

Prevalence, severity, and under-diagnosis of COPD in primary care setting

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ABSTRACT

Background. COPD is a common disease with steadily increasing prevalence and mortality. However, recent epidemiological estimates largely differ depending on population studied and methods used.

Aim. We aimed to investigate prevalence, severity, and burden of COPD in a primary care setting.

Methods. From 4730 patients registered in a single primary care practice, all 2250 patients aged 40 years or more were invited to participate. Participants completed a questionnaire on smoking, respiratory symptoms, education, and social status. A physical examination was followed by pre and post bronchodilator (BD) spirometry.

Results. Of the eligible patients, 1960 (87%) participated. Ninety two percent of spirometric tests met the ATS criteria. Airflow limitation was demonstrated in 299 (15%) of the participants pre-BD and 211 (11%) post-BD. COPD was diagnosed in 183 patients (9.3%). Of these patients, the degree of post-BD airflow limitation was mild in 30.6%, moderate in 51.4%, severe in 15.3%, and very severe in 2.7%. Only 18.6% of these patients had previously been diagnosed with COPD; and almost all of these had severe or very severe airflow limitation. As a result of the study, a diagnosis of asthma was made in 122 patients.

Conclusions. The prevalence and under-diagnosis of COPD in the adult patients in this primary care setting made case-finding worthwhile. Large number of newly detected patients were symptomatic and needed treatment. Limiting investigations to smokers would have reduced the number of COPD diagnosis by 26%.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common disabling disease. Mortality from COPD is increasing world-wide [1]. Prevalence estimates of COPD differ largely depending on the diagnostic instruments employed and the population studied [2]. Another major sources of difference in COPD prevalence estimates are related to different spirometric criteria for bronchial obstruction (FEV₁/FVC fixed ratio vs. lower limit of normal), type of spirometric test (pre or post bronchodilator) and a cut-off level of FEV₁ percent predicted (>80% or <80% of predicted). According to ATS/ERS [3] and GOLD guidelines [4], a presumptive diagnosis of COPD should be confirmed by spirometry. Metaanalysis of epidemiological investigations based on spirometry testing showed COPD prevalence of 9-10% [5].

The prevalence of physician-diagnosed COPD is much lower than suggested by population-based spirometric surveys: 1.5% in the UK [6] and 3% in Canada [7]. Thus only a fraction of those with COPD have been diagnosed (9.4% [8] to 22% [9]). The aim of our study was to investigate in the primary care setting: 1) the prevalence and severity of COPD in adult patients; 2) the fraction already diagnosed and treated; and 3) COPD risk factors.

METHODS

The study was performed in Sierpc, a town with 20,000 inhabitants. No significant sources of air pollution are located in the town itself or in the perimeter of 50 km. Investigations were performed in one of 3 primary care practices in Sierpc. This practice cares for both urban and rural populations. Two full-time primary care physicians care for a total of 4730 registered patients (children and adults).

All patients registered at the primary care practice aged 40 or more years were invited to participate. Of the 2250 eligible adult patients, 967 (43%) were men; 1462 lived in Sierpc and 788 lived in a nearby village.

Full investigations were performed in 1960 patients, 87.1% of those eligible; 174 (7.7%) patients refused to participate, 90 (4%) persons were unable to attend (handicapped by stroke, with impaired mental functions, or poor performance status due to malignancy or other debilitating disease); and 26 (1.2%) of the patients were not able to perform valid spirometric tests. Age and sex structure of the participating patients did not differ from those of the population of Sierpc (Online supplement Table 1).

Adult patients were recruited using a personalized letter from the primary care physician explaining the nature and aim of the study. Causes, symptoms, signs, and the natural history of COPD were described. The importance of early diagnosis for prevention of severe, life threatening disease, was emphasized. The higher risk of lung cancer, coronary artery disease, and stroke in patients with abnormal spirometry results was also mentioned. A practice nurse then called eligible patients to arrange a convenient time for an office visit for the study. A home visit was arranged for 80 patients who expressed difficulty coming to the office for the study.

Each visit started with weight and height measurements, and completion of a questionnaire including questions on details of birth, smoking habits, dyspnoea [10], education, economic status, environmental or professional exposure to dusts, fumes or smoke, and a history of respiratory diseases.

Spirometry testing was performed using portable battery powered spirometer (EasyOne Diagnostic, model 2001, ndd Medical Technologies, Zurich, Switzerland). The spirometer measures flow using ultrasound transit-time principle. Measurements were performed with a person in a sitting position without a nose clip. Forced expiratory manoeuvres were repeated until three acceptable and reproducible tests were obtained [11]. The best FEV₁ and forced vital capacity (FVC) were recorded, and the FEV₁/FVC ratio was

calculated. In patients with FEV₁/FVC below the fifth percentile of the predicted value in baseline spirometry, 200µg of salbutamol was given by inhalation delivered through a spacer device and spirometry was repeated 15 minutes later (post-BD).

Spirometry tests were performed by two primary care nurses who had been trained during two separate 4-hour sessions in a reference Lung Function Laboratory at the National Research Institute of TB and Lung Diseases in Warsaw. The results of spirometric tests (numbers, flow/volume and volume/time curves) were sent electronically to one of the authors (MB) for quality control. Overall, 91.8% of the tests fulfilled the ATS goals for a good quality test session. The remaining 8.2% tests were also included into analysis as they all showed results above predicted values and were accepted as normal. Staging of COPD using post-BD spirometry results was performed according to ATS/ERS guidelines [3] using ECCS predicted values [12].

The study was approved by the local Institutional Review Board, and all participating patients gave written informed consent.

Statistical analyses were performed using Statistica version 6.0 software (StatSoft, Inc., version 2001, Tulsa, Oklahoma, USA). Tests were considered significant when $p < 0.05$. Data distribution was analysed using the Kolmogorov-Smirnov test with Lilliefors correction. Quantitative data were described using mean \pm SD. Between groups characteristics were described using t-test or analysis of variance. Homogeneity of variance was assessed using Levene's test. If a variable demonstrated normal distribution and homogenous variance, the F ANOVA test was applied. Otherwise, a nonparametric Kruskal-Wallis H test was used. To characterize the strength of relationships between continuous variables, Pearson correlations were used. Categorized, qualitative, between groups analyses were performed using Pearson chi-square test with appropriate corrections for N. Pre-test probability for post-bronchodilator airflow limitation was assessed using logistic regression models.

RESULTS

A total of 1960 patients were investigated, 87.1% of the eligible cohort. There were 1196 women (93% of eligible) and 764 men (79% of eligible) in the studied group. See table 1 for detailed patients' characteristics. The mean age was 56.7 ± 11.6 years; and the age range was 40-93 years in men and 40-91 years in women. About two-thirds lived in town.

Table 1. Characteristics of eligible patients and participating patients

Age (years)	Males		Females		χ^2	p
	Eligible N	Investigated N (%)	Eligible N	Investigated N (%)		
40-49	313	253 (76.7)	418	407 (97.4)	2.708	0.099
50-59	272	252 (92.6)	371	358 (96.5)	0.089	0.766
60-69	162	126 (77.8)	217	206 (94.9)	1.494	0.222
70-79	159	111 (69.8)	203	186 (91.6)	2.629	0.105
≥ 80	61	22 (36.1)	74	39 (52.7)	1.082	0.298
Total	967	764 (79.0)	1283	1196 (93.2)	6.752	0.009
Current smokers		301 (39.4)		279 (23.3)	30.14	0.0001
Ex-smokers		286 (37.3)		202 (16.9)	60.65	0.0001

Never smokers		177 (23.3)		715 (59.8)	100.7	0.0001
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Footnote: Chi square test and p values regarding age categories refer to differences between the eligible versus investigated groups. Chi square test and p values regarding smoking status refer to differences between men and women.

Spirometry. The pre-BD FEV₁/FVC% was below the fifth percentile in 299 patients (15.3%). Airflow obstruction was present post-BD in 211 patients (29.4% fewer than pre-BD). (Online supplement figures 1 and 2). From 88 patients in whom FEV₁/FVC ratio returned to normal range 60% presented with mild and 40% with moderate airflow obstruction.

In all subjects with post BD airflow obstruction patients' notes were inspected for history of respiratory events in the past and earlier respiratory diagnoses. In 20 patients there was a history of asthma documented by attacks of dyspnoea, remissions, eosinophilia, and in some patients positive results of prick tests. In eight patients additional tests were performed (white blood differential count, IgE, prick test) confirming diagnosis of asthma. Fourteen patients showed large bronchodilating response. This was considered as a sign suggestive of asthma, but only in combination with other symptoms and signs. This resulted in separation of 28 patients with the diagnosis of asthma and airflow obstruction which was not fully reversible. COPD was diagnosed in 183 patients (9.3%) of the total, 12.8% of males and 7.1% of females. The mean increase of FEV₁ post-BD was 1.2±8.5%. The majority of patients with COPD had mild (30.6%) or moderate (51.4%) stage of the disease. Only 15.3% were severe and 2.7% very severe stage (Table 2). Ventilatory impairment in female COPD patients was less severe, with a mean FEV₁% of predicted of 71±18.3% versus 64±20% in males (Table 3).

Table 2. Spirometric classification of COPD severity

	Airflow obstruction				
	Mild N (%)	Moderate N (%)	Severe N (%)	Very severe N (%)	Total N (%)
Males	24 (24.5)	50 (51.0)	21 (21.4)	3 (3.1)	98 (53.6)
Females	32 (37.6)	44 (51.8)	7 (8.2)	2 (2.3)	85 (46.4)
Together	56 (30.6)	94 (51.4)	28 (15.3)	5 (2.7)	183 (100)
p	0.25	0.94	0.09	0.87	0.41

Footnote: post-BD ATS/ERS staging [3]

Table 3. Spirometric variables in subjects with COPD (mean ±SD)

	Age years	FEV ₁ L	FEV ₁ % of pred.	FVC L	FVC % of pred.	FEV ₁ /FVC % of pred.	FEV ₁ /FVC RSD
Males N=98	63.4 ±11.0	2.00 ±0.84	64.2 ±20.3	3.61 ±1.1	92.0 ±19.8	70.8 ±11.8	-3.07 ±1.22
Females N=85	59.9 ±11.5	1.60 ±0.52	71.1 ±18.3	2.65 ±0.7	99.5 ±22.8	77.0 ±8.1	-2.73 ±0.96
Together N=183	61.7 ±11.3	1.83 ±0.75	67.2 ±19.7	3.2 ±1.1	95.2 ±21.4	73.5 ±10.8	-2.92 ±1.13
P	0.05	0.001	0.05	0.0001	0.05	0.0005	0.052

Footnote: RSD – residual standard deviation, p values refer to difference between genders

The prevalence of COPD increased with age, from 5.2% in the fifth decade to 16.8% in patients aged 70 years or more, reaching in males 28.5% (Fig 1). In women aged 70+ years there was no further increase in COPD prevalence. From 19 women in that age group 16 were never smokers.

To analyse the pre-test probability for COPD diagnosis a model of logistic regression was applied. The analysis revealed a role of smoking status, exertional dyspnoea, chronic phlegm production and gender as potential indicators of COPD in primary care (Table 4).

Table 4. Indicators for COPD in logistic regression model

In 34 patients (18.6%) COPD had already been diagnosed, 27 of them presented with

	Regression coefficient (Beta)	Standard Error	Wald Probability (p)	Exp(Beta) Odds Ratio
Ever smoker	1.075	0.006	<0.0001	2.93
Dyspnoea on exertion	0.772	0.003	<0.0001	2.16
Chronic phlegm production	0.438	0.007	<0.0001	1.55
Gender (male)	0.352	0.005	<0.0001	1.42
Age (years)	0.021	0.0002	<0.0001	1.02
Chronic cough	-0.093	0.007	<0.0001	0.91

severe, and 4 with very severe stage COPD. Two patients with severe and one patient with very severe disease had not been previously diagnosed. There was no patient who had previously been diagnosed with COPD but had normal post-BD spirometry. A restrictive pattern of ventilatory impairment was found in 108 (5.5%) patients ($FEV_1/FVC\%$ above the fifth percentile and $FVC < 80\%$ of predicted).

Symptoms. Patients diagnosed with COPD frequently had symptoms, chronic cough (45%), sputum production (38%) and dyspnoea on exertion (52.5%). Only 59 (32%) did not report any symptom. Dyspnoea MRC grade 1 was reported by 43 (23.5%), grade 2 by 36 (19.7%), grade 3 by 12 (6.6%), and grade 4 by 5 (2.7%) patients. Relations between symptoms, COPD stage, and smoking status are shown in Table 5. Frequency and number of symptoms increased with the disease severity.

Table 5. Relations between symptoms, COPD stage and smoking status

	mild (n=56)		moderate (n=94)		severe (n=28)		v. severe (n=5)	
	ever smoker (n=38)	never smoker (n=18)	ever smoker (n=70)	never smoker (n=24)	ever smoker (n=24)	never smoker (n=4)	ever smoker (n=3)	never smoker (n=2)
no symptoms	13 34.2%	12 66.7%	23 32.9%	7 29.2%	4 16.7%	1 25.0%	0 0%	0 0%
cough	19 50.0%	1 5.6%	30 42.9%	11 45.8%	17 70.8%	3 75.0%	3 100%	2 100%
phlegm	12 31.6%	1 5.6%	27 38.6%	5 20.8%	18 75.0%	2 50.0%	3 100%	2 100%
dyspnoea	18 47.4%	6 50.0%	32 45.7%	12 50.0%	23 95.8%	3 75.0%	3 100%	2 100%

Smoking habits. There was a large gender difference in smoking habits in the studied cohort. Only 23.3% of the men were never smokers, compared to 60% of the women (Table 1). This difference was even more pronounced in COPD patients. Ninety six percent of the men with COPD were ever-smokers, with a mean tobacco exposure of 40 pack-years. Former smokers had a higher tobacco exposure (46.6 pack-years) than current smokers (35.5 pack-years). In female COPD patients, 52% were never smokers. Of the women who had ever smoked, 13% were former smokers and 35% were current smokers, with a mean total tobacco exposure of 20 pack-years.

Initiation of smoking was earlier in men than women ($p < 0.0001$). The intensity of tobacco smoking (cigarettes smoked per day) was twice as high in males than in females ($p < 0.0001$). Despite a lower cumulative exposure to nicotine in females, the difference in the Fagerström nicotine dependence test (FNDT) between males and females was lower than in tobacco exposure ($p < 0.001$) (Table 1).

Other risk factors. The relatively high prevalence of COPD in never smoking women led us to a post-hoc case-control survey about combustible material used by women for cooking (gas, coal, or wood). Eighty five never-smoking women with COPD were compared to 85 age-matched asymptomatic women with normal spirometry (healthy control subjects). Coal and wood material was used by 68.3% of women with COPD compared to being used by 44.7% of healthy control subjects ($p < 0.003$). Never smoking patients with COPD (both sexes) were older ($p < 0.0001$); more frequently lived in rural area ($p < 0.001$); and were more likely to have been born prematurely ($p < 0.002$) when compared to patients with no respiratory problems.

There was a significant relation between risk of developing COPD and education level. Three quarters of patients with COPD received only primary education compared to half of patients with no respiratory symptoms ($p < 0.0001$).

Low economic status was also associated with a higher risk of COPD compared to patients with no respiratory problems who more often declared satisfactory or good economic status ($p < 0.0001$).

DISCUSSION

In patients aged 40 years or older from this primary care practice, the prevalence of COPD was 9.3%. Only 19% of these patients had already been diagnosed and treated. Our results are strengthened by a high attendance rate (87%), and very high accuracy of spirometry tests (92% met ATS goals).

Results of our investigations are consistent with the results of epidemiological surveys of COPD in Poland. In a representative population sample of Warsaw, aged 42-71 years, COPD was diagnosed in 10.7% [13]. In a study performed in Silesia, a heavy polluted industrial region of Poland, the COPD prevalence in 19-69 year old adults was 10.2% [14]. We found higher prevalence of severe COPD than reported in country-wide epidemiological surveys of COPD in adults. Fukuchi et al. [8] found only 6% of adults with an FEV₁ lower than 50% of predicted. Severe COPD was found in 13% of adults surveyed in Spain [9].

We reduced over-diagnosis of COPD by using post-BD FEV₁/FVC to diagnose COPD. There were other factors that may have prevented over-diagnosis of COPD, like trained and supervised nurses, spirometer with quality grades, and feedback. Others [15] also reported a 27% lower COPD prevalence by using post-BD spirometry instead of pre-BD spirometry (thereby excluding some people with asthma). We also reduced over-diagnosis of COPD applying the 5th percentile of the FEV₁/FVC as a lower limit of normal [16] instead of a fixed 0.7 ratio [17, 18].

Gender. Our study did not confirm recent reports of a high prevalence of COPD among women [19, 20]. That finding may reflect pattern of smoking in Poland, with 40% of males vs. 23% of females smoking. In our study COPD was diagnosed in 12.8% of men and 7.1% of women. Only 50% of women diagnosed with COPD were current or ex-smokers. Also, total exposure to tobacco smoke was 50% lower in women than in men.. However, use of coal and biomass fuel by almost 70% of women with COPD might have influenced COPD rate in women [21]. Severe and very severe COPD ($FEV_1 < 50\%$ of predicted) was more than twice as frequent in men than in women (24.5% vs 11.7%). Proportions of men and women with COPD in our study was similar to that reported by recent surveys on COPD prevalence in five major Latin American cities [22] and Norway [15].

Spirometry in primary care. Our study confirmed that good quality spirometry testing can be accomplished in a primary care setting when several conditions are fulfilled. The spirometer model we selected met NLHEP criteria for office spirometers, including instant maneuver quality checks and messages [23]. This spirometer has been shown to retain long-term accuracy [24]. The two nurses performing the spirometry tests underwent two hands-on training courses in a reference pulmonary function laboratory. A strict quality assurance program closely monitored and reported the quality of the test sessions.

Poor quality spirometry tests increase the risk of misinterpreting the results, causing unnecessary stress to the patients due to falsely positive diagnoses. The cost and side effects of unnecessary treatment must also be considered. Low accuracy of spirometric tests in primary care was reported by Eaton et al [25]. However, more recent data from 8 rural primary care practices in Canada showed good quality spirometry testing performed with a portable office spirometer [26]. Under-utilization of spirometry in COPD diagnosis and management by primary care practitioners [27, 28] has led some experts to question the value of wide-spread COPD case-finding by primary care physicians [29]. However, proper training and monitoring of test quality may produce low misclassification rates in selected primary care settings [30, 31].

Widespread use of good quality spirometric testing in primary care would have a positive impact on the diagnosis, management, and prevention of severe stages COPD when disability is substantial, quality of life poor and costs of treatment very high [4]. Around 80% of COPD patients are in a mild or moderate stage of the disease. Early diagnosis allows many more years for successful anti-smoking activities [32], counseling and smoking cessation treatment [33]. Smoking cessation counseling combined with spirometry testing was shown to increase smoking cessation rate in COPD patients in some studies [34, 35], but not in others [36]. Long term follow-up of the Lung Health Study cohort have clearly shown that smoking cessation stops progression of the disease [37] and reduces mortality [38].

In many recent investigations on COPD detection by case-finding in primary care the percentage of newly diagnosed patients presenting with respiratory symptoms was strikingly high, attaining almost 50% [31, 36]. In our COPD group 68% were symptomatic with at least one symptom (cough, phlegm or dyspnoea) reported. Those patients qualify for treatment that may result in the considerable reduction in symptoms, increase in exercise capacity and improvement in health-related quality of life.

Patients with airflow limitation have high risk of lung cancer [39], coronary artery disease [40] and stroke [41]. A large proportion of patients with COPD die from non-pulmonary diseases [42, 43]. Preventive measures should be undertaken. Early diagnosis and treatment of cardiovascular diseases may be especially rewarding [44].

Risk factors. Smoking was by far the most important risk factor for COPD in these patients, especially the men. However, 52% of females with COPD never smoked. Looking for other

potential risk factors in never-smoking women, we found that they were significantly more often using coal or wood for cooking than women with normal lung function. Biomass fuels and coal used for cooking also account for COPD among non-smoking women in other regions of the world [21].

Another COPD risk factors in some of the non-smoking women was passive exposure to cigarette smoke and heavy physical work in the farm in unfavorable weather conditions, resulting in frequent respiratory infections. Passive smoking [45], and recurrent lower respiratory tract infections [46] may contribute to development and progression of COPD.

Our data warn against screening for COPD limited to current or ex-smokers. Half of women diagnosed with COPD never smoked. Analysis of relation between smoking status and symptoms in all COPD patients showed that 77% ever smokers were symptomatic compared to 23% in never smokers. However, among 44 never smoking women with COPD 28 (64%) were symptomatic. By screening only smokers we would have missed COPD diagnosis in 26% of cases. Screening only symptomatic patients would result in 32% missed cases.

Socioeconomic status. Patients with COPD declared low income and low educational level significantly more often than patients with normal respiratory function. Low educational level was found to be an independent risk factor for COPD in several large studies [47, 48].

Study limitations. Our study has several limitations. We used ECCS predicted values for spirometry that have been developed some decades ago and may not exactly fit for the current generation of adults in Poland. The recent prediction equations for Caucasians populations [49] may have resulted in lower COPD prevalence rates. However, as ECCS predicted values are still widely used in Europe we decided to follow a routine. Non-smoking status was not objectively verified. However, we believe that investigated subjects' declaration was true.

Our results may not apply to other communities and countries. Good quality spirometry testing may remain a problem in some primary care settings, despite physician and nurse training programs.

In summary, our study confirmed that COPD affected around 9% of the adult patients seen in a primary care setting in Poland. However, the disease was largely under-diagnosed without spirometry: only patients with severe disease ($FEV_1 < 50\%$ predicted) had been diagnosed and treated. Large number of newly detected patients were symptomatic and needed treatment. Limiting screening to smokers would have reduced the number of COPD diagnosis by 26%. COPD case-finding should be done using office spirometry in high risk patients, smokers and subjects with respiratory symptoms.

Acknowledgements

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Legends

Tables

Table 1. Characteristics of eligible patients and participating patients

Table 2. Spirometric classification of COPD severity

Table 3. Spirometric variables in subjects with COPD (mean \pm SD)

Table 4. Indicators for COPD in logistic regression model

Table 5. Relations between symptoms, COPD stage and smoking status

Figures

Figure 1. COPD prevalence and severity in relation to gender, age and smoking status.

Online Appendix

Table 1. The patients studied represented the local population.

Figure 1. Distribution of the pre-BD FEV₁/FVC showing 15.3% of patients (299) below the fifth percentile (mean minus 1.64 times the standardized residual).

Figure 2. Distribution of the FEV₁/FVC in 229 patients with post-BD airflow limitation.

Supplement online

Table 1. The patients studied represented the local population.

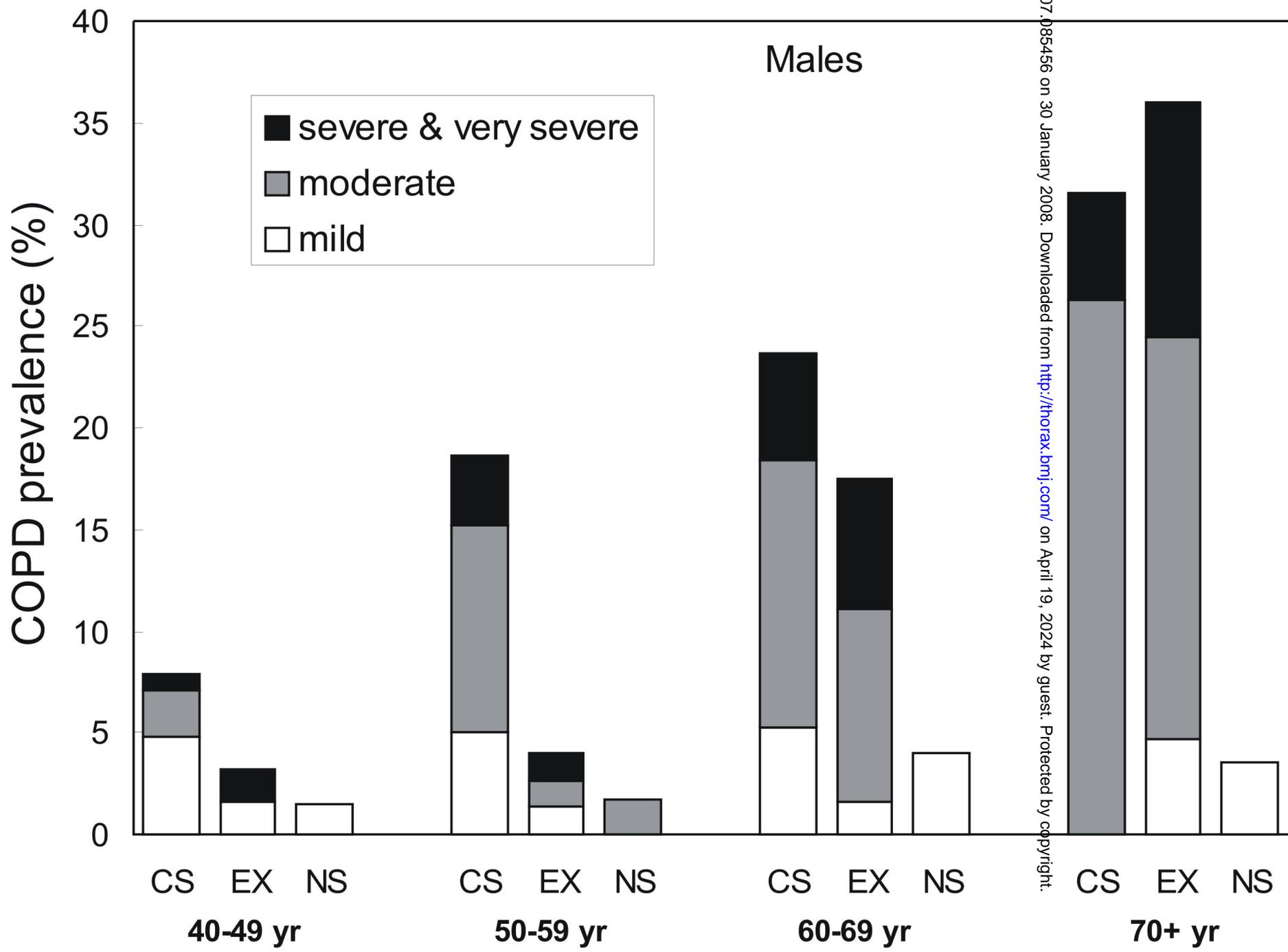
Age (years)	Population of Sierpc			Participating Patients			p
	Females N	Males N	Together N (%)	Females N	Males N	Together N (%)	
0-18	1981	2134	4115 (21.2)	501	489	990 (20.9)	NS
19-39	3347	3037	6384 (32.9)	770	720	1490 (31.5)	NS
40-65	3797	3347	7144 (36.8)	923	689	1612 (34.1)	NS
> 65	1023	757	1780 (9.2)	360	278	638 (13.5)	NS
Total, N (%)	10148 (52.2)	9275 (47.8)	19423 (100)	2554 (54.0)	2176 (46.0)	4730 (100)	NS

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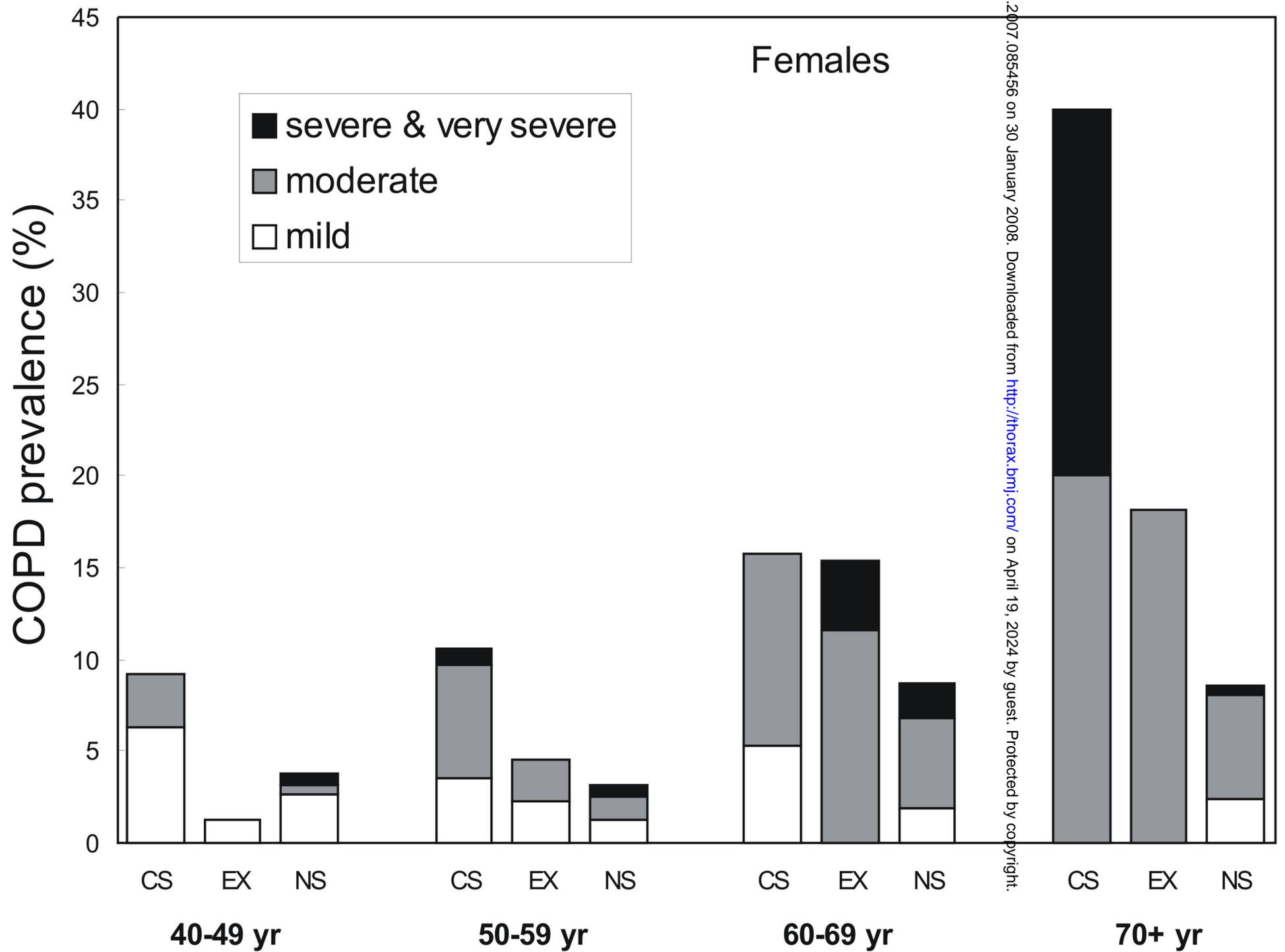
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