ล

health and probability of disease. Studies that assess the relationship between lung function and health outcomes will advance this goal.

There are tradeoffs between use of race-specific versus multiracial reference equations, and a shift from one approach to the other will have adverse consequences in different settings. Townsend and Cowl provide an interesting historical example of how a change to a racespecific approach may have increased access to job opportunities for Black individuals. Similarly, there are examples of how race-specific equations may increase access to treatments or surgeries that require lung function to be above a threshold. There are also compelling examples of how a race-specific approach could delay diagnosis of lung disease or limit access to disability benefits for Black individuals. Collectively, these examples highlight the limitations of approaches that rely on threshold values and the urgent challenge to think more broadly about potential solutions that prioritize health equity.

Rather than viewing our analysis as a means to discount ancestry (race)-specific equations, we approached the study question with an overall goal of investigating how lung function is associated with health outcomes, as a means of reexamining how we define normal. We do not contend that race should be ignored but rather that additional work is needed to eliminate health disparities that may contribute to the differences that have been demonstrated in lung function. Our findings caution that integrating the lower lung function observed among Black Americans in the definition of normal may have the potential to obscure adverse health implications.

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

Meredith McCormack, M.D., M.H.S.* Aparna Balasubramanian, M.D., M.H.S. Robert A. Wise, M.D. Corinne A. Keet, M.D., Ph.D. Johns Hopkins University Baltimore, Maryland

Elizabeth C. Matsui, M.D., M.H.S. Dell Medical School Austin, Texas

Roger D. Peng, Ph.D. Johns Hopkins Bloomberg School of Public Health Baltimore, Maryland

ORCID ID: 0000-0003-1702-3201 (M.M.).

*Corresponding author (e-mail: mmccor16@jhmi.edu).

References

- McCormack MC, Balasubramanian A, Matsui EC, Peng RD, Wise RA, Keet CA. Race, lung function, and long-term mortality in the National Health and Nutrition Examination Survey III. Am J Respir Crit Care Med 2022;205:723–724.
- Sin DD, Wu L, Man SF. The relationship between reduced lung function and cardiovascular mortality: a population-based study and a systematic review of the literature. *Chest* 2005;127:1952–1959.
- Elmaleh-Sachs A, Balte P, Oelsner EC, Allen NB, Baugh A, Bertoni AG, 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;205:700–710.

- Baugh AD, Shiboski S, Hansel NN, Ortega V, Barjakteravic I, Barr RG, et al. Reconsidering the utility of race-specific lung function prediction equations. Am J Respir Crit Care Med 2022;205:819–829.
- American Thoracic Society. Lung function testing: selection of reference values and interpretative strategies. *Am Rev Respir Dis* 1991;144: 1202–1218.
- Quanjer PH, Stanojevic S, Cole TJ, Baur X, Hall GL, Culver BH, 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;40:1324–1343.
- Borrell LN, Elhawary JR, Fuentes-Afflick E, Witonsky J, Bhakta N, Wu AHB, et al. Race and genetic ancestry in medicine - a time for reckoning with racism. N Engl J Med 2021;384:474–480.
- Witonsky J, Elhawary JR, Eng C, Rodríguez-Santana JR, Borrell LN, Burchard EG. Genetic ancestry to improve precision of race/ethnicitybased lung function equations in children. *Am J Respir Crit Care Med* 2022;205:725–727.

Copyright © 2022 by the American Thoracic Society

Check for updates

Reply to Townsend and Cowl

From the Authors:

We were thrilled to receive the letter from Drs. Townsend and Cowl, which highlights important issues in the use of race in spirometry. They emphasize the potential risk of alternative systems of reporting lung function that do not use race, whereas we had aimed to demonstrate how its current usage can mislead about the importance of socio-environmental influence and clinical severity (1). Each is a critical point worthy of further exploration. We have always hoped that our work would inspire a fulsome debate about current practice.

³This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0. For commercial usage and reprints, please e-mail Diane Gern (dgern@thoracic.org).

Supported by NHLBI grants U01HL137880, K24HL137013, K23HL125551, HL137013, and F32HL158160. SPIROMICS was supported by contracts from the NIH/NHLBI (HHSN268200900013C HHSN268200900014C, HHSN268200900015C, HHSN268200900016C, HHSN268200900017C, HHSN268200900018C, HHSN268200900019C, HHSN268200900020C), grants from the NIH/NHLBI (U01 HL137880 and U24 HL141762), and supplemented by contributions made through the Foundation for the NIH and the COPD Foundation from AstraZeneca/MedImmune; Bayer; Bellerophon Therapeutics; Boehringer-Ingelheim Pharmaceuticals, Inc.; Chiesi Farmaceutici S.p.A.; Forest Research Institute, Inc.; GlaxoSmithKline; Grifols Therapeutics, Inc.; Ikaria, Inc.; Novartis Pharmaceuticals Corporation; Nycomed GmbH; ProterixBio; Regeneron Pharmaceuticals, Inc.; Sanofi; Sunovion; Takeda Pharmaceutical Co.; and Theravance Biopharma and Mylan. The above entities had no role in the analysis or interpretation of the data; the preparation, review, or approval of the manuscript; or the decision to submit the manuscript for publication.

Author Contributions: A.D.B. drafted the first version of the manuscript. All authors contributed to the conceptualization, revision for important intellectual content, and approval of the final work.

Originally Published in Press as DOI: 10.1164/rccm.202204-0655LE on May 3, 2022

As scientists and humanitarians, we should aspire to a standard that both assures individuals are not being arbitrarily excluded from job opportunities, and simultaneously that they are not put in situations that would compromise their health because they occupy a genuinely elevated risk stratum. The current state of knowledge is not sufficient to address either concern. Therefore, we strongly agree that all possible causes of lung function differences should be vigorously investigated. However, it is helpful in this regard to understand the direction of prior scientific work. Anthropometry as a cause of difference in mean racial lung function has been investigated persistently since the mid-19th century, but has never been found to explain the majority of the difference (2, 3). Helpfully, though, its origins have been shown to be socially influenced, and not solely genetic. Despite moving away from the equator, Mayan immigrants have in contravention of Allen's Rule (4) developed progressively longer limbs and shorter trunks as they've arrived in more affluent nations (5). This suggests a complex, multifactorial relationship that might be predicted from the need for all determinants of lung function to be mediated through some biological mechanism. But skewed trends in scientific investigation are not well-poised to capture these dynamics. Over a decade ago, genetic and genomic-centered projects were among the top ten areas for publicly funded healthcare research funds disbursed in the United States (6). By contrast, proposals that prominently feature ideas like socioeconomic status or psychosocial environment have been less commonly funded (7). Relative to the ability to capture genetic influences, assessing the impact of environmental exposures is still in its infancy (8). So, too, is our understanding of the connection between lung function and clinical outcomes. Perhaps like the study of transplant, deepening our knowledge will reveal that we have over-estimated the importance of lung function relative to other determinants in our inquiries of greatest interest (9).

As for all professions that routinely measure lung function, cotton workers with ethnically normal but globally abnormal lung function may be at unique risk, equivalent risk, or lung function may not be a meaningful determinant of risk at all. In the interval, we agree that omitting race is not an appropriate or reasonable solution. We have advocated the use of composite equations derived from multiple racial and ethnic groups that reflect the rich diversity of our population. This approach naturally accounts for greater variance to address the concerns raised in the case of cotton worker standards, and improves on the current standard's handling of multiracial individuals and those for whom there are not currently appropriate race-specific equations elaborated.

Recognizing that these questions are unresolved is one important step to promoting their continued study. Gathering the data to resolve these unknowns will not only help address health disparities, it will augment our ability to care for all people by advancing our knowledge of physiology and disease. This is an important mission to which all healthcare professionals are called.

<u>Author disclosures</u> are available with the text of this letter at www.atsjournals.org.

Aaron D. Baugh, M.D.* Neeta Thakur, M.D., M.P.H. Prescott G. Woodruff, M.D., M.P.H. University of California San Francisco San Francisco, California

ORCID ID: 0000-0002-9527-691X (A.D.B.).

*Corresponding author (e-mail: Aaron.baugh@ucsf.edu).

References

- Baugh AD, Shiboski S, Hansel NN, Ortega V, Barjakteravic I, Barr RG, et al. Reconsidering the utility of race-specific lung function prediction equations. Am J Respir Crit Care Med 2022; 205:819–829.
- Jacobs DR Jr, Nelson ET, Dontas AS, Keller J, Slattery ML, Higgins M. Are race and sex differences in lung function explained by frame size? The CARDIA Study. *Am Rev Respir Dis* 1992;146:644–649.
- Harik-Khan RI, Muller DC, Wise RA. Racial difference in lung function in African-American and White children: effect of anthropometric, socioeconomic, nutritional, and environmental factors. *Am J Epidemiol* 2004;160:893–900.
- Allen AJ. The influence of physical conditions in the genesis of species. Radical Rev 1877;1:108–140.
- Bogin B, Smith P, Orden AB, Varela Silva MI, Loucky J. Rapid change in height and body proportions of Maya American children. *Am J Hum Biol* 2002;14:753–761.
- Pohlhaus JR, Cook-Deegan RM. Genomics research: world survey of public funding. *BMC Genomics* 2008;9:472.
- Hoppe TA, Litovitz A, Willis KA, Meseroll RA, Perkins MJ, Hutchins BI, et al. Topic choice contributes to the lower rate of NIH awards to African-American/Black scientists. Sci Adv 2019;5: eaaw7238.
- Braun L, Wolfgang M, Dickersin K. Defining race/ethnicity and explaining difference in research studies on lung function. *Eur Respir J* 2013;41: 1362–1370.
- Shweish O, Dronavalli G. Indications for lung transplant referral and listing. J Thorac Dis 2019;11:S1708–S1720.

Copyright © 2022 by the American Thoracic Society

Check for updates

Genetic Ancestry Has the Same Major Problems as Phenotypic Ancestry

To the Editor:

Using genetic scores to identify ethnic background (1) is more precise but no different in principle from using physical characteristics and carries the same hazards for the misuse of "race" as a variable in medicine. Skin tone is largely inherited, and even among African Americans it is associated with educational level, income, and employment either as a manager or professional (2, 3). Nobody would believe that these indicators of social advantage are genetically determined. Using genotyping to "improve" the determination of what social position an individual ought to aspire to would horrify

ิล

³ This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial No Derivatives License 4.0. For commercial usage and reprints, please e-mail Diane Gern (dgern@thoracic.org).

Originally Published in Press as DOI: 10.1164/rccm.202204-0702LE on May 3, 2022