Current clinical guideline definitions of airflow obstruction and COPD overdiagnosis in primary care

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ABSTRACT: The aim of the present study was to establish the agreement between two recommended definitions of airflow obstruction in symptomatic adults referred for spirometry by their general practitioner, and investigate how rates of airflow obstruction change when pre-bronchodilator instead of post-bronchodilator spirometry is performed.

The diagnostic spirometric results of 14,056 adults with respiratory obstruction were analysed. Differences in interpretation between a fixed 0.70 forced expiratory volume in one second (FEV_1)/ forced vital capacity (FVC) cut-off point and a sex- and age-specific lower limit of normal cut-off point for this ratio were investigated.

Of the subjects, 53% were female and 69% were current or ex-smokers. The mean post-bronchodilator FEV_1/FVC was 0.73 in males and 0.78 in females. The sensitivity of the fixed relative to the lower limit of normal cut-off point definition was 97.9%, with a specificity of 91.2%, positive predictive value of 72.0% and negative predictive value of 99.5%. For the subgroup of current or ex-smokers aged $\geqslant$50 yrs, these values were 100, 82.0, 69.2 and 100%, respectively. The proportion of false positive diagnoses using the fixed cut-off point increased with age. The positive predictive value of pre-bronchodilator airflow obstruction was 74.7% among current or ex-smokers aged $\geqslant$50 yrs.

The current clinical guideline-recommended fixed 0.70 forced expiratory volume in one second/ forced vital capacity cut-off point leads to substantial overdiagnosis of obstruction in middle-aged and elderly patients in primary care. Using pre-bronchodilator spirometry leads to a high rate of false positive interpretations of obstruction in primary care.

KEYWORDS: Chronic obstructive pulmonary disease, diagnostics, lung function measurements, primary care

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Chronic obstructive pulmonary disease (COPD) is a respiratory condition that is predominantly caused by smoking, and is characterised by airflow obstruction that is progressive in nature and not fully reversible [1]. Recent estimates for the population prevalence of COPD in adults aged >40 yrs range 11–26% for countries throughout the world [2]. As the majority of patients with COPD are diagnosed and managed in primary care, timely diagnosis and subsequent staging both require primary care spirometry in order to confirm the presence and severity of airflow obstruction [3].

Airflow obstruction in COPD is present when a patient shows a disproportionate reduction in the maximal airflow from the lungs in relation to the maximal volume that can be displaced from the lungs [4]. According to current COPD guideline recommendations for primary [5, 6] and secondary care [1, 7, 8], this is determined by measuring the forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) ratio. Without exception, the guidelines recommend a fixed 0.70 cut-off point for FEV_1/FVC in deciding whether or not airflow obstruction is present, regardless of the sex and age of the subject involved. However, it is well documented that ageing is associated with a range of postural and physiological changes that influence respiratory function in both sexes [9]. Several reports from studies in healthy nonsmokers indicate that the cut-off point for an abnormal FEV_1/FVC ratio indeed depends upon the sex and age of an individual [10–12]. Hence the use of the fixed 0.70 FEV_1/FVC cut-off point may lead to a substantial proportion of middle-aged and elderly

males and females unjustly being considered to have COPD. Indeed, this has been shown in several general population studies [13–18].

Taking the point of view that a cut-off value for any physiological or biochemical index used in medicine should be able to reliably differentiate between normal and abnormal function, it seems that the ''one size fits all'' approach with a fixed FEV_1/FVC cut-off point for everyone is inadequate. A definition based on the lower limit of normal (LLN) of the FEV_1/FVC, as observed in an appropriate reference population, is regarded the scientifically justified and preferred way of rendering justice to the sex and age dependency of the ratio [4].

Since COPD is generally first diagnosed in primary care, the issue of which definition to use in deciding whether or not airflow obstruction is present is especially relevant for general practitioners (GPs). Given the frequent comorbidity that occurs in older current or ex-smokers, such as, for example, heart failure [19], using an inappropriate cut-off point further increases the chance of an incorrect diagnosis and subsequent, potentially avoidable, healthcare costs.

The aim of the present study was to compare the agreement between the two recommended definitions of airflow obstruction (*i.e.* the clinical guideline-recommended fixed cut-off point for FEV_1/FVC versus the LLN cut-off point) and severity classification based on predicted FEV_1 in a population of subjects with respiratory complaints but without a prior diagnosis of chronic respiratory disease who were referred by their GP to a primary care diagnostic centre for spirometry. It was also investigated how rates of airflow obstruction in this study population change when pre-bronchodilator instead of post-bronchodilator spirometric values are used.

METHODS

Study population

The present study was based on all of the available spirometric results (October 2001 to May 2007) from the General Practice Laboratory Foundation Etten-Leur/Breda (Etten-Leur, the Netherlands; SHL), a regional primary care diagnostic centre that has provided a range of diagnostic and healthcare services (including spirometry) for >330 GPs in the south-western area of the Netherlands since 1997. GPs refer patients they suspect of having COPD or asthma to the SHL for diagnostic spirometry on the basis of presentation with respiratory symptoms or other problems for which the GP considers spirometry to be indicated. The SHL performs ~5,000 spirometric tests annually. Approximately half are of the tests are for diagnostic purposes, the other half are being carried out as part of the regular monitoring of patients with COPD or asthma. The spirometric results and accompanying demographic (sex and age), anthropometric (height and weight) and medical history information (smoking habit and respiratory symptoms (sputum, cough, dyspnoea and exacerbations during the past year)) are recorded during each visit using a standard format. For the current study, all subjects for whom a post-bronchodilator spirometric test result was available were selected. If two or more spirometric results were available for a particular subject, only the first one was used for the present study. From this, the subset of subjects aged ⩾50 yrs that were current or ex-smokers were selected because of their higher

prior probability of being diagnosed with COPD. The medical ethics review board of the Radboud University Medical Centre Nijmegen (Nijmegen, the Netherlands) approved the present study. Since only routine lung function data were used for the present retrospective database analysis and the investigators had no access to the patients' medical records or information on patient identity, no written informed consent was obtained.

Measurement and definition of airflow obstruction

The SHL operates in 21 different locations where spirometric testing is performed. Five certified lung function technicians perform these tests. Each of them performs a minimum of 100 spirometric tests annually. The technicians are regularly supervised in central meetings. Personal computer-based digital volume sensor spirometers (SpiroPerfect®; WelchAllyn, Delft, the Netherlands) are used at all locations. This spirometer satisfies American Thoracic Society (ATS) standards [20]. The lung function technicians always use the same spirometer, and all follow a standard operating procedure for calibration of the spirometer on a daily basis using a 1-L syringe. Within-test volume deviations of <3% are considered acceptable. Air temperature and ambient pressure are measured and entered into the spirometric software in order to correct for body temperature and ambient pressure saturation [20]. Patient instruction, assessment of acceptability of forced expiratory manoeuvres and criteria for test reproducibility are based on ATS recommendations [20]. Pre- and post-bronchodilator measurements are performed with subjects seated at rest before and 15 min after administration of four doses of 100 μg aerosolised salbutamol by Volumatic® spacer (GlaxoSmithKline, Brentford, UK). The prediction equations of the European Community for Steel and Coal (ECSC) [12], which are applied quite universally in Europe, were used to determine predicted values of FEV_1 and FEV_1/FVC. In order to calculate sex-, age- and height-specific predicted values of FEV_1, a correction factor of 1.08 was applied [21], as recommended for the Dutch population in the current COPD guideline of the Netherlands College of General Practitioners [6].

Analysis

The post-bronchodilator FEV_1/FVC was used to determine whether or not airflow obstruction was present in the study subjects. The following two definitions of obstruction were used.

1) Fixed cut-off point definition: FEV_1/FVC of <0.70. This is the definition that is currently recommended in all major clinical COPD guidelines [1, 7, 8].

2) LLN cut-off point definition: FEV_1/FVC below the sex- and age-specific LLN. This is the definition recommended by lung function experts [4]. The LLN was determined by subtracting the predicted FEV_1/FVC from the measured FEV_1/FVC in each study subject and dividing this difference by the residual SD (0.0717 in males and 0.0651 in females) derived from the ECSC reference population [12]. When the resulting SD score was <-1.645, airflow obstruction was present according to the LLN definition. This corresponds to the estimated 5th percentile.

A similar procedure was followed in determining severity of airflow obstruction based on either the FEV_1 expressed as a
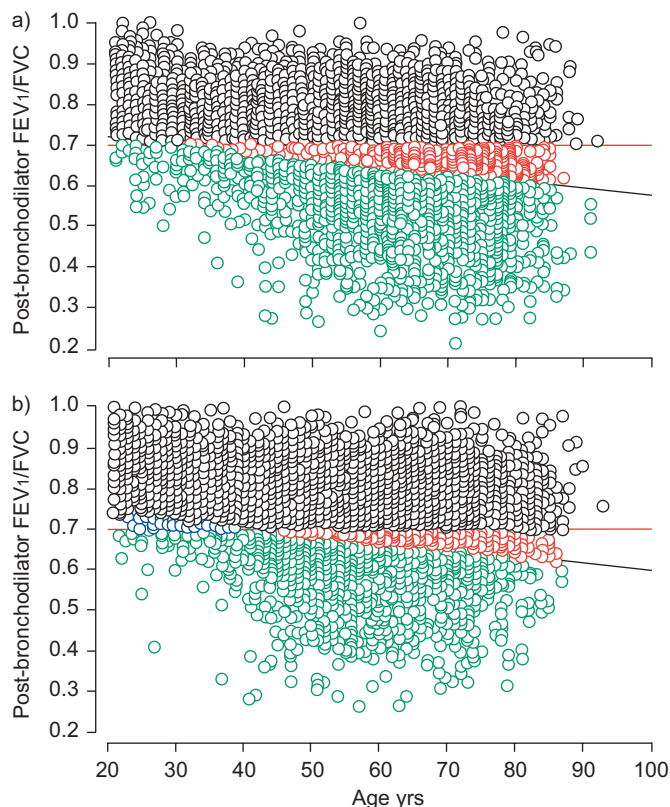
TABLE 1	Characteristics of study sample and the subgroup of older current or ex-smokers[#]			
	Total population		**Subgroup**	
	Males	**Females**	**Males**	**Females**
Subjects n	6597	7459	3473	2543
Age yrs	54.2±15.2	51.9±15.1	64.5±8.9	61.9±8.3
Age range %				
21–30 yrs	7.3	9.3		
31–40 yrs	13.9	15.5		
41–50 yrs	18.1	21.4	1.6	2.7
51–60 yrs	23.5	23.4	36.4	47.5
61–70 yrs	21.0	18.2	34.3	32.0
71–80 yrs	13.6	10.1	23.4	15.5
⩾81 yrs	2.6	2.1	4.4	2.2
Height m	1.77±0.08	1.65±0.07	1.75±0.01	1.63±0.06
Smoking status %				
Never-smoker	20.3	35.7		
Ex-smoker	42.8	28.3	62.3	53.0
Current smoker	32.9	32.1	37.7	47.0
Missing	4.0	4.0		
Respiratory symptoms %[¶]				
Exercise-related dysp[+]	60.4	69.1	64.0	68.8
Nocturnal dysp	21.3	24.6	19.4	22.0
Cough	66.3	73.6	67.2	73.1
Sputum	61.5	59.2	62.9	60.9
Exacerbation(s) in past year	37.6	47.1	35.8	47.7
FEV1				
Pre-bronch L	2.83±0.98	2.18±0.70	2.35±0.81	1.77±0.57
Post-bronch L	3.00±0.98	2.31±0.70	2.50±0.81	1.87±0.56
Post-bronch % pred	77.3±18.3	81.5±17.5	72.4±19.6	75.7±19.5
FVC				
Pre-bronch L	3.97±1.06	2.87±0.77	3.49±0.91	2.47±0.62
Post-bronch L	4.09±1.03	2.94±0.75	3.62±0.88	2.55±0.60
Post-bronch % pred	83.0±14.2	83.6±13.9	80.7±15.3	81.6±15.1
FEV1/FVC				
Pre-bronch	0.70±0.13	0.75±0.11	0.67±0.13	0.71±0.12
Post-bronch	0.73±0.13	0.78±0.11	0.68±0.13	0.73±0.12

Data are presented as mean±SD, unless otherwise indicated. dysp: dyspnoea; FEV1: forced expiratory volume in one second; bronch: bronchodilator; FVC: forced vital capacity; % pred: % predicted. [#]: 6,016 current or ex-smokers aged ⩾50 yrs; [¶]: based on a 15% (n=2,100) random sample of study subjects; [+]: ⩾2 on UK Medical Research Council scale.

FIGURE 1. Association between forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) and age in symptomatic: a) males (n=6,597); and b) females (n=7,459). The horizontal red line indicates the fixed 0.70 FEV1/FVC cut-off point that is currently recommended by all major clinical chronic obstructive pulmonary disease guidelines [1, 5, 6, 8]; the black diagonal line indicates the lower limit of normal for healthy nonsmoking males and females, respectively. Green circles: true positive (unique subjects considered to have airflow obstruction according to both definitions); black circles: true negative; red circles: false positive (subjects in whom discordant conclusions regarding the presence of airflow obstruction are drawn); blue circles: false negative.

percentage of the predicted value [1, 7, 8] or the LLN based on the distribution of FEV1 [4] in the reference population [12]. Finally, 3×3 tables were constructed in order to compare the presence and severity of airflow obstruction based on the fixed FEV1/FVC cut-off point and percentage predicted FEV1 classification (*i.e.* no, mild and moderate-to-very severe obstruction) on the one hand and LLN of FEV1/FVC and FEV1 on the other.

The sensitivity, specificity, positive and negative predictive value [22], and the 95% confidence intervals (CIs) were calculated for the fixed FEV1/FVC definition, considering the LLN definition the gold standard for assessment of airflow obstruction [4]. For these calculations, all subjects with obstruction according to a particular definition (regardless of the severity of obstruction, *i.e.* mild or moderate-to-very severe obstruction) were combined. The aforementioned diagnostic test characteristics (sensitivity, *etc.*) were also calculated for the use of pre-bronchodilator spirometry for the demonstration of airflow obstruction compared with the gold standard, *i.e.* post-bronchodilator spirometry.

RESULTS

Study population

Spirometric results were available in the primary care laboratory database for 14,056 subjects aged ⩾21 yrs who had been referred for lung function testing by their GP. Table 1 shows the demographic and lung function characteristics of the males and females in the present study population. At 54.2±15.2 yrs, the males' mean±SD age was higher than that

of the females (51.9±15.1 yrs). Of all of the subjects, 69.1% were current or ex-smokers. The post-bronchodilator FEV1/FVC was 0.73±0.13 in males and 0.78±0.11 in females.

The subgroup of subjects aged ⩾50 yrs with a smoking history consisted of 3,473 (57.7%) males and 2,543 females, with a mean±SD age of 63.4±8.8 yrs (table 1). Of these, 1,308 males and 1,195 females (41.6% of subgroup) were current smokers. The post-bronchodilator FEV1/FVC was 0.68±0.13 in the males and 0.73±0.12 in the females. Compared with the females in the subgroup, post-bronchodilator FEV1 was lower in males (72.4±19.6 versus 75.7±19.5% pred).

Distribution of post-bronchodilator airflow obstruction

Figure 1 shows the relationship between the FEV1/FVC ratio and age in males and females in the study sample. Both graphs clearly show that the discrepancy between the two definitions of airflow obstruction increases with the age of the subjects. The graphs also show that, particularly in females aged <40 yrs, use of the fixed FEV1/FVC ratio cut-off point leads
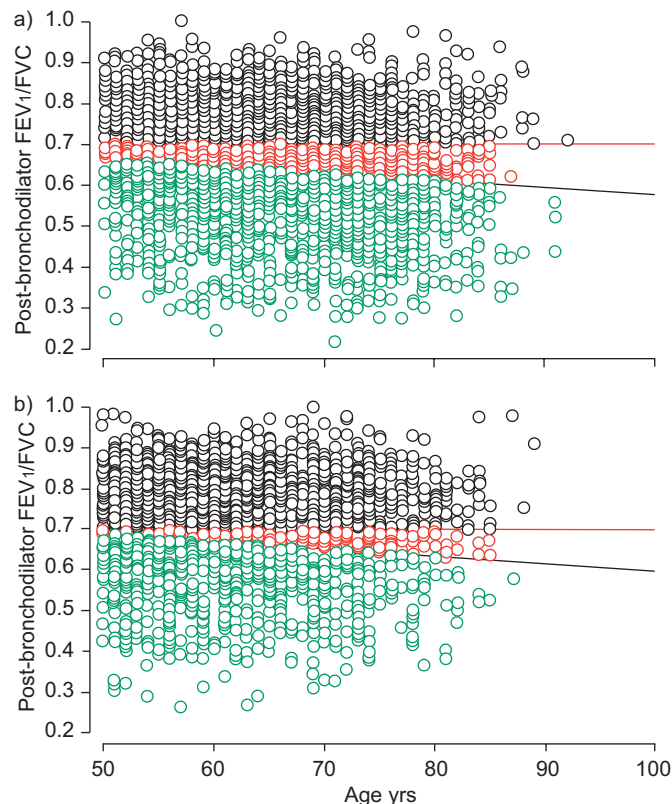
FIGURE 2. Association between forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) and age in symptomatic current and ex-smokers aged ⩾50 yrs referred for spirometric testing by their general practitioner: a) males (n=3,473); and b) females (n=2,543). The horizontal red line indicates the fixed 0.70 FEV1/FVC cut-off point that is currently recommended by all major clinical chronic obstructive pulmonary disease guidelines [1, 5, 6, 8]; the black diagonal line indicates the lower limit of normal for healthy nonsmoking males and females, respectively. Green circles: true positive (unique subjects considered to have airflow obstruction according to both definitions); black circles: true negative; red circles: false positive (subjects in whom discordant conclusions regarding the presence of airflow obstruction are drawn).

to a small number of subjects being unjustly considered to have no airflow obstruction, whereas, according to their sex- and age-specific LLN, they do show obstruction. For the subgroup of current or ex-smokers aged ⩾50 yrs, no such cases were observed (fig. 2).

Agreement between definitions of post-bronchodilator airflow obstruction

Table 2 shows the concordance and discordance between the fixed FEV1/FVC cut-off point and LLN cut-off point definitions of airflow obstruction. For all male and female study subjects combined, the sensitivity of the fixed cut-off point relative to the LLN cut-off point definition was 97.9% (95% CI 97.7–98.1%), with a specificity 91.2% (95% CI 90.7–91.7%), positive predictive value of 72.0% (95% CI 71.3–72.7%) and negative predictive value of 99.5% (95% CI 99.4–99.6%).

The agreement between the two definitions for the subgroup of current and ex-smokers aged ⩾50 yrs is shown in table 3. In this subgroup, the sensitivity of the fixed FEV1/FVC cut-off point relative to the LLN cut-off point definition was 100%, the specificity 82.0% (95% CI 81.0–83.0%), the positive predictive value 69.2% (95% CI 68.0–70.4%) and the negative predictive value 100%.

Figure 3 shows the true positive, false positive, true negative and false negative rates of the fixed cut-off point definition in relation to age for the whole study sample. Starting from subjects aged 30 yrs, there was a steady increase in the rate of false positive diagnoses of airflow obstruction. For subjects in the 31–40-yr age stratum, the proportion of false positive diagnoses based on the fixed cut-off point definition was 8.9% (95% CI 7.7–10.1%) of all positive diagnoses. For the other age strata, the proportions of false positive diagnoses using the fixed cut-off point definition were 15.5% (95% CI 14.2–16.8%) for those aged 41–50 yrs, 23.9% (95% CI 22.4–25.4%) for those aged 51–60 yrs, 33.2% (95% CI 31.0–35.4%) for those aged 61–70 yrs, 38.7% (95% CI 35.7–41.7%) for those aged 71–80 yrs and 42.7% (95% CI 37.3–48.1%) for those aged ⩾81 yrs (p<0.001 in Chi-squared test).

Figure 4 shows the prevalence of post-bronchodilator airflow obstruction by diagnostic definition and age group for the total study population.

Airflow obstruction with pre-bronchodilator versus post-bronchodilator spirometry

Table 4 shows the concordance and disconcordance between pre- and post-bronchodilator rates of airflow obstruction for the fixed cut-off point definition (i.e. FEV1/FVC of <0.70 versus FEV1/FVC of ⩾0.70). For the total study population, the sensitivity of an observed pre-bronchodilator airflow obstruction was 94.5% (95% CI 94.1–94.9%), with a specificity of 89.0% (95% CI 88.5–89.5%), positive predictive value of 74.7% (95% CI 74.0–75.4) and negative predictive value of 97.9% (95% CI 97.7–98.1%). In the subgroup of current and ex-smokers aged ⩾50 yrs, the corresponding figures were 94.6% (95% CI 94.0–95.2%), 87.4% (95% CI 86.6–88.2%), 84.2% (95% CI 83.3–85.1%) and 95.8% (95% CI 95.3–96.3%), respectively (data not shown).

TABLE 2	Comparison of definitions by level of obstruction[#]			
	LLN cut-off			**Total**
	Moderate-to-very severe[¶]	**Mild[+]**	**None[§]**	
Fixed cut-off				
Moderate-to-very severe[f]	2277	124	740	3141
Mild[##]	16	164	265	445
None[¶¶]	44	12	10414	10470
Total	2337	300	11419	14056

LLN: lower limit of normal (*i.e.* SD score of <-1.645). [#]: based on post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) and FEV1 in all study subjects (n=14,056); [¶]: FEV1/FVC<LLN and FEV1<LLN; [+]: FEV1/FVC<LLN and FEV1⩾LLN; [§]: FEV1/FVC⩾LLN; [f]: FEV1/FVC <0.70 and FEV1 <80% of predicted value; [##]: FEV1/FVC <0.70 and FEV1 ⩾80% pred; [¶¶]: FEV1/FVC ⩾0.70.

TABLE 3	Comparison of definitions by level of obstruction[#] in the older current and ex-smoker subgroup[¶]			
	LLN cut-off			**Total**
	Moderate-to-very severe[+]	**Mild[§]**	**None[f]**	
Fixed cut-off				
Moderate-to-very severe[##]	1552	100	571	2223
Mild[¶¶]	0	78	199	227
None[++]	0	0	3516	3516
Total	1552	178	4286	6016

LLN: lower limit of normal (*i.e.* SD score of <-1.645). [#]: based on post-bronchodilator forced expiratory volume in one second (FEV1)/forced vital capacity (FVC) and FEV1; [¶]: 6,016 current or ex-smokers aged ⩾50 yrs; [+]: FEV1/FVC<LLN and FEV1<LLN; [§]: FEV1/FVC<LLN and FEV1⩾LLN; [f]: FEV1/FVC⩾LLN; [##]: FEV1/FVC <0.70 and FEV1 <80% of predicted value; [¶¶]: FEV1/FVC <0.70 and FEV1 ⩾80% pred; [++]: FEV1/FVC ⩾0.70.

DISCUSSION

In the present study, diagnostic outcomes were compared when two recommended but different definitions of airflow obstruction based on FEV1/FVC were applied in a large
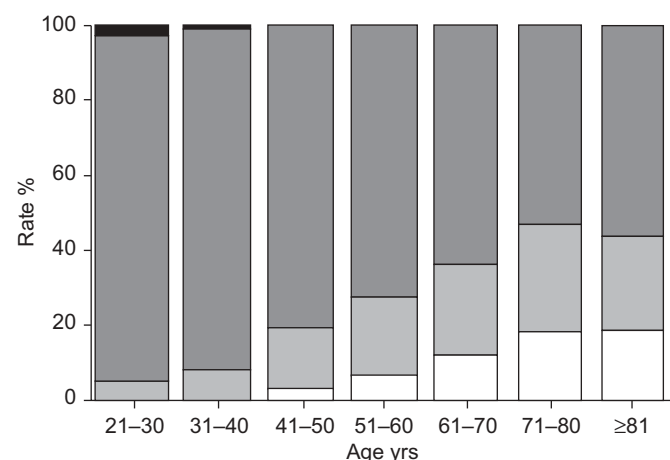
FIGURE 3. Concordant and discordant classification of airflow obstruction in 14,056 adult males and females referred for spirometric testing by their general practitioner when comparing the 0.70 fixed forced expiratory volume in one second/ forced vital capacity ratio cut-off point definition with the sex- and age-specific lower limit of normal cut-off point as the gold standard definition. □: false positive; ▨: true positive; ▦: true negative; ■: false negative.

population of subjects without a prior diagnosis of chronic respiratory disease referred for diagnostic spirometry by their GP. The present findings show that the older such subjects are, the more pronounced the discrepancy between the widely recommended 0.70 fixed FEV1/FVC cut-off point and a sex- and age-specific LLN cut-off point for this ratio becomes. Although the negative predictive value of the fixed ratio definition was very high (99.4% for the whole sample and 100% for the subgroup of older current and ex-smokers with a high prior probability of COPD), the positive predictive value of the fixed ratio was insufficient (72.0% overall and 69.2% in the aforementioned subgroup). Since spirometry is used as a diagnostic test for the verification of obstruction (rather than its exclusion), these predictive values are insufficient. When using the fixed FEV1/FVC cut-off point definition in middle-aged and elderly current or ex-smokers, at least a quarter of all subjects with airflow obstruction should be considered false positives when sex and age are taken into account. This clearly has implications for the GP's diagnostic interpretation in individuals who present with respiratory symptoms, and, consequently, may have an undesirable impact upon those who are incorrectly confronted with a positive diagnosis of COPD and are treated as such. Conversely, it is important to realise that, in daily practice, there will always be the risk of false positive and false negative results, especially in the borderline area between normal and abnormal function. Careful follow-up of patients and confirmation of the initial result can largely overcome this.
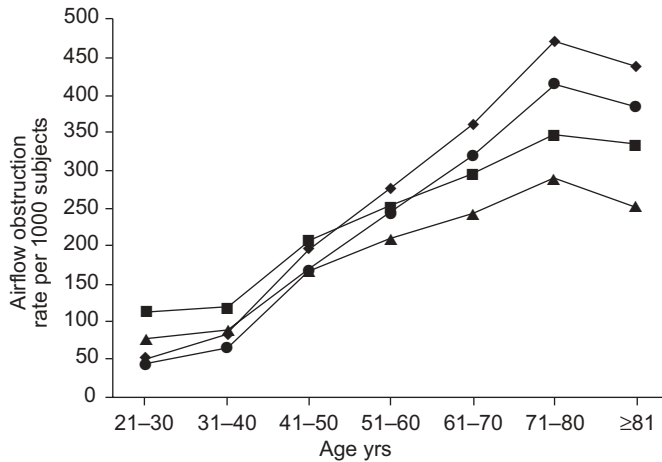
FIGURE 4. Prevalence of post-bronchodilator airflow obstruction in the total study population (n=14,056), by age group and diagnostic definition. ♦: fixed forced expiratory volume in one second (FEV_1)/forced vital capacity (FVC) cut-off of <0.70; ●: FEV_1/FVC of <0.70 plus FEV_1 ⩽50% pred (Global Initiative for Chronic Obstructive Lung Disease stages II–IV); ■: FEV_1/FVC <88% of predicted value in males and <89% pred in females; ▲: lower limit of normal of FEV_1/FVC cut-off.

Use of pre-bronchodilator instead of post-bronchodilator spirometry to demonstrate airflow obstruction in the present study population resulted in an acceptable outcome with regard to sensitivity and negative predicted value, but also in a less favourable outcome with regard to specificity and, especially, positive predictive value; the rate of false positive interpretations of obstruction when using the fixed 0.70 FEV_1/FVC cut-off point was 25.3% in the present total study population of symptomatic subjects, and 15.8% in the subgroup of symptomatic current or ex-smokers aged ⩾50 yrs. Similar rates of overestimation of the prevalence of airflow obstruction have previously been reported in general population studies [23, 24].

Comparison with existing literature

The main origin of the choice of the arbitrary 0.70 fixed FEV_1/FVC cut-off point is probably the publication of the first Global Initiative for Chronic Obstructive Lung Disease (GOLD) workshop report in 2001 [7]. Ever since its publication, the GOLD

guideline has served as the point of departure for many other COPD guidelines around the world, including the National Institute for Health and Clinical Excellence guideline [1]. However, the initial 2001 GOLD workshop report had already stated that the proposed classification system for airflow obstruction was a ''pragmatic approach aimed at practical implementation and should only be regarded as an educational tool'' [7]. In the latest update of the GOLD guideline (2006), the authors emphasise that the recommended fixed FEV_1/FVC cut-off point (as well as the percentage predicted FEV_1 cut-off points for COPD severity staging) is recommended for the sake of simplicity, and that the use of the fixed 0.70 value may result in overdiagnosis of COPD in the elderly. In the present authors' view, there is now sufficient scientific evidence from a number of different population studies [13–18] showing that undifferentiated use of the fixed 0.70 cut-off point for the FEV_1/FVC is afflicted with an age bias that may lead to an unacceptably high proportion of middle-aged and elderly subjects being unjustly diagnosed with airflow obstruction. The present real-life data from subjects referred by their GP with a directed indication for a diagnostic spirometric test confirm this presumption. Although it is obvious that the fixed FEV_1/FVC ratio cut-off point definition is a very convenient way of defining airflow obstruction, the resultant mismatch between the simplicity and the unfavourable rate of false positive results for the main diagnostic criterion for COPD should definitely give rise to reconsideration of this approach [25].

It was recently reported that subjects classified as normal when applying the LLN definition but as obstructive when applying the fixed ratio are more likely to die and show a higher risk of COPD related hospitalisation during follow-up [26]. Although this is an interesting observation, the study distracts from the real debate, since demonstration of airflow obstruction in the work-up involved in diagnosing chronic respiratory conditions is quite a different thing from using lung function measurements for the prediction of mortality or hospital admission [27]. Other conditions that influence respiratory function (e.g. heart failure) are likely to be responsible for the increased risk of mortality and hospitalisation in such patients. COPD patients with mild obstruction according to the fixed FEV_1/FVC definition show significant physiological limitation as regards exercise capacity [28], which raises the possibility that even mild abnormality in lung function may be important in some circumstances. This should be all the more reason to make sure that sex and, particularly, age are taken into account when defining (mild) airflow obstruction.

Strengths and limitations

To the best of the present authors' knowledge, the present study is the first to analyse post-bronchodilator spirometric results obtained in a primary care population with a wide age range. The GPs considered a spirometric test indicated as a part of their diagnostic work-up in individuals who presented with symptoms that may point to a chronic respiratory condition. In contrast with the population screening studies that have recently been reported [15–18], the subjects in the present study population had a higher prior probability of underlying chronic respiratory illness and truly reflect the group of people in which spirometry is applied in primary care practice. One limitation of the present study was that it was not

TABLE 4	Concordance and disconcordance of rates of pre- and post-bronchodilator airflow obstruction in all study subjects[#]		
	Post-bronchodilator FEV_1/FVC		**Total**
	Obstruction[¶]	**No obstruction[+]**	
Pre-bronchodilator FEV_1/FVC			
Obstruction[¶]	3390	1149	4539
No obstruction[+]	196	9321	9517
Total	3586	10470	14056

Data are presented as n. FEV_1: forced expiratory volume in one second; FVC: forced vital capacity. [#]: n=14,056; [¶]: FEV_1/FVC of <0.70; [+]: FEV_1/FVC of ⩾0.70.

possible to check the quality of the spirometric test according to current standards [29]. Conversely, poor-quality spirometric tests are often interpreted nonetheless, and poor test performance will affect the outcome of both definitions of airflow obstruction equally. A final limitation was that follow-up data were not yet available for the present study subjects; only time can tell whether or not the subjects will exhibit the progressive lung function decline that is typical of COPD.

One aspect that should be borne in mind when reconsidering the choice of a more rational definition of airflow obstruction is that physicians and nurses may lack sufficient biostatistical knowledge to fathom approaches based on reference population distributions [30]. Conversely, there are examples of using LLN approaches in medical practice, for instance when expressing the results of bone mineral density measurements for osteoporosis [31] and assessing thinness or overweight in children and adolescents [32, 33]. Contemporary electronic spirometers and spirometric software should be able to support its interpretation if a more sophisticated definition of airflow obstruction were to be used in clinical practice. Several spirometers that calculate, show and print LLN and/or SD scores are commercially available.

It is important to realise that the choice of definition of airflow obstruction also has a substantial impact on prevalence rates of obstructive lung disease. Depending upon the definition used, population prevalence rates for COPD may double, or even triple, as a consequence of the age bias in the fixed ratio definition of airflow obstruction [34–36]. The present findings, as depicted in figure 4, suggest a similar increase in positive diagnosis of airflow obstruction in subjects who seek medical care because of respiratory symptoms.

Conclusion

In conclusion, the previously reported sex and age dependency of the forced expiratory volume in one second/forced vital capacity ratio, the main criterion for demonstrating airflow obstruction when diagnosing chronic obstructive pulmonary disease, leads to substantial overdiagnosis of obstruction in the middle aged and elderly. In both males and females, the rate of false positive diagnoses increases with age when the widely recommended fixed 0.70 forced expiratory volume in one second/forced vital capacity cut-off point is used. As in previously reported population studies, the use of pre- instead of post-bronchodilator spirometry leads to overestimation of the prevalence of airflow obstruction in subjects who present to their general practitioner with respiratory symptoms. Although diagnosis of chronic obstructive pulmonary disease obviously requires more than a spirometric test (*i.e.* symptoms, smoking history and additional diagnostic tests), a definition of airflow obstruction that is based on lower limits of normal from an appropriate reference population would diminish the rate of false positive interpretations. The individual, as well as the societal, burden of chronic obstructive pulmonary disease is sufficiently large to warrant critical appraisal of the main criterion on which the diagnosis of this disease is based.

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