ORIGINAL RESEARCH

Acute respiratory illness as a trigger for detecting chronic bronchitis in adults at risk of COPD: a primary care survey

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Abstract

Aim: To evaluate the impact of chronic bronchitis in patients identified among subjects at risk of chronic obstructive pulmonary disease (COPD) but currently free from any known chronic respiratory disorder, visiting a general practitioner for an acute respiratory episode.

Method: A multicentre, cross-sectional survey carried out in primary care.

Results: Primary care practitioners (n=772) examined 14,030 patients with acute cough (male: 56.9%, age 50.6 ± 16.5 years). Of these, 3,615 were at risk of COPD (>40 years and tobacco use >10 pack-years) and constituted the study population: 79.8% reported current symptoms of chronic bronchitis. Compared to patients without chronic bronchitis, they were older, more frequently exposed to occupational pollutants or to passive smoking, had more tobacco use (p < 0.001), reported dyspnoea ≥ Grade 2 more frequently, and had poorer quality of life as assessed by the EuroQOL-5D questionnaire.

Conclusions: In this survey, previously unrecognised chronic bronchitis was diagnosed in a high proportion of at-risk patients with acute respiratory episodes. Chronic bronchitis was associated with significantly poorer health status. Acute respiratory illness could be an appropriate opportunity for screening those patients at risk of COPD with lung function testing.

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N Roche *et al. Prim Care Resp J* 2010; **19**(4): 371-377
doi:10.4104/pcrj.2010.00042

Keywords COPD, exacerbation, hospitalisation, telephone support, service development

Introduction

Chronic obstructive pulmonary disease (COPD) is a leading cause of world-wide mortality and disability.[1] Its long-lasting course is characterised by irreversible decline in the forced expiratory volume in one second (FEV_1), increasing dyspnoea, progressive deterioration of health status, and acute exacerbations leading to an increased use of health services.[2-4]

A diagnosis of airflow obstruction may increase the success rate of smoking cessation attempts – thereby slowing disease progression and increasing life expectancy – and may allow early initiation of appropriate treatments, thereby reducing disability.[2-6] However, a definitive diagnosis is required. In France, as in other industrialised countries, spirometry data in the population suggest a prevalence of COPD (as defined by an FEV_1/FVC ratio < 0.7%) ranging from 5%–15% in adults.[7,8] The prevalence of COPD varies markedly depending on the age group studied, making it difficult to compare populations of different age ranges. However, currently available data suggest that the prevalence reaches more than 20% in current or former smokers over the age of 40 and even 50% in persistent smokers over the age of 65.[9,10] Most often, the diagnosis is established in subjects who have been smokers for several decades, after a long course of structural and functional changes in the lungs. Consequently, the 10-year survival rate following diagnosis is

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rather low (about 50%), with more than a third of patients dying due to respiratory failure.[11,12] In a recent survey in French prevention centres, chronic airflow obstruction was found in 7.5% of subjects aged 45 years or more.[13] In 93.9% of these subjects, no respiratory disease had been diagnosed previously. Despite the predominantly mild to moderate severity of airflow obstruction, it was associated with an impaired health status and work loss.[13]

Under- or late diagnosis is a consequence of the insidious development of COPD: patients tend to adapt to their condition and under-estimate symptoms, thus making early detection difficult.[14,15] To combat this, standardised questionnaires have been developed to help case-finding.[16] In parallel, the cost-effectiveness of early detection by systematic spirometry in asymptomatic smokers is still debated.[17]

As acute exacerbations represent major events in the natural history of COPD and as they usually prompt patients to seek medical advice, they may be an opportunity to diagnose the disease. A first step could be to identify patients with chronic bronchitis (CB), who are at increased risk of developing COPD,[18,19] even if chronic bronchitis itself is not included in the latest GOLD classification.[20] It would also be useful to determine the impact of the respiratory disease in these patients: demonstration of a poorer health status would substantiate the use of chronic bronchitis for case-finding, and increase the awareness of COPD in primary care and the motivation of physicians towards early detection of this disease.

Thus, the objectives of the present study were to assess:
(i) the health status of patients with (previously undiagnosed) chronic bronchitis (CB), compared to that of patients without chronic bronchitis – i.e. to determine whether subjects with chronic bronchitis identified whilst visiting a general practitioner (GP) for an acute respiratory episode already have impaired health status despite being previously undiagnosed.
(ii) the proportion of subjects with chronic bronchitis among at-risk individuals (age > 40 years, smoking > 10 pack-years) identified when visiting a GP with an apparent clinical presentation of acute bronchitis and no known underlying chronic respiratory disease.

Material and methods

This French multicentre observational cross-sectional survey was conducted during 2006-2007 in primary care practice. The study protocol was approved by the National Council of the French Medical Association, the French Consultative Committee on Data Processing in Biomedical Research and the French National Data Protection Committee. Informed consent was obtained from all patients.

Figure 1. Studied populations and subgroups.
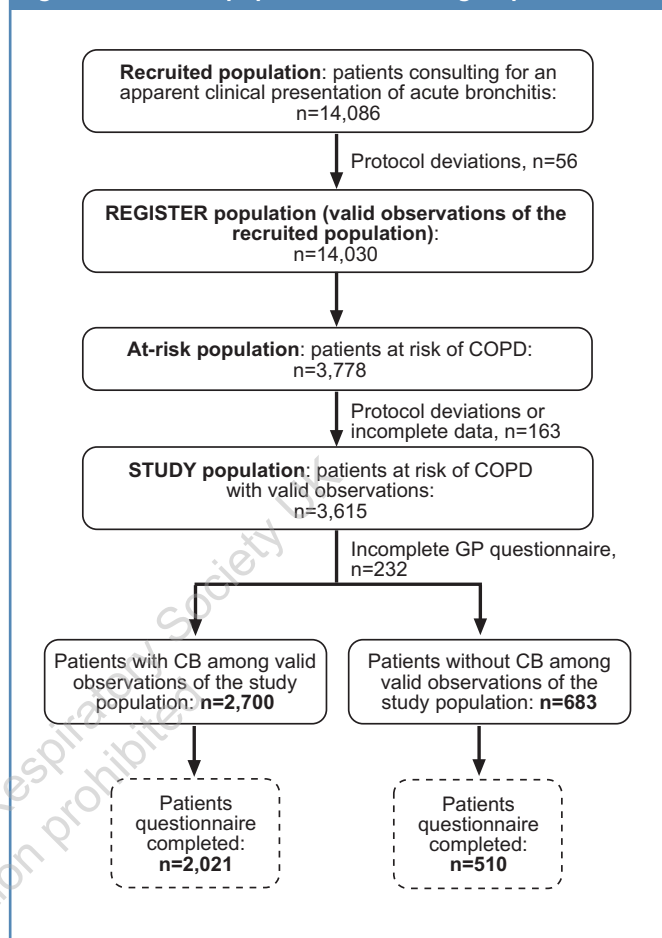
Study populations (see Figure 1)

Nine hundred GPs located throughout mainland France were asked to participate. Each had to include the first 20 consecutive adult patients (age >18 years) with a clinical presentation of acute bronchitis (the **recruited population**) – i.e. with acute (< 1 week) sudden cough, with or without expectoration, retrosternal pain or fever, whose clinical state did not justify hospitalisation. Valid observations of the recruited population constituted the "register population". Amongst these patients, each GP had to select the first five consecutive patients considered to be at risk of COPD – i.e. aged over 40 years, with a smoking history > 10 pack-years (the **at-risk population**). Valid observations of the at-risk population constituted the "study population".

Data collection

For the total population, collected data were age, gender, tobacco use, and the presence/absence of known chronic respiratory disease or lung function testing [LFT] within the past two years.

For the at-risk population, GPs had to record information related to chronic respiratory symptoms (cough, expectoration, chronic shortness of breath), tobacco use, previous episodes of

acute bronchitis and treatment prescriptions. Patients had to report information related to usual symptoms (cough, expectoration, shortness of breath), tobacco use, occupational exposures and previous episodes of acute bronchitis on a self-administered questionnaire (derived from the European Respiratory Community Health Survey questionnaire).[21] Perceived health status and global quality of life [QoL] were assessed by the EuroQOL-5D questionnaire.[22] Chronic bronchitis was defined as chronic productive cough for at least three months per year for at least two consecutive years, as assessed by GP questionnaires. The same definition was applied for patient-recorded data. In patients with chronic bronchitis, the acute respiratory episode at the origin of the visit was subsequently named "acute exacerbation of chronic bronchitis" (AECB).

Statistical analyses

Considering an expected prevalence of chronic bronchitis of at least 20% in current or former smokers over the age of 40 years, expecting up to 15% of non-valuable files and requiring a precision of 2% for prevalence estimation, 4,500 patients were to be included in the study population to obtain 3,825 valid observations in the study population. This calculation took account of the clustered nature of the sample. The number of clusters (i.e. the number of participating physicians) and of statistical units (i.e. subjects) were calculated to ensure reliable variance estimation and to minimise the risk of sampling errors, knowing that there was only one stage of clustering. Considering a proportion of at-risk subjects of at least 1/3 of the total population, a sample of 13,500 individuals had to be recruited in that population.

All analyses were restricted to valid observations (no protocol deviation) with exploitable questionnaires. In the register population, the study evaluated the proportion of individuals at risk of COPD (> 40 years, tobacco use > 10 pack-years, without known chronic respiratory disease) and the proportion of patients with chronic bronchitis. In the study population, patients' characteristics were described according to the presence or absence of underlying newly diagnosed chronic bronchitis. The statistical tests used for these univariate analysis according to the nature of the analysed variables were the Student's t-test with Sattherwaite's correction if variances were not equal, Shapiro-Wilk test, Chi-squared or Fischer's exact test and Wilcoxon-Mann-Whitney test. Risk factors which best predicted the presence of chronic bronchitis in the at-risk population were determined using multivariate logistic regression analysis: the most discriminating parameters on univariate analyses ($p<0.2$) were included in a stepwise procedure to build the best regression model and Odds ratio were calculated.

All tests were two-sided with a significance threshold of 5%. The statistical analyses were carried out using SAS® software, version 8.2, SAS® Institute, NC, Cary, USA.

Results

Studied populations

Seven hundred and seventy-two GPs located throughout mainland France actively participated in the survey and recruited 14,086 patients with a primary diagnosis of acute bronchitis (Figure 1). Valid observations were available for 14,030 of them (the "register population": age 50.6 ± 16.5 years; male gender: 56.9%; smokers or ex-smokers ≥10 pack-years: 54.4%). A known underlying respiratory disease was reported by 24% (n=3,320). Among the remaining subjects, 3,778 (27% of the register population) were at risk of COPD (>40 years old, >10 pack-years). Of these, 3,615 (95.7%) observations were valid (i.e. no protocol deviation) and represented the study population. The GP questionnaire was completed in 3,383 cases (93.6%). In that population, the investigators identified underlying chronic bronchitis in 79.8% of cases (n=2,700, 95%CI: 78.5 -81.2%).

Characteristics of patients with chronic bronchitis in the study population

The demographic characteristics and respiratory risk factors of patients in the study population, according to the presence or absence of chronic bronchitis, are presented in Table 1. Patients with chronic bronchitis had been or were more frequently exposed to occupational pollutants (p <0.001).

Patients with chronic bronchitis suffered from higher degrees of dyspnoea (Figure 2).

Table 1. Cohort population (patients at risk of COPD) - demographic characteristics and respiratory risk factors according to the presence/absence of CB.

	with CB n = 2,700	without CB n = 683	p value
Gender % (n)			
Male	68.8% (1,855)	67.0% (457)	0.367
Female	31.2% (841)	33.0% (225)	
Age (years)	57.0 ± 10.3	53.5 ± 10.2	< 0.001
[40 - 65] years % (n)	78.9% (2,129)	85.5% (584)	< 0.001
>65 years % (n)	21.1% (571)	14.5% (99)	
BMI (kg/m²)	26.3 ± 4.8	25.4 ± 4.4	< 0.001
Smoking status			
Current smokers % (n)	42.8% (1,144)	49.0% (333)	0.003
Former smokers % (n)	57.2% (1,530)	51.0% (346)	
Age the patient stopped smoking (years)	52.8 ± 10.2	47.2 ± 9.9	<0.001
Age the patient started to smoke (years)	18.7 ± 4.2	19.2 ± 4.0	0.002
Smoking duration (years)	32.8 ± 11.2	27.9 ± 10.7	<0.001
Patients exposed to other people tobacco smoke ≥2 hours/day			
Patients quest. % (n)	63.7% (1,280)	52.6% (266)	<0.001
Patients exposed to occupational and environmental pollutants			
Patients quest. % (n)	43.8% (879)	31.0% (157)	<0.001

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Figure 2. Grade of dyspnoea in patients without and with CB (as assessed by GPs and patients).

Grades of dyspnoea
Grade 1: dyspnoea with strenuous exercise
Grade 2: dyspnoea when walking rapidly on a flat ground or walking up one floor or a mild slope
Grade 3: dyspnoea when walking at normal speed for the age on flat ground
Grade 4: dyspnoea when walking slowly for the age on a flat ground
Grade 5: dyspnoea when washing or dressing
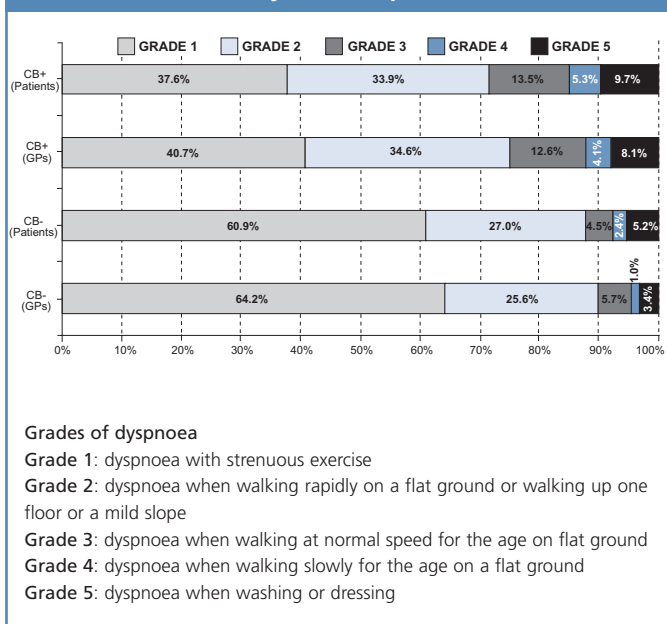
Figure 3. Patients' quality of life according to the absence or presence of CB.

Mobility: 0 = no problem; 1 = problems for walking; 2 = confined to bed
Autonomy: 0 = no problem; 1 = problems for washing/dressing;
2 = unable to wash/dress
Usual activities: 0 = no problem; 1 = problems for accomplishing them;
2 = unable to accomplish them
Pain-Discomfort / Anxiety/Depression: 0 = none; 1 = moderate; 2 = severe
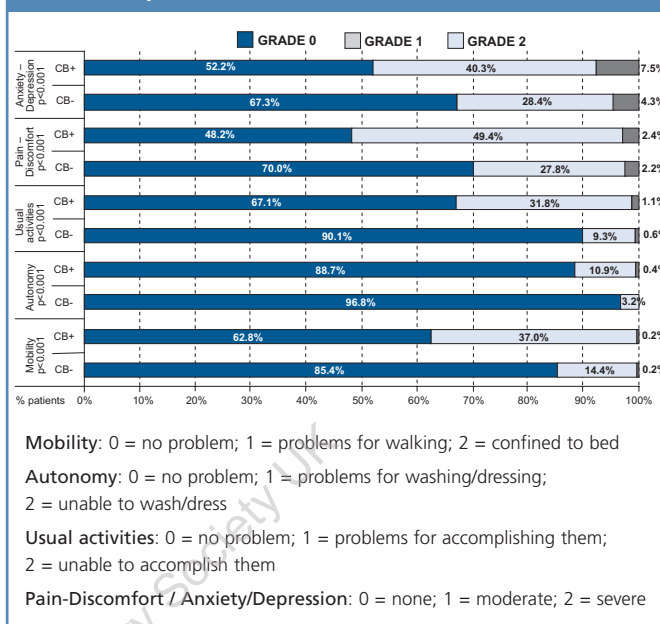
The prevalence of chronic bronchitis was 1.5 times higher in patients aged more than 55 years (p = 0.011), 2.2 times higher in patients presenting more than two acute bronchitis episodes per year (p = 0.004), and consequently 2.3 times higher in patients having been treated by antibiotics more than twice during the past year (p = 0.009).

Impact of chronic bronchitis on patients' quality of life and activity

The global QoL, as assessed by the patients on the 100mm visual analogue scale of the EuroQOL-5D questionnaire, was more altered in patients with chronic bronchitis: 58.4 ± 17.5 versus 68.9 ± 17.7 mm (p < 0.001). For each domain of the EuroQOL-5D questionnaire (mobility, autonomy, problems in daily activities, pain and discomfort, anxiety or depression), QoL was significantly impaired in patients with chronic bronchitis (p < 0.001) (see Figure 3).

Within the past three years, the proportion of patients having stopped their activities due to respiratory disorders was 62.2% in patients with chronic bronchitis compared to 22.6% of the patients without AECB (p < 0.001). Consequently, the time lost from work due to respiratory disorders was higher in patients with, than without, chronic bronchitis (p < 0.001) (see Figure 4). Altogether, chronic bronchitis was 3.7 times more frequent in patients with more than four weeks lost from work in the previous year due to respiratory disorders (p < 0.001).

Compared to patients with less than two weeks lost from work, patients who stopped working for two or more weeks within the past year presented with a lower global QoL

Figure 4. Time lost from work due to respiratory disorders within past year in patients with and without CB.
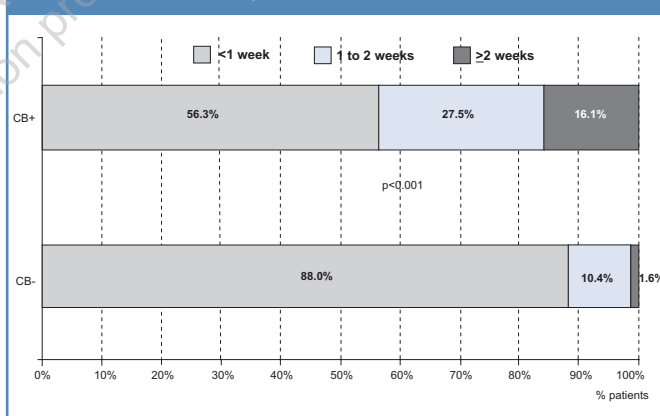
(respectively: 63.0 ± 17.4 vs 51.7 ± 16.9 - p < 0.001). They also reported more frequently an impairment in mobility (25.0% vs 60.0% - p < 0.001), autonomy (6.2% vs 21.8% - p < 0.001) and ability to accomplish usual activities (20.9% vs 51.3% - p < 0.001). Pain or discomfort was also more frequent in these subjects (41.3% vs 68.6% - p < 0.001), as well as anxiety or depression (41.1% vs 60.6% - p < 0.001).

Care-seeking and previous acute respiratory episodes

The frequency of acute respiratory episodes and care-seeking in patients with or without chronic bronchitis are summarised in Table 2. The proportion of patients having already been consulted and consequently having received antibiotic treatments for acute bronchitis was higher among patients with underlying chronic bronchitis.

Table 2. Respiratory disorders frequency and care seeking.

Number of patients with complete autoquestionnaire	with CB n = 2,021	without CB n = 510	p value
Number of patients whose physician already spoke about chronic bronchitis			
Patients quest. % (n)	74.6% (1,496)	8.3% (42)	< 0.001
Number of patients already followed up for chronic bronchitis			
Patients quest. % (n)	45.5% (917)	2.6% (13)	< 0.001
Number of patients followed up for cardiovascular disease			
Patients quest. % (n)	30.5% (613)	20.3% (103)	< 0.001
Number of acute bronchitis per year (GPs' questionnaire)			
Mean ± SD	2.7 ± 1.4	1.5 ± 0.9	< 0.001
Patients having consulted for previous similar episodes			
Patients quest. % (n)	88.8% (1,781)	62.5% (317)	< 0.001
Patients treated with antibiotics for similar episodes within past year			
GPs quest. % (n)	96.4% (2,603)	79.8% (544)	< 0.001
Patients quest. % (n)	83.6% (1,546)	60.3% (293)	< 0.001

Number of antibiotic treatments within past year	1	2	≥2	1	2	≥2	
GPs quest. %	19.2	36.1	41.1	45.0	27.1	7.6	< 0.001
Patients quest. %	26.9	37.0	36.1	64.3	26.4	9.3	< 0.001

Patients having already consulted for the current episode and received antibiotics			
GPs quest. % (n)	23.5% (629)	11.1% (75)	< 0.001
Antibiotics % (n)	81.0% (498)	78.4% (58)	0.593
Patients quest. % (n)	20.3% (408)	9.9% (50)	< 0.001
Antibiotics % (n)	79.8% (320)	65.3% (32)	0.020

Figure 5. Management planned and treatments prescribed for the acute respiratory episode in patients without and with CB.
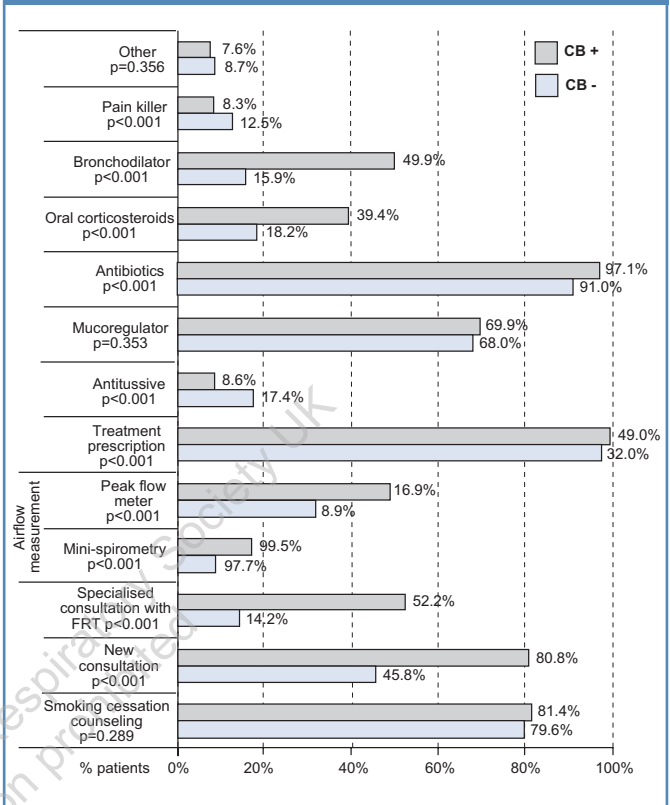
The planned management and treatments prescribed for the current episode in patients with or without chronic bronchitis are shown in Figure 5. The presence of acute bronchitis was associated with closer and more specialised follow-up, as well as with more frequent prescriptions of antibiotics, inhaled bronchodilators and oral corticosteroids, and less frequent use of anti-cough agents.

Discussion

In this study of 14,030 adult patients consulting a GP with a primary diagnosis of acute bronchitis, 43% were at risk of COPD (> 40 years of age and tobacco use > 10 pack-years). Among these, 79.8% were diagnosed with underlying chronic bronchitis. Compared to patients without chronic bronchitis, they were older, had been or were more exposed to occupational or environmental pollutants, and had a longer history of tobacco use. They also more frequently reported dyspnoea of Grade 2 or more. Most importantly, their QoL was more altered and they reported more time lost from work due to respiratory disorders and more acute respiratory episodes and visits to physicians.

Some potential sources of bias may have influenced the results of this survey. The lack of exhaustive and consecutive enrolment could have led to a selection of patients presenting more risk factors and/or symptoms. Thus, we cannot draw any conclusion regarding the prevalence of risk factors and chronic bronchitis in the studied population, but this was not the main goal of the study.

The targeted size of the study population (n=3,825) was not reached, but the actual number of subjects (n=3,615) only marginally affected the power of the study (precision of the estimate: 2.1% vs 2.0%).

Since spirometry was not performed, it is not possible to determine the frequency of underlying COPD in the studied population. Thus, we cannot distinguish between the impact of chronic sputum production and that of airflow obstruction. In any case, our results show that, in subjects with a clinical presentation and primary diagnosis of acute bronchitis, it is worth identifying those with risk factors for COPD and, among them, those with previously undiagnosed chronic bronchitis. In these subjects, poorer QoL, work loss and consumption of healthcare resources suggest ill health.

Some cases of acute episodes and symptoms of chronic bronchitis may be related to asthma in the studied population. However, subjects reporting that a doctor ever mentioned a diagnosis of asthma were excluded from the study. Other diseases such as bronchiectasis cannot be ruled out either, but

they are far less frequent in the general population. In any case, the impairment in QoL and activity in subjects with symptoms of chronic bronchitis suggests that spirometry might be useful in these subjects, whichever underlying chronic respiratory disease is finally diagnosed.

The diagnosis of COPD is based on spirometry. Some studies have shown that systematic spirometry in smokers in general practice may permit detection of previously undiagnosed COPD in 10%–20% of screened subjects, a substantial proportion of them having moderate to severe disease.[23] However, systematic screening of smokers who do not recognise or report symptoms has been discouraged by recent guidelines,[24] which state that it would not be cost effective in terms of number-needed-to-screen to prevent one exacerbation. This position can be debated since it is not known whether early detection could delay handicap or death through the early implementation of appropriate treatment and advices.

Nevertheless, symptom-based case-finding by GPs may be more realistic, especially in settings such as France where spirometry is not performed in primary care. Simple patient self-administered questionnaires have been developed in order to identify patients with a high likelihood of COPD, and for whom spirometry has to be performed.[16] The sensitivity of a COPD diagnostic questionnaire was found to be as high as 80% with a 70% specificity in its initial development study, making it potentially useful in routine primary care practice. Indeed, the use of this questionnaire was subsequently advocated in the guideline for Chronic Airways Diseases of the International Primary Care Airways Group. However, a study of its external validity recently provided rather disappointing results, with a high false-positive rate and low area under the ROC curve.[25] Such results are likely to prevent this questionnaire from being generalised.

Our data suggest that acute respiratory episodes (which were not part of the above-mentioned questionnaire) could be a useful entry in the screening approach. The recurrence of such episodes should also be a trigger for screening, as shown by the higher number of acute respiratory episodes in subjects with chronic bronchitis. Spirometry-based studies are required to determine the proportion of COPD cases in at-risk subjects with chronic bronchitis detected using this approach. This proportion should be compared to that observed in at-risk patients without chronic bronchitis. This will allow one to determine the performance of screening for chronic bronchitis, as a tool to help detecting underlying COPD or other chronic respiratory diseases.

Interestingly, clinical practice appears to be modified when chronic bronchitis is discovered, with a higher rate of prescription of bronchodilators, oral corticosteroids and antibiotics. As shown in figure 5, more frequent and specialised follow-up is also planned in subjects with newly diagnosed chronic bronchitis. In the present study, we obviously have no way to determine

whether these decisions lead to better outcomes. As mentioned above, this will require further prospective studies.

Conclusion

These survey results show a high prevalence of chronic bronchitis in at-risk patients visiting their GP for an acute bronchitis episode. Although no diagnosis of chronic respiratory disease had been made before in most patients, the burden of chronic bronchitis was high in terms of health status, consumption of healthcare resources and work loss. As patients tend to adapt to the insidious onset of COPD symptoms and seek medical advice only late in the course of the disease, acute respiratory episodes could be a useful opportunity for spirometry screening and initiating active COPD prevention and management.

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