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Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking Report from the Obstructive Lung Disease in Northern Sweden Studies

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KEYWORDS
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Severity;
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Summary
Background: There is a lack of epidemiological data on COPD by disease severity. We have estimated the prevalence and underdiagnosis of COPD by disease severity defined by the British Thoracic Society (BTS) and Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. The impact of smoking was evaluated by the population attributable fraction of smoking in COPD.
Methods: A random sample of 1500 responders of the third postal survey performed in 1996 of the Obstructive Lung Disease in Northern Sweden (OLIN) Studies' first cohort (6610 subjects recruited in 1985) were invited to structured interview and spirometry. One thousand two hundred and thirty-seven subjects (82%) performed spirometry.
Results: The prevalence of mild BTS-COPD was 5.3%, moderate 2.2%, and severe 0.6% (GOLD-COPD: mild 8.2%, moderate 5.3%, severe 0.7%, and very severe 0.1%). All subjects with severe COPD were symptomatic, corresponding figures among mild COPD were 88% and 70% (BTS and GOLD), Subjects with severe BTS-COPD reported a physician-diagnosis consistent with COPD in 50% of cases, in mild BTS-COPD 19%, while in mild GOLD-COPD only 5% of cases. The major risk factors, age and smoking,

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had a synergistic effect on the COPD-prevalence. The Odds Ratio (OR) for having COPD among smokers aged 76–77 years was 59 and 34 (BTS and GOLD) when non-smokers aged 46–47 was used as reference population.
Conclusions: Most subjects with COPD have a mild disease. The underdiagnosis is related to disease-severity. Though being symptomatic, only a half of the subjects with severe COPD are properly labelled. Smoking and increasing age were the major risk factors and acted synergistic.

Introduction

Chronic obstructive pulmonary disease (COPD) is a common and disabling disease and a growing cause of mortality world wide.[1–3] During 1990s, several guidelines for management of COPD and diagnosing the disease were developed, among them were the British Thoracic Society (BTS) and the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines.[1,2] The prevalence of COPD is largely dependent on the age distribution of the studied population samples, their smoking habits, and which criteria for disease that has been used.[4] Whereas numerous cross-sectional studies of respiratory symptoms and diseases among young people and adults up to middle ages have been reported, there is still little data from studies including lung function among middle aged and elderly.[5,6] Thus, there are still limited data about prevalence of COPD according to recent guidelines among middle-aged and elderly subjects, in whom COPD is most common.[7–9] Further, data about disease severity and the size of the proportion of subjects with COPD who never were smokers as well are even more rare . Data from population studies are needed in order to explore these topics, as the slowly progressive nature of COPD[1] means that the disease usually remains undetected for years.[8–10]

The Obstructive Lung Disease in Northern Sweden (OLIN) Studies started in 1985–86,[11] and now several cohorts are under study. The age composition of the OLIN Studies first cohort, together with the large participation rate, provides an opportunity to study the epidemiology of COPD in relevant ages. The third postal survey of the cohort was performed in 1996 and was followed by structured interviews and lung function tests. COPD was strongly related to increasing age and smoking.[8] The main aim of this study was to measure prevalence and underdiagnosis of COPD by disease severity as defined by BTS[1] and GOLD guidelines[2] and to assess the proportion of symptomatics by degree of severity. Further aims were to study combined effects of increasing age and smoking as risk for COPD, and to evaluate the epidemiological concept population attributable fraction (PAF) with regard to smoking and COPD.

Material and methods

Study population

A random sample of 1500 subjects living in the northernmost province of Sweden was invited to structured interviews and lung function tests in 1996, and 1237 (82%), 51% women, completed a lung function test with acceptable technique.[8] Of women, 26% were current smokers versus 24% of men, 47% of men were ex-smokers versus 24% of women, while 51% of women were non-smokers versus 29% of men. Smoking was most common among subjects in the youngest age group both among men and women.[8]

The study sample was drawn from the responders of the postal questionnaire to the third survey[12,13] of the OLIN Studies' first cohort. The first survey of the OLIN cohort I was performed in 1985/86. All 6610 subjects born in 1919–20, 1934–35, and 1949–1950 living in eight areas were invited.[11] In 1996, 5892 subjects could be traced to the third survey, and 5189 (88%) responses were received, or 79% of the original study cohort from 1985. The study was approved by the Ethics Committee at Umeå University.

Methods

Structured interview

The interview questionnaire consisted of questions about respiratory symptoms, use of medicines, past and present smoking habits including exposure to environmental tobacco smoke, occupation, socio-economic group, and family history of obstructive airway diseases (OADs).[14] Questions about symptoms including cough, sputum production, wheezing, and dyspnoea were included. The OLIN postal questionnaire was developed from the original

British Medical Research Council (MRC) questionnaire and has been used in several Northern European studies,[15,16] and has also previously been described in detail.[15,17]

Lung function test

The lung function tests were performed by using a dry spirometer (Mijnhardt Vicatest 5) by following the ATS guidelines.[18] Reference values reported by Berglund[19] were used, which conforms to the symptom-free population of the OLIN Studies.[14] A reversibility test by using 4×0.2 mg Ventoline Discus® was performed in subjects with a ratio of FEV_1/FVC or $VC < 0.7$, or $FEV_1 < 90\%$ of predicted.

Definitions

COPD was classified according to the criteria developed by BTS (1) and GOLD (2). GOLD define COPD as $FEV_1/FVC < 0.7$, and BTS criteria include both $FEV_1/FVC < 0.7$ and $FEV_1 < 80\%$ of predicted values. The GOLD criteria include lung function after reversibility test, while the BTS criteria are not clear on that point. The BTS criteria mention both VC and FVC as denominators for the ratio. We have used the values after reversibility test, and the highest value of either VC or FVC. Further, BTS states that asthma with chronic obstruction may be included in COPD, while GOLD criteria do not clearly recommend to distinguish between asthma with chronic obstruction and COPD. Thus, subjects with chronic obstruction who stated that they had asthma have been included in the analyses.

The classification of smoking status was based on the answers to questions regarding smoking habits in the structured interview. Subjects who currently smoked every week or had stopped smoking within 12 months prior to the study were classified as smokers, while those who had stopped > than 12 months previously were classified as ex-smokers. Ever smokers include current- and ex-smokers. Never smokers refer to subjects who have never been smokers, i.e. they are not current- or ex-smokers.

Use of "airway medicines" included affirmative answers to questions regarding regular or as-needed use of beta-2-agonists and/or inhaled anticholinergics and/or inhaled glukocorticosteroids and/or expectorantia.

Grading of severity

The severity of COPD is defined by level of FEV_1 in % of predicted, and the grading of severity vary: BTS defines severe COPD as $FEV_1 < 40\%$ predicted, moderate COPD as $FEV_1 \geqslant 40\% < 60\%$ predicted and mild COPD as $FEV_1 \geqslant 60\% < 80\%$ predicted. GOLD defines very severe disease as $FEV_1 < 30\%$ predicted, severe COPD as $FEV_1 \geqslant 30\% < 50\%$ predicted, moderate COPD as $FEV_1 \geqslant 50\% < 80\%$ predicted, and mild COPD as $FEV_1 > 80\%$ predicted. Very severe COPD according to GOLD includes also subjects with $FEV_1 \geqslant 30\% < 50\%$ predicted in case of having hypoxemia. In the current study, blood gases were not measured.

Analyses

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS). χ^2-square test was used for bi-variate calculations. Determinants for COPD were calculated by multiple logistic regression analysis, in which the independent variables were age, gender, smoking habits, socio-economic group based on occupation,[20] and family history of OAD, i.e. of asthma, chronic bronchitis, emphysema or COPD. Age groups and smoking habits created a combined variable with nine categories. Odds ratios (ORs) are reported with 95% confidence intervals (CI). P-values < 0.05 were regarded statistically significant.

The risk difference (RD) or attributable risk for ever smoking was calculated: risk exposed (ever smoker) (R_e)—risk un-exposed (never-smoker) (R_0). The population attributable risk (PAR) was calculated: RD × prevalence of ever smoker (p), which is the occurrence of the disease attributable to exposure. The PAF is the fraction of all cases in the population due to exposure and was calculated: (prevalence of ever smoker (p)(Risk Ratio (RR)−1))/(1+p(RR−1)).[21,22]

Result

The prevalence of COPD was strongly smoking dependent and increased considerably with increasing age (Table 1). The prevalence of COPD increased almost linear from the age of 47 years in smokers, while in non-smokers the increase started after the age of 62 years (Fig. 1).

COPD by disease severity

The distribution of the disease severity among the subjects with COPD according to the BTS criteria was: 65% mild disease, 27% moderate, and 8% severe disease. The corresponding distribution of COPD according to the GOLD criteria was: 57% mild,

Table 1 Prevalence of COPD by age and smoking according to the BTS and GOLD criteria, respectively.

Criteria	Category	46–47 years	61–62 years	76–77 years	All	Difference (*P*-value)	
						Age	Smoking
GOLD	Non-smoker	3	5	21	7.8		
	Ex-smokers	6	14	33	14.5		
	Smokers	11	42	50	24.6		
	Total	6.5	17.1	28.7	14.3	<0.001	<0.001
BTS	Non-smokers	1	2	16	3.8		
	Ex-smokers	2	7	20	7.6		
	Smokers	5	24	45	14.1		
	Total	2.8	9.0	19.7	8.1	<0.001	<0.001

Difference (*P*-value) by age and smoking habits.

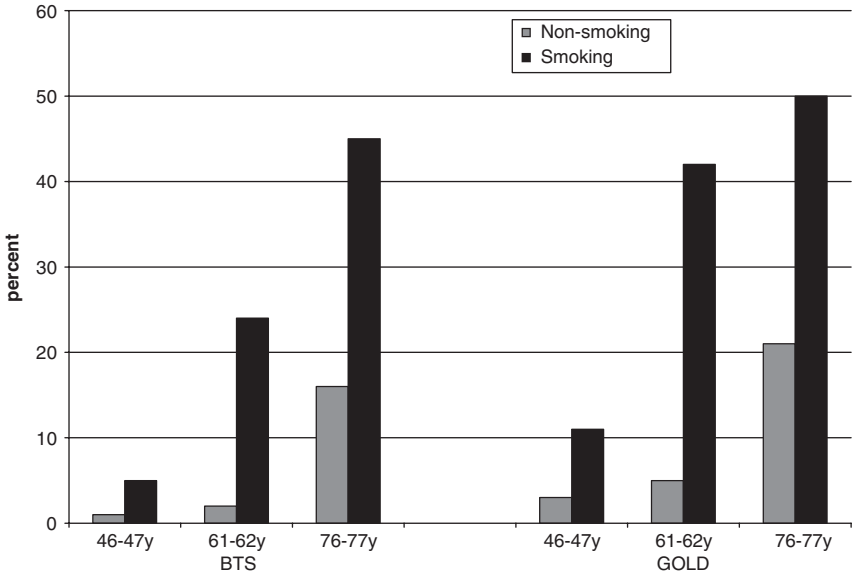

Figure 1 Prevalence of COPD according to the BTS and GOLD criteria by age, in smokers and non-smokers.

37% moderate, 5% severe, and 1% very severe disease (Fig. 2). Estimated at population level, the prevalence of mild COPD according to BTS was 5.3%, moderate 2.2%, and severe 0.6%. Corresponding prevalence rates according to GOLD were mild COPD 8.2%, moderate 5.3%, severe 0.7%, and very severe disease 0.1%.

Underdiagnosis and symptoms by disease severity

Of the subjects fulfilling the criteria for COPD and having $FEV_1 < 40\%$ of predicted (severe COPD according to BTS), 88% had chronic productive cough, and 100% had either longstanding cough, sputum production, recurrent wheeze, attacks of shortness of breath, or dyspnoea of at least MRC grade 2. Among them, 50% were diagnosed as having chronic bronchitis, emphysema, or any labelling synonymous with COPD, and 100% used airway medicines (Table 2). The corresponding figures for mild COPD according to GOLD were as follows: 21% reported chronic productive cough, 70% were symptomatic, and only 5% were diagnosed as having chronic bronchitis, emphysema, or COPD, and 10% were using airway medicines. Further, among subjects with mild COPD according to GOLD, 18% were either using airway medicines, or reported a diagnosis of chronic bronchitis, emphysema, COPD, or asthma prior to the survey (Table 2).

Multivariate relationships

The combined effects of age and smoking have been explored more in detail by multiple logistic

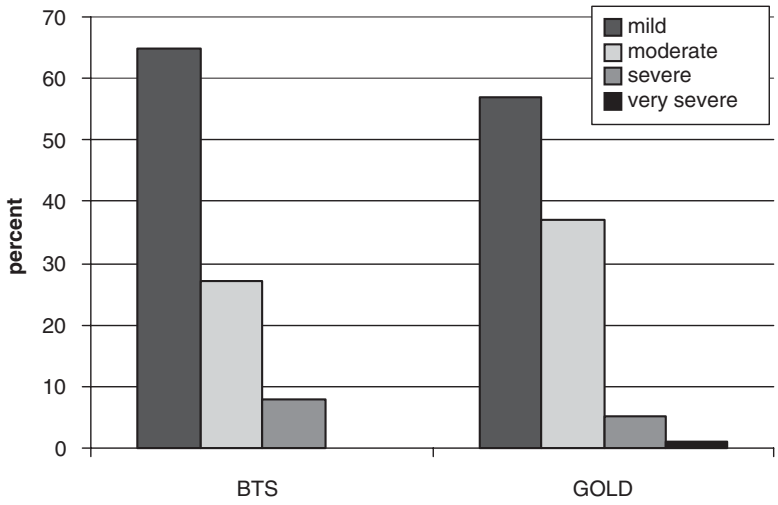

Figure 2 Prevalent cases of COPD according to the BTS and GOLD criteria, distribution by disease severity.

Table 2 Proportion (%) of diagnosed subjects, symptomatics, users of airway medicines or expectorantia, including *N*-acetylcysteine, and self-reported obstructive airway disease (OAD) among subjects with COPD ($FEV_1/VC < 0.7$) by different levels of FEV_1.

Condition	$FEV_1 < 40\%$ of predicted	FEV_1 40–59% of predicted	FEV_1 60–79% of predicted	$FEV_1 \geqslant 80\%$ of predicted
Symptomatics	100	91	88	70
Chronic productive Cough	88	63	51	21
Physician-diagnosed chronic bronchitis, emphysema or COPD	50	28	19	5
Use of medicines	100	47	26	10
Use of medicines, or any self-reported OAD	100	63	42	18

regression analysis. Other independent variables included in the multivariate model were gender, socio-economic group based on occupation, and family history of OAD. Gender was not significantly associated with COPD, while family history of OAD was significantly related with COPD according to BTS. In comparison with non-smokers in the subjects aged 46–47 years, the non-smokers aged 61–62 years yielded an OR of 1.36 for having COPD according to BTS and of 2.09 for COPD according to GOLD, both without reaching a significant difference. However, the effect of age was stronger among non-smoking subjects aged 76–77 years, and the OR for COPD according to BTS was 11.71 (95% CI 3.34–41.03), while it was 9.97 (95% CI 4.17–23.84) for COPD according to GOLD (Table 3).

In smoking subjects aged 46–47 years, the OR was 3.38 (95% CI 0.90–12.69) for having COPD according to BTS, while it was 4.48 (95% CI 1.89–10.65) for COPD according to GOLD. The combined effect of smoking and age appeared highly significant among subjects aged 61–62 years and yielded odds rations > 20 for COPD according to both criteria. The ORs for smokers aged 76–77 years were 58.96 and 33.66 (COPD according to BTS and GOLD, respectively), and both highly significant compared with non-smokers aged 46–47 years. The combined effect of increasing age and smoking illustrates a multiplicative effect (Table 3).

COPD and smoking

In subjects with COPD according to BTS 76% were ever smokers (GOLD 77%), and the proportion was 89% among men (GOLD 84%) and 64% in women (GOLD 68%) (Table 4). All men with severe COPD according to BTS were smokers or ex-smokers, while 86% with moderate and 90% with mild COPD were smokers or ex-smokers. In all subjects with

Table 3 Risk factors (Odds ratios, OR and 95% confidence intervals, CI) for COPD according to GOLD (COPD-GOLD) and BTS (COPD-BTS) criteria, respectively, by multiple logistic regression analysis.

Independent variables	Dependent variables			
	COPD-GOLD		COPD-BTS	
	OR	95% CI	OR	95% CI
Sex				
Men	1		1	
Women	1.12	0.66–1.88	1.32	0.72–2.23
Family history of OAD				
No	1		1	
Yes	1.33	0.92–1.95	1.94	1.21–3.12
Age and smoking habits combined				
Age 46–47 years, non-smoker	1		1	
Age 46–47 years, ex-smoker	2.35	0.94–5.92	1.43	0.32–6.50
Age 46–47 years, smoker	4.48	1.89–10.65	3.38	0.90–12.69
Age 61–62 years, non-smoker	2.09	0.81–5.35	1.36	0.30–6.15
Age 61–62 years, ex-smoker	5.84	2.46–13.87	5.41	1.48–19.85
Age 61–62 years, smoker	22.02	9.45–51.34	20.97	6.15–71.43
Age 76–77 years, non-smoker	9.97	4.17–23.84	11.71	3.34–41.03
Age 76–77 years, ex-smoker	15.75	6.59–37.66	17.2	4.84–61.07
Age 76–77 years, smoker	33.66	10.53–107.58	58.96	13.82–251.48

The independent variables include sex, family history of obstructive airway disease (OAD), and the combination of smoking habits and age-class.

COPD (BTS) in the age groups 46–47 years, 81% were ever smokers, and in those aged 61–62 years 90% (GOLD 85% in both age groups), while in the age group 76–77 years it was 62–61% according to both criteria. The corresponding figures among women with COPD according to BTS were 83% in severe, 69% in moderate and 59% in mild disease. The proportion of smokers and ex-smokers was similar by disease severity of COPD according to GOLD.

Attributable fraction and population attributable risk

The PAF of ever smoking in COPD according to BTS was 41% (men 64%, women 29%). The corresponding figures for COPD according to GOLD were similar but yielded somewhat smaller gender differences (Table 4). Further, the PAR of ever smoking in COPD was calculated (Table 4). The fraction of COPD according to BTS in the population attributable to ever smoking was also calculated by age, and was in subjects aged 46–47 years 47% (GOLD 58%), in those aged 61–62 years 76% (GOLD 65%), while it was lower in the elderly aged 76–77 years, 21% (GOLD 22%).

Table 4 Proportions of ever smokers (prop %) among subjects with COPD according to the BTS and GOLD in men and women.

Criteria	Category	Prop (%)	PAF*	PAR†
COPD-BTS	All	76	41	0.033
	Men	89	64	0.050
	Women	64	29	0.025
COPD-GOLD	All	77	43	0.073
	Men	84	46	0.087
	Women	68	37	0.056

Population attributable fraction (PAF) and population attributable risk (PAR) of ever smoking in COPD.
*Attributable fraction in the study population, percent.
†Population attributable risk.

Discussion

In order to further deepen the knowledge of the descriptive epidemiology of COPD, we have examined the prevalence and underdiagnosis of COPD by disease severity. In addition to calculation of single risk factors for COPD, the risk combination of increasing age and smoking and the PAR of ever smoking in COPD were estimated. We have

previously reported the prevalence of COPD and its major risk factors in the same age-stratified sample of the general population.[8]

The major findings of this study are that increasing age and smoking are the two dominating risk factors for COPD. Among men, 89% were current or ex-smokers of the subjects fulfilling the spirometric criteria (BTS) for COPD. The proportion of never smokers among subjects classified as having COPD (BTS) was somewhat greater than expected among women, 36%. These findings will be further discussed. Secondly, although the majority of subjects suffering from COPD had a mild disease, a large proportion of this population >45 years, 3–6%, had a moderate or severe COPD.

There are limited data in the literature about COPD by disease severity. The overall prevalence of COPD in Northern Sweden conforms well to results from large studies in USA, Spain, Italy and Norway.[7,9,23,24] Regarding disease severity, the prevalence of mild COPD was 5.3% (BTS)–8.2% (GOLD), or similar to the 6.9% according to GOLD found in the US NHANES III survey.[25] Moderate, severe and very severe COPD according to GOLD was in our study 6.1% versus 6.6% in the NHANES III. Analyses of NHANES I from 1970s found severe and very severe COPD with $FEV_1 < 50\%$ of predicted normal value to be 1.7% in the US population,[26] and this proportion was similar 20 years later[9] and somewhat higher than in our study, in which it was 0.9%. Distribution by severity of incident COPD (GOLD) over 15 years in the Copenhagen City Heart Study conforms also well with the overall impression; mild COPD accounted for 7.2%, moderate for 5.8%, and severe for 0.2%.[27] The prevalence of severe COPD (i.e. identical with severe BTS according to the later published BTS Guidelines) in Bergen, Norway, was 0.2% compared with 0.6% in our study.[23] We have to keep in mind that the average age particularly in the NHANES and the Norwegian studies were younger than in our study. Further, the very low proportion of severe COPD in this cross-sectional setting has to be studied also prospectively, as it may reflect poor survival.

Only 20–30% of the subjects fulfilling the criteria for COPD had been correctly identified prior to the study. The underdiagnosis of COPD was related to disease severity. In severe COPD according to BTS every other subject had a diagnosis consistent with COPD, and they all reported respiratory symptoms. Of subjects with mild disease (GOLD), only 5% were diagnosed as having chronic bronchitis, emphysema, or labellings synonymous with COPD, while 18% either used medicines for the airways or reported any diagnosis of a respiratory disease. The overall degree of underdiagnosis conforms to previous findings.[9,10,28]

The combined effect of smoking and age, as given in uncorrected estimates of prevalence in Fig. 1, and in terms of adjusted odds ratios in Table 3, is the largely dominating determinant of COPD in a cross-sectional setting. The studied sample consisted of middle-aged and elderly, and the majority of smokers have been smoking since decades. The average age of start of smoking was 14 years.[11] It would have been an advantage if the exposure could have been expressed in quantitative terms as pack-years. However, retrospective assessments of pack-years are accompanied with uncertainty, and dividing the smokers by exposure categories would have enlarged the already very wide confidence intervals. Analysis of cotinine levels can increase the strength of data on smoking-status, but no lab-tests were performed in this study. Though a recall bias on previous smoking history is known (mainly underestimating previous smoking), it is considered reliable to use self-reported smoking status in population-based studies.[29,30]

Smoking and increasing age are the major risk factors for COPD, and among men with severe COPD all were current or ex-smokers. Some of the women fulfilling the criteria of COPD reported no history of smoking, most frequent among elderly women, aged 76–77 years, and women with mild COPD (63% and 41%, respectively). The overall non-smoking cases of COPD were most commonly found in elderly aged 76–77 years. The strong relationship between smoking and COPD found in this study was on a similar level as reported by the NHANES III,[26] while in the Copenhagen City Heart Study the association with smoking and COPD was found to be weaker.[27]

Non-smokers with COPD has only rarely been studied, but have been recognised among others by Siafakas et al.[31] Smoking was more common in the past in Sweden and most Nordic countries as well. Environmental tobacco smoke may contribute to COPD in non-smokers,[32] but also overall airborne exposure over the lifetime and a low socio-economic status.[23] However, among the elderly the combination of normal ageing and the use of the fixed ratio defining COPD contribute to an overestimation of COPD.[6] This may have a major impact on the proportion of non-smokers among subjects defined as having COPD as the majority were elderly subjects with mild COPD. There is a need for further studies on this sub-population of elderly never smokers in order to clarify to which extent there is an overestimation of COPD, in how many cases asthma contributes to a chronic

obstruction, how many can really be regarded as having COPD or can be considered respiratory healthy. After taking these questions into account, further analysis of risk factors for COPD among non-smokers could be evaluated. It is already known that the proportion of subjects with alpha-1-anti-trypsine deficiency is not big enough to have any major influence on population level.[33]

Close to 90% of men with COPD were smokers or ex-smokers and age is an important risk factor, but also other risk factors as the total amount of airborne exposure contributes to COPD. However, smoking can almost be regarded as a necessary risk factor for COPD, especially among subjects with severe COPD. The PAF include evaluation of and correction for several risk factors contributing to a disease. PAF is regarded as a measure of the public health impact of a certain exposure, while it is a function of the potential harm of the exposure (through the relative risk) and how common the exposure is (through its prevalence, in this study proportion of ever-smokers). It has been used in evaluating occupational exposure in COPD.[34] The PAF in COPD of ever smoking express the proportion of the population with COPD that is or has been attributed to smoking. Our results demonstrate the importance of smoking as the PAF of smoking in COPD increased to almost 80% in ages 61–62 years but it was less in the elderly (76–77 years). The probable explanation of the decreased importance of smoking in elderly is the use of the fixed ratio for the definition of airway obstruction. As previously discussed, the spirometric criteria of COPD with a fixed quotient will overestimate COPD among elderly and include also non-smokers without respiratory symptoms.[6] Further, as stated in the section definition, patients with chronic obstruction due to asthma but fulfilling the spirometric criteria of COPD were not excluded, and we can expect that asthma contributed to some of the non-smoking cases of COPD. The guidelines definition of COPD[1,2] does not exclude asthma as a cause of chronic obstruction, and the proportion of non-smokers in COPD, though low, has to be interpreted in accordance. The PAF of smoking in COPD has to be evaluated in relation to factors as age, definition of COPD, disease severity, but also concomitant asthma, otherwise the public health impact of smoking in COPD may be underestimated.

In this epidemiological study, the data collected were based on structured interview and spirometry and the diagnosis of COPD was based on spirometric criteria. The results are to be interpreted in accordance with the methods used. The diagnosis and possible overestimation of COPD among elderly has been discussed here and also by others.[6] Further, the possible heterogeneity of subjects classified as having mild COPD, especially among elderly, has to be surveyed and is also an important area for future epidemiological studies. PAF is a well-known epidemiological concept, but previously hardly used in the aspect of describing the impact of smoking in COPD. It is of importance to increase the knowledge in the descriptive epidemiology of COPD, but also important, as discussed, to evaluate both the strength and weakness when using new methods.

In conclusion, in a cross-sectional setting, the majority of subjects with COPD irrespective of criteria had mild COPD, but almost a half had a moderate or severe COPD. The small proportion having severe COPD may reflect a poor survival and has to be studied longitudinally. Smoking and increasing age are the dominating risk factors for COPD. The PAF of smoking for COPD was close to 80% in ages 61–62 years. However, PAF was related to age and is most probably related also to disease severity and needs further evaluation with respect to these factors when assessing the public health impact of smoking in COPD.

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