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IMPACT OF CHRONIC AIRFLOW OBSTRUCTION IN A WORKING POPULATION

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ABSTRACT (199 words)

Data on the individual and collective impact of chronic airflow obstruction at a population level are scarce. In a nationwide survey, dyspnea, quality of life, and missed working days were compared between subjects with and without spirometry-diagnosed chronic airflow obstruction.

Subjects aged 45 years or more were recruited in French health prevention centres (n=5008). Results of pre-bronchodilator spirometry and questionnaires (European Community Respiratory Health Survey-derived and EuroQOL-5D questionnaires) were collected. Adequate datasets were available in 4764 subjects aged 60 ± 10 years (only 2% were 80 years old or more).

Prevalence of airflow obstruction ($FEV_1/FVC<0.70$) was 7.5%. The vast majority (93.9%) of cases had not been diagnosed previously. Health status was significantly influenced by dyspnoea. Both were associated with the number of missed working days. Despite mild-to-moderate severity, subjects with chronic airflow obstruction had more dyspnea, poorer quality of life and higher numbers of missed working days (mean values: 6.71 days *vs* 1.45 days per patient per year in patients without airflow obstruction, p=0.0015, for the population with no known heart or lung disease).

In conclusion, even mild-to-moderate airflow obstruction is associated with an impaired health status, which represents an additional argument in favour of early detection in COPD.

KEY WORDS: COPD, prevalence, dyspnoea, work loss, quality of life

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of mortality, handicap and health care costs worldwide [1, 2]. Prevalence is high, ranging from 4% to 10% [3], but the disease remains largely under-diagnosed [4, 5][6]. This may relate to the relatively late occurrence and underestimation of symptoms [7], which correlate poorly with lung function [8].

COPD alters quality of life, mainly through dyspnea and exacerbations, and is associated with several extra-respiratory manifestations [9, 10]. Ultimately, it leads to respiratory failure and premature death. Based on these assumptions, guidelines advocate the need for early detection of the disease, to (i) motivate patients towards smoking cessation [11] and (ii) allow the use of treatments that can reduce the impact of COPD on symptoms, activities, quality of life and healthcare costs [1, 2, 12, 13]. However, this impact has been seldom evaluated at the general population level: in most cases, subjects recruited in quality of life studies were patients with known COPD, which excludes the most prevalent fraction of the diseased population, *i.e.*, the less severe and undiagnosed cases. Thus, it is difficult to estimate the global consequences of the disease on health status in the population, and the possible effect of early detection at this level.

The present analysis was designed to assess the impact of chronic airflow obstruction on dyspnea, quality of life (measured with a generic questionnaire) and missed working days in a population sample, which was constituted with the primary objective of determining the prevalence of chronic airflow obstruction [14].

MATERIAL AND METHODS

Study design

Subjects were recruited in 31 health prevention centres which are accessible to all workers. The sample was built according to national statistics on age and sex distribution in the general population of the considered age range (subjects aged 40 years and more). Subjects filled a standardized auto-questionnaire and a technician who was not aware of answers to the questionnaire measured FEV_1 and FVC. All subjects received an information note before their participation.

Questionnaire and spirometry

Data obtained from each individual included usual demographic and anthropometrical description, information on risk factors, clinical symptoms, associated chronic diseases and presumptive diagnosis, and previous assessment of lung function.

The questionnaire was derived from the European Community Respiratory Health Survey (ECRHS) questionnaire [15]. Details on its content have already been published. Dyspnoea was measured using the 0-4 modified MRC scale and quality of life was assessed using a generic 5-dimension questionnaire, EuroQOL 5D [16]. Declared missed working days during the previous year were recorded.

Spirometry was performed pre-bronchodilator by trained technicians using daily-calibrated spirometers. Three measures were performed, the best technically adequate being chosen for analysis. Subjects were excluded from the analyses when only one spirometric measurement was adequate or when the variation between the two highest FEV_1 values exceeded 200 ml. Predicted values were calculated using ERS equations [17, 18]. Airflow obstruction was defined by a FEV_1/FVC ratio <0.70.

Statistical analysis

The study was powered to assess the prevalence of chronic airflow obstruction in the population. Considering the expected prevalence of airflow obstruction at about 5%, an allowed risk of error of 0.5% of this percentage, and a possible analysis on 2 strata, 4500 individuals had to be recruited for the survey.

Analysis were performed using SAS software (SAS Institute, Cary, NC, USA). Results are expressed as percentages or means $\pm$ one standard deviation.

Based on questionnaire data, analyses were performed in three populations: the whole population, non asthmatics and subjects with no declared respiratory or cardiac disease.

In each of these populations, percentages have been compared by two-way and multiway frequency analysis, and means by analysis of variance and t-tests. Relations between continuous variables were assessed using linear regression. A difference was considered significant if $p<0.05$. Bonferroni corrections were performed for multiple comparisons.

Finally, multivariate logistic regression analyses were performed to identify independent predictors of quality of life and work loss. For these analysis, dependent variables were (i) scores of each EQ-5D domain and (ii) presence or absence of at least one missed working day, respectively. This last analysis was restricted to the active fraction of the population, *i.e.* subjects aged<65 years.

RESULTS

Characteristics of the studied population (table 1)

A total of 5008 subjects were included in the survey during an 8-month recruitment period; this corresponded to a 93.5% response rate among subjects initially asked to participate. Adequate questionnaire and spirometry data were available in 4764 subjects (95.1%). Mean age was 60 years; 81% of subjects were less than 70 years of age and only 2% were more than 80 years old. Already known chronic respiratory diseases were reported by 9.1% of subjects for asthma, 2.6% for COPD and 5.8% for chronic bronchitis. Questions on symptoms found that chronic bronchitis was actually present in 3.9% of subjects. Prevalence of chronic airflow obstruction in non-asthmatics was 7.5%. In the majority of these patients ($FEV_1 \geq 80\%$ predicted: 59%), the severity of airflow obstruction was mild and chronic bronchitis was absent. Severity of airflow obstruction was moderate (FEV_1 [50-80]% predicted) in 36.1%, severe or very severe ($FEV_1 < 50\%$ predicted) in 4.8%. Among non-asthmatic subjects in whom airflow obstruction was found, only 6.1% had been previously diagnosed as having a chronic respiratory disease.

Impact of chronic airflow obstruction: dyspnoea, quality of life

In the whole population and in subjects with no known heart or lung disease, dyspnoea grade correlated significantly ($p<0.0001$) but weakly ($r=0.28$) with EQ-5D visual analogic scale score. There were also significant relationships between dyspnoea grade and EQ-5D sub-scores (mobility, activity, anxiety, autonomy and pain: all, $p<0.001$; data in the whole population are shown in table 2).

Altogether, 7.2% of subjects with dyspnoea grade 0 had airflow obstruction versus 10.7% of those with dyspnoea grade ≥ 1, 14.8% of those with dyspnoea grade ≥ 2

and 21.8% of those with dyspnoea grade = 4.

In subjects without known chronic respiratory or heart disease, but who were diagnosed as actually having airflow obstruction during the examination, severity of dyspnea increased with that of airflow obstruction (figure 1).

In the whole population, patients who declared having asthma, COPD or chronic heart failure had lower aggregated EQ-5D scores than controls, all domains of the questionnaire being affected (data not shown). In patients with no chronic respiratory or cardiac disease, scores on EQ-5D visual analogic scale decreased with FEV_1 % pred (mean score 70.5 $\pm$ 14.8 vs 72.8 $\pm$ 14.8 in subjects with versus without aiflow obstruction, p=0.004) while, in all EQ-5D domains, airflow obstruction was associated with lower proportions of patients declaring no limitation than in subjects with no airflow obstruction : 87% versus 93% for mobility, 97% versus 99% for autonomy; 90% versus 93% for activity, 38% versus 46% for pain and 49% versus 55% for anxiety (all, $p<0.05$). Multivariate analysis showed that age and FEV_1 were independent predictors of all EQ-5D domains except anxiety, which was mainly influenced by gender (table 3).

Missed working days

The number of missed working days was significantly associated with (i) health status, as measured by EQ-5D visual analogic scale and all EQ-5D domains except autonomy and (ii) dyspnoea grade (data not shown; $p<0.01$ for all analysis).

On average, most subjects reported no missed working day during the year preceding the examination (figure 2). However, in all groups (whole population, non-asthmatics, subjects with no declared respiratory or cardiac disease) a decreased FEV_1/FVC ratio was associated with an increase in missed working days (subjects with no respiratory or heart disease: 6.71 ± 39.09 *vs* 1.45 ± 14.33; p=0.0015). In the

whole population and in non-asthmatics, number of missed working days was higher in subjects reporting symptoms of chronic bronchitis than in other subjects (5.56 ± 15.45 *vs* 1.75 ± 16.54, p=0.05) and patients with a FEV_1 between 50% and 80% predicted missed more working days than those with a $FEV_1 \geq 100\%$ predicted (4.62 ± 32.80 *vs* 1.54 ± 13.90; p=0.04). These differences were not significant in non-asthmatics declaring no co-morbid respiratory or cardiac disease. Other differences between FEV_1 categories were also not significant. In multivariate analysis, chronic bronchitis was the only independent predictor of missed working days (p<0.0001, OR: 95% CI:)(table 3), and interacted strongly with airglow obstruction (test for interaction: p<0.001).

DISCUSSION

In this sample of 4764 subjects visiting health prevention centres, airflow obstruction was present in 7.5% of non-asthmatics and was of mild-to-moderate severity in the vast majority of cases. In these subjects, exertional dyspnea was more frequent, quality of life assessed by the EuroQOL-5D generic questionnaire was poorer and the number of missed working days was greater than in other subjects. The vast majority (93.9%) of subjects with airflow obstruction were not previously known as suffering from any kind of chronic respiratory disease.

Limitations and strengths of the study

To our knowledge, this is one of the largest spirometry-based population study assessing the impact of chronic airflow obstruction, using a validated quality of life questionnaire.

Airflow obstruction was defined according to pre-bronchodilator spirometry, which is not in accordance with current guidelines. However, this was inevitable since French health prevention centres are not allowed to deliver any kind of medication. In addition, the use of pre-bronchodilator values is in line with several recent epidemiological studies such as those by De Marco et al. [15, 19]. In their most recent paper, these authors conclude that the use of pre-bronchodilator values exposes to a risk of overestimating the prevalence of COPD. They also show that this risk is minimized by exclusion of asthmatic subjects. For this reason, all analysis were performed in the whole population, in non asthmatics only and in subjects with no known heart or respiratory disease. Regarding FEV_1/FVC ratio, the use of the fixed 0.70 cut off rather than lower limit of normal to diagnose airflow obstruction may overestimate the prevalence of the disease in the elderly (and underestimate it in

younger adults, but these were not part of our study population). However, for practical reasons the fixed cut off is the recommended way of diagnosing chronic airflow obstruction in current guidelines. In addition, elderly subjects and those < 40 years represented a small part of our population, which limits the overall risk of error.

The mode of recruitment was certainly a source of bias: since (i) the main purpose of health examination centres is prevention and (ii) visits to these centres are offered mainly to the working population, subjects of the studied population are less likely to exhibit symptoms or be known as having any disease than the general population ("healthy worker effect"). Accordingly, the proportion of patients with a known diagnosis of COPD (6.1%) was lower than in other studies [4, 5, 20]. Thus, the prevalence and impact of chronic airflow obstruction may be underestimated, which may help explaining the low number of subjects with FEV_1<50% predicted and the low proportion of subjects with airflow obstruction who reported symptoms of chronic bronchitis, severe dyspnea or a previously known diagnosis of respiratory disease. In addition, the results presented here can not be extrapolated to the non working population. Despite these considerations, overall prevalence data were very similar to that of other studies in developed countries regarding both asthma, chronic bronchitis and airflow obstruction [4, 5, 21-23].

Another limitation is the declarative nature of data on work loss. We have no way to assess how this may have affected the results. We can only assume that, since missed working days are important events in the life of workers, they are likely to be remembered accurately enough and not significantly overestimated.

Impact of airflow obstruction

Despite mild severity, patients with chronic airflow obstruction had poorer quality of life and increased dyspnoea and number of missed working days. This observation

remained true even in patients with no known heart or lung illness.

Dyspnea

In our patients, quality of life impairment was influenced by dyspnea, although this symptom was much less severe than in patients with possible COPD identified in the Confronting COPD survey [6]: for instance, among persistent smokers with GOLD stage >1 airflow obstruction (in whom dyspnea was the most prevalent), only 8.3% reported dyspnea grade of 3 or more, whereas the corresponding figure in the Confronting COPD survey was 42.6%. Thus, even mild levels of dyspnea can be associated with impaired quality of life.

Quality of life

In subjects with chronic airflow obstruction identified in the general population, a diagnosis of COPD is more likely when quality of life is more impaired [24]. In addition, lung function is an independent predictor of all EQ-5D domains except anxiety. However, despite the under-representation of severe cases and marked underdiagnosis of COPD in our study, quality of life was impaired by airflow obstruction. In the United States, the National Health and Nutrition Examination Survey also showed that undiagnosed airflow obstruction in the general population is associated with impaired health and functional status. In that study, health status was not assessed using a dedicated questionnaire but with questions about general health status, walking 1/4 mile, lifting or carrying something as heavy as 10 lb, or needing help with personal care [25]. In the Confronting COPD Survey [6], patients with airflow obstruction also reported activity restrictions related to their respiratory condition: depending on the considered item, 30% to 70% of subjects with or at-risk of COPD reported limitations in sports and recreation, physical exertion, social life,

sleep, household chores and sex life. In line with these findings, data from the Spanish EPIDEPOC study found a significant impairment in quality of life measured with the SF-12 questionnaire in stable COPD subjects followed in primary care, even in mild disease stages [26].

Impact on work

COPD is not only a disease of the elderly: its prevalence in subjects aged 65 years or less is not neglectable and has a noticeable impact on resource utilization and health-care costs [27]. In these subjects, ability to work is an important determinant of life satisfaction [28]. In the Confronting COPD survey, 35.7% of patients reported that "their condition prevented them from working, limited their ability to work or had caused them working time loss in the past year". This percentage increased to 45.3% in subjects aged less than 65 years, who were less likely to be part of the 54.8% of the population who were retired [7]. The proportion of retired subjects was much lower in our population (1.3%), which is related to the mode of recruitment: health examination centres target only working subjects. The much lower proportion of subjects reporting work loss in our population is probably related to several factors: slightly younger age (60 years *versus* 63 years in the Confronting COPD survey), different mode of recruitment (systematic prevention visits by subjects who presume they are healthy *versus* general population) and studied variable: we used only the number of missed working days to assess disease consequences on work, while Rennard et al. also included reported "limitations in the ability to work" in their assessment; this introduces a possibly more subjective component, the contribution of which is difficult to assess. Finally, we have no way to determine if airflow obstruction was less severe in our population than in the Confronting COPD survey, since lung function was not assessed in that study.

In the National Health and Nutrition Examination Survey (NHANES) III, even patients with spirometry-graded mild COPD were less likely to be in the labor force than controls: more precisely, mild, moderate, and severe COPD was associated with a 3.4%, 3.9%, and 14.4% reduction in the labor force participation rate relative to those without COPD [29].

Finally, multivariate analysis did not identify lung function as an independent predictor of missed working days while chronic bronchitis was. Thus when the COPD fraction of a population has mostly mild or mild-to-moderate disease, work loss seems to relate more to chronic bronchitis than to airflow obstruction. However, this result has to be taken with some caution since the power of the analysis was relatively low, due to the small number of subjects reporting any missed working day (n=69) among the population restricted to those aged<65 years with no cardiac or respiratory comorbid illness (n=1310). This also prevented us from performing reliable multivariate analysis with the number of missed working days divided in sub-categories.

In conclusion, this study in a large sample from health prevention centres found a significant impact of mild-to-moderate airflow obstruction on dyspnea, quality of life and missed working days despite a very low proportion of subjects who spontaneously reported symptoms or a known respiratory disease. Such findings suggest that systematic screening for COPD may be justified in the general population since identified cases suffer from a significant although underestimated impact of the disease, which might be limited by early implementation of preventive and therapeutic measures.

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References

1. Celli BR, Macnee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. *Eur Respir J*. 2004;23:932-46
.
2. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. *Am J Respir Crit Care Med*. 2001;163:1256-76.

3. Halbert RJ, Isonaka S, George D, Iqbal A. Interpreting COPD prevalence estimates: what is the true burden of disease? *Chest*. 2003;123:1684-92.

4. Mannino DM, Gagnon RC, Petty TL, Lydick E. Obstructive lung disease and low lung function in adults in the United States: data from the National Health and Nutrition Examination Survey, 1988-1994. *Arch Intern Med*. 2000;160:1683-89.

5. Pena VS, Miravitlles M, Gabriel R, Jimenez-Ruiz CA, Villasante C, Masa JF, Viejo JL, Fernandez-Fau L. Geographic variations in prevalence and underdiagnosis of COPD: results of the IBERPOC multicentre epidemiological study. *Chest 2000 Oct ;118 (4):981 -9*.118:981-89.

6. Halbert R, Natoli J, Gano A, Tinkelman D. Prevalence of undiagnosed COPD: systematic review and meta-analysis. *Eur Respir J*. 2007;30:34s.

7. Rennard S, Decramer M, Calverley PM, Pride NB, Soriano JB, Vermeire PA, Vestbo J. Impact of COPD in North America and Europe in 2000: subjects' perspective of Confronting COPD International Survey. *Eur Respir J*. 2002;20:799-805.

8. Mahler DA, Harver A. A factor analysis of dyspnea ratings, respiratory muscle strength, and lung function in patients with chronic obstructive pulmonary disease. *Am Rev Respir Dis*. 1992;145:467-70.

9. Jones PW, Kaplan RM. Methodological issues in evaluating measures of health as outcomes for COPD. *Eur Respir J Suppl*. 2003;41:13s-8s.

10. Jones PW, Agusti AG. Outcomes and markers in the assessment of chronic obstructive pulmonary disease. *Eur Respir J*. 2006;27:822-32.

11. Gorecka D, Bednarek M, Nowinski A, Puscinska E, Goljan-Geremek A, Zielinski J. Diagnosis of airflow limitation combined with smoking cessation advice increases stop-smoking rate. *Chest*. 2003;123:1916-23.

12. Société de Pneumologie de Langue Française. Recommandations pour la prise en charge de la bronchopneumopathie chronique obstructive. *Rev Mal Respir*. 2003;20:294-329.

13. Halpin D. NICE guidance for COPD. *Thorax*. 2004;59:181-82.

14. Roche N, Dalmay F, Perez T, Kuntz C, Vergnenegre A, Preux PM, Neukirch F, Giordanella J-P, Huchon G. Variation in the prevalence of chronic airflow obstruction with the definition used. *Proc Am Thorac Soc*. 2006;3:A616.

15. de Marco R, Accordini S, Cerveri I, Corsico A, Sunyer J, Neukirch F, Kunzli N, Leynaert B, Janson C, Gislason T, Vermeire P, Svanes C, Anto JM, Burney P. An international survey of chronic obstructive pulmonary disease in young adults according to GOLD stages. *Thorax*. 2004;59:120-125.

16. Rutten-van Molken MP, Oostenbrink JB, Tashkin DP, Burkhart D, Monz BU. Does quality of life of COPD patients as measured by the generic EuroQol five-dimension questionnaire differentiate between COPD severity stages? *Chest*. 2006;130:1117-28.

17. 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 Suppl*. 1993;16:5-40:5-40.

18. Quanjer PH, Lebowitz MD, Gregg I, Miller MR, Pedersen OF. Peak expiratory flow: conclusions and recommendations of a Working Party of the European Respiratory Society. *Eur Respir J Suppl*. 1997;24:2S-8S:2S-8S.

19. de Marco R, Accordini S, Cerveri I, Corsico A, Anto JM, Kunzli N, Janson C, Sunyer J, Jarvis D, Chinn S, Vermeire P, Svanes C, Ackermann-Liebrich U, Gislason T, Heinrich J, Leynaert B, Neukirch F, Schouten JP, Wjst M, Burney P. Incidence of chronic obstructive pulmonary disease in a cohort of young adults according to the presence of chronic cough and phlegm. *Am J Respir Crit Care Med*. 2007;175:32-39.

20. Wouters EF. Economic analysis of the Confronting COPD survey: an overview of results. *Respir Med*. 2003;97 Suppl C:S3-14.

21. Viegi G, Pedreschi M, Pistelli F, Di Pede F, Baldacci S, Carrozzi L, Giuntini C. Prevalence of airways obstruction in a general population: European Respiratory Society vs American Thoracic Society definition. *Chest*. 2000;117:339S-45S.

22. Zielinski J, Bednarek M. Early detection of COPD in a high-risk population using spirometric screening. *Chest*. 2001;119:731-36.

23. Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J*. 2006;28:523-32.

24. Miravitlles M, Ferrer M, Pont A, Luis VJ, Fernando MJ, Gabriel R, Jimenez-Ruiz CA, Villasante C, Fernandez-Fau L, Sobradillo V. Characteristics of a population of COPD patients identified from a population-based study. Focus on previous diagnosis and never smokers. *Respir Med*. 2005;99:985-95.

25. Coultas DB, Mapel D, Gagnon R, Lydick E. The health impact of undiagnosed airflow obstruction in a national sample of United States adults. *Am J Respir Crit Care Med*. 2001;164:372-77.

26. Carrasco GP, de Miguel DJ, Rejas GJ, Centeno AM, Gobartt VE, Gil dM, Garcia CM, Jimenez GR. Negative impact of chronic obstructive pulmonary disease on the health-related quality of life of patients. Results of the EPIDEPOC study. *Health Qual Life Outcomes*. 2006;4:31.

27. Tinkelman DG, George D, Halbert RJ. Chronic obstructive pulmonary disease in patients under age 65: utilization and costs from a managed care sample. *J Occup Environ Med*. 2005;47:1125-30.

28. Sturesson M, Inga-Britt B. Life satisfaction in subjects with chronic obstructive pulmonary disease. *Work*. 2000;14:77-82.

29. Sin DD, Stafinski T, Ng YC, Bell NR, Jacobs P. The impact of chronic obstructive pulmonary disease on work loss in the United States. *Am J Respir Crit Care Med*. 2002;165:704-7.

Table 1: description of the studied population

	N (%) unless otherwise indicated		
	All	**Women**	**Men**
Sex ratio M/F	0.92 (2290/2474)	-	-
Age (years)	59.9 ± 10.1	60.4 ± 10.3	59.3 ± 9.9
Socioeconomic status			
Manual workers	3208 (67.3 %)	1718 (69.4 %)	1490 (65.1 %)
Managers	1493 (31.3 %)	700 (28.3 %)	793 (34.6 %)
Nonworking population (retired, others)	63 (1.3 %)	56 (2.3 %)	7 (0.3 %)
Habitat			
rural	1327 (28.0 %)	661 (26.9 %)	666 (29.2 %)
town < 50,000 inhabitants	1451 (30.6 %)	738 (30.0 %)	713 (31.3 %)
town > 50,000 inhabitants	1960 (41.4 %)	1059 (43.1 %)	901 (39.5 %)
Known Diagnosis			
COPD	123 (2.6 %)	63 (2.6 %)	60 (2.6 %)
Chronic bronchitis	275 (5.8 %)	145 (5.9 %)	130 (5.7 %)
Co-morbid illness			
Asthma	429 (9.1 %)	236 (9.5 %)	193 (8.4 %)
Bronchiectasis	54 (1.1 %)	30 (1.2 %)	24 (1.1 %)
Heart failure	119 (2.5 %)	52 (2.1 %)	67 (3.0 %)
Smoking status			
Never-smoker	2297 (49.6 %)	1561 (64.2 %)	736 (33.4 %)
Ex-smoker	1473 (31.8 %)	544 (22.4 %)	929 (42.2 %)
Current smoker	862 (18.6 %)	326 (13.4 %)	536 (24.4 %)
Cumulative smoking of current and ex-smokers (pack-years category, % of total population)			
1-14	816 (40.9 %)	339 (48.5 %)	477 (36.8 %)
15-24	510 (25.6 %)	169 (24.2 %)	341 (26.3 %)
≥25	669 (33.5 %)	191 (27.3 %)	478 (36.9 %)
Daily cigarette consumption			
≤1	50 (2.4 %)	30 (4.0 %)	20 (1.5 %)
2-20	1722 (81.9 %)	628 (83.8 %)	1094 (80.8 %)
≥21	331 (15.7 %)	91 (12.1 %)	240 (17.7 %)
Occupational exposure to dusts, gas, fumes	1423 (30.3%)	480 (19.8 %)	943 (41.5 %)
Dyspnoea grade			
0	3700 (79.5 %)	1836 (76.4 %)	1864 (82.7 %)
1	706 (15.2 %)	412 (17.1 %)	294 (13.0 %)
2	128 (2.7 %)	70 (2.9 %)	58 (2.6 %)
3	89 (1.9 %)	63 (2.6 %)	26 (1.2 %)
4	33 (0.7 %)	22 (0.9 %)	11 (0.5 %)
Chronic cough and sputum production			
No cough nor expectoration	4142 (86.9 %)	2197 (88.8 %)	1945 (84.9 %)
Chronic cough only	310 (6.5 %)	152 (6.1 %)	158 (6.9 %)
Chronic expectoration only	127 (2.7 %)	47 (1.9 %)	80 (3.5 %)
Chronic cough + Chronic expectoration	185 (3.9 %)	78 (3.2 %)	107 (4.7 %)

Table 2: relationship between dyspnoea grade and EQ-5D domains in the whole population / in non asthmatic patients with airflow obstruction. Data are reported as the percentage of patients with the considered dyspnoea grade who report no limitation / impairment in the considered EQ-5D domain.

Dyspnoea grade	EQ-5D domains				
	Mobility	Autonomy	Activity	Anxiety	Pain
0	95.6 / 91.5	99.3 / 98.0	95.7 / 93.1	54.7 / 57.4	50.3 / 45.6
1	86.1 / 82.1	98.3 / 100.0	87.5 / 89.5	36.9 / 29.9	29.6 / 35.8
2	74.2 / 61.1	95.3 / 88.9	79.7 / 77.8	33.9 / 38.9	14.8 / 16.7
3	55.1 / 53.3	90.9 / 86.7	67.1 / 66.7	22.5 / 26.7	17.2 / 26.7
4	54.6 / 40.0	81.8 / 80	63.6 / 40.0	30.3 / 20.0	3.0 / 0.0

Table 3: predictors of quality of life and missed working days in multivariate logistic regression analysis in subjects without a known diagnosis of COPD, asthma or any other pre-defined co-morbid illness[§]. Mobility, activity, anxiety and pain are the four EQ-5D domains.

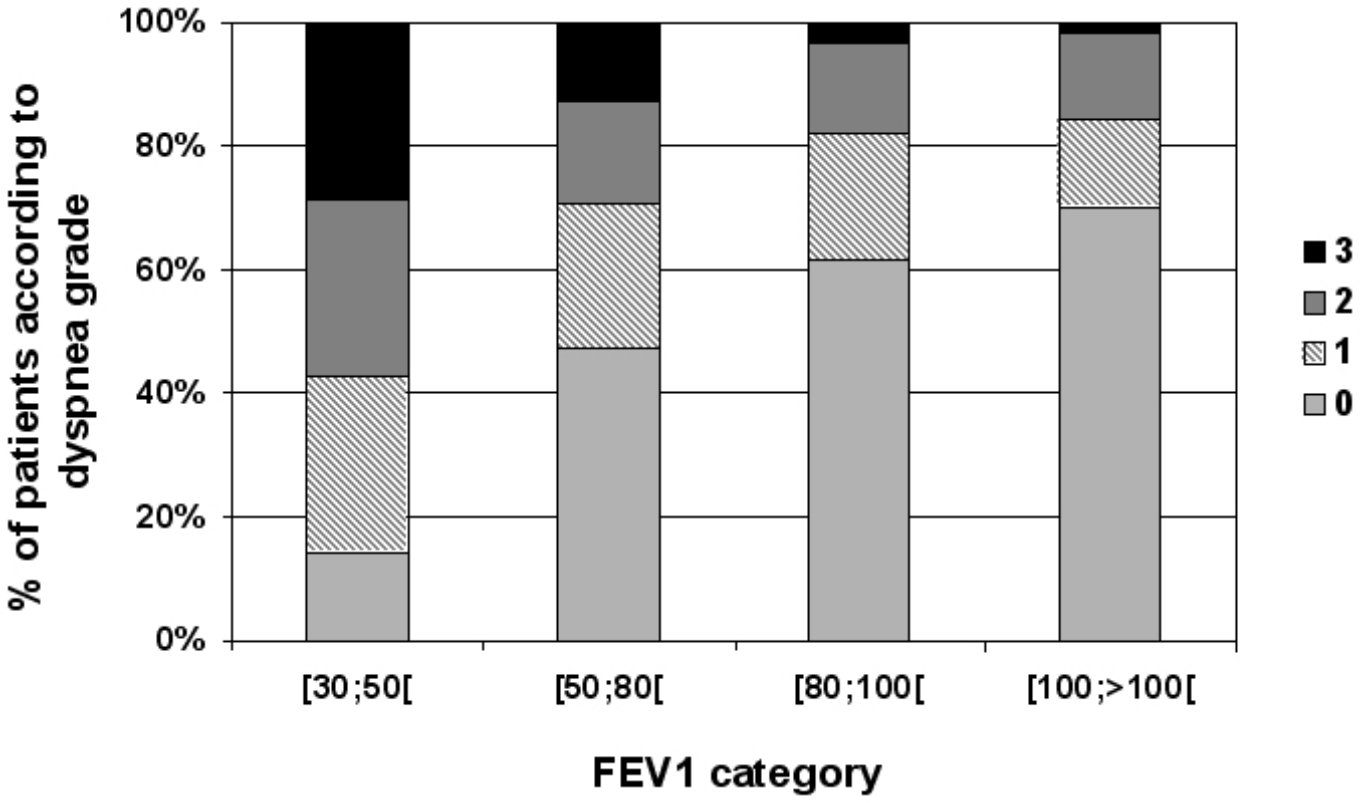
	Reference	Odds Ratio	95% confidence interval	p
Health status*				
Mobility 2	1			
FEV1 % predicted [30-50[	≥80%	13.8	[2.6– 73.9]	0.0022
FEV1 % predicted [50-80[	≥80%	1.8	[1.1–3.0]	0.0208
Age [class] ≥75	[45-54]	3.1	[1.0–9.4]	0.0428
Activity 2	1			
FEV1 % predicted [50-80[	≥80%	2.0	[1.2–3.4]	0.0062
Age [class] ≥75	[45-54]	5.0	[1.5–16.6]	0.0089
Number of cigarettes [≥21[	[2-20]	2.1	[1.1–3.9]	0.0198
Anxiety 2	1			
Female gender	Male	2.1	[1.7-2.7]	<0.0001
Anxiety 3	1			
Female gender	Male	3.7	[2.3-6.0]	<0.0001
Pain 2	1			
FEV1 % predicted [50-80[	≥80%	1.4	[1.1–1.9]	0.0190
Age [class] ≥75	[45-54]	1.9	[1.1–3.4]	0.0325
Pain 3	1			
Age [class] [55-64]	[45-54]	3.0	[1.4–6.4]	0.0048
Age [class] [65-74]	[45-54]	3.6	[1.0–12.2]	0.0432
Age [class] ≥75	[45-54]	4.4	[1.1–18.4]	0.0414
FEV1 % predicted [50-80[	≥80%	2.1	[1.1–4.0]	0.0212
At least one missed working day[#]				
Chronic bronchitis	None	6.0	[2.8-12.7]	<0.0001

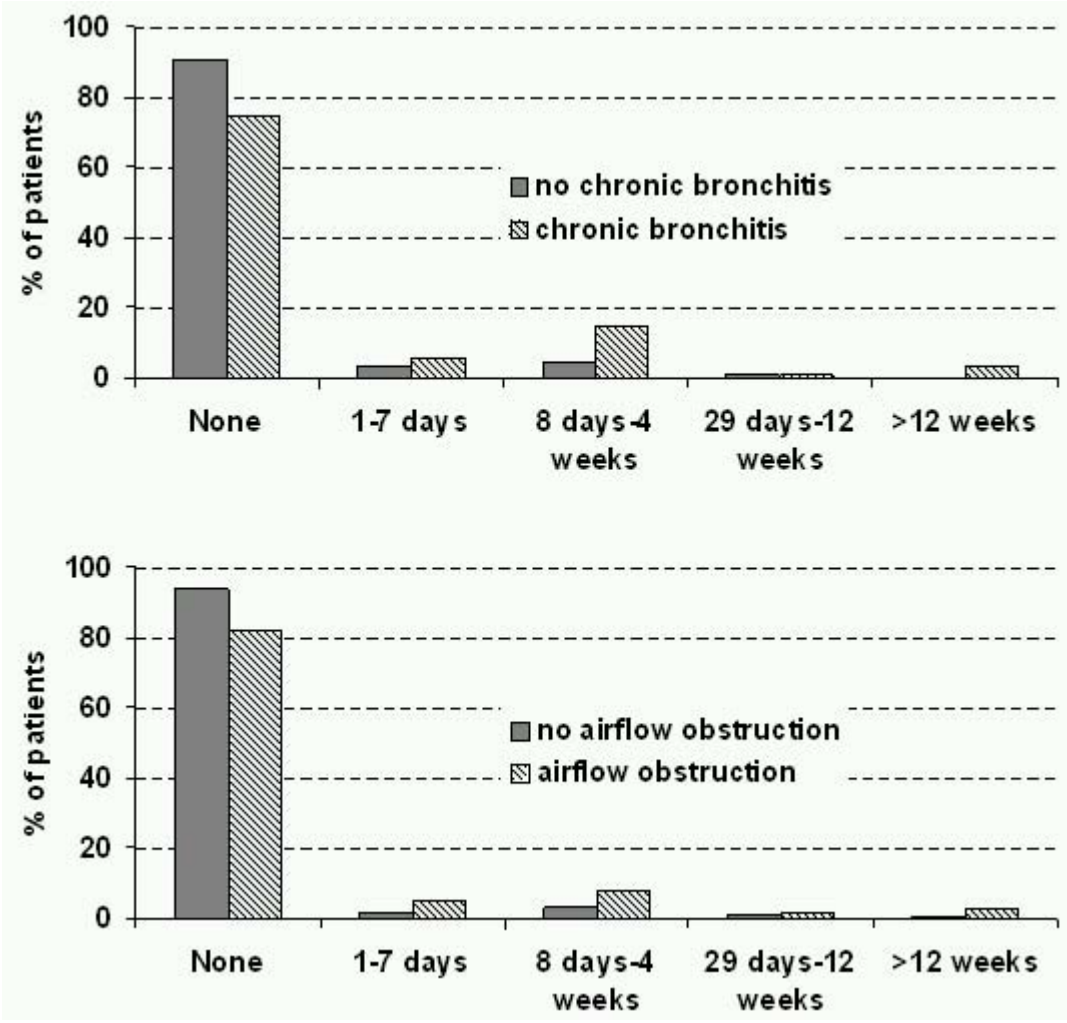
§ bronchiectasis, chronic heart failure
*No independent predictor was found for Mobility class 3 and Activity class 3.
[#] this analysis was restricted to the population aged <65 years, n=1310.

LEGENDS

Figure 1: MRC dyspnea grades according to % predicted FEV_1 in subjects with no known heart or lung disease in whom chronic airflow obstruction (FEV1/FVC<0.70) was demonstrated. No subject of this category reported grade 4 dyspnea.

Figure 2: distribution of the number of missed working days reported during the previous year in the population with no known lung or heart disease, according to the presence or absence of chronic bronchitis (top) and airflow obstruction (bottom).


% of patients according to dyspnea grade
100%
80%
60%
40%
20%
0%
[30;50[
[50;80[
[80;100[
[100;>100[
FEV1 category
3
2
1
0


100
80
60
40
20
0
% of patients
no chronic bronchitis
chronic bronchitis
None
1-7 days
8 days-4 weeks
29 days-12 weeks
>12 weeks
100
80
60
40
20
0
% of patients
no airflow obstruction
airflow obstruction
None
1-7 days
8 days-4 weeks
29 days-12 weeks
>12 weeks