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Reply by McCormack *et al.* to Townsend and Cowl, and to Miller *et al.*

From the Authors:

We appreciate the opportunity to respond to the points raised by Drs. Miller, Graham and Thompson and Drs. Townsend and Cowl regarding our publication "Race, Lung Function, and Long-Term Mortality in the National Health and Examination Survey III" (1). Our findings caution that integrating the lower lung function observed among Black Americans in a definition of normal may have the potential to obscure adverse health implications. Miller and colleagues argue for the use of race-specific reference equations for interpretation of lung function by arguing that using all-cause mortality as an outcome lacks validity and that categories defined by the Global Lung Function Initiative (GLI) reference equations represent the effects of "geographic ancestry" on lung function. We agree that studying overall mortality has inherent limitations. However, lung function has consistently been linked to all cause mortality, and poor lung function affects not only respiratory mortality but also cardiovascular mortality (2), the leading cause of death in the United States. Further, Elmaleh-Sachs and colleagues, and others, have recently shown similar results for chronic lung related events and mortality (3, 4).

Miller uses the term "geographic ancestry," a term which has unclear meaning. The concept of geography in lung function seems to harken back to recommendations that existed before the availability of large datasets of normative values to gather data from local populations to develop normal values for individual labs (5). A perceived benefit of such an approach was that geographic conditions that may affect lung function, such as living at altitude, would be addressed by local norms. However, a major limitation was the lack of standardization between labs, a problem addressed by the use of much larger datasets such as National Health and Nutrition Examination Survey (NHANES) and GLI reference equations.

It is not correct to state that GLI subgroups from which reference equations are based represent "geographic ancestry." Reference data for Black/African American populations were drawn solely from U.S. cohorts, including NHANES and Multi-Ethnic Study of Atherosclerosis, where race was self-reported. Data from other groups was also based on a concept of race rather than geography resulting in vast heterogeneity in geography within subgroups. For example, the GLI Caucasian subgroup includes individuals of various ethnicities in Northern Africa, North America, South America, Europe, Asia, the Middle East, and Australia (6).

Further, the concept of ancestry often implies genetic data, and it is important to note that neither the GLI nor NHANES include genetic data. There is ongoing work to define the extent to which genetic ancestry contributes to the observed variation in lung function and may be applied to improve precision of GLI equations, as well as the practical limitations of implementing such approaches (7, 8). These questions are beyond the scope of our work. Further, focus on "geographic ancestry" has the potential to distract from the possible harms that may stem from classifying groups according to race, which Miller and colleagues agree is a social rather than biologic construct.

A strength of the NHANES data is that this is a publicly available resource, providing the opportunity to ensure reproducibility. Miller and colleagues recapitulate the figure in our manuscript, replicating our finding that that race-specific comparisons normalize the lower lung function among Black (African American) individuals apparent when using a universal, multi-racial approach. Miller and colleagues argue that "the probability distribution graphs in the study should use percent of people rather than numbers of people"; our goal in showing the raw numbers of individuals was not only to show the distribution of lung function outcomes but also to allow the reader to see how much data was contributing to our mortality estimates at each strata of lung function.

Both Miller, Townsend, and their colleagues note the potential contribution of anthropomorphic differences to the observed differences in lung function by race. They also note that there is reduced precision with a multiracial approach compared with race-specific, demonstrated by the wider confidence intervals surrounding the curves estimating normal lung function. Future steps, including anthropometric measurements for those being tested, would increase precision without the negative impact of including race in medical decision-making. However, we would emphasize that a more important goal is to improve accuracy and that the goal of measuring lung function is to quantify

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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 race-specific 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.

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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.

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