ORIGINAL ARTICLE

Normal Lung Function and Mortality in World Trade Center Responders and National Health and Nutrition Examination Survey III Participants

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Abstract

Rationale: Low FEV_1 is a biomarker of increased mortality. The association of normal lung function and mortality is not well described.

Objectives: To evaluate the FEV_1–mortality association among participants with normal lung function.

Methods: A total of 10,999 Fire Department of the City of New York (FDNY) responders and 10,901 Third National Health and Nutrition Examination Survey (NHANES III) participants, aged 18–65 years with FEV_1 ⩾80% predicted, were analyzed, with FEV_1 percent predicted calculated using Global Lung Function Initiative Global race-neutral reference equations. Mortality data were obtained from linkages to the National Death Index. Cox proportional hazards models estimated the association between FEV_1 and all-cause mortality, controlling for age, sex, race/ethnicity, smoking history, and, for FDNY, work assignment. Cohorts were followed for a maximum of 20.3 years.

Measurements and Main Results: We observed 504 deaths (4.6%) of 10,999 for FDNY and 1,237 deaths (9.4% [weighted]) of 10,901 for NHANES III. Relative to FEV_1 ⩾120% predicted, mortality was significantly higher for FEV_1 100–109%, 90–99%, and 80–89% predicted in the FDNY cohort. In the NHANES III cohort, mortality was significantly higher for FEV_1 90–99% and 80–89% predicted. Each 10% higher predicted FEV_1 was associated with 15% (hazard ratio, 0.85; 95% confidence interval, 0.80–0.91) and 23% (hazard ratio, 0.77; 95% confidence interval, 0.71–0.84) lower mortality for FDNY and NHANES III, respectively.

Conclusions: In both cohorts, higher FEV_1 is associated with lower mortality, suggesting higher FEV_1 is a biomarker of better health. These findings demonstrate that a single cross-sectional measurement of FEV_1 is predictive of mortality over two decades, even when FEV_1 is in the normal range.

Keywords: FEV_1; pulmonary medicine; occupational health; firefighters; emergency responders

FEV_1 is an essential measure of lung function that can help diagnose and monitor lung diseases (1, 2). Standardized spirometry techniques enable results from independent cohorts to be compared (3, 4). In 1999, a cross-sectional analysis of never smokers without respiratory symptoms enrolled in the Third National Health and Nutrition Examination Survey (NHANES III) cohort produced widely used predicted values of FEV_1 as a function of age and height, stratified by sex and race/ethnicity, often referred to as "Hankinson reference values" (5). Recently, the disadvantages of race-based prediction equations for pulmonary function have resulted in the American Thoracic Society adopting the Global Lung Function Initiative

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This article has a related editorial.

A data supplement for this article is available via the Supplements tab at the top of the online article.

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At a Glance Commentary

Scientific Knowledge on the Subject: Low FEV_1 is associated with mortality in community and occupational cohorts.

What This Study Adds to the Field: FEV_1 at the beginning of longitudinal follow-up was associated with reduced mortality over the next 20 years in both an occupational cohort and a community-based validation cohort with normal FEV_1 (at least 80% predicted). FEV_1 throughout its range may be a simple biomarker of subsequent mortality.

race-neutral reference equations (GLI Global) (6).

Low FEV_1 is a risk factor for mortality in community and occupational cohorts (7–10). The association of FEV_1 and mortality among those with average to above average lung function has received less attention. The Fire Department of the City of New York (FDNY) World Trade Center (WTC) rescue and recovery workers have been followed for over 20 years (11). Previously, we demonstrated an association between longitudinal FEV_1 decline and increased mortality (12). In the present study, we investigated the association between pre-WTC exposure FEV_1 and subsequent mortality among those with $FEV_1 \geq 80\%$ predicted using GLI Global reference equations. Because of the unique aspects of WTC exposure, we sought to validate our findings in a cohort of NHANES III participants, aged 18–65 years with $FEV_1 \geq 80\%$ predicted, who are more representative of the general population with lung function in the normal range.

Methods

Study Population

The source population for the primary cohort included 12,323 WTC firefighters and emergency medical service providers (EMS) who were actively employed by FDNY on September 11, 2001. Participants without a pulmonary function test (PFT) between January 1, 1998, and September 10, 2001, with high-quality (grade A or B) FEV_1 measurements were excluded ($n = 1{,}059$). We excluded participants with below average lung function ($FEV_1 < 80\%$ predicted; $n = 265$), resulting in a primary cohort of 10,999 participants (Figure 1). FDNY participants provided written informed consent. The Albert Einstein College of Medicine Institutional Review Board approved this study.

The source population for the validation cohort included 17,705 NHANES III participants with a PFT between October 18, 1988, and October 15, 1994. Participants without a mortality status ($n = 420$) or a reproducible FEV_1 measurement with two or more acceptable trials ($n = 1{,}592$) were excluded. Because 65 years is the FDNY mandatory retirement age, no members of the FDNY cohort were older than 65 at the time of their PFT. Therefore, all NHANES III participants over age 65 at the time of PFT were excluded ($n = 3{,}355$) so that the NHANES III cohort would be more comparable to the FDNY cohort. Participants with $FEV_1 < 80\%$ predicted ($n = 1{,}437$) were also excluded, resulting in a validation cohort of 10,901 participants (Figure 1). NHANES III data were publicly available and deidentified.

Pulmonary Function Testing (Prebronchodilator Spirometry)

FEV_1 was the exposure of interest for all analyses. The FDNY protocol for PFTs is described elsewhere (13, 14). The PFT closest to September 10, 2001, was used. Spirometry data for the NHANES III cohort were obtained from the public release Examination Data File (15). FEV_1 percent predicted values were calculated by dividing participants' observed measurements by expected values, given sex, height, and age, derived from the GLI Global race-neutral reference equations (16).

Mortality Ascertainment

Mortality data for the FDNY cohort were ascertained via linkages to the National Death Index through December 31, 2021. Public use linked mortality data from the National Death Index were available through 2019 for the NHANES III cohort (17).

Cohort Characteristics

In the FDNY cohort, age at examination, sex, height, race/ethnicity, and work assignment were obtained from the FDNY WTC Health Program database. Smoking history was obtained via self-administered surveys conducted at periodic medical evaluations. The survey closest to the date of spirometry was used. Smoking history was missing for six FDNY participants (<0.1%) and was imputed as "never smoker." In the NHANES III cohort, age at examination, sex, race/ethnicity, and smoking history were obtained from the public release NHANES III Household Adult Data File (18). Height was obtained from the Examination Data File (15).

Sample Weighting (NHANES III Cohort)

The NHANES III cohort was sampled using a stratified, multistage probability design. The sample was not intended to be representative of the general U.S. population, because it oversampled subpopulations and was subject to biases due to nonresponse, the exclusion of certain types of housing, and other factors. However, sample weight, cluster, and strata variables were provided so that estimates could be obtained that would reflect the entire noninstitutionalized, civilian U.S. population at the time (18). Measurements and analyses of the NHANES III cohort in the present study were weighted according to the NHANES III Analytic and Reporting Guidelines (19).

Statistical Methods

FDNY cohort characteristics were summarized as counts/proportions and means/SDs. NHANES III cohort characteristics were summarized as weighted means/SEs and weighted proportions/SEs.

Standardized mortality ratios (SMRs) were estimated for five categories of FEV_1 percent predicted: *1*) 80–89%, *2*) 90–99%, *3*) 100–109%, *4*) 110–119%, and *5*) ⩾120%. Deaths and person-time in the two cohorts were stratified by age group, race/ethnicity, sex, and calendar period. The expected number of deaths for each stratum was estimated using the corresponding stratum mortality rate for the general U.S. population from the National Institute for Occupational Safety and Health Life Table Analysis System 1960–2021 rate file (20, 21). SMRs for the NHANES III cohort were weighted so that they would reflect the demographic distribution of the general U.S. population. A supplementary analysis was performed with FEV_1 percent predicted values that were calculated using the Hankinson race-adjusted reference equations for comparison with the analysis based on the GLI race-neutral reference equations (5). The Hankinson reference equations provide reliable estimates only for White, Black, and

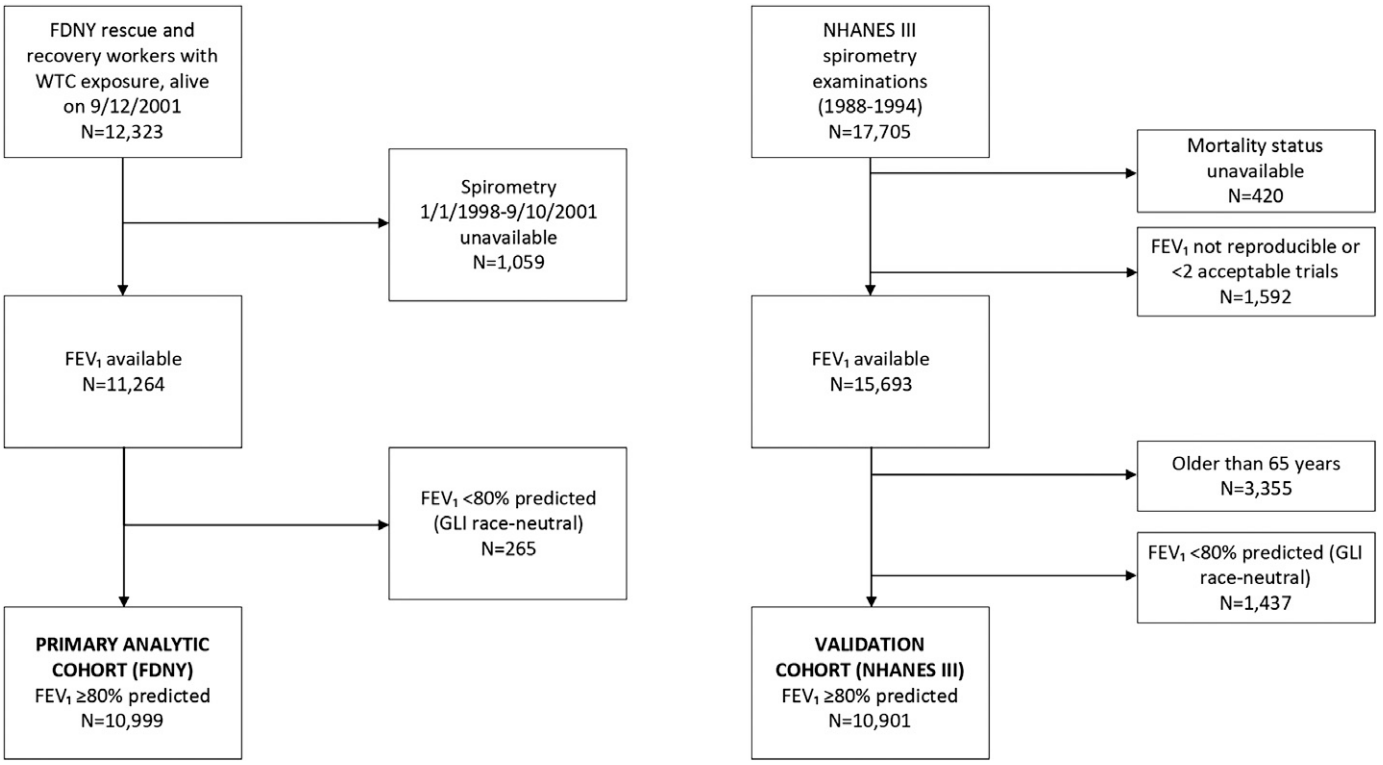

Figure 1. Study population of Fire Department of the City of New York (FDNY) rescue and recovery workers and Third National Health and Nutrition Examination Survey (NHANES III) participants aged 18–65 years with FEV_1 ⩾80% predicted. Shown is the source population of 12,323 FDNY rescue and recovery workers who were employed by the FDNY on September 11, 2001, present at the WTC site between September 11, 2001, and July 24, 2002, alive on September 12, 2001, and consented to research; 11,264 had A or B grade spirometry available between January 1, 1998, and September 10, 2001. The final study population of 10,999 had FEV_1 ⩾80% predicted. Validation analyses were derived from 17,705 NHANES III participants with spirometry performed between October 18, 1988, and October 15, 1994. The validation cohort had 15,693 participants with reproducible spirometry and National Death Index mortality linkage. The final study population included 10,901 participants aged 18–65 years with FEV_1 ⩾80% predicted. GLI = Global Lung Function Initiative; WTC = World Trade Center.

Mexican American individuals. Nation of origin was not available for Hispanic FDNY members. Therefore, we restricted the cohorts to non-Hispanic White and Black individuals (FDNY, $n = 10{,}266$; NHANES III, $n = 6{,}786$) for this analysis.

Multivariable Cox proportional hazards models were used to evaluate the association between FEV_1 and mortality. Because FDNY participants had to be alive on September 12, 2001, to be included in the study cohort, follow-up began on September 12, 2001, rather than the date of spirometry to mitigate the potential for immortal time bias. End of follow-up occurred at the earlier of December 31, 2021, or death, for a maximum follow-up of 20.3 years. In the NHANES III cohort, follow-up began at the date of spirometry examination. Follow-up ended at the earlier of death date or 20.3 years after examination (to be comparable to the FDNY follow-up period). FEV_1 percent predicted was evaluated as both a continuous and categorical predictor of all-cause mortality. In categorical models, FEV_1 percent predicted was categorized as defined above. FDNY FEV_1 percent predicted models were adjusted for age at examination, sex, race/ethnicity, smoking, and work assignment (firefighter/EMS). NHANES III models were adjusted for age at examination, sex, race/ethnicity, and smoking. Plots of survival curves estimated from the above models were generated for each category of FEV_1 percent predicted. For these plots, the Breslow estimator based on the empirical cumulative hazard function was used to estimate baseline hazards that are not specified in the Cox model (22, 23). The association between absolute FEV_1 (in L) and mortality was also evaluated. To account for variations by height, these models were adjusted for height and height squared in addition to the same covariates included in the percent predicted models. Covariates were selected *a priori* on the basis of our conceptual framework. Potential interaction between FEV_1 and WTC exposure (defined as arrival at the WTC site on September 11, 2001, vs. September 12, 2001, or later) in the FDNY models was assessed. Sensitivity analyses were performed that included participants with FEV_1 <80% predicted and in which the six participants missing smoking history were assigned as "ever smoker." NHANES III analyses were weighted. The proportional hazards assumption was assessed using plots of log-log survival curves and Schoenfeld residuals. Plots of restricted cubic spline models were generated for each cohort to illustrate the hazard across the distribution of FEV_1 percent predicted. Analyses were conducted using SAS (version 9.4; SAS Institute Inc.) and R (version 4.3.1; R Foundation for Statistical Computing).

Results

Cohort Characteristics

The mean age at examination in the FDNY cohort was 38.7 years (SD, 7.6). The maximum age was 64.8 years (mandatory retirement age for FDNY firefighters is 65 yr).

Table 1. Selected Characteristics of FDNY and NHANES III Participants Aged 18–65 Years with FEV_1 ⩾80% Predicted

Variable	FDNY (n = 10,999) Mean (SD)/n (%)	NHANES III (n = 10,901) Weighted Mean (SE)/ Weighted Proportion (SE)*
Age at examination, yr	38.7 (7.6)	37.7 (0.2)
Sex		
Male	10,666 (97.0%)	49.2% (0.5)
Female	333 (3.0%)	50.8% (0.5)
Race/ethnicity		
White Non-Hispanic	9,733 (88.5%)	76.3% (1.3)
Black Non-Hispanic	533 (4.9%)	9.5% (0.6)
Hispanic	673 (6.1%)	10.7% (0.9)
Other	60 (0.6%)	3.4% (0.4)
Height (cm)	176.5 (7.0)	169.5 (0.2)
Smoking history		
Never	7,866 (71.5%)	47.6% (0.8)
Ever	3,127 (28.4%)	52.4% (0.8)
Missing	6 (<0.1%)	
Work assignment		
Firefighter	9,381 (85.3%)	n/a
EMS	1,618 (14.7%)	n/a
FEV_1, % predicted	110.4 (14.3)	103.2 (0.3)
FEV_1, L	4.3 (0.7)	3.5 (0.02)
Deceased	504 (4.6%)	9.4% (0.5)
Years of follow-up†	20.0 (1.8)	19.6 (0.04)

Definition of abbreviations: EMS = emergency medical services; FDNY = Fire Department of the City of New York; n/a = not applicable; NHANES III = Third National Health and Nutrition Examination Survey.
*Because of the weighting procedures, only SEs rather than SDs could be derived for the NHANES III cohort.
†In the FDNY cohort, follow-up began on September 12, 2001, and ended at death or December 31, 2021. In the NHANES III cohort, follow-up began at the date of examination (conducted between October 18, 1988, and October 15, 1994) and ended at death or 20.3 years after examination.

The weighted mean age at examination in the NHANES III cohort, which was restricted to participants aged 18–65 years, was 37.7 years (SE, 0.2). The FDNY cohort was mostly White (88.5%), male (97.0%), and never smokers (71.5%). Weighted percentages in the NHANES III cohort reflected the general U.S. population, aged 18–65 years with FEV_1 ⩾80% predicted, between 1988 and 1994. The cohort was 76.3% White, 49.2% male, and 47.6% never smokers, using sample weights. Compared with the NHANES III cohort, the FDNY cohort had more never smokers, was taller, and had higher FEV_1 (Table 1). FEV_1 ⩾100% predicted occurred in 76.1% of the FDNY cohort and 60.3% of the weighted NHANES III cohort (Table 2). FEV_1 and FVC were strongly correlated in the FDNY cohort (Spearman's rho = 0.882; $P < 0.001$) and the NHANES III cohort (Spearman's rho = 0.808; $P < 0.001$).

Crude Mortality and SMRs by Lung Function

The FDNY cohort had 504 deaths over 20.3 years of follow-up with an overall crude mortality rate of 4.6%. The NHANES III cohort had 1,237 deaths over 20.3 years of follow-up with an overall weighted crude mortality rate of 9.4%. In the FDNY cohort, crude mortality was 8.3% for those with FEV_1 80–89% predicted, 6.1% for FEV_1 90–99% predicted, 4.7% for FEV_1 100–109% predicted, 3.4% for FEV_1 110–119% predicted, and 3.6% for FEV_1 ⩾120% predicted. In the NHANES III cohort, weighted crude mortality was 17.0% for those with FEV_1 80–89% predicted, 10.9% for FEV_1 90–99% predicted, 7.6% for FEV_1 100–109% predicted, 6.4% for FEV_1 110–119% predicted, and 6.2% for FEV_1 ⩾120% predicted (Table 2). Eighteen (3.6%) of the deaths in the FDNY cohort and 44 (4.0% [weighted]) of the deaths in the NHANES III cohort were related to respiratory disease.

The FDNY cohort had low mortality compared with the entire U.S. population. The SMR for the entire FDNY study cohort was 0.35 (95% confidence interval [CI], 0.32–0.39). The strata-specific SMRs were 0.61 (95% CI, 0.20–1.90) for the subgroup with FEV_1 80–89% predicted, 0.48 (95% CI, 0.40–0.57) for FEV_1 90–99% predicted, 0.38 (95% CI, 0.33–0.43) for FEV_1 100–109% predicted, 0.26 (95% CI, 0.18–0.36) for FEV_1 110–119% predicted, and 0.26 (95% CI, 0.21–0.32) for FEV_1 ⩾120% predicted (Table 2). The NHANES III study cohort had similar mortality relative to the entire U.S. population (SMR, 0.99; 95% CI, 0.89–1.09). Strata-specific SMRs were 1.59 (95% CI, 1.33–1.90) for FEV_1 80–89% predicted, 1.12 (95% CI, 0.96–1.31) for FEV_1 90–99% predicted, 0.86 (95% CI, 0.72–1.03) for FEV_1 100–109% predicted, 0.69 (95% CI, 0.54–0.89) for FEV_1 110–119% predicted, and 0.62 (95% CI, 0.44–0.86) for FEV_1 ⩾120% predicted (Table 2). Results were similar when FEV_1 percent predicted was calculated using the Hankinson race-adjusted reference equations (*see* Table E1 in the online supplement).

Adjusted Cox Proportional Hazards Models

Relative to those with FEV_1 ⩾120% predicted, those with FEV_1 100–109%, 90–99%, and 80–89% predicted had significantly elevated mortality in the FDNY cohort (hazard ratio [HR], 1.35; 95% CI, 1.05–1.75 for FEV_1 100–109%; HR, 1.68; 95% CI, 1.28–2.19 for FEV_1 90–99%; HR, 1.90; 95% CI, 1.36–2.65 for FEV_1 80–89%; Figure 2). In the NHANES III cohort, mortality was significantly elevated for FEV_1 90–99% predicted (HR, 1.69; 95% CI, 1.17–2.44) and 80–89% predicted (HR, 2.40; 95% CI, 1.51–3.80) compared with FEV_1 ⩾120% predicted (Figure 2). For both cohorts, adjusted survival curves showed greater survival with higher FEV_1, although the curves for the two highest categories (FEV_1 110–119% and ⩾120% predicted) almost overlapped in the FDNY cohort, whereas in the NHANES III cohort, they diverged. Similarly, there was less divergence between the two lowest categories (FEV_1 80–89% and 90–99% predicted) in the FDNY cohort compared with the NHANES III cohort (Figure 3). Higher FEV_1 percent predicted as a continuous variable in the average to above average range (⩾80% predicted) was associated with decreasing mortality in both the FDNY and NHANES III cohorts. Each 10% higher predicted FEV_1 was associated with a 15% decrease in mortality in the FDNY cohort (HR, 0.85; 95% CI, 0.80–0.91) and a 23% decrease in mortality in the NHANES III cohort (HR, 0.77; 95% CI, 0.71–0.84). Each 1-L higher

Table 2. All-Cause Mortality by FEV_1 Percent Predicted in FDNY and NHANES III Cohorts

FEV_1 % Predicted	Frequency	Percent*	Deaths	Crude Mortality*	SMR† (95% CI)
FDNY cohort					
⩾120%	2,864	26.0%	103	3.6%	0.26 (0.21, 0.32)
110–119%	2,618	23.8%	88	3.4%	0.26 (0.18, 0.36)
100–109%	2,891	26.3%	137	4.7%	0.38 (0.33, 0.43)
90–99%	1,939	17.6%	119	6.1%	0.48 (0.40, 0.57)
80–89%	687	6.3%	57	8.3%	0.61 (0.20, 1.90)
Entire study cohort	10,999	100.0%	504	4.6%	0.35 (0.32, 0.39)
NHANES III cohort (weighted)					
⩾120%	1,107	9.6%	77	6.2%	0.62 (0.44, 0.86)
110–119%	2,101	20.7%	178	6.4%	0.69 (0.54, 0.89)
100–109%	2,994	30.0%	292	7.6%	0.86 (0.72, 1.03)
90–99%	2,827	25.8%	357	10.9%	1.12 (0.96, 1.31)
80–89%	1,872	13.9%	333	17.0%	1.59 (1.33, 1.90)
Entire study cohort	10,901	100.0%	1,237	9.4%	0.99 (0.89, 1.09)

Definition of abbreviations: CI = confidence interval; FDNY = Fire Department of the City of New York; NHANES III = Third National Health and Nutrition Examination Survey; SMR = standardized mortality ratio.
*Weighted percent and weighted crude mortality for NHANES III cohort.
†SMRs are stratified by age group, race/ethnicity, sex, and calendar period and compared with the general U.S. population using data from the National Institute for Occupational Safety and Health Life Table Analysis System 1960–2021 rate file (20, 21, 36).

absolute FEV_1 was associated with a 32% decrease in mortality for FDNY (HR, 0.68; 95% CI, 0.57–0.81) and a 55% decrease for NHANES III (HR, 0.45; 95% CI, 0.33–0.60) (Table 3). Sensitivity analyses including participants with FEV_1 <80% predicted produced similar results (Table E2 and Figures E1 and E2). Results did not meaningfully change when missing smoking history was imputed with "ever smoker" instead of "never smoker" (data not shown). Interaction of FEV_1 and WTC exposure (arrival at the WTC site on September 11, 2001, vs. September 12, 2001, or later) on mortality was assessed in the FDNY models. Interaction was not significant in the model using FEV_1 percent predicted or the model using absolute FEV_1. When evaluating the proportional hazards assumption for FEV_1, no significant violations were observed.

Plots of HRs generated by restricted cubic spline models showed similar associations of FEV_1 and mortality in the FDNY and NHANES III cohorts. In the FDNY cohort, the HR decreased continuously throughout the 80–120% predicted range of FEV_1 and then increased slightly for FEV_1 above 120% predicted. In the NHANES III cohort, the HR decreased throughout the entire range of FEV_1 percent predicted, although the effect was attenuated above 110% predicted FEV_1 (Figure 4).

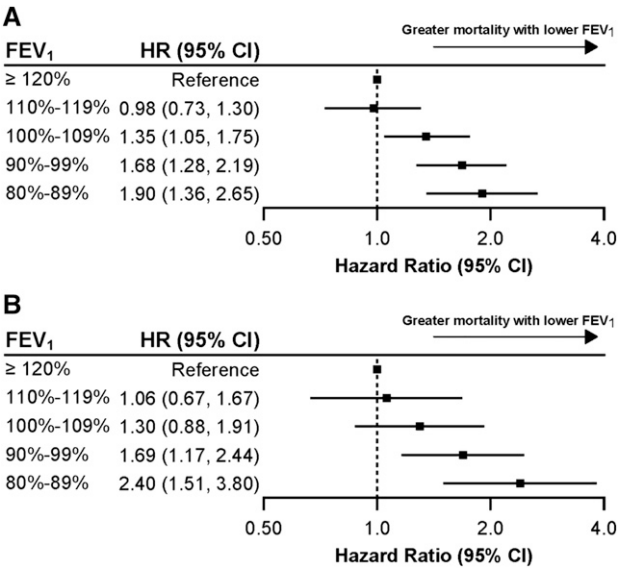

Figure 2. Multivariable Cox proportional hazards models of the association between categorical FEV_1 percent predicted and all-cause mortality. (*A*) FDNY cohort: complete data for 10,999 participants, with 504 deaths between September 12, 2001, and December 31, 2021. Adjusted for age at examination, sex, race/ethnicity, smoking history, and work assignment. (*B*) NHANES III cohort: complete data for 10,901 participants, with 1,237 deaths during the 20.3 years after spirometry examination. Adjusted for age at examination, sex, race/ethnicity, and smoking history. Weighted for cohort sampling designs. CI = confidence interval; FDNY = Fire Department of the City of New York; HR = hazard ratio; NHANES III = Third National Health and Nutrition Examination Survey.

Discussion

Low FEV_1 is a biomarker for lung disease and is associated with increased mortality in multiple cohorts (7, 24–29). However, few studies have assessed higher FEV_1 in the average to above average range as a biomarker of good health. Our observations support the conclusion that high FEV_1 is a biomarker for reduced mortality in the average to above average range of lung function. A single cross-sectional FEV_1 measurement was predictive of all-cause mortality across two decades in both the

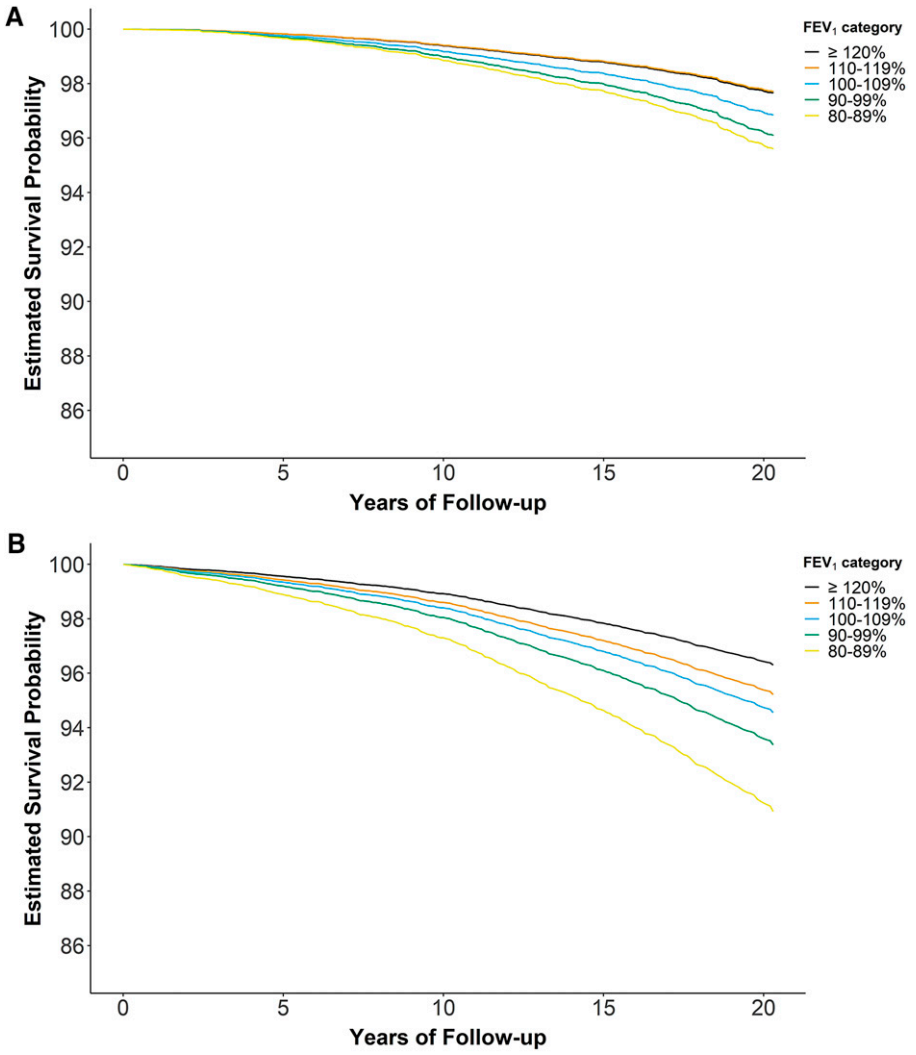

Figure 3. Adjusted survival curves for categories of FEV_1 percent predicted for (*A*) FDNY and (*B*) NHANES III (weighted for sampling designs) from the models shown in Figure 2 using the Breslow estimator for baseline hazards. FDNY = Fire Department of the City of New York; NHANES III = Third National Health and Nutrition Examination Survey.

FDNY and NHANES III cohorts, even among those with average to above average lung function ($FEV_1 \geqslant 80\%$ predicted), demonstrating the utility of FEV_1 as a measure of general health.

This 20-year prospective cohort study followed 10,999 FDNY firefighters and EMS providers and 10,901 NHANES III participants, a cohort representative of the U.S. population when sample weights are applied. In the FDNY cohort, FEV_1 100–109%, 90–99%, and 80–89% predicted were associated with a 35%, 68%, and 90% greater risk of mortality, respectively, when compared with those with $FEV_1 \geqslant 120\%$ predicted. In the NHANES III cohort, FEV_1 90–99% and 80–89% predicted were associated with a 69% and 140% greater risk of mortality, respectively (Figure 2). Our results are similar to those of an analysis of non–chronic obstructive pulmonary disease participants followed for 3–8 years in the 2007–2012 NHANES cohort, which found significantly higher mortality among participants with FEV_1 between 80% and 90% predicted compared with those with $FEV_1 \geqslant 100\%$ predicted (30).

This study used GLI Global race-neutral equations to calculate FEV_1 percent predicted. Although age, sex, and height are biological characteristics, race and ethnicity are social constructs. They are still, however, associated with both lung function and mortality because of differential exposures and could thus confound the association between lung function and mortality (6, 31). Therefore, we treated race/ethnicity as a confounder and adjusted for it in our statistical models. The SMRs for each level of FEV_1 percent predicted were similar when Hankinson race-adjusted FEV_1 percent predicted was substituted for GLI Global race-neutral FEV_1 percent predicted. This suggests that the relationship between FEV_1 percent predicted and mortality might not be dependent on the reference population used to derive the expected FEV_1. Shifts in cut point–based diagnostic criteria when race-neutral reference equations are substituted for race-adjusted reference equations are under active investigation (32).

The findings from this study were robust. Regardless of whether FEV_1 was analyzed as a categorical or a continuous variable, Cox proportional hazards models evaluating the association between lung function and mortality consistently demonstrated a strong exposure–response relationship, although the association appears to be attenuated above 110% predicted FEV_1. The same was true when FEV_1 was examined as an absolute measure or as a percent predicted of normative values. Although the cut points for the five categories of FEV_1 percent predicted may be considered arbitrary, our findings led us to the same conclusion that greater FEV_1 is associated with lower mortality. Although participants with $FEV_1 < 80\%$ predicted were not included in this study, this group is already known to have poor mortality outcomes (30). Reduced mortality with continuous improvements in lung function is analogous to the observation that lowering of blood pressure throughout its range is associated with decreasing mortality (33, 34). Only 3.6% of the deaths in the FDNY cohort and 4.0% (weighted) of the deaths in the NHANES III cohort were related to respiratory disease, suggesting that poor lung function was not a proximal cause of death for most participants. Instead, FEV_1 may reflect a higher level of functional reserve in multiple organ systems (7) and thus could be an indicator of general systemic health. Further research can evaluate associations between FEV_1 and cause-specific mortality to elucidate this relationship.

The FDNY cohort had a lower overall crude mortality rate than the NHANES III cohort (4.6% vs. 9.4% [weighted]). The lower mortality in the FDNY cohort could be an indication of the healthy worker effect.

Table 3. Multivariable Cox Proportional Hazards Models of Association between Continuous FEV_1 and All-Cause Mortality

Lung Function	Hazard Ratio	95% Confidence Interval		*P* Value
		Lower	Upper	
FDNY analyses				
FEV_1 per 10% predicted increment*	0.85	0.80	0.91	<0.001
FEV_1 per 1-L increment†	0.68	0.57	0.81	<0.001
NHANES III analyses (weighted)				
FEV_1 per 10% predicted increment‡	0.77	0.71	0.84	<0.001
FEV_1 per 1-L increment†	0.45	0.33	0.60	<0.001

Definition of abbreviations: FDNY = Fire Department of the City of New York; NHANES III = Third National Health and Nutrition Examination Survey.
*Complete data for 10,999 with 504 deaths by December 31, 2021. Adjusted for age at examination, sex, race/ethnicity, work assignment, and smoking history.
†Secondary models using absolute FEV_1 instead of FEV_1 percent predicted as the measure of lung function. Adjusted for the same confounders, as well as height and height squared.
‡Complete data for 10,901 with 1,237 deaths during the 20.3 years after spirometry examination. Adjusted for age at examination, sex, race/ethnicity, and smoking history.

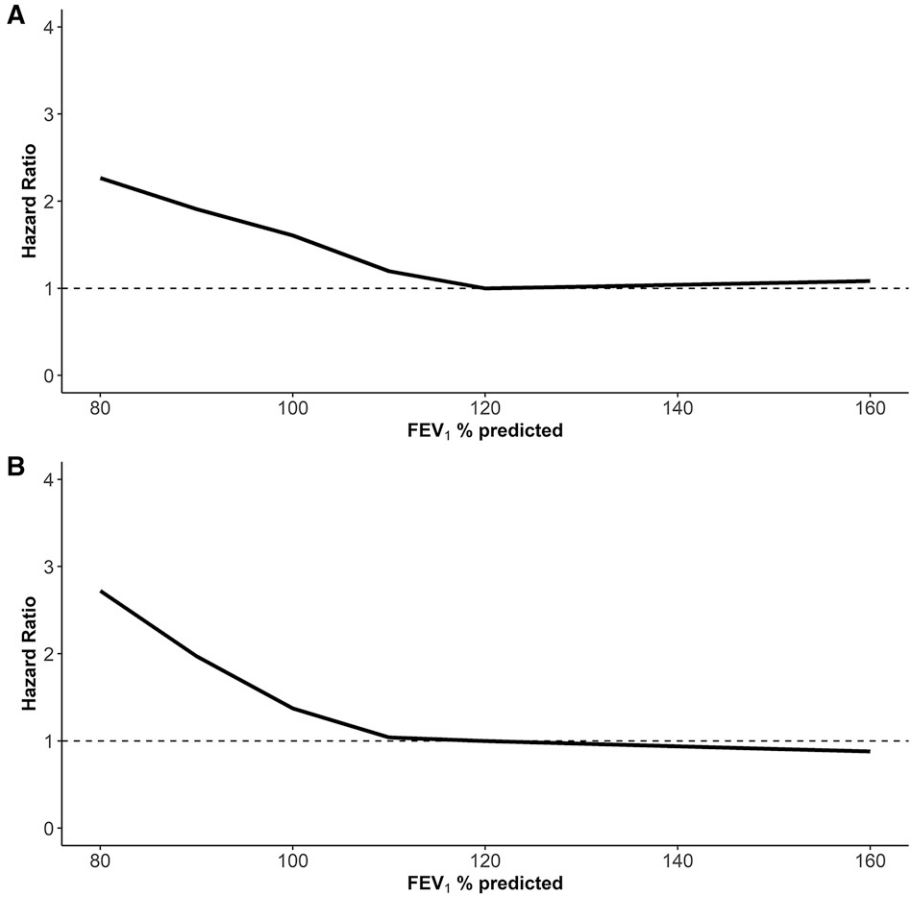

Figure 4. Plots of hazard ratios for FEV_1 percent predicted generated by restricted cubic spline models. (*A*) FDNY cohort: complete data for 11,264 participants with 540 deaths. Adjusted for age at examination, sex, race/ethnicity, smoking history, and work assignment. (*B*) NHANES III cohort: complete data for 12,338 participants with 1,714 deaths. Adjusted for age at examination, sex, race/ethnicity, and smoking history. Weighted for cohort sampling designs. FDNY = Fire Department of the City of New York; NHANES III = Third National Health and Nutrition Examination Survey.

FDNY uniformed employees must meet strict nationally mandated preemployment physical requirements to qualify for employment (35). This selection resulted in a higher proportion of individuals with $FEV_1 \geq 100\%$ than in the age- and FEV_1-restricted NHANES III cohort (76.1% vs. 60.3% [weighted]). Employment selection also resulted in a lower proportion of members with $FEV_1 < 80\%$, who were excluded from the primary analysis (2.4% vs. 8.7% [weighted]; Figure 1). The differences in FEV_1 between the FDNY and NHANES III cohorts suggest that FEV_1 could be a strong biomarker of the healthy worker effect, although the similar findings in an occupational cohort and a cohort representing the general U.S. population suggest that the association between above average FEV_1 and decreased mortality in the FDNY cohort is generalizable to the U.S. population.

This study's strengths are the sizes of both the analytic and validation cohorts, the 20 years of follow-up, and the use of a nonoccupational cohort representative of the general U.S. population to validate the findings in our occupational cohort. Date of death was ascertained rigorously using linkages to the National Death Index. FEV_1 percent predicted values were calculated using the GLI Global race-neutral reference equations, according to current American Thoracic Society recommendations (6). This study has some limitations. Unmeasured confounding due to competing occupational and community exposures in the FDNY and NHANES III cohorts is possible. Although

we have cross-sectional lung function data on FDNY and NHANES III, we lack data on many other health conditions before the FEV_1 measurement. Measurement error due to smoking status is possible, although it is unlikely to result in a significant bias among participants in this range of lung function.

In summary, this study provides evidence that higher lung function in the average to above average range is associated with reduced all-cause mortality after controlling for important confounders. This association between greater lung function and decreased mortality was significant whether FEV_1 percent predicted was analyzed as a continuous variable or as a categorical variable. Our findings also show the utility of FEV_1 as a general health measure as a single cross-sectional measurement predicted mortality over a 20-year follow-up period. Although aspects of this occupational cohort are unique, these findings were replicated in a representative weighted sample of the U.S. population, suggesting that they are generalizable to the U.S. population between the ages of 18 and 65 years. Further research can evaluate potential pathways for the association between lung function in the average to above average range and mortality. ■

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