Effect of Race and Ethnicity on Pulmonary Function Testing Interpretation

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An American College of Chest Physicians (CHEST), American Association for Respiratory Care (AARC), American Thoracic Society (ATS), and Canadian Thoracic Society (CTS) Evidence Review and Research Statement

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BACKGROUND: Calls have been made to discontinue the routine use of race and ethnicity in medicine. Specific to respiratory medicine, the use of race- and ethnicity-specific reference equations for the interpretation of pulmonary function test (PFT) results has been questioned.

RESEARCH QUESTIONS: Three key questions were addressed: (1) What is the current evidence supporting the use of race- and ethnicity-specific reference equations for the interpretation of PFTs? (2) What are the potential clinical implications of the use or nonuse of race and ethnicity in interpreting PFT results? and (3) What research gaps and questions must be addressed and answered to understand better the effect of race and ethnicity on PFT results interpretation and potential clinical and occupational health implications?

STUDY DESIGN AND METHODS: A joint multisociety (American College of Chest Physicians, American Association for Respiratory Care, American Thoracic Society, and Canadian Thoracic Society) expert panel was formed to undertake a comprehensive evidence review and to develop a statement with recommendations to address the research questions.

RESULTS: Several assumptions and gaps, both in the published literature and in our evolving understanding of lung health, were identified. It seems that many past perceptions and practices regarding the effect of race and ethnicity on PFT results interpretation are based on limited scientific evidence and measures that lack reliability.

INTERPRETATION: A need exists for more and better research that will inform our field about these many uncertainties and will serve as a foundation for future recommendations in this area. The identified shortcomings should not be discounted or dismissed because they may enable flawed conclusions, unintended consequences, or both. Addressing the identified research gaps and needs would allow a better—a more informed—understanding of the effects of race and ethnicity on PFT results interpretation.   CHEST 2023; 164(2):461-475

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Across many disciplines of medicine, race and ethnicity historically have been used to guide clinical care and have been assumed to reflect biological differences between populations (ie, race and ethnicity are viewed as biological variables). But race and ethnicity similarly can be viewed as socially defined; meanings have changed over time and definitions vary between countries and are used differently in different situations (eg, clinical medicine vs occupational medicine as outlined for the Cotton Dust Standard spirometry threshold explained herein) where, for example, a low predicted threshold may increase sensitivity for the detection of disease in the clinical setting, but potentially may limit use in the occupational setting. Concern is growing that the use of race and ethnicity in medicine, often arbitrarily inferred based on appearance, as biological variables may perpetuate inequalities in outcomes. Several calls have been made to discontinue the routine use of race and ethnicity in medicine.[1-3] Specific to respiratory medicine, the use of race- and ethnicity-specific reference equations for the interpretation of pulmonary function test (PFT) results warrants reconsideration.[4]

Pulmonary function testing is essential to the field of pulmonary and respiratory medicine. In addition to informing patient care and the assessment of symptoms in individuals, testing also often is required for the surveillance of occupational health and determining

suitability for employment; for screening and targeted testing of individuals, populations, or both who may be at increased risk of nonoccupational disease; and for evaluation and monitoring of overall population respiratory health.

The American Thoracic Society (ATS), and later in collaboration with the European Respiratory Society (ERS), developed recommendations for spirometry performance and standardization of testing technique (1979-2019) and interpretation of results (1991-2022). When interpreting results, measured values are compared with the range of values observed from a comparative healthy population—a reference population. The characteristics of reference populations have evolved over time; in the 1960s, reference populations included primarily White men (including tobacco users) free of respiratory disease, and predicted values were based on height and age. Later reference value studies included White women and men who were not tobacco users. In the 1970s, it became clear some Black individuals were ineligible for employment in US cotton mills because their lung volumes were smaller than required for employment.[5] Although race-based differences in spirometry had been appreciated for some time,[6] to correct discriminatory hiring practices, the US Occupational Safety and Health Administration mandated that a 0.85 scaling factor be applied to predicted values from existing White reference populations when Black job applicants were assessed.[7] It was not until the late 1990s that the Third National Health and Nutrition Examination Survey (NHANES III) measured thousands of Black, White, and Mexican American people from across the United States and race-specific reference equations were developed.[8] In 2012, the Global Lung Function Initiative (GLI) developed all-age reference equations in which four distinct ethnic groups were summarized: Caucasian, African American. South East Asian, and North East Asian.[9] The term *Caucasian* has been used widely in the literature to reflect the White population, predominately of European ancestry. However, in much of this work, no explanation was provided of how race and ethnicity categories were defined and no reliability statistics for these categories were reported. When a person did not identify with any of the four groups or was of mixed ethnic origin, a fifth group, GLI-Other, was created based on the mathematical average of the statistical coefficients used to derive the GLI equations. A problem with GLI-Other is that it is heavily weighted toward GLI-Caucasian values. To address this, and as a potential solution to the

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uncertainty in an individual's race or ethnicity, a new equation, called GLI-Global, was created that adjusts the statistical contribution of the four GLI groups to have equal weighting and has been suggested as a more valid representation of the composite GLI data.[10]

The 2019 ATS and ERS updated spirometry measurement technical statement[11] and the 2022 ERS and ATS updated lung function interpretation standard[12] recommended that a patient's self-identified race or ethnicity be obtained to interpret results. No guidance is provided for defining race and ethnicity, but uncertainty when it comes to the interpretation of PFT results is acknowledged.

The ERS and ATS interpretation standards, including the 2022 update, recommend comparing patients with a reference population that includes non-tobacco-using, asymptomatic, healthy individuals. The definition was developed in 1961 when Kory et al[13] wanted to avoid respiratory abnormalities that might affect predicted lung function measurements. Non-tobacco users were studied from the 1970s onward to avoid the impact of smoking on the predicted values. Today, we know that many principal factors influence lung health, including air quality, nutrition, and occupational exposures. Also recent awareness has developed of temporal lung function changes in populations, independent of increasing height over time, that potentially may impact diagnostic criteria for various lung diseases.[14] Studies have demonstrated that healthy reference populations that do not account for these and other residual factors disproportionately will mislabel individuals from marginalized communities with impaired lung function as healthy.[15-18] Several recent studies have highlighted that people of color living in the United States, predominantly Black Americans, seem to show greater respiratory symptoms, morbidity, and mortality for the same percent predicted value of lung function impairment based on race-specific reference values as White individuals, but this difference is mitigated when percent predicted values are based on both groups using the same race-neutral reference standard. This difference highlights how race-specific reference values may be normalizing the lower lung function seen in Black individuals compared with White individuals of the same age, sex, and height.[19-21] Increasing awareness about the intersectionality between disparities and race and ethnicity will help to ensure that PFT results interpretation is appropriate and optimal.

Moreover, a complex relationship exists between genetic ancestry and lung function. An implicit assumption in race correction is that genetic differences track reliably with race, but this has not been demonstrated with certainty in the case of lung function. The reality that Black American ancestry correlates with low socioeconomic status also makes it difficult to disentangle genetic influences on interpretation of PFT results.[22] The primary aims of this joint international, multiprofessional society evidence review and research statement are: (1) to determine the current evidence for the use of race- and ethnicity-specific equations for the interpretation of PFT results, (2) to identify potential clinical and occupational implications of using or not using race-specific reference equations in the interpretation of PFT results, and (3) to identify research priorities needed to understand better the role of race and ethnicity as a part of PFT results interpretation.

Study Design and Methods

Expert Panel Composition

The chair of the panel (D. D. M.) was appointed by the American College of Chest Physicians and approved by the other organizations' leadership. The panel comprised expert representatives from the American College of Chest Physicians, the American Association for Respiratory Care, the ATS, and the Canadian Thoracic Society. The final joint panel consisted of the chair, 14 panelists, and a methodologist (J. M. I.). All panelists were reviewed for conflicts of interest, with potential conflicts of interest managed by disclosure (e-Appendix 1). All members of the panel completed the Kirwin Institute for the Study of Race and Ethnicity's Implicit Bias Module Series (https://kirwaninstitute.osu.edu/implicit-bias-training).

Question Development

The panel developed three key questions to provide a framework for this evidence review and research statement (Table 1). The questions focused on areas initially agreed to by leadership from the four organizations and were developed to fulfill the goal of identifying research gaps and needs. All panel members participated in the refinement and approval of the key questions, which was unanimous.

Literature Search and Study Selection

A comprehensive search using MEDLINE via PubMed was performed to identify evidence that could inform the key questions. The search was conducted using a combination of the National Library of Medicine's Medical Subject Headings and key words pertaining to each key question. Unique searches of studies published in the English language were used for Key Questions 1 and 2, with results from both searches used to inform and address Key Question 3. Additional relevant studies were identified by reviewing the references of included studies and by the expert panel members.

Studies identified during the literature search were reviewed for relevance by panel members in two steps. Citations from the search

TABLE 1] Key Questions for Assessing the Effect of Race and Ethnicity on Pulmonary Function Test Results Interpretation

Key Question 1	What is the current evidence supporting the use of race- and ethnicity-specific reference equations for the interpretation of PFT results?
Key Question 2	What are the potential clinical implications of the use or nonuse of race or ethnicity in interpreting PFT results?
Key Question 3	What research gaps and questions must be addressed and answered to understand better the effect of race and ethnicity on PFT results interpretation and potential clinical and occupational health implications?

For the intention of this work, PFTs included spirometry, lung volumes, and diffusion capacity. PFT = pulmonary function test.

results were screened for potential relevance to the key questions. Potentially relevant studies then were reviewed in full to determine if they directly addressed the key question. Single case reports, reviews, editorials, and expert opinion statements were excluded. Studies also were excluded if they included fewer than 300 participants to avoid sampling bias (see Key Question 1),[23] did not adjust for socioeconomic factors (see Key Question 1), and did not assess clinical impairment or use clinically relevant end points (see Key Question 2). Studies on which panelists disagreed regarding inclusion or exclusion underwent secondary review by a designated panelist who made a final determination. Included studies were reviewed and summarized.

Results

Key Question 1: What Is the Current Evidence Supporting the Use of Race- and Ethnicity-Specific Reference Equations for the Interpretation of PFT Results?

The literature search found 516 initial citations for Key Question 1, from which seven studies were selected for inclusion (Fig 1). Included studies are listed in Table 2.[24-30] Most of the published literature included only spirometry outcomes. A few studies included diffusing capacity of the lungs for CO_2 and lung volumes, but these were limited and lacked generalizability. Of these seven selected studies, six were convenience samples[24-29] and one was a random sample of the population.[30] All studies were cross-sectional. The number of participants ranged from 1,038[28] to 9,658.[24] Three studies investigated differences between Black and White individuals living in the United States, two studies were conducted in the United Kingdom, and three studies were conducted elsewhere in the world.

In general, the study populations were not particularly well described, both in terms of how *healthy* was defined, nor how study participants were assigned a race and ethnic group. Race and ethnicity often were self-reported, were investigator assigned, or were based on parental country of origin and used fixed categories without an option to select more than one category; no study reported reliability metrics for race
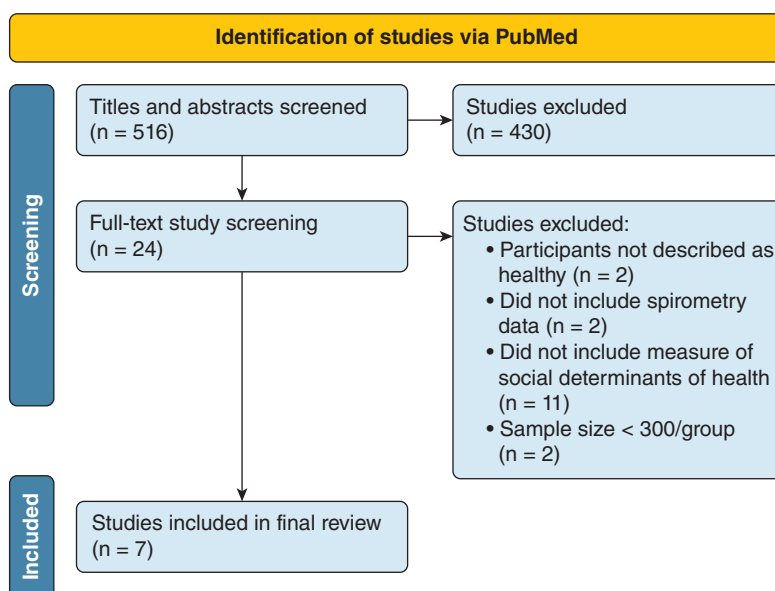

Figure 1 – *Preferred Reporting Items for Systematic Reviews and Meta-analyses diagram showing race adjustment in pulmonary function test results for Key Question 1.*

TABLE 2] Included Studies (n = 7) Addressing Key Question 1: What Is the Current Evidence Supporting the Use of Race- and Ethnicity-Specific Reference Equations for the Interpretation of PFT Results?

Study	Country	Year	Sample Size	Age Range, y	Race or Ethnicity Definition	SES
Harik-Khan et al[25]	United States	2001	1,242 White; and 1,084 Black	≥ 18	Self-identified	Education, poverty index
Harik-Khan et al[26]	United States	2004	623 White; 839 Black	8-17	Self-identified	Education, poverty index
Whitrow and Harding[30]	United Kingdom	2008	757 White; 597 Black African; 518 Black Caribbean; 307 Indian; and 381 Pakistan/ Bangladesh	11-13	Self-defined or according to Census	Access to standard of living items, overcrowding, parental employment status, psychological well-being
Van Sickle et al[24]	United States	2011	9,658 African American and White men and women	20-80	Self-identified	Education
Lum et al[27]	United Kingdom	2015	664 White; 543 Black; 462 South Asian; and 232 other	5-11	Birth country: child, parents, grandparents	Income, Family Affluence Scale scores and free meals, Index of Multiple Deprivation
Sonnappa et al[28]	India and United Kingdom	2015	311 Indian British; 382 Indian urban; 188 Indian semiurban; and 158 Indian rural	5-12	Not specified	Family Affluence Scale
Arigliani et al[29]	Sub-Saharan Africa	2017	306 Angola; 377 Democratic Republic of Congo; and 399 Madagascar	6-12.8	Country of origin	Malnutrition defined as a z score BMI < –2, stunted growth as a z score height < –2, public school attendance or thinness = low SES

PFT = pulmonary function test; SES = socioeconomic status.

or ethnicity. Differences also were found in how socioeconomic status was defined (eg, income, education, family wealth, malnutrition). In most studies, both standing and sitting height (or upper body segment) were used to measure chest dimensions.

Overall, all seven studies identified statistically significant differences in lung function between people of different racial and ethnic groups. For the same standing height, age, and sex, people of White European ancestry on average showed larger FEV_1 and FVC values compared with those of African or Asian ancestry. Differences in body proportions as well as

socioeconomic factors explained some, but not all, of the observed differences.[25,26,28-30]

In a series of analyses of the NHANES III data in children and adults, Harik-Khan et al[25,26] demonstrated that differences in chest size (using sitting height as a proxy) explained more of the variability in lung function than socioeconomic factors. These findings subsequently were replicated in a large UK study of children.[30] A subsequent reanalysis of unselected NHANES III data by Van Sickle et al[24] demonstrated that exclusion criteria to define healthy differentially excluded individuals by age, race, and education, which could lead to underestimation of the

contribution of socioeconomic factors. In a study of 1,000 school children in London, differences in lung function persisted even after adjustment for anthropometric differences in chest dimensions and socioeconomic circumstances.[27] Using the Family Affluence Scale (a four-item measure of family wealth developed by the World Health Organization) as a social determinant of health, in addition to the Index of Multiple Deprivation, the study adjusted for comprehensive measures of socioeconomic status and multiple measures of chest dimensions. The observation that ethnic differences persisted after accounting for both chest dimensions differences and socioeconomic status was cited to support the use of ethnicity-specific reference equations. The same group compared lung function in South Asian children living in London with that of children in rural and urban regions of India. Differences in lung function were observed between rural and urban children in India, but not between South Asian children living in an urban area of India compared with those living in London. South Asian children (in both London and urban India) on average typically showed lower lung function compared with White British children. The FEV_1 to FVC ratio between ethnic groups for both studies was not different,[27,28] suggesting proportional differences in the FEV_1 and FVC between ethnic groups and that differences are the result of smaller lungs, and hence the differences are not the result of airflow obstruction. In one study, malnutrition (measured by thinness) was used as a measure of

socioeconomic status. Minimal differences were found in lung function between Black children in three African countries compared with African American children in the NHANES III data, whereas significant reductions in lung function were found in the African children who were malnourished.[29]

Key Question 1 Summary: Statistically significant differences in FEV_1 and FVC (but not FEV_1 to FVC ratio) have been observed between different racial and ethnic groups. People of White European ancestry have, on average, larger FVC and FEV_1 values compared with those of African or Asian ancestry. Although participants in most studies self-identified their race or ethnicity, this was carried out without definitions, thereby limiting the validity of this measure. Healthy was defined almost exclusively as non-tobacco-using, asymptomatic individuals. Adjusting body proportions (chest size), socioeconomic status, or both attenuated the observed differences between racial and ethnic groups, but did not account for all the observed differences in lung function between people of different racial and ethnic groups.

Key Question 2: What Are the Potential Clinical Implications of the Use or Nonuse of Race or Ethnicity in Interpreting PFT Results?

The literature search found 835 citations for Key Question 2, from which 22 studies were selected for inclusion (Fig 2). Studies included are listed in Table 3. Among the 22 included studies, eight described new
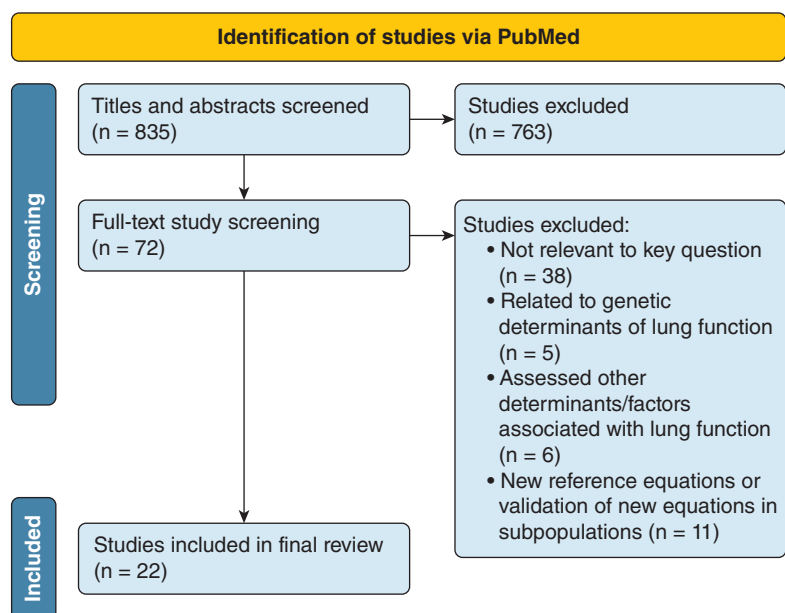

Identification of studies via PubMed

Screening

Titles and abstracts screened (n = 835) → Studies excluded (n = 763)

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Full-text study screening (n = 72) → Studies excluded:
• Not relevant to key question (n = 38)
• Related to genetic determinants of lung function (n = 5)
• Assessed other determinants/factors associated with lung function (n = 6)
• New reference equations or validation of new equations in subpopulations (n = 11)

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Included

Studies included in final review (n = 22)

Figure 2 – *Preferred Reporting Items for Systematic Reviews and Meta-analyses diagram showing race adjustment in pulmonary function test results for Key Question 2.*

TABLE 3] Included Studies (n = 22) Addressing Key Question 2: What Are the Potential Clinical Implications of the Use of Race in Interpreting PFT Results?

Study	Country	Year	Sample Size	Age Range, y	Race and Ethnicity Definition	Clinical Implication
Harber et al[31]	United States	1983	900 Black and White	≥ 18	Self-identified	Disability benefits
Enright et al[32]	United States	1996	3,246 White; and 575 Black	≥ 65	Self-identified	Spirometry
Saad et al[33]	Tunisia	2002	1,192 Tunisian	18-60	Country of origin	Obstructive and restrictive lung disease
Golshan et al[34]	Iran	2003	4,341 Persian	5-80	Country of origin	Spirometry
Sylvester et al[35]	United Kingdom	2005	80 Afro-Caribbean	4-17	Self-identified	Obstructive and restrictive lung disease
Arnall et al[36]	United States	2009	580 Navajo	6-14	Self-identified	Spirometry
Collen et al[37]	United States	2009	4,463 African American	19-91	Self-identified	Restrictive and obstructive lung disease
Hankinson et al[38]	United States	2010	270 White; 210 African American; 245 Hispanic; and 343 Asian American	≥ 18	Self-identified	Spirometry
Kiefer et al[39]	Untied States	2010	567 White; 470 African American; 492 Hispanic (Mexican) American; 113 Chinese American; and 51 Hispanic (non-Mexican) American	≥ 18	Self-identified	Spirometry
Burney et al[21]	United States	2012	6125 White; and 1,364 African American	45-64	Self-identified	Spirometry, mortality
Quanjer and Weiner[40]	United States	2014	4,034 White; and 746 Black	6-18	Self-identified	Obstructive lung disease (spirometry)
Kim et al[41]	Korea	2015	498 Korean, non-ethnic-Korean migrants	20-40	Country of origin	Spirometry
Chhabra and Madan[42]	India	2018	12,323 North Indian	≥ 18	Country of origin	Restrictive and obstructive lung disease
Al-Qerem et al[43]	Jordan	2021	1,036 Jordanian	14-17	Country of origin	Asthma diagnosis
Baugh et al[20]	United States	2021	2,122 non-Hispanic White; and 530 African American	≥ 18	Self-identified	COPD diagnosis

(Continued)

TABLE 3] *(Continued)*

Study	Country	Year	Sample Size	Age Range, y	Race and Ethnicity Definition	Clinical Implication
Elmaleh-Sachs et al[44]	United States	2021	1,187 White; 844 Black; 755 Hispanic; and 558 Asian	45-84	Self-identified	Chronic lower respiratory disease events, mortality
Gaffney et al[45]	United States	2021	5,294 White; 3,743 Black	≥ 18	Self-identified	Spirometry, mortality
Heraganahally et al[46]	Australia	2021	212 Australians	≥ 18	Country of origin	Obstructive and restrictive lung disease
McCormack et al[47]	United States	2021	8,798 White; and 3,972 Black	18-79	Self-identified	Spirometry, mortality
Miller and Cooper[48]	United Kingdom	2021	12,394 European ancestry; and 1,435 non-European ancestry	20-97	Country of origin	Lung gas transfer, mortality
Sood et al[49]	United States	2022	10,597 non-Hispanic White; 3,416 African American; 378 Hispanic; and 2,467 American Indian	45-80	Self-identified	Obstructive lung disease (COPD)
Liu et al[19]	United States	2022	1,247 Black; and 1,427 White	43-55	Self-identified	Emphysema on chest CT scan

PFT = pulmonary function test.

reference equations for subpopulations or compared different reference equations applied within a subpopulation. Adult subpopulations included in these articles were North African, Iranian, Australian Aboriginal, Native American, Malay, Chinese, and Indian populations, as well as Asian migrant workers. Children and adolescents included in these studies were from Jordanian, urban Zimbabwean, Navajo nations, Afro-Caribbean, Polynesian, Chinese, European, and Hong Kong backgrounds. Findings often demonstrated differences in percent predicted values or *z* scores based on applying region-specific reference equations compared with GLI or NHANES III equations.

The evidence may be summarized into three main categories:

1. Development and validation of reference standards in different subpopulations, typically in comparison with reference standards from NHANES III or GLI.

Regarding comparisons with NHANES III equations, Arnall et al[36] developed new reference equations for Navajo children 6 to 14 years of age and found that they were similar to those of the equivalent NHANES III White population, provided that maximal effort was given (which should always be attained). Two other studies found that ethnic references values improved accuracy over NHANES III equations. Golshan et al[34] found that Iranian reference values were more accurate than NHANES III equations based on the mean differences between measured and predicted values, but the differences were small. Further, Kim et al[41] found that ethnicity-specific values were lower for Asian migrant workers compared with NHANES III predicted values, so fewer workers received a diagnosis of an abnormality. The differences in FEV_1 and FVC % predicted were significant, and up to 25% and 30%, respectively, when comparing ethnicity-specific values with values derived from the NHANES III.

Three studies showed mixed effects when comparing ethnic reference equations with GLI equations. Heraganahally et al[46] demonstrated that the Australian aboriginal population does not fit GLI equations even when using the GLI-Other reference standards for FEV_1 and FVC, but values for FEV_1 to FVC ratio were similar.

Similarly, Ben Saad et al[33] found that North African adults were not described appropriately by GLI equations. GLI overestimated normal and underestimated obstruction and possible restriction compared with ethnicity-specific equations derived from North African adults. However, Al-Qerem et al[43] found that the GLI-Caucasian values fit the lung function of Jordanian adolescents better than the two selected regional equations or the GLI-Other equation.

Two lung volume studies demonstrated that ethnicity-specific reference equations eliminated differences between White and Afro-Caribbean children. Greenough et al[50] found differences in functional residual capacity by helium dilution in 88 children with asthma of different ethnic origins. Functional residual capacity was elevated in all children compared with normal values; however, functional residual capacity of White children was higher than that of Afro-Caribbean children if using absolute or % predicted for height when using the same regression equation, but similar when using ethnic-specific regression equations. Sylvester et al[35] also examined lung volumes in 80 Afro-Caribbean children 4 to 17 years of age measured by body plethysmography and found that ethnic-specific equations were needed. To see if White values could be used, they adjusted by sitting height or by 77% or 90% factors and found that differences persisted.

2. Changing from one reference equation to another can change the quantification of relative lung function of individuals in comparison with reference values. This series of articles demonstrated that the proportion of individuals labeled as having obstructive impairment or restrictive impairment differed based on which reference equation was selected. None of the studies used a clinically relevant end point or gold standard to define impairment.

Harber et al[31] found that adjustment for race and sex had significant effects on disability determination among 900 case records. As mentioned in the discussion of that publication, "The American Thoracic Society has recommended [1982] that race correction not be employed because prediction equations are not available for all race and race subgroups. We have found that incorporation of a 15% reduction in the FEV_1, FVC, and maximal voluntary ventilation values predicted for blacks had a major effect upon the relative distribution of impairment assignments. We believe that the concern about employing sex and race corrections represents a complex matter with both scientific and sociopolitical considerations."

Chhabra and Madan[42] found that NHANES III and GLI White and GLI-Other equations predicted higher values for a North Indian population, so more values were labeled low, and therefore abnormal. Compared with ethnicity-specific equations, up to one-third of patients showed a change in category of disease, with more having a restrictive and mixed pattern.

Collen et al[37] found discordance in interpretation of lung function in African American patients using Morris, Knudson, Glindmeyer vs NHANES III equations, less so for Crapo vs NHANES III equations. Morris, Knudson, and Crapo equations were used applying a correction factor of 0.88. Glindmeyer equations were used without any adjustment because they were derived directly from an African American population. Meanwhile in children, Quanjer and Weiner[40] found that transitioning from NHANES III and Wang equations to GLI equations was accurate in 6- to 18-year-old individuals with low FEV_1, FVC, and FEV_1 to FVC ratio; conversely, equations from Knudson, Polgar, and Zapletal were not. Similar findings were published by Sood et al,[49] who found that changing from older reference standards to NHANES III equations among 1,106 non-Hispanic White patients assessed at a single PFT laboratory resulted in a change in both the prevalence and severity of any spirometric abnormality, with a greater change seen in the prevalence. A difficulty in interpreting this and similar work is the lack of clinical outcome comparisons, that is, data were compared only with labels for a given numerical threshold.

Kiefer et al[39] examined whether a single equation could be applied to participants in the NHANES III population. They found no effect modification for race or ethnicity (interaction of age, height, or sex on FEV_1, FVC, and FEV_1 to FVC ratio among White, African American, and Mexican American participants who contributed NHANES III data), thus statistically justifying a single multiethnic equation. Mean lung function was similar in White and Mexican American participants, but lower in African American participants, for a given age, sex, and height.

Regarding adjustment factors, two articles examined the use of Caucasian values in relationship to people of other ethnicities. Enright et al[32] found that among

participants 65 years of age and older in the cardiovascular health study, a correction factor of 6% was more accurate than 12% for African American participants compared with White participants (ie, that the FVC was 6% lower in African American individuals than White individuals among healthy non-tobacco users), even after correcting for standing height, sitting height, and age. In the Multi-Ethnic Study of Atherosclerosis population of older adults, Hankinson et al[38] showed that NHANES III equations performed well. They specified that the "correction factor" for Asian American individuals should be 0.88 instead of 0.94, which minimized the difference of observed minus predicted values.

McCormack et al[47] found that among 12,770 individuals in NHANES III, applying GLI race-specific equations increased the FEV_1 % predicted by 7.6% among Black participants and decreased the FEV_1 % predicted among White participants by 7% compared with the racial composite of GLI-Other. Similarly, Baugh et al[20] quantified the impact of incorporating race into the interpretation of lung function. They showed that in a study of 2,652 participants in the SubPopulations and InteRmediate Outcome Measures In COPD Study (SPIROMICS) cohort of those who had ever used tobacco with or at risk of COPD, the average FEV_1 % predicted for Black participants was 76.8% using NHANES III African American equations, 64.7% using NHANES III non-Hispanic White equations, and 70.0% using GLI-Other equations. These findings demonstrate that the approach chosen can result in significant and clinically relevant changes in the interpretation of spirometry results.

3. Comparing how the choice of reference equation influences diagnosis and the prediction of important health outcomes.

Regarding mortality, Burney and Hooper[21] investigated the Atherosclerosis Risk in Communities study population and demonstrated that although African American individuals showed lower FVC values on average, no difference was found in the association between absolute lung function and survival between African American and White American individuals. This lack of difference was masked when using race-specific reference values from NHANES III because mortality then seemed greater in Black participants (lower absolute FVC value for same % predicted value). The authors concluded, "In assessing the severity of disease, if a given FVC carries the same prognosis for both ethnic groups, the use of ethnically specific norms may disadvantage African-Americans." Thus, they recommended using the same reference equation for White and Black individuals, in this case, the White equations from NHANES III. To repeat this study in a larger population, Gaffney et al[45] studied mortality in the NHANES III population itself and found that the apparent increased mortality for Black individuals predicted by ethnicity-specific reference equations disappeared when using White equations for everyone or when using absolute values rather than % predicted values. The risk for all-cause mortality was the same when Black and White individuals were compared for the same age, sex, height, and absolute FVC values, but when FVC was expressed by a race-specific standard as a % predicted, Black participants showed higher mortality when matched for the same FVC % predicted (because the absolute FVC value would be lower in this situation for Black individuals). Thus, they validated the findings of Burney and Hooper. In a similar strategy, McCormack et al[47] applied the GLI reference equations to the NHANES III population and found that when applying GLI-Other as a multiracial approach to interpreting lung function, the association between FEV_1 and mortality did not differ between Black and White participants. Findings were similar for FVC. These results support using a single, race-neutral equation when interpreting lung function in relationship to mortality. For the same z score, Black individuals seemed to have a higher mortality when using race-specific reference equations, because the same z score reflects a lower absolute FVC in Black participants. When using GLI-Other, Black individuals would have a less inflated z score than when using a race-specific equation, so matching z scores with White individuals reflected closer matching of absolute FVC and thereby similar mortality. One study that did not find an advantage of using race neutral reference equations was by Miller and Cooper,[48] who investigated the association between transfer factor for carbon monoxide (diffusing capacity of the lungs for CO_2) and mortality. These authors concluded that applying 2020 GLI equations (FVC coefficients) for ethnic adjustments to transfer factor for carbon monoxide equations improved survival prediction, thus demonstrating the importance of using race- and ethnicity-specific equations; however, this study involved only 10% of patients of non-European ancestry.

Regarding morbidity, Baugh et al[20] found that among participants in the SPIROMICS study, race-specific

equations underestimated severity among African American individuals with COPD or at risk of COPD. The association between lung function and COPD outcomes, including the COPD Assessment Test, St. Georges Respiratory Questionnaire, and chest CT scan findings were examined, and investigators concluded that FEV_1 and FVC % predicted values derived from universally derived equations more accurately reflected clinically relevant outcomes than % predicted values derived from race-specific equations. In the Multi-Ethnic Study of Atherosclerosis, Elmaleh-Sachs et al[44] examined lung function as a predictor of clinical events (hospitalizations or deaths attributed to chronic lower respiratory disease) and found that race-specific equations (GLI race-specific or NHANES III equations) were not better than race-neutral equations (GLI-Other) in predicting clinical events. Similarly, use of race-specific equations based on GLI failed to improve prediction of breathlessness or prognosis in the NHANES III population compared with race-neutral equations (GLI-Other).[51] A similar finding was reported by Liu et al,[19] who demonstrated that use of race-specific equations to define normal lung function led to substantially higher prevalence of emphysema on CT imaging in Black participants compared with White participants, but this difference was attenuated when using race-neutral reference equations. All these studies provide increasing evidence that use of race-specific reference equations in Black individuals tends to mask the relationship between low absolute lung function and morbidity and mortality.

Key Question 2 Summary: We found studies demonstrating: (1) that ethnicity-specific reference equations generally were more precise in describing the local population than applying NHANES III or GLI equations for groups not specified in either of those two reference datasets; (2) that the proportion of individuals classified as having a lung function impairment by lung function testing strongly depends on the reference set chosen; and (3) that important population health outcomes (eg, mortality, clinical events in COPD) are predicted better by using a standard reference set for all individuals, rather than ethnicity-specific reference values, implying that race-specific values may be masking modifiable risk factors for low lung function seen in non-White ethnic groups. These conclusions are tempered by the limitations that methodology was not standardized between studies, that self-identification of race and ethnicity was highly variable (eg, African American,

Black, Hispanic), and importantly, that no gold standard was used in classifying disease categories.

Key Question 3: What Research Gaps and Questions Must Be Addressed and Answered to Understand Better the Effect of Race and Ethnicity on PFT Results Interpretation and Potential Clinical and Occupational Health Implications?

The expert panel identified several priorities for further research to inform and help clinicians and others to understand better the effect of race and ethnicity on PFT results interpretation. Each of the 10 recommendations achieved 100% consensus and support from panel members. These include the following research gaps (Table 4).

A. It is evident that race and ethnicity have been used as biological variables, and solely using genetics as an indicator of race also has limitations. It similarly should be recognized that social realities, in particular oppression, may have effects that could be reflected in biological variables. Rather than use race or ethnicity as proxies for differences in genetics, body proportions, or both as they currently are, future studies should investigate ways to measure true biological variables more precisely.

In addition, when race or ethnicity are assessed, our understanding would be advanced if consistent guidance and definitions for race and ethnicity were provided and used,[52] along with reliability metrics for this variable. An advantage of objectively collecting data on race and ethnicity would be to identify the source of and to quantify health disparities that align with race and ethnicity, not to assume and include race and ethnicity as biological variables.

Research Gap:

1. **Use clear, practical, and standardized definitions of terms such as *race* and *ethnicity* for research intentions (with aligned clinical utility and/or benefits).**
2. **Establish practical guidance for how and when, or if at all, race and ethnicity should be used in studies assessing lung function.**
3. **Assess, derive, and incorporate precise measures and study methods into interpretation of pulmonary function. For example, if ancestry is being considered, genetics should be studied; if chest dimensions are being considered, detailed measurements of chest size should be assessed.**

TABLE 4] Identified Research Gaps and Needs to Understand Better the Effect of Race and Ethnicity on PFT Results Interpretation and Potential Clinical Implications

1. Use clear, practical, and standardized definitions of terms such as *race* and *ethnicity* for research intentions (with aligned clinical utility and/or benefits).

2. Establish practical guidance for how and when, or if at all, race and ethnicity should be used in studies assessing lung function.

3. Assess, derive, and incorporate precise measures and study methods into interpretation of pulmonary function. For example, if ancestry is being considered, genetics should be studied; if chest dimensions are being considered, detailed measurements of chest size should be assessed.

4. Generate consistent and robust investigations using validated instruments for assessing the effects of social determinants of health on lung health outcomes.

5. Research studies assessing differences in lung function between populations should include measures of standardized clinical relevance and outcomes.

6. Develop a more thorough understanding and inclusive definition of *normal* lung function by better understanding all important factors that contribute to lung health and safety. When reporting normal populations, all factors or attributes used to make that assumption should be listed.

7. A definition and understanding of a 'gray zone' is required—either borderline normal or borderline abnormal—that appreciates the reality of more than a binary interpretation of test results. There is a parallel need to clearly identify and guide circumstances and settings where further investigation or longitudinal follow-up may then be appropriate.

8. Evaluate and develop updated, equitable guidelines relating to pulmonary function testing for assessing employability, impairment and disability, and occupational health and safety that are cognizant of the complex and multiple regulatory requirements and constraints.

9. Construct and standardize research study designs that allow for meaningful comparisons and with a dataset of accepted and commonly utilized comparisons.

10. Research funding and efforts must be [re-]directed to appropriately address the many and significant identified research gaps related to the complex relationship between race/ethnicity and lung function. Common study protocols must be developed to guide this research, and as an important early step, it is strongly recommended that a multisociety initiative be established to advance these relevant and important needs.

PFT = pulmonary function test.

B. In addition to body proportions, the differences observed between ethnic groups may reflect the social and environment circumstances of an individual

longitudinally over the life span, and potentially also across several generations for exposures from chronic poverty and racism. Although differences in lung function are observed between people of different geographical ancestry, what proportion of these differences can be attributed to socioenvironmental factors remains poorly understood because heterogeneity exists between studies in terms of how social constructs were selected, defined, and measured, resulting in disparate findings.

Research Gap:

4. Generate consistent and robust investigations using validated instruments for assessing the effects of social determinants of health on lung health outcomes.

C. Differences between racial and ethnic groups, or between populations, frequently are reported, but very few studies have evaluated whether the differences are clinically relevant (either for the intention to define impairment or to predict risk of future respiratory outcomes, in an individual or for a population). Both an opportunity and need exist to re-evaluate how we use lung function to view the normal vs abnormal framework where lung function is used to aid in diagnosis. For example, better correlating important individual or population health interventions or outcomes (eg, treatments and therapies, transplantation referrals, unwanted or adverse clinical events, mortality, and so on) with reference sets for all individuals would be of significant benefit.

Research Gap:

5. Research studies assessing differences in lung function between populations should include measures of standardized clinical relevance and outcomes.

D. Measures of lung function are essential for the diagnosis and management of respiratory diseases, but how do we confidently differentiate (normal) smaller lungs from impaired lung function, recognizing that it is well established that lower lung function is associated with poor health outcomes and early mortality. The current view of normal is problematic because marginalized populations disproportionately may be underdiagnosed and may be misclassified as healthy. This is compounded by definitions of health that differentially exclude individuals by age, race, and education[24]; have a single threshold for normal

compared with abnormal; or both. In addition, exposures and settings such as second-hand smoke, air pollution, and premature births that impact lung growth and development are observed disproportionately in areas of poor socioeconomic status. Finally, instead of primarily relying on limits of normal using a healthy population, it would be desirable also to track lung function change(s) longitudinally over time and to anchor the findings to clinically relevant end points and outcomes.

Research Gap:

6. **Develop a more thorough understanding and in-clusive definition of *normal* lung function by better understanding all important factors that contribute to lung health and safety. When reporting normal populations, all factors or attributes used to make that assumption should be listed.**
7. **A definition and understanding of a 'gray zone' is required—either borderline normal or borderline abnormal—that appreciates the reality of more than a binary interpretation of test results. There is a parallel need to clearly identify and guide cir-cumstances and settings where further investigation or longitudinal follow-up may then be appropriate.**

E. Equitable evidence-informed guidelines relating to pulmonary function testing for employability and occupational health and safety must be developed. The realities and needs are unique in the varied employment and occupational settings and include protecting potentially vulnerable workers, assessing and monitoring risk regarding exposure effect, and others. In addition, the regulatory environments in these settings are complex and similarly unique. It also may be warranted to be specific when considering implications of pulmonary function test interpretation, that is, rather than PFTs in general, benefit may exist in different approaches when considering race and ethnicity regarding FEV_1, FVC, and FEV_1 to FVC ratio, in varying settings.

8. **Evaluate and develop updated, equitable guidelines relating to pulmonary function testing for assessing employability, impairment and disability, and occupational health and safety that are cognizant of the complex and multiple regulatory requirements and constraints.**

F. A need exists for large, representative population studies that include lung function measurements (not limited to spirometry) of excellent quality using harmonized protocols and measures of anthropometric and genetic differences between populations. A need

also exists for transparent and harmonized reporting of the study population (ie, not limiting for health [non-tobacco users, no respiratory disease], social determinants of health, reporting units (milliliters, % predicted, % differences attributed) and race and ethnicity.

Research Gap:

9. **Construct and standardize research study designs that allow for meaningful comparisons and with a dataset of accepted and commonly utilized comparisons.**
10. **Research funding and efforts must be [re-]directed to appropriately address the many and significant identified research gaps related to the complex relationship between race/ethnicity and lung function. Common study protocols must be developed to guide this research, and as an important early step, it is strongly recommended that a multisociety initiative be established to advance these relevant and important needs.**

Discussion

This review has identified assumptions and gaps, both in the published literature and in our evolving understanding of lung health. It has become evident that many past perceptions and practices regarding the effect of race and ethnicity on PFT results interpretation are based on limited scientific evidence and measures that lack reliability. These shortcomings should not be discounted or dismissed, because they may enable flawed conclusions, unintended consequences, or both. Addressing the identified research gaps and needs (Table 4) would allow a better—a more informed—understanding of the effects of race and ethnicity on PFT results interpretation.

It must be emphasized that this current document is not meant to provide clinical guidance. This multiprofessional society document evaluates past research that addresses this key area and identifies research gaps and questions as well as best methods to address these research gaps and questions in relationship to the effect(s) of race and ethnicity on PFT results interpretation. In essence, this document identifies key research priorities that can help to inform and guide future clinical interpretation statements or standards.

Given the current limitations in methods and conflicting results that race- and ethnic-specific

equations may perform better for matching specific physiologic features in a limited number of individuals, but worse for predicting mortality and health outcomes, and that lung function classification is influenced strongly by the choice of reference standard used in interpretation, the panel proposes that we, and our field, proceed with caution. Understandably, people who use PFT results to make clinical and occupational decisions currently may be confused and in need of guidance and direction. Regardless of any short-term solution(s) that are proposed, our review of the evidence underlines the challenges and limitations of past studies and highlights the need for additional scientific research and rigor.

It is also important to appreciate the scope of this issue: those individuals or areas that require additional thoughtfulness compared with those individuals or areas where stronger evidence exists. For example, it is evident that regardless of techniques or equations used, the reduction in FEV_1 and FVC are proportional, leading to relative stability in the FEV_1 to FVC ratio. In addition, and importantly, the issues and factors under discussion that seem to influence the impact of race and ethnicity in the interpretation of PFT results likely do not influence results that easily are normal or decidedly abnormal. Alternatively, and even if they do in the setting of easily normal or decidedly abnormal, the impact in these settings is clinically insignificant. However, for others and as noted above (Research Gap 7) (Table 4), the concept or identification of a borderline or gray zone may have merit and may signal the practical need for additional testing or assessment. In the clinical setting, pulmonary function testing is only one of many tools available to the clinician.

In undertaking future work and research to advance our understanding of the effect of race and ethnicity on PFT results interpretation, several key principles also should guide our work and approaches:

1. Solutions need to be patient centric and globally applicable;
2. Solutions must be evidence based and informed; and
3. Solutions need to appreciate and account for varied clinical, occupational, and epidemiologic testing environments, including affecting both individuals and populations.

An urgent need exists for more and better research that will inform our field about these many uncertainties and serve as a foundation for future recommendations in this area. We need to be ready to accept and implement new guidance considering this evidence and acknowledge that the solutions available today may not be ideal and require careful consideration of the individual context.

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Conflicts of interest are listed in e-Appendix 1.

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