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Research Paper

# Prognostic implications of differences in forced vital capacity in black and white US adults: Findings from NHANES III with long-term mortality follow-up

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ABSTRACT

*Background:* Because Forced Vital Capacity (FVC) is reduced in Black relative to White Americans of the same age, sex, and height, standard lung function prediction equations assign a lower "normal" range for Black patients. The prognostic implications of this race correction are uncertain.
*Methods:* We analyzed 5,294 White and 3,743 Black participants age 20–80 in NHANES III, a nationally-representative US survey conducted 1988–94, which we linked to the National Death Index to assess mortality through December 31, 2015. We calculated the FVC-percent predicted among Black and White participants, first applying NHANES III White prediction equations to all persons, and then using standard race-specific prediction equations. We used Cox proportional hazard models to calculate the association between race and all-cause mortality without and with adjustment for FVC (using each FVC metric), smoking, socioeconomic factors, and comorbidities.
*Findings:* Black participants' age- and sex-adjusted mortality was greater than White participants (HR 1.46; 95%CI:1.29, 1.65). With adjustment for FVC in liters (mean 3.7 L for Black participants, 4.3 L for White participants) or FVC percent-predicted using White equations for everyone, Black race was no longer independently predictive of higher mortality (HR∼1.0). When FVC-percent predicted was "corrected" for race, Black individuals again showed increased mortality hazard. Deaths attributed to chronic respiratory disease were infrequent for both Black and White individuals.
*Interpretation:* Lower FVC in Black people is associated with elevated risk of all-cause mortality, challenging the standard assumption about race-based normal limits. Black-White disparities in FVC may reflect deleterious social/environmental exposures, not innate differences.
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## 1. Introduction

Within populations free of known lung disease or respiratory symptoms, Black Americans have lower lung function, on average, than White Americans of similar age, sex, and height [1,2]. Consequently, lung function prediction equations used to transform raw spirometry measurements into clinically useful metrics of "percent-predicted" (i.e. relative to "normal" as defined statistically in the general population) have been derived separately for different racial/ethnic groups, effectively adjusting the normal range downward for Black patients [1,2]. The use of such race-specific equations is the norm in clinical practice [3].

For decades, scholars have debated whether the Black: White difference in lung function stems from genetic, or purely environmental exposures [4–15]. Skeptics of genetic explanations [4–6] point to ubiquitous socioeconomic status (SES) gradients in lung function, [16–18] and Black individuals' greater exposure to air pollution. Ascribing lung function differences to race-specific genetic factors, moreover, has troubling historical roots [4]. However, some worry that failure to use race-specific equations could lead to harmful over diagnosis of pulmonary disease among Black patients [10]. Moreover, studies have found that controlling for readily observed socioeconomic factors explains little of the Black: White disparity in lung

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**Research in context**

*Evidence before this study*

We searched Pubmed for studies examining the prognostic significance of racial differences in lung function in the general US population, up to March 16, 2021, using the key words ("pulmonary function" OR "ventilatory function" OR "lung function") AND ("race" or "ethnicity"). A large body of literature has explored racial and ethnic differences in lung function, and some studies have explored potential etiologies for these differences. However, few have examined the prognostic implications of using race-specific equations. Most notably, a previous study found that US Black and White individuals of the same age, sex, height, and forced vital capacity (FVC) in liters had similar mortality, suggesting that adjustment for lung function may incorrectly underestimate the deleterious impact of lung disease on Black people. However, this study examined only four US communities, and may not be generalizable to the overall US population.

*Added value of this study*

Using the NHANES III, a nationally-representative health survey conducted 1988–94, we found that Black adult participants' FVC was lower than White participants' and that their mortality was elevated (HR 1.46) over more than twenty-years of follow-up. This mortality differential was not affected by adjustment for percent predicted FVC using race-specific equations, but was largely eliminated when adjusted for FVC in liters or when using the equation usually applied only to White patients to everyone. The reduced FVC of Black adults relative to White adults is hence associated with increased mortality that is obscured with the use of race-specific pulmonary function equations.

*Implication of all the available evidence*

The lower lung function of Black Americans is associated with higher mortality, and may reflect disadvantageous social and environmental conditions rather than "innate" differences.

function [19,20], and one study identified an association between genetic markers linked to ancestry and pulmonary function [21].

Rather than examining the *cause* of racial differences in lung function, Burney and Hooper [9] focused on the clinical *consequences* of using race-specific prediction equations. They observed that Black and White individuals of the same age, sex, height, and forced vital capacity (FVC) in liters had similar mortality, and argued that adjusting lung function for race may inappropriately underestimate the toll of lung disease in Black people [9].

However, Burney and Hooper studied only four US communities (one of which only enrolled Black individuals), and their findings may not be generalizable. Using a nationally-representative US cohort, we examined the prognostic implications of Black-White differences in FVC to shed light on the clinical ramifications of using race-specific prediction equations.

## 2. Methods

### 2.1. Data and population

We analyzed the publicly-available 1988–1994 National Health and Nutrition Examination Survey (NHANES III), described elsewhere [22–24] and in the appendix. Respondents underwent physical examinations and laboratory testing, including spirometry.

We linked the NHANES III to the National Death Index (NDI) [25] (see appendix for details). The latest NDI file provides time, in months, from examination to death, or censuring on December 31, 2015; our mortality follow-up ranged from 21 to 27 years. The NDI listed principal cause-of-death in 10 broad categories, but not contributing (or secondary) causes.

Appendix E-Fig. 1 diagrams the formation of our study cohort, and our handling of missing data (also see the appendix note). In brief, our final cohort included 9037 Black or White adults ages 20–80 with acceptable spirometry data (i.e. meeting standard acceptability and reproducibility criteria as detailed in the appendix), as well as data on measured height (needed to calculate percent-predicted values for FVC), vital status and follow-up time.

### 2.2. Variables

Race/ethnicity was self-reported, and categorized by the NHANES as non-Hispanic White (hereinafter "White"), non-Hispanic Black ("Black"), Mexican American, or other.

We used individuals' age at the time of spirometry to calculate predicted lung function; when that was unavailable, we used age at interview.

NHANES III's spirometry methods adhered to contemporaneous guidelines [26,27] from the American Thoracic Society. Details are available elsewhere [28] and in the online appendix. For each subject, we calculated the FVC percent-predicted, and the lower limit of normal (LLN) for FVC, using age, height, sex- and race-specific NHANES III prediction equations [1] (hereinafter "race-specific" assessment). Next, we recalculated percent-predicted and LLN without adjustment for race, i.e. applying the NHANES III prediction equations usually reserved for White adults to all subjects (a "race-non-specific" or "colorblind" assessment) [9].

### 2.3. Outcome

Our primary outcome was all-cause mortality. We also tabulated cause of death in the 10 broad categories available in the NDI.

### 2.4. Analytic plan

We first examined three metrics of lung function stratified by race: (1) mean FVC in liters; (2) FVC percent-predicted using White prediction equations for all subjects; and (3) FVC percent-predicted using race-specific equations. We also tabulated the proportion with abnormally low FVC, defined as an FVC$<$ LLN calculated using each equation. Means were compared using univariate linear regression and proportions using the Pearson chi-square test.

Next, to evaluate whether Black/White FVC differences were associated with differences in mortality (our main outcome), we performed Cox proportional hazard regressions adjusted for race and the other covariates described below, with and without adjustment for each of the three metrics of FVC, drawing on the approach of Burney and Hooper [9].

We performed 12 Cox regressions: [9] four base models (A1-A4) that assess the mortality hazards of Black vs. White race, one adjusted only for age and sex, and three others, each adjusted for one of our three FVC metrics; four similar models (B1-B4) with additional adjustment for smoking and body mass index (BMI) and co-morbidities; and four models (C1-C4) with additional adjustment for SES.

Specifically, our first model (A1) assessed the mortality hazard ratio (HR) associated with race, adjusted only for age and sex, i.e. with no control for lung function. The second model (A2) assessed the HR for race after additional control for height and FVC in liters; the third (A3) adjusted for age and FVC percent predicted using colorblind equations (which incorporate age, sex and height). The HRs for Black individuals in Models A2-A3 hence represent the excess

mortality risk in Black vs. White individuals adjusted for measured lung function, but without assuming that "normal" FVC is lower in Black individuals. The fourth model (A4) assesses the HR for Black individuals after adjustment for FVC percent-predicted using race-specific equations (now the standard in clinical practice), which incorporate the assumption that normal FVC is lower in Black individuals.

Models B1-B4 repeat the regressions in A1-A4, with additional control for: sex (in all models), smoking (defined as ≥ 100 cigarettes in lifetime, and treated as a three-category variable: former, never, and current); four comorbidities based on subjects' reports of physicians' diagnoses (stroke, congestive heart failure [CHF], heart attack, and diabetes mellitus); hypertension (measured average systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥90 mmHg, or subjects' reports that they were currently taking antihypertensive medication); and measured BMI (≤18.5, 18.5−24.99, 25−25.99, 30+ kg/m$^2$).

Adjustment for SES in studies examining the effects of race is controversial, because racial SES differences stem from the legacies of slavery and discrimination. Consequently, adjustment may 'over-control' for the health harms attributable to discrimination [29]. However, for sensitivity analyses, we repeated regressions B1-B4 with additional adjustment for education (0−8 years, 9−11 years, 12 years, 13+ years) and family income (<$10,000, $10,000-$29,999, $30,000-$49,999, and $50,000+). We label this set of models C1-C4.

For each set of models (A, B, and C) the change in the HR for Black race between Model 1 and Models 2−3 reflects how differences in FVC between the two racial groups impact mortality prediction when FVC is assessed "color-blind", i.e. using raw FVC in liters or the same equation (the White equation) for all subjects. In contrast, the difference between Model 1 and Model 4 in each set of models (A, B, and C) reflects FVC's effect on mortality prediction when FVC is assessed using race-specific equations that implicitly assume that Black's lower average FVC is normal, i.e. non-indicative of pathology.

We used STATA/SE 16.1, NHANES-provided weights that permit extrapolation to the non-institutionalized US population, procedures that account for the survey's complex sampling for all analyses, and Stata's *stcox* procedure for Cox regressions. The Cambridge Health Alliance's Institutional Review Board waived review of this analysis of publicly-available, deidentified data.

Role of the funding source: No special funding.

## 3. Results

### 3.1. Population characteristics

Our final study population included 5294 White and 3743 Black adults; Table 1 provides their characteristics. Black participants (mean age = 39.8 years) were younger than White participants (44.0 years) ($p < 0.001$), but had similar heights (169.5 vs. 169.8 cm); a slightly higher proportion (54.1% vs. 51.0%) were female ($p = 0.007$). Black individuals had lower SES (e.g. 22.4% vs. 7.3% with family income <$10,000) ($p < 0.001$), were more likely to reside in Southern states (54.2% vs. 32.2%) ($p < 0.001$), and were more often obese (27.9% vs. 20.8%) ($p<0.001$). Black individuals were less likely than White participants to be former smokers (15.6% vs. 27.7%), but more likely to be current (35.8% vs. 30.0%) or never smokers (48.6% vs. 42.3%) ($p < 0.001$). Rates of stroke and CHF were similar and low in both groups, while Black individuals had slightly lower rates of previous heart attacks ($p = 0.013$) but higher rates of diabetes mellitus ($p = 0.001$) and hypertension ($p < 0.001$).

### 3.2. Lung function

Table 2 shows our three FVC metrics stratified by race. As expected, mean FVC (in liters) was significantly lower among Black individuals (3.7 L) than White participants (4.3 L). Consequently, the mean FVC percent-predicted using colorblind equations was lower for Black individuals (84.5%) than White participants (98.3%). In contrast, applying the standard, race-specific equations, the FVC percent-predicted was slightly (but significantly) higher among Black (101.1%) than White individuals (98.3%). In other words, using the standard race-specific equations shifted the assessment of average lung health of Black individuals from substantially worse than White participants' to slightly better. Similarly, when using the LLN derived from race-specific equations, as is standard in clinical practice, Black individuals were significantly less likely than White participants to be categorized as having an abnormally low FVC (4.8% vs. 8.8%). However, when using the White-specific equations for both groups, Black individuals were significantly more likely than White participants to be categorized as having an abnormally low FVC (39.9% vs. 8.8%). ($p < 0.001$ for all Black-White comparisons).

**Table 1**
Characteristics of White and Black participants ($n$ = 9037).

| | White ($n$ = 5294) | Black ($n$ = 3743) | $p$-Value |
|---|---|---|---|
| Female (%) | 51.0 | 54.1 | 0.007 |
| Age (mean, ± SE) | 44.0 ± 0.47 | 39.8 ± 0.36 | <0.001 |
| Region (%) | | | <0.001 |
| Northeast | 21.8 | 16.0 | |
| Midwest | 27.0 | 19.9 | |
| South | 32.2 | 54.2 | |
| West | 19.0 | 9.8 | |
| Education (%) | | | <0.001 |
| 0−8 years | 6.2 | 9.1 | |
| 9−11 years | 11.7 | 18.4 | |
| 12 years | 35.2 | 39.1 | |
| 13 years | 46.9 | 33.5 | |
| Income (%) | | | <0.001 |
| < $10,000 | 7.3 | 22.4 | |
| $10,000-$30,000 | 34.3 | 45.5 | |
| $30,000-$50,000 | 29.5 | 21.6 | |
| $50,000+ | 28.9 | 10.4 | |
| Congestive heart failure (%) | 1.4 | 1.8 | 0.086 |
| Previous stroke (%) | 1.4 | 1.3 | 0.83 |
| Previous heart attack (%) | 3.0 | 2.0 | 0.013 |
| Diabetes mellitus (%) | 4.4 | 6.2 | 0.001 |
| Hypertension (%) | 20.9 | 26.3 | <0.001 |
| Height (cm) | 169.8 ± 0.16 | 169.5 ± 0.21 | 0.242 |
| BMI category (%) | | | <0.001 |
| <18.5 kg/m$^2$ | 2.3 | 2.2 | |
| 18.5−24.99 kg/m$^2$ | 44.2 | 37.4 | |
| 25−29.99 kg/m$^2$ | 32.6 | 32.5 | |
| 30+ kg/m$^2$ | 20.8 | 27.9 | |
| Smoking status (%) | | | <0.001 |
| Never | 42.3 | 48.6 | |
| Former | 27.7 | 15.6 | |
| Current | 30.0 | 35.8 | |

SE=standard error; BMI = body mass index.
$p$-values calculated using univariate linear regression (age) or Pearson chi-square (all other variables).
Individuals with missing data out of study sample of $n$ = 9037: education ($n$ = 18 [0.3%] among White participants; $n$ = 22 [0.6%] Black participants); income ($n$ = 306 [4.8%] White participants; $n$ = 324 [8.0%] Black individuals); CHF ($n$ = 7 [0.1%] White participants; $n$ = 2 [0.0%] Black individuals); previous stroke ($n$ = 2 [0.0%] White participants; $n$ = 0 [0.0%] Black individuals); previous heart attack ($n$ = 31 [0.9%] White participants; $n$ = 43 [1.1%] Black individuals); diabetes mellitus ($n$ = 8 [0.1%] White participants; $n$ = 2 [0.0%] Black individuals); hypertension ($n$ = 9 [0.2%] White participants; $n$ = 5 [0.2%] Black participants); smoking status ($n$ = 0 [0.0%] White participants, $n$ = 1 [0.0%] Black individuals). All percentages and means are weighted.

### 3.3. Mortality

During 184,206 person-years of follow-up, 3064 deaths occurred. The average age at death was 66.4 years among Black decedents and 74.5 years among White decedents ($p < 0.001$). Table 3 provides the weighted proportion of decedents in each of the 10 broad causes of death; overall, proportions differed between Black and White

**Table 2**
Measures of forced vital capacity (FVC) of White and Black participants ($n$ = 9037) ages 20–80, NHANES III.

| | White ($n$ = 5294) | Black ($n$ = 3743) | $p$-value |
|---|---|---|---|
| Mean FVC (±SE) | | | |
| FVC (Liters) | 4.3 ± 0.03 | 3.7 ± 0.02 | <0.001 |
| FVC, percent predicted (White equation) | 98.3 ± 0.36 | 84.5 ± 0.28 | <0.001 |
| FVC, percent predicted (race-specific equation) | 98.3 ± 0.36 | 101.1 ± 0.34 | <0.001 |
| Proportion with reduced (<LLN) FVC (±SE) | | | |
| Using White prediction equation (%) | 8.8 ± 0.6 | 39.9 ± 1.2 | <0.001 |
| Using race-specific prediction equation (%) | 8.8 ± 0.6 | 4.8 ± 0.4 | <0.001 |

$p$-values calculated using uni-variate linear regression (Mean FVC) or Pearson chi-square (Proportion with reduced FVC).
Note: FVC=forced vital capacity; SE=standard error; LLN = lower limit of normal. Percent predicted and LLN calculated using NHANES III prediction equations.[1].

**Table 3**
Causes of death among Black and White US adults ages 20–80 in NHANES III deceased as of December 31, 2015 ($n$ = 3055).

| | White ($n$ = 1982) | Black ($n$ = 1073) |
|---|---|---|
| Heart disease | 20.7% | 18.7% |
| Malignant neoplasms | 25.6% | 26.5% |
| Chronic lower respiratory disease | 6.0% | 3.1% |
| Accidents | 3.2% | 4.1% |
| Cerebrovascular disease | 5.5% | 5.7% |
| Alzheimer's disease | 2.6% | 1.5% |
| Diabetes mellitus | 2.5% | 4.8% |
| Influenza and Pneumonia | 2.2% | 1.8% |
| Kidney disease | 0.7% | 1.7% |
| All other causes | 31.1% | 32.2% |

Notes:.
Pearson chi-square $p$-value for overall differences in cause of death among Black and White decadents = 0.002.
$N$ = 3064 deaths in our sample. $N$ = 9 individuals had no cause of death provided, and are excluded from this table. Proportions are weighted.
Average age of White decedents = 74.5 years; average age of Black decedents = 66.4 years; $p$-value for this difference (uni-variate linear regression) <0.001.

individuals ($p$ = 0.002). The most frequent cause, accounting for nearly one-third of deaths, was "all other causes." Only 6.0% of White decedents and 3.1% of Black decedents had chronic lower respiratory tract disease listed as the cause of death.

Table 4 provides results of Cox regression analyses, including the base set of models (A1-A4), the set with additional adjustment for smoking and health factors (B1-B4), and the set of models with additional adjustment for smoking, health factors and SES (C1-C4).

In model A1 (adjusted only for age and sex), Black individuals HR for death relative to White participants was 1.46 (95% CI 1.29–1.65; $p < 0.001$). In model A2, which includes adjustment for height and FVC (L), the Black: White HR fell to 1.03 (95% CI 0.91–1.16; $p$ = 0.621). As expected, Model A3, which is adjusted for FVC-percent-predicted using colorblind equations that incorporate height, produced similar results to Model A2. In contrast, model A4, which is adjusted for FVC-percent-predicted using the standard, race-specific equations (essentially adjusting lung function for race), the Black: White HR was slightly higher than in base model A1 (HR 1.52; 95% CI 1.35, 1.70; $p < 0.001$), and much higher than in Models A2 and A3.

In other words, there was substantial unexplained mortality in Black individuals relative to White participants in models with either no adjustment for lung function (model A1) or with lung function adjustment based on race-specific equations (A4). In contrast, colorblind adjustment for lung function, i.e. without any assumption that normal FVC differed between the racial groups (models A2 and A3), reduced Black individuals' HR to about 1, suggesting that the reduced FVC in the Black population is a close correlate of their higher mortality.

Models B1-B4, which add adjustment for sex (in all models), smoking and baseline health factors, produced similar results, with some attenuation of the effect of Black race. Analyses that included additional adjustment for SES (C1-C4) further attenuated the HRs of the association between race and mortality. Consequently, racial differences in risk of death were not statistically significant in models C1-C3. However, in model C4, which includes adjustment for FVC-percent-predicted using race-specific equations, Black race was significantly associated with higher mortality (HR 1.15, 95% CI 1.03, 1.29; $p$ = 0.017) as in models A4 and B4.

## 4. Discussion

In this nationally representative cohort, the lower average lung function of Black adults relative to White adults helped explain the all-cause mortality differential between the groups. Our results suggest that Black and White individuals of the same age, sex, height, health, and FVC (in liters) had similar risks of all-cause mortality over more than two decades of follow-up; conversely, they suggest that a

**Table 4**
Hazard ratio (for death), Black vs. White race among US adults ages 20–80 in NHANES III ($n$ = 9037).

| Model | Covariates | Hazard Ratio, Black vs. White Race | 95% Confidence Interval | | $p$-value |
|---|---|---|---|---|---|
| A1 | Age and sex | 1.46 | 1.29 | 1.65 | <0.001 |
| A2 | Age, sex, and height (cm) plus FVC (L) | 1.03 | 0.91 | 1.16 | 0.621 |
| A3 | Age plus FVC percent predicted (White equation) | 1.05 | 0.93 | 1.18 | 0.445 |
| A4 | Age plus FVC percent predicted (race-specific equations) | 1.52 | 1.35 | 1.70 | <0.001 |
| B1 | Age, sex, smoking status, diabetes mellitus, heart attack, CHF, stroke, hypertension, and BMI | 1.23 | 1.10 | 1.37 | <0.001 |
| B2 | B1 covariates plus FVC (L) and height (cm) | 1.00 | 0.90 | 1.12 | 0.974 |
| B3 | B1 covariates plus FVC percent predicted (White equation) | 1.02 | 0.92 | 1.13 | 0.702 |
| B4 | B1 covariates plus FVC percent predicted (race-specific equations) | 1.32 | 1.18 | 1.47 | <0.001 |
| C1 | Age, sex, smoking status, income, education, diabetes mellitus, heart attack, CHF, stroke, hypertension, and BMI | 1.08 | 0.95 | 1.21 | 0.224 |
| C2 | C1 covariates plus FVC (L) and height (cm) | 0.91 | 0.80 | 1.02 | 0.107 |
| C3 | C1 covariates plus FVC percent predicted (White equation) | 0.92 | 0.82 | 1.03 | 0.156 |
| C4 | C1 covariates plus FVC percent predicted (race-specific equations) | 1.15 | 1.03 | 1.29 | 0.017 |

Notes:.
*Race indicator variable (Black vs. White) included in all models.*
*cm=centimeter; L=liter; FVC=forced vital capacity; CHF=congestive heart failure; BMI=body mass index.*
*N = 9037 for models A1-A4; N = 8927 for models B1-B4; N = 8277 for models C1-C4.*
*Smoking is defined as ≥ 100 cigarettes in lifetime, and treated as a three-category variable: former, never, and current. Income and education categories as per Table 1; diabetes mellitus, heart attack, CHF and stroke reflect self-reported diagnoses by a medical professional; BMI categories are <18.5, 18.5 – 25, 25–30, 30+ kg/m$^2$; and hypertension is defined as measured average systolic blood pressure ≥140, diastolic blood pressure ≥90, or taking antihypertensives. FVC percent predicted using NHANES III prediction equations.*[1].

Black adult with a lower FVC (in liters), but a similar race-specific FVC percent predicted as an otherwise similar White individual, would have a higher risk of mortality.

The lower average lung function of the US Black population, often assumed to be innate or genetic in origin but that could also stem from social or environmental disadvantage, is hence associated with worse health outcomes. The use of race-specific prediction equations, which "adjust away" such differences in lung function (and which left substantial unexplained mortality associated with Black race in our regression models), could thereby underestimate Black patients' greater risk of mortality in clinical settings.

Our national data confirms an earlier study by Burney and Hooper, [9] which similarly found that all-cause mortality for a given FVC did not vary by race in four US communities. However, neither study necessarily implicates lower FVC as the cause of racial disparities in mortality. Indeed, only a small share of the deaths in our cohort were attributed principally to chronic respiratory disease; the proportion was actually lower among Black compared to White decedents (although Black decedents on average were younger). Lower lung function among the US Black population may hence serve as a general but non-specific indicator of adversity and disadvantage, which in turn is independently linked to a shortened life-span. However, it is also possible that reduced lung function is on the causal pathway between adversity and early mortality for some individuals.

Thomas Jefferson first suggested that Black individuals had innately inferior lung function, writing that a "difference of structure in the pulmonary apparatus" inclined them to plantation labor [4](pp 27–28). Racial differences in vital capacity were first documented in the mid-nineteenth century among enslaved Black people by a prominent Southern physician slave owner [4]. Subsequently, such racial differences were repeatedly demonstrated, including in large, well-conducted surveys like the NHANES [1].

These observations led to the routine use of racial "correction factors," and later race-specific pulmonary function equations, in clinical practice. Controversy persists, however, about the etiology of these racial differences, and the appropriateness of adjusting for them. In the 1980s and 1990s, two South African physicians first argued against racial adjustment of lung function [4–6], noting that variability in lung function within races was as extensive as variability between races; that social class also influenced lung function; and that race-specific prediction equations could have harms, e.g. inadequate recognition and remediation of (and compensation for) occupational lung disease [5].

Since then, socioeconomic gradients in lung function have been identified in diverse populations [16,17,30–32]. However, analyses have found that controlling for SES explains only part of the Black: White differences in lung function, that anthropometric differences (e.g. relative leg length) explain a greater portion, and that much of the difference remains unexplained [19,20]. Such findings, however, do not prove a genetic etiology for racial differences in lung function. First, because cohorts from which lung function prediction equations are derived exclude subjects with respiratory symptoms or a smoking history, researchers may underestimate the impact of socioeconomic factors on lung function [33]. Second, environmental and socioeconomic exposures themselves affect, in complex ways, anthropometric measures [34], which exhibit secular change within societies over time [35]. Third, and perhaps more importantly, adjustment for socioeconomic factors such as occupation, education, or income may fail to account for the totality of Black: White differences in social disadvantage and environmental exposures affecting lung function. For instance, Black individuals have particularly high exposure to PM 2.5, ozone, and traffic-related air pollutants [36,37], toxins that reduce pulmonary function both in childhood and adulthood [38–40]. Relative to White individuals, Black individuals also experience more pulmonary infections [41,42], which inhibit lung growth [43].

Our analyses focused not on the nature/nurture debate *per se*, but on the prognostic implications of FVC differences by race, and by extension the clinical ramifications of the use of race-specific equations. Because forced expiratory volume in 1 s ($FEV_1$) and FVC are both lower in Black relative to White individuals, the use of race-specific standards has little effect on the $FEV_1$ /FVC ratio which is used to diagnose obstructive disease [2,3,12,13]. However, we found that the use of colorblind rather than race-specific equations would cause an 8-fold increase in the share of Black individuals meeting spirometric criteria for possible restrictive disease.

These findings echo those of an international study which found that use of colorblind equations labeled a large share — in some instances a majority — of the population in some low-income nations as having restrictive ventilatory deficits [44]. Those low-income nations were ethnically diverse, making it unlikely that genetics *per se* accounted for the low FVCs shared across their populations [44]. Deprivation appeared to be the common link.

Etiologic debates aside, use of colorblind prediction equations in US clinical practice would label a much higher share of Black individuals with possible restrictive ventilatory deficits, few of whom are likely to have identifiable restrictive lung diseases, which are relatively rare [10,12]. Such reclassification would have important ramifications for both clinical care and environmental hazard control, and should not be undertaken lightly.

For those with established lung disease, however, the use of race-specific equations might lead to inadvertent discrimination against Black patients. For such patients, clinicians use $FEV_1$ and FVC percent predicted to gage disease severity [45], determine prognosis, select treatments [46], and inform decisions about referral for lung transplantation [47], and these measures influence the Lung Allocation Score used to prioritize the allocation of organs [48]. Hence, use of race-specific prediction equations could lead Black patients with the same lung function (in liters) and mortality-risk as an otherwise similar White patient to receive less medical treatment, be referred for lung transplantation later in the course of illness, and have a lower likelihood of transplant once wait-listed. Similar concerns have been raised with respect to the clinical use of other race-based algorithms, [49] particularly kidney function equations [50,51.]

The use of race-specific pulmonary function prediction equations also has implications for surveillance and compensation for occupational lung disease. Federal regulations specify the use of NHANES III prediction equations for monitoring $FEV_1$ in coal miners [52]. Hence, to be notified of an abnormality, and/or removed from exposure, a Black miner would need to have greater respiratory impairment — and, our data imply, a higher risk of death—than an otherwise similar White miner. Race-specific NHANES III prediction equations are also used in the assessment of respiratory disability [53]. Although criteria differ among compensation systems, in some cases to qualify for workers' compensation, a Black worker needs to have a lower FVC in liters (and higher risk of death) than an otherwise identical White worker.

Our study has limitations. The public-use NDI lumps causes of death in ten broad categories, with no information on contributing causes, and many deaths categorized as "other." Consequently, the mechanism of elevated death rates associated with reduced lung function in our study, as in some previous studies [54,55], is uncertain. The frequent misattribution of cause of death among those with chronic lung disease, a known problem [56], further complicates disentangling causality.

NHANES III predated the most recent ATS guidance on performance of spirometry. However, the survey used methods mostly similar to current guidelines; the small differences are unlikely to substantively impact results. We lacked data on total lung capacity, which is used clinically to confirm restrictive ventilatory deficits. Consequently, our primary measure was FVC, and not the absence or presence of a fully-verified, restrictive ventilatory deficit. We

additionally lacked imaging, and so do not know whether those with low FVC had parenchymal lung diseases or other processes, or indeed had any identifiable lung disease at all. Finally, our analysis focused on the general population; the implications of our findings for the prognostication and treatment of patients with such lung diseases as asthma, COPD, and interstitial lung disease are unclear. Further research, including with chest imaging, lung volume measurement and other biomarkers, and in populations with diverse respiratory diseases, would help elucidate the clinical implications of using race-specific lung function equations for pulmonary patients.

Black Americans have faced adversity since before the nation's birth, and continue to have lower income and wealth than White individuals; inferior access to healthcare [57]; more exposure to environmental pollutants [37] and other stressors; and a greater burden of morbidity and mortality from some but not all lung diseases [58–60]. Their lower lung function is associated with higher mortality, and may serve as a general marker of exposure to adverse social and environmental factors. Adjusting away racial differences in lung function, as is now standard, may further disadvantage some Black patients and workers.

## Data sharing statement

The data used in this study is freely available for download by the public at: https://wwwn.cdc.gov/nchs/nhanes/nhanes3/default.aspx.

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## Declaration of Competing Interests

The authors have nothing to declare.

## Author contributions

All authors contributed to study design, data interpretation, and drafting or critical review/editing of the manuscript. Adam Gaffney conducted the data analyses; Adam Gaffney and David Himmelstein verified the underlying data.

## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.eclinm.2021.101073.

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