

# Early detection of COPD in primary care: screening by invitation of smokers aged 40 to 55 years

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## SUMMARY

**Background:** The incidence of chronic obstructive pulmonary disease (COPD) is increasing in developed countries, as is the mortality rate. The main cause of COPD is smoking, and COPD is usually diagnosed at a late stage.

**Aim:** To evaluate a method to detect COPD at an early stage in smokers in a young age group (40–55 years).

**Design of study:** Prospective descriptive study.

**Setting:** The city of Motala (45 000 inhabitants) and its surrounding rural areas (43 000 inhabitants) in south-east Sweden. Nineteen thousand, seven hundred and fifty subjects were between 40 and 55 years of age. According to Swedish statistics, approximately 27% of this population are smokers.

**Method:** Smokers aged between 40 and 55 years were invited to have free spirometry testing in primary healthcare centres. Placards were placed in pharmacies and health centres and advertising was carried out locally twice a year.

**Results:** A total of 512 smokers responded. The prevalence of COPD was 27% (n = 141). The COPD was classified as mild obstruction in 85% (n = 120), moderate in 13% (n = 18) and severe in 2% (n = 3) according to the European Respiratory Society classification. Knowledge of the disease COPD was acknowledged by 39% of the responders to the questionnaire. Logistic regression analysis showed that age, male sex, number of pack years, dyspnoea and symptoms of chronic bronchitis significantly increased the odds of having COPD. The adjusted odds ratio was significant for having > 30 pack years.

**Conclusions:** This method of inviting relatively young smokers selected a population of smokers with a high incidence of COPD, and may be one way of identifying smokers with COPD in the early stages.

**Keywords:** bronchitis, chronic; logistic regression; pulmonary disease, chronic obstructive; screening; smoking; spirometry.

## Introduction

THE incidence of chronic obstructive pulmonary disease (COPD) is increasing in developed countries, as is the mortality rate.<sup>1</sup> In 1990, COPD was the sixth most common cause of death worldwide, and it has been estimated that it will be the third most common cause of death in 2020.<sup>2</sup> Except during the earliest stages of the disease, COPD has a great impact on healthcare systems and causes increasing costs to society owing to absence from work, visits to the doctor's surgery, medication, and hospital admissions.<sup>3</sup>

COPD is characterised by a slowly progressing, irreversible airflow limitation caused by chronic inflammation in the bronchioles.<sup>1</sup> It is diagnosed by performing spirometry. In the early stages, COPD can be symptomless, although long episodes of coughing, often with sputum production, are common. In the later stages, when there are also symptoms of dyspnoea on exertion, a large portion of the lung capacity may already have been lost. COPD is usually diagnosed in the later stages, and this diagnostic delay may either be due to the patient's gradual adaptation to a decreasing lung function or because doctors are unaware of, or not responding to, the symptoms of the patient.<sup>4,5</sup>

The main cause of COPD is smoking,<sup>1,5</sup> and COPD often manifests itself after someone has been smoking more than 20 cigarettes a day over 20 years (20 pack years). A smoker who is sensitive to cigarette smoke may therefore have spirometric changes between the ages of 40 to 45 years if they started smoking as a teenager. It has been estimated that 15–20% of smokers develop COPD,<sup>6</sup> but more recent research suggests that as many as 50% develop COPD if the smoker reaches a high age.<sup>7</sup> Since there is no treatment that can restore lung function, the key method to prevent development of severe COPD is to identify smokers at an early stage of the disease so that they can be encouraged to stop smoking. Smoking cessation is the most important treatment for COPD.<sup>8</sup>

It has been estimated that only 25% of all smokers with COPD have been diagnosed with it.<sup>5</sup> In one Swedish epidemiological survey, the prevalence of COPD in smokers in the age group 47–48 years was 13%, when adhering to the European Respiratory Society (ERS) definition of COPD.<sup>7</sup> In a Spanish survey, 15% of the smokers in the age group 40–69 years had COPD.<sup>9</sup>

It is not feasible to screen the entire population of smokers for COPD at an early stage, at least not in areas where smoking is common. However, since many smokers have incipient symptoms of COPD, an invitation to perform a lung function test could attract and identify a population of smokers

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**HOW THIS FITS IN**

*What do we know?*

The incidence of chronic obstructive pulmonary disease (COPD) is increasing, as is the mortality rate. The main cause is smoking, and COPD is usually first diagnosed in the later stages, when a major portion of lung function has been lost.

*What does this paper add?*

This study demonstrates a method of identifying smokers with a high frequency of COPD in the early stages in a relatively young age group, 40–55 years old. The odds of having COPD increased with the number of pack years and symptoms of chronic bronchitis.



**Are you a smoker?**

TAKE THE OPPORTUNITY TO HAVE YOUR LUNG FUNCTION TESTED

If you are a smoker between 40 and 55 years old, we are offering you the chance to have your lung function tested. The aim is to detect the lung disease COPD at an early stage. The disease is also known by the names 'smokers' lung' and emphysema. COPD is caused by smoking and characterised by obstruction due to inflammation in the bronchi. COPD manifests itself as a decreased lung function. Breathlessness is the predominant symptom.

Box 1. Example of an advertisement placed in a local newspaper.

with a high frequency of COPD at an early stage. We therefore invited smokers between the ages of 40 and 55 years, using placards and advertisements, to have spirometry in primary care centres.

**Method**

*Population*

The study was performed in south-east Sweden, in the city of Motala (45 000 inhabitants) and the surrounding suburban areas (43 000 inhabitants). The population is served by nine primary healthcare centres. In the study area a total of 19 750 inhabitants were between the age of 40 and 55 years. According to Swedish statistics, approximately 27% of this population in this age group are smokers.<sup>13</sup>

*Method*

Placards were displayed in each healthcare centre. An advertisement was placed in the local newspaper twice in the spring and twice in the autumn of one year (Box 1). The placards and advertisements invited smokers between the ages of 40 and 55 years to have a pulmonary function test (spirometry) performed free of charge, as well as giving the information that the aim of the test was to diagnose COPD at an early stage. Patients who already had a diagnosis of COPD were excluded from the study. Information about the relation between smoking and COPD was also given. A smoker was defined as someone who smoked at the time of the study or had stopped smoking less than 3 months before the study.

*Pulmonary function testing*

The participants performed at least three dynamic spirometries during their visit to trained asthma and COPD nurses, all of whom had had at least 5 years' experience in the field. The models of spirometers used were: Flowscreen, version 3.10gb; Vitalograph Compact II; Vitalograph Alpha; and the Vicatest P2a. The spirometry was performed and interpreted according to the American Thoracic Society's recommendations.<sup>10</sup> The results from all the spirometries performed by the nurses were re-evaluated by one experienced physician. If the spirometry was judged as not being optimal or showing obstruction, the participants were asked to perform another spirometry, performed by the same physician and using a Flowscreen version 3.10gb.

*Diagnostic criteria of COPD*

Slow vital capacity (SVC), forced vital capacity (FVC) and forced expiratory volume at one second (FEV<sub>1</sub>) were measured. The greatest values of SVC or FVC were used as maximum vital capacity (VC<sub>max</sub>). The FEV<sub>1</sub>/VC<sub>max</sub> ratio (FEV%) and FEV% of predicted value were calculated. The results were classified as obstruction if the FEV% was <88% of predicted for males and <89% for females, in accordance with ERS definition.<sup>5</sup> The obstruction was classified as mild if the FEV<sub>1</sub> predicted was ≥70, moderate if the FEV<sub>1</sub> predicted was 50–69, and severe if the FEV<sub>1</sub> was <50% predicted, in accordance with the ERS definition.

The spirometry results were also classified according to the guideline of the Global Initiative for Chronic Obstructive Lung Disease (GOLD), 2003.<sup>1</sup> The obstruction was classified as: stage 0 (at risk) in smokers with normal lung function and chronic cough; stage I (mild) if the FEV<sub>1</sub> was ≥80% predicted; stage II (moderate) if 50% ≤ FEV<sub>1</sub> <80% predicted; stage III (severe) if 30% ≤ FEV<sub>1</sub> <50% predicted; and stage IV (very severe) if the FEV<sub>1</sub> was <30% predicted or FEV<sub>1</sub> <50% predicted, with the presence of respiratory failure or clinical signs of right heart failure.

Early in the study it was observed that some spirometry results that were classified as non-obstructive according to the current ERS and GOLD definitions showed a low mid-expiratory flow at 50% of vital capacity (MEF<sub>50</sub>) alone, or a lower FEV% than predicted but which was not below the diagnostic criteria for obstruction. These spirometry results were therefore classified as pre-COPD and defined as those with a FEV% predicted 89–93 for males and of 90–93 for females or an MEF<sub>50</sub> ≤ 60 predicted. This is in accordance with the Finnish national guidelines, which state that MEF<sub>50</sub> is a parameter that should be taken into consideration when diagnosing COPD.<sup>11</sup>

If the spirometry showed obstruction, further investigation to rule out asthma was performed, which included a β<sub>2</sub>-agonist reversibility test involving the inhalation of three 0.5 mg doses of terbutaline and a steroid test involving a 14 day course of oral prednisolone 30 mg daily. A chest X-ray was also taken to exclude other pulmonary disease.

*Questionnaire*

All participants were asked to fill in a questionnaire indicating their age, sex, smoking habits, profession, and symptoms of

Table 1. Age distribution in relation to sex, number of pack years, chronic bronchitis and lung function.

Age in years	Sex <i>n</i>	Mean pack years <sup>a</sup> (SD)	Dyspnoea <i>n</i>	Chronic bronchitis <i>n</i>	Normal lung function <i>n</i>	COPD <i>n</i>	Percentage with COPD by age group
40-44							
Male	49	25 (10)	25	27	42	7	14
Female	75	21 (9)	25	28	57	18	24
45-49							
Male	69	30 (12)	27	32	52	17	25
Female	92	24 (10)	30	43	65	27	29
50-55							
Male	103	31 (15)	30	35	71	32	31
Female	124	28 (13)	41	58	84	40	32
Total	512	27 (12)	178	223	371	141	27

<sup>a</sup>There are 11 missing.

Table 2. Smokers with COPD. Age distribution and sex in relation to FEV<sub>1</sub>% predicted according to ERS 1995 and GOLD 2003 definitions.

Age in years	ERS			GOLD				
	Mild <i>n</i>	Moderate <i>n</i>	Severe <i>n</i>	Stage 0 <i>n</i>	Stage I <i>n</i>	Stage II <i>n</i>	Stage III <i>n</i>	Stage IV <i>n</i>
40-44								
Male	6	1	0	22	6	4	0	0
Female	18	0	0	18	9	4	0	0
45-49								
Male	14	3	0	23	10	8	0	0
Female	26	1	0	28	20	6	0	0
50-55								
Male	24	7	1	17	23	16	1	0
Female	32	6	2	33	27	14	2	0
Total	120	18	3	141	95	52	3	0

dyspnoea and chronic bronchitis. The participants were given the diagnosis of chronic bronchitis if they had had a productive cough for more than 3 months per year for at least 2 consecutive years.<sup>12</sup> In addition, they were asked if they had knowledge of COPD (or emphysema or 'smokers' lung') as a disease which could affect smokers before the study. To these questions they could answer 'yes' or 'no'.

### Definition

A pack year is the number of years of smoking multiplied by the average number of cigarettes smoked per day, divided by 20 (the number of cigarettes in a standard packet).

### Ethical approval

Informed consent was obtained and the study was approved by the Ethics Committee, University Hospital, Linköping, Sweden.

### Statistics

SPSS version 11.5 and MINITAB version 13 were used for the different analyses. The mean differences in pack years for sex, chronic bronchitis and COPD were calculated with CIA version 2. The variables age, sex, chronic bronchitis, pack years, and dyspnoea were examined for their association with COPD. First, a univariate logistic regression and then both forward and backward stepwise logistic regression was

done to estimate the influence of the explanatory variables on the odds of having COPD. The numbers of pack years were categorised into four groups (1-20, 21-30, 31-40, >40) and age into three groups (40-44, 45-49, 50-55 years). A Spearman rank correlation matrix between the five explanatory variables was done to examine if any relationships existed between those five variables.

### Results

Of the total population in the study area, 19 750 participants were between the ages of 40 and 55 years. The approximate number of smokers in this population was calculated to be 5332, and 512 (9.6%) participants responded to the advertisement and were included in the study. The mean age was 48 years, 43% were males, and 57% were females (Table 1).

In the first screening by the nurses, 160 spirometries showed obstruction or a questionable result. All these 160 participants performed a new spirometry, of which 147 still showed obstruction, and 13 were judged to be normal. Of the 147 smokers with obstruction, 90% performed a  $\beta_2$ -agonist reversibility test and 74% a steroid test. These tests indicated that six of the smokers had asthma. Therefore, in total, 371 (73%) of the smokers did not have any obstruction and 141 (27%) were classified as having COPD (Table 1, Figure 1). The COPD was classified as mild in 120 (85%), moderate in 18 (13%), and severe in three (2%) of them, according to the

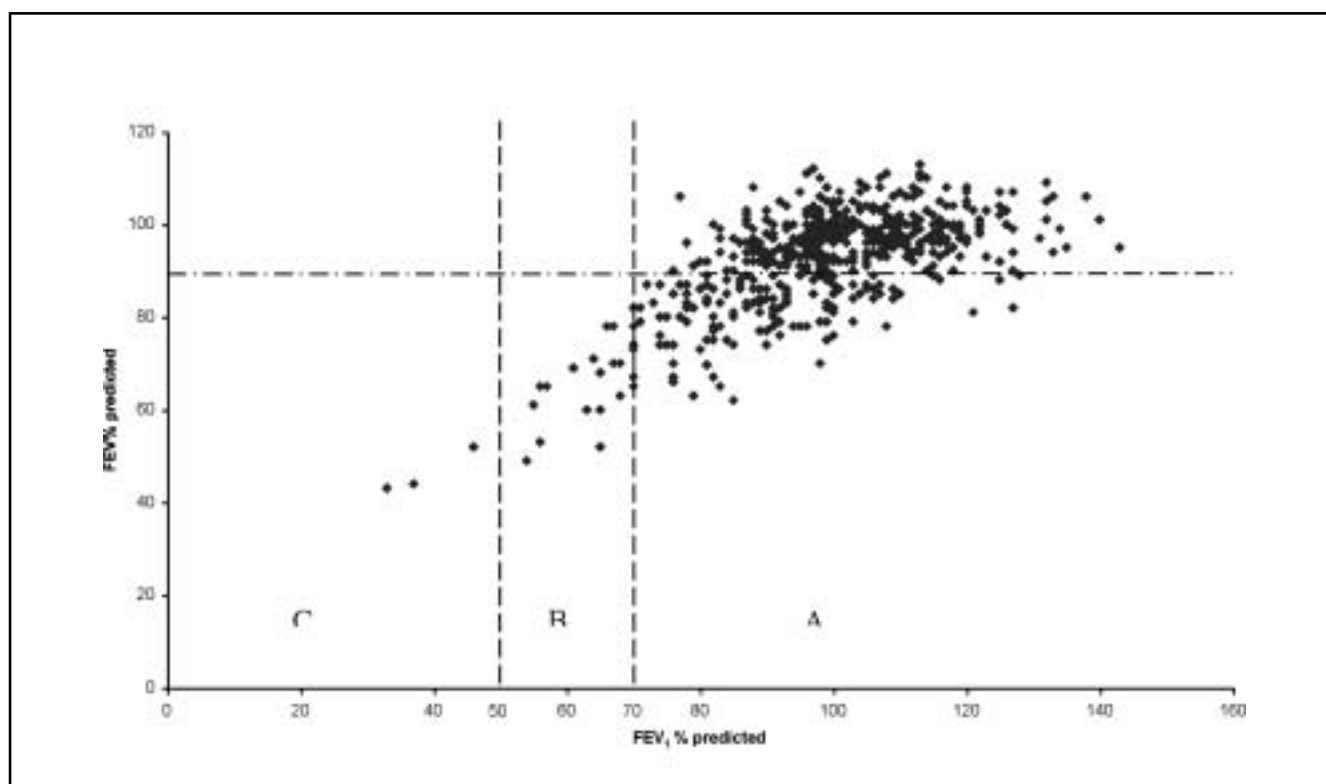


Figure 1. Result of all spirometries. COPD was classified into mild, moderate and severe according to the ERS definition. The degree of obstruction was classified as A) mild if FEV<sub>1</sub>% predicted was  $\geq 70$ , B) moderate if FEV<sub>1</sub>% predicted was 50–69 and C) severe if FEV<sub>1</sub> was <50% predicted, in accordance with the ERS definition.

ERS classification (Table 2). According to the GOLD classification, 150 (29%) had COPD. Of the smokers with normal lung function, 141 (38%) had chronic bronchitis and were classified as stage 0 (at risk) according to the GOLD definition. According to our definition, pre-COPD was found in 57 (11%) of the participants (Table 3). Of these 57 with pre-COPD, 27 had chronic bronchitis and were at stage 0 (at risk) according to GOLD.

The questionnaire showed that the mean number of pack years was 27 (standard deviation [SD] = 12.4) and that 223 (44%) participants had symptoms in accordance with the definition of chronic bronchitis (Table 3). Dyspnoea was experienced by 178 (35%) participants during physical

activity. Of the responders to the questionnaire, knowledge of the disease COPD (or emphysema or 'smokers' lung') was acknowledged by 39%. Of the participants, 41 (8%) had taken early retirement, the majority for musculoskeletal problems. Only 7% had a college education, and there was no indication of any particular profession being related to COPD.

Fewer males than females responded to our invitation, but the males had significantly more pack years than females: 29.5 and 25.1 pack years, respectively, with a difference of 4.35 (95% confidence interval [CI] = 1.24 to 7.46). COPD was correlated to a higher number of pack years than if respiratory function was normal: 32.1 and 25, respectively, with a difference of 7.08 (95% CI = 3.73 to 10.43) (Table 3). In

Table 3. Mean values (SD) of pack years and spirometry in relation to classification of COPD according to the ERS definition.<sup>a</sup>

	Normal spirometry according to ERS		COPD			Total
	Normal	Pre-COPD	Mild (n = 120)	Moderate (n = 18)	Severe (n = 3)	
Pack years <sup>b</sup>	24 (11)	29 (14)	31 (12)	35 (18)	45 (14)	27 (12)
VC <sub>max</sub> % predicted	109 (15)	104 (12)	111 (14)	98 (12)	85 (8)	108 (14)
FEV <sub>1</sub> %	78 (4)	71 (3)	64 (5)	52 (7)	36 (4)	73 (9)
FEV <sub>1</sub> % predicted	99 (5)	93 (2)	80 (6)	66 (9)	46 (5)	98 (6)
FEV <sub>1</sub> % predicted	106 (12)	94 (9)	87 (11)	63 (5)	39 (7)	98 (16)
MEF <sub>50</sub> % predicted	91 (20)	60 (8)	44 (12)	24 (6)	11 (5)	74 (29)

<sup>a</sup>Those with normal lung function according to ERS definitions were divided into those with normal spirometry and those with pre-COPD, according to our definitions (MEF<sub>50</sub>  $\geq 60$  or FEV<sub>1</sub>% predicted 89–93 for males or 90–93 for females). FEV<sub>1</sub>% predicted = FEV<sub>1</sub> of predicted value. <sup>b</sup>There are 11

participants with 1–20 pack years, 15% had COPD; in those with 21–30 pack years, 27% had COPD; in those with 31–40 pack years, 38% had COPD; and in those with >40 pack years, 48% had COPD. Symptoms of chronic bronchitis were evident in 223 (44%) of the 512 participants and 82 (37%) of them had COPD. Of the 141 participants with COPD, 82 (57%) had chronic bronchitis, and among those with normal pulmonary function, 38% had chronic bronchitis.

The univariate logistic regression, with COPD as the dependent variable, showed that these variables: age (odds ratio [OR] = 1.34), male sex (OR = 1.2), pack years (OR = 1.73), chronic bronchitis (OR = 2.26) and dyspnoea (OR = 1.61) influenced the odds of having COPD (Table 4). In the multiple regression model, 31–40 pack years (OR = 3.05) and >40 pack years (OR = 4.58) remained independently associated with COPD.

## Discussion

### Summary of main findings

In this study, 40 to 55-year-old inhabitants who smoked were invited, using placards and advertisements, to have spirometry performed. Of the approximately 5332 eligible smokers in the area, 512 (9.6%) responded, and 73% had a normal spirometry and 27% had COPD. Of the participants with a normal spirometry, 11% had pre-COPD according to our definition.

### Strengths and limitations

In Sweden, approximately 27% of the studied age group smoke,<sup>13</sup> and the high frequency of COPD among the responders suggests that they represented a selection of smokers with more symptoms than smokers have in general. Therefore, this method of inviting smokers for spirometry probably results in an overestimation of the average frequency of COPD in the studied age group. In addition, 10% did not have a reversibility test with  $\beta_2$  agonists and 26% did not have a test with steroids. Fear of the side effects of steroids, or not being able to take more time off from their work, were the main reasons. In this study, six out of the 147 smokers with obstruction had asthma, and the diagnosis was obtained after a  $\beta_2$ -agonist reversibility test. The chest X-ray and the steroid test that were included in the investigation to exclude other causes than COPD for obstruction may not be necessary in clinical practice.

### Relationship to existing literature

The response rate to the campaign (9.6%) was lower than expected. However, considering that the investigated population was only aged between 40 and 55 years, a high prevalence of COPD was found, and, as expected, most subjects had a degree of COPD that would be classified as mild according to the standards of the ERS (Table 2). Our method was aimed at identifying people at high risk of a disease (COPD) who probably would not have consulted a health-care facility until a later stage of their disease.<sup>14</sup> It is therefore difficult to compare the prevalence of 27% that we found with other studies, since definitions of COPD, diagnostic criteria and the included population or age groups may differ. FEV<sub>1</sub> and the variable FEV<sub>1</sub> predicted are regarded as

Table 4. Odds ratios estimated by univariate logistic regression.<sup>a</sup>

Variables	Univariate regression analyses (95% CI)	Multiple regression analyses (95% CI)	P-value
Age (years)	1.34 (1.04 to 1.72)		
40–44	1 (1)		
45–49	1.49 (0.85 to 2.61)		
50–55	1.84 (1.09 to 3.10)		
Male sex	1.20 (0.82 to 1.80)		
Pack years	1.73 (1.41 to 2.12)		
1–20	1 (1)		
21–30	2.04 (1.19 to 3.48)	1.82 (1.05 to 3.15)	0.034
31–40	3.34 (1.89 to 5.91)	3.05 (1.68 to 5.53)	0.001
>40	5.06 (2.55 to 10.04)	4.58 (2.25 to 9.31)	0.001
Chronic bronchitis	2.26 (1.52 to 3.35)	1.77 (1.17 to 2.7)	0.07
Dyspnoea	1.61 (1.04 to 2.49)		

<sup>a</sup>The stepwise logistic regression was performed with factors chosen from the univariate analysis. Both backward and forward analysis were performed with identical results.

sensitive measures of early obstruction.<sup>5</sup> We used FEV<sub>1</sub> predicted, since it reduces the importance of the age factor and the risk of both under- and overdiagnosing. One epidemiological study, using the same ERS criteria and performing reversibility tests, showed a prevalence of COPD of 15% in smokers between the ages of 40 and 69 years.<sup>9</sup> A Polish study, using a similar method and using local media, showed a prevalence of airway obstruction in 30.6% of the smokers aged between 40 and 89 years. However, in that study, reversibility tests were not performed, and subjects older than 55 years were included.<sup>15</sup>

Studies have shown chronic bronchitis to be a risk factor for the development of COPD, and it has been regarded as one stage in the development of COPD.<sup>1</sup> In this study, 38% of subjects with normal lung function had chronic bronchitis (stage 0 according to GOLD) but only 57% of those with COPD had chronic bronchitis. Consequently, a clinical history of chronic bronchitis is not enough to identify patients with COPD. In our study, age, male sex, the number of pack years, chronic bronchitis and dyspnoea were associated with COPD, but only having more than 30 pack years was independently associated with COPD (Table 4). These data indicate that lung function tests to identify COPD should be performed on all smokers, especially those with more than 30 pack years.

Abnormal small airway disease, not detectable by spirometry, may exist in smokers who still have spirometric measurements within the normal range.<sup>16</sup> Furthermore, it has been shown that asymptomatic smokers have signs of neutrophil inflammation activity in bronchoalveolar lavage fluid and a reduced diffusion capacity, as in COPD.<sup>17</sup> In this study, we identified a subgroup of smokers with signs of reduced lung function (pre-COPD), but who were classified as normal according to the ERS. The classification of pre-COPD is only from spirometry. Smokers with pre-COPD should be interpreted as a group of smokers at risk of developing COPD, but they cannot be compared to those with stage 0 disease according to the GOLD definition, since GOLD only include

smokers with symptoms of chronic bronchitis.

### Clinical implications

The identification of smokers with COPD is an important matter for discussion, since smoking cessation is indicated, irrespective of diagnosis. A recent study indicated that when patients perceived that their symptoms were smoking related they were more likely to intend to stop smoking.<sup>18</sup> The knowledge that they have a smoking-related diagnosis, with a prognosis highly affected by smoking, may strengthen the patient's resolve to stop smoking, and it is the only way to reduce morbidity and mortality in COPD.<sup>5,6</sup> In addition, when infected, the diagnosis would be acute exacerbation of COPD, and not acute bronchitis, which may have implications regarding evaluation of severity and for treatment.

The knowledge that smoking can cause lung cancer is widespread, but knowledge about COPD among smokers is low. This was confirmed in this study, since only 39% had heard of COPD or knew that its main cause is smoking, in spite of the fact that we also included the alternatives emphysema or 'smokers' lung' in the information. This stresses the importance of providing information to the public. Furthermore, the general belief that a smokers' cough is normal, and not a symptom of disease, may cause the patient to delay seeking help. A doctor's delay may be caused by the fact that smokers often consult healthcare facilities only when they have a cold, which results in treatment with cough suppressants or antibiotics, and the possible underlying disease, COPD, is not considered.

Mass screening of the population with spirometry has been controversial and is not regarded as feasible.<sup>4</sup> Our method of inviting smokers at a relatively young age to have a lung function test shows that a majority of the responders had experienced symptoms of chronic bronchitis or dyspnoea, and that the prevalence of COPD was high (27%). The method used may be one way of identifying relatively young smokers with COPD in the early stages.

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