

ORIGINAL RESEARCH

COPD prevalence and the differences between newly and previously diagnosed COPD patients in a spirometry program

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Abstract

Aims: To evaluate the prevalence and severity of COPD in a primary care population participating in a spirometry program. Differences between newly and previously diagnosed COPD patients were identified.

Methods: A spirometry program was conducted in 15 primary care centres. Visitors aged over 30 years who were willing to perform spirometry were included in this program.

Results: A total of 1,526 subjects provided acceptable spirometries. COPD prevalence in our population was 18.4%, of whom 69.0% were newly diagnosed. Most patients were classified as GOLD stages I and II (26.0% and 54.0%, respectively). COPD diagnosis was related to gender (men), age (older subjects), history of repeated respiratory infection in childhood, smoking (>10 pack-years) and presence of symptoms (cough, dyspnoea, wheezing). Variables related to newly diagnosed COPD were younger age and absence of chronic cough.

Conclusions: A primary care spirometry program may identify a large proportion of undiagnosed COPD patients especially in the early stages of the disease. Newly diagnosed COPD patients were of younger age and presented with less symptoms. These results support the need for spirometry programs in primary care for early COPD detection.

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The full version of this paper, with online Appendix, is available at www.thepcrj.org

Introduction

Chronic obstructive pulmonary disease (COPD) is characterised by airflow limitation that is not fully reversible. The development of COPD depends on the patient's exposure to noxious particles or gases, the most important being tobacco smoke.¹ The symptoms of the disease are mainly cough, sputum production and dyspnoea. Chronic cough and sputum production may precede the development of airflow limitation for years, yet significant airflow obstruction may develop without cough and sputum production.¹ Therefore, COPD

remains largely underdiagnosed and underperceived.²

Early diagnosis of COPD is important, especially in current smokers, since smoking cessation is the only intervention which delays the rate of decline in lung function.³ Although early diagnosis of COPD does not lead directly to a delay in the rate of decline in lung function, there is evidence that smokers with COPD quit smoking more often.^{4,5} A previous study tried to identify the successful factors in quitting smoking between smokers with and without airflow limitation; the results indicated that the predictors of success in quitting smoking were older age, a smaller pack-year history of tobacco smoking, and poorer lung function.⁶

The diagnosis of COPD requires a high suspicion for

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identifying subjects at risk, combined with implementation of good quality spirometry that is necessary for the detection of airflow limitation, the appropriate classification of patients, and which is mandatory for treatment decisions.¹ Early implementation of spirometry for subjects at risk may identify the disease in the early stages.⁷ Both screening and case finding studies have addressed the question of COPD prevalence, with different results.⁷⁻¹⁰ Recently, the BOLD study estimated that the overall prevalence of COPD at stage II or higher was 10.1% with significant variation between countries.¹¹ In Greece, Tzanakis *et al.* estimated a COPD prevalence of 8.4%, reaching 15.1% in men in rural areas.¹² Despite the growing body of evidence suggesting that early intervention may affect the clinical manifestations of COPD,¹³ COPD is generally not diagnosed in its early stages. Reasons for this include the limited use of spirometry in primary care^{1,14-16} along with nihilistic personal views and failure in communication between patients and doctors.¹⁷ Therefore, identifying the characteristics of newly diagnosed COPD patients in primary care may help in the early diagnosis of COPD.

The aims of the present study included the evaluation of the prevalence and severity of COPD in a population attending primary care offices for a spirometry program, and the identification of differences between newly and previously diagnosed patients with COPD.

Methods

The study was conducted in 15 primary health care centres in Thessaly, Greece, during an 18-month period (January 2006 to June 2007). All subjects were over 30 years of age, resided near a primary health care practice, and were able and willing to participate in a spirometry program. The program took place in the first week of each month, when study co-ordinators visited the primary care practices. Public invitation to participate in the spirometry program with local advertising preceded the spirometry program in each health centre. Subjects were excluded from participation if they had a history of upper or lower respiratory tract infection during the previous four weeks or were unable to perform spirometry. The study was approved by the Ethics Committee of the University Hospital of Larissa and all subjects provided written informed consent.

Study design

A study questionnaire was completed upon arrival for all subjects, who were subsequently submitted to physical examination. Body mass index (BMI) and pre- and post-bronchodilation spirometry were assessed. BMI was calculated as the body weight divided by the square of height (expressed in kg/m²).

Study questionnaire

The study questionnaire (see Appendix 1, available online at www.thepcrj.org) included questions about smoking habits, occupational exposure, history of common respiratory infections,

and chronic respiratory symptoms (i.e. cough, sputum production, wheezing and dyspnoea). Subjects with a history of >100 cigarettes smoked during their lifetime were considered as smokers, whereas ex-smokers were smokers who had quit smoking for at least 12 months.^{12,18} Smoking status was measured by pack-years (PYS), defined as the number of cigarettes smoked per day divided by 20 and multiplied by the number of years of smoking. According to their smoking history, subjects were classified into five categories: never-smokers; ex-smokers with < 10 PYS; ex-smokers with > 10 PYS; current smokers with < 10 PYS; and current smokers with > 10 PYS. The cut-off limit of 10 PYS was chosen in accordance with previous epidemiologic studies.¹¹

Spirometry

Spirometry was performed with a dry spirometer (KoKo Legend, Ferraris, UK), according to American Thoracic Society (ATS) recommendations.¹⁹ Calibration checks were performed every morning, 30 minutes before the beginning of the spirometry program. Spirometry testing was performed by physicians who had undergone a special training program by two pneumonologists. Forced expiratory manoeuvres were repeated until three reproducible acceptable tests were obtained and the best forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio, were recorded.¹⁹ A bronchodilator reversibility test using 400mcg of salbutamol was performed in all patients with obstructive spirometry. Obstructive spirometry was defined as an FEV₁/FVC ratio <0.7 in accordance with GOLD guidelines.¹ An increase in FEV₁ >12% and >200 ml from baseline was considered significant.²⁰ Patients who had used their regular long-acting bronchodilators in the morning prior to spirometry were included in the study, and their spirometric values were considered as post-bronchodilation since all spirometries were performed in the morning. Patients who had received only short-acting bronchodilators followed the above-mentioned bronchodilation protocol.

Diagnosis of COPD

After completion of the study questionnaire, all participants were evaluated by experienced chest physicians (KK, CH, KIG), who established the diagnosis of COPD. COPD diagnosis was based on the global assessment of patients, including a history of exposure to noxious particles or gases (especially smoking, but also occupational dusts and indoor air pollution), compatible symptoms (e.g. cough, sputum production, dyspnoea), and an obstructive spirometry pattern (post-bronchodilator FEV₁/FVC ratio <0.7).¹ Classification of COPD was based on post-bronchodilator FEV₁, according to GOLD guidelines (Stage I – mild COPD, FEV₁ ≥80.0% predicted; Stage II – moderate COPD, 50.0% ≤ FEV₁ < 80.0% predicted; Stage III – severe COPD, 30.0% ≤ FEV₁ < 50.0%; Stage IV – very severe COPD, 30.0% ≤ FEV₁ or FEV₁ < 50.0% predicted with respiratory failure).¹

A previous diagnosis of COPD was based on patients' medical

records and drugs received, as well as previous spirometries, whenever possible. All patients with a previous diagnosis of COPD were thoroughly evaluated by the study physicians and current spirometry was used for the confirmation of the diagnosis and the classification of the patient according to GOLD stages.

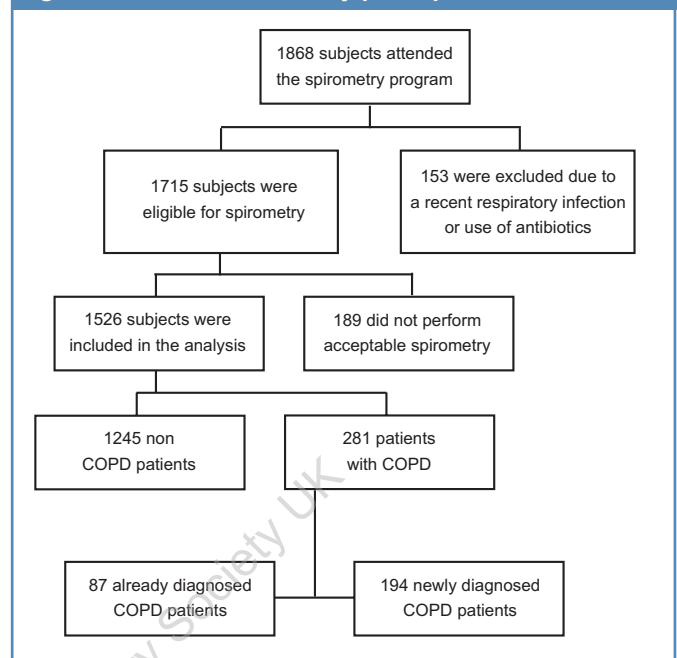
In terms of the differentiation between COPD and asthma, asthma diagnosis was based on pre-defined criteria, as previously described in a similar population – i.e. briefly, the presence of a long standing history of asthma-like symptoms from childhood or adolescence, along with seasonal distribution and a history of atopy, and the presence of significant reversibility of airway obstruction on spirometry.²¹ Again, the final diagnosis was based on the global clinical evaluation by the study physicians. Patients with asthma were included in the analysis as non-COPD patients.

Statistical analysis

Demographic data are presented as mean \pm standard deviation (SD), with the exception of spirometric values which are presented as median (interquartile range). Comparisons of proportions were performed using chi-square tests, whereas differences in numerical variables between groups were performed with unpaired t-tests or Mann-Whitney U-tests for normally and skewed data, respectively.

For the evaluation of variables related to the diagnosis of COPD, sex, age, BMI, occupational exposure, frequency of respiratory infections, smoking habit (PYS), cough, sputum production, wheezing and dyspnoea were included as

Figure 1. Flow chart of study participants.



independent variables in univariate and multivariate analyses, with the diagnosis of COPD being the dependent variable. The variable PYS was included as a categorical variable, according to the predefined classification. Univariate analyses were performed using binary logistic regression analysis whereas multivariate

Table 1. Patient's characteristics.

	Total (n=1526)	Non COPD (n=1245)	COPD (n=281)	Previously diagnosed COPD (n=87)	Newly diagnosed (n=194)
Male/Female, n	902/624	656/589	246/35	77/10	169/25
Age (years)	63.9 \pm 13.7	62.3 \pm 13.9	70.9 \pm 10.1 †	73.3 \pm 7.3	69.8 \pm 10.9*
BMI (kg/m ²)	28.01 \pm 4.42	28.15 \pm 4.38	27.37 \pm 4.53 †	27.51 \pm 4.67	27.31 \pm 4.48
Occupational exposure	349 (22.9%)	248 (19.9%)	101 (35.9%) †	30 (34.5%)	71 (36.6%)
Often respiratory infections	60 (3.9%)	34 (2.7%)	26 (9.2%) †	7 (8.1%)	19 (9.8%)
Smoking status					
Current smoker	507 (33.2%)	378 (30.4%)	129 (45.9%) †	34 (39.1%)	95 (49.0%)
PYS	47.27 \pm 34.4	38.8 \pm 27.85	71.6 \pm 39.4 †	76.7 \pm 39.4	69.8 \pm 39.5
Non Smoker	681 (44.6%)	639 (51.3%)	42 (15.0%) †	12 (13.8%)	30 (15.5%)
Ex Smoker	338 (22.2%)	228 (18.3%)	110 (39.1%) †	41 (47.1%)	69 (35.6%)*
PYS	47.9 \pm 39.4	38.9 \pm 33.4	66.3 \pm 44.3 †	68.1 \pm 48.9	65.3 \pm 41.7
Cough	387 (25.4%)	224 (18.0%)	163 (58.0%) †	65 (74.7%)	98 (50.5%)*
Sputum	307 (20.1%)	172 (13.8%)	135 (48.0%) †	55 (63.2%)	80 (41.2%)*
Wheezing	214 (14.0%)	117 (9.4%)	97 (34.5%) †	38 (43.7%)	59 (30.4%)*
Dyspnoea	260 (17.0%)	134 (10.8%)	126 (44.8%) †	53 (60.9%)	73 (37.6%)*
FEV ₁ (% pred.)	88 (73-100)	92 (80-103)	53 (64-77)	56 (45-71)	67 (57-80)
FVC (% pred.)	88 (74-100)	90 (77-101)	61 (75-92)	70 (55-83)	77 (65-93)
FEV ₁ /FVC ratio (%)	79.6 (73-84)	81 (77-86)	66 (59-69)	66 (56-70)	66 (60-69)

Categorical data are presented as n with percentage in parenthesis, whereas numerical data are presented as mean \pm SD and spirometric values are presented as median (interquartile range). † Comparisons between non-COPD and COPD groups (p < 0.05); * Comparisons between newly and previously diagnosed COPD groups (p < 0.05). Spirometry data presented are post-BD

analyses were performed using forward stepwise binary logistic regression analysis. The same dependent variables were analysed in a similar way in order to identify variables related to newly diagnosed COPD. Data were analysed using SPSS 15.0 for Windows (SPSS Co, Chicago, IL, USA). P-values <0.05 were considered statistically significant.

Results

The flow chart of the study subjects is presented in Figure 1. In the spirometry program 1,868 patients were examined of whom 1,715 (91.8%) were eligible for spirometry. Among the 1,715 participants, 1,526 subjects (88.9%) provided an acceptable spirometry and were included in the analysis. Asthma was diagnosed in 218 subjects (14.2%). The demographics of the 1,526 subjects included are presented in Table 1.

COPD was diagnosed in 281 of the 1526 subjects providing an overall COPD prevalence of 18.4% in our population. Newly diagnosed COPD patients (n=194) represented 69.0% of the COPD patients. Table 2 shows the distribution of patients according to disease severity and sex. Interestingly, 73.7% of the COPD patients belonged to COPD stages II or higher. Of these patients, 65.7% were newly diagnosed. According to our data, 75.6% of patients in stages I and II respectively are newly diagnosed (Table 2). There were 35 women (12.5%)

Table 2. Distribution of COPD patients according to GOLD COPD stages and by sex.

	COPD (n=281)	COPD old (n=87)	COPD new (n=194)
Stage I	74 (26.3%)	16 (18.4%)	58 (29.9%)
Men/Women	60/14	14/2	46/12
Stage II	152 (54.1%)	39 (44.8%)	113 (58.3%)
Men/Women	136/16	34/5	102/11
Stage III	53 (18.9%)	30 (34.5%)	23 (11.8%)
Men/Women	48/5	27/3	21/2
Stage IV	2 (0.7%)	2 (2.3%)	0 (0%)
Men/Women	2/0	2/0	0/0

Data are presented as actual numbers with percentages in every subgroup in parenthesis.

among the 281 COPD patients. The vast majority of women with COPD (25 out of 35) were newly diagnosed. Of these, 92% were classified as COPD stages I and II (Table 2).

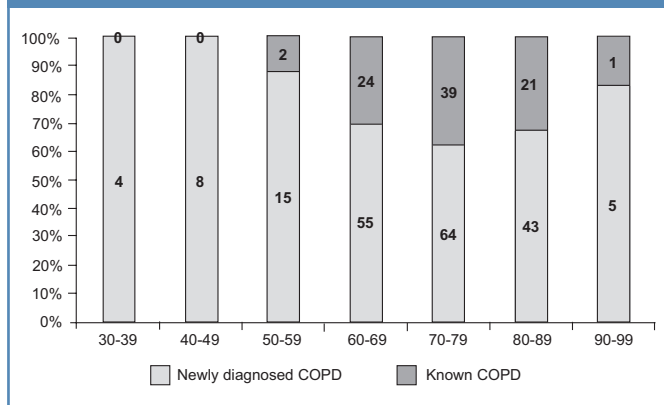
Differences between COPD and non-COPD patients

COPD patients were more often male, older in age, and had a lower BMI compared to subjects without COPD. COPD patients were also more often smokers (current and ex-smokers), with a higher smoking habit. All respiratory symptoms were more often present in COPD patients (Table 1).

Table 3. Univariate and multivariate analysis.

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Comparison between COPD and non-COPD patients						
Male Sex	6.27	4.32 – 9.09	<0.001	2.27	1.42 – 3.62	0.001
Age	1.06	1.04 – 1.07	<0.001	1.06	1.05 – 1.07	<0.001
BMI	0.96	0.93 – 0.99	0.008			
Occupational exposure	2.26	1.70 – 2.99	<0.001			
Often respiratory infections during childhood	3.63	2.14 – 6.16	<0.001	2.93	1.48 – 5.77	<0.001
PYS	1.46	1.35 – 1.58	<0.001	1.41	1.25 – 1.59	<0.001
Cough	6.30	4.77 – 8.32	<0.001	2.48	1.7 – 3.6	<0.001
Sputum	5.77	4.34 – 7.66	<0.001			
Wheezing	5.08	3.72 – 6.94	<0.001	1.52	1.01 – 2.32	<0.05
Dyspnoea	6.74	5.01 – 9.06	<0.001	2.4	1.64 – 3.52	<0.001
Comparison between newly and previously diagnosed COPD patients						
Male Sex	0.87	0.40 – 1.89	ns			
Age	0.96	0.94 – 0.99	0.007	0.96	0.93 – 0.99	0.004
BMI	0.99	0.94 – 1.05	ns			
Occupational exposure	1.01	0.65 – 1.86	ns			
Often respiratory infections during childhood	1.24	0.50 – 3.07	ns			
PYS	1.08	0.91 – 1.29	ns			
Cough	0.35	0.20 – 0.60	<0.001	0.35	0.20 – 0.62	<0.001
Sputum	0.41	0.24 – 0.69	0.001			
Wheezing	0.56	0.33 – 0.95	0.031			
Dyspnoea	0.39	0.23 – 0.65	<0.001			

Figure 2. 100% stacked columned chart representing known versus newly diagnosed COPD patients distributed by patients' ages and by sex. Numbers in columns represent the absolute numbers of patients with COPD.



Univariate and multivariate analyses are shown in Table 3. In univariate analysis, the comparison between COPD patients and non-COPD patients showed that all factors examined are related to the presence of COPD. In multivariate analysis, male sex ($p=0.001$), older age ($p<0.001$), frequent respiratory infections in childhood ($p<0.001$), a smoking habit of more than 10 PYS ($p<0.001$), and the presence of respiratory symptoms ($p<0.001$) were the most significant factors related to the presence of COPD. The most important factor was the history of frequent respiratory infections during childhood, followed by the presence of cough and dyspnoea.

Age distribution of newly diagnosed COPD patients

Figure 2 shows the distribution of newly diagnosed versus known COPD patients based on their age. Patients between 30 and 50 years old were all newly diagnosed, whereas the percentage of newly diagnosed COPD patients decreases as age increases until the age group 70-79 years. Interestingly, in the two last age groups, the percentage of newly diagnosed COPD patients increases again, providing a U-shaped distribution of newly diagnosed COPD patients (Figure 2). Comparison of the proportions of newly diagnosed COPD patients between age groups showed that these differences were statistically significant ($p<0.001$). However, at all ages the percentage of newly diagnosed COPD patients remained over 60.0% in this population (Figure 2).

Differences between newly and previously diagnosed COPD

Differences are presented in Table 1. Newly diagnosed COPD patients were younger and had less frequent respiratory symptoms (cough, sputum, wheezing and dyspnoea) compared to previously diagnosed COPD patients (Table 1). They had a smaller number of pack-years smoking history than already diagnosed COPD patients, for both the current and ex-

smokers group, but this difference did not reach statistical significance. However, diagnosed COPD patients had a higher percentage of ex-smokers.

In the univariate analysis, the variables that were related to newly diagnosed COPD in the spirometry program were younger age ($p=0.007$) and less frequent presence of all respiratory symptoms (cough, sputum, wheezing and dyspnoea, $p<0.05$). In the multivariate analysis, only younger age ($p=0.004$) and less frequent presence of chronic cough ($p<0.001$) remained significant predictors of newly diagnosed COPD (Table 3).

Discussion

In this study we have shown that a significant proportion of patients with COPD can be diagnosed by the implementation of a spirometry program in primary care. We have additionally shown that 69% of patients with COPD were newly diagnosed and that 88.2% of newly diagnosed patients were classified as GOLD stages I and II, providing a possible target for early intervention. Spirometry programs should be implemented in primary care for the identification of patients with COPD, since newly diagnosed patients with COPD were of younger age and presented with fewer symptoms.

The overall prevalence of COPD in our population is 18.4% and these patients were mainly classified as GOLD stages I and II (26.0% and 54.0%, respectively). These percentages are similar to those estimated by Shahab *et al.* from a cross-sectional household survey in England,²² and by Bednarek *et al.* who investigated the burden of COPD in a single primary care practice in Poland,²³ despite the fact that our population differs significantly from those two studies. Several case finding studies in smokers have shown a higher prevalence of COPD.^{7,24} These differences can be attributed to differences between study populations. Our study included eligible subjects attending primary care offices for any reason after public invitation through local advertising, so it does not fulfil the criteria for a screening study. However, our data further support the under-diagnosis of COPD in primary care settings that has been highlighted in previous studies.

Previous data from our group have shown that primary care physicians underdiagnose and undertreat COPD,^{25,26} which may reflect the limited access to spirometry and to specialist pneumonologists in rural areas of Greece. The underdiagnosis of COPD remains a problem in several countries, and several studies have highlighted the importance of spirometry for the identification of obstructive lung disease in primary care.²⁷ The current evidence that spirometry is underused by primary care physicians,^{16,28} combined with the fact that the development of screening questionnaires is not yet satisfactory,²⁹ has led to the suggestion that the problem of COPD underdiagnosis in primary care may be addressed by the provision of good quality

spirometry in the primary care setting,³⁰⁻³² – as is the case in our study. The implementation of current recommendations on spirometry standards in primary care may also lead to an improvement in the diagnosis of COPD.³³ Moreover, the implementation of guidelines from the International Primary Care Respiratory Group (IPCRG)³⁴ may further help primary health care physicians raise the standards of health care provided for patients with COPD.

Recent guidelines from the American College of Physicians recommend against spirometry screening in asymptomatic individuals.³⁵ However, several studies have revealed a high prevalence of COPD among smokers and ex-smokers with minimal symptoms or no symptoms at all. In a case finding study, Vandervoort *et al.* reported high proportions of undiagnosed patients with COPD in the early stages of the disease.²⁴ In that study, factors independently associated with newly diagnosed COPD were younger age and less reporting of chronic cough and fatigue.²⁴ In a screening study from Sweden only 21% of patients with mild COPD had symptoms.¹⁸ Interestingly, data from the European Community Respiratory Health Survey have shown that a considerable percentage of young adults aged 24-44 years old suffer from COPD.³⁶ The fact that patients with newly diagnosed COPD in our study were younger and less symptomatic further supports the need for spirometry programs that will identify patients in the early stages of the disease.

The importance of early diagnosis of COPD is supported from studies suggesting that a diagnosis of COPD may improve smoking cessation rates in intervention programs.⁴ Recent data from the UK have additionally shown that spirometry results provided in the form of “lung age” (defined as the age of the average healthy individual who would perform spirometry similarly to the patient) significantly increased the rates of smoking cessation.³⁷ Moreover, the treatment of patients with moderate COPD with a long-acting anticholinergic bronchodilator may reduce the rate of decline of FEV₁.³⁸ This evidence, along with the limited effect of treatment options on the natural history of advanced COPD, suggest that the identification of patients in the early stages of the disease may represent the best intervention in terms of long-term outcomes for these patients.

Another important finding from our study is that the diagnosis of COPD was associated with a history of frequent respiratory infections in childhood. The presence of this factor may involve a significant recollection bias. However, recent data indicate that frequent respiratory infections in childhood were associated with lower FEV₁ in adult life.³⁹ Moreover, there is accumulating evidence connecting genetic susceptibility and early life events – including antenatal influences on lung growth and frequent respiratory infections in childhood – with the risk of future development of COPD.⁴⁰ This finding is consistent with the

results of the present study, where patients with COPD report frequent respiratory tract infections three times more often compared to patients without COPD.

Interestingly, in our study the percentage of women with COPD was only 12.5%. The BOLD study estimated that the prevalence of COPD in women was 8.5%, with significant variations between different areas.¹¹ The low percentage of women with COPD in our study is probably related to the low smoking habit of Greek women in rural areas. It has recently been shown that 96% of women above the age of 60 in northern Greece were non-smokers.⁴¹ Additionally, it is likely that more smokers and especially those with respiratory symptoms may have attended the spirometry program, and this may further account for the lower number of female participants in our study.

We chose to include both smokers and non-smokers in our study for the following reasons. Firstly, we wanted our population to be representative of the general population attending primary care offices. Secondly, recent studies have shown that passive smoking,⁴² as well as indoor and outdoor air pollution, occupational hazards, and infections,⁴³ are also important. Finally, an analysis of the BOLD study revealed a significant proportion of never-smokers with COPD.⁴⁴ Bednarek *et al.* have also shown that 50% of women with COPD in their population had never smoked.²³

A significant limitation of our study lies in the subject selection based on local advertising and targeting of the population attending primary care centres. This may have influenced the reported prevalence of COPD in our population, primarily due to the fact that current smokers and subjects with respiratory symptoms were more likely to attend the program. This may further account for the higher number of male participants, since they represent the vast proportion of smokers in rural areas of Greece. However, we followed this approach in order to increase the likelihood for participation in the spirometry program. Another limitation is that the diagnosis of COPD in our study was based on the GOLD criteria that use an FEV₁/FVC ratio <0.70 to define airway obstruction.¹ Several authors have recommended the use of the lower limit of normal (LLN),^{45,46} since the FEV₁/FVC ratio decreases with increasing age and thus the use of a fixed ratio may lead to misclassification.⁴⁷ However, Mannino *et al.* have shown that the use of the 0.7 fixed ratio can identify patients at increased risk of death or hospitalisation, even among older adults.⁴⁸ Based on the aforementioned studies and the fact that we wanted our results to be more easily applicable in clinical practice, we chose to use the fixed ratio of 0.70 for the diagnosis of COPD.

Conclusion

Our data suggest that an invitation strategy for patients to undergo spirometry in primary care offices may identify a

Summary box

Underdiagnosis of COPD in primary care remains a significant problem in Greece. Current and ex-smokers with respiratory symptoms should have access to spirometry and should be evaluated for the presence of COPD. The implementation of a spirometry program in primary care may be useful for the identification of COPD patients in the early stages of the disease. Undiagnosed patients with COPD are younger and have less symptoms, especially cough. The most cost-effective strategy for eliminating the problem of COPD underdiagnosis remains to be determined.

large proportion of patients with undiagnosed COPD, therefore contributing to the early diagnosis of COPD. The fact that the majority of diagnosed patients had mild-to-moderate COPD, and that newly diagnosed COPD patients in this program were younger and less symptomatic than COPD patients who were already diagnosed, further supports the need for spirometry programs in primary care for the early detection of COPD.

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Conflict of interest declaration

None of the authors presents any conflicts of interest related to this manuscript.

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Appendix 1. Study questionnaire

No..... Name..... Male/Female.....

Age..... Occupation.....

Height..... Weight..... BMI.....

Did you have a respiratory infection during the last 4 weeks?

Did you receive any antibiotics during the last 4 weeks?

Do you smoke or have you previously smoked?

If you smoke NOW What is your starting age? How many cigarettes/day? PYS.....	If you smoked IN THE PAST What is your starting age? What is the age you stopped smoking? How many cigarettes/day did you smoke? PYS.....
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At your occupation, do you have exposure to noxious particles or gases?

What kind of heating and cooking devices do you use at home?

At your childhood, do you remember to have often respiratory infections?

Do you have a previous history/diagnosis of COPD?

Do you use any inhaler medications?

If yes, what and for what reason.....

Do you have cough?

Do you produce sputum/phlegm?

Do you have wheezing?

Do you have dyspnea/chest tightness?