Respiratory Medicine 217 (2023) 107347

Contents lists available at ScienceDirect

Respiratory Medicine

journal homepage: www.elsevier.com/locate/rmed

Original Research

Underdiagnosis and misclassification of COPD in Sweden – A Nordic Epilung study

Malin Axelsson [a,*], Helena Backman [b], Bright I. Nwaru [c,d], Caroline Stridsman [e], Lowie Vanfleteren [c,f], Linnea Hedman [b], Päivi Piirilä [g], Juuso Jalasto [g], Arnulf Langhammer [h,i], Hannu Kankaanranta [c,j,k], Madeleine Rådinger [c], Linda Ekerljung [c], Eva Rönmark [b], Anne Lindberg [e]

[a] Department of Care Science, Faculty of Health and Society, Malmö University, Malmö, Sweden
[b] Department of Public Health and Clinical Medicine, Section of Sustainable Health/ the OLIN unit, Umeå University, Umeå, Sweden
[c] Krefting Research Centre, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden
[d] Wallenberg Centre for Molecular and Translational Medicine, Institute of Medicine, University of Gothenburg, Gothenburg, Sweden
[e] Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden
[f] COPD Center, Department of Respiratory Medicine and Allergology, Sahlgrenska University Hospital, Gothenburg, Sweden
[g] Unit of Clinical Physiology, HUS Medical Diagnostic Center, University Central Hospital, Helsinki, Finland and University of Helsinki, Finland
[h] HUNT Research Centre, Department of Public Health and Nursing, NTNU, Norwegian University of Science and Technology, Levanger, Norway
[i] Levanger Hospital, Nord-Trøndelag Hospital Trust, Levanger, Norway
[j] Department of Respiratory Medicine, Seinäjoki Central Hospital, Seinäjoki, Seinäjoki, Finland
[k] Faculty of Medicine and Life Sciences, University of Tampere, Tampere, Finland

ARTICLE INFO

Keywords:
COPD
Population study
Epidemiology
Underdiagnosis
Misclassification

ABSTRACT

Introduction: The prevalence of COPD tends to level off in populations with decreasing prevalence of smoking but the extent of underdiagnosis in such populations needs further investigation.
Aim: To investigate underdiagnosis and misclassification of COPD with a focus on socio-economy, lifestyle determinants and healthcare utilization.
Method: The 1839 participants were selected from two ongoing large-scale epidemiological research programs: The Obstructive Lung Disease in Northern Sweden Studies and the West Sweden Asthma Study. $COPD_{GOLD}$ was defined according to the fixed post-bronchodilator spirometric criteria FEV1/FVC<0.70 in combination with respiratory symptoms.
Results: Among the 128 participants who fulfilled the criteria for $COPD_{GOLD}$, the underdiagnosis was 83.6% (n = 107) of which 57.9% were men. The undiagnosed participants were younger, had higher FEV1% of predicted and less frequently a family history of bronchitis. One in four of the undiagnosed had utilized healthcare and had more frequently utilized healthcare due to a burden of respiratory symptoms than the general population without COPD. Underdiagnosis was not related to educational level. Misclassification of COPD was characterized by being a woman with low education, ever smoker, having respiratory symptoms and having a previous asthma diagnosis.
Conclusion: In the high income country Sweden, the underdiagnosis of COPD was highly prevalent.
Reduced underdiagnosis can contribute to risk factor modification, medical treatment and self-management strategies in early stages of the disease, which may prevent disease progression and improve the quality of life among those affected. Therefore, there is a need to increase the use of spirometry in primary care to improve the diagnostic accuracy.

* Corresponding author. Department of Care Science, Faculty of Health and Society, Malmö University, SE-205 06, Malmö, Sweden.
E-mail address: malin.axelsson@mau.se (M. Axelsson).

https://doi.org/10.1016/j.rmed.2023.107347
Received 27 April 2023; Received in revised form 27 June 2023; Accepted 1 July 2023
Available online 3 July 2023

1. Introduction

Chronic Obstructive Pulmonary Disease (COPD), is a common disease that poses a high economic burden on health care and society [1] and it is the third leading cause of death in the world according to the World Health Organization [2]. A recent systematic review estimated the global prevalence of COPD to 10.3%, corresponding to around 391.9 million people aged 30–79 years [3]. Until recently, the prevalence has steadily increased [4] but in some high-income countries where tobacco smoking has decreased in the population, the prevalence of COPD seems to be levelling or even decreasing [5–9]. Although the prevalence may be leveling off, underdiagnosis of COPD is still high worldwide and a majority of those suffering from COPD are not identified as having COPD or any other obstructive airway disease [4,10–14].

In Europe and North America, around and after the millennium shift, the underdiagnosis of COPD ranged from 70% to 90% according to several large-scale population studies [10–13], and in Latin America, the underdiagnosis was estimated at around 90% [14]. From a global perspective, the range for underdiagnoses varies between 10 and 95% [15]. Even though increasing attention has been paid to COPD in health care and the public awareness has increased, underdiagnosis of COPD has remained high also in the Scandinavian countries [16–18]. Besides underdiagnosis, misclassification of COPD is common. Recent results from the large scale, multinational Burden of Obstructive Lung Disease (BOLD) study have revealed that a large proportion of study participants given the diagnosis of COPD did not fulfil the spirometry criteria for the disease [19], which also has been reported in a study conducted in Italy [20] and in a quite recent review [13]. Similar misclassification has also been found in Scandinavia [21,22]. Major reasons for both underdiagnosis and misclassification of COPD have been related to under-utilization of spirometry and lack of uniformity in diagnostic criteria [15]. Accurate and early diagnosis of COPD is crucial for secondary prevention of the disease progression [1], mainly by means of smoking cessation [23], modification of other riskfactors regarding environmental exposures and lifestyle, and by pharmacological intervention [1].

Two ongoing large-scale epidemiological research programs focusing on obstructive respiratory diseases include surveys of random samples of the population in northern [24] and southwestern Sweden [25]. Results from these programs have shown a COPD prevalence of 7.0%, in age group 21–78 years, based on post-bronchodilator spirometric criteria in combination with respiratory symptoms [8]. While our previous study investigated the prevalence of COPD after decades of changing smoking habits [8], the current study aimed to investigate underdiagnosis and misclassification of COPD with a focus on socio-economy, lifestyle determinants and healthcare utilization.

2. Methods

2.1. Study areas

The study was performed in the regions of Norrbotten in northern Sweden and Västra Götaland in southwestern Sweden and is based on two ongoing large-scale epidemiological research programs: The Obstructive Lung Disease in Northern Sweden (OLIN) Studies, in progress since 1985 [16,26–28] and the West Sweden Asthma Study (WSAS), which started in 2008 with a similar basic study design [25,29–31]. The Regional Ethical Review Boards in Umeå and Gothenburg, Sweden, have approved the research programs (Dnr 1991–236, 2005-157 M and 2008-593–08).

2.2. Study population

In 2006, two random samples of the population in Norrbotten, aged 20–69 years and 30–84 years, were invited to a postal questionnaire survey and 12 055 participated, corresponding to a response-rate of 80% [32]. In 2008-2009, after stratification by age and sex to resemble the population demographics in Norrbotten, a random sample of 1016 responders to the postal questionnaire was invited to a clinical examination including pre- and post- bronchodilator spirometry and a structured interview. In total, 726 (71.5%) participants performed an adequate quality spirometry measurement and completed the structured interview [33].

In 2008, a postal questionnaire was sent to 30 000 randomly selected inhabitants in Västra Götaland aged 16–75 years. In total, 18 087 responded, which corresponds to a response-rate of 62% and a study of late- and non-response verified a high representativeness [34]. In 2009-2012, after stratification by age and sex to resemble the population demographics in Västra Götaland, a random sample of 2000 responders to postal questionnaire was invited to a clinical examination including pre- and post-bronchodilator spirometry and a structured interview. In total, 1158 (58%) participants performed an adequate quality spirometry measurement and completed the structured interview [25,30,31].

Data from the clinical examinations of the participants from both OLIN and WSAS in the overlapping age range 21–78 years have been pooled in the current study. Thus, the sample of this study comprised 1839 participants; mean age 51.1 years (SD 14.8 years), and 52.6% women.

2.3. Questionnaire

The Swedish OLIN-questionnaire [24] was used in both study areas. It has been used in several epidemiological studies both nationally and internationally [35–38], and it has been validated against the Global Allergy and Asthma European Network (GA^2LEN) questionnaire [39]. It consists of a self-administrated short version for postal surveys, and a longer version for structured interviews. In addition, questions from the Swedish version of the GA^2LEN questionnaire were included [40,41]. The questionnaires includes questions about respiratory symptoms, respiratory diseases, medication, potential risk factors for respiratory diseases, such as family history of obstructive airway diseases, socio-economic status and smoking habits and healthcare utilization related to respiratory problems.

2.4. Spirometry

A daily calibrated Masterscope (Jaeger) spirometer was used in both study areas. Height and weight were measured before the spirometry and, at least three and a maximum six forced vital capacity (FVC) measurements were performed. The difference between the two highest values of both FVC and forced expiratory volume during the first second of the expiration (FEV_1) values had to be <5% and <150 ml, or <100 ml for values < 2.0 L. In OLIN, the bronchodilation test was performed using 0.4 mg salbutamol via discus, while in WSAS, a combination of 0.4 mg salbutamol and 80 mcg ipratropium-bromide via spacer was used. The OLIN reference values for spirometry were used [42].

2.5. Definitions

COPD was defined based on spirometric criteria and, in addition respiratory symptoms were required. We used the spirometric criteria of GOLD (Global Initiative of Obstructive Lung Disease) and LLN (Lower Limit of Normal) divided into the categories 1-3 presented below. The following chronic or recurrent respiratory symptoms within the last 12 months; longstanding cough, chronic productive cough, sputum production, mMRC dyspnea scale≥2, recurrent wheeze, persistent wheeze and/or attacks of shortness of breath were also required to define:

1. $COPD_{GOLD}$: Post-bronchodilator (post-BD) $FEV_1/FVC<0.70$
2. $COPD_{GOLD>2}$: Post-BD $FEV_1/FVC<0.70$ & $FEV_1<80\%$ of predicted

3. $COPD_{LLN}$: Post-BD FEV_1/FVC < LLN, i.e. the lower 5th percentile of the reference value in line with the European Respiratory Society and the American Thoracic Society [43].

Underdiagnosis was defined as participants fulfilling the above criteria of COPD but who did not have a self-reported diagnosis of COPD. See below definitions of self-reported diagnosis.

Misclassification was defined as participants not fulfilling the above criteria of COPD but who had a self-reported diagnosis of COPD. See below definitions of self-reported diagnosis.

Self-reported physician-diagnosed COPD was defined as an affirmative answer to: Have you been diagnosed as having chronic obstructive pulmonary disease by a doctor?

Self-reported physician-diagnosed chronic bronchitis, COPD, or emphysema was defined as an affirmative answer to: Have you been diagnosed as having chronic bronchitis (CB), chronic obstructive pulmonary disease (COPD) or emphysema by a doctor?

Self-reported physician-diagnosed asthma was defined as an affirmative answer to: Have you been diagnosed as having asthma by a doctor?

Self-reported medication use for obstructive airway disease was defined as an affirmative answer to: Have you been using medication for obstructive airway disease during the last 12 months?

Self-reported Any obstructive airway disease (OAD) was defined as any of Self-reported physician-diagnosed COPD/chronic bronchitis, COPD, or emphysema/asthma or Have you used medication for obstructive airway disease during the last 12 months?

Smoking habits were divided into never-smokers, ex-smokers or current smokers. Ever smokers were defined as ex-smokers or current smokers. Pack years were calculated for ever smokers.

Occupational exposure to gas, dust or fumes (GDF) was defined as an affirmative answer to: Have you been heavily exposure to gas, dust or fumes at work?

Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meter and classified according to the WHO definition and then dived into two categories (<25 and ≥ 25).

Socioeconomic status was based on educational level: high educational level = university education and low educational level = high school or less.

Family history of asthma was defined as an affirmative answer to: Have any of your parents, brothers or sisters had asthma?

Family history of chronic bronchitis was defined as an affirmative answer to: Have any of your parents, brothers or sisters had chronic bronchitis?

2.5.1. Definitions of healthcare utilization

- *Ever medical care* = Ever medical care due to respiratory symptoms
- *Medical care* 12 months = Medical care due to respiratory symptoms last 12 months
- *Ever hospitalized* = Ever hospitalized due to respiratory symptoms
- *Ever emergency care* = Ever emergency care due to respiratory symptoms

2.6. Statistical analyses

The IBM SPSS Statistics version 26 (Armonk, NY: IBM Corp) was used for statistical analyses. Descriptive statistics were used to describe the study population. Chi-square tests were used to test for differences in proportions and t-tests to compare mean values between groups. P-values <0.05 were considered statistically significant.

3. Results

In total, approximately, 38% of the participants were inhabitants in Norrbotten and 62% in Västra Götaland (in total 49% in the City of Gothenburg and 13% outside the city). Of the total sample (n = 1839 participants), 128 (7.0%) fulfilled the criteria for $COPD_{GOLD}$, corresponding to 8.3% in men and 5.8% in women. The criteria for $COPD_{GOLD}$ ≥2 was fulfilled by 65 in while the criteria for $COPD_{LLN}$ was fulfilled by 84 participants. In the total sample, the prevalence of $COPD_{GOLD}$ by age groups was 2.2% among those <40 years, 5.4% in 40–60 years and 12.8% among those >60 years.

Participants with $COPD_{GOLD}$ were in general more frequently male, older, current or ex-smokers, had more pack years, lower educational level and had more often a family history of chronic bronchitis, respiratory symptoms, occupational exposure to GDF and healthcare contacts compared to those without $COPD_{GOLD}$ (Table 1).

In the total sample, aged 21–78 years, self-reported physician-diagnosed prevalence of COPD was 1.5%, 4.5% for chronic bronchitis, COPD or emphysema, and 18.8% for any obstructive airway disease. Those with self-reported physician-diagnosed COPD were more likely to have lower educational level and to report occupational exposure to GDF than those without self-reported physician diagnosed COPD. The broader the definition of obstructive airway disease used, the greater the proportion reporting occupational exposure to GDF tended to be (Table 2).

4. Underdiagnosis of COPD

Among the 128 individuals with $COPD_{GOLD}$, 16.4% had a self-reported physician-diagnosed COPD and 23.4% reported a physician-diagnosis of chronic bronchitis, COPD or emphysema (Table 3). Distribution of self-reported COPD, chronic bronchitis, COPD or emphysema, asthma, medication and OAD did not differ significantly when comparing between sexes, between high or low level of education or occupational exposure of GDF or not (Table 3).

Further analyses when participants with self-reported physician-diagnosed asthma (n = 38) were removed, showed that out of the remaining 90 participants 14 (15.6%) reported physician-diagnosed COPD, 19 (21.1%) reported a physician-diagnosis of chronic bronchitis, COPD or emphysema and 20 (22.2%) reported any OAD.

Fig. 1 illustrates the underdiagnosis in relation to different definitions of COPD: among those with $COPD_{GOLD}$, 83.6% did not have a previous physician diagnosis of COPD, corresponding percentages for underdiagnosis among those with $COPD_{LLN}$ and $COPD_{GOLD}$ ≥2, were 81.0% and 73.8% respectively.

Among the 107 (83.6%) undiagnosed participants with $COPD_{GOLD}$, 57.9% were men and they were younger (mean age 59.6 (SD12.2) vs. 65.0 years (SD 8.2), p = 0.021) and had higher FEV_1% of predicted (82.9 (SD 14.4) vs. 65.2 (SD 18.0), p = 0.001) compared to those reporting a physician diagnosis of COPD. The undiagnosed had less frequently family history of bronchitis, chronic productive cough, recurrent wheeze, and they were less likely to seek medical and emergency care due to respiratory symptoms compared to those reporting a physician diagnosis (Fig. 2). No differences were found with regard to sex, hospitalization, occupational exposure to GDF and educational level (Fig. 2). When comparing the 107 undiagnosed participants with $COPD_{GOLD}$ with those without COPD (n = 1711) regarding healthcare utilization, a higher proportion of those with undiagnosed $COPD_{GOLD}$ had ever have sought medical care (68.2% versus 55.4%, p = 0.010), emergency care (25.5% and 11.8%, p = 0.001) and, more frequently been hospitalized (14.0% and 5.2%, p = 0.001) due to respiratory symptoms than participants without COPD. No difference was, however, found regarding seeking medical care last 12 months due to respiratory symptoms among those with undiagnosed COPD and those without COPD (27.0% and 23.3%, p = 0.471).

The undiagnosed participants had fewer packyears (mean 22.4 (SD15.3) vs 39.9 (SD21.2), p = 0.001) and a higher proportion never smokers (p = 0.009) than the diagnosed (Fig. 3.)

4.1. Misclassification of COPD

Twenty-seven participants reported a physician-diagnosis of COPD

Table 1
Demographics and characteristics of the total sample and among participants with and without $COPD_{GOLD}$ respectively. Presented as n(%) expressing distribution within group when relevant, unless otherwise stated.

	All n = 1839 N (%)	Non COPD n = 1711 N (%)	$COPD_{GOLD}$ n = 128 N (%)	P-value Chi-square tests and Independent samples t-tests
Sex				**0.037**
Men	871 (47.4)	799 (46.7)	72 (56.3)	
Age, mean (SD)	51.1 (14.8)	50.3 (14.8)	60.5 (11.8)	**<0.001**
BMI ≥ 25	1139 (61.9)	1060 (62.0)	79 (61.7)	0.958
Smoking habits				**<0.001**
Never-smoker	966 (52.6)	933 (54.6)	33 (25.8)	
Ex-smoker	637 (34.7)	580 (33.9)	57 (44.5)	
Current smoker	235 (12.8)	197 (11.5)	38 (29.7)	
Pack years (n=858)				
Pack years, mean (SD)	14.5 (13.8)	13.1 (12.5)	26.1 (18.4)	**<0.001**
Occupational exposure to gas, dust or fume (GDF)	495 (27.3)	445 (26.3)	50 (39.1)	**0.001**
Level of education				**0.004**
High school or less	1061 (58.6)	972 (57.7)	89 (70.6)	
Family history of asthma	364 (19.8)	341 (19.9)	23 (18.0)	0.591
Family history of bronchitis	162 (8.8)	143 (8.4)	19 (14.8)	**0.002**
Chronic productive cough	223 (12.3)	187 (11.1)	36 (28.8)	**0.001**
Recurrent wheeze	284 (15.5)	222 (13.0)	62 (48.4)	**0.001**
Any wheeze	468 (25.5)	387 (22.6)	81 (63.3)	**0.001**
Healthcare utilization due to respiratory symptoms				
Ever medical care	1041 (56.7)	948 (55.5)	93 (72.7)	**0.001**
Medical care last 12 months	258 (24.5)	224 (23.3)	34 (36.2)	**0.006**
Ever emergency care	240 (13.1)	201 (11.8)	39 (30.7)	**0.001**
Ever hospitalized	109 (5.9)	89 (5.2)	20 (15.6)	**0.001**

(Table 2) and 21 (77.8%) of these fulfilled the criteria for $COPD_{GOLD}$ (Table 3). Thus, 6 out of the 27 with self-reported physician-diagnosed COPD were misclassified. They had 31.5 (SD 13.7) pack years and their mean age was 60.9 (SD 6.4). Of these six misclassified, four were women, five had low educational level i.e. highschool or less, four had chronic productive cough, four had recurrent wheeze, five had any wheeze, four had physician-diagnosed asthma and all were ever smokers i.e. ex- or current smokers.

5. Discussion

This population-based study illustrates that a large underdiagnosis of COPD remains despite the attention given to COPD in health care and, a raising public awareness of COPD. Only 16.4% of the participants who fulfilled the criterion for $COPD_{GOLD}$ i.e. fixed post-bronchodilator chronic airway obstruction $FEV_1/FVC<0.70$ together with respiratory symptoms, reported a physician diagnosis of COPD which corresponds to an underdiagnosis of 83.6%. Even more alarming is that when using a wider and perhaps more clinically realistic measure, any obstructive airway disease, still the underdiagnosis was above 50%, as merely 45.3% of those with $COPD_{GOLD}$ confirmed a physician diagnosis of any obstructive airway disease. Also when using more narrow spirometric criteria, $COPD_{LLN}$ or $COPD_{GOLD} \geq 2$, the underdiagnosis was large as only 19% and 26.2% of the participants, respectively, reported a physician-diagnosis of COPD.

The estimated underdiagnosis of 83.6% in $COPD_{GOLD}$ is indeed alarming but corroborates previous worrying reports of 70%–90% from large-scale population studies being undiagnosed [10–14,16,17]. However, some improvement has been noticed after the millennium shift in Scandinavian countries [33,44–46]. Moreover, in northern Sweden over 15 years from 1994 to 2009 the proportion of participants with moderate to very severe COPD, who had been diagnosed with either COPD, emphysema, or chronic bronchitis increased from 15 to 29% [33].

Importantly, our results show that a noteworthy percentage of those with undiagnosed $COPD_{GOLD}$ had utilized healthcare due to respiratory symptoms, which indicates that those with undiagnosed COPD have a clinical relevant disease. It was also evident that those with undiagnosed $COPD_{GOLD}$ more frequently had sought medical care, emergency care and been hospitalized due to respiratory symptoms in comparison to participants without COPD i.e. consuming more healthcare than the general population. This further implies that there is a lack of adequate diagnostic procedures, i.e. poor routines for use of spirometry in primary care when patients seek health care due to respiratory complaints, and also a lack of screening of smoking patients, which have been described as main causes of underdiagnosis of COPD [5,12,47–49]. Other possible explanations may be that patients deny or have difficulty accepting the COPD diagnosis [50] or low awareness among patients and physicians of other risk factors for COPD than tobacco smoking [15]. Previous studies have shown that low socioeconomic status and occupational exposure to GDF are associated with COPD [51,52], which was confirmed also in the current study where we used interview data on occupational exposure and educational level as indicator of socioeconomic status. However, neither educational level nor occupational exposure were associated with underdiagnosis of COPD. Other potential explanations for underdiagnosis are poor adherence to treatment guidelines for COPD [51] and omission to use case-finding strategies by performing spirometry in high-risk groups of patients with smoking history och healthcare utilization due to respiratory tract [52]. Salinas et al. reported that only 23.4% of the investigated physicians in primary health care ordered spirometry when patients presented with symptoms of COPD [53]. The current results show that undiagnosed participants were treated in healthcare due to burden of respiratory symptoms and in addition that a large majority had the most common riskfactor for COPD namely ever smoking but still not have been diagnosed with COPD is alarming. This points towards poor adherence to guidelines, which leads to unequal care in that undiagnosed persons are prevented from access to necessary

Table 2
In the total sample (n = 1839), prevalence, presented as n(%), of *self-reported* physician-diagnosed COPD, Chronic bronchitis (CB), COPD or emphysema, asthma, medication for obstructive airway disease and any obstructive airway disease (OAD) by sex, level of education and occupational exposure to gas, dust or fumes (GDF).

		Sex			Level of edcuation			GDF		
Self-reports of:	All n = 1839	Women n = 968	Men n = 871	P-values[1]	High n = 750	Low n = 1061	P-values[1]	No n = 1320	Yes n = 495	P-values[1]
COPD	27 (1.5)	15 (1.6)	12 (1.4)	0.424	5 (0.7)	21 (2.0)	**0.021**	15 (1.1)	12 (2.4)	**0.044**
CB, COPD, emphysema	82 (4.5)	47 (4.9)	35 (4.0)	0.385	19 (2.5)	61 (5.7)	**0.001**	48 (3.6)	33 (6.7)	**0.005**
Asthma	226 (12.3)	120 (12.4)	106 (12.2)	0.882	93 (12.4)	128 (12.1)	0.830	142 (10.8)	81 (16.4)	**0.001**
Medication	240 (13.4)	140 (14.5)	100 (11.5)	0.058	98 (13.1)	137 (12.9)	0.923	151 (11.4)	89 (18.0)	**0.001**
OAD	345 (18.8)	198 (20.5)	147 (16.9)	**0.050**	141 (18.8)	199 (18.8)	0.981	226 (17.1)	115 (23.3)	**0.003**

[1]Chi-square tests were used for comparisons between groups. P-values in bold indicate significant differences.

Table 3
Among participants with $COPD_{GOLD}$ (n = 128), prevalence, presented as n(%), of *self-reported* physician-diagnosed COPD, Chronic bronchitis (CB), COPD or emphysema, asthma, medication for obstructive airway disease and any obstructive airway (OAD) disease by sex, level of education and occupational exposure to gas, dust and fumes (GDF).

		Sex			Level of edcuation			GDF		
Self-reports of:	All n = 128	Women n = 56	Men n = 72	P-values[a]	High n = 37	Low n = 89	P-values[a]	No n = 76	Yes n = 50	P- values[a]
COPD	21 (16.4)	11 (19.6)	10 (13.9)	0.383	5 (13.5)	16 (18.0)	0.540	13 (17.1)	8 (16.0)	0.871
CB, COPD, emphysema	30 (23.4)	14 (25.0)	16 (22.2)	0.713	8 (21.6)	22 (24.7)	0.710	18 (23.7)	12 (24.0)	0.968
Asthma	38 (29.7)	16 (28.6)	22 (30.6)	0.807	11 (29.7)	26 (29.2)	0.954	23 (30.3)	13 (26.0)	0.604
Medication	43 (33.6)	19 (33.9)	24 (33.3)	0.944	10 (27.0)	32 (36.0)	0.333	23 (30.3)	20 (40.0)	0.259
OAD	58 (45.3)	25 (44.6)	33 (45.8)	0.893	15 (40.5)	42 (47.2)	0.495	33 (43.4)	23 (46.0)	0.776

[a] Chi-square tests were used for comparisons between groups.

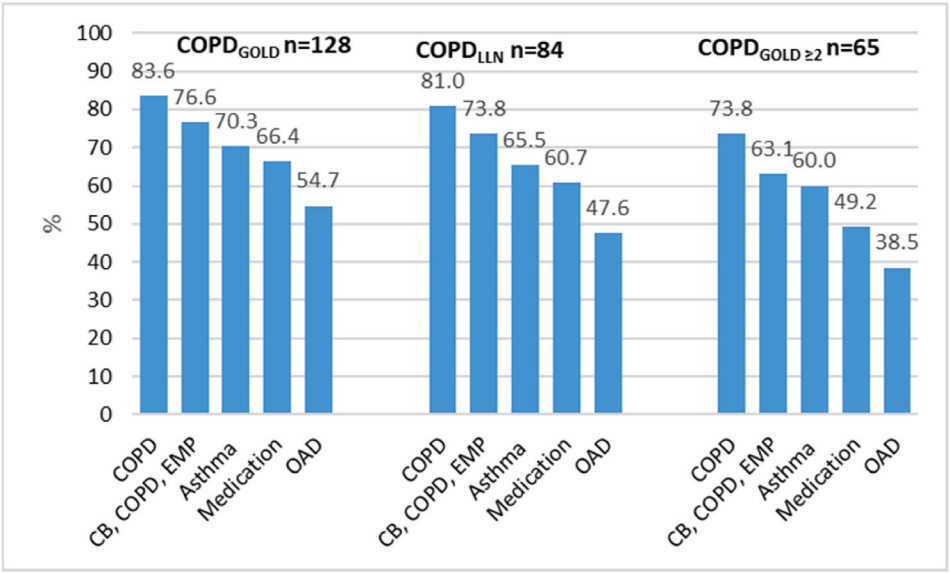

Fig. 1. Underdiagnosis assessed by self-reported physician diagnosis of COPD (COPD), Chronic bronchitis, COPD or emphysema (CB, COPD, EMP), asthma, medication for obstructive airway disease (Medication) or any obstructive airway disease (OAD) in relation to different definitions of COPD: requirement of respiratory symptoms in addition to the spirometric criteria $COPD_{GOLD}$, $COPD_{LLN}$ or $COPD_{GOLD\ >2}$.

treatment and support with self-management strategies aimed to prevent disease progression, which in turn has implications for their quality of life.

A further reason to the magnitude of the underdiagnosis is probably the fact that several middle-aged and elderly with asthma have developed chronic airway obstruction, and could thus have been labelled as having both asthma and COPD corresponding to asthma-COPD overlap (ACO) [54,55] or as in our study reporting a physician-diagnosis of asthma. About one third of the participants fulfilling the criteria for COPD in our study reported a physician-diagnosis of asthma and this proportion was even greater if using the $COPD_{LLN}$ or $COPD_{GOLD}$ ≥2 criteria, 34.5% and 40.0%, respectively. This is in line with a previous study from United Kingdom [56], where 47% of those with severe COPD had been diagnosed with any of the obstructive airway diseases including COPD. The proportion reporting a physician diagnosis of asthma in our study corresponds with the prevalence of ACO in the two studied areas in Sweden, up to about 20% [55,57].

We found that above 80% of those with $COPD_{GOLD}$ (i.e. spirometric criteria + respiratory symptoms) were undiagnosed and despite stepwise wider criteria for physician diagnosis until the widest, any obstructive airway disease, the majority remained undiagnosed. This indicates that differences in diagnostic patterns of obstructive airway disease exist, which we previously have reported [46]. Delayed diagnosis most likely negatively impact on disease progression leading to

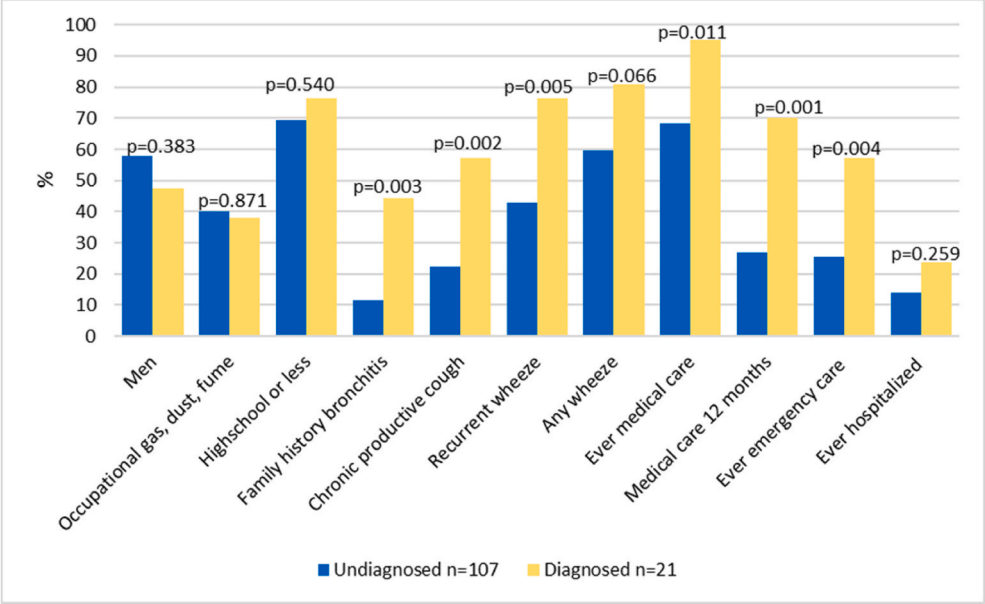

Fig. 2. Characteristics and differences between the 107 participants with $COPD_{GOLD}$ but without self-reported physician-diagnosed COPD (Undiagnosed) and the 21 participants with $COPD_{GOLD}$ with self-reported physician-diagnosed COPD (Diagnosed).

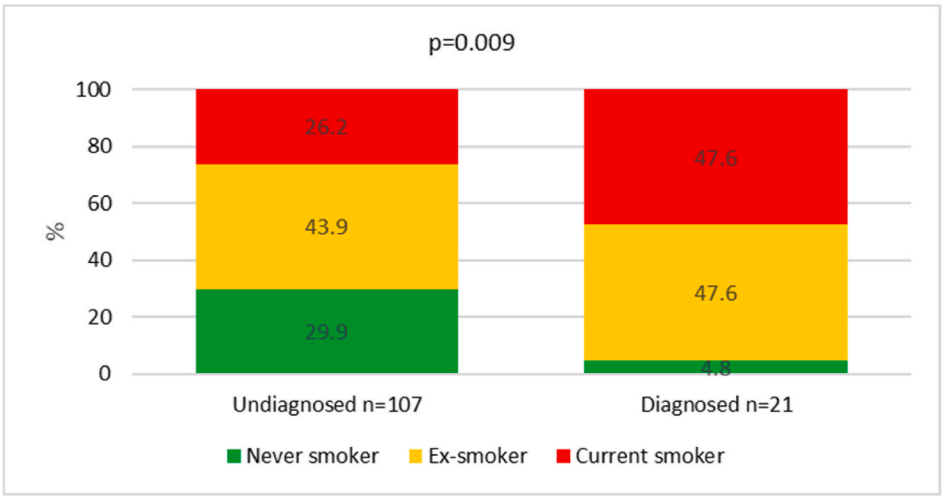

Fig. 3. Differences in smoking habits between the 107 participants with $COPD_{GOLD}$ but without self-reported physician-diagnosed COPD (undiagnosed) and the 21 participants with $COPD_{GOLD}$ with self-reported physician-diagnosed COPD (diagnosed).

unnecessary suffering and reduced of quality of life. A review by Welte et al. showed that smoking cessations slow down the progression of COPD and the earlier smoking cessation is initiated the better and, the review also showed that even patients with mild COPD had impaired quality of life [23]. Early recognition of COPD is indeed essential to initiate preventive measures as smoking cessation but also through treatment to reduce symptoms and to prevent the risks of exacerbations and hospitalizations [1]. Independent of definitions used, our results show a considerable underdiagnosis of COPD and even any obstructive airway disease. Despite some improvements over the last decades [46], our results highlight a persistent important clinical message, i.e. the need of correct diagnosis of obstructive airway diseases in order to reduce the underdiagnosis of COPD [15].

Misclassification of COPD has been reported by several large-scale studies [13,19,20]. Data from the BOLD Study indicate a considerable misclassification, among those reporting a physician diagnosis of COPD, airway obstruction could not be confirmed in 62% [19]. Smoking and high age have been associated with misclassification of COPD, as well as female sex and high educational level [18]. In the current study, 6 participants out of 27 reporting a physician diagnosis of COPD did not fulfil the definition of $COPD_{GOLD}$. This is considerably lower than reported by others, but the low numbers do not allow detailed evaluation of misclassification. However, they had about the same amount of packyears as those with $COPD_{GOLD}$.

5.1. Strenghts and weaknesses

Estimations of underdiagnosis and misclassification of COPD requires population-based studies. The study area for the current study includes approximately 20% of the general population in Sweden, and based on random samples from both northern and south-western Sweden covering both rural and urban areas. A further strength is that both large-scale epidemiological research programs, the OLIN studies and WSAS, have had high participation rates throughout and the samples reflect well the adult general population in the areas and further, studies of non-response in the areas have verified a good representativeness

[58–60]. The same spirometers, the Jaeger's Masterscope, was used in both areas by well trained and experienced study staffs who had practised together in order to avoid inter-observer bias. A strength is that the OLIN reference values were used as these have been validated internally and externally and reflect the healthy general population in both areas somewhat better than the Global Lung Initiative (GLI) reference values [42,61]. Furthermore, the OLIN questionnaires used in the current study have been validated [39]. The study size allowed analyses of underdiagnosis with reasonable statistical power, but on the other hand, the low numbers of participants with self-reported physician-diagnosed COPD is a limitation and did not allow in depth analysis of misclassification of COPD. Another limitation is that self-reported diagnoses have not been verified by medical records meaning that there can be participants, who have been diagnosed as having mild COPD but being unaware of it or may have forgotten given information, i.e. recall bias. However, a study of intermethod reliability showed good agreement between self-reports and medical records for respiratory conditions [62].

6. Conclusion

In a high income country as Sweden, the underdiagnosis of COPD was still highly prevalent, independent of definition of COPD, and true also for moderate to severe COPD. Some misclassification was also observed, however of less magnitude than in other studies. Importantly, the undiagnosed individuals with COPD contacted health care due to respiratory complaints. Thus case-finding strategies would matter, and there is an urgent need to increase both the use of spirometry and the interpretation of spirometry results in primary care to improve the diagnostic accuracy. Reduced underdiagnosis can contribute to risk factor modification, medical treatment and support with self-management in early stages of the disease, which most likely improve the health-related quality of life among those affected. Additionally, support with smoking cessation will influence prognosis.

Credit author statement

(1) MA and AL conceived and designed the study, (2) HB performed data management, MA conducted the analyses, MA and AL interpreted the analyses, (3) MA drafted the manuscript and AL supported with critical review and intellectual content. HB, BN, CS, LV, LH, PP, JJ, ALA, HK, MR, LE, ER, AL, revised the manuscipt critically for important intellectual content, (4) all authors approved the final version for submission.

Funding scources

Supported by grants from The Swedish Heart & Lung Foundation, The Swedish Research Council, the Herman Krefting Foundation for Asthma and Allergy Research, regional agreements between University of Gothenburg and the Region of Västra Götaland (ALF) and between Umeå University and Västerbotten County Council (ALF), Norrbotten County Council, the Swedish Asthma-Allergy Foundation, and VISARE NORR Fund: Northern county councils Regional federation. The Nordic Council of Ministers: NordForsk Foundation (Nordic EpiLung Study)

Declaration of competing interest

Malin Axelsson declares no conflicts of interest.

Helena Backman reports personal fees for scientific lectures from Boehringer Ingelheim, AstraZeneca and GlaxoSmithKline, outside the submitted work.

Bright I. Nwaru reports personal fees for scientific consulting from DBV Technologies, outside the submitted work.

Caroline Stridsman declares no conflicts of interest.

Lowie Vanfleteren declares no conflicts of interest related to this manuscript. Outside the submitted work: payment for lectures or advisory boards from GSK, AstraZeneca, Chiesi, Boehringer, Novartis, Pulmonx.

Linnea Hedman declares no conflicts of interest.

Juuso Jalasto declares no conflicts of interest.

Päivi Piirilä declares no conflicts of interest.

Arnulf Langhammer reports fees for lectures and consulting from AstraZeneca, Boehringer-Ingelheim, GSK, and Diagnostica Ltb, outside the submitted work.

Hannu Kankaanranta reports fees for lectures and consulting from AstraZeneca, Boehringer-Ingelheim, Chiesi Pharma, GSK, MSD, Novartis, Orion Pharma and SanofiGenzyme, outside the submitted work.

Madeleine Rådinger declares no conflicts of interest.

Linda Ekerljung declares no conflicts of interest.

Eva Rönmark declares no conflicts of interest.

Anne Lindberg reports personal fees for advisory board work for AstraZeneca, GlaxoSmithKline, Novartis and Boehringer Ingelhem, as well as personal fees for scientific lectures for Boehringer Ingelheim and Novartis, both outside the submitted work.

Acknowledgement

The late professor emeritus Bo Lundbäck, the initiator of the OLIN-studies and later also the West Sweden Asthma study.

References

[1] Global Strategy for the Diagnosis, Management and Prevention of COPD, Global Initiative for Chronic Obstructive Lung Disease, 2023.
[2] Organization WH, The top 10 causes of death 2020 [Available from: https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.
[3] D. Adeloye, P. Song, Y. Zhu, H. Campbell, A. Sheikh, I. Rudan, et al., Global, regional, and national prevalence of, and risk factors for, chronic obstructive pulmonary disease (COPD) in 2019: a systematic review and modelling analysis, Lancet Respir. Med. 10 (5) (2022) 447–458.
[4] B.B.P. Lundbäck, T. Ingebrigtsen, P. Lange, A. Lindberg, J.B. Soriano, J. Vestbo, Chapter on Chronic Obstructive Pulmonary Disease in Respiratory Epidemiology, Monograph European Respiratory Society Publications, Sheffield, United Kingdom, 2014.
[5] J.B. Soriano, J. Ancochea, M. Miravitlles, F. Garcia-Rio, E. Duran-Tauleria, L. Munoz, et al., Recent trends in COPD prevalence in Spain: a repeated cross-sectional survey 1997-2007, Eur. Respir. J. 36 (4) (2010) 758–765.
[6] T.M. Vasankari, O. Impivaara, M. Heliovaara, S. Heistaro, K. Liippo, P. Puukka, et al., No increase in the prevalence of COPD in two decades, Eur. Respir. J. 36 (4) (2010) 766–773.
[7] E.S. Ford, D.M. Mannino, A.G. Wheaton, W.H. Giles, L. Presley-Cantrell, J.B. Croft, Trends in the prevalence of obstructive and restrictive lung function among adults in the United States: findings from the National Health and Nutrition Examination surveys from 1988-1994 to 2007-2010, Chest 143 (5) (2013) 1395–1406.
[8] H. Backman, L. Vanfleteren, A. Lindberg, L. Ekerljung, C. Stridsman, M. Axelsson, et al., Decreased COPD prevalence in Sweden after decades of decrease in smoking, Respir. Res. 21 (1) (2020) 283.
[9] H. Melbye, J. Helgeland, O. Karlstad, I. Ariansen, A. Langhammer, T. Wisloff, et al., Is the disease burden from COPD in Norway falling off? A study of time trends in three different data sources, Int. J. Chronic Obstr. Pulm. Dis. 15 (2020) 323–334.
[10] J.B. Soriano, J. Zielinski, D. Price, Screening for and early detection of chronic obstructive pulmonary disease, Lancet 374 (9691) (2009) 721–732.
[11] M. Miravitlles, J.B. Soriano, F. Garcia-Rio, L. Munoz, E. Duran-Tauleria, G. Sanchez, et al., Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities, Thorax 64 (10) (2009) 863–868.
[12] B. Lamprecht, J.B. Soriano, M. Studnicka, B. Kaiser, L.E. Vanfleteren, L. Gnatiuc, et al., Determinants of underdiagnosis of COPD in national and international surveys, Chest 148 (4) (2015) 971–985.
[13] N. Diab, A.S. Gershon, D.D. Sin, W.C. Tan, J. Bourbeau, L.P. Boulet, et al., Underdiagnosis and overdiagnosis of chronic obstructive pulmonary disease, Am. J. Respir. Crit. Care Med. 198 (9) (2018) 1130–1139.
[14] C. Talamo, M.M. de Oca, R. Halbert, R. Perez-Padilla, J.R. Jardim, A. Muino, et al., Diagnostic labeling of COPD in five Latin American cities, Chest 131 (1) (2007) 60–67.
[15] T. Ho, R.P. Cusack, N. Chaudhary, I. Satia, O.P. Kurmi, Under- and over-diagnosis of COPD: a global perspective, Breathe 15 (1) (2019) 24–35.
[16] A. Lindberg, A. Bjerg, E. Rönmark, L.G. Larsson, B. Lundbäck, Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking report from the obstructive lung disease in northern Sweden studies, Respir. Med. 100 (2) (2006) 264–272.
[17] K. Jyrki-Tapani, A. Sovijarvi, B. Lundbäck, Chronic obstructive pulmonary disease in Finland: prevalence and risk factors, COPD 2 (3) (2005) 331–339.

[18] T.S. Ingebrigtsen, J.L. Marott, J. Vestbo, J. Hallas, B.G. Nordestgaard, M. Dahl, et al., Characteristics of undertreatment in COPD in the general population, Chest 144 (6) (2013) 1811–1818.

[19] L. Sator, A. Horner, M. Studnicka, B. Lamprecht, B. Kaiser, M.A. McBurnie, et al., Overdiagnosis of COPD in subjects with unobstructed spirometry: a BOLD analysis, Chest 156 (2) (2019) 277–288.

[20] E. Heffler, C. Crimi, S. Mancuso, R. Campisi, F. Puggioni, L. Brussino, et al., Misdiagnosis of asthma and COPD and underuse of spirometry in primary care unselected patients, Respir. Med. 142 (2018) 48–52.

[21] R.W. Thomsen, P. Lange, B. Hellquist, E. Frausing, P.D. Bartels, B.R. Krog, et al., Validity and underrecording of diagnosis of COPD in the Danish national patient registry, Respir. Med. 105 (7) (2011) 1063–1068.

[22] M. Arne, K. Lisspers, B. Ställberg, G. Boman, H. Hedenstrom, C. Janson, et al., How often is diagnosis of COPD confirmed with spirometry? Respir. Med. 104 (4) (2010) 550–556.

[23] T. Welte, C. Vogelmeier, A. Papi, COPD: early diagnosis and treatment to slow disease progression, Int. J. Clin. Pract. 69 (3) (2015) 336–349.

[24] B. Lundbäck, L. Nyström, L. Rosenhall, N. Stjernberg, Obstructive lung disease in northern Sweden: respiratory symptoms assessed in a postal survey, Eur. Respir. J. 4 (3) (1991) 257–266.

[25] B.I. Nwaru, L. Ekerljung, M. Radinger, A. Bjerg, R. Mincheva, C. Malmhäll, et al., Cohort profile: the West Sweden Asthma Study (WSAS): a multidisciplinary population-based longitudinal study of asthma, allergy and respiratory conditions in adults, BMJ Open 9 (6) (2019), e027808.

[26] A. Lindberg, A.C. Jonsson, E. Rönmark, R. Lundgren, L.G. Larsson, B. Lundbäck, Ten-year cumulative incidence of COPD and risk factors for incident disease in a symptomatic cohort, Chest 127 (5) (2005) 1544–1552.

[27] S. Hagstad, H. Backman, A. Bjerg, L. Ekerljung, X. Ye, L. Hedman, et al., Prevalence and risk factors of COPD among never-smokers in two areas of Sweden - occupational exposure to gas, dust or fumes is an important risk factor, Respir. Med. 109 (11) (2015) 1439–1445.

[28] B. Lundbäck, A. Lindberg, M. Lindström, E. Rönmark, A.C. Jonsson, E. Jonsson, et al., Not 15 but 50% of smokers develop COPD?–Report from the obstructive lung disease in northern Sweden studies, Respir. Med. 97 (2) (2003) 115–122.

[29] J. Lötvall, L. Ekerljung, E.P. Rönmark, G. Wennergren, A. Linden, E. Rönmark, et al., West Sweden Asthma Study: prevalence trends over the last 18 years argues no recent increase in asthma, Respir. Res. 10 (2009), 94-9921-10-94.

[30] M. Axelsson, L. Ekerljung, J. Eriksson, S. Hagstad, E. Rönmark, J. Lötvall, et al., Chronic bronchitis in West Sweden - a matter of smoking and social class, Eur. Clin. Respir.J 3 (2016), 30319.

[31] L. Ekerljung, A. Bjerg, A. Bossios, M. Axelsson, K. Toren, G. Wennergren, et al., Five-fold increase in use of inhaled corticosteroids over 18 years in the general adult population in west Sweden, Respir. Med. 108 (5) (2014) 685–693.

[32] H. Backman, L. Hedman, S.A. Jansson, A. Lindberg, B. Lundbäck, E. Rönmark, Prevalence trends in respiratory symptoms and asthma in relation to smoking - two cross-sectional studies ten years apart among adults in northern Sweden, World. Allergy.Organ.J 7 (1) (2014), 1-4551-7-1.

[33] H. Backman, B. Eriksson, E. Rönmark, L. Hedman, C. Stridsman, S.A. Jansson, et al., Decreased prevalence of moderate to severe COPD over 15 years in northern Sweden, Respir. Med. 114 (2016) 103–110.

[34] J. Lötvall, L. Ekerljung, E.P. Rönmark, G. Wennergren, A. Linden, E. Rönmark, et al., West Sweden Asthma Study: prevalence trends over the last 18 years argues no recent increase in asthma, Respir. Res. 10 (2009) 94.

[35] M. Lindström, J. Kotaniemi, E. Jonsson, B. Lundbäck, Smoking, respiratory symptoms, and diseases : a comparative study between northern Sweden and northern Finland: report from the FinEsS study, Chest 119 (3) (2001) 852–861.

[36] M. Meren, A. Raukas-Kivioja, L. Jannus-Pruljan, H.M. Loit, E. Rönmark, B. Lundbäck, Low prevalence of asthma in westernizing countries-myth or reality? Prevalence of asthma in Estonia–a report from the "FinEsS" study, J. Asthma 42 (5) (2005) 357–365.

[37] P. Pallasaho, E. Rönmark, T. Haahtela, A.R. Sovijarvi, B. Lundbäck, Degree and clinical relevance of sensitization to common allergens among adults: a population study in Helsinki, Finland, Clin. Exp. Allergy 36 (4) (2006) 503–509.

[38] H.T. Lam, E. Rönmark, N.V. Tu'o'ng, L. Ekerljung, N.T. Chuc, B. Lundbäck, Increase in asthma and a high prevalence of bronchitis: results from a population study among adults in urban and rural Vietnam, Respir. Med. 105 (2) (2011) 177–185.

[39] L. Ekerljung, E. Rönmark, J. Lotvall, G. Wennergren, K. Toren, B. Lundbäck, Questionnaire layout and wording influence prevalence and risk estimates of respiratory symptoms in a population cohort, Clin. Res. J 7 (1) (2013) 53–63.

[40] A. Bjerg, L. Ekerljung, R. Middelveld, S.E. Dahlen, B. Forsberg, K. Franklin, et al., Increased prevalence of symptoms of rhinitis but not of asthma between 1990 and 2008 in Swedish adults: comparisons of the ECRHS and GA(2)LEN surveys, PLoS One 6 (2) (2011), e16082.

[41] J. Bousquet, P.G. Burney, T. Zuberbier, P.V. Cauwenberge, C.A. Akdis, C. Bindslev-Jensen, et al., GA2LEN (Global Allergy and Asthma European Network) addresses the allergy and asthma 'epidemic', Allergy 64 (7) (2009) 969–977.

[42] H. Backman, A. Lindberg, A. Oden, L. Ekerljung, L. Hedman, A. Kainu, et al., Reference values for spirometry - report from the obstructive lung disease in northern Sweden studies, Eur Clin Respir J 2 (2015).

[43] S. Stanojevic, D.A. Kaminsky, M.R. Miller, B. Thompson, A. Aliverti, I. Barjaktarevic, et al., ERS/ATS technical standard on interpretive strategies for routine lung function tests, Eur. Respir. J. 60 (1) (2022).

[44] H. Melbye, E. Drivenes, L.G. Dalbak, T. Leinan, S. Hoegh-Henrichsen, A. Ostrem, Asthma, chronic obstructive pulmonary disease, or both? Diagnostic labeling and spirometry in primary care patients aged 40 years or more, Int. J. Chronic Obstr. Pulm. Dis. 6 (2011) 597–603.

[45] T. Vasankari, A. Pietinalho, K. Lertola, S.Y. Junnila, K. Liippo, Use of spirometry and recording of smoking habits of COPD patients increased in primary health care during national COPD programme, BMC Fam. Pract. 12 (2011) 97.

[46] M. Axelsson, P. Ilmarinen, H. Backman, L. Ekerljung, L. Hedman, A. Langhammer, et al., Differences in diagnostic patterns of obstructive airway disease between areas and sex in Sweden and Finland - the Nordic EpiLung study, J. Asthma 58 (9) (2021) 1196–1207.

[47] E.T. Thomas, P. Glasziou, C.C. Dobler, Use of the terms "overdiagnosis" and "misdiagnosis" in the COPD literature: a rapid review, Breathe 15 (1) (2019) e8–e19.

[48] D. Price, G. Brusselle, Challenges of COPD diagnosis, Expert Opin. Med. Diagn. 7 (6) (2013) 543–556.

[49] S. Hangaard, T. Helle, C. Nielsen, O.K. Hejlesen, Causes of misdiagnosis of chronic obstructive pulmonary disease: a systematic scoping review, Respir. Med. 129 (2017) 63–84.

[50] S. Lindgren, S.L. Storli, L. Wiklund-Gustin, Living in negotiation: patients' experiences of being in the diagnostic process of COPD, Int. J. Chronic Obstr. Pulm. Dis. 9 (2014 May 6) 441–451, https://doi.org/10.2147/COPD.S60182. PMID: 24851046; PMCID: PMC4018318.

[51] H. Sandelowsky, C. Janson, F. Wiklund, G. Telg, S. de Fine Licht, B. Stallberg, Lack of COPD-related follow-up visits and pharmacological treatment in Swedish primary and secondary care, Int. J. Chronic Obstr. Pulm. Dis. 17 (2022) 1769–1780.

[52] H. Sandelowsky, B. Stallberg, A. Nager, J. Hasselstrom, The prevalence of undiagnosed chronic obstructive pulmonary disease in a primary care population with respiratory tract infections - a case finding study, BMC Fam. Pract. 12 (2011) 122.

[53] G.D. Salinas, J.C. Williamson, R. Kalhan, B. Thomashow, J.L. Scheckermann, J. Walsh, et al., Barriers to adherence to chronic obstructive pulmonary disease guidelines by primary care physicians, Int. J. Chronic Obstr. Pulm. Dis. 6 (2011) 171–179.

[54] P. Lange, Y. Colak, T.S. Ingebrigtsen, J. Vestbo, J.L. Marott, Long-term prognosis of asthma, chronic obstructive pulmonary disease, and asthma-chronic obstructive pulmonary disease overlap in the Copenhagen City Heart study: a prospective population-based analysis, Lancet Respir. Med. 4 (6) (2016) 454–462.

[55] H. Backman, S.A. Jansson, C. Stridsman, H. Muellerova, K. Wurst, L. Hedman, et al., Chronic airway obstruction in a population-based adult asthma cohort: prevalence, incidence and prognostic factors, Respir. Med. 138 (2018) 115–122.

[56] L. Shahab, M.J. Jarvis, J. Britton, R. West, Prevalence, diagnosis and relation to tobacco dependence of chronic obstructive pulmonary disease in a nationally representative population sample, Thorax 61 (12) (2006) 1043–1047.

[57] L. Ekerljung, R. Mincheva, S. Hagstad, A. Bjerg, G. Telg, G. Stratelis, et al., Prevalence, clinical characteristics and morbidity of the Asthma-COPD overlap in a general population sample, J. Asthma : official journal of the Association for the Care of Asthma (2017) 1–9.

[58] E.P. Rönmark, L. Ekerljung, J. Lotvall, K. Toren, E. Ronmark, B. Lundback, Large scale questionnaire survey on respiratory health in Sweden: effects of late- and non-response, Respir. Med. 103 (12) (2009) 1807–1815.

[59] E. Rönmark, A. Lundqvist, B. Lundbäck, L. Nyström, Non-responders to a postal questionnaire on respiratory symptoms and diseases, Eur. J. Epidemiol. 15 (3) (1999) 293–299.

[60] P. Raisanen, L. Hedman, M. Andersson, C. Stridsman, A. Lindberg, B. Lundbäck, et al., Non-response did not affect prevalence estimates of asthma and respiratory symptoms - results from a postal questionnaire survey of the general population, Respir. Med. 173 (2020), 106017.

[61] H. Backman, A. Lindberg, A. Sovijarvi, K. Larsson, B. Lundbäck, E. Rönmark, Evaluation of the global lung function initiative 2012 reference values for spirometry in a Swedish population sample, BMC Pulm. Med. 15 (2015) 26.

[62] L. Iversen, P.C. Hannaford, D.J. Godden, D. Price, Do people self-reporting information about chronic respiratory disease have corroborative evidence in their general practice medical records? A study of intermethod reliability, Prim. Care Respir. J. 16 (3) (2007) 162–168.