Race in pulmonary function test interpretation: history, clinical implications, challenges, and alternatives

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Associate Professor
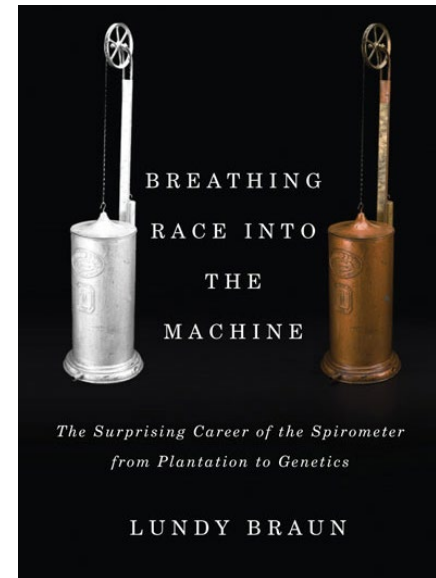Division of Pulmonary and Critical Care Medicine
University of California, San Francisco
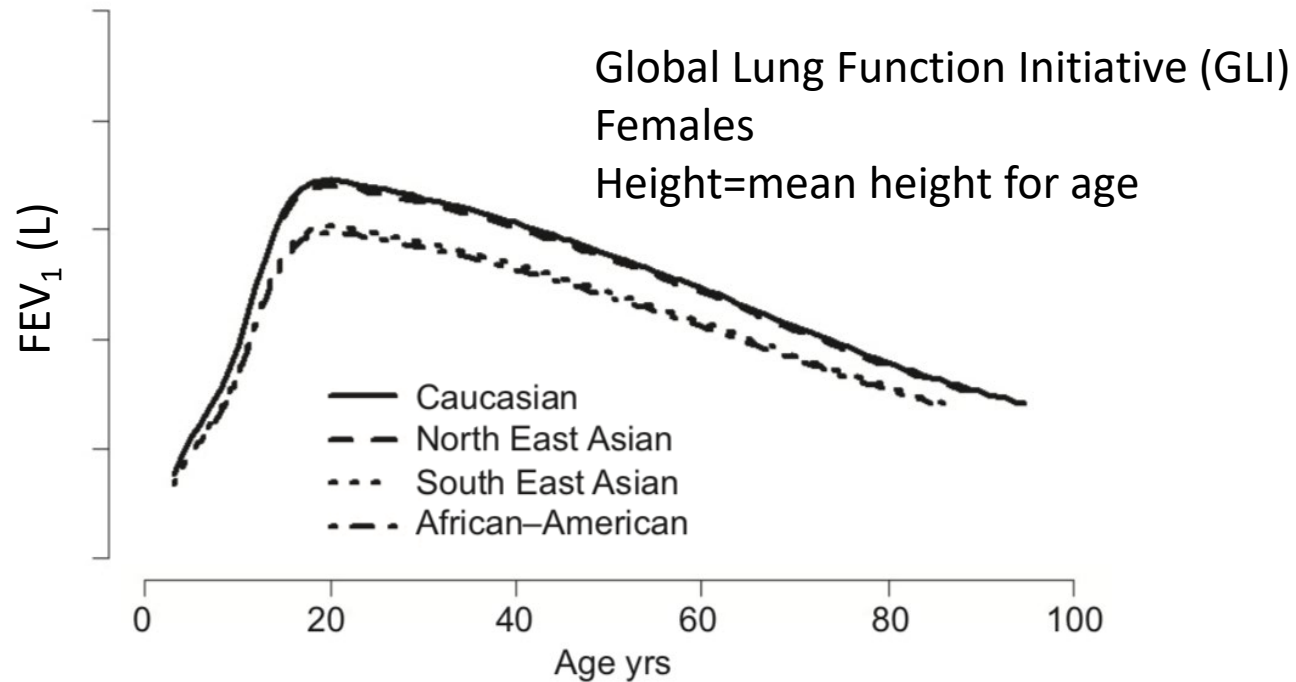Associate Director, Adult Pulmonary Function Laboratory
Vice-chair of the American Thoracic Society PFT Committee

7/11/2023

History: race-centric, biased, unquestioned

- Views that racial categories reflected innate characteristics drove the organization of pulmonary function observations while ignoring other factors.

- Disproportionate emphasis on race limited understanding of determinants of pulmonary function.

- Majority of research that formed the evidence base for lower lung function in non-White populations did not examine socioeconomic status (Braun ERJ 2013).

- Physiologists justified race from differences in the ratio of limb length to chest height, but this view is:
  - Quantitatively insufficient
  - Expected to reflect the environment, ≠ all innate

BREATHING RACE INTO THE MACHINE

The Surprising Career of the Spirometer from Plantation to Genetics

LUNDY BRAUN

The race-specific approach to pulmonary function

Global Lung Function Initiative (GLI)
Females
Height=mean height for age

Caucasian
North East Asian
South East Asian
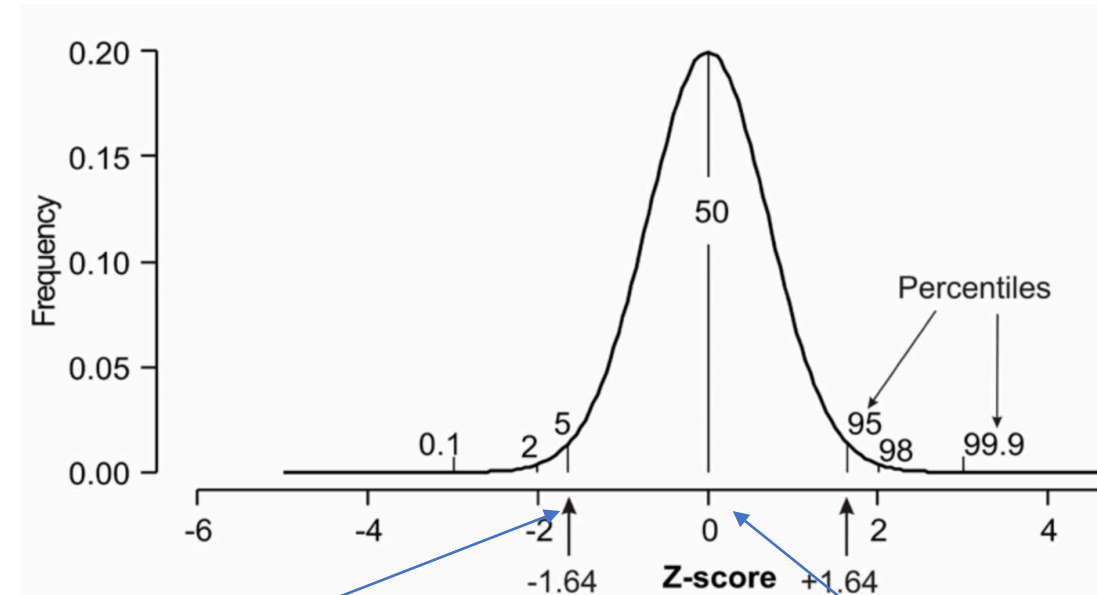African–American

FEV$_1$ (L)

Age yrs

47-year-old female
5'5" (165.1 cm)
Measured FEV$_1$ 2.0 L

GLI African-American Predicted FEV$_1$ 2.53 L
➢ 79% of predicted, z -1.46
➢ 2.0 > lower limit of 1.93 L

Lower limit of normal, 5th percentile

Predicted value

47-year-old female
5'5" (165.1 cm)
Measured FEV$_1$ 2.0 L

GLI African-American Predicted FEV$_1$ 2.53 L
➢ 79% of predicted, z -1.46
➢ 2.0 > lower limit of 1.93 L

Conclude: Normal

GLI White Predicted FEV$_1$ 2.94 L
➢ 68% of predicted, z -2.43
➢ 2.0 < lower limit of 2.31 L

Conclude: Abnormal

47-year-old female
5'5" (165.1 cm)
Measured FEV$_1$ 2.0 L

GLI African-American Predicted FEV$_1$ 2.53 L   GLI White Predicted FEV$_1$ 2.94 L

THIS DECISION WE CREATED HAS REAL IMPLICATIONS
- Will respiratory disease be considered? Additional tests done?
- Referral for lung transplantation evaluation?
- Denied lung cancer resection?
- Eligible for disability?
- Eligible to work as a firefighter or diver?

Challenges with race

- Not uniformly defined across time and location

- Can mask modifiable risks for reduced lung function and disease

- Not a proxy for genetics: variation in genome within races categories is large

- Limited categories and they do not account for effects of acculturation and mixed backgrounds

- Residual differences in lung function between race categories justified idea of innate inferiority

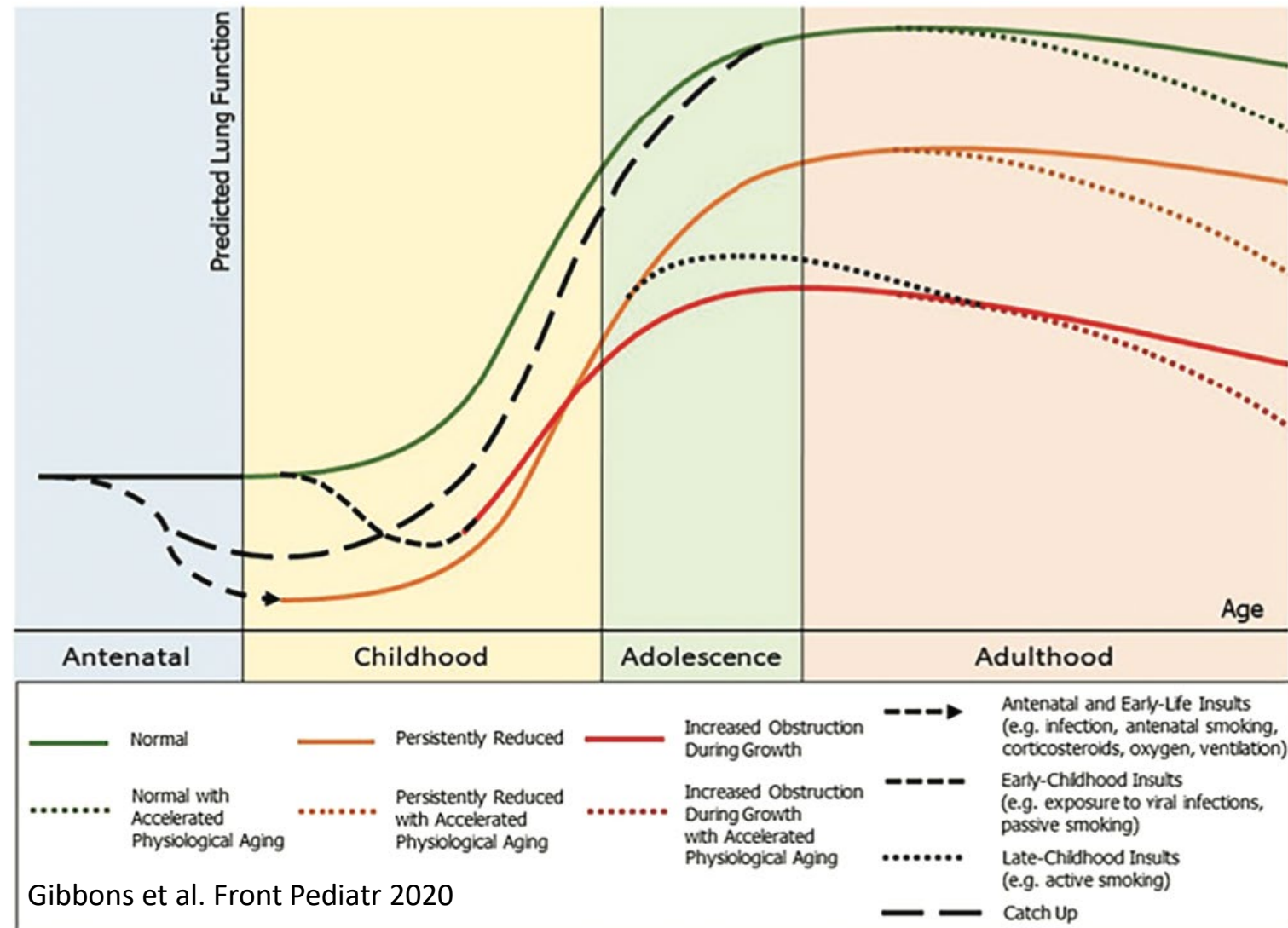From: https://www.inclusionhub.com/articles/lauren-stiller-rikleen

Race and Ethnicity in Pulmonary Function Test Interpretation
An Official American Thoracic Society Statement

Nirav R. Bhakta, Christian Bime, David A. Kaminsky, Meredith C. McCormack, Neeta Thakur, Sanja Stanojevic, Aaron D. Baugh, Lundy Braun, Stephanie Lovinsky-Desir, Rosemary Adamson, Jonathan Witonsky, Robert A. Wise, Sean D. Levy, Robert Brown, Erick Forno, Robyn T. Cohen, Meshell Johnson, John Balmes, Yolanda Mageto, Cathryn T. Lee, Refiloe Masekela, Daniel J. Weiner, Charlie G. Irvin, Erik R. Swenson, Margaret Rosenfeld, Richard M. Schwartzstein, Anurag Agrawal, Enid Neptune, Juan P. Wisnivesky, Victor E. Ortega, and Peter Burney; on behalf of the American Thoracic Society Committees on Pulmonary Function Testing and on Health Equity and Diversity

Determinants of pulmonary function

- Early-life
- Prematurity
- Infections
- Nutrition: over and under
- Second-hand smoke
- Indoor/outdoor pollution
- Discrimination, stress
- Genetics
  - Genetic ancestry vs
  - SNPs

Gibbons et al. Front Pediatr 2020

Current practice:
Age, height, sex, race/ethnicity

interpretation

To triage respiratory symptoms

Diagnosis (e.g. COPD)

Occupational: Eligibility Disability

Severity, prognosis, decision on risk:benefit ratio for treatments including chemo, transplant, resection

Inclusion criteria for trials

Measured lung function

Implementation factors

- Software updates, availability, cost
- PFT reports:
  - Language and education
  - Include prior approach for a limited time?
- Electronic health record trending and interoperability: HL7, LOINC, OBX
- Speaking to patients and colleagues
- Still need to engage with the many users of PFTS external to clinical medicine: e.g., disability insurance evaluation, occupational evaluation, life insurance.
- Trends in absolute lung function often most important.
- Race and ethnicity categories have a role in understanding impact of structural racism on lung health and function

Remaining challenges

- Ideal reference population uncertain
- Need for reference equations uncertain: absolute FEV1, FEV1Q
- What the right amount of FEV_1, FVC, TLC, and DLCO is for body size and task/exposure is poorly understood.
- Role for adjustment for chest dimensions uncertain
- How to incorporate environmental influences
- Decreasing value of normalized FEV_1, FVC, TLC, DLCO in the era of widespread availability of others tests (CT, TTE, V/Q, cath).
- Thresholds used to make decisions based on PFTs are largely not evidence-based
- Need to anchor use of PFTs on patient-centered outcomes rather than normal vs abnormal.

Acknowledgments
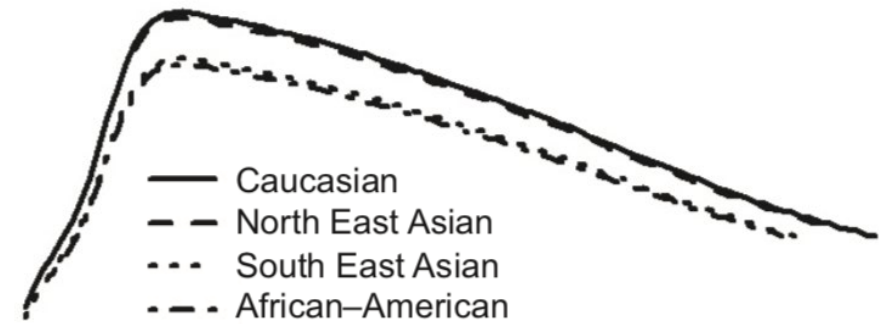
Christian Bime
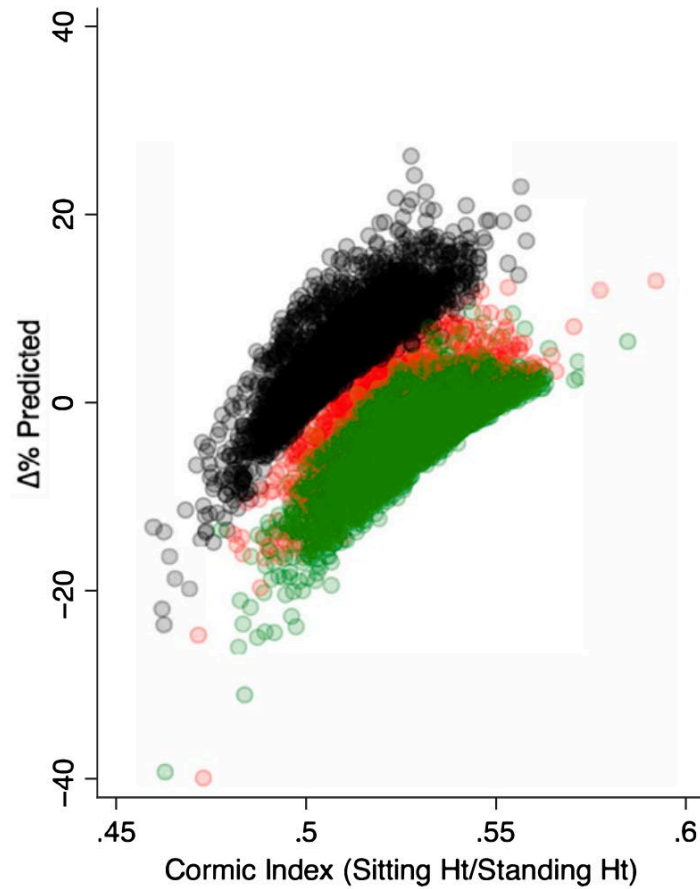Workshop members
ATS Executive Committee

Extra slides, primarily supporting data
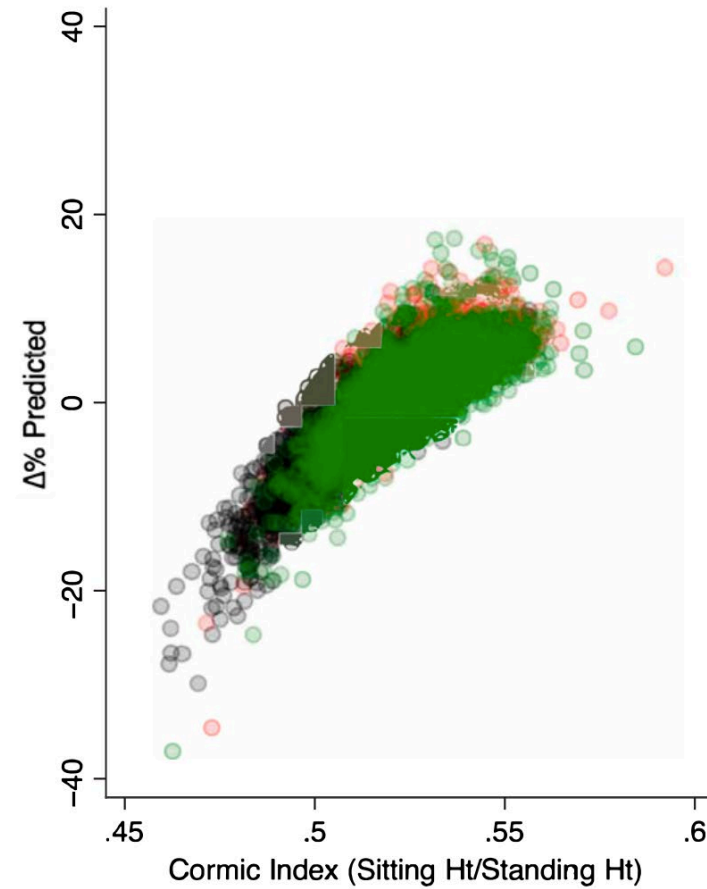
Clinical implications

- In most cases, GLI Global shifts the <u>mean predicted value and lower limit of normal</u> to values that are:
  - Higher compared to African American and South East Asian equations
  - Lower compared to White and North East Asian equations

- Thus, application of GLI Global yields <u>relative values (z scores and % of predicted)</u> that are:
  - Lower compared to African American and South East Asian equations
  - Higher compared to White and North East reference equations

- FEV_1/FVC has relatively minor variation between equations

A NHANES Ethnic Specific - NHANES Sit/Stand/Cormic

B NHANES Standing - NHANES Sit/Stand/Cormic

Δ% Predicted

Cormic Index (Sitting Ht/Standing Ht)

○ White ○ Black ○ Mexican American

Bowerman et al. AJRCCM. 2023

The Contribution of Anthropometry and Socioeconomic Status to Racial Differences in Measures of Lung Function

A Systematic Review

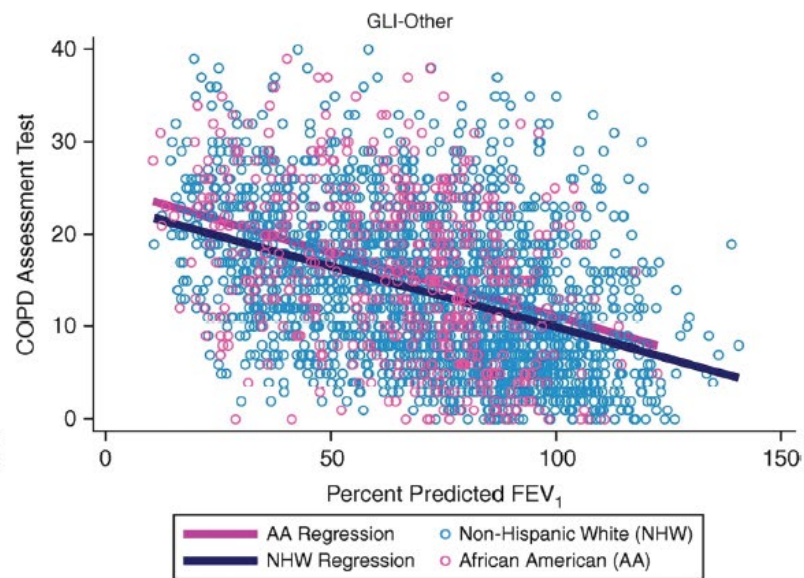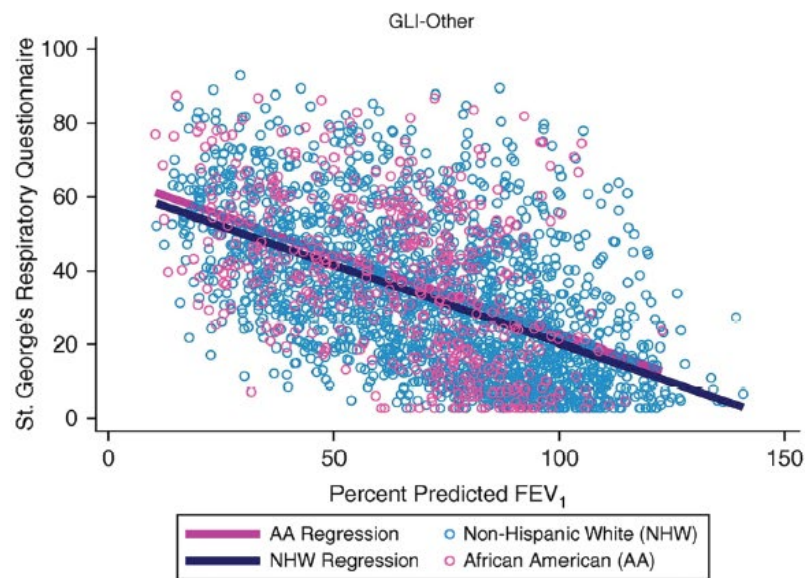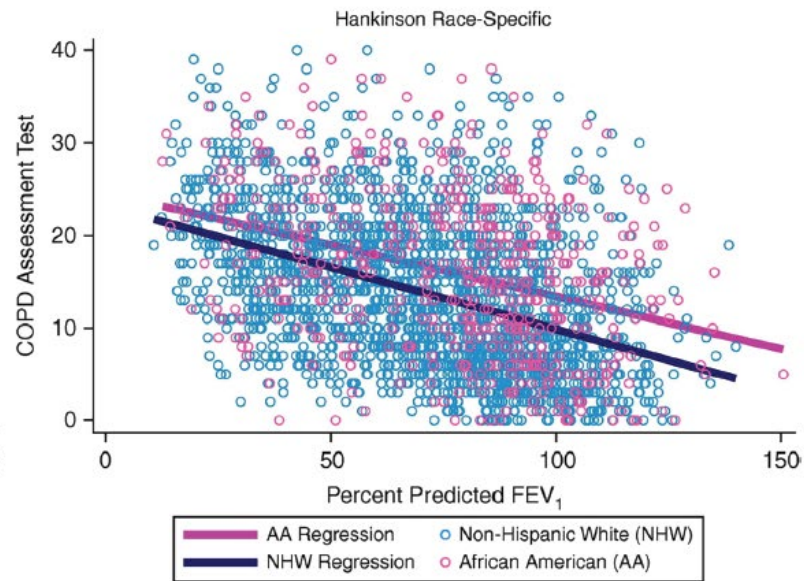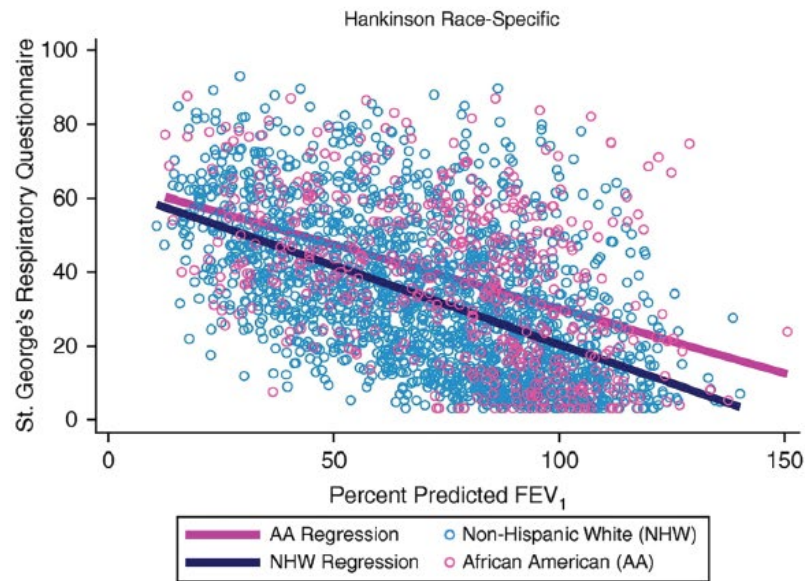*Rachel Holland, BSc; Cole Bowerman, MSc; and Sanja Stanojevic, PhD*

BACKGROUND: The current approach to interpretation of lung function measurements assumes that differences in lung function between racial and ethnic groups represent inherent and biological differences. Observed differences in lung function between White and Black populations are often attributed to physiological differences in body proportions (eg, chest size, leg length); however, most studies investigating the observed differences have not considered the impact of socioeconomic status (SES).

RESEARCH QUESTION: What proportion of the differences in lung function between Black and White populations can be attributed to SES and/or differences in body proportions?

STUDY DESIGN AND METHODS: PubMed and EMBASE were searched up to March 2022 for articles relating to Black race, SES, and lung function. A total of 4,673 titles and abstracts were screened, followed by assessment for extractable data; 11 articles were ultimately included in this systematic review.
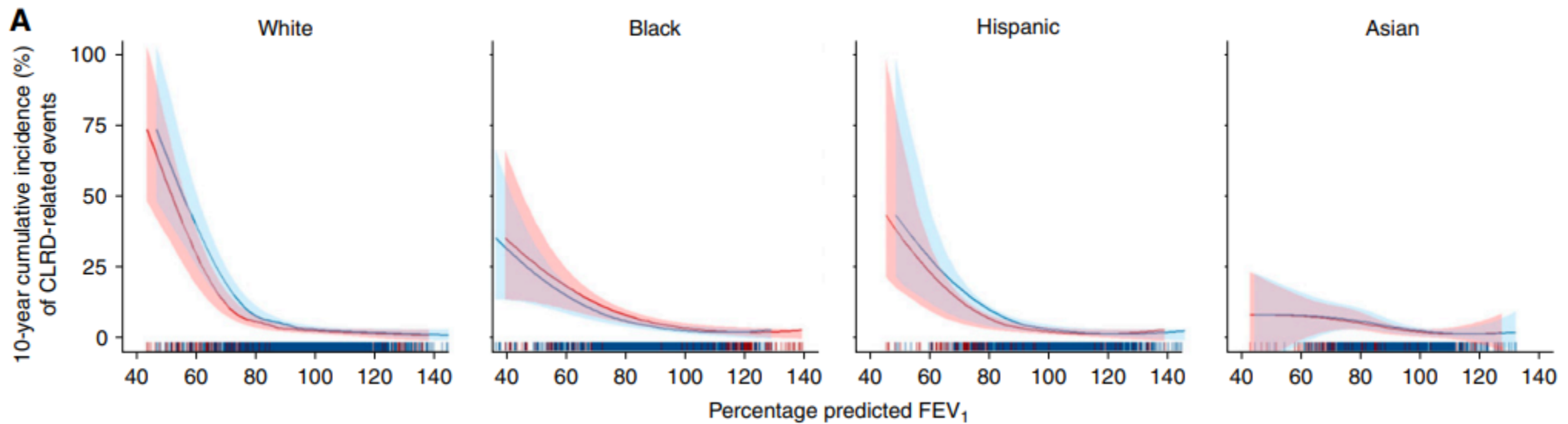
RESULTS: There is substantial heterogeneity in the contribution of SES and body proportions to the observed differences in lung function between Black and White individuals. The proportion of differences between Black and White study participants attributable to SES factors ranged from 2.2% to 43.3% in FEV_1 and from 4.1% to 41.9% for FVC. Studies that adjusted for sitting height explained 3% to 31.7% of the racial difference in lung function.
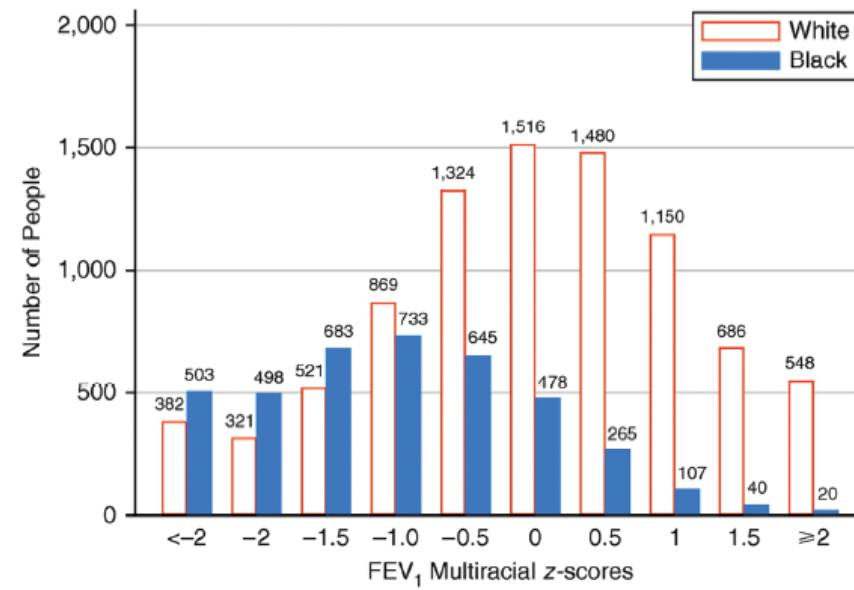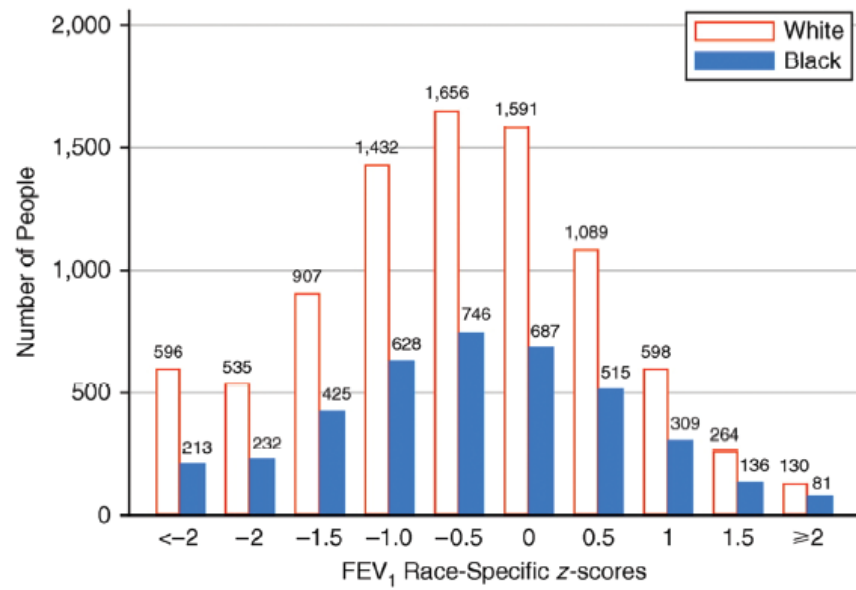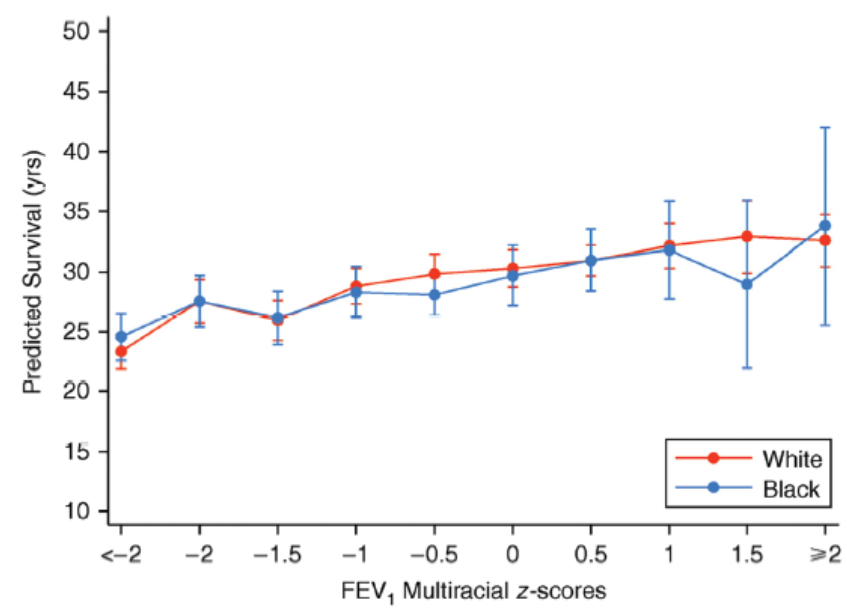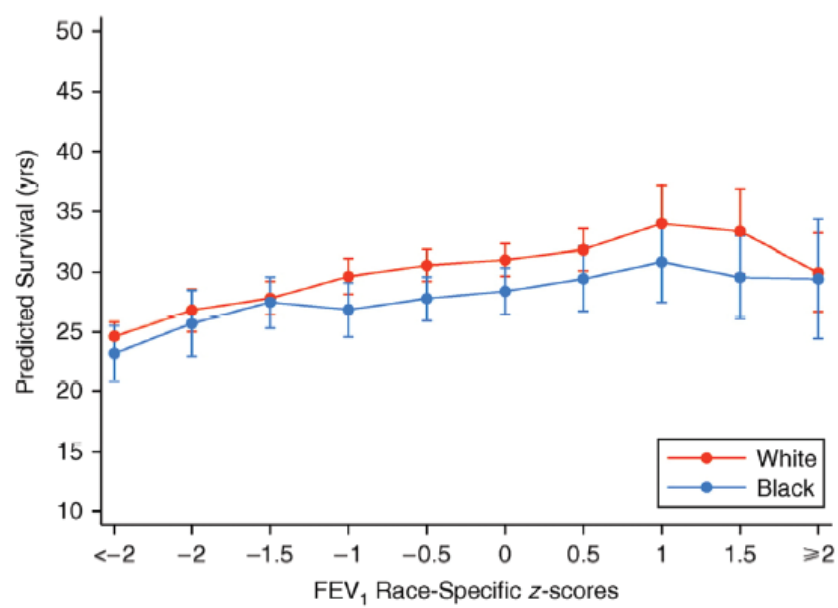
INTERPRETATION: Reproducible research aimed at explaining the etiology of the differences in lung function between populations is difficult to achieve. The evidence to support the use of race/ethnic specific equations is limited, and the practice needs to be re-evaluated.

Baugh et al. AJCRCCM 2022

General Population Evidence

Elmaleh-Sachs et al. AJRCCM 2022

McCormack et al. AJCRCCM 2022

2023 ATS Statement Recommendations

Use sex-specific reference equations that represent an average across many people:

- GLI Global for spirometry

Embrace uncertainty and individual patient factors when interpreting PFTs

NO LONGER REPORT OR INTERPRET PFTS USING RACE OR ETHNICITY

No adjustments for D_{LCO} and lung volumes.

Recognize agreement in FEV_1/FVC between equations

Longitudinal data