Role of Race in the Interpretation of Pulmonary Function Tests

The American Thoracic Society's Efforts to Mitigate Bias in Its Clinical Guidance

Technical standards developed by the American Thoracic Society (ATS) and the European Respiratory Society in 2005 recommended race-specific interpretation of pulmonary function tests rather than race adjustment (1). In race-specific interpretation, the reference values used for a patient of a particular race are estimated from populations of the same race. This approach was maintained when the ATS/European Respiratory Society technical standards were updated in 2021 (2).

Concerns regarding the use of race in clinical algorithms prompted an ATS project to explore the role of race and ethnicity in the interpretation of pulmonary function tests (3). The project yielded a new recommendation to use a global average equation to derive reference values for patients of all races, replacing race-specific interpretation. The evidence, rationale, and recommendation are published in this issue of the *Journal* as an official ATS statement (4).

ATS's leadership is aware that the recommendation may be controversial and may initiate passionate debate. However, it sees the statement as an important first step to ignite discussion and accelerate research regarding not only race in pulmonary function testing but also race in other areas of pulmonary, critical care, and sleep medicine. ATS's leadership expects the recommendation to evolve as new evidence is created. Future changes will be viewed as further advances rather than an admonition of prior guidance.

It is important to reassure stakeholders that the statement is not intended to be a political statement. Rather, it is intended to be an evidence-based, scientific expression of a group of experts on a topic important to pulmonary patients. To mitigate bias, creation of the statement followed the same steps that all official ATS documents must follow, steps that have been in place for more than a decade and are designed to minimize biased decision making.

Project Selection

Mitigation of bias in official ATS documents begins with project selection. Applicants submit proposals, which compete for approval. Among the considerations by which a proposal is judged is whether there exist preconceived outcomes or recommendations. The ATS wants projects that ask questions, consider the evidence, and then draw conclusions or make recommendations based on the evidence. Therefore, proposals with preconceived conclusions or recommendations are typically rejected.

Task force composition is essential in preventing bias and is carefully reviewed before a project is approved. Successful projects propose a task force that is diverse in terms of sex, seniority, specialty, discipline, race, ethnicity, and geographical location. The presumption is that including individuals with a variety of attributes is more likely to yield a diversity of perspectives, guarding against "groupthink" and biased decision making.

ATS rigorously manages potential conflicts of interest among its task force members. All participants must disclose potential conflicts of interest to the ATS at the beginning of the project and annually during document development and must disclose new potential conflicts of interest to other participants before each meeting. Individuals who have potential conflicts that are viewed as potentially biasing the project are instructed not to participate in certain activities during document development. Task force disclosures are published with the document.

In the case of the statement on race and ethnicity in the interpretation of pulmonary function tests, there were no preconceived conclusions, the task force was diverse, and conflict of interest was managed per routine.

Document Development

Official ATS document task forces are instructed to focus on science, and attempts are made to isolate the task force from external political and economic pressures. In the case of the statement on race and ethnicity in the interpretation of pulmonary function tests, ATS leadership was pushed relentlessly by various advocacy groups to make public statements condemning the use of race in the interpretation of pulmonary function tests. To ATS leadership's credit, they adopted the views that *1*) the ATS had its experts addressing the question, *2*) the issue is complicated and therefore requires a thoughtful approach that may take time, and *3*) the task force should be protected from external influences. Although it is impossible to isolate task force members from the political environment, stakeholders may be assured that the task force never received any pressure from ATS leadership to reach a certain conclusion or make a certain recommendation.

Peer Review

Peer review is essential to identify previously unrecognized bias in a document. It is also important that peer reviewers not interject bias. These goals are achieved by using multiple peer reviewers with a diversity of perspectives. In the case of the statement on race and ethnicity in the interpretation of pulmonary function tests, there were four peer reviewers: *1*) a senior investigator with experience working on pulmonary function test technical standards, *2*) a senior clinician-scientist with expertise in health inequities, *3*) a midcareer investigator with expertise in the effect of race on pulmonary function

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testing, and *4*) a senior clinician-scientist with expertise in pulmonary function testing and research methods. The peer reviews were passionate, provided a wide variety of perspectives, and were both thoughtful and detailed.

It is noteworthy that the project began as a workshop. However, after the first round of peer review, the authors indicated that they could not address the reviewers' comments without considering evidence published after the workshop. In other words, the workshop was already outdated. Therefore, the task force was granted permission to consider the new evidence, and the project was changed from a workshop to a statement.

Board of Directors Approval

Finally, all official ATS documents undergo review and approval by the ATS Board of Directors. This offers an additional layer of review and therefore an additional opportunity to identify bias by those with fiduciary responsibility for anything that bears the imprimatur of the ATS.

Conclusion

The ATS welcomes discussion and debate about this important topic. It looks forward to advocating for additional research on topics that address racism in medicine and healthcare disparities. Its only plea is that the debate and decision making be grounded in evidence, consistent with its identity as a leading scientific professional organization. ■

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

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"KEAP"ing Alveolar Macrophage Mitochondria Content in Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease (COPD) is associated with persistent macrophage infiltration in the lung parenchyma and alveolar space even after smoking cessation (1), which correlates with disease severity and areas of lung destruction (2). Macrophages isolated from BAL in COPD are derived from both tissue-resident macrophages with the capacity for self-renewal and circulating peripheral blood monocytes that migrate to the lung under a variety of stimuli (3, 4). Despite the increased abundance of airway and alveolar macrophages (hereafter termed alveolar macrophages [AMs]) in COPD, recurrent respiratory infections are abundant, accelerating disease progression and mortality (5). This may be attributed to the inability of these cells to carry out efficient phagocytosis and efferocytosis (6, 7), which may be closely linked to mitochondrial dysfunction in these cells (8–10).

Cellular energy metabolism governs macrophage adaptation and responses to a variety of environmental signals (11). At steady state, macrophages can generate ATP via several metabolic pathways, including aerobic oxidative phosphorylation (OXPHOS), glycolysis, and fatty acid oxidation. Macrophages display robust metabolic plasticity to reprogram ATP production from the most efficient metabolic pathways available. For example, stimulated bone marrow–derived macrophages predominantly use glycolysis (11) to rapidly generate ATP for proinflammatory effector functions, whereas AMs that inhabit a low-glucose, high-lipid environment in the healthy lung rely on OXPHOS to meet energy demands (12, 13). AMs from individuals with COPD display a defect in mitochondrial respiration (10, 13), with lower compensatory glycolysis and alterations in metabolite abundance (4, 12). Yet how this metabolic rewiring relates to the functional capacity of AMs and whether this phenomenon can be therapeutically reversed with beneficial effects had yet to be defined.

In this issue of the *Journal*, Ryan and colleagues (pp. 998–1011) build on their own earlier findings (14) to show that both alveolar and

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