

STUDY REPORT SUMMARY

ASTRAZENECA PHARMACEUTICALS

FINISHED PRODUCT: Not applicable

ACTIVE INGREDIENT: Not applicable

Study No: NIS-RGR-DUM-2010/1

A cross sectional study for the assessment of the words used by patients and physicians to express the symptoms of chronic obstructive pulmonary disease and the limitations of patients' activities in primary care.

The « COPD Language » Study

Developmental Phase: NIS

Study Completion Date: 28 March 2011

Date of Report: 14 October 2011

OBJECTIVES:

Primary Objective

- To evaluate the most frequently used words by the patients and the physicians to express COPD symptoms as well as the limitations of activities caused by COPD.

Secondary Objectives

- To describe the health status of COPD patients (as assessed by CCQ).
- To assess the correlation between the health status and the words used by the patients.
- To describe the actions recommended by the physician or those initiated by the patient that are associated with words that express chronic daily symptoms.
- To describe the actions recommended by the physician or those initiated by the patient when the symptoms worsen.
- To describe the severity level with which the patient experiences the words expressing the COPD symptoms as well as the assessment of the severity of symptoms by the physician.
- To describe the most frequently used words (lexical intensity) by the patient and the physician when an inhaled reliever treatment is used.
- To look for the factors (CCQ score, years with symptoms, age, residency, marital status, smoking history, educational level, treatment, number of exacerbations within last year, co-morbidities) associated with the use of these words by the patients when expressing their COPD symptoms and the limitations of activities caused by COPD.

METHODS:

Study Design

This is a cross-sectional observational study that has been conducted by a representative sample of 70 office-based physicians, under the coordination of two hospital-based lung specialists, who have been selected through pre-defined eligibility assessment process from a population of primary care practitioners who treat patients with COPD and practice in different regions of Greece.

Before the commencement of any study related procedure, the patients were informed about the nature of the study and signed accordingly the informed consent form. Each physician was requested to complete a questionnaire with his/her personal data (physician's questionnaire) and a paper case report form (pCRF) for the first 10 consecutive patients who visited his/her office and who met the eligibility criteria for enrolment into the study. In addition, every participating patient has completed a questionnaire.

The study has been completed in one single patient visit which took place within the normal clinical practice.

Selection Criteria

Inclusion criteria

For inclusion in the study subjects had to fulfill all of the following criteria:

- Aged 45-75 years
- Current or former smokers
- Known history of COPD for at least 6 months before enrolment documented by spirometry ($FEV_1/FVC < 70\%$)
- Patients with stable COPD (with no exacerbation within the last month prior to enrolment into the study) under treatment with a long-acting inhaled bronchodilator (LABA and/or LAMA) alone or in combination with an inhaled corticosteroid
- Written consent for participation in the study
- Patients able to complete by themselves in Greek a questionnaire on COPD.

Exclusion criteria

Any of the following was regarded as a criterion for exclusion from the study:

- Patients with diagnosed asthma
- Patients with any psychiatric, neurological or other disorder that render them unable to complete the COPD questionnaire by themselves
- Patients who were participating in another study.

Target Patient Population, Study Disease and Sample Size

Overall 700 patients with stable COPD fulfilling the study-specific eligibility criteria were enrolled and completed the study. 61.4% of patients (430/700) were enrolled by physicians practicing outside Attica whereas the rest 38.6% (270/700) by primary healthcare practitioners inside Attica.

The primary variable of the study was the determination of the most frequently used words by the patients and the physicians to express COPD symptoms and the limitations of daily activities caused by COPD, in primary healthcare settings. According to the published literature

dyspnea/shortness of breath is the most common symptom reported by patients with COPD. Assuming that in the present study dyspnoea/shortness of breath will represent the most frequently reported word by 75% of the participating patients to express their COPD symptoms, the assessment of 625 subjects was required in order to detect this value in the study population with power 80%, significance level $\alpha=0.05$ and two-tailed test. The observed value will be tested against a theoretical value of 0.70 (H_0). With this sample size ($n=625$) the study will have power 80% to yield a statistically significant result with a precision of approximately plus/minus 0.03 points. Taking into account that approximately 10% of patients would not provide evaluable data, approximately 700 patients should be enrolled, and were finally included and completed the current study.

Statistical Methods

Descriptive statistical analysis has been applied to all study data. All categorical variables are expressed in counts (N) and percentages (%). Continuous variables are summarized with the use of descriptive statistical measures [mean value, standard deviation (SD), median, and extreme values].

The normality of distribution of continuous variables has been examined using the Kolmogorov Smirnov test (K-S test) in order to determine whether or not to use parametric methods for the analysis of the sample data.

Pearson's chi-square test of independence has been used to test the relationship between categorical variables while Mann-Whitney test for independent samples has been applied to estimate potential differences between continuous variables.

For the primary endpoint the most frequently words used to express COPD symptoms as well as the 7 relevant groups of words tabulated by the two responders' categories (physicians and patients) are presented in frequency tables (n,%). A similar table is displayed for the most frequently used words to express the limitations of patients' daily activities caused by COPD. With regard to secondary variables, patients' health status is displayed through the mean (SD) total CCQ score as well as the mean (SD) score of the 3 domains (symptoms score, functional state and mental state score).

Furthermore, descriptive methods have being applied for the presentation of the actions recommended or initiated by the physicians and the patients respectively that are associated with words that express chronic daily symptoms as well as when the symptoms worsen.

The severity level with which the patients experience the words expressing the COPD symptoms as well as the assessment of the severity of symptoms by the physicians are tabulated using descriptive statistics (mean value, standard deviation (SD), median, and extreme values).

RESULTS:

Subject Demographic and Baseline Characteristics

The mean age of the study population was 61.2 ± 7.8 years, with a clear preponderance of males over females, and a male-to-female ratio of 1.5 (males/females: 60.0%/40.0%) [Table 1].

Table 1 Subjects' socio-demographic characteristics

Subjects' socio-demographic characteristics					
Age (years)	Mean	SD	Median	Min	Max
	61.2	7.8	62.0	45.0	75.0
Gender	N		%		
<i>Male</i>	420		60.0		
<i>Female</i>	280		40.0		
Place of residence	N		%		
<i>Urban</i>	499		71.3		
<i>Semi-urban</i>	103		14.7		
<i>Rural</i>	98		14.0		
Native Greek speaker	N		%		
<i>Yes</i>	694		99.1		
<i>No</i>	6		0.9		
Marital status	N		%		
<i>Single</i>	38		5.4		
<i>Married</i>	569		81.3		
<i>Divorced/widowed</i>	93		13.3		
Educational background	N		%		
<i>Primary education</i>	196		28.0		
<i>Secondary education</i>	295		42.1		
<i>Post-secondary</i>	109		15.6		
<i>Higher education</i>	100		14.3		
Occupation	N		%		
<i>Unemployed</i>	7		1.0		
<i>Housework</i>	97		13.9		
<i>Private sector employee</i>	60		8.6		
<i>Public sector employee</i>	83		11.9		
<i>Farmer</i>	53		7.6		
<i>Craftsman</i>	41		5.9		
<i>Freelancer</i>	62		8.9		
<i>Trader/businessman</i>	52		7.4		
<i>Retired</i>	245		35.0		

Subjects' medical history

The vast majority of patients (72.4%; 507/700) suffered from at least one co morbid disease apart from COPD. Hypertension and diabetes were the most frequent co-morbidities observed among the study population (reported by 56.7% and 19.6% of patients, respectively) and were under treatment in the majority of patients. It is noteworthy to mention that only 6.4% (45/700) of the study participants had a history of bronchiectasis.

Subjects' COPD history & treatment patterns

The vast majority of patients (89.3%; 625/700) had been diagnosed with COPD for more than 1 year prior to study visit, and the median duration of COPD symptoms reported was 5 years (range 0-30). Mean FEV₁/FVC was 0.62 (\pm 0.06) and the median number of exacerbations reported during last year was 1 (range 0-30), whereas the median number of hospitalizations due to COPD was 0.0 (range 0-4). The vast majority of patients (85.3%) were treated with combination drug therapy while only 14.7% with monotherapy [Table 2]. As far as patients' adherence to their current COPD therapy is concerned, a great proportion of patients (38.3%) reported that they sometimes forget to take their medications, 22.5% mentioned that they take their medication only when their condition gets worse, while the frequency of COPD prescription refills was once monthly as indicated by the majority of patients (68%).

Table 2 Subjects' COPD history & treatment patterns

COPD history & treatment patterns					
Years since COPD diagnosis		N		%	
< 1 year		75		10.7	
> 1 year		625		89.3	
Symptoms duration & lung function	Mean	SD	Median	Min	Max
<i>Duration of COPD symptoms (years)</i>	6.8	5.1	5.0	0.0	30.0
<i>FEV₁/FVC (indicative of COPD)</i>	0.62	0.06	0.65	0.32	0.69
Smoking status		N		%	
<i>Active smokers</i>		354		50.6	
<i>Ex-smokers</i>		346		49.4	
Pack-years	Mean	SD	Median	Min	Max
<i>Active smokers</i>	40.7	22.8	37.5	0.5	140.0
<i>Ex-smokers</i>	40.4	31.3	33.0	1.0	225.0
Exacerbations/hospitalisations last year	Mean	SD	Median	Min	Max
<i>No of COPD exacerbations</i>	1.8	2.1	1.0	0.0	30.0
<i>No of hospitalisations due to COPD</i>	0.2	0.5	0.0	0.0	4.0
Hospitalisation due to COPD		N		%	
<i>No of patients who had been hospitalized</i>		158		22.6	
<i>No of patients who had not been hospitalized</i>		542		77.4	
Current treatment for COPD		N		%	
<i>Drug therapy only</i>		604		86.3	
<i>Drug therapy plus oxygen treatment</i>		96		13.7	
Type of drug therapy		N		%	
<i>Monotherapy</i>		103		14.7	
<i>Combination therapy</i>		597		85.3	

Primary Objective

Most frequently used words by patients and physicians to express COPD symptoms

Among the most common words used by the physicians to express patients' COPD chronic daily symptoms was cough/coughing (for 44.4% of patients), dyspnoea (38.8%), shortness of breath (30.3%) and sputum (28%). Accordingly, the words that were most commonly used by the

patients to express their COPD chronic daily symptoms was cough/coughing (38.6% of patients), shortness of breath (33.9%), phlegm (32.3%) and chest sounds (24.6%) [Table 3].

Table 3 Most frequently used words by patients and physicians to express COPD symptoms

Words expressing COPD symptoms	Words used by Physicians		Words used by Patients	
	N _{patients}	%	N _{patients}	%
Sputum	196	28.0	162	23.1
Whistling	147	21.0	121	17.3
Dyspnoea	269	38.4	158	22.6
Discomfort in the chest	101	14.4	127	18.1
Chest sounds	152	21.7	172	24.6
Dry cough	79	11.3	109	15.6
Cough/coughing	311	44.4	270	38.6
Tiredness in breathing	73	10.4	107	15.3
Cat's meow	95	13.6	152	21.7
Expectoration	182	26.0	70	10.0
Pressure/tightness in chest	65	9.3	72	10.3
Bronchospasm	64	9.1	4	0.6
Phlegm	118	16.9	226	32.3
Shortness of breath	212	30.3	237	33.9
Difficulty to get air into and out of the lungs	25	3.6	35	5.0
Discomfort in breathing	84	12.0	86	12.3
Smoker's cough	109	15.6	134	19.1
Chocking	24	3.4	38	5.4
Cannot get enough air	42	6.0	66	9.4
Difficulty in breathing	82	11.7	75	10.7

Most frequently used words by patients and physicians to express limitations of daily activities caused by COPD

As depicted in Table 4, COPD was causing limitations in daily activities in 83.4% of patients (584/700) according to treating physicians' perception, and in 82% (574/700) of patients as reported by the patients themselves.

Table 4 Limitations in daily activities due to COPD as reported by physicians and patients

Limitations in daily activities due to COPD	Physicians		Patients	
	N _{patients}	%	N _{patients}	%
COPD causes limitations in daily activities	584	83.4	574	82.0
COPD does not cause limitations in daily activities	116	16.6	126	18.0
Total	700	100.0	700	100.0

Interestingly, for 87.4% of the patients (612/700) physicians' and patients' perception on whether COPD was limiting patients' daily activities coincided, whereas for the rest 88 patients (12.6%) different perception among physicians and patients was observed.

Among the most common words used by the physicians to express patients' COPD-related limitations of daily activities was walking uphill (for 64.1% of patients), stair climbing (60.9%), brisk walking (51.1%) and sports (21.9%) [Table 5]

Similarly, the words that were most frequently used by the patients to express the daily activities that were limited by COPD were walking uphill (61.9% of patients), stair climbing (59.1%) and brisk walking (48.3%) whereas 21.9% of patients reported that they could not do everything they want due to COPD.

Table 5 Most frequently used words by patients and physicians to express limitations of daily activities caused by COPD

Daily activities limited by COPD	Words used by Physicians		Words used by Patients	
	N _{patients}	%	N _{patients}	%
Stair climbing	426	60.9	414	59.1
Brisk walking	358	51.1	338	48.3
Walking uphill	449	64.1	433	61.9
Household activities	95	13.6	95	13.6
Sports	153	21.9	158	22.6
Shopping	80	11.4	93	13.3
Difficulty at work	76	10.9	78	11.1
Weight lifting	133	19.0	155	22.1
Visiting friends	18	2.6	21	3.0
Entertainment	23	3.3	26	3.7
Intense smells	44	6.3	68	9.7
Playing with children	27	3.9	34	4.9
Cannot stand smoky areas	71	10.1	96	13.7
Difficulty in speaking	18	2.6	35	5.0
Difficulty in singing	5	0.7	28	4.0

Daily activities limited by COPD	Words used by Physicians		Words used by Patients	
	N _{patients}	%	N _{patients}	%
Difficulty in laughing	12	1.7	20	2.9
Hobbies activity	24	3.4	17	2.4
Sexual activity	35	5.0	48	6.9
Difficulty with humidity and south wind	133	19.0	167	23.9
Cannot do everything I want	145	20.7	195	27.9

Secondary Objectives

Health status of COPD patients as assessed by CCQ (weekly version)

The CCQ was administered to all patients who were asked to recall their COPD status over the past week prior to the study visit. The CCQ is self-administered and contains 10 items, subdivided into three domains: symptoms, functional state and mental state. Subjects responded to each question using a 7 point scale from 0 = asymptomatic or no-limitation, to 6 = extremely symptomatic or totally limited. For the calculation of the total score the following algorithm was used: $(\text{symptom domain score}) \times 4 + (\text{functional state domain score}) \times 4 + (\text{mental state domain score}) \times 2 / 10 = \text{CCQ total score}$. As shown in Table 6, the mean CCQ total score was 1.8 ± 0.9 , whereas the symptom domain score was 2.1 ± 0.9 , the functional domain score was 1.5 ± 1.1 , and the mental domain score was 1.6 ± 1.3 , respectively.

Table 6 Clinical COPD questionnaire score

	Mean	SD	Median	Min	Max	N*
Total CCQ score	1.8	0.9	1.7	0.1	5.3	696
<i>Symptom domain</i>	2.1	0.9	2.0	0.0	5.8	699
<i>Functional state domain</i>	1.5	1.1	1.5	0.0	5.5	698
<i>Mental state domain</i>	1.6	1.3	1.5	0.0	6.0	699

**4 patients were excluded from total CCQ calculation due to missing data (1 patient from symptoms domain, 2 patients from functional state domain and 1 patient from mental state domain)*

Correlation between patients' health status and words chosen by patients to express COPD symptoms and limitations of daily activities due to COPD

Concerning the correlation between health status and words used by the patients to express COPD symptoms, it has been demonstrated that patients using the words 'dyspnoea', 'discomfort (bloating) in the chest', 'tiredness in breathing', 'pressure/tightness in chest', 'shortness of breath', 'difficulty to get air into and out of the lungs', 'discomfort in breathing', 'choking', 'cannot get enough air', and 'difficulty in breathing' had significantly poorer health status in comparison to those who did not use these words to express their symptoms. Surprisingly, with regard to cough, it has been shown that patients who used the word 'cough' had significantly lower CCQ score i.e., better health status compared to those who did not [Table 7].

With regard to the correlation between health status and the limitations in daily activities, it has been shown that the subgroup of patients who reported that COPD does not cause any limitation in their daily living had significantly better health status (lower mean CCQ score) compared to

those who reported at least one COPD-related limitation. Moreover, a statistically significant correlation has been demonstrated between health status and almost all COPD-related limited activities apart from sports, hobbies activities and inability to stand smoky areas [Table 8].

Table 7 Correlation between patients' health status and words chosen by patients to express COPD symptoms

Total CCQ score (n=696)	Mean	SD	Median	Min	Max	N	p-value**
Sputum	1.7	0.8	1.7	0.1	4.1	161	0.382
No sputum	1.8	0.9	1.7	0.2	5.3	535	
Whistling	1.7	0.9	1.7	0.2	4.9	121	0.832
No whistling	1.8	0.9	1.7	0.1	5.3	575	
Dyspnoea	2.0	0.9	2.0	0.4	4.4	158	<0.001*
No dyspnoea	1.7	0.9	1.6	0.1	5.3	538	
Discomfort in the chest	1.9	0.9	1.8	0.3	4.9	127	0.030*
No discomfort in the chest	1.7	0.9	1.6	0.1	5.3	569	
Chest sounds	1.7	0.8	1.7	0.1	4.3	170	0.857
No chest sounds	1.8	0.9	1.6	0.1	5.3	526	
Dry cough	1.7	0.9	1.6	0.3	4.4	108	0.326
No dry cough	1.8	0.9	1.7	0.1	5.3	588	
Cough/coughing	1.7	0.8	1.5	0.3	4.4	267	0.010*
No cough/coughing	1.8	0.9	1.7	0.1	5.3	429	
Tiredness in breathing	1.9	0.9	1.9	0.3	4.3	106	0.026*
No tiredness in breathing	1.7	0.9	1.6	0.1	5.3	590	
Cat's meow	1.7	0.8	1.7	0.3	4.1	150	0.748
No cat's meow	1.8	0.9	1.7	0.1	5.3	546	
Expectoration	1.9	0.9	1.8	0.1	4.3	69	0.324
No expectoration	1.8	0.9	1.6	0.1	5.3	627	
Pressure/tightness in chest	2.0	0.9	1.9	0.4	4.9	72	0.006*
No pressure/tightness in chest	1.7	0.9	1.6	0.1	5.3	624	
Bronchospasm	3.0	1.2	3.5	1.1	3.7	4	0.054
No bronchospasm	1.8	0.9	1.7	0.1	5.3	692	
Phlegm	1.7	0.8	1.7	0.2	4.3	224	0.725
No phlegm	1.8	0.9	1.7	0.1	5.3	472	
Shortness of breath	1.9	0.8	1.8	0.4	4.9	237	0.007*
No shortness of breath	1.7	0.9	1.6	0.1	5.3	459	
Difficulty to get air into and out of the lungs	2.6	1.0	2.6	0.4	5.3	35	<0.001*
No difficulty to get air into and out of the lungs	1.7	0.9	1.6	0.1	4.9	661	
Discomfort in breathing	2.0	1.0	1.8	0.4	4.3	86	0.021*
No discomfort in breathing	1.7	0.9	1.6	0.1	5.3	610	
Smoker's cough	1.7	0.9	1.5	0.2	4.1	134	0.156

Total CCQ score (n=696)	Mean	SD	Median	Min	Max	N	p-value**
No smoker's cough	1.8	0.9	1.7	0.1	5.3	562	
Chocking	2.4	1.2	2.3	0.8	5.3	38	<0.001*
No chocking	1.7	0.9	1.6	0.1	4.9	658	
Cannot get enough air	2.1	0.9	2.0	0.3	5.3	66	0.006*
No 'cannot get enough air'	1.7	0.9	1.6	0.1	4.9	630	
Difficulty in breathing	2.2	1.0	2.2	0.6	5.3	75	<0.001*
No difficulty in breathing	1.7	0.9	1.6	0.1	4.9	621	

*Statistical significance; **U- Mann Whitney test

Table 8 Correlation between patients' health status and words chosen by patients to express COPD limitations in daily activities

Total CCQ score (n=696)	Mean	SD	Median	Min	Max	N	p-value**
Limitations in daily activities	1.9	0.9	1.8	0.1	5.3	571	<0.001*
No limitations in daily activities	1.1	0.7	1.0	0.1	3.6	125	
Stair climbing	2.0	0.9	1.9	0.1	5.3	412	<0.001*
No stair climbing	1.4	0.8	1.2	0.1	4.1	284	
Brisk walking	2.0	0.9	1.9	0.3	4.4	337	<0.001*
No brisk walking	1.6	0.8	1.4	0.1	5.3	359	
Walking uphill	2.0	0.9	1.9	0.3	4.9	431	<0.001*
No walking uphill	1.4	0.8	1.2	0.1	5.3	265	
Household activities	2.4	0.9	2.4	0.3	4.4	95	<0.001*
No household activities	1.7	0.8	1.6	0.1	5.3	601	
Sports	1.8	0.9	1.7	0.3	4.4	158	0.386
No sports	1.7	0.9	1.6	0.1	5.3	538	
Shopping	2.3	0.9	2.3	0.4	4.4	93	<0.001*
No shopping	1.7	0.9	1.6	0.1	5.3	603	
Difficulty at work	2.3	1.0	2.2	0.5	4.4	78	<0.001*
No difficulty at work	1.7	0.9	1.6	0.1	5.3	618	
Weight lifting	2.2	0.9	2.1	0.5	5.3	154	<0.001*
No weight lifting	1.6	0.8	1.5	0.1	4.9	542	
Visiting friends	3.1	0.8	3.0	1.4	4.4	21	<0.001*
No visiting friends	1.7	0.9	1.6	0.1	5.3	675	
Entertainment	2.7	1.0	2.8	1.1	4.4	26	<0.001*
No entertainment	1.7	0.9	1.6	0.1	5.3	670	
Intense smells	2.1	1.0	1.9	0.6	4.3	68	0.002*
No intense smells	1.7	0.9	1.6	0.1	5.3	628	
Playing with children	2.3	0.9	2.0	1.0	4.3	34	0.001*
No "Playing with children"	1.7	0.9	1.6	0.1	5.3	662	
Cannot stand smoky areas	1.7	0.9	1.6	0.1	5.3	95	0.198

Total CCQ score (n=696)	Mean	SD	Median	Min	Max	N	p-value**
No "Cannot stand smoky areas"	1.9	1.0	1.7	0.3	4.9	601	
Difficulty in speaking	2.9	0.9	3.0	1.0	5.3	35	<0.001*
No difficulty in speaking	1.7	0.8	1.6	0.1	4.9	661	
Difficulty in singing	2.2	0.9	2.5	0.7	3.7	28	0.007*
No difficulty in singing	1.7	0.9	1.6	0.1	5.3	668	
Difficulty in laughing	2.7	1.1	2.8	0.8	4.3	20	<0.001*
No difficulty in laughing	1.7	0.9	1.6	0.1	5.3	676	
Hobbies activity	2.1	0.9	2.0	1.0	4.0	17	0.102
No hobbies activity	1.8	0.9	1.7	0.1	5.3	679	
Sexual activity	2.3	1.0	2.2	0.6	4.4	48	<0.001*
No sexual activity	1.7	0.9	1.6	0.1	5.3	648	
Difficulty with humidity and south wind	2.2	0.9	2.1	0.3	5.3	167	<0.001*
No difficulty with humidity and south wind	1.6	0.8	1.5	0.1	4.4	529	
Cannot do everything I want	2.2	0.9	2.1	0.3	4.9	195	<0.001*
No "Cannot do everything I want"	1.6	0.8	1.5	0.1	5.3	501	

*Statistical significance; **U- Mann Whitney test

Actions recommended by the physicians or those initiated by the patients associated with words expressing COPD symptoms

With regard to actions recommended by the physicians associated with words expressing COPD symptoms, it is noteworthy to mention that rescue medication intake was recommended most frequently in patients with dyspnoea (68%), bronchospasm (67.2%), difficulty in breathing (64.6%), difficulty to get air into and out of the lungs (64%), discomfort in breathing (61.9%) and difficulty in getting enough air (61.9%). Furthermore, the increase in maintenance therapy dose was more commonly recommended in patients with difficulty to get air into and out of the lungs (60%), bronchospasm (59.4%), and difficulty in breathing (54.9%).

Concerning the actions initiated by the patients themselves, it is worthwhile to mention that rescue medication intake was initiated by patients most frequently due to difficulty to get air into and out of the lungs (71.4%), difficulty in getting enough air (66.7%) and pressure/tightness in chest (56.9%). Furthermore, the increase in inhaled drug dose was initiated by patients most commonly due to bronchospasm (75%), choking (42.1%), difficulty in getting enough air (40.9%), and difficulty to get air into and out of the lungs (40%).

Actions recommended by the physicians or those initiated by the patients when symptoms worsen

When COPD symptoms worsen, the most frequently recommended actions as reported by physicians was telephone contact (in 83.7% of patients), followed by intake of rescue medication or inhaled/systemic corticosteroids (in 54.3% of patients) and increase of dose of maintenance treatment (in 45.1% of the patients) [Table 9]. Likewise, the most frequently initiated actions by the patients themselves was to contact their doctor by phone (81.8%), receive rescue medication (44.6%) and increase the doses of the inhaled drug (33.9%) [Table 10].

Table 9 Actions recommended by the physicians when symptoms worsen (n=700)

Actions recommended by the physicians	N _{patients}	%
Telephone contact	586	83.7
Receive rescue medication or inhaled/systemic corticosteroids	380	54.3
Increase of dose of maintenance treatment	316	45.1
Receive antibiotics	167	23.9
Emergency department visit	85	12.1
No specific advice	33	4.7

Table 10 Actions initiated by the patients when symptoms worsen (n=699*)

Actions initiated by the patients	N _{patients}	%
Contact the doctor by phone	572	81.8
Receive medication for symptom relief	312	44.6
Increase the doses of the inhaled drug	237	33.9
Receive antibiotics	127	18.2
Visit an emergency department	97	13.9
Continue treatment without changes	92	13.2
Take pills (or injection) with cortisone	49	7.0

*1 patient with no available data

Severity level with which patients experience the words expressing the COPD symptoms as well as assessment of symptoms' severity by physicians

Both patients and physicians were requested to assess the severity of COPD symptoms (reflected by the most commonly used words) in a 7-point scale ranging for '0' (mild) to '6' (very severe). As depicted in Tables 11 and 12, the mean severity score for all words used by physicians ranged from 2.1 to 3.2, whereas for the words used by patients ranged from 2.2 to 3.6, indicating mild to moderate severity of symptoms reported by both physicians and patients.

Table 11 Symptoms severity level as reported by physicians

Symptoms severity rating (reported by physicians)	Mean	SD	Median	Min	Max	N
Sputum	2.1	1.0	2.0	0.0	5.0	196
Whistling	2.2	1.0	2.0	0.0	5.0	147
Dyspnoea	2.7	1.1	3.0	0.0	5.0	269
Discomfort in the chest	2.6	1.1	3.0	0.0	5.0	101
Chest sounds	2.3	1.0	2.0	0.0	5.0	152
Dry cough	2.3	1.1	2.0	0.0	5.0	79
Cough/coughing	2.4	0.9	2.0	0.0	5.0	311
Tiredness in breathing	2.4	1.1	2.0	0.0	5.0	73
Cat's meow	2.2	1.0	2.0	0.0	5.0	95
Expectoration	2.4	1.0	2.0	0.0	5.0	182

Pressure/tightness in chest	2.3	1.0	2.0	1.0	5.0	65
Bronchospasm	2.8	1.0	3.0	1.0	5.0	64
Phlegm	2.3	1.1	2.0	0.0	5.0	118
Shortness of breath	2.4	1.1	2.0	0.0	5.0	212
Difficulty to get air into and out of the lungs	3.2	1.4	3.0	0.0	5.0	25
Discomfort in breathing	2.4	1.0	2.0	1.0	5.0	84
Smoker's cough	2.3	1.1	2.0	0.0	5.0	109
Chocking	2.5	1.2	2.0	0.0	5.0	24
Cannot get enough air	2.7	1.3	2.5	0.0	5.0	42
Difficulty in breathing	2.9	1.3	3.0	0.0	5.0	82

Table 12 Symptoms severity level as reported by patients

Symptoms severity rating (<i>reported by patients</i>)	Mean	SD	Median	Min	Max	N
Sputum	2.2	1.2	2.0	0.0	5.0	161
Whistling	2.2	1.2	2.0	0.0	5.0	119
Dyspnoea	2.7	1.2	3.0	0.0	5.0	157
Discomfort in the chest	2.8	1.1	3.0	0.0	5.0	124
Chest sounds	2.4	1.0	2.0	0.0	5.0	166
Dry cough	2.3	1.1	2.0	0.0	5.0	109
Cough/coughing	2.3	1.1	2.0	0.0	5.0	268
Tiredness in breathing	2.7	1.2	3.0	1.0	5.0	104
Cat's meow	2.4	1.1	2.0	0.0	5.0	151
Expectoration	2.4	1.2	2.0	0.0	5.0	69
Pressure/tightness in chest	2.9	1.2	3.0	1.0	5.0	70
Bronchospasm	3.5	1.3	3.5	2.0	5.0	4
Phlegm	2.4	1.1	2.0	0.0	5.0	222
Shortness of breath	2.7	1.1	3.0	0.0	5.0	229
Difficulty to get air into and out of the lungs	3.6	1.0	4.0	1.0	5.0	35
Discomfort in breathing	2.8	1.2	2.5	1.0	5.0	84
Smoker's cough	2.5	1.2	2.0	0.0	5.0	132
Chocking	3.7	1.4	4.0	1.0	5.0	37
Cannot get enough air	2.9	1.3	3.0	1.0	5.0	63
Difficulty in breathing	3.2	1.3	3.0	0.0	5.0	72

Most frequently used words (lexical intensity) by the patients and the physicians when an inhaled reliever treatment is used

The most frequently used words by physicians when an inhaled reliever treatment is recommended include dyspnoea (35.7%), cough (26.6%), and shortness of breath (19.3%).

Similarly, among the words that were most commonly used by the patients when an inhaled reliever treatment is initiated are shortness of breath (22.9%), cough (19.8%), and dyspnoea (19.2%).

Factors associated with the 4 most frequently words used by patients when expressing their COPD symptoms and the limitations of daily activities caused by COPD

For the 4 most frequent words used by the patients when expressing their COPD symptoms [*i.e.*, ‘cough’, ‘shortness of breath’, ‘phlegm’ and ‘chest sounds’] and the limitations of activities caused by COPD [*i.e.*, ‘walking uphill’, ‘stair climbing’, ‘brisk walking’, and ‘cannot do everything I do’] the chi-square test has been applied in order to look for possible association with factors such as gender, place of residence, marital status, smoking history, education level, therapy and co-morbidities. Furthermore, Mann Whitney test has been used in order to explore the potential correlation between the aforementioned variables and the age, the CCQ score, the years with COPD symptoms, and the number of exacerbations.

- **Association between gender and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation between gender and the words most frequently used by patients to express COPD symptoms and limitations in their daily activities concerned the word ‘phlegm’ ($p=0.011$) which was found to be used most frequently by males compared to females.

- **Association between marital status and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

No statistically significant correlation between marital status and the words most frequently used by patients to express COPD symptoms and limitations in their daily activities has been demonstrated.

- **Association between educational background and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation between educational background and the words most frequently used by patients to express COPD symptoms and limitations in their daily activities concerned the words ‘phlegm’ ($p=0.021$), ‘chest sounds’ ($p=0.008$) and ‘walking uphill’ ($p=0.002$) which were found to be more commonly used by patients with a lower educational level (up to secondary education graduates) compared to higher education level graduates.

- **Association between smoking status and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The word ‘shortness of breath’ was significantly most commonly used by ex-smokers ($p=0.018$) and patients with a smoking history over 40 pack-years ($p=0.018$) while ‘chest sounds’ was most commonly used by active-smokers ($p=0.035$).

Additionally, patients with a smoking history over 40 pack-years used significantly more commonly the word 'phlegm' in comparison to those with < 40 pack-year smoking history (p=0.004).

Furthermore, ex-smokers used more frequently 'stair climbing' (p=0.018) to express the limitation in daily activities, whereas 'walking uphill' (p<0.001), 'stair climbing' (p=0.032), 'brisk walking' (p<0.001) and 'cannot do everything I want' (p=0.001) were most frequently used by heavier smokers (≥ 40 pack-years).

- **Association between place of residence and 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation between place of residence and the words most frequently used by patients to express COPD symptoms and limitations in their daily activities concerned the word 'chest sounds' (p<0.001) which was found to be more commonly used by patients living in rural areas compared to residents in urban areas.

Furthermore, patients from rural or semi-urban areas use significantly more frequently the word 'walking uphill' (p=0.023) to express the limitation in their daily activities.

- **Association between age and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The subgroup of patients that used the word 'phlegm' (p<0.001) was older in age than those who did not, while 'chest sounds' (p=0.002) was most commonly used by younger ones.

Additionally, the cohort of patients that used the 4 most frequently words expressing limitations in daily activities were older than those who did not.

- **Association between years since COPD diagnosis and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation between years since COPD diagnosis and the words most frequently used by patients to express COPD symptoms concerned the word 'cough' (p=0.005) which was found to be more commonly used by patients who had been diagnosed with COPD less than one year.

Furthermore, patients diagnosed with COPD more than 1 year used significantly more frequently the expression 'I cannot do everything I want' (p=0.007) to indicate the limitation of their daily activities caused by COPD.

- **Association between health status and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The subgroup of patients who used the word 'shortness of breath' (p=0.007) and the 4 most frequently used words (p<0.001) regarding COPD-limited activities had significantly poorer health status (higher CCQ score) than those who did not. With regard to cough, the cohort of patients who used the word 'cough' (p=0.01) had better health status compared to those who did not.

- **Association between hospitalization and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation between hospitalization and the words most frequently used by patients to express COPD symptoms concerned the word ‘cough’ ($p < 0.001$) which was found to be used more commonly by patients who had not previously been hospitalized due to COPD and the word ‘phlegm’ ($p = 0.02$) that was used more frequently by patients who had previously been hospitalized.

Furthermore, the cohort of patients previously hospitalized due to COPD used significantly more frequently each of the 4 chosen words ($p < 0.001$) expressing the limitations in daily activities compared to the population of patients not previously hospitalized.

- **Association between current COPD therapy and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The word ‘cough’ ($p = 0.03$) was used significantly more frequently by patients who were treated with drug therapy only in comparison with those being on combined drug and oxygen therapy.

Furthermore, the cohort of patients who were on drug plus oxygen therapy as well as those being treated with combination drug therapy used significantly more frequently each of the 4 chosen words expressing the limitations in daily activities compared to those being treated with drug monotherapy without concomitant oxygen administration.

- **Association between symptoms duration and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The subgroup of patients who used the word ‘cough’ ($p = 0.004$) had statistically significantly shorter duration of COPD symptoms than those who did not.

Additionally, the cohort of patients who used the 4 most frequently words expressing limitations in daily activities had significantly longer duration of COPD symptoms compared to those who did not.

- **Association between number of COPD exacerbations and 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The subgroup of patients that used the word ‘phlegm’ ($p = 0.006$) and ‘chest sounds’ ($p < 0.001$) had experienced significantly more COPD exacerbations during the past year compared to those who did not.

Moreover, the cohort of patients who used the most frequently words expressing limitations in daily activities apart from brisk walking had experienced significantly more COPD exacerbations during the past year compared to those who did not.

- **Association between comorbidities and the 4 most frequently used words by patients to express their COPD symptoms and the limitations of daily activities caused by COPD**

The only statistically significant correlation demonstrated between comorbidities and the 4 most frequently used words by the patients concerns the word ‘shortness of breath’ ($p = 0.012$) which

was significantly more frequently used by the subgroup of patients with heart failure compared to those with no heart failure.

With regard to the correlation between comorbidities and the words used by patients to express the limitations of their daily activities, it has been demonstrated that patients with arterial hypertension used significantly more frequently all 4 words in comparison to the cohort of patients without hypertension, whereas patients suffering from heart failure, peripheral arterial disease or bronchiectasis used more frequently the words 'stair climbing' and 'cannot do everything I want' to express their daily activities that were limited due to COPD.

Furthermore, patients with depression and diabetes mellitus used significantly more frequently the words 'stair climbing' and 'cannot do everything I do' respectively, to express the limitations of daily activities due to COPD.