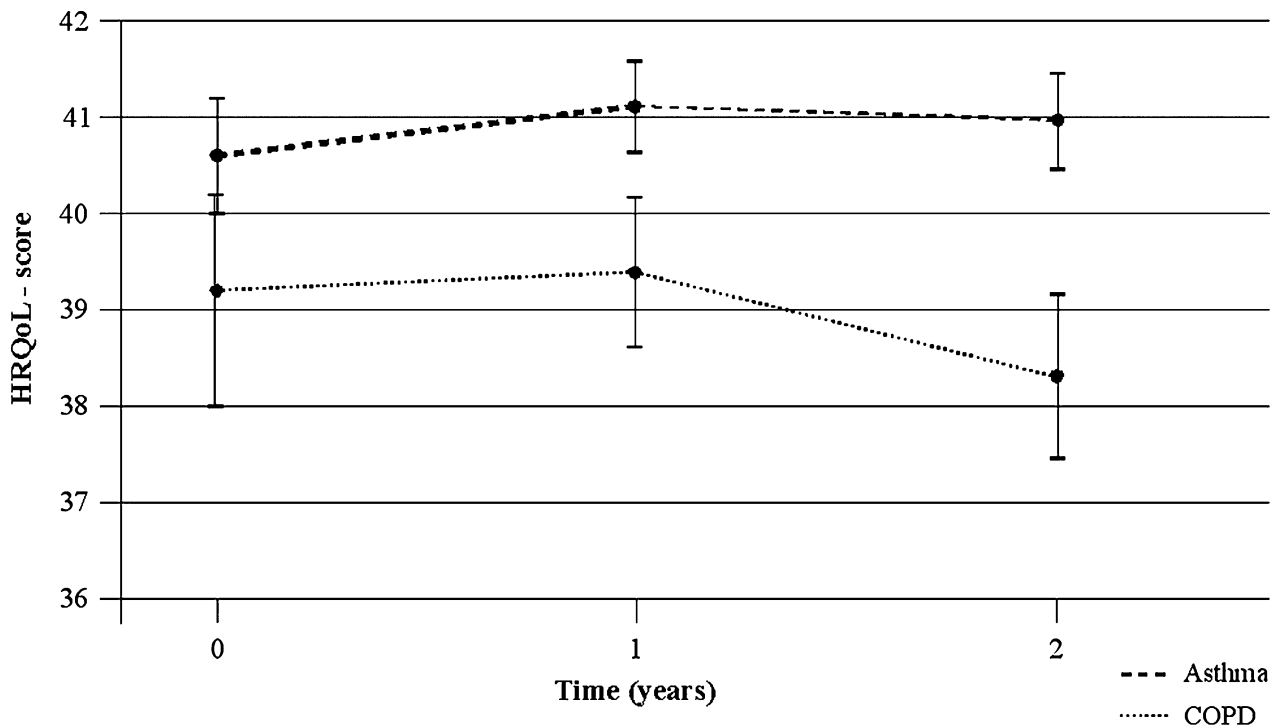


FIGURE 2.—HRQoL at baseline, after one and after two years.

TABLE 2.—Predictive value of baseline patient and disease characteristics regarding changes in FEV<sub>1</sub> and HRQoL during 2 years follow-up: results of univariate analyses (regression coefficients (β) and 95% CI), for asthma, and COPD separately.

Characteristics	Asthma (n = 380)		COPD (n = 120)	
	FEV <sub>1</sub> β [95%CI]	HRQoL β [95%CI]	FEV <sub>1</sub> β [95%CI]	HRQoL β [95%CI]
Gender (men)	0.95 [−0.91, 2.81]	0.60 [−0.22, 1.41]*	−1.02 [−3.58, 1.54]	1.32 [−0.16, 2.80]*
Age (years)	−0.10 [−0.16, −0.04]*	−0.04 [−0.07, −0.01]*	−0.18 [−2.28, −0.08]*	−0.06 [−0.11, 0]*
Education level				
Medium vs low	2.47 [0.54, 4.39]*	0.31 [−0.57, 1.19]	1.07 [−2.04, 4.18]	1.51 [−0.23, 3.24]*
High vs low	0.31 [−2.32, 0.55]	0.34 [−0.74, 1.42]	1.35 [−2.90, 5.60]	1.75 [−0.61, 4.11]*
Body weight	−0.06 [−0.11, 0]*	−0.01 [−0.04, 0.01]	0.08 [−0.01, 0.17]*	0.04 [−0.01, 0.09]*
Region of living <sup>a</sup>				
East vs west	2.05 [−0.40, 4.49]*	−0.58 [−1.69, 0.53]	4.49 [1.45, 7.53]*	−0.13 [−1.90, 1.64]
Northwest vs west	4.58 [1.63, 7.53]*	0.67 [−0.42, 1.77]	3.97 [1.96, 7.94]*	−0.98 [−3.16, 1.20]
Co-morbidity	1.32 [−3.09, 0.44]*	−0.64 [−1.45, 0.17]*	−1.92 [−4.39, 0.55]	−0.99 [−2.39, 0.42]*
Smoking				
Former vs never	−0.58 [−2.58, 1.43]	−0.54 [−1.44, 0.36]	−2.82 [−6.09, 0.45]*	−1.33 [−3.20, 0.55]*
Current vs never	−0.12 [−2.30, 2.07]	−0.29 [−1.27, 0.69]	−5.31 [−8.62, −2.0]*	−0.67 [−2.59, 1.26]
Medication <sup>b</sup>				
Step 2 vs step 1	−0.33 [−0.44, 1.79]	−0.39 [−1.33, 0.57]	2.12 [−2.05, 6.28]	−0.84 [−3.13, 1.45]
Step 3 & 4 vs step 1	−1.16 [−3.94, 1.62]	−0.59 [−1.85, 0.67]	2.11 [−2.35, 6.57]	−2.46 [−4.86, −0.06]*
Compliance				
Not compliant vs compliant	0.61 [−1.44, 2.65]	−0.77 [−1.70, 0.16]*	1.67 [−1.04, 3.87]	0.22 [−1.32, 1.77]
Missing vs compliant	0.65 [−1.49, 2.78]	0.53 [−0.43, 1.48]	0.26 [−3.51, 4.03]	1.10 [−1.05, 3.24]
Duration of disease (years)	−0.02 [−0.08, 0.04]	−0.03 [−0.05, 0]*	0.01 [−0.05, 0.07]	0 [−0.04, 0.03]
Allergy test				
Positive vs negative	−0.60 [−2.41, −0.65]	0.54 [−0.27, 1.35]	1.92 [−0.72, 4.56]*	1.53 [0.03, 3.03]*
Missing vs negative	1.06 [−2.65, 4.77]	0.24 [−1.46, 1.93]	2.02 [−3.49, 7.53]	0.80 [−2.30, 3.91]
Hyperreactivity	0.96 [−0.92, 2.84]	−0.41 [−1.32, 0.5]*	0.03 [−2.54, 2.60]	0.45 [−0.84, 2.09]
Dyspnea-grades <sup>c</sup> (score)	−0.39 [−1.14, 0.37]	−0.54 [−0.93, −0.14]*	−0.12 [−1.15, 0.91]	−0.78 [−1.46, −0.10]*
Wheeze				
Ever vs never	−1.92 [−5.24, 5.24]	0.75 [−0.74, 2.23]	3.9 [−0.03, 7.83]*	−0.59 [−2.85, 1.66]
Most days and nights vs never	−1.28 [−0.506, 2.50]	0.98 [−0.75, 2.70]	2.86 [−1.64, 7.36]	−1.24 [−3.85, 1.38]
Chronic cough or sputum production present	1.72 [0.01, 3.44]*	−0.17 [−0.98, 0.64]	−1.70 [−4.2, 0.8]	−0.26 [−1.75, 1.20]
Days or nights disturbed by respiratory complaints <sup>d</sup>	0.52 [0.16, 0.89]*	−0.13 [−0.31, 0.05]*	−0.24 [−0.61, 0.14]*	−0.47 [−0.71, −0.22]*
Use of β-agonists <sup>d</sup>	0 [−0.14, 0.15]	−0.06 [−0.13, 0.01]*	−0.21 [−0.47, 0.04]*	−0.03 [−0.18, 0.11]
PEFR (low (morning)%predicted) <sup>d</sup>	0.09 [0.04, 0.15]*	0.04 [0.01, 0.06]*	0.22 [0.13, 0.31]*	0.06 [0.01, 0.10]*
FEV <sub>1</sub>		0.01 [−0.01, 0.04]		0.08 [0.03, 0.12]*
HRQoL	−0.10 [−0.25, 0.04]*		0.10 [−0.11, 0.31]	

\*p-value < 0.20.

<sup>a</sup>Region of living: west is urban, east and northwest are suburban.

<sup>b</sup>Stepped care therapy: step 1, β-agonists only; step 2, low or moderate dose corticosteroids or cromoglycine; step 3, moderate-dose corticosteroids or cromoglycine and long-acting β-agonists; and step 4, high-dose corticosteroids or cromoglycine with long-acting β-agonists.

<sup>c</sup>Higher score indicates less severe dyspnea.

<sup>d</sup>Measured by day chart over a period of 14 days.

TABLE 3.—Predictive value of baseline patient and disease characteristics regarding changes in FEV<sub>1</sub> and HRQoL during 2 years follow-up: results of multivariate analyses (regression coefficients (β) and 95% (CI) for asthma and COPD separately: best predicting model.

Characteristics	Asthma (n = 380)		COPD (n = 120)	
	FEV <sub>1</sub> β [95%CI]	HRQoL β [95%CI]	FEV <sub>1</sub> β [95%CI]	HRQoL β [95%CI]
Gender (men)				2.48 [1.07, 3.89] <sup>§</sup>
Age (years)	−0.10 [−0.15, −0.04] <sup>§</sup>	−0.03 [−0.06, 0]*	−0.14 [−0.23, −0.04] <sup>§</sup>	
Education level				
Medium vs low				1.36 [−0.22, 2.93]
High vs low				2.09 [−0.08, 4.26]*
Body weight (kg)	−0.07 [−1.2, −0.01] <sup>¶</sup>			0.05 [0, 0.10] <sup>¶</sup>
Region of living <sup>a</sup>				
East vs west	1.84 [−0.50, 4.17]		2.93 [0, 07, 5.79] <sup>¶</sup>	
Northwest vs west	2.83 [0.04, 5.62] <sup>¶</sup>		2.63 [−0.94, 6.20]	
Smoking				
Former vs never			−1.81 [−4.78, 1.16]	
Current vs never			−2.94 [−5.99, 0.11]*	
Compliance				
Not compliant vs compliant		−0.87 [−1.79, 0.04]*		
Missing vs compliant		0.43 [−0.51, 1.37]		
Dyspnea-grades <sup>b</sup>		−0.37 [−0.77, 0.02]*		−0.80 [−1.43, 0.17] <sup>¶</sup>
Chronic cough or sputum production present	1.74 [0.07, 3.41] <sup>¶</sup>			
Days or nights disturbed by respiratory complaints <sup>c</sup>	0.70 [0.3, 1.06] <sup>§</sup>			−0.41 [−0.64, −0.17] <sup>§</sup>
PEFR (low (morning)%predicted) <sup>c</sup>	0.11 [0.06, 0.16] <sup>§</sup>	0.03 [0.01, 0.06] <sup>§</sup>	0.16 [0.06, 0.25] <sup>§</sup>	

p-value: <sup>§</sup> < 0.01, <sup>¶</sup> < 0.05, and \* < 0.10.

<sup>a</sup>Region of living: west is urban, east and northwest are suburban.

<sup>b</sup>Higher score indicates less severe dyspnea.

<sup>c</sup>Measured by day chart over a period of 14 days.

FEV<sub>1</sub>. Female gender, higher level of education, and greater body weight were associated with an increase in HRQoL. More dyspnea and more frequent respiratory symptoms were associated with a decline in HRQoL. For example, for every point a patient who scored lower on the dyspnea scale, a mean decline of 0.80 was found in HRQoL.

#### DISCUSSION

Both FEV<sub>1</sub> and HRQoL were poorer in patient with COPD than in asthma patients. Furthermore, COPD patients showed a greater decline in FEV<sub>1</sub> and HRQoL over a period of 2 years. Longitudinal multivariate analyses showed different predictors of changes in FEV<sub>1</sub> and HRQoL in both asthma and COPD patients. Older age, living in an urban area, and low PEFR at baseline were associated with a decline in FEV<sub>1</sub> in both asthma and COPD patients. In patients with asthma, a greater body weight, no chronic cough or sputum production, and less frequent respiratory symptoms also predicted a decline in FEV<sub>1</sub>, whereas current smoking predicted a decline in FEV<sub>1</sub> in COPD patients. A decline in HRQoL was in both asthma and COPD predicted by a higher degree of dyspnea. Other predictors of a decline of HRQoL in asthma patients were older age, poor compliance, and lower PEFR, whereas in COPD patients these were male gender, lower body weight, and more frequent respiratory symptoms.

#### *The Course of FEV<sub>1</sub> and HRQoL Over a Period of 2 Years*

Over a period of 2 years the mean change in FEV<sub>1</sub> and HRQoL in asthma patients was small. In contrast, patients with COPD showed a significant decline in FEV<sub>1</sub> over a period of 2 years and a significant decline in HRQoL in the second year. These results are in line with expectations regarding the course of these diseases (5, 21, 22). It might be true that a study period of 2 years is too short to demonstrate important mean changes in FEV<sub>1</sub> or HRQoL, especially in asthma patients. However, there was sufficient variation in the changes in FEV<sub>1</sub> and HRQoL among the patients to identify a number of relevant predictors.

These longitudinal findings confirm previous cross-sectional findings that respiratory symptoms are poorly associated with objective disease parameters such as FEV<sub>1</sub>, but more strongly associated with subjective disease parameters such as HRQoL (1, 23). Chronic cough or sputum production and frequent respiratory symptoms at baseline even predicted an improvement in FEV<sub>1</sub> in the asthma patients. However, this finding, may very well reflect the changeable, episodic nature of the disease and may indicate that respiratory problems disappear over time.

#### *Predictors of Changes in FEV<sub>1</sub> and HRQoL Over a Period of 2 Years*

In both asthma and COPD patients, more severe dyspnea at baseline was associated with a subsequent decline in HRQoL. Since other researchers also found a strong correlation between dyspnea and HRQoL (3, 4, 24) and dyspnea can be easily measured in a clinical setting, it might be worthwhile to make a standard assessment of dyspnea in clinical practice (4, 25).

The results of previous research are inconsistent with respect to the associations between PEFR and HRQoL (26). In the present study a significant but weak association was found between low PEFR at baseline and a decline in HRQoL. A stronger association was found between a low mean PEFR at baseline and a decline in FEV<sub>1</sub> in both asthma and COPD patients.

As expected, the results showed that smoking predicts a stronger decline in FEV<sub>1</sub> in COPD patients (5). Living in an urban region (west) compared to a suburban region (east or northwest) predicted a decline in FEV<sub>1</sub> in both asthma and COPD patients. A possible explanation for this result might be a difference in the measurement conditions. However, since the same spirometer was used in the east and the west, and the training instructions for the research assistants were very similar, this is not likely. Another more likely explanation is the difference in the grade of urbanization. Patients living in more urbanized areas may be more severely affected, receive less optimal treatment, or live in poorer conditions, compared to those in suburban areas.

As far as we know, only a few studies have investigated the change in FEV<sub>1</sub> over time, and none have studied changes in HRQoL in patients in a primary care. Most other studies that investigated predictors of FEV<sub>1</sub> and HRQoL had a cross-sectional design (11). The strength of the present study is that it was possible to identify predictors of changes within patients over a period of 2 years and investigate the predictive value of several patient and disease characteristics.

The participants in this study were patients in primary care who used medication and had reported some respiratory complaints during selection. The present study group may not be representative for patients with even milder forms of asthma or COPD in general practice, for well-controlled asthma patients (no symptoms), or for patients in secondary care. However, we feel that the study population does represent an average population of patients with mild to moderate asthma or COPD in primary care.

#### CONCLUSION

FEV<sub>1</sub> and HRQoL appear to be influenced by different predictors (27). This suggests that besides FEV<sub>1</sub> measurements, HRQoL should also be taken into account by physicians, as this clearly reflects a different aspect of the disease. Dyspnea seems to be an important predictor of decline in HRQoL in both asthma and COPD patients. More research is needed to determine whether a short dyspnea questionnaire can be of value in routine general practice to anticipate a decline in HRQoL in individual patients (25). Finally, a few additional factors might help physicians to identify patients who are at risk for a decline in FEV<sub>1</sub> (older age, living in an urban area, and smoking) or a decline in HRQoL (lower level of education, poor compliance with treatment, and more frequent respiratory complaints).

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## REFERENCES

1. Wijnhoven HA, Kriegsman DM, Hesselink AE, Penninx BW, de Haan M. Determinants of different dimensions of disease severity in asthma and COPD: pulmonary function and health-related quality of life. *Chest* 2001; 119:1034–1042.
2. Moy ML, Israel E, Weiss ST, Juniper EF, Dube L, Drazen JM. Clinical predictors of health-related quality of life depend on asthma severity. *Am J Respir Crit Care Med* 2001; 163:924–929.
3. Ferrer M, Alonso J, Morera J, Marrades RM, Khalaf A, Aguar MC, Plaza V, Prieto L, Anto JM. Chronic obstructive pulmonary disease stage and health-related quality of life. The quality of life of Chronic Obstructive Pulmonary Disease Study Group. *Ann Intern Med* 1997; 127:1072–1079.
4. Curtis JR, Deyo RA, Hudson LD. Pulmonary rehabilitation in chronic respiratory insufficiency. 7. Health-related quality of life among patients with chronic obstructive pulmonary disease. *Thorax* 1994; 49:162–170.
5. Celli BR. The importance of spirometry in COPD and asthma: effect on approach to management. *Chest* 2000; 117(2 suppl.): 15S–24S.
6. van Schayck CP. Is lung function really a good parameter in evaluating the long-term effects of inhaled corticosteroids in COPD? *Eur Respir J* 2000; 15:238–239.
7. Hansen EF, Phanareth K, Laursen LC, Kok-Jensen A, Dirksen A. Reversible and irreversible airflow obstruction as predictor of overall mortality in asthma and chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1999; 159(4 Pt. 1):1267–1271.
8. Fan VS, Curtis JR, Tu SP, McDonnell MB, Fihn SD. Using quality of life to predict hospitalization and mortality in patients with obstructive lung diseases. *Chest* 2002; 122:429–436.
9. Nishimura K, Izumi T, Tsukino M, Oga T. Dyspnea is a better predictor of 5-year survival than airway obstruction in patients with COPD. *Chest* 2002; 121:1434–1440.
10. Jones PW. Interpreting thresholds for a clinically significant change in health status in asthma and COPD. *Eur Respir J* 2002; 19:398–404.
11. van Schayck CP, Dompeling E, Putters R, Molema J, van Weel C. Asthma and chronic bronchitis. Can family physicians predict rates of progression? *Can Fam Physician* 1995; 41:1868–1876.
12. Geijer RMM, Thiadens HA, Smeele IJM, Sachs APE, Bottema BJAM, van Hensbergen W, van Schayck CP, van Weel C, Rosmalen CF. NHG-standaard COPD en astma bij volwassenen: diagnostiek. *Huisarts en Wet* 2001; 44:107–117.
13. Standardisation of Spirometry, 1994 Update. Statement of The American Thorax Society. 1995; 1522:1107–1198.
14. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J* 1993; 16(suppl.):5–40.
15. Maille AR, Koning CJ, Zwinderman AH, Willems LN, Dijkman JH, Kaptein AA. The development of the “Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)”: a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. *Respir Med* 1997; 91:297–309.
16. Geijer RMM, Van Hensbergen W, Bottema BJAM, Bottema BJAM, van Schayck CP, Sachs APE, Smeele IJM, van Weel C, Thiadens HA, Rosmalen CF. NHG-standaard astma bij volwassenen: behandeling. *Huisarts en Wetenschap*: 2001; 44:153–164.
17. Matricardi PM, Nisini R, Pizzolo JG, D’Amelio R. The use of Phadiatop in mass-screening programmes of inhalant allergies: advantages and limitations. *Clin Exp Allergy* 1990; 20:151–155.
18. Reddel HK, Salome CM, Peat JK, Woolcock AJ. Which index of peak expiratory flow is most useful in the management of stable asthma? *Am J Respir Crit Care Med* 1995; 151:1320–1325.
19. Hesselink AE, Penninx BW, van der Windt DAWM, van Duin BJ, Vries de P, Twisk JWR, Bouter LM, van Eijk JThM. An education programme for asthma and COPD patients conducted by a general practice assistant: results from a randomized controlled trial. *Patient Education and Counselling* 55; 2004:121–128.
20. Ulrik CS, Lange P. Decline of lung function in adults with bronchial asthma. *Am J Respir Crit Care Med* 1994; 150:629–634.
21. Morgan WK, Reger RB. Rise and fall of the FEV(1). *Chest* 2000; 118:1639–1644.
22. Teeter JG, Bleecker ER. Relationship between airway obstruction and respiratory symptoms in adult asthmatics. *Chest* 1998; 113:272–277.
23. Smeele IJ, Van Schayck CP, van den Bosch WJ, van den Hoogen HJ, Muris JW, Grol RP. Quality of life of patients with asthma and COPD in general practice. *Eur J Gen Pract* 1998; 4:121–125.
24. Bestall JC, Paul EA, Garrod R, Garnham R, Garnham R, Jones PW, Wedzicha JA. Usefulness of the Medical Research Council (MRC) dyspnea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax* 1999; 54:581–586.
25. Marks GB, Dunn SM, Woolcock AJ. An evaluation of an asthma quality of life questionnaire as a measure of change in adults with asthma. *J Clin Epidemiol* 1993; 46:1103–1111.
26. Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ, Walters EH. Self-management education and regular practitioner review for adults with asthma. *Cochrane Database Syst Rev* 2003; (2):CD001117. Oxford: Update Software.
27. Gigliotti F, Grazzini M, Stendardi L, Romagnoli I, Scano G. Quality of life and functional parameters in patients with chronic obstructive pulmonary disease (COPD): an update. *Respir Med* 2002; 96(6):373–374.