The burden of chronic obstructive pulmonary disease in the Middle East and North Africa: Results of the BREATHE study

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Summary
COPD is a progressive pulmonary disease which may have a profound impact on general health status and quality of life. This article presents data on the burden of COPD obtained from the BREATHE study in the Middle East, North Africa and Pakistan. This study was a large general population survey of COPD conducted in eleven countries of the region using a standardised methodology. A total of 62,086 subjects were screened, of whom 2,187 fulfilled the "epidemiological" definition of COPD. Data on symptoms, perceived disease severity, impact on work, limitations in activities and psychological distress were collected. 1,392 subjects were analysable of whom 661 (47.5%) reported experiencing an exacerbation of their respiratory condition, 49.4% reported comorbidities and 5.5% reported

severe breathlessness as measured with the MRC breathlessness questionnaire. The degree of breathlessness, as well as the perceived severity, was correlated with the overall disease impact as measured with the COPD Assessment Test ($p < 0.001$). 374 subjects (28.4%) reported that their respiratory condition prevented them from working and this proportion rose to 47.8% in subjects who perceived their respiratory condition as severe. 47.9% of subjects reported difficulties in normal physical exertion, 37.5% in social activities and 31.7% in family activities. Psychological distress was reported by between 42.3% and 53.2% of subjects, depending on the item. In conclusion, the burden of COPD is important, and covers central aspects of daily life. For this reason, physicians should take time to discuss it with their patients, and ensure that the management strategy proposed addresses all their needs.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of chronic morbidity and mortality worldwide.[1–4] The impact of COPD on health and quality of life is considerable, particularly in patients with severe stages[5,6] (GOLD 2009 stages 3 and 4,[1] or GOLD 2011 groups C and D).[7] It has also been suggested that symptom burden in these is comparable to that of patients with cancer, although patients with COPD tend to live longer.[8]

The *Confronting COPD* international survey,[6] published in 2002, which evaluated the impact of COPD in North America and Europe, showed that COPD carried a significant burden to subjects, society and the economies of these countries. For example, 44% of subjects in the USA with COPD in this survey reported getting breathless when washing or dressing, 51% reported that their symptoms limited their ability to work, 52% felt that they were not in control of their breathing.

In particular, the impact of COPD on work has been investigated in several studies. For example, a study comparing employees with COPD to those without COPD[9] performed in the United States,[9] indicated that the former reported a significantly lower quality of life with worse mental and physical component summary scores and health utilities and a greater decline in productivity, more absenteeism, and more impairment in work and daily activities than those without COPD. In addition, a higher healthcare resource consumption was reported by employed adults with COPD than by those employed without COPD, particularly in those experiencing exacerbations.[9,10]

There are few studies assessing the burden of COPD in developing countries. This lack of information may lead to an underestimation of the real impact of the disease and thus minimise the need for a holistic approach to the management of COPD taking into account the burden of the disease with respect to activities of daily living. We have recently performed the BREATHE study, a large epidemiological survey of subjects reporting COPD-related symptoms in the general populations of eleven countries in the Middle East and North Africa (MENA) region.[11] This study collected data on the subjects' perception of COPD and on the burden of disease in terms of work, daily activities and psychological condition. This information was collected using a similar questionnaire to that used in *Confronting COPD*, which allows the findings to be compared with those of the latter study.

Methods

The BREATHE study was a cross-sectional epidemiological survey of COPD conducted in eleven countries (Algeria, Egypt, Jordan, Lebanon, Morocco, Pakistan, Saudi Arabia, Syria, Tunisia, Turkey and UAE) between June 2010 and December 2011. A detailed description of the methodology used in the study can be found in another article in this supplement.[11] The present article presents the data obtained on the burden of the disease across the region.

Study sample

A general population sample of 10,000 subjects was generated from random telephone numbers of each country or zone of the MENA region. All subjects (men and women) aged ⩾40 years who agreed to participate in the study were included and a structured telephone interview was carried out with all eligible subjects. Subjects not domiciled in the country or zone in question, or those of foreign origin who had been resident in the country for <6 months at the time of the study were excluded from the study, as were subjects with comorbid mental illness.

Data collection

When initial telephone contact with each subject was established, the interviewer explained the goal of the study and the next steps. Subjects who agreed to participate in the study completed a first screening questionnaire which collected data on demographics, respiratory symptoms and smoking habits.[11–13]

Subjects were considered to have symptomatic COPD if they fulfilled the two criteria for the epidemiological definition of COPD used in this study and outlined in the methodology paper.[11] The first criterion was EITHER a diagnosis of COPD, emphysema or chronic bronchitis OR the presence of coughing with phlegm or sputum (productive cough), breathlessness or symptoms consistent with chronic bronchitis. The second criterion was a lifetime smoking exposure of ⩾10 pack·years. Subjects in the COPD population were considered as positively screened and were invited to undergo a second more detailed telephone questionnaire on the disease (detailed COPD questionnaire). This second questionnaire consisted of 77 questions collecting information on risk factors, comorbidities, disease history,

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Box 1.

Which of the following best describes how breathless you get, these days?

Grade 1:   Not troubled by breathlessness except on strenuous exercise

Grade 2:   Short of breath when hurrying on the level or walking up a slight incline

Grade 3:   Walk slower than most people on the level, stop after a mile or so, or stop after 15 minutes walking at own pace

Grade 4:   Stop for breath after walking about 100 yards or after a few minutes on level ground

Grade 5:   Too breathless to leave the house, or breathless when undressing

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Box 2.

Q14.   Does your respiratory condition keep you from working?

Q15.   Are you limited in the kind or amount of work you can do because of your respiratory condition?

Q16.   Have you missed work in the past 12 months due to your respiratory condition?

Q17.   How many work days have you lost in the past 12 months as a result of your respiratory condition?

Q18.   Has your respiratory condition caused any other household member to miss work in the past 12 months?

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clinical symptoms and burden and management of the disease. Many of the items in this questionnaire, and notably those related to burden of disease, were adopted from the *Confronting COPD* study questionnaire.[6]

This detailed COPD questionnaire collected data on the severity of breathlessness using the modified MRC (Medical Research Council) breathlessness scale.[14,15] Subjects were asked to choose which of five statements, proposed in decreasing order of severity, best described their recent condition (Box 1). Each statement was assigned to a grade. Grades 1 and 2 indicated mild breathlessness, Grades 3 and 4 moderate breathlessness and Grade 5 severe breathlessness.[15] Overall symptom severity was also assessed with the COPD Assessment Test (CAT),[16,17] an eight-item patient-reported outcome measure which scores severity on a forty-point ordinal scale (0: no impairment; 40: high impairment). In addition, data on the subject's overall perception of severity of COPD were also collected by asking a single question *'Overall, how severe is your Respiratory Condition now?'* with three proposed responses (mild, moderate or severe).

Information was also collected on disease exacerbations in the previous six months. Since the BREATHE study questionnaire addressed members of the general population in non-medical terms, the number of exacerbations was not explicitly documented and the presence of an exacerbation was thus determined operationally. An exacerbation was taken to have occurred in the previous six months if the subject fulfilled any of the following criteria:

- Criterion 1: In the last 6 months, have you been told by your physician that you have had worsening of your "Respiratory Condition"? – **YES**
- Criterion 2: In the last 6 months, have you been told by your physician that you have had acute bronchitis? – **YES**
- Criterion 3: In the last 6 months, what aspects of your "Respiratory Condition" have worsened? (cough during the daytime, cough during the night, phlegm, breathlessness

or shortness of breath and fatigue, ability to perform regular activities) – **At least two symptoms cited**

On the basis of their CAT score and their exacerbation history (yes or no), subjects were assigned to one of four severity grades according to an adaptation of the 2011 GOLD classification.[7] GOLD group A consisted of subjects with a CAT score < 10 and without exacerbation, GOLD group B concerned subjects with a CAT score ⩾ 10 and without exacerbation, GOLD group C those with a CAT score < 10 and with exacerbation and GOLD group D consisted of subjects with a CAT score ⩾ 10 and with exacerbation.

The impact of COPD on work was assessed using five items (Box 2) in the detailed questionnaire. Question 14 had three response modalities (*Yes*, *No* or *Retired*). Questions 15 and 16 were only asked to subjects who replied '*No*' to Question 14 and had two response modalities (*Yes* and *No*). Question 17 was only asked to subjects who replied '*Yes*' to Question 16. Question 18 was asked to all subjects and had two possible responses (*Yes* and *No*).

The impact of COPD on subjects' activities of daily living and on a number of psychological variables was assessed using two multi-item questions (Box 3) in the detailed COPD questionnaire. The questions related to activities of daily living had four possible response modalities (*a lot*, *some*, *only a little* or *not at all*), which were concatenated into a dichotomous variable (a lot or some *versus* only a little or not at all). The questions related to psychological distress had only two possible response modalities (*Yes* and *No*).

Statistical analysis

Data presentation is principally descriptive, with continuous variables being presented as mean values ±SEM and categorical variables as frequency counts (%). Missing data were not replaced and the relatively few subjects for whom data were missing were excluded from the calculation of frequency rates. The relationship between the MRC

Box 3.

Q22.   Would you agree with each of the following statements?

1.   My cough or breathing is embarrassing in public

2.   I expect my condition to get worse

3.   I panic or get afraid when I cannot get my breath

4.   I feel that I am not in control of my breathing problem

5.   I often worry about having an exacerbation (increase in severity of symptoms) when I am away from home

6.   I have a hard time making plans because I never know how I will be feeling

7.   The health care system could do a lot better job helping people with my condition

Q24.   How much do you feel that your respiratory condition limits what you can do in each of the following areas? Do you feel it restricts you a lot, some, only a little or not at all in

a.   Sports and recreation

b.   Normal physical exertion

c.   Social activities

d.   Sleeping

e.   Housekeeping chores

f.   Sexual intercourse

g.   Famility activities

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breathlessness scores and the CAT scores was assessed using analysis of variance (ANOVA). The relationship between different categorical variables and perceived severity was determined using the χ^2 test and between perceived severity and GOLD severity grade using log-linear analysis.

Variables assessing the impact of COPD on daily activities (variables a to g) and on the psychological status (variables 1 to 7), as well as gender, overall severity, work impact and CAT scores were entered into a Multiple Correspondence Analysis (MCA) in order to identify relationships between the different variables, and the findings displayed as a factorial map. Close proximity between the centres of gravity of two different variables on the factorial map is indicative of a strong association between the variables, and the separation between the centres of gravity of the two response modalities (for example yes and no) of a given variable is indicative of the discriminatory power of the variable.

Results

Study sample

A total of 62,086 subjects completed the screening questionnaire. Of these, 2,187 subjects fulfilled the epidemiological definition of COPD,[11] of whom 1,392 (63.6%) completed the detailed COPD subject questionnaire and constituted the study population. No relevant differences in terms of age, gender and COPD symptoms (productive cough, breathlessness or symptoms consistent with chronic bronchitis) were found when comparing the COPD population who completed the detailed questionnaire with all 2,187 subjects who fulfilled the epidemiological definition of COPD.

The demographic features of the COPD population are presented in Table 1. Three-quarters (75.6%) of the study population were male (from 49.5% male in Lebanon to 96.2% in Algeria). Smoking $\geqslant$10 pack·years was part of the epidemiological definition of COPD, and around two-thirds of subjects were current smokers at the time of the survey (range: 48.5% in Algeria to 82.4% in the UAE). A total of 696 subjects (50.1%) considered themselves to be in good, very good or excellent health.

Symptom presentation

Symptom presentation in participating subjects in the COPD population was documented with respect to onset of exacerbations in the last six months and breathlessness. Exacerbation history was established using the operational definition provided in the Methods section. Overall, nearly half of the study population (n = 661; 47.5% [95% CI: 44.9–50.1%]) reported experiencing an exacerbation of their respiratory condition in the previous six months, ranging from 36.0% [95% CI: 31.0–41.1%] in Turkey to 76.7% [95% CI: 61.5–91.8%] in Pakistan (Fig. 1).

COPD symptoms were evaluated using the MRC breathlessness questionnaire, which was completed by 1,091 subjects (78.3%). The distribution of MRC breathlessness questionnaire grades is presented in Fig. 2. Overall, the most frequently reported grade of breathlessness was "*short of breath when hurrying on the level or walking up a slight incline*" (Grade 2) by around one third of subjects (32.8%; [95% CI: 30.1–35.7%]). Less than six percent of subjects reported the highest breathlessness grade (too breathless to leave the house). A positive association was observed between the MRC breathlessness questionnaire grades and CAT symptom severity scores ($p < 0.001$; $r_s = 0.293$; Fig. 3).

Table 1
Demographics of the study population of each participating country

|	Algeria	Egypt	Jordan	Lebanon	Morocco	Pakistan	Saudi Arabia	Syria	Tunisia	Turkey	UAE	Total
Age group	**105**	**172**	**140**	**111**	**77**	**30**	**216**	**114**	**53**	**347**	**27**	**1,392**
40–49 years	26 (24.8%)	68 (39.5%)	64 (45.7%)	34 (30.6%)	36 (46.8%)	8 (26.7%)	116 (53.7%)	48 (42.1%)	19 (35.8%)	101 (29.1%)	15 (55.6%)	535 (38.4%)
50–59 years	42 (40.0%)	61 (35.5%)	36 (25.7%)	38 (34.2%)	22 (28.6%)	10 (33.3%)	68 (31.5%)	44 (38.6%)	17 (32.1%)	139 (40.1%)	10 (37.0%)	487 (35.0%)
⩾60 years	37 (35.2%)	43 (25.0%)	40 (28.6%)	39 (35.1%)	19 (24.7%)	12 (40.0%)	32 (14.8%)	22 (19.3%)	17 (32.1%)	107 (30.8%)	2 (7.4%)	370 (26.6%)
Gender	**105**	**172**	**140**	**111**	**77**	**30**	**216**	**114**	**53**	**347**	**27**	**1,392**
Male	101 (96.2%)	149 (86.6%)	117 (83.6%)	55 (49.5%)	72 (93.5%)	25 (83.3%)	185 (85.6%)	81 (71.1%)	50 (94.3%)	192 (55.3%)	25 (92.6%)	1,052 (75.6%)
Female	4 (3.8%)	23 (13.4%)	23 (16.4%)	56 (50.5%)	5 (6.5%)	5 (16.7%)	31 (14.4%)	33 (28.9%)	3 (5.7%)	155 (44.7%)	2 (7.4%)	340 (24.4%)
Cigarette smokers	**101**	**111**	**126**	**85**	**77**	**29**	**160**	**83**	**52**	**236**	**17**	**1,077**
Current smokers	49 (48.5%)	69 (62.2%)	84 (66.7%)	61 (71.8%)	47 (61.0%)	20 (69.0%)	86 (53.8%)	65 (78.3%)	42 (80.8%)	158 (66.9%)	14 (82.4%)	695 (64.5%)
Ex-smokers	52 (51.5%)	42 (37.8%)	42 (33.3%)	24 (28.2%)	30 (59.0%)	9 (31.0%)	74 (46.2%)	18 (21.7%)	10 (19.2%)	78 (33.1%)	3 (17.6%)	382 (35.5%)
Comorbidities	**105**	**172**	**140**	**111**	**77**	**30**	**216**	**114**	**53**	**347**	**27**	**1,392**
None	60 (57.1%)	73 (42.4%)	50 (35.7%)	41 (36.9%)	34 (44.2%)	22 (73.3%)	84 (38.9%)	55 (48.2%)	23 (43.4%)	249 (71.8%)	13 (48.1%)	704 (50.6%)
Cardiovascular disease	21 (20.0%)	53 (30.8%)	47 (33.6%)	40 (36.0%)	11 (14.3%)	2 (6.7%)	49 (22.7%)	33 (28.9%)	11 (20.8%)	67 (19.3%)	10 (37.0%)	344 (24.7%)
Diabetes	11 (10.5%)	39 (22.7%)	34 (24.3%)	30 (27.0%)	8 (10.4%)	2 (6.7%)	66 (30.6%)	17 (14.9%)	10 (18.9%)	26 (7.5%)	7 (25.9%)	250 (17.8%)
Asthma	4 (3.8%)	6 (3.5%)	7 (5.0%)	10 (9.0%)	1 (1.3%)	5 (20.8%)	22 (10.2%)	6 (5.3%)	None	36 (10.4%)	2 (7.4%)	99 (7.1%)
Any comorbidity	45 (42.9%)	99 (57.6%)	90 (64.3%)	70 (63.1%)	33 (55.8%)	8 (26.7%)	132 (61.1%)	59 (51.8%)	30 (56.6%)	98 (28.2%)	14 (51.9%)	688 (49.4%)
General health status	**102**	**172**	**140**	**111**	**77**	**30**	**216**	**114**	**52**	**347**	**27**	**1,388**
Excellent	0 (0.0%)	9 (5.2%)	11 (7.9%)	10 (9.0%)	1 (1.3%)	2 (6.7%)	29 (13.4%)	8 (7.0%)	1 (1.9%)	2 (0.6%)	5 (18.5%)	78 (5.6%)
Very good to good	50 (49.0%)	66 (38.4%)	81 (57.9%)	44 (39.6%)	42 (54.5%)	9 (30.0%)	137 (63.4%)	47 (41.2%)	34 (65.4%)	100 (28.8%)	8 (29.6%)	618 (44.5%)
Fair	44 (43.1%)	76 (44.2%)	36 (25.7%)	40 (36.0%)	26 (33.8%)	10 (33.3%)	31 (14.4%)	42 (36.8%)	14 (26.9%)	40 (11.5%)	12 (44.4%)	371 (26.7%)
Poor to very poor	8 (7.8%)	21 (12.2%)	12 (8.6%)	17 (15.3%)	8 (10.4%)	9 (30.0%)	19 (8.8%)	17 (14.9%)	3 (5.8%)	205 (59.1%)	2 (7.4%)	321 (23.1%)
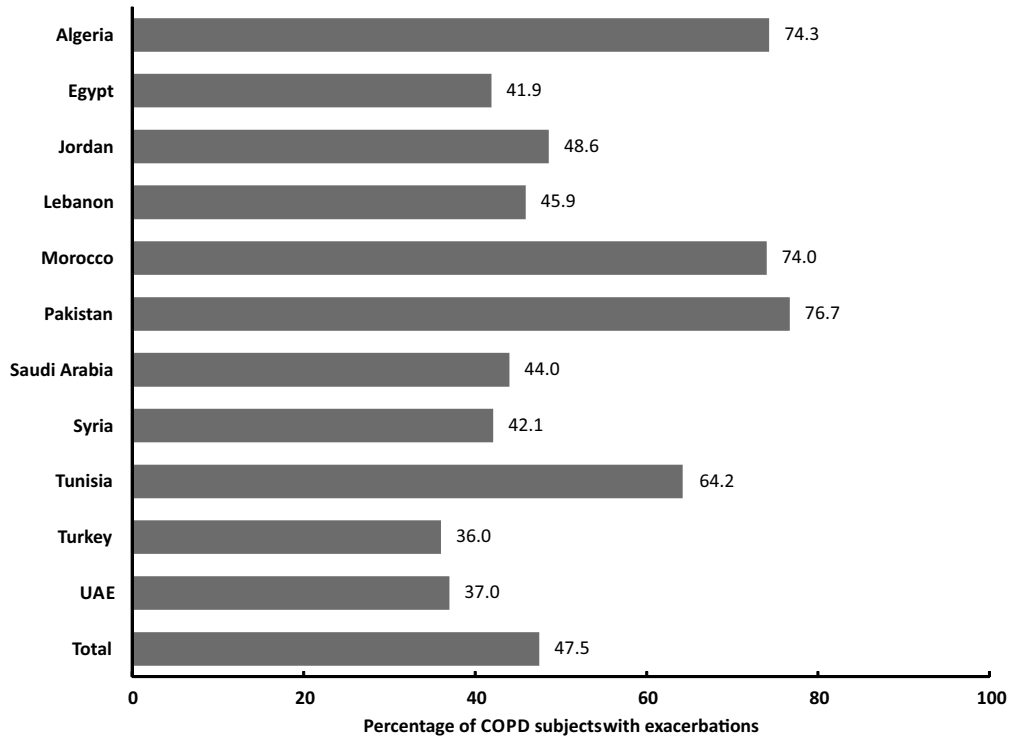
Figure 1. Rate of COPD exacerbations in participating countries of the MENA region. The definition of exacerbation used in our study is described in the Methods section.
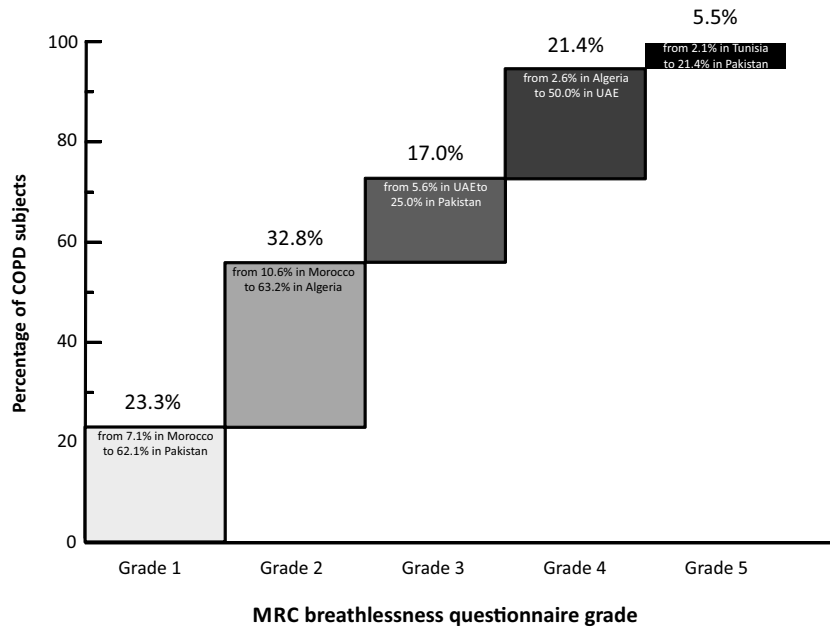

Figure 2. Distribution of MRC breathlessness questionnaire grades. The number of respondents to this questionnaire was 1,091.

Comorbidities

Around half (49.4%) of the study population reported having comorbidities, ranging from 26.7% in Pakistan to 64.3% in Jordan (Table 1). Specific information was collected with respect to cardiovascular comorbidity, diabetes and asthma. The proportion of subjects reporting these comorbidities was 24.7% for cardiovascular disease, 17.8% for diabetes and 7.1% for asthma. The extent of reporting of these comorbidities was quite variable between countries, with the proportion of patients reporting diabetes ranging from 6.7% in Pakistan to 30.6% in Saudi Arabia, and that of asthma from 1.3% in Morocco to 20.8% in Pakistan.
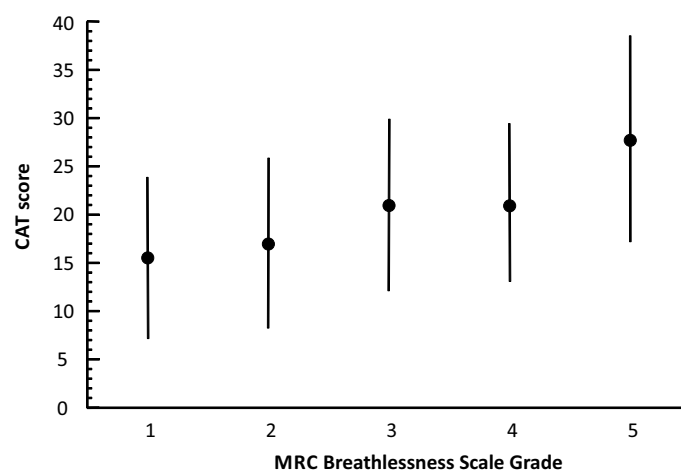
Figure 3. Relationship between scores of the MRC breathlessness scale and scores of the CAT questionnaire. Data are presented as mean CAT scores and standard deviations.
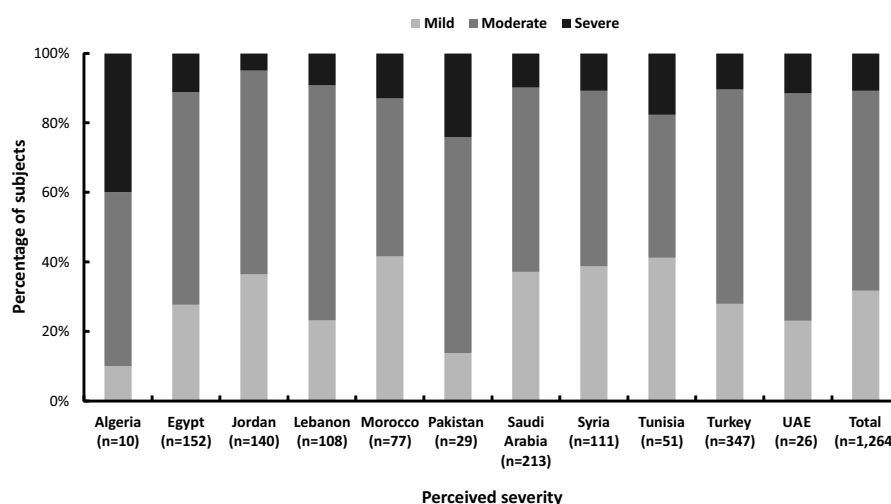
Figure 4. Overall perceived severity of COPD symptoms by country.

Perceived severity of COPD symptoms

Data relating to the perceived severity of COPD (mild, moderate or severe) were collected for 1,264 subjects and are presented by country in Fig. 4. Overall, the majority of subjects considered that their respiratory condition was of moderate severity (57.5%) and around one third (31.7%) considered it to be mild (Fig. 4). The highest proportions of subjects considering their symptoms to be severe were observed in the Maghreb countries and in Pakistan, and the highest proportions of patients considering them mild in Jordan, Morocco, Syria and Tunisia.

Perceived severity was also assessed according to subjects' demographics, CAT score and exacerbations, and is summarised for all countries in Tables 2 and 3. The perception of severity was not associated with age, gender or the existence of comorbidities. However, subjects were more likely to consider their symptoms to be moderate or severe if they recalled having received a diagnosis of COPD ($p < 0.0001$) and if they had experienced exacerbations ($p < 0.0001$). In addition, mean CAT scores increased incrementally with perceived severity ($p < 0.0001$) (Table 2).

Subjects with a higher grade of perceived severity were more likely to have consulted a doctor, been hospitalised or made an emergency room visit because of their respiratory symptoms ($p < 0.0001$) (Table 3).

The relationship between perceived severity and GOLD severity group was also evaluated. A total of 1,014 subjects in the COPD population could be classified into one of four groups (GOLD Group A, B, C and D) according to CAT score and exacerbation history (Table 4). Subjects in the higher-grade GOLD group reported having a more severe condition ($p < 0.0001$) and a poorer general health status ($p < 0.0001$). Overall, the relationship between perceived severity and general health status on the one hand and CAT scores and exacerbation on the other, appeared to be stronger for CAT score than for exacerbations (0.0003 and 0.0238 respectively). Using a log-linear analysis for a 3-way contingency table, a significant association was found between perceived severity on the one hand and both exacerbations and CAT scores on the other ($p < 0.001$ in each case).

Table 2
Perceived severity according to subject characteristics

	Mild (N = 401)	Moderate (N = 727)	Severe (N = 136)	p
Age group				
40–49 years	163 (40.6%)	289 (39.8%)	44 (32.4%)	
50–59 years	142 (35.4%)	243 (33.4%)	53 (39.0%)	0.3774
≥60 years	96 (23.9%)	195 (26.8%)	39 (28.7%)	
Gender				
Men	304 (75.8%)	531 (73.0%)	99 (72.8%)	
Women	97 (24.2%)	196 (27.0%)	37 (27.2%)	0.5702
COPD diagnosis	95 (23.7%)	271 (37.3%)	74 (54.4%)	<0.0001
CAT Score	14.8±8.8	18.6±9.0	25.0±9.1	<0.0001
Exacerbations	157 (39.2%)	340 (46.8%)	94 (69.1%)	<0.0001
Comorbidities	203 (50.6%)	355 (48.8%)	75 (55.1%)	0.3872

Table 3
Healthcare resource utilisation during the previous year according to perceived severity level

	Mild (N = 401)	Moderate (N = 727)	Severe (N = 136)	p
Consultations	243 (60.6%)	456 (62.7%)	106 (77.9%)	0.0001
Hospitalisations	57 (14.2%)	158 (21.7%)	61 (44.8%)	<0.0001
Emergency visits	52 (13.0%)	142 (19.5%)	46 (33.8%)	<0.0001

Table 4
Classification of COPD subjects (n = 1,014) according to symptoms (CAT score) and exacerbation history

Variables	Exacerbation			
	No		Yes	
	CAT score <10 Group A (N = 147)	CAT score ≥10 Group B (N = 233)	CAT score <10 Group C (N = 86)	CAT score ≥10 Group D (N = 548)
Perceived severity [a]				
Mild	67 (52.8%)	78 (33.8%)	28 (32.6%)	125 (24.8%)
Moderate	58 (45.7%)	139 (60.2%)	29 (33.7%)	297 (58.9%)
Severe	2 (1.6%)	14 (6.1%)	3 (3.5%)	82 (16.3%)
General health status				
Poor to very poor	14 (9.5%)	62 (26.6%)	7 (8.1%)	132 (24.1%)
Fair	30 (20.4%)	47 (20.2%)	23 (26.7%)	175 (31.9%)
Good to very good	81 (55.1%)	112 (48.1%)	49 (57.0%)	221 (40.3%)
Excellent	20 (13.6%)	12 (5.2%)	7 (8.1%)	20 (3.6%)
Comorbidities	66 (44.9%)	115 (49.4%)	38 (44.2%)	298 (54.4%)

[a] CAT scores were not documented for 20 subjects of Group A, 2 subjects of Group B, 26 subjects of Group C and 44 subjects of Group D. Percentages are calculated according to each resulting denominator.

Impact of respiratory symptoms

Work

Overall, 374 subjects (28.4%) reported that their respiratory condition prevented them from working, and this proportion rose to 47.8% in subjects who perceived their respiratory condition as severe (Fig. 5). In those subjects who were in full- or part-time employment, 21.5% (n = 125) reported that they were limited in the kind or amount of work that they could do and 17.2% (n = 103) reported having missed work in the previous year due to their respiratory symptoms. The mean number of days lost was 17.7±38.2. The proportion
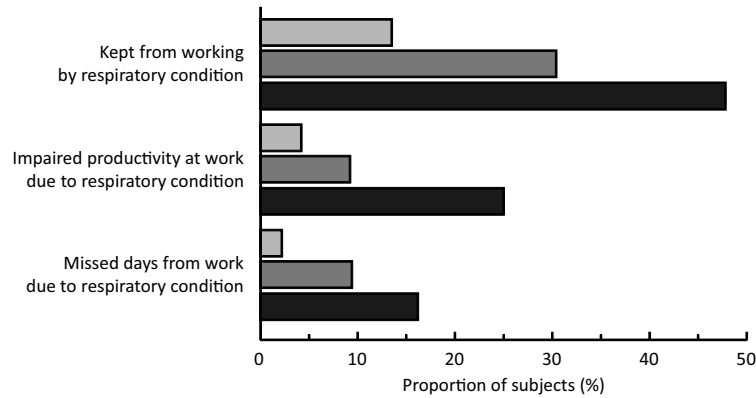
Figure 5. Impact on work activities according to the degree of perceived severity. Open bars: mild disease severity; grey bars: moderate disease severity; black bars: severe disease severity. Data are presented for the 1,264 subjects providing data on perceived disease severity and on impact on work.
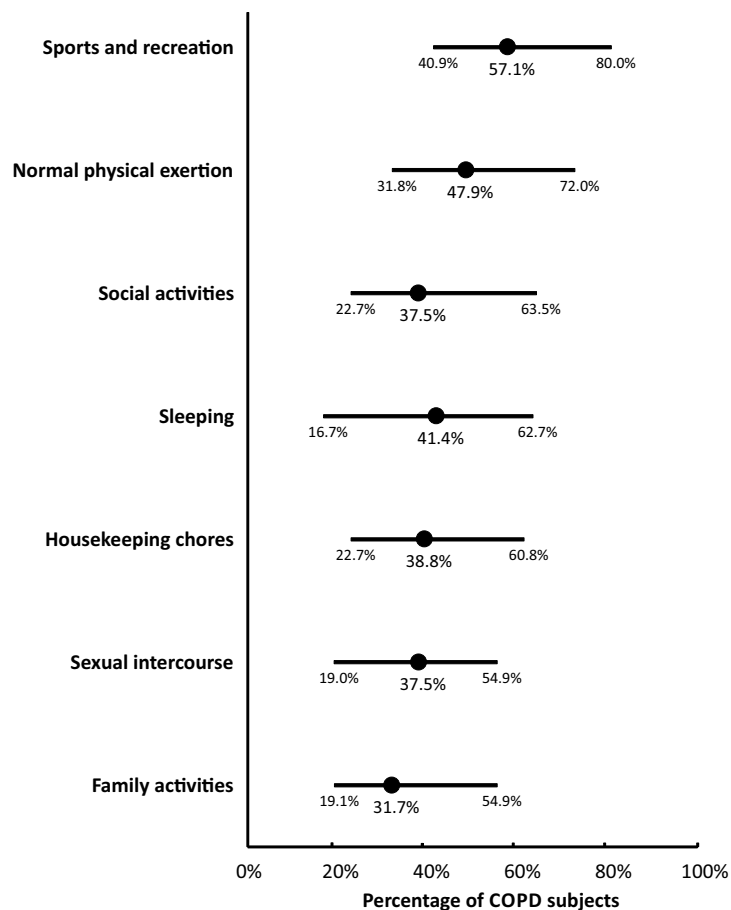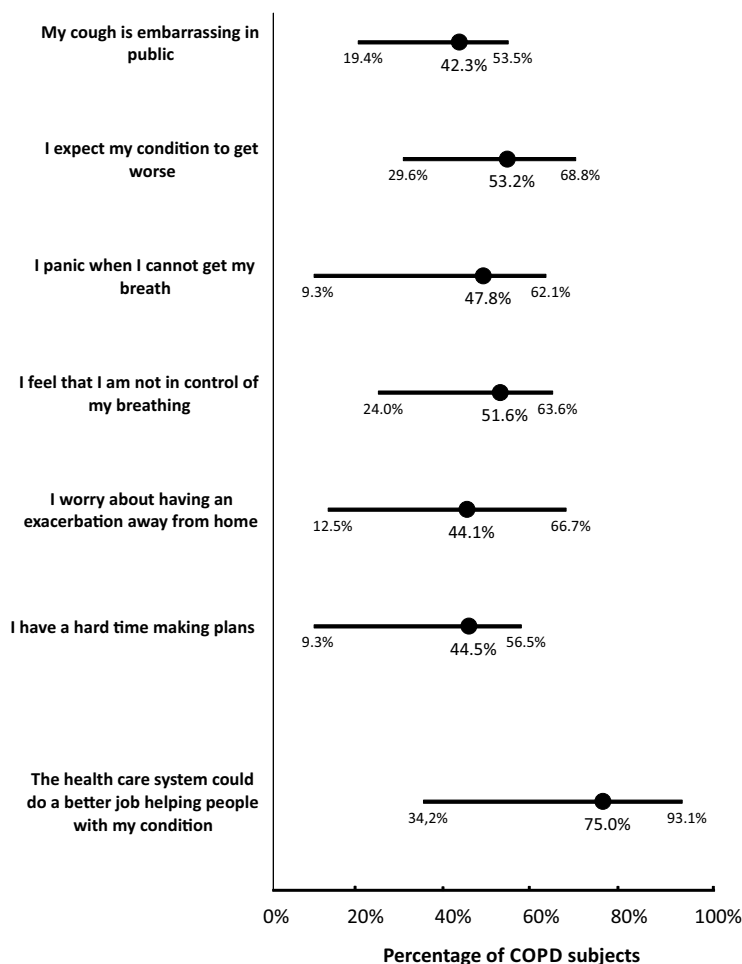

Figure 6. Percentage of COPD subjects reporting 'some' or 'a lot' of limitation with various activities. Data presented are the mean values for all countries combined. The black bars indicate the inter-country range between the countries with the lowest and the highest agreement rates.

of subjects reporting impaired work productivity or days missing work also increased significantly with perceived disease severity ($p < 0.0001$) (Fig. 5). In addition, 102 respondents (8.1%) reported that their respiratory condition had caused another member of their household to miss work at least once in the previous year.

Limitations in activities of daily living

The reported impact of respiratory symptoms on activities of daily living was assessed. Overall, a lot or some limitations were reported for all areas of daily life considered in at least thirty percent of subjects, ranging from 31.7% of subjects limited in their family activities to 57.1% limited in sports activities (Fig. 6). The impact of respiratory symptoms on

Figure 7. Impact of respiratory symptoms on psychological variables. Data presented are the mean values for all countries combined. The black bars indicate the inter-country range between the countries with the lowest and the highest agreement rates.

each area was analysed according to whether the subject reported having received a diagnosis of COPD and according to the presence or absence of comorbidities. These analyses showed that subjects who reported having received a diagnosis of COPD reported limitations in all their daily activities significantly more often than those who did not ($p < 0.0162$). In contrast, no significant association between the presence of comorbidities and limitations in activities of daily living was observed, except for family activities, which were more limited in subjects with comorbidities ($p = 0.0019$).
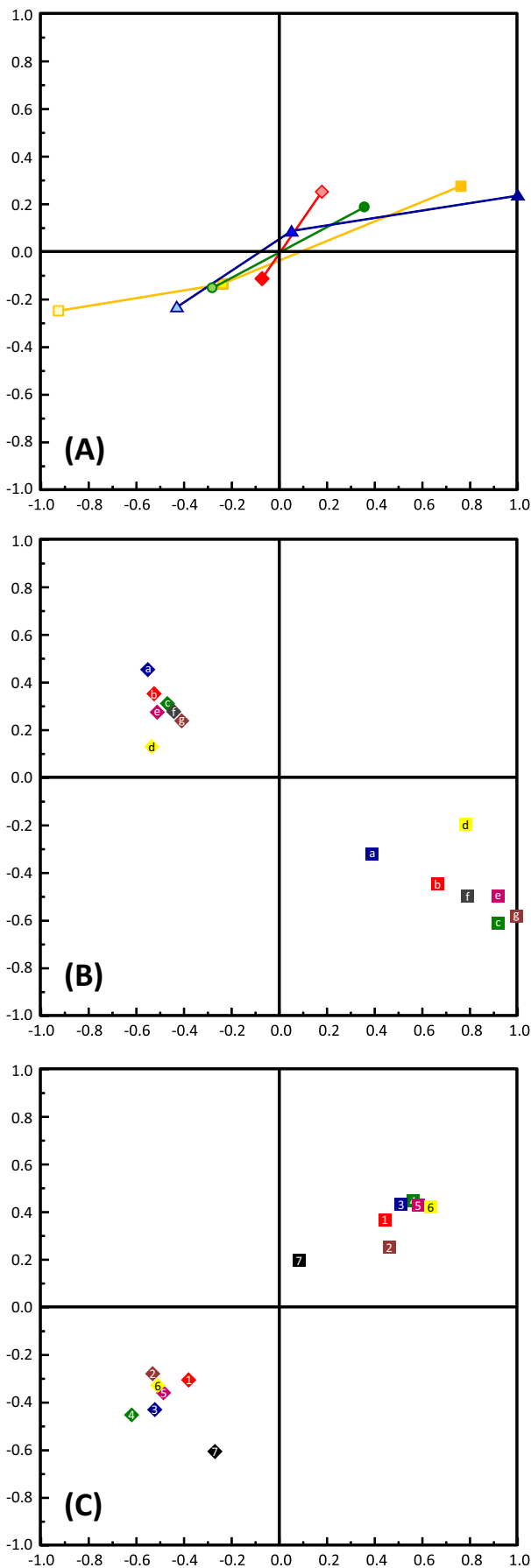
Psychological distress

The impact of symptoms on a number of psychological variables related to anxiety and distress was also evaluated. Impact on all the psychological variables assessed was reported by between forty and eighty percent of subjects (Fig. 7). In addition, three-quarters of subjects considered that the healthcare system could do more for them than it does. Subjects who reported having received a diagnosis of COPD were more likely to report an impact on all psychological well-being items ($p < 0.0026$). In contrast, no significant association was observed between the

presence of comorbidities and psychological impact, with the exception of the items related to anxiety about having an exacerbation outside the house and to embarrassment about cough or breathing in public ($p < 0.005$).

Factors associated with the burden of the disease

In order to identify factors potentially associated with the burden of the disease, a multiple correspondence analysis was performed. Variables assessing the impact of COPD on subjects' daily activities (variables a to g) and those assessing psychological distress (variables 1 to 7), as well as gender, overall severity and CAT scores were entered into the analysis. The results are presented in Fig. 8. Disease severity grades (panel A), whether measured by the CAT or with the perceived severity, were well discriminated by the horizontal axis of the factorial map and were aligned along this dimension. The vertical axis discriminated the severity items less well. Impact upon work was also aligned along the horizontal axis. Female gender was associated with more severe disease. The psychological distress items (panel C) were all aligned with the severity grades, with the presence of psychological distress being associated with more severe disease. The individual psychological distress

Figure 8. Factorial analysis of variables potentially associated with burden of disease. (A) Gender, diamond symbols; men (light), women (dark); perceived severity, squares; mild (light); moderate (medium); severe (dark); CAT score (triangles: <10; (light), 10–20 (medium), ⩾20 (dark); impact on work, circles; no impact (light), impact (dark). (B) Limitations in activities of daily living: a–g correspond to items as defined in Box 2; square symbols: a lot or some limitations; diamond symbols: a little or not at all limited. (C) Psychological distress items: 1–7 correspond to items as defined in Box 2; square symbols: agree with the statement; diamond symbols: disagree with the statement.

items were also closely associated with each other, except for item 7 (the healthcare system could do a lot better job helping people with my condition). The limitations in activities of daily living items (Panel B) were also discriminated by the horizontal (severity) axis with the 'no or few limitations' subgroups on the left-hand (low severity) side of the factorial map. However, the limitations items showed a different relationship with the vertical axis to the severity and psychological distress items, with the 'no or few limitations' subgroups lying in the upper half and the 'some or a lot of limitations' in the lower half of the map. This indicates that something other than severity influences how subjects perceive limitations in their daily activities. All individual limitations items were closely associated with each other.

Discussion

The current study assessed the burden of COPD in a representative sample of the general population of eleven countries of the MENA region in 2011. The analysis was performed in a total of 1,392 subjects fulfilling the epidemiological definition of COPD and focuses on how they perceived the severity of their COPD symptoms and how they estimated the impact of these symptoms on their life. In this large study population, respiratory symptoms significantly interfered with all activities of daily living assessed and thus contribute to a significant burden of disease. These findings are consistent with the results of other studies such as the *Confronting COPD* surveys in North America and Europe[5,6] which used a similar methodology and questionnaire to the BREATHE study (Table 5).

The impact of breathlessness was determined in the BREATHE study using the MRC breathlessness questionnaire. The 2011 GOLD guidelines[7] propose that this scale may be used as an alternative to the CAT for the assessment of symptom severity in order to assign a severity grade and thus identify the most appropriate management strategy, although they consider the CAT to be the preferred option. In this context, it is important that the CAT and the MRC breathlessness questionnaire show substantial coherence. In the BREATHE study sample of individuals in the general population with COPD symptoms, the MRC breathlessness questionnaire grade was shown to be positively associated with the CAT score, which supports the idea that the two measures are coherent. This is also consistent with a large study of patients in primary care with spirometrically

Table 5
Comparison of the burden of COPD in the past year[a] in the MENA region and in the United States[5,20,21]

	BREATHE study MENA region	Confronting COPD USA[5,20,21]
MRC scale	N = 1,091	N = 573
Grade 1	23.3%	15.0%
Grade 2	**32.8%**	25.0%
Grade 3	17.0%	17.0%
Grade 4	21.4%	**32.0%**
Grade 5	5.5%	8.0%
Perceived severity	N = 1,264	N = 573
Mild	31.7%	34.0%
Moderate	**57.5%**	**38.0%**
Severe	10.8%	23.0%
Impact of COPD		
Limitations in work	N = 582–1,315[b]	NA
Keeps from working	**28.4%**	**34.0%**
Limited kind or amount of work	21.5%	17.0%
Workdays lost in past year	17.2%	4.0%
Limitations in daily activities	N = 1,210–1,258[b]	NA
Sport and recreation	**57.1%**	**72.0%**
Normal physical exertion	47.9%	70.0%
Social activities	37.5%	53.0%
Sleeping	41.4%	50.0%
Household chores	38.8%	56.0%
Sexual intercourse	37.5%	37.0%
Family activities	31.7%	46.0%
Psychological distress	N = 1,258–1,280[b]	N = 573
My cough or breathing is embarrassing in public	42.3%	52.0%
I expect my condition to get worse	**53.2%**	**66.0%**
I panic or get afraid when I cannot get my breath	47.8%	58.0%
I feel that I am not in control of my breathing	51.6%	52.0%
I worry about having an exacerbation away from home	44.1%	39.0%
I have a hard time making plans	44.5%	48.0%

NA: not available.
[a] Values in boldface type indicate the most frequently cited responses for each domain.
[b] The number of responder subjects was different for each item: the range is provided.

defined COPD,[18] which reported very similar findings to the present ones regarding the relationship between CAT score and MRC breathlessness questionnaire grade, even though this population was apparently more severe than the BREATHE population. The observation of an association between the CAT score and the different items of the MRC breathlessness scale also supports the notion of a 'ladder of severity' recently proposed by Jones et al.,[19] whereby increasing CAT scores are associated with more and more limitations in activities.

Around half of the COPD population had experienced at least one operationally-defined exacerbation of their COPD

symptoms in the previous six months, and these subjects reported a greater perceived severity of their respiratory condition and a poorer general health status. The proportion of patients with exacerbations identified using this definition is within the range of that reported in other studies in which exacerbations were ascertained by the physician.[18,22] However, the operational definition used has not been previously validated, and it would be useful to compare the performance of this definition against physician-ascertained exacerbations in a future study.

Half of the study population reported having comorbidities. This proportion was similar to that reported in

two large cohorts from the US where 50.1% of COPD subjects reported at least one comorbidity.[23] Cardiovascular comorbidities were reported by 24.7% of subjects and diabetes by 17.8%. Asthma was reported by 7.1% of subjects. These findings are comparable to those reported in many other studies performed in the US and Europe.[20,21,23,24] Nonetheless, it is probable that diabetes is under-reported in the BREATHE population due to incomplete diagnosis, since the proportions of affected subjects are generally lower than prevalence rates for diabetes in subjects over 45 years of age reported in general population studies in countries in the region.[25–31] However, the between-country variability in the proportion of subjects reporting diabetes does reflect known regional variation in the prevalence of diabetes, being highest in peninsular Arabia and lower in Pakistan, Turkey and North Africa.[32] There is little published data on the prevalence of asthma in the adult general population in countries of the region. The proportion of subjects in the BREATHE study reporting asthma was lower than adult prevalence estimates in Morocco and Tunisia,[33] again perhaps reflecting under-diagnosis, but similar in Algeria.[33] For Turkey, on the other hand, the proportion of subjects with COPD reporting comorbid asthma (10.4%) is higher than that reported in a recent general population survey,[34] and this may potentially be explained by individuals with COPD believing that their symptoms are due to asthma.

Overall, the percentage of subjects in the BREATHE study reporting their symptoms to be of mild severity was comparable with that observed in the *Confronting COPD*[5,6] study (31.7% *versus* 31.8%), although the proportion of subjects reporting severe symptoms was lower in the BREATHE study (10.4%) compared to the *Confronting COPD* study (21.0%).[5] These differences might be explained by lower health expectations in the MENA region compared to North America. This would be supported by the observation that half of the BREATHE study population considered themselves to be in excellent, very good or good health, even though when asked about individual activities of daily living, it was clear that the impact of their respiratory condition on their lives was substantial, and equivalent to that observed in the USA population of the *Confronting COPD* study.[5,20,23] Subjects with a higher grade of perceived severity were more likely to have consulted a doctor, been hospitalised or made an emergency room visit because of their respiratory symptoms (p < 0.0001).

An association was observed between, on the one hand, the severity of the respiratory condition perceived by the patient and, on the other, the CAT score and the occurrence of exacerbations. Nonetheless, in the BREATHE study as well as in the *Confronting COPD* study,[5,35,36] a considerable disparity was observed between the degree of severity of respiratory symptoms determined using the CAT or the MRC scale and the subjective overall perception of its severity reported by the subject. For example, in the BREATHE study, 26.9% of subjects scored 4 or 5 on the MRC breathlessness scale, consistent with severe COPD, whereas only 5.9% perceived their symptoms to be severe. This underestimation of perceived severity was also apparent in *Confronting COPD*, in which 40% of subjects scored 4 or 5 on

the MRC breathlessness scale but only 23% of them perceived their symptoms to be severe. Another international study including Turkey, the *COPD Uncovered* study,[10] found that 37.0% of interviewees fulfilled criteria for severe COPD using the MRC breathlessness scale (Grade 4 or 5).

The perceived severity of COPD was not associated with age or gender. This suggests that the symptoms of COPD did not systematically worsen in elderly male subjects, challenging the stereotypic image of the COPD patient as an elderly male smoker. Nonetheless, since over eighty percent of subjects in the BREATHE study considered that their respiratory condition would inevitably get worse with time, regardless of how it was managed,[37] this lack of association between perceived severity and age may also reflect adjustments in expectations about what can be considered 'normal' respiratory health with ageing. Moreover, and somewhat surprisingly, the presence of comorbidities did not influence the grade of perceived severity. This result differed from the one reported in the *COPD Uncovered*[10] study where it was shown that subjects with mild COPD reported less comorbidity than those with more severe COPD.

The results of the BREATHE study indicate that COPD has a substantial impact on work given that overall 28.4% of subjects reported that their respiratory condition kept them from working altogether. This percentage was consistent with the findings of the *COPD Uncovered* study[10] which reported a rate of 26.0% and somewhat lower than that described in the *Confronting COPD* survey in the United States which reported a rate of 34.0%[5,35,36] and in the *COPD-Life* study[38] in Turkey (45.3%, compared to 33.4% of the Turkish subjects of the BREATHE study). However, it should be noted that the economic consequences of stopping work completely or of absenteeism in the region may be a stronger disincentive than in the USA or Europe, where social security protection is greater. Of those in work, around one quarter were obliged to stop working for a mean number of 17.8±38.2 days in the last year. Not surprisingly, the proportion of subjects kept from working or who reported an impact of their respiratory condition on their work was higher in subjects with a higher disease severity. This is consistent with findings reported in the literature, such as in the *COPD Uncovered* study.[10]

The impact of symptoms on the daily activities and on a number of psychological variables related to anxiety and distress was also evaluated. Impact on all variables assessed was reported by between thirty and sixty percent of subjects, which is consistent with the results of the *Confronting COPD* survey in the United States.[5,35,36] Factorial analysis of the data suggested that limitations in activities of daily living may represent a supplementary dimension of burden of disease to severity. Psychological distress, on the other hand, appeared to be closely related to severity.

In conclusion, the burden of disease perceived by subjects fulfilling the epidemiological definition of COPD was important, and covered all aspects of daily life considered in the survey. This burden may be underestimated in everyday clinical practice due to the tendency of individuals to report the perceived severity of their respiratory condition as less

than it really is. For this reason, physicians should take time to discuss the burden of respiratory symptoms on the daily lives of their patients, and ensure that the management strategy proposed addresses all the needs of the patient.

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