CHEST

Original Research

LUNG FUNCTION TESTING

Spirometric Criteria for Airway Obstruction*

Use Percentage of FEV_1/FVC Ratio Below the Fifth Percentile, Not < 70%

James E. Hansen, MD, FCCP; Xing-Guo Sun, MD; and Karlman Wasserman, PhD, MD, FCCP

Background: **Current authoritative spirometry guidelines use conflicting percentage of FEV_1/FVC ratios (FEV_1/FVC%) to define airway obstruction. The American Thoracic Society/European Respiratory Society Task Force characterizes obstruction as a FEV_1/FVC% below the statistically defined fifth percentile of normal. However, many recent publications continue to use the Global Initiative for Chronic Obstructive Lung Disease (GOLD) primary criterion that defines obstruction as a FEV_1/FVC% < 70%. Data from the Third National Health and Nutrition Examination Survey (NHANES-III) should identify and quantify differences, help resolve this conflict, and reduce inappropriate medical and public health decisions resulting from misidentification.**

Methods: **Using these two guidelines, individual values of FEV_1/FVC% were compared by decades in 5,906 healthy never-smoking adults and 3,497 current-smokers of black (African American), Hispanic (Latin), or white ethnicities aged 20.0 to 79.9 years.**

Results: **In the never-smoking population, the lower limits of normal used in other reference equations fit reasonably well the NHANES-III statistically defined fifth percentile guidelines. But nearly one half of young adults with FEV_1/FVC% below the NHANES-III fifth percentile of normal were misidentified as normal because their FEV_1/FVC% was > 70% (abnormals misidentified as normal). Approximately one fifth of older adults with observed FEV_1/FVC% above the NHANES-III fifth percentile had FEV_1/FVC% ratios < 70% (normals misidentified as abnormal).**

Conclusions: **The GOLD guidelines misidentify nearly one half of abnormal younger adults as normal and misidentify approximately one fifth of normal older adults as abnormal.**

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Key words: airway obstruction; percentage of predicted FEV_1/FVC; reference values; spirometry

Abbreviations: ATS = American Thoracic Society; BA = both abnormal; BN = both normal; ERS = European Respiratory Society; FEV_1/FEV_6% = percentage of FEV_1/forced expiratory volume in 6 s; FEV_1/FVC% = percentage of FEV_1/FVC; FN = false negative; FP = false positive; GOLD = Global Initiative for Chronic Obstructive Lung Disease; LLN = lower limit/limits of normal; NHANES-III = Third National Health and Nutritional Examination Survey; NPV = negative predictive value; PPV = positive predictive value; VC = vital capacity

In 1966, Sobol and Weinheimer[1] pointed out the error of using fixed percentages of spirometric predicted values to define abnormality. In 1988, Miller and Pincock[2] emphasized the necessity of using statistically derived lower limits of normal (LLN). Currently, however, respected organizations of pulmonary specialists have defined spirometric airway obstruction in conflicting ways, resulting in ongoing confusion regarding the prevalence of air-

*From the Division of Respiratory and Critical Care Physiology and Medicine, Department of Medicine, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, CA.

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Correspondence to: James E. Hansen, MD, FCCP, Box 405, Harbor-UCLA Medical Center, Torrance, CA 90509; e-mail: jhansen@labiomed.org

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way obstruction in a general or specific population. The most recent guideline of the American Thoracic Society (ATS)/European Respiratory Society (ERS) Task Force interpretative strategies,[3] with which the authors agree, states that an "obstructive ventilatory defect . . . is defined as a reduced forced expiratory volume in one second/vital capacity ratio (FEV_1/VC) below the fifth percentile of the predicted value." This definition contrasts with that described by the Global Initiative for Chronic Obstructive Lung Disease (GOLD),[4] and reinforced in the most current GOLD guidelines[5] and the 2004 ATS/ERS standards for diagnosis and treatment of patients with COPD, as summarized in their position statement.[6] These latter publications primarily define airway obstruction as percentage of FEV_1/FVC (FEV_1/FVC%) $< 70\%$, even though it is recognized that this fixed ratio identifies an unusually high incidence of obstruction in older never-smoking individuals unexposed to noxious particles or gases.[7] Despite this recognition and its lack of statistical justification, many current reports[8–13] continue to use the fixed limit of FEV_1/FVC% $< 70\%$ to identify and define airway obstruction, a usage that tends to underestimate airway obstruction in the young and overestimate it in older adults. Minor considerations are as follows: (1) the ratio denominator should be FVC or vital capacity (VC), since the latter is often larger in those with airway obstruction[14]; (2) spirometric values after aerosolized bronchodilators are necessary[4]; and (3) a reduction in FEV_1 is necessary to diagnose airflow obstruction. To further explore the potential magnitude of the problem and importance of selecting good criteria of airflow obstruction, the authors used high-quality spirometric data from nearly 10,000 ethnically defined, healthy never-smokers and current-smokers in the United States[15] to quantify the degree of overidentification and underidentification of airway obstruction as related to age.

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Materials and Methods

Subjects

Subjects were 5,906 never-smoking adults without recognized respiratory or musculoskeletal disease and 3,497 current-smoking adults from the Third National Health and Nutrition Examination Survey (NHANES-III) database[16] from ages 20.0 to 79.9 years (third to eighth decades). Each subject selected (Table 1) was classified ethnically as black, Latin, or white, and had performed repeated spirometric maneuvers meeting ATS standards.[15,16] These data from unidentified subjects had been ethically obtained with informed consent and Institutional Review Board approval.

Analysis and Statistics

First, Hankinson et al[17] LLN equations for FEV_1/FVC% specific for sex, ethnicity, and age, and derived from healthy NHANES-III never-smokers were used. By decade, sex, and ethnicity, the 9,403 individual subjects in each never-smoking and current-smoking group were identified as being above or below the fifth percentile of normal. If above, such individuals were identified as *normal*; if below, they were considered to have a $< 5\%$ chance of being normal and were therefore identified as *abnormal*.[18] Second, by decade, sex, and ethnicity, the individual subjects in each never-smoking and current-smoking group who had FEV_1/FVC% $< 70\%$ were similarly identified.

Third, by sex and smoking status, grouping all ethnicities together, we identified the number and percentage of subjects in

Table 1—*Number of NHANES-III Subjects Included in Study*

	Women			Men			
Decade of Life	Black	Hispanic	White	Black	Hispanic	White	Totals
Never-smokers							
Third	371	426	224	289	303	181	1,794
Fourth	306	312	274	135	165	178	1,370
Fifth	191	201	209	91	95	113	900
Sixth	98	84	221	44	46	86	576
Seventh	103	160	201	50	71	119	704
Eighth	78	58	293	24	19	90	562
Total	1,147	1,241	1,425	633	699	764	5,906
Current-smokers							
Third	153	91	201	147	197	159	948
Fourth	204	72	172	224	143	159	974
Fifth	127	44	115	155	102	134	677
Sixth	69	28	95	90	32	111	425
Seventh	48	23	59	68	64	78	340
Eighth	11	4	45	21	12	40	113
Total	612	262	687	705	550	681	3,497

each decade with the following characteristics: (1) obstruction as per both guidelines (both abnormal [BA]); (2) normal by both guidelines (both normal [BN]); (3) below the fifth percentile but with $FEV_1/FVC\%$ ratio $\geq 70\%$ (false negative [FN]); or (4) above or equal to the fifth percentile but $FEV_1/FVC\%$ ratio $< 70\%$ (false positive [FP]). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were calculated for each decade by gender and smoking status (Table 2).

Fourth, considering the Hankinson et al[17] fifth percentile as the "correct" and "gold standard," we calculated for each decade and smoking status the normal and abnormal subjects misidentified by substituting the $FEV_1/FVC\% < 70\%$ or $\geq 70\%$ standard: abnormals misidentified as normals, FN/(FN +BA), *ie*, 1 – sensitivity; and normals misidentified as abnormals, FP/(FP + BN), *ie*, 1 − specificity. Fifth, to further assess the validity of the formulae used by Hankinson et al,[17] we compared two other frequently used American $FEV_1/FVC\%$ formulae[19,20] for never-smokers with well-defined fifth percentile limits to see if the number per decade of the "abnormal" 2,189 white never-smoking individuals from the NHANES-III database[16] approximated 5%.

Results

The percentage of NHANES-III never-smokers with $FEV_1/FVC\% < 70\%$ are shown by decade of age, sex, and ethnicity in Figure 1, *top*, *A*. For each group, the prevalence was < 5% for the third and fourth decades; thereafter, it increased to 6 to 14% for the sixth decade, 11 to 18% for the seventh decade, and 19 to 33% for the eighth decade. If ethnic- and sex-specific groups were weighted equally, mean values for the third through eighth decades, respectively, were 2.0%, 2.6%, 4.7%, 8.3%, 14.6%, and 25.3%. These values contrast with an optimal 5% during each decade. Figure 1, *bottom*, *B*, shows similar values for the current-smoking population. With equal weighting, mean values for the third through eighth decades, respectively, were 3.2%, 5.1%, 14.1%, 31.9%, 42.2%, and 54.4%. For 11 of the 12 group/decade comparisons, the percentages for men exceeded those of women, likely because men normally have lower $FEV_1/FVC\%$ values than women of the same age.

Table 2—*Summary of Abbreviations and Formulae Used*

Groupings
BA = FEV_1/FVC < 5th percentile and $FEV_1/FVC < 70\%$
BN = $FEV_1/FVC \geq$ 5th percentile and $FEV_1/FVC \geq 70\%$
FN = FEV_1/FVC < 5th percentile and $FEV_1/FVC \geq 70\%$
FP = $FEV_1/FVC \geq$ 5th percentile and $FEV_1/FVC < 70\%$
Formulae
Sensitivity, % = 100 × BA/(BA + FN)
Specificity, % = 100 × BN/(BN + FP)
PPV, % = 100 × BA/(BA + FP)
NPV, % = 100 × BN/(BN + FN)
Abnormals misidentified as normals, % = 100 × FN/(FN + BA)
Normals misidentified as abnormals, % = 100 × FP/(FP + BN)

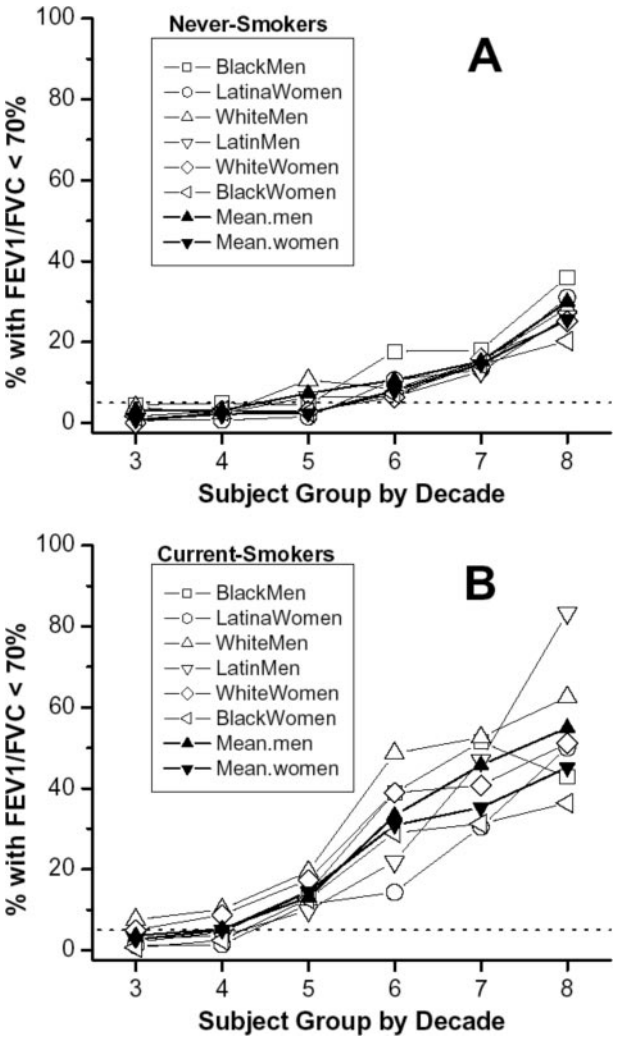

Figure 1. Percentages of healthy 5,906 NHANES-III never-smokers (*top*, *A*) and 3,497 current-smokers (*bottom*, *B*), by sex, ethnicity, and decade, with observed $FEV_1/FVC\% < 70\%$. Observed $FEV_1/FVC\% < 70\%$, rather than the statistically valid fifth percentile, is the primary GOLD spirometric criterion used to screen for airway obstruction. Among never-smokers, all of those above the expected fifth percentile dashed line will be improperly identified as "airway obstruction" using the GOLD $FEV_1/FVC\% < 70\%$ criterion. Among current-smokers, some of those above the expected fifth percentile dashed line will be improperly identified as "airway obstruction" using the GOLD $FEV_1/FVC\% < 70\%$ criterion.

Table 3 gives details of the third analysis. Sensitivities were low in all groups in the third and fourth decades, so that overall sensitivity from 20 to 39.9 years is only 41% (bottom of Table 3). After the fifth decade, the percentages of FN cases are negligible, but FP-observed $FEV_1/FVC\%$ values continue to increase. For the seventh and eighth decades, specificity (correct diagnosis of nonobstruction) has declined from 100 to 81% while the PPV (percentage of reliability of positive test results) has declined from 100 to 55%.

Table 3—*Comparison of Observed $FEV_1/FVC\% < 70\%$ or Greater Than or Equal to the Fifth Percentile LLN with Observed $FEV_1/FVC\% < 70\%$ or $\geq 70\%$***

Decade of Life	$FEV_1/FVC\%$ $< 5\%$ LLN and $< 70\%$ (BA)	$FEV_1/FVC\%$ $\geq 5\%$ LLN and $\geq 70\%$ (BN)	$FEV_1/FVC\%$ $< 5\%$ LLN and $\geq 70\%$ (FN)	$FEV_1/FVC\%$ $\geq 5\%$ LLN and $< 70\%$ (FP)	Sensitivity: BA/ (BA + FN)	Specificity: BN/ (BN + FP)	PPV: BA/ (BA + FP)	NPV: BN/ (BN + FN)
Male never-smokers								
Third	2.6	94.0	3.4	0.0	43	100	100	97
Fourth	2.9	95.5	1.6	0.0	64	100	100	98
Fifth	6.0	92.3	0.7	1.0	90	99	86	99
Sixth	5.5	90.2	0.0	4.3	100	95	56	100
Seventh	4.6	85.0	0.0	10.4	100	89	31	100
Eighth	6.0	73.7	0.0	20.3	100	78	23	100
Female never-smokers								
Third	0.8	95.8	3.5	0.0	19	100	100	97
Fourth	1.7	94.7	3.6	0.0	32	100	100	96
Fifth	2.2	95.5	2.3	0.0	48	100	100	98
Sixth	6.2	92.5	0.5	0.7	93	99	89	99
Seventh	9.3	85.5	0.2	5.0	98	94	65	100
Eighth	12.1	76.7	0.0	11.2	100	87	52	100
Male current-smokers								
Third	4.2	90.9	5.0	0.0	46	100	100	95
Fourth	5.9	89.7	4.4	0.0	57	100	100	95
Fifth	14.1	82.9	2.3	0.8	86	99	95	97
Sixth	32.2	58.8	0.0	9.0	100	87	78	100
Seventh	34.3	49.5	0.0	16.2	100	75	68	100
Eighth	42.9	37.7	0.0	19.5	100	66	69	100
Female current-smokers								
Third	2.7	88.1	9.2	0.0	23	100	100	91
Fourth	4.7	89.3	6.0	0.0	44	100	100	94
Fifth	14.3	81.1	4.5	0.0	76	100	100	95
Sixth	30.7	68.2	0.0	1.0	100	98	97	100
Seventh	25.4	64.6	0.0	10.0	100	87	72	100
Eighth	31.3	50.0	0.0	18.8	100	73	63	100
All adults								
Third and fourth	2.8	92.9	4.3	0.0	41	100	100	95
Seventh and eighth	15.5	73.2	0.0	11.3	99	81	55	100

*Data are presented as %.

Figure 2 shows the results of the fourth analysis, in which abnormals were misidentified, FN/(FN + BA), and normals were misidentified, FP/(FP + BN), using data from Table 3. More than one half of those in the third and fourth decades and one fifth in the fifth decade with an observed $FEV_1/FVC\%$ below the fifth percentile for their age were wrongly identified (abnormals misidentified) as not having airway obstruction because their observed $FEV_1/FVC\%$ was $\geq 70\%$. Further, approximately one fourth of current-smokers and one eighth of never-smokers in the seventh and eighth decades who had observed $FEV_1/FVC\%$ above the fifth percentile were wrongly identified (normals misidentified) as having airway obstruction because their observed $FEV_1/FVC\%$ was $< 70\%$. Thus, the standard of $FEV_1/FVC\% < 70\%$ or $\geq 70\%$ underidentifies airway obstruction in the younger adults, and overidentifies airway obstruction in older adults. Table 4 shows that, for each decade, approximately 5% of the NHANES-III never-smokers had observed $FEV_1/FVC\%$ values below the fifth percentile, whether the Hankinson et al,[17] Crapo et al,[19] or Knudson et al[20] reference equations were used.

Discussion

This study illustrates the importance of using statistically valid spirometric criteria to identify the prevalence of airway obstruction. Use of the GOLD criterion to identify obstruction as an $FEV_1/FVC\% < 70\%$ results in finding an inappropriately high prevalence of obstruction in adults in seventh and eighth decades, among never-smokers and probably among current-smokers. Confirmatory evidences in these decades are the relatively low specificity and very low PPV (Table 3) and high ratios of normals misidentified as abnormals (Fig 2). The latter indicate that approximately one seventh of never-smokers and one fifth of current-smokers in these decades with $FEV_1/FVC\%$ above the fifth percentile LLN

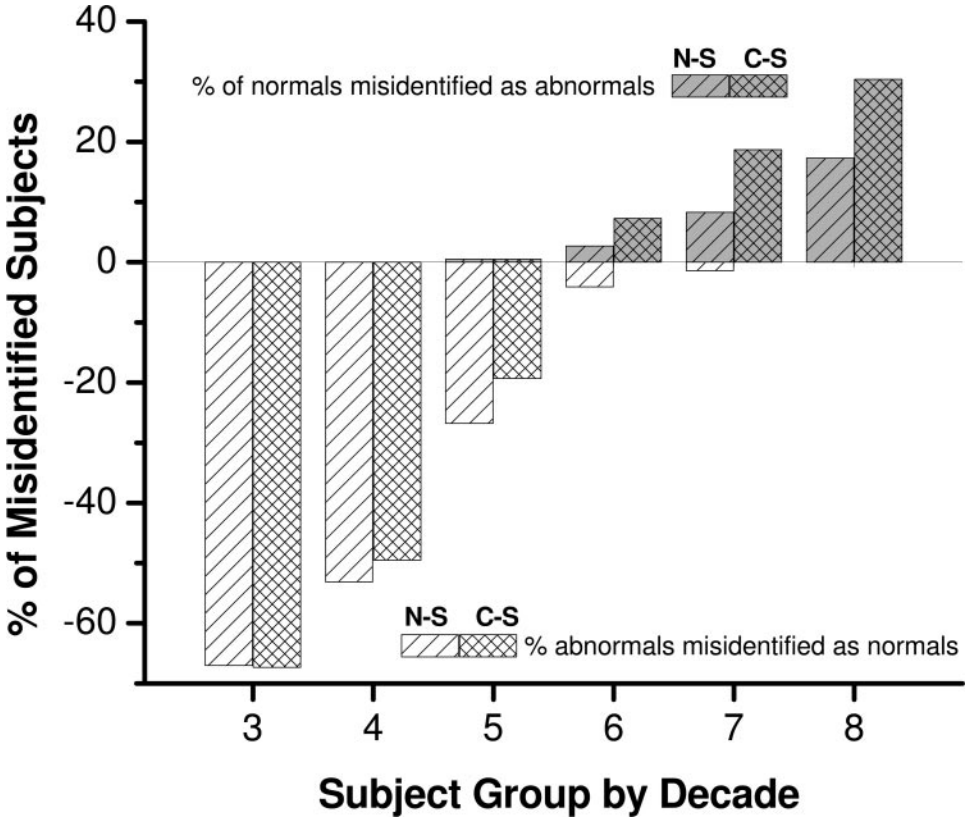

FIGURE 2. Underidentification and overidentification of airway obstruction, by decade, in 5,906 never-smokers and 3,497 current-smokers using the GOLD 70% of $FEV_1/FVC\%$ as a criterion. For each decade, the left of the paired columns are never-smokers (N-S) and the right of the paired columns are current smokers (C-S). The columns below the zero line are abnormals misidentified as normals; the columns above zero line are normals misidentified as abnormals. This criterion causes underidentification of airway obstruction in the younger subjects, reasonable identification in early middle age, and overidentification in the older subjects.

would be misidentified as having airway obstruction using the GOLD $FEV_1/FVC\%$ criterion (Fig 2).

Also importantly, the observed GOLD $FEV_1/FVC\%$ criterion fails to identify airway obstruction in many in the third to fifth decades of life. Confirming this finding are the 19 to 46% sensitivity in the third decade and the 32 to 64% sensitivity in the fourth decade (Table 3), plus the high frequency of misidentified normal subjects (approximately two thirds in the third decade, one half in the fourth decade, and one fifth in the fifth decade (Fig 2). The latter indicates that in these decades, nearly half of those with observed $FEV_1/FVC\%$ values below fifth percentile LLN values would not be considered to have airway obstruction by the GOLD criterion because their observed $FEV_1/FVC\% \geq 70\%$.

Table 4—*NHANES-III Never-Smoking White Adults With $FEV_1/FVC\%$ Below the Fifth Percentile LLN Using Three Sets of Reference Values

Decade of Life	Patients, No.	Abnormal Values		
		Hankinson et al[17]	Crapo et al[19]	Knudson et al[20]
Third	405	22 (5.4)	31 (7.7)	26 (6.4)
Fourth	452	22 (4.9)	29 (6.4)	23 (5.1)
Fifth	322	24 (7.5)	28 (8.7)	26 (8.1)
Sixth	307	12 (3.9)	16 (5.2)	17 (5.5)
Seventh	320	19 (5.9)	27 (8.4)	32 (10.0)
Eighth	383	27 (7.0)	31 (8.1)	57 (14.9)
Total	2,189	126 (5.8)	162 (7.4)	181 (8.3)

*Data are presented as No. (%).

The continuing use of the GOLD 70% criterion, with inherent lowered sensitivity, specificity, and PPV, seems both unfortunate and unnecessary. We do not question the numeric value of the observed $FEV_1/FVC\%$, only an interpretation based on a fixed standard for all adults.

The 2005 ATS/ERS definition of airway obstruction,[3] *ie*, a $FEV_1/FVC\%$ below the fifth percentile of a normal never-smoking population of similar age, is statistically valid. In cross-sectional studies, although the FEV_1 begins to decline earlier than the FVC

with increasing age in never-smoking populations after maturity,[17] decline in FEV_1/FVC% appears to be quite linear within each gender and ethnic group, at least in survivors to age 70 or 80 years.[17,20–22] Confirmatory is the finding in three commonly used reference groups that approximately 5% of healthy never-smoking adults have FEV_1/FVC% below the 95% confidence limits.

The high percentage of older never- and current-smoking adults with observed FEV_1/FVC% $< 70\%$ noted in Figure 1 deserves comment. Clearly, many of these individuals have FEV_1/FVC% that are well within normal limits for their age and should not be identified or treated as having airways obstruction. As also found, many current-smoking adults in their third and fourth decades with FEV_1/FVC% below the LLN should not be dismissed as normal because their FEV_1/FVC% is $> 70\%$ (Fig 2).

Spirometric surveys do not identify the specific cause of airway obstruction or the presence or absence of disease. Nevertheless, spirometry can help identify lung injury due to exposure to occupational hazards, tobacco smoke, and other noxious inhalants. Clinical findings including history, physical examination, response to inhaled bronchodilators, and measurement of gas transfer index are useful in recognizing if airway obstruction may be due to asthma, chronic bronchitis, emphysema, acute or chronic infection, or acute or chronic inhalant exposure. Using poor spirometric criteria may lead to misdirection of resources, unnecessary costs, and individual and societal harm. The planning for and necessity of preventative or therapeutic interventions and their cost/benefit ratio should be based on the best available spirometric criteria.

GOLD defends its definition of airway obstruction as an FEV_1/FVC% $< 70\%$ on the basis of its simplicity and ease of remembrance.[4] To the authors, these reasons seem unimportant compared to the objective of being able to properly detect airway obstruction in the young or prevent the overdiagnosis and treatment of older individuals who do not have airway obstruction. For example, in this era, the use of the body mass index to define obesity is not discarded because the formula uses the square of height. The additional GOLD criterion[4] requiring a reduction in the absolute value of FEV_1 to identify airway obstruction can be questioned because in three commonly used reference groups,[17,19,20] coefficients of variation for volume measures such as FEV_1 and FVC for a given age, gender, and height are approximately 1.5 to 3 times those for the FEV_1/FVC ratio. However, the GOLD criterion[4] that concerns response to bronchodilators should be helpful in differential diagnosis, but the prebronchodilator spirometric values are key in identifying whether or not baseline airway obstruction is present.

Following are some examples in which use of GOLD criteria could lead to ill-advised actions. Lundback et al,[8] Wilson et al,[23] and Celli et al al[13] correctly noted that the prevalence of airway obstruction in their studies depended on what spirometric criteria were used, yet they failed to advocate using fifth percentile values. Kim et al,[12] on the basis of FEV_1/FVC% $<70\%$, concluded that 26% of Korean men and 10% of Korean women > 45 years old have COPD. Of those > 45 years, 20% of men and 91% of women were never-smokers. Behrendt,[11] using the NHANES-III data for 7,526 never-smokers and a cut-off for FEV_1/FVC% of 70%, concluded that 16 to 18% of those never-smokers aged 60 to 69 years and 25 to 30% of those aged 70 to 79 years had COPD. The high prevalence in both latter studies[11,12] is undoubtedly due to not using appropriate age-specific fifth percentile values.

Normal aging changes should not be considered disease or abnormal. Other examples of aging-related physiologic changes in which age is factored into predicted values are peak heart rate, peak oxygen uptake, VC, and FEV_1. As previously noted, the primary measurement of airway obstruction, FEV_1/FVC% declines linearly with age, at least in American and European never-smoking populations.[17,19–22,24] Only when these normal declines are exceeded should the spirometric finding of airway obstruction be made. Because of the variability of spirometric values within the general population, minimized by reference to age, height, sex, and ethnicity, values below fifth percentile have been recommended for use in identifying abnormality since 1991.[25] Of the several measurements advocated to identify airway obstruction, the FEV_1/FVC%, the percentage of forced expiratory volume in 3 s/FVC, and percentage of predicted FEV_1/forced expiratory volume in 6 s (FEV_1/FEV_6%), all ratios of volume/volume, have lower coefficients of variation than those of individual lung volumes[17,19,20,22,24] and much lower coefficients of variation than measures of flow dependent on volume, such as forced expiratory flow, mid-expiratory range, or forced expiratory flow at 50% of VC.[17,19,20] A proper concern is whether the FVC alone, without obtaining the slow or unforced VC for expressing the percentage of FEV_1/VC, suffices as a denominator in ascertaining the presence of airway obstruction.[14] In the our experience, when evaluating a general population, the VC and FVC are usually quite similar; but with moderate-to-severe obstructive disease, the VC may be considerably larger, strengthening the evidence of airway obstruction.

The FEV_1/FEV_6% has been proposed as a substitute for the FEV_1/FVC% in screening for airway obstruction.[26] Although the FEV_1/FEV_6% ratio may suffice adequately in patients with known significant airway obstruction,[27–29] it seems to discriminate airway obstruction less well in a general population.[30]

A recent suggestion to use mean values of FEV_1/FVC% minus 1 SD to identify airway obstruction[23] seems unwise, since approximately an additional 15% of normal never-smokers would be identified with airway obstruction using this criterion. In conclusion, we recommend that the GOLD criterion of airway obstruction as an observed FEV_1/FVC% $< 70\%$ be discarded. Its usage causes significant underidentification of airway obstruction in the young and overidentification in older individuals and populations.

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