ORIGINAL ARTICLE

Application of Global Lung Function Initiative Global Spirometry Reference Equations across a Large, Multicenter Pulmonary Function Lab Population

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Abstract

Rationale: Global Lung Function Initiative (GLI) Global spirometry reference equations were recently derived to offer a "race-neutral" interpretation option. The impact of transitioning from the race-specific GLI-2012 to the GLI Global reference equations is unknown.

Objectives: Describe the direction and magnitude of changes in predicted lung function measurements in a population of diverse race and ethnicity using GLI Global in place of GLI-2012 reference equations.

Methods: In this multicenter cross-sectional study using a large pulmonary function laboratory database, 109,447 spirometry tests were reanalyzed using GLI Global reference equations and compared with the existing GLI-2012 standard, stratified by self-reported race and ethnicity.

Measurements and Main Results: Mean FEV_1 and FVC percent predicted increased in the White and Northeast Asian groups and decreased in the Black, Southeast Asian, and mixed/other race groups. The prevalence of obstruction increased by 9.7% in the White group, and prevalences of possible restriction increased by 51.1% and 37.1% in the Black and Southeast Asian groups, respectively. Using GLI Global in a population with equal representation of all five race and ethnicity groups altered the interpretation category for 10.2% of spirometry tests. Subjects who self-identified as Black were the only group with a relative increase in the frequency of abnormal spirometry test results (32.9%).

Conclusions: The use of GLI Global reference equations will significantly impact spirometry interpretation. Although GLI Global offers an innovative approach to transition from race-specific reference equations, it is important to recognize the continued need to place these data within an appropriate clinical context.

Keywords: GLI Global; racial groups; ethnicity; spirometry; health disparities

In 2012, the Global Lung Function Initiative (GLI) issued four sets of "multiethnic" spirometry reference equations derived from data collected from 74,187 healthy nonsmokers representing different race and ethnicity groups (White, Black, Northeast [NE] Asian, and Southeast [SE] Asian) (1). Unweighted averages of these four equations were used to derive "GLI-Other," a reference equation to be used for patients of other, unknown, or mixed self-reported race and ethnicity. The variables used to compute predicted lung function in the GLI-2012 equations are age, sex, standing height, and, controversially, race (1). Importantly, the GLI-2012 equations recognized that the relationship between lung function and these variables is not linear and that the standard deviation from the predicted mean values is not constant.

Reference equations hold significant clinical, occupational, and social importance.

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This article has a related editorial.

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At a Glance Commentary

Scientific Knowledge on the Subject: Race-specific Global Lung Function Initiative (GLI)-2012 reference equations have been the recommended standard for spirometry interpretation. The new GLI Global equations offer a "race-neutral" approach, an important step toward eliminating racial bias in the interpretation of lung function.

What This Study Adds to the Field: This study evaluates the impact of transitioning from GLI-2012 to GLI Global equations on lung function interpretations in a large, diverse patient population. It shows that this transition could significantly alter spirometry interpretations, and emphasizes the importance of placing these data within an appropriate clinical context.

They are used to diagnose pulmonary diseases, determine eligibility for procedures or transplantation, evaluate the ability to work in some industries, and establish disability status (2, 3). The use of race- and ethnicity-specific equations in spirometry is based on the assumption that differences in lung function seen in patients of various ancestral origins can be explained by genetic factors (4). Historical adjustments for race, such as the 15% reduction in predicted lung function proposed for Black individuals by the 1978 Occupational Health and Safety Administration Cotton Dust Standard, were required to avoid discriminatory hiring practices at a time when reference standards were available only for White individuals (5, 6). However, there is abundant evidence that these assumptions are an oversimplification of the complex factors that impact lung function in the increasingly multicultural communities across the globe. Sitting height, which may more accurately estimate chest size and reduce the observed differences in lung volume measurements between Black and White individuals using standing height, for example, is impacted by early-life nutrition and genetics (7, 8). Other socioeconomic factors such as education, occupation, wealth, and social determinants of lung health, including exposure to tobacco, respiratory infections, and air pollution, have also been shown to significantly impact lung function (4, 9, 10).

There are substantial concerns that the use of race-specific equations underestimates predicted lung function in certain populations, perpetuates health disparities, and may cause unintended harm by delaying appropriate diagnoses and access to treatment (9, 11). Recognizing that race is a complex sociopolitical—rather than biological—construct has led to a concerted effort by the medical community to eliminate race from clinical equations and algorithms (12, 13). This included the recent development of GLI Global, a set of sex-stratified, "race-neutral" weighted-average reference equations for spirometry interpretation (14). In the development of GLI Global, an inverse probability weight was assigned to each data point based on the sex-stratified proportion of the corresponding GLI race and ethnicity group, thereby treating each of the four race and ethnicity groups as equal contributors to the overall reference equations. Although the GLI Global reference equations represent a major step toward reducing racial bias in pulmonary function test (PFT) interpretation, clinicians need to understand the impact of their adoption. The objective of this study was to describe the frequency, direction, and magnitude of interpretive changes when GLI Global reference equations were applied to a large, real-world population of patients of diverse race and ethnicity referred for PFTs at multiple sites within a large healthcare system consisting of community and quaternary care centers. Further analysis was conducted to examine the modified Medical Research Council (mMRC) dyspnea scale score and lung volume measurements, when available, in patients whose spirometry interpretation had changed with the use of GLI Global compared with GLI-2012 reference equations. Some of the results of this study have been previously reported in the form of an abstract (15).

Methods

The Mayo Clinic PFT Database

Our PFT database encompasses all testing performed and interpreted at the clinical pulmonary function laboratories at the Mayo Clinic locations in Rochester, MN, Jacksonville, FL, and Eau Claire, WI, between January 1, 2016, and May 31, 2022. It includes reported PFT data, patient age, sex at birth, self-reported race and ethnicity, standing height, weight, and mMRC dyspnea scale score at the time of testing. Our PFT laboratories follow American Thoracic Society technical standards and consensus recommendations for quality assurance and perform daily equipment calibration and monthly biological quality control testing (16, 17). Self-reported race and ethnicity was provided by each patient through a questionnaire completed on the day of testing and confirmed by the pulmonary function technician performing the test. All spirometry and static lung volume measurements were obtained using Masterscreen Classic or Realtime and Vyntus BODY or ONE testing systems with SentrySuite v.3.10.5 software (Vyaire Medical Inc.). Predicted spirometry values in the database were calculated using the race- and ethnicity-specific GLI-2012 reference equations. Predicted lung volume measurements were calculated using GLI reference equations for individuals of European ancestry (18).

Interpretation of Spirometry Results

Spirometry results were divided into four broad categories using the following definitions: (*1*) normal spirometry (FEV_1, FVC, and FEV_1/FVC ratio above a *z*-score of −1.64, which will subsequently be referred to as the lower limit of normal [LLN]), (*2*) indeterminate reduction in FEV_1 (only $FEV_1 \leq$ LLN; FVC and FEV_1/FVC ratio $>$ LLN), (*3*) obstruction (FEV_1/FVC ratio $\leq$ LLN; FEV_1 and FVC may or may not be above the LLN), and (*4*) possible restriction (FVC $\leq$ LLN with FEV_1/FVC ratio $>$ LLN; FEV_1 may or may not be above the LLN).

Sample Selection and Data Analysis

The study was approved by the Mayo Clinic Institutional Review Board (study ID 22-008578). The database included 335,949 spirometry tests, of which 181,287 tests were initial measurements (i.e., without influence from additional interventions such as bronchodilation or bronchoprovocation). Among these, we excluded 15,222 for the following reasons: (*1*) 142 tests involved patients aged $<$5 years or $>$95 years, which are outside of the age range included in GLI Global (ages 5–95 years) and GLI-2012 (ages 3–95 years) reference equations, and (*2*) 15,080 tests were conducted on patients who

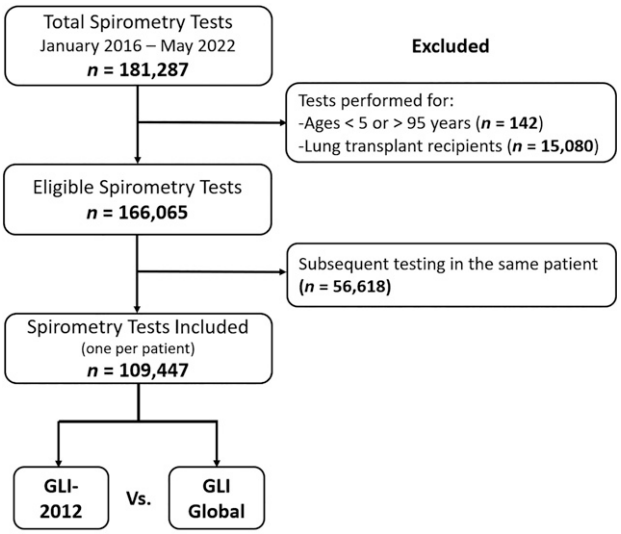

Figure 1. Of the 181,287 baseline spirometry tests considered in this analysis, 142 belonging to 63 patients outside the age ranges for Global Lung Function Initiative (GLI) reference equations and 15,080 belonging to 1,006 lung transplant recipients were excluded. The remaining 166,065 spirometry tests were reanalyzed using the race-neutral GLI Global reference equation. To avoid duplications, only the first test was included for patients who had undergone more than one test. The final data set for comparison included 109,447 tests, each corresponding to a unique patient. The resultant predicted lung function measures were compared with those previously computed with the race- and ethnicity-based GLI-2012 reference equations.

had undergone lung transplantation, in whom donor race and ethnicity was not known and lung function was dependent on more complex physiologic interactions, which could confound subsequent analysis. After these exclusions, a total of 166,065 spirometry tests were reevaluated using GLI Global reference equations. To minimize bias from repeated measurements from the same individual, only the first test performed on each patient was included in our analysis, resulting in a final sample of 109,447 tests (Figure 1).

In a separate subgroup analysis conducted on spirometry tests that met the criteria for obstruction or possible restriction using the GLI-2012 or GLI Global reference equation but not the other ($n = 10{,}723$), we identified all corresponding lung volumes measured during the same visit ($n = 6{,}720$). We limited this cohort to individuals between ages 5 and 80 years, in line with the age limits of the GLI lung volume reference equations for individuals of European ancestry (18). In total, 5,441 unique patients were included. A comprehensive breakdown of this sample selection process is presented in Figure E1 in the online supplement.

JMP 14 and GraphPad Prism 9 were used to analyze the data and create descriptive diagrams. An ANOVA was used to compare means of continuous variables across different race and ethnicity groups, and a χ^2 test of independence and Fisher's exact test were used to compare proportions of categorical variables with two or more levels. An independent *t* test was conducted to compare distributions of continuous variables across spirometry tests with and without changes in interpretation. The statistical significance level was set at $P < 0.05$.

Results

Patient Characteristics and Baseline Lung Function Measures

Baseline patient characteristics, mMRC scores, and lung function measurements are summarized in Table 1 and stratified by self-reported race and ethnicity. The mixed/other race group had the youngest patient population, and the Black group had the highest proportion of mMRC scores ⩾2 (36.7%). Absolute FEV_1 and FVC were highest in the NE Asian (2.51 and 3.19 L, respectively) and White (2.47 and 3.36 L) groups and lowest in the Black group (2.15 and 2.77 L). Using GLI-2012 reference equations, lung function measurements consistent with obstruction were most common in the SE Asian group (22.1%), whereas those indicative of a possible restriction were most common in the Black group (21.9%).

Changes in Percent Predicted FEV_1 and FVC Measures with the Application of GLI Global

When GLI Global reference equations were used in place of GLI-2012, the mean FEV_1 and FVC (% predicted) increased in the White and NE Asian groups and decreased in the Black, SE Asian, and mixed/other race groups (Figure 2). The change in FEV1 % predicted and FVC % predicted were greatest in the Black group, decreasing by 8.4% and 8.6%, respectively. More detailed descriptions of the distribution and change in mean and median FEV_1% predicted and FVC% predicted across groups are displayed in Table E1 and Figure E2.

Relative Changes in the Interpretation of Spirometry Test Results with the Application of GLI Global

The prevalence of obstruction increased from 19.7% to 21.6% (a relative increase of 9.7%) in the White group and decreased in all other groups (Figure 3A). The decrease was smallest in the Black group (from 14.7% to 14.4%, a relative decrease of 1.8%) and greatest in the SE Asian group (from 22.1% to 14.7%, a relative decrease of 33.7%). The prevalence of possible restriction increased substantially with the use of GLI Global equations in the Black (from 21.9% to 33.1%, a relative increase of 51.1%) and SE Asian (from 13.9% to 19.1%, a relative increase of 37.1%) groups and decreased in all other groups (Figure 3B). The decrease was largest for the NE Asian group (from 19.9% to 11.9%, a relative decrease of 40.4%), followed by the White group (from 14.3% to 10.6%, a relative decrease of 26.3%). Summaries of the direction and magnitude of all relative changes are displayed in Table E2 and Figure E3.

Overall, the use of GLI Global in place of GLI-2012 reference equations altered the interpretation of 8,296 (7.6%) spirometry test results in our sample (Table 2). This alteration in interpretations increased to 10.2% when each of the five race and ethnicity groups were represented equally. This percentage corresponds to the average of the individual changes observed in each group, regardless of their size. The highest proportion of alterations was seen in the Black group (14.9%), whereas the lowest was

Table 1. Patient Characteristics and Lung Function Measures Using GLI-2012 Reference Sets Stratified by Self-Reported Race and Ethnicity ($N = 109,447$)

Characteristic	White ($n = 101,010$)	Black ($n = 4,476$)	Northeast Asian ($n = 236$)	Southeast Asian ($n = 1,472$)	Mixed/Other ($n = 2,253$)	Total ($N = 109,447$)
Age, yr	59.5 ± 18.5	52.0 ± 18.1	53.9 ± 20.9	51.9 ± 19.6	48.7 ± 21.1	58.9 ± 18.7
Female sex	52,089 (51.6)	2,624 (58.6)	129 (54.7)	779 (52.9)	1,151 (51.1)	56,772 (51.9)
Height, cm	168.5 ± 11.3	167.1 ± 11.8	162.5 ± 10.9	160.4 ± 11.6	164.2 ± 13.7	168.2 ± 11.4
Weight, kg	84.0 ± 24.1	86.7 ± 25.9	64.4 ± 14.9	66.3 ± 18.0	76.1 ± 24.5	83.7 ± 24.2
BMI, kg/m^2	29.4 ± 7.4	30.8 ± 8.2	24.2 ± 4.4	25.5 ± 5.6	27.7 ± 7.3	29.3 ± 7.4
mMRC score,* *n* (%)						
0	31,618 (35.9)	1,640 (40.9)	96 (50.8)	562 (45.8)	639 (35.0)	34,555 (36.2)
1	27,151 (30.8)	898 (22.4)	57 (30.2)	371 (30.2)	576 (31.6)	29,053 (30.5)
2	13,897 (15.8)	557 (13.9)	18 (9.5)	130 (10.6)	281 (15.4)	14,883 (15.6)
3	10,370 (11.8)	548 (13.7)	11 (5.8)	103 (8.4)	193 (10.6)	11,225 (11.8)
4	4,964 (5.6)	360 (9.0)	7 (3.7)	58 (4.7)	132 (7.2)	5,521 (5.8)
Lung function (GLI-2012)						
FEV_1, L	2.47 ± 0.97	2.15 ± 0.81	2.51 ± 0.89	2.21 ± 0.86	2.41 ± 0.95	2.45 ± 0.96
FVC, L	3.36 ± 1.15	2.77 ± 0.98	3.19 ± 1.08	2.85 ± 1.04	3.12 ± 1.17	3.32 ± 1.15
FEV_1/FVC ratio	72.9 ± 12.3	77.7 ± 11.0	78.8 ± 9.54	77.4 ± 10.5	77.3 ± 11.2	73.2 ± 12.2
Normal	63,798 (63.2)	2,756 (61.6)	159 (67.4)	903 (61.3)	1,361 (60.4)	68,977 (63.0)
Indeterminate ↓FEV_1	2,857 (2.8)	84 (1.9)	1 (0.4)	28 (2.6)	41 (1.8)	3,021 (2.8)
Obstruction	19,901 (19.7)	657 (14.7)	29 (12.3)	326 (22.1)	424 (18.8)	21,337 (19.5)
Possible restriction	14,454 (14.3)	979 (21.9)	47 (20.0)	205 (13.9)	427 (19.0)	16,112 (14.7)

Definition of abbreviations: ↓ = reduced; GLI = Global Lung Function Initiative; mMRC = modified Medical Research Council.
Variables are reported as mean ± standard deviation where applicable. Values in parentheses are percentages. Differences in distribution and percentages across all self-reported race and ethnicity groups were statistically significant ($P < 0.001$).
*Discrepancies between the sum of tests and column total may be attributed to missing variables. mMRC data were missing for 14,210 patients. All other variables were available for all patients.

seen in the mixed/other race group (5.6%). Alterations in spirometry interpretation were slightly more common in patients identified as female at birth and were more likely to impact tests with measurements near the LLN (Table E3). Figure 4 illustrates the changes in spirometry interpretation that would be expected with the use of GLI Global in a population with equal representation of all five race/ethnicity groups.

Lung Volumes and mMRC Scores in Spirometry Tests with Discordant Interpretations by GLI Global versus GLI-2012

Spirometry test results indicating obstruction by GLI Global alone were 1.7 (95% CI, 1.2–2.5; $P = 0.006$) times more likely to be associated with an mMRC score ⩾2 and 2.6 (95% CI, 1.4–5.1; $P = 0.003$) times more likely to present with air trapping (defined by residual volume of at least the upper limit of normal) than those indicating obstruction by GLI-2012 alone (Figure 5). The corresponding odds of hyperinflation (defined by a total lung capacity of at least the upper limit of normal) did not reach statistical significance (2.7; 95% CI, 0.7–11.4). Spirometry test results showing possible restriction by GLI Global alone were 3.3 (95% CI, 2.7–4.2) times more likely to be associated with a low total lung capacity (defined as no greater than the LLN) than those showing possible restriction by GLI-2012 alone ($P < 0.001$). A detailed analysis of the sample composition for this subgroup is provided in Table E4.

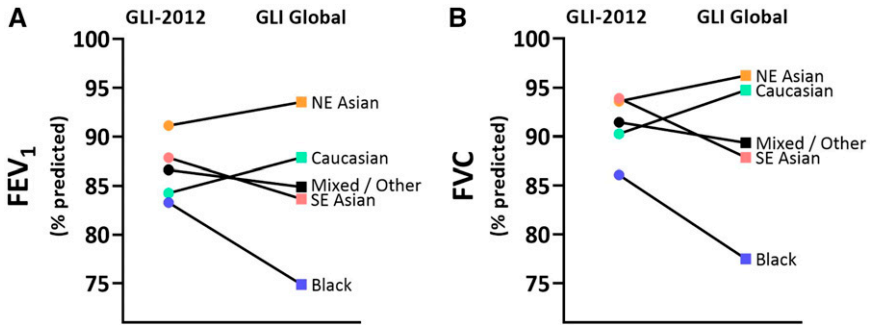

Figure 2. Absolute change in mean (*A*) FEV_1% predicted and (*B*) FVC% predicted values using Global Lung Function Initiative (GLI)-2012 and GLI Global reference equations. In White and NE Asian groups, mean FEV_1% predicted increased by 3.6% and 2.4% predicted and mean FVC% predicted increased by 4.5% and 2.6% predicted, respectively. In Black, SE Asian, and mixed/other groups, mean FEV_1% predicted decreased by 8.4%, 4.2%, and 1.7% predicted and mean FVC% predicted decreased by 8.6%, 6.1%, and 2.1% predicted, respectively. NE = northeast; SE = southeast.

Discussion

GLI Global offers a "race-neutral" approach to the interpretation of lung function measurements, motivated by efforts to eliminate health disparities and structural racism in medicine. The use of self-identified race and ethnicity oversimplifies the interplay between genetics and the myriad socioeconomic, environmental, and other risk factors that impact lung function (19–23). The GLI Global authors and others have called for careful examination of the

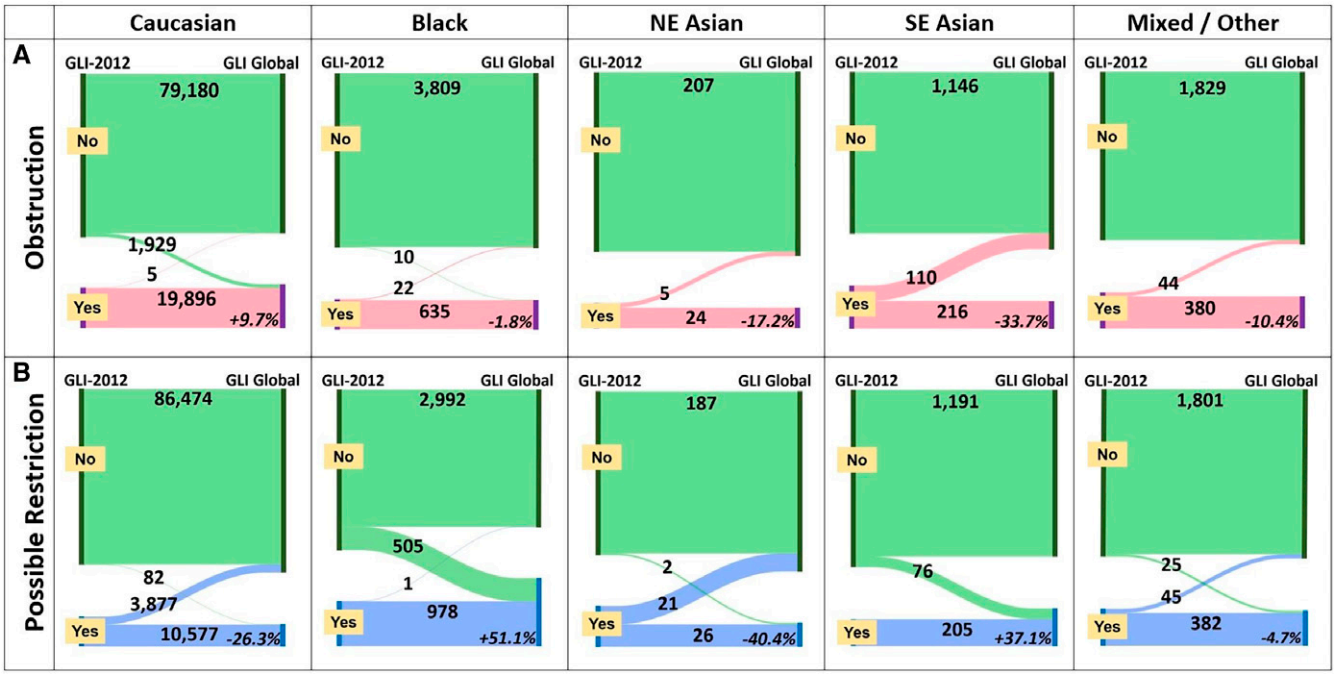

Figure 3. Relative change in lung function measure interpretations by self-declared race and ethnicity. (*A*) Changes relating to obstruction defined as $FEV_1/FVC \leq$ lower limit of normal (LLN). "No" denotes no obstruction whereas "yes" indicates the presence of obstruction. (*B*) Changes relating to possible restriction defined as $FVC \leq LLN$ with FEV_1/FVC ratio $>$ LLN. "No" denotes no restriction, whereas "yes" indicates the presence of possible restriction. For instance, there was a relative decrease of 33.7% in obstruction in the Southeast Asian group with the use of GLI Global in place of GLI-2012, whereas there was a relative increase in possible restriction of 51.1% in the Black group.
NE = northeast; SE = southeast.

use of these reference equations in real-world populations to better understand the resulting impact in spirometry interpretation (14, 24).

Our study demonstrated that the application of GLI Global in place of the race- and ethnicity-specific GLI-2012 equations resulted in a different interpretation of nearly 1 of every 13 spirometry tests in our sample. This change would be larger in centers with greater demographic representation of individuals who self-identify as Black or SE Asian and does not include additional changes in the severity of impairment (i.e., mild to moderate obstruction). Changes in interpretation were more likely to occur in patients whose measurements were near the LLN, emphasizing the need for clinicians to recognize the uncertainty around such diagnostic thresholds and the impact of the reference equation that is used.

The highest percentage of lung function interpretation changes was seen in Black patients, with a 32.9% relative increase in the prevalence of abnormal results. These changes were primarily driven by a proportional decrease in mean FEV_1% predicted and FVC% predicted, resulting in an increase in possible restriction. In fact, this significant decrease in mean FEV_1% predicted among Black subjects aligns with concerns that race-specific reference equations might underestimate the severity of COPD in Black individuals (25). Patients who self-identified as Black had a similar percentage of normal spirometry test results by GLI-2012 as all other race and ethnicity groups except the NE Asian group, while also having the lowest absolute measures of FEV_1 and FVC and the highest proportion of mMRC scores $\geq$2.

Spirometry interpretations in patients who identified as SE Asian demonstrated a significant decrease in obstruction and increase in possible restriction using GLI Global, leading to comparable prevalences of both abnormalities. White individuals were the only group in whom the use of GLI Global was associated with an increase in the frequency of obstruction, albeit with an expected decrease in its severity graded using FEV_1% predicted. The GLI-2012 mixed/other race reference values are an unweighted racial composite that, not surprisingly, exhibited the least change compared with GLI Global weighted composite values. It is important to note that changes in the % predicted values are driven by shifts in the LLN when using GLI Global. Decreases in % predicted values correspond to increases in the LLN and vice versa. This is particularly relevant because the determination of abnormalities is based on these LLN values.

Obstruction and possible restriction using GLI Global equations more strongly correlated with air trapping and reduced total lung capacity on lung volume measurements, respectively, compared with GLI-2012. Although these findings may seem to affirm that GLI Global more accurately stratifies patients by their underlying lung physiology, we caution that they are far from definitive. Because the database used for the present study provides no "gold standard" for the presence of disease, further research is necessary to explore the correlation of these findings with more standardized clinical measures and outcomes (11, 26).

The pursuit by Bowerman and colleagues to produce race-neutral GLI Global reference equations that aim to reduce the risk of systematic bias is a

Table 2. Frequency of Change in Lung Function Interpretations and Relative Change in Abnormal Interpretations by Race and Ethnicity

Race and Ethnicity	Change in Lung Function Interpretation*	Change in Abnormal Interpretation (Obstruction, Possible Restriction, ↓FEV_1)†		
		Abnormal by GLI-2012	Abnormal by GLI Global	Relative Change, %
White (n = 101,010)	7,305 (7.2)	37,212	34,418	−7.5
Black (n = 4,476)	667 (14.9)	1,720	2,286	+32.9
Northeast Asian (n = 236)	27 (11.4)	77	54	−29.9
Southeast Asian (n = 1,472)	173 (11.8)	569	539	−5.3
Mixed/other (n = 2,253)	124 (5.6)	892	846	−5.2
Total (N = 109,447)	8,296 (7.6)	40,470	38,143	−5.8
Equally weighed sample‡	NA (10.2)	NA	NA	−3.0

Definition of abbreviations: ↓ = reduced; GLI = Global Lung Function Initiative; NA = not applicable.
Values in parentheses are percentages.
*"Change in Lung Function Interpretation" describes the number and frequency of spirometry tests with change in categorization with the switch from GLI-2012 to GLI Global.
†"Change in abnormal interpretation" represents the number of abnormal interpretations falling into one of three categories: obstruction, possible restriction, and indeterminate reduction in FEV_1. Relative change is calculated as ([GLI Global value − GLI-2012 value]/GLI-2012 value) × 100%.
‡"Equally weighed sample" refers to a sample in which all five race and ethnicity groups (Black, White, Northeast Asian, Southeast Asian, and mixed/other) are represented in equal proportions. The percentages correspond to the average of the individual frequencies/changes observed in each group regardless of their size.

laudable goal (14). Burney and Hooper demonstrated that White individuals had a better survival rate than Black individuals with the same FVC% predicted using race-specific equations, but that this survival differential was eliminated with the use of absolute measures of FVC (in liters) and/or race-neutral reference equations (27). Concern for the continued use of GLI-2012 equations has focused on the risk of underestimating lung function impairment in individuals who identify as a race or ethnicity other than White and the consequent withholding of important therapies or early referral to lung transplantation compared with White individuals with similar absolute lung function (28–30). Conversely, moving away from GLI-2012 equations may affect the eligibility of persons of different race or ethnicity for specific occupations (e.g., military, firefighting), lead to higher insurance premiums, or limit eligibility for lung cancer resection surgery (11). Understanding the real-world implications of these changes will help inform the complex discussions regarding the most appropriate selection and use of normative spirometry values. The intricacies regarding the inclusion of self-reported race and ethnicity are discussed more fully in the recent American Thoracic Society statement, "Race and Ethnicity in Pulmonary Function Test Interpretation" (11).

GLI Global is not entirely devoid of racial and ethnic influences, but rather aims to minimize the impact of race/ethnicity on spirometry interpretation. As the developers of GLI Global have noted, no reference equation is ideal, and many questions regarding the best approach to measure lung function in our diverse global population remain unanswered. There is some merit to using locally derived reference standards that are region-specific. However, this requires well-conducted and regularly updated epidemiological studies that can be difficult to perform (31). Moreover, such local reference values are unlikely to perform well in diverse, multiethnic communities in which there are high rates of migration, both national and international. Although the GLI offers the best normative data set to date, it still lacks representation from many important world populations. The absence of an objective gold standard for disease still underlines the importance of careful clinical assessment to clarify the uncertainty that persists with lung function categorization

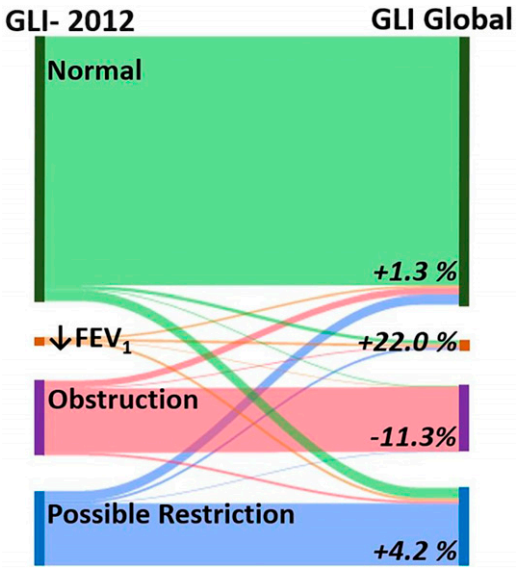

Figure 4. The application of Global Lung Function Initiative (GLI) Global to a population with equal representation of all five race and ethnicity groups (Black, White, Northeast Asian, Southeast Asian, and mixed/other) resulted in a change in interpretation in 10.2% of tests performed. The displayed changes in lung function interpretation represent the relative (or percent) change in categorization with the switch from GLI-2012 to GLI Global.

near the LLN. This highlights the urgent need for further research examining the impact of the transition to GLI Global reference values on patient-centered clinical outcomes, including symptom burden, quality of life, healthcare utilization, and mortality (32). Perhaps most importantly, even though race-neutral equations may increase the sensitivity of disease detection for individuals of certain ancestral origins—albeit at the expense of potential "false-positive" results—it will do nothing to eliminate racial disparities in access to and quality of health care and insurance.

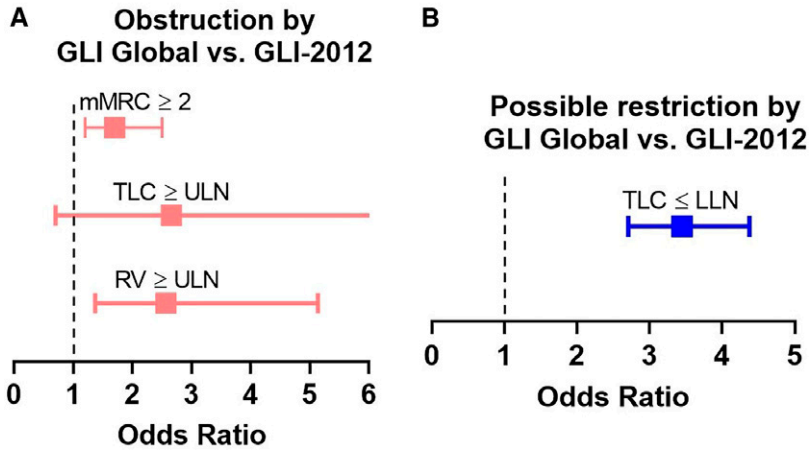

Figure 5. (*A*) Patients with obstruction on spirometry by Global Lung Function Initiative (GLI) Global alone were 1.7 (95% CI, 1.2–2.5; $P = 0.006$) times more likely to present with a modified Medical Research Council score ⩾2 and 2.6 (95% CI, 1.4–5.1) times more likely to exhibit air trapping (defined as residual volume at least at the upper limit of normal) compared with those with obstruction by GLI-2012 alone. (*B*) Patients with possible restriction on spirometry by GLI Global alone were 3.3 (95% CI, 2.7–4.2) times more likely to exhibit low total lung capacity (defined as at or lower than the LLN) compared with those with possible restriction by GLI-2012 alone. LLN = lower limit of normal; mMRC = modified Medical Research Council; RV = residual volume; TLC = total lung capacity; ULN = upper limit of normal.

Differences in socioeconomic and environmental factors that impact health will also persist or become even more stark as providers pursue further evaluation to explain abnormal PFT findings. Solving these problems remains fundamental to meaningful progress toward healthcare equity.

Our study has limitations. Our database included a relatively small number of individuals who identified as NE Asian, despite encompassing more than 6 years of data from three medical centers in our health system. As such, caution should be exercised when generalizing these results to individuals who identify with this demographic group. Furthermore, our subgroup analysis, while informative, addresses a smaller proportion of patients and is influenced by the racial composition of our sample. It should also be noted that the reference equations used for lung volumes were derived exclusively from individuals of White race, and the implications for their applicability to other racial or ethnic groups remain unclear. Although our study offers valuable insights into the use of GLI Global for spirometry interpretation, further research is necessary to ascertain whether the changes in spirometry interpretations correlate with patient symptoms, other objective testing abnormalities, and clinical diagnoses at the time of testing. As it stands, the clinical significance of the observed changes in interpretation using GLI Global remains to be determined.

Conclusions

Although GLI Global provides innovative "race-neutral" reference equations aimed at reducing systematic bias, our findings reveal that transitioning to these equations significantly changes interpretation within a large, diverse, multicenter PFT database. These changes are likely to be greater in communities with greater racial diversity than was seen in our cohort. It is crucial to consider the intended use of spirometry interpretation and acknowledge the continued importance of placing these data within an appropriate clinical context. More research is needed to understand the clinical implications of the changes in interpretation we observe using the GLI Global reference equations. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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