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COMMENTARY

Rethinking the Role of Race in Lung Function: The Shift to Race-Neutral Spirometry Interpretation

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Normative values for lung function have traditionally been determined by age, sex, height, and self-reported race.[1] The inclusion of race has become increasingly controversial, as it implies that the observed differences in lung function among individuals of different races are solely due to genetic factors.[2]

Although hereditary factors may play some role, lung function is influenced by numerous environmental factors such as access to prenatal care, smoke exposure (both direct and secondhand), childhood infections, nutrition, and ambient air quality (Figure). These factors, many linked to social determinants of health, likely play a larger role in the observed differences in lung function between races than ancestral origin.[2] Conflating race—a predominantly social construct—with inherent biological differences has been increasingly recognized as a fundamentally flawed approach to pulmonary function test interpretation.

Spurred by these discussions, and with a clear agenda to reduce racial bias in pulmonary function test interpretation, the American Thoracic Society recommended the worldwide adoption of a "race-neutral" set of spirometry reference equations in pulmonary function laboratories in 2023.[3] In this article, we outline the complexities associated with this recommendation and the resulting impact on spirometry interpretation and patient care.

What Does Race-Neutral Spirometry Mean?

Mayo Clinic and many other pulmonary function laboratories internationally currently employ the Global Lung Function Initiative (GLI) 2012 "multiethnic" spirometry reference equations.[1] These equations provide normative values for 4 ancestral origin categories: White, Black (including African American), Northeast Asian (including individuals from Korea and China; north of the Huaihe River and Qinling Mountains), and Southeast Asian (including individuals from Thailand, Taiwan, and China; south of the Huaihe River and Qinling Mountains).[1] For patients who do not self-identify in these categories, GLI investigators have recommended the use of "Other/Mixed" reference equations, which represent an average of the equations for the other 4 categories (GLI-Other).

The race-composite GLI-Other equations have been proposed as a race-neutral option[4] but faced criticism due to the White predominance in the database used to develop these reference values. In response, GLI-Global equations were recently created by assigning different weights to each of the 4 ancestral origin categories to ensure that the final equations represent an equal contribution from all 4 categories.[5]

The GLI-Global equations don't include race, only age, sex, and height.

We simulated the impact of transitioning from GLI-2012 multiethnic to race-neutral GLI-Global equations on spirometry interpretation in more than 100,000 Mayo Clinic patients.[6] Using GLI-Global changed spirometry interpretation (ie, normal, obstruction, or preserved ratio impaired spirometry [PRISm]) in 10% of patients, with the greatest change seen among Black and Southeast Asian individuals. The most common change was the increased frequency of PRISm, defined as a reduced forced expiratory volume in the first second

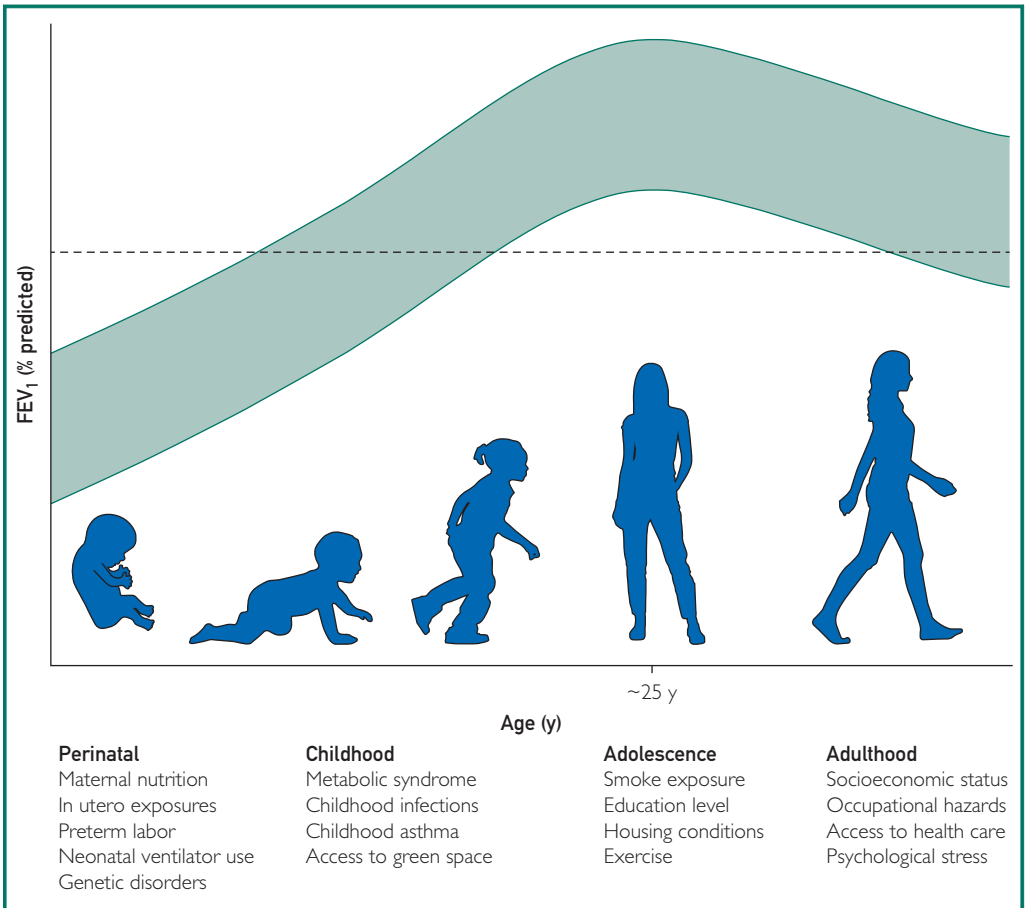

FIGURE. Determinants of lung health encompass a broad range of factors, including genetic predisposition, exposures during in utero development, nutrition, level of education, childhood infections, exercise, smoking, air quality, and access to health care. These factors are often intertwined with race, underscoring the importance of addressing systemic racism and socioeconomic inequities as part of a systematic public health strategy to improve lung health across different racial groups. Although the risk factors listed here are subdivided into distinct time periods, many risk factors exert a negative effect on lung health across the age spectrum. FEV_1, forced expiratory volume in the first second.

Somewhat complex measures of lung function are needed for medical purposes.

For our purposes, all that we really need to know is that this diagnostic test measures how much air can be exhaled in one breath. This, then, indicates lung capacity.

(FEV_1) and/or forced vital capacity (FVC) with a normal FEV_1/FVC ratio.[6] Further testing with lung volume measurements is recommended in this setting to determine whether these findings are due to a restrictive process or occult obstruction.[7]

Although transitioning to a race-neutral approach does not change the frequency of obstruction (ie, low FEV_1/FVC ratio) in Black individuals, GLI Global does result in a reduction in percent predicted FEV_1 in these patients. In practice, this reduction translates into increased severity grading of airflow obstruction in Black patients. Two recent studies have suggested that about 20% of Black patients would be impacted, with the most common change being a reclassification from mild to moderate obstruction.[7,8] Table 1 provides a summary of other changes in lung function interpretation resulting from the use of a race-neutral approach.

The Impact of a Race-Neutral Approach on Patients and Patient Care

Race adjustment in spirometry testing normalizes the lower mean observed lung function in certain racial/ethnic groups,

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TABLE 1. Changes in Lung Function Interpretation Resulting From the Use of GLI-Global[a,b]

Variable	Affected spirometry test results	PRISm	Obstruction	Severity of impairment
Black	15%	↑↑↑↑	—	Increased
White	7%	↓↓	↑	Decreased
Northeast Asian	11%	↓↓↓	↓↓	Decreased
Southeast Asian	12%	↑↑↑	↓↓↓	Increased

[a]GLI-Global, Global Lung Function Initiative global (race-neutral) reference equations; PRISm, preserved ratio impaired spirometry; ↑, increase; ↓, decrease; —, relative change by <5%; 1 arrow, 5%-15%; 2 arrows, 16%-30%; 3 arrows, 31%-50%; 4 arrows, >50%.
[b]Individuals who self-identify as Black are most affected by this transition.[6]

including Black and Southeast Asian individuals. This factor can lead to underdiagnosis of lung disease and may contribute to health inequities.[9]

Benefits of Adopting a Race-Neutral Approach. An important benefit of adopting a race-neutral approach is the potential for earlier diagnosis of pulmonary disease in underrepresented populations. For example, adoption of race-neutral reference equations in Black children led to a doubling in the number of diagnoses of uncontrolled asthma.[10] Earlier diagnosis and assessment of greater disease severity should in turn lead to earlier initiation and appropriate escalation of treatment for such patients. Similarly, the increased identification of PRISm may lead to earlier diagnosis of restrictive lung disease such as pulmonary fibrosis.[6]

A race-neutral approach also stands to benefit underrepresented populations by qualifying them earlier for specific treatments that rely on predicted lung function thresholds, such as noninvasive ventilation for neuromuscular disease[11] or pulmonary rehabilitation for chronic obstructive pulmonary disease.[12] When compared with standard multiethnic equations, the use of race-neutral equations led to higher lung allocation scores for Black patients, potentially increasing their priority for lung transplant.[13,14]

The transition to a race-neutral approach may also allow members of underrepresented groups to qualify more readily for disability compensation that relies on impairment assessments that use percent predicted lung function cutoffs.[3]

Challenges of Adopting a Race-Neutral Approach. Conversely, adopting a single set of reference equations may disqualify patients from necessary treatments in certain instances. For example, surgical resection remains the preferred treatment for early-stage lung cancer over radiation or chemotherapy. When thoracic surgeons were presented with spirometry data for Black patients using race-neutral rather than race-specific reference equations, the absolute likelihood of recommending surgical treatment dropped by 26%.[15] This decrease would only deepen disparities that Black patients already encounter when accessing surgical procedures in the United States.[16,17]

Originally, race adjustment was implemented to enable more Black Americans to work in cotton processing mills in the 1970s. The reference values used at that time, derived from White males, prevented Black job applicants from being hired when preemployment spirometry tests were required.[18] A transition back to a single reference approach may exclude people who are not White from certain jobs that require occupational spirometry screening, such as firefighting. Without widespread awareness of how implementation of race-neutral equations affects lung function estimates, this approach could add systematic bias in job opportunities, compounding implicit and explicit biases already entrenched in societal hiring practices.

Transitioning to a race-neutral approach might also result in higher premiums for life and health insurance, further compounding existing disparities in health care access. Although a race-neutral approach could

uncover previously unidentified health risks and more severe lung disease in certain racial/ethnic groups,[3] subsequent recommendations for additional diagnostic testing and management could potentially aggravate the socioeconomic inequities in health care access that these groups have historically and continue to face due to long-standing racial discrimination. Moreover, this transition could potentially heighten stress and concern among these groups, who may perceive their lung function as worsening solely because of a change in a prediction equation. This issue highlights the need for both health care provider and patient education about these changes.

Areas of Uncertainty. The effects of adopting a race-neutral approach for spirometry interpretation on White individuals are less clear. Although changes in predicted lung function using various race-neutral equations tend to be less prominent for this group,[6] the overall number of individuals potentially affected in most US communities is likely higher compared with other groups. Potential unintended consequences for White individuals vary depending on the specific equation used and may include delayed diagnoses and reduced eligibility for specific treatments.[3,13]

Another area of uncertainty concerns the impact of this approach on underrepresented populations other than Black individuals. Although GLI equations for White individuals include those who are Hispanic,[19] significant variability exists within Hispanic subgroups. In the United States, adults of Hispanic/Latino ethnicity (ie, Dominican and Puerto Rican individuals) have been previously found to have a lower mean predicted FEV_1 and FVC than other Hispanics, and the impact of a race-neutral approach on these subgroups remains unclear.[20] In addition, a general observation from our study indicated that the use of the GLI-Global equation resulted in worse predicted lung function in Southeast Asian individuals and slightly better in Northeast Asian people.[6] The smallest change when transitioning to GLI-Global was among those who did not self-identify in these 4 ancestral origin categories.[6] Further studies are necessary to better understand the full implications of these findings.

It is also important to note that the database used to develop GLI-Global also lacks representation from many large global populations, especially from Africa, Asia, and South America. Further research is needed in these wider populations to truly move toward globally representative race-neutral equations. Lastly, research is needed to better clarify if incorporation of social determinants of health into predictive lung function values should be considered.

Is Race-Neutral Spirometry Interpretation Ready for Implementation?

The exclusion of race from normative values in lung function assessments can reduce inherent biases and expose modifiable risk factors associated with structural racism. Current studies suggest that single-reference equations in spirometry are as effective, if not superior, to race-adjusted equations when considering clinical and radiographic end points.[3,21] For example, race-neutral approaches may more accurately estimate breathlessness,[22] better correlate with lung volume measurements,[6] and match race-specific approaches in explaining abnormalities on computed tomography of the chest.[7] Race-neutral approaches may also better predict overall survival,[23,24] although this result might be coincidental given that lung disease does not significantly contribute to the mortality gap between Black and White individuals.[3]

Many argue that, as a profession, we also have a collective ethical responsibility to minimize risk for historically disadvantaged groups already at higher risk for lung disease.[7] In this context, a strategy that favors increased sensitivity over specificity may be of greater overall benefit,[7] albeit with the potential for greater health care utilization. Other potential negative consequences of implementing race-neutral equations can be mitigated. As an example, greater use of alternative methods for lung function assessment such as cardiopulmonary exercise testing may obviate the potential pitfalls of a race-neutral approach

TABLE 2. Pros and Cons of Adopting a Race-Neutral Approach in Spirometry Interpretation

Pros	Cons
General population:	General population:
Better correlation with disease burden	Scarcity of effective race-neutral options
Better correlation with overall survival	Uncertain impact on White individuals and non-Black underrepresented groups
Unmasking modifiable SDH	Black individuals:
Black individuals:	Decreased candidacy for lung surgery
Earlier evaluation and diagnosis of lung diseases	Increased premiums
Enhanced eligibility for treatments (eg, pulmonary rehabilitation, noninvasive ventilation)	Concerns for employment
Enhanced eligibility for lung transplant	
Enhanced eligibility for compensation in disability cases	

SDH, social determinants of health.

to spirometry interpretation in patients who are being considered for lung cancer resection or certain occupations. Longitudinal follow-up and in-depth counseling may also help address patient concerns, although this issue may be more intricate and demanding than it initially appears.[25]

As societies become increasingly diverse and multicultural, more people may feel that they do not fit into a specific race/ethnicity category. Indeed, those who self-identified in the Other/Mixed category in our study were also the youngest.[6] However, as we search for the perfect race-neutral approach, we should be aware of the unintended consequences of its application. A summary of the pros and cons of transitioning to a race-neutral approach in spirometry interpretation is presented in Table 2. Some experts have also raised important questions about whether this "one-size-fits-all" race-composite approach represents a step away from precision medicine in an era in which "omics"-based strategies are increasingly employed to tailor diagnoses and therapies at the individual level.[26]

Finally, it is worth emphasizing that discussions on the impact of a race-neutral approach in spirometry must extend beyond its impact on testing interpretation and consistently both acknowledge and address the broader sources of ingrained racial bias that persist in our US health care system. There remains an urgent need for systemic reforms to eliminate the deep-seated racial inequalities in health care. Expanding the dialogue and looking for methods to remove race from spirometric measurements represents just one small step in the long overdue journey to meaningful change.

Conclusion

Continued use of race-specific normative equations is not a viable long-term strategy as we seek to reduce systemic racism in medicine. Transitioning to a race-neutral method like GLI-Global is a promising alternative to race-specific approaches in spirometry interpretation that attempts to reduce bias and inequities in pulmonary function test interpretation. Professional societies endorsing it have highlighted research gaps and the need for more studies on the impact of race on spirometry interpretation. Until these gaps are filled, careful consideration should be given to the application of spirometry results, recognizing uncertainties in categorizing lung function that falls near the lower limit of normal, and underlining the continued importance of placing pulmonary function testing results within an appropriate clinical context.

POTENTIAL COMPETING INTERESTS

The authors report no competing interests.

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REFERENCES

1. Quanjer PH, Stanojevic S, Cole TJ, et al; ERS Global Lung Function Initiative. Multi-ethnic reference values for spirometry for the 3-95-yr age range: the Global Lung Function 2012 equations. *Eur Respir J*. 2012;40(6):1324-1343.
2. Vyas DA, Eisenstein LG, Jones DS. Hidden in plain sight — reconsidering the use of race correction in clinical algorithms. *N Engl J Med*. 2020;383(9):874-882.
3. Bhakta NR, Bime C, Kaminsky DA, et al. Race and ethnicity in pulmonary function test interpretation: an official American Thoracic Society statement. *Am J Respir Crit Care Med*. 2023;207(8):978-995.
4. Connolly MJ, Donohue PA, Palli R, Khurana S, Cai X, Georas SN. Diagnostic impact of a race-composite pulmonary function test results interpretation strategy. *Chest*. 2023;164(5):1290-1295.
5. Bowerman C, Bhakta NR, Brazzale D, et al. A race-neutral approach to the interpretation of lung function measurements. *Am J Respir Crit Care Med*. 2023;207(6):768-774.
6. Kanj AN, Scanlon PD, Yadav H, et al. Application of Global Lung Initiative Global spirometry reference equations across a large, multicenter pulmonary function lab population. *Am J Respir Crit Care Med*. 2024;209(1):83-90.
7. Non AL, Bailey B, Bhatt SP, et al. Race-specific spirometry equations do not improve models of dyspnea and quantitative chest CT phenotypes. *Chest*. 2023;164(6):1492-1504.
8. Moffett AT, Bowerman C, Stanojevic S, Eneanya ND, Halpern SD, Weissman GE. Global, race-neutral reference equations and pulmonary function test interpretation. *JAMA Netw Open*. 2023;6(6):e2316174.
9. Beaverson S, Ngo VM, Pahuja M, Dow A, Nana-Sinkam P, Schefft M. Things We Do For No Reason™: Race adjustments in calculating lung function from spirometry measurements. *J Hosp Med*. 2023;18(9):845-847.
10. Burbank AJ, Atkinson CE, Espaillat AE, et al. Race-specific spirometry equations may overestimate asthma control in Black children and adolescents. *Respir Res*. 2023;24(1):203.
11. Miller RG, Jackson CE, Kasarskis EJ, et al. Quality Standards Subcommittee of the American Academy of Neurology. Practice parameter update: the care of the patient with amyotrophic lateral sclerosis: drug, nutritional, and respiratory therapies (an evidence-based review); report of the Quality Standards Subcommittee of the American Academy of Neurology. Published corrections appear in *Neurology*. 2009;73(24):2134 and *Neurology*. 2010;74(9):781. *Neurology*. 2009;73(15):1218-1226
12. Rochester CL, Alison JA, Carlin B, et al. Pulmonary rehabilitation for adults with chronic respiratory disease: an official American Thoracic Society clinical practice guideline. *Am J Respir Crit Care Med*. 2023;208(4):e7-e26.
13. Brems JH, Balasubramanian A, Psoter KJ, et al. Race-specific interpretation of spirometry: impact on the lung allocation score. *Ann Am Thorac Soc*. 2023;20(10):1408-1415.
14. Colon Hidalgo D, Ramos KJ, Harlan EA, et al. Historic use of race-based spirometry values lowered transplant priority for Black patients. *Chest*. 2024;165(2):381-388.
15. Bonner SN, Lagisetty K, Reddy RM, Engeda Y, Griggs JJ, Valley TS. Clinical implications of removing race-corrected pulmonary function tests for African American patients requiring surgery for lung cancer. *JAMA Surg*. 2023;158(10):1061-1068. Published correction appears in *JAMA Surg*. 2023;158(10):1116 (doi: 10.1001/jamasurg.2023.5321).
16. Roberts SE, Rosen CB, Keele LJ, et al. Rates of surgical consultations after emergency department admission in Black and White Medicare patients. *JAMA Surg*. 2022;157(12):1097-1104.
17. Best MJ, McFarland EG, Thakkar SC, Srikumaran U. Racial disparities in the use of surgical procedures in the US. *JAMA Surg*. 2021;156(3):274-281.
18. Townsend MC, Cowl CT. U.S. occupational historical perspective on race and lung function. *Am J Respir Crit Care Med*. 2022;206(6):789-790.
19. Elmaleh-Sachs A, Balte P, Oelsner EC, et al. Race/ethnicity, spirometry reference equations, and prediction of incident clinical events: the Multi-Ethnic Study of Atherosclerosis (MESA) Lung Study. *Am J Respir Crit Care Med*. 2022;205(6):700-710.
20. LaVange L, Davis SM, Hankinson J, et al. Spirometry reference equations from the HCHS/SOL (Hispanic Community Health Study/Study of Latinos). *Am J Respir Crit Care Med*. 2017;196(8):993-1003.
21. Marciniuk DD, Becker EA, Kaminsky DA, et al. Effect of race and ethnicity on pulmonary function testing interpretation: 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. *Chest*. 2023;164(2):461-475.
22. Ekström M, Backman H, Mannino D. Clinical implications of the Global Lung Function Initiative race-neutral spirometry reference equations in terms of breathlessness and mortality. *Am J Respir Crit Care Med*. 2024;209(1):104-106.
23. Gaffney AW, McCormick D, Woolhandler S, Christiani DC, Himmelstein DU. Prognostic implications of differences in forced vital capacity in black and white US adults: findings from NHANES III with long-term mortality follow-up. *EClinicalMedicine*. 2021;39:101073.
24. Burney PGJ, Hooper RL. The use of ethnically specific norms for ventilatory function in African-American and white populations. *Int J Epidemiol*. 2012;41(3):782-790.
25. Baugh A, Adegunsoye A, Connolly M, et al. Towards a race-neutral system of pulmonary function test results interpretation. *Chest*. 2023;164(3):727-733.
26. Mannino DM, Townsend MC. Spirometry in 2022: is a single set of prediction equations for all the best path forward [editorial]? *Am J Respir Crit Care Med*. 2023;207(6):659-661.