Respiratory Impairment in Older Persons: When Less Means More

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ABSTRACT

BACKGROUND: Among older persons, within the clinical context of respiratory symptoms and mobility, evidence suggests that improvements are warranted regarding the current approach for identifying respiratory impairment (ie, a reduction in pulmonary function).

METHODS: Among 3583 white participants aged 65 to 80 years (Cardiovascular Health Study), we calculated the prevalence of respiratory impairment using the current spirometric standard from the Global Initiative for Obstructive Lung Disease (GOLD) and an alternative spirometric approach termed “lambda-mu-sigma” (LMS). Results for GOLD- and LMS-defined respiratory impairment were evaluated for their (cross-sectional) association with respiratory symptoms and gait speed, and for the 5-year cumulative incidence probability of mobility disability.

RESULTS: The prevalence of respiratory impairment was 49.7% (1780/3583) when using the GOLD and 23.2% (831/3583) when using LMS. Differences in prevalence were most evident among participants who had no respiratory symptoms, with respiratory impairment classified more often by the GOLD (38.1% [326/855]) than LMS (12.3% [105/855]), as well as among participants who had normal gait speed, with respiratory impairment classified more often by the GOLD (46.4% [1003/2164]) than LMS (19.3% [417/2164]). Conversely, the 5-year cumulative incidence probability of mobility disability for respiratory impairment was higher for LMS than GOLD (0.313 and 0.249 for never-smokers, and 0.352 and 0.289 for ever-smokers, respectively), but was similar for normal spirometry by LMS or GOLD (0.193 and 0.185 for never-smokers, and 0.219 and 0.216 for ever-smokers, respectively).

CONCLUSIONS: Among older persons, the LMS approach (vs the GOLD approach) classifies respiratory impairment less frequently in those who are asymptomatic and is more strongly associated with mobility disability.

Published by Elsevier Inc. • The American Journal of Medicine (2013) 126, 49-57

KEYWORDS: Gait speed; Mobility disability; Respiratory impairment; Respiratory symptoms

Funding: Dr Vaz Fragoso is a recipient of a Career Development Award from the Department of Veterans Affairs and an R03 award from the National Institute on Aging (R03AG037051). Dr Gill is the recipient of a National Institute on Aging Midcareer Investigator Award in Patient-Oriented Research (K24AG021507). Dr Concato is supported by the Department of Veterans Affairs Cooperative Studies Program.

Conflict of Interest: The study was conducted at the Veterans Affairs Clinical Epidemiology Research Center and the Yale Claude D. Pepper Older Americans Independence Center (P30AG2134). The investigators retained full independence in the conduct of this research. The Cardiovascular Health Study (CHS) was conducted and supported by the National Heart, Lung, and Blood Institute (NHLBI) of the United States in collaboration with the CHS Study Investigators. This manuscript was prepared using a limited access dataset obtained from the NHLBI and does not necessarily reflect the opinions or views of the CHS or the NHLBI.

Authorship: All authors had access to the data and played a role in writing this manuscript.

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Among older persons, respiratory symptoms and reduced mobility are highly prevalent and associated with important adverse outcomes. In this setting, an underlying mechanism is likely to include a respiratory impairment (ie, a reduction in pulmonary function), given that cumulative exposures to tobacco smoke, respiratory infections, air pollutants, and occupational dusts frequently occur across the lifespan. Accordingly, the method by which respiratory impairment is established in older persons is pertinent to providers in primary care, pulmonary medicine, and other specialties. In particular, because nonrespiratory factors also may lead to respiratory symptoms and reduced mobility in older persons, it is essential that respiratory impairment be identified with a high level of diagnostic relevance.

Respiratory impairment is typically established by spirometric measures of pulmonary function, subsequently categorized as airflow limitation (eg, chronic obstructive pulmonary disease or asthma) or restrictive pattern (eg, interstitial lung disease or heart failure). The criteria that define airflow limitation and restrictive pattern are often based on diagnostic thresholds published by the Global Initiative for Obstructive Lung Disease (GOLD), but these have serious limitations for 2 major reasons. First, the GOLD defines airflow limitation on the basis of a value less than 0.70 for the ratio of forced expiratory volume in 1 second to forced vital capacity (FEV1/FVC). Because aging is associated with increased rigidity of the chest wall and decreased elastic recoil of the lung, an FEV1/FVC less than 0.70 frequently occurs in otherwise healthy never-smokers aged more than 65 years. Second, the GOLD defines restrictive pattern based on FVC less than 80% predicted. Because aging is associated with increased variability in spirometric performance, an increased disparity between percent predicted values and the lower limit of normal is found with advancing age. Given these age-related limitations, GOLD thresholds may misidentify respiratory impairment in older persons.

An alternative approach for establishing respiratory impairment has been promoted, one that defines the lower limit of normal for FEV1/FVC and FVC based on the fifth percentile distribution of z scores, as calculated by lambda-mu-sigma (LMS). This method has a strong mathematical rationale because LMS-calculated z scores account for age-related changes in pulmonary function, including variability in spirometric performance and skewness of reference data. A strong clinical rationale for the LMS approach also exists, supported by analyses of data from 3 large cohorts of aging populations. Specifically, prior work has shown that LMS-defined respiratory impairment, including airflow limitation and restrictive pattern, is associated with respiratory symptoms, slow gait speed, hospitalization, and death. As additional evidence supporting the LMS approach in clinical practice, z scores are routinely used to diagnose osteoporosis (bone mineral density) and the LMS method is widely applied to construct growth charts.

Whether LMS yields advantages over the GOLD within the clinical context of respiratory symptoms and mobility has not been evaluated in older persons. Accordingly, and using data from a large cohort of community-living persons aged 65 to 80 years, we evaluated the association of LMS- and GOLD-defined respiratory impairment with respiratory symptoms, gait speed, and the 5-year cumulative incidence probability of mobility disability.

## Materials and Methods

### Study Population

We used data from the Cardiovascular Health Study (CHS) after obtaining institutional review board approval. The CHS is a population-based, longitudinal study of 5888 Americans aged 65 to 100 years, assembled in 1989 and 1990 as a random sample of Medicare beneficiaries.

For the present study, eligible participants were white and aged 65 to 80 years, and completed at least 2 acceptable spirometric maneuvers at baseline, as defined by the American Thoracic Society (ATS). Our analyses were limited to white participants aged 65 to 80 years because reference values derived from the LMS method were not yet available for nonwhites and those aged more than 80 years. To focus on “irreversible” pathology as the principal group for airflow limitation (ie, chronic obstructive pulmonary disease), participants with self-reported asthma were excluded. As per convention, we did not exclude participants on the basis of spirometric reproducibility criteria. The final sample included 3583 participants.

### Spirometry

Participants underwent spirometry during the baseline examination, as per ATS protocols. For each participant, the measured FEV1/FVC was calculated from the largest set of FEV1 and FVC values that were recorded in any of the spirometric maneuvers meeting ATS acceptability criteria. The respiratory status of each participant was

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**CLINICAL SIGNIFICANCE**

- Among older persons, a z score–based spirometric approach (termed “lambda-mu-sigma”) identified respiratory impairment less frequently in those who were asymptomatic and was more strongly associated with mobility disability compared with the current Global Initiative for Obstructive Lung Disease standard.
- As 2 potential benefits of adopting spirometric z scores, both the designation of respiratory impairment in asymptomatic individuals and the unnecessary use of medications for (“false-positive”) respiratory disease could be reduced.
then categorized as normal spirometry (normal FEV1/FVC and normal FVC) or respiratory impairment, including air-flow limitation (reduced FEV1/FVC) or restrictive pattern (normal FEV1/FVC but reduced FVC). The diagnostic thresholds for FEV1/FVC and FVC were based on LMS and GOLD criteria, as described in the Appendix.16,17,19,20,36

**Demographic and Clinical Characteristics**

These included age, sex, education, body mass index, smoking status, chronic conditions, health status, dyspnea and other respiratory symptoms, gait speed, and mobility disability.32,33,40 Dyspnea severity was graded by an ATS-published 5-level scale (ATS-DLD-78-A), with moderate-to-severe dyspnea corresponding to an ATS grade III—“yes” response to “Do you ever have to stop for breath when walking at your own pace on the level?”33,38

Respiratory symptoms included the following:32,33,38 (1) chronic cough or sputum production—“yes” response to “Do you usually cough on most days for 3 consecutive months or more during the year?” or “Do you bring up phlegm on most days for 3 consecutive months or more during the year?”; (2) dyspnea-on-exertion—“yes” response to “Are you troubled by shortness of breath when hurrying on the level or walking up a slight hill?”; (3) wheezing—“yes” response to “Does your chest ever sound wheezy or whistling occasionally apart from colds?” Gait speed was measured at a usual pace during a timed 15-feet walk, with less than 0.8 m/s denoting slow gait speed.32,39,40 Mobility status was ascertained annually during in-person interviews.32 In the present study, we used the first 5 years of follow-up and a definition for mobility disability based on a “yes” response to “a lot of difficulty or unable to walk up 10-steps or walk a half-mile.”7,41,42

**Statistical Analysis**

Baseline characteristics were summarized as mean values accompanied by standard deviations or counts accompanied by percentages. In a cross-sectional analysis, the frequency distributions of LMS- and GOLD-defined spirometric categories, including normal spirometry and respiratory impairment, were presented in a 2-by-2 agreement table. Because all participants who had GOLD-defined normal spirometry also had LMS-defined normal spirometry, but not vice versa, discordant designations occurred exclusively as respiratory impairment by the GOLD but normal by LMS, hereafter termed the “discordant respiratory impairment group.”

The frequency distributions of LMS- and GOLD-defined respiratory impairment also were evaluated within 4 clinical groups: (1) asymptomatic, defined by the absence of respiratory symptoms and chronic conditions; (2) respiratory symptoms, defined by the composite of chronic cough or sputum production, dyspnea on exertion, or wheezing; (3) moderate-to-severe dyspnea, defined by an ATS grade III or higher; and (4) slow gait speed, defined by a speed less than 0.8 m/s. Each of these clinical groups was stratified further by smoking status as never-smokers or ever-smokers.

To obtain a longitudinal measure of absolute risk, and because mobility disability may have occurred at a variable point in time during the interval between annual follow-up visits, a complementary log-log model for interval-censored event times was used to estimate the cumulative incidence probabilities of new-onset mobility disability over 5 years among participants who did not have mobility disability at baseline.43 Three separate models were estimated, including one each for LMS- and GOLD-defined spirometric categories, and a third for discordant respiratory impairment, and these models were adjusted for age and stratified by smoking status.

Among the 3583 study participants, 149 (4.2%) and 699 (19.5%) had missing baseline and follow-up mobility disability evaluations, respectively. In addition, 142 (4.0%) were deceased before the development of mobility disability. Consequently, after investigating the extent and nature of missing data with a random-effects/pattern-mixture model, sequential regression imputation was used to multiply impute binary values for the missing mobility disability values.44,46 This process included the imputation of 11 values for each missing value, and the process was performed separately for each of the 6 waves of data (baseline and 5 annual follow-up visits). The 11 multiply imputed data sets for each wave were then merged, and the complementary log-log interval censored model was fit to the longitudinal data sets.37 Next, the multiple results were integrated using the IVEware software package,48 and a single set of parameter estimates was used to calculate the probabilities of mobility disability. Finally, plots of cumulative incidence probabilities over time, stratified by LMS- and GOLD-defined spirometric categories and discordant respiratory impairment, were created separately for never- and ever-smokers, with a mean age of 71 years used to obtain age-adjusted cumulative incidence probabilities. SAS 9.2 (SAS Institute Inc, Cary, NC) and the IVEware software package were used for all analyses, with $P < .05$ (2-sided) denoting statistical significance.48,49

**RESULTS**

As shown in Table 1, the mean age was 71.5 years and the mean body mass index was 26.3 kg/m$^2$; 57.7% (2066/3583) were female and 55.9% (2002/3583) were ever-smokers. The mean number of chronic conditions was 1.0, and 20.4% (732/3583) had fair-to-poor health status. Respiratory symptoms were reported by 43.6% (1561/3583), and moderate-to-severe dyspnea was reported by 10.2% (365/3583). A slow gait speed was recorded in 38.5% (1378/3583).

**Table 2** shows frequency distributions of participants according to baseline spirometric category. GOLD-defined respiratory impairment was present in 49.7% (1780/3583), whereas LMS-defined respiratory impairment was present in only 23.2% (831/3583). The discordant respiratory impairment group (ie, respiratory impairment by GOLD, but
normal by LMS) comprised 26.5% (949/3583) of all participants.

Table 3 shows frequency distributions of participants within clinical groups, according to baseline respiratory impairment. In all clinical groups, the prevalence of respiratory impairment was greater when determined by the GOLD than by LMS. For example, among asymptomatic participants (no respiratory symptoms and no chronic conditions), the prevalence of respiratory impairment using GOLD was 38.1% (326/855), but only 12.3% (105/855) using LMS. Likewise, among participants who had respiratory symptoms, moderate-to-severe dyspnea, or slow gait speed, GOLD identified respiratory impairment in 58.5% (913/1561), 67.4% (246/365), and 54.9% (757/1378), respectively, whereas LMS identified only 32.2% (502/1561), 44.7% (163/365), and 29.3% (404/1378), respectively. The differences in prevalence rates for respiratory impairment were especially prominent in never-smokers. In particular, among asymptomatic never-smokers, the GOLD classified 31.6% (134/424) as having respiratory impairment, whereas LMS identified only 8.7% (37/424).

Table 3 also shows frequency distributions of baseline discordant respiratory impairment within clinical groups, indicating that the prevalence of discordant respiratory impairment was similar across all clinical groups (21.3%-29.3%). In particular, the prevalence of discordant respiratory impairment was nearly identical in asymptomatic never-smokers (22.9% [97/424]) vs ever-smokers who had moderate-to-severe dyspnea (23.5% [54/230]).

Figure 1 shows the age-adjusted cumulative incidence of mobility disability over 5 years of annual follow-up, based on spirometric category and smoking status. For both never- and ever-smokers, the 5-year trajectory of incident mobility disability showed a greater slope for LMS- versus GOLD-defined respiratory impairment. In contrast, LMS- and GOLD-defined normal spirometry, as well as discordant respiratory impairment, had lower and nearly identical trajectories of incident mobility disability.

Table 4 shows the age-adjusted cumulative incidence probability of mobility disability at the fifth annual follow-up visit, according to spirometric category and smoking status. By using LMS, the 5-year cumulative incidence probability of incident mobility disability for respiratory impairment in never- and ever-smokers was 0.313 and 0.352, respectively, representing a 62.2% and 60.7% increase relative to normal spirometry, respectively. In contrast, using the GOLD, the 5-year cumulative incidence probability of incident mobility disability for respiratory impairment in never- and ever-smokers was lower at 0.249 and 0.289, respectively, representing only a 34.6% and 33.8% increase relative to normal spirometry, respectively. In contrast, the 5-year cumulative incidence probability of incident mobility disability was similar for LMS- and GOLD-defined normal spirometry, and for discordant respiratory impairment.

**DISCUSSION**

In a representative population of older persons, we found that twice as many participants are given a designation of respiratory impairment using the GOLD versus LMS, with approximately one half versus one quarter of participants, respectively, classified as abnormal. Subsequent analyses revealed that the GOLD results in overdiagnosis according to clinically based assessments. For example, among asymptomatic never-smokers, the GOLD was 4-fold more...
likely than LMS to assign a “diseased” designation. In addition, the 5-year trajectory of incident mobility disability for respiratory impairment showed a greater slope for LMS versus GOLD, such that the percentage increase in the 5-year cumulative incidence probability of mobility disability for respiratory impairment (compared with normal spirometry) was 2-fold greater for LMS versus GOLD. Of note, the designation of discordant respiratory impairment (ie, respiratory impairment by GOLD but normal by LMS) did not differ substantially in prevalence across clinical groups, including asymptomatic never-smokers versus symptomatic ever-smokers, nor did it differ substantially in the 5-year cumulative incidence probability of mobility disability relative to LMS- and GOLD-defined normal spirometry.

Overall, these results indicate that, among older persons, LMS-defined respiratory impairment is established less frequently in those who are asymptomatic and, in turn, is more strongly associated with mobility disability compared with GOLD-defined respiratory impairment. These results also suggest that a “GOLD abnormal” but “LMS normal” determination is best characterized as clinically normal.

Strengths of the current study include assessing outcomes that have high clinical relevance. For example, respiratory symptoms are the most distressing feature of respiratory disease and can lead to disability and increased healthcare use and mortality.1-5 Gait speed, an objective measure of mobility, is strongly associated with disability, hospitalization, and mortality.7,11 Mobility disability, as defined in the present study, is associated with higher rates of morbidity, self-care disability, social isolation, healthcare use, and mortality.6,7,41,42,50

The present study also provides direct evidence to justify the claim that the excess rate of respiratory impairment identified when using the GOLD (ie, the group designated as having discordant respiratory impairment) is not clinically meaningful for several reasons. First, prevalence rates for discordant respiratory impairment did not vary substantially when stratified by clinical group, and second, the probability of incident mobility disability for discordant respiratory impairment was comparable to that of LMS-defined normal spirometry.

### Table 3

<table>
<thead>
<tr>
<th>Clinical Group</th>
<th>N</th>
<th>GOLD</th>
<th>LMS</th>
<th>Discordant</th>
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</thead>
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<tr>
<td><strong>Symptom based</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Asymptomatic†</td>
<td>855</td>
<td>326</td>
<td>105</td>
<td>221</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>424</td>
<td>134</td>
<td>37</td>
<td>97</td>
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<tr>
<td>Ever-smokers</td>
<td>431</td>
<td>192</td>
<td>68</td>
<td>124</td>
</tr>
<tr>
<td>Respiratory symptoms‡</td>
<td>1561</td>
<td>913</td>
<td>502</td>
<td>411</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>602</td>
<td>253</td>
<td>106</td>
<td>147</td>
</tr>
<tr>
<td>Ever-smokers</td>
<td>959</td>
<td>660</td>
<td>396</td>
<td>264</td>
</tr>
<tr>
<td>Moderate-to-severe dyspnea§</td>
<td>365</td>
<td>246</td>
<td>163</td>
<td>83</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>135</td>
<td>67</td>
<td>38</td>
<td>29</td>
</tr>
<tr>
<td>Ever-smokers</td>
<td>230</td>
<td>179</td>
<td>125</td>
<td>54</td>
</tr>
<tr>
<td><strong>Function based</strong></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Normal gait speed</td>
<td>2164</td>
<td>1003</td>
<td>417</td>
<td>586</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>927</td>
<td>313</td>
<td>83</td>
<td>230</td>
</tr>
<tr>
<td>Ever-smokers</td>
<td>1237</td>
<td>690</td>
<td>334</td>
<td>356</td>
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<tr>
<td>Slow gait speed¶</td>
<td>1378</td>
<td>757</td>
<td>404</td>
<td>353</td>
</tr>
<tr>
<td>Never-smokers</td>
<td>635</td>
<td>256</td>
<td>121</td>
<td>135</td>
</tr>
<tr>
<td>Ever-smokers</td>
<td>743</td>
<td>501</td>
<td>283</td>
<td>218</td>
</tr>
</tbody>
</table>

GOLD = Global Initiative for Obstructive Lung Disease; LMS = lambda-mu-sigma.

*The symptom-based groups are not mutually exclusive.
†No respiratory symptoms and no chronic conditions.
‡Chronic cough or sputum production, dyspnea on exertion, or wheezing.
§ATS dyspnea grade III or higher, representing a select subgroup of participants who had respiratory symptoms.
||Equal to or greater than 0.8 m/s.
¶Less than 0.8 m/s.
#See footnote to Table 2 for definitions of respiratory impairment.
As implications of this research, the GOLD approach among older persons may misidentify respiratory impairment and, in turn, may lead to inappropriate use of respiratory therapies with known side effects, as well as potential delays in the consideration of alternative diagnoses.51-53 Conversely, because z scores rigorously account for age-related changes in pulmonary function, and because corresponding diagnostic thresholds are associated with health outcomes, the LMS method has a high level of mathematic and clinical validity when establishing respiratory impairment. Accordingly, adopting the LMS approach could lead to more targeted delivery of respiratory therapies.12,26-30,51

The finding that the prevalence of respiratory impairment was 4-fold greater for GOLD versus LMS in otherwise very
low-risk individuals (ie, never-smokers who had no respiratory symptoms and no chronic conditions) also has important implications for epidemiologic surveys of older populations. In particular, the GOLD may incorrectly suggest respiratory impairment as occurring in almost epidemic proportions. Moreover, clinical trials of respiratory therapies in older populations also can be affected adversely when using the GOLD, because enrollment may include persons at very low risk of having a clinically meaningful respiratory impairment.

We did not evaluate relative risks for mobility disability among participants who had LMS- or GOLD-defined respiratory impairment relative to their respective “internal” reference group of normal spirometry, which may represent a limitation of our study. This analytic strategy was intentionally not selected, however, because the reference groups that define normal spirometry for LMS and GOLD differ, and these reference groups would serve as the basis for calculating relative risks. Accordingly, inferences made from a direct comparison of such relative risks would be an “apples-to-oranges comparison” and would be flawed, particularly given the high likelihood that the GOLD misclassifies normal spirometry in older persons.

Our results were limited to participants who were white and aged 65 to 80 years. With new LMS equations having been published recently for other racial and ethnic groups, as well as for age up to 95 years, future work can extend these results to include nonwhites and those aged more than 80 years. In addition, the longitudinal analysis that yielded cumulative incidence probabilities for mobility disability was limited because the outcome was recorded within relatively large intervals (yearly), preventing explicit handling of death as a competing risk. Last, our longitudinal analysis involved missing data for mobility disability, but this was addressed by using multiple imputation techniques.

CONCLUSIONS
Among older persons and on the basis of respiratory symptoms and mobility, respiratory impairment is more clinically meaningful when defined by LMS compared with the GOLD. As 2 potential “less-is-more” benefits of adopting the LMS approach, both the designation of respiratory impairment in asymptomatic individuals and the unnecessary use of medications for (“false positive”) respiratory disease could be reduced.

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**APPENDIX**

Participants underwent spirometry at baseline, as per ATS
protocols. For each participant, the measured FEV$_1$/FVC
values were calculated from the largest set of FEV$_1$ and FVC
values that were recorded in any of the spirometric maneuvers.
meeting ATS acceptability criteria. The respiratory status of each participant was then categorized as normal spirometry (ie, normal FEV$_1$/FVC and normal FVC) or respiratory impairment, including airflow limitation (ie, reduced FEV$_1$/FVC) or restrictive pattern (ie, normal FEV$_1$/FVC but reduced FVC), with diagnostic thresholds based on LMS and GOLD, as described next.

LMS diagnostic thresholds use spirometric z scores that include specific elements of a distribution, namely, the median (mu), representing how spirometric measures change on the basis of predictor variables; the coefficient of variation (sigma), representing the spread of reference values and adjusting for nonuniform dispersion; and skewness (lambda), representing the departure from normality. Using this methodology, z scores for FEV$_1$/FVC and FVC were calculated as $[(\text{measured} \div \text{predicted median}) \times \text{lambda} \times \sigma]$ with predicted values for the median, lambda, and skewness derived from LMS equations; a z score of −1.64 defined the lower limit of normal as the fifth percentile of distribution (5 LMS-tile). By using the 5 LMS-tile as the diagnostic threshold, normal spirometry was then established by FEV$_1$/FVC and FVC, both $\geq$ 5 LMS-tile, airflow limitation by FEV$_1$/FVC $< 5$ LMS-tile, and restrictive pattern by FEV$_1$/FVC $\geq 5$ LMS-tile and FVC $< 5$ LMS-tile.

The GOLD establishes normal spirometry by FEV$_1$/FVC $\geq$ 0.70 and FVC $\geq 80\%$ predicted, airflow limitation by FEV$_1$/FVC $\geq 0.70$, and restrictive pattern by FEV$_1$/FVC $\geq 0.70$ and FVC $< 80\%$ predicted. Percent predicted values were calculated as $[(\text{measured} \div \text{predicted mean}) \times 100]$, with predicted values derived from published equations.