



OPEN Associations between life's essential 8 and preserved ratio impaired spirometry

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Preserved ratio impaired spirometry (PRISm) is a prevalent yet under-researched state of diminished lung function, which has been proposed as a pre-clinical abnormal spirometry associated with chronic obstructive pulmonary disease (COPD) or early-stage COPD. PRISm is closely associated with cardiovascular disease. Preventing and improving quality of life in PRISm subjects is important. We aimed to examine the relationship between American Heart Association's Life's Essential 8 (LE8) and PRISm. This cross-sectional study utilized data of 2,869 adults aged ≥ 20 years from the National Health and Nutrition Examination Survey (NHANES) in 2007–2012. Multivariable logistic regression models were employed to examine the association between LE8 score, health behavior score, health factor score, each component of LE8 score, and PRISm. Moreover, the study explored this correlation in greater depth using restricted cubic spline curves and subgroup analyses. Of the 2,869 participants, the mean age was 44.09 ± 0.44 years, and 316 (11.01%) were defined as having PRISm. In fully adjusted models, higher LE8 scores were associated with a reduced odds ratio for PRISm (OR = 0.97; 95% CI, 0.96–0.98). A linear relationship between the LE8 score and PRISm was observed. Similar patterns emerged for health behavior and health factor subscores, with a particularly stronger correlation between health factors and PRISm. In the subgroup analysis, the inverse association between LE8 and PRISm was significantly more pronounced among those with high income. A higher LE8 score was associated with a lower likelihood of developing PRISm. Promoting optimal adherence to the LE8 metrics may improve PRISm and offers a meaningful approach for its prevention and management.

Keywords PRISm, Life's essential 8, NHANES, COPD

Abbreviations

PRISm	Preserved ratio impaired spirometry
COPD	Chronic obstructive pulmonary disease
FVC	Forced vital capacity
FEV ₁	Forced expired volume in the first second
LE8	Life's Essential 8
LS7	Life's Simple 7
NHANES	National Health and Nutrition Examination Survey
IGT	Impaired glucose tolerance
BMI	Body mass index
PIR	Poverty to income ratio

Chronic obstructive pulmonary disease (COPD) can cause airflow obstruction, which is a major contributor to global mortality, morbidity, and healthcare utilization¹. COPD is defined by a ratio of forced expired volume in the first second to forced vital capacity (FEV₁/FVC) of less than 0.70 on post-bronchodilator spirometry. Moreover, COPD can develop due to abnormal lung development and/or accelerated lung aging². Preserved ratio impaired spirometry (PRISm), defined as FEV₁/FVC ratio of ≥ 0.7 with an FEV₁ of $< 80\%$ of the predicted value on spirometry, was served as a more informative term that distinguishes its pattern from “restriction” and “nonspecific abnormality”³.

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PRISm has been proposed as a pre-clinical COPD abnormal spirometry or early-stage COPD^{3,4}. Recently studies have found that individuals with PRISm have a high rate of transitioning to other lung function categories⁵, and are more susceptible to developing COPD^{6,7}. The global prevalence of PRISm is high, estimated to be 7–20%^{7–12}. Compared to individuals with normal spirometry, those with PRISm are associated with increased respiratory symptoms⁴, limitations in physical strength, a higher body mass index (BMI), poor health-related quality of life¹³, diabetes, hypertension, and a continuous increase in all-cause mortality rates^{5,7,14,15}.

In recent years, a growing number of studies have been conducted on PRISm, including epidemiology, aetiology, disease subtyping, and relationship with other diseases. However, there remains a deficiency in established guidelines for diagnostic evaluation and management¹⁶. PRISm is significant linked to a multitude of health concerns, including obesity, diabetes, hypertension, heart failure, coronary artery disease, and stroke¹⁴. Additionally, individuals with PRISm were at higher risk for various cardiovascular outcomes¹⁷. The American Heart Association's "Life's Essential 8" health metrics emerge as a novel framework of cardiovascular health to prompting and preserving throughout the lifespan of individuals and populations¹⁸. The Life's Essential 8 consists of two main aspects, comprising eight metrics: health behaviors (diet, physical activity, nicotine exposure, and sleep health) and health factors (BMI, blood lipids, blood glucose, and blood pressure), thereby providing a comprehensive construct for health improvement.

A previous study has examined the relationship between "Life's Simple 7" (LS7) and lung function, as well as COPD¹⁹. However, a targeted investigation of the association between the Life's Essential 8 metrics and PRISm remains scarce. While these indicators primarily emphasize cardiovascular health, they also play a crucial role in overall health and quality of life. Individuals with PRISm often experience a reduced health-related quality of life¹³, highlighting the importance of promoting healthy lifestyles to improve their overall well-being. This study aims to address this gap by examining the correlation between the Life's Essential 8 metrics and PRISm, offering innovative insights and strategies for the sustained health management and lifestyle interventions of individuals with PRISm.

Methods

Data sources

The National Health and Nutrition Examination Survey (NHANES) is an ongoing, nationally representative cross-sectional study in the United States, which stratified multistage probability sampling approach. Conducted by the National Center for Health Statistics, this survey aims to accurately assess the health and nutritional status of the U.S. population. More details on ethical approvals and procedures for informed consent can be obtained from the National Center for Health Statistics (<http://www.cdc.gov/nchs/nhanes.htm>). Extensive information on the design, methodology, and weighting of NHANES has been previously published²⁰. From 2007 to 2020, the NHANES employed a stratified, complex multistage sampling methodology to select households from random clusters. Within these households, a subset of adults was randomly chosen to participate in a survey encompassing questions about health status, healthcare utilization, lifestyle risk factors, prevalent diseases, and other pertinent health-related matters²⁰. Trained investigators conducted personal interviews to gather the required data. Exclusion criteria established by the study design included the following:¹ age < 20 years;² missing data of particular weights² missing data on lung function;³ missing data for an incomplete Life's essential 8 score;⁴ diagnosis with COPD or asthma, and emphysema⁵ respondents with incomplete main covariates. The selection process is detailed in Fig. 1.

Definition of life's essential 8 (LE8)

The Life's Essential 8 (LE8) initiative, introduced by the American Heart Association, comprises eight essential components: Four health behaviors (diet, physical activity, nicotine/tobacco exposure, and sleep health) and four health factors [body mass index (BMI), levels of non-high-density lipoprotein cholesterol (non-HDL), blood glucose, and blood pressure]¹⁸. The diet metric was assessed using the Healthy Eating Index-2015 (HEI-2015)²¹, derived from the average values of dietary components gathered through 2 days of dietary recalls at outset²². The metrics for physical activity, nicotine/tobacco exposure and sleep health were assessed via self-reported questionnaires. Weight, height, and blood pressure measurements were obtained during physical examinations, while blood lipid and glucose levels were collected through laboratory analyses. Detailed calculation methods are provided in the Supplementary Table 1. Each of the eight indicators is scored on a scale ranging from 0 to 100. The overall LE8 score is derived from the unweighted average of these indicators. To determine the levels of individual cardiovascular health (CVH) factors, cutoff points of 50 and 79 were used to classify participants into low (0–49 points), moderate (50–79 points), and high (80–100 points)^{18,23}.

Spirometry and PRISm definitions

Spirometry data included FVC, FEV1, and the FEV1/FVC ratio. These spirometry values were used for this analysis. Calculations of the percentage predicted for FEV1 were performed based on sex, age, and height according to Hankinson's²⁴ predictive equation: (FEV1 predicted for males = $0.5536 - 0.01303 \times \text{age} - 0.000172 \times \text{age}^2 + 0.00014098 \times \text{Height}^2$ and FEV1 predicted for females = $0.4333 - 0.00361 \times \text{age} - 0.000194 \times \text{age}^2 + 0.00011496 \times \text{Height}^2$) for all race/ethnicities^{25,26}. Due to more than 90% missing values for post-bronchodilator test result, COPD diagnosis was based on pre-bronchodilator, a method consistent with previous studies^{19,27}. COPD was defined by the Global Initiative for Chronic Obstructive Lung Disease as FEV1/FVC ratio less than 0.7². PRISm was defined as FEV1/FVC ratio greater than or equal to 0.70 and an FEV1 less than 80% predicted¹⁴. Asthma was assessed by an affirmative answer to the question "Have you ever been told by a doctor or other health professional that you had asthma?". Emphysema was assessed by an affirmative answer to the question "Have you ever been told by a doctor or other health professional that you had emphysema?". Individuals without COPD, PRISm, asthma or emphysema were classified as normal subjects.

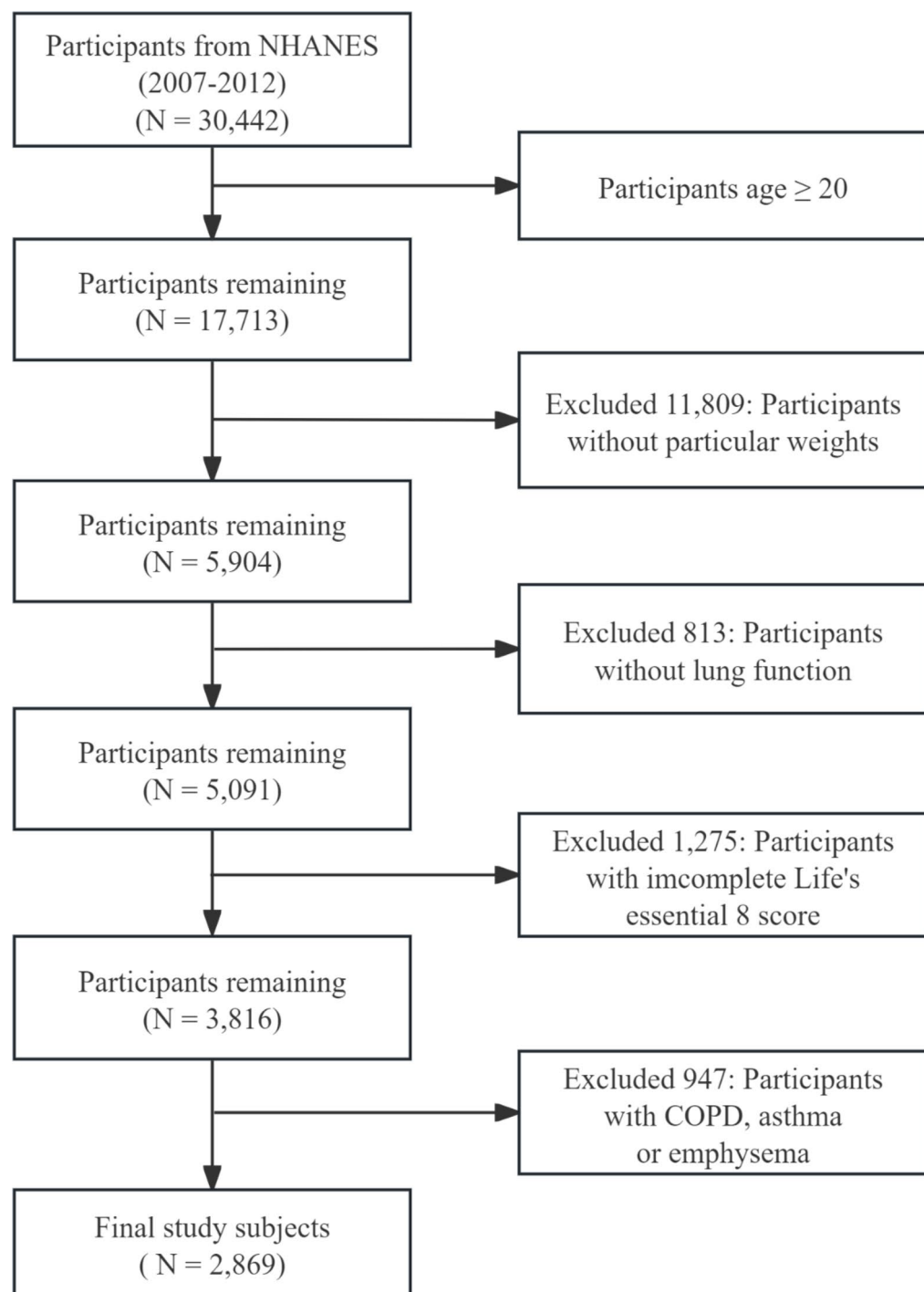


Fig. 1. Flowchart of the study design and participants.

Covariates

In light of prior studies and clinical experiences^{25,28}, we identified essential demographic factors such as age, sex (male and female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Mexican American, and Other), educational attainment [completed of ≤ 12 th grade, completed of high school or equivalent, completed of some college or an Associate in Arts degree (GED/AA), and completed of college or higher education)], marital status (unmarried, married or living with a partner, divorced or separated, and widowed), Poverty-to-Income ratio (PIR) levels (low-income: $\text{PIR} < 1$, middle-income: $\text{PIR} 1-4$, high-income: $\text{PIR} > 4$)²⁹, the body mass index (BMI) groups (underweight and normal weight: $\text{BMI} < 25$, overweight: $25 \leq \text{BMI} < 30$, and obesity: $\text{BMI} \geq 30$).

Smoking status was classified into three groups: never (smoked fewer than 100 cigarettes in their lifetime), former (smoked at least 100 cigarettes in their lifetime but were not currently smoking), and current (smoked at least 100 cigarettes in their lifetime and were currently smoking either some days or every day).

Alcohol consumption was divided into five categories: mild (having a history of daily binge drinking), moderate (consuming ≥ 2 drinks per day for females, ≥ 3 drinks per day for males), heavy (consuming ≥ 3 drinks per day for females, ≥ 4 drinks per day for males), former (consumed ≥ 2 drinks in one year but had not drunk in the last year, or consumed ≥ 12 drinks in a lifetime but had not drunk in the last year), and never (consumed < 12 drinks in a lifetime)³⁰.

Hypertension diagnosis was based on either systolic blood pressure ≥ 130 mmHg, diastolic blood pressure ≥ 80 mmHg, or taking antihypertensive drugs. Diabetes category was further broken down into diabetes mellitus (DM) (self-reported a doctor-diagnosed diabetes; taking diabetic medication or insulin; HbA1c $\geq 6.5\%$; fasting glucose ≥ 7.0 mmol/L; random blood glucose ≥ 11.1 mmol/L, 2-h OGTT blood glucose ≥ 11.1 mmol/L), including impaired fasting glycemia (IFG) (fasting glucose ≥ 6.1 and < 7.0 mmol/L without DM), and impaired glucose tolerance (IGT) (2-h OGTT blood glucose ≥ 7.7 and < 11.1 mmol/L without DM).

Statistical analyses

In this study, we combined data from three 2-year circle (2007–2008, 2009–2010, 2011–2012) of NHANES dataset into a unified dataset and excluded individuals with missing information. All analyses adhered to the Centers for Disease Control and Prevention guidelines for NHANES data analysis and were conducted using sample weights to generate accurate nationwide estimates in the U.S. Continuous variables were presented as mean and standard error (SE), and categorical variables were expressed as counts and percentages (%). Bivariate analyses of continuous and binary variables were performed using t-tests and Wald chi-square tests, respectively. Relative risk ratios for LE8 scores, health behavior score, health factor score, each component of LE8 score and PRISm were assessed using weighted multiple logistic regression models. We examined different models through stepwise adjustment for various risk factors. Model 1 represented the original unadjusted model without considering any potential confounders. Model 2 was adjusted for age, sex. Model 3 additionally accounted for race, education, marital status, PIR, and alcohol consumption. Adjusted odds ratios (ORs) were calculated based on these data, with 95% confidence intervals (CIs). Additionally, subgroup and interaction analyses were conducted to explore whether the association was modified by age, sex, race, education status, marital status, PIR, alcohol consumption. The restricted cubic spline (RCS) analysis method with three nodes was applied to investigate potential nonlinear associations among LE8 scores, health behavior score, health factor score and PRISm. Missing values for covariates, including both continuous or categorical variables, were imputed in this study using the covariate multiple imputation by mice package. Supplementary Table 2 provides comprehensive data on the missing covariates. All statistical analyses were conducted using R version 4.2.1 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided P value of less than 0.05 was considered statistically significant.

Results

Baseline characteristics of participants

The study included of 2,869 participants, representing 97,390,625 individuals in the U.S. Among these participants, 11.01% had PRISm. The main characteristics of the analyzed participants are presented in Table 1. The mean age of participants was 44.09 ± 0.44 years, the mean LE8 score was 70.54 ± 0.45 . The mean age of participants with PRISm was 47.61 ± 1.03 , while participants with normal spirometry was 43.78 ± 0.51 .

Compared to participants with normal spirometry, those with PRISm had a higher percentage of non-Hispanic black individuals, divorced or separated, obese, former or never alcohol user, hypertension, and diabetes. However, they had a lower percentage of non-Hispanic white individuals, married or partnered marital status, high education level, and low PIR.

Association between LE8 score and PRISm

The associations between PRISm and LE8 score, health behavior score, and health factor score are presented in Table 2. Treating the LE8 score as a continuous variable, revealed that each unit increase in the LE8 score was associated with a reduction in the odds of PRISm across all models [Model 1: OR = 0.96, 95% CI (0.95, 0.97), $p < 0.001$; Model 2: OR = 0.96, 95% CI (0.95, 0.97), $p < 0.001$; Model 3: OR = 0.97, 95% CI (0.96, 0.98), $p < 0.001$]. Additionally, a 10-point increase in LE8 score showed ORs of 0.67(0.60, 0.74), 0.68(0.60, 0.75), and 0.73(0.64, 0.83) for Model 1, 2, and 3, respectively. The trends persisted when the analysis was conducted with the LE8 score as a categorical variable. Compared to the low LE8 score group, the moderate LE8 score group showed a significantly OR for PRISm [0.42, 95% CI (0.27, 0.64), $p < 0.001$], as did the high LE8 score group [0.18, 95% CI (0.10, 0.32), $p < 0.001$].

For the health behavior score, there was a significant association with PRISm across all models: Model 1 [OR = 0.98, 95% CI (0.97, 0.99), $p = 0.002$], Model 2 [OR = 0.98, 95% CI (0.97, 0.99), $p = 0.001$], and Model 3 [OR = 0.98, 95% CI (0.97, 1.00), $p = 0.027$]. Additionally, there was a significant association between the health factor score and PRISm [Model 1: OR = 0.98, 95% CI (0.97, 0.98), $p < 0.001$; Model 2: OR = 0.98, 95% CI (0.97, 0.98), $p < 0.001$; Model 3: OR = 0.98, 95% CI (0.98, 0.99), $p < 0.001$]. Moreover, within the health behavior score group, only in Model (1, 2) did the moderate and high score groups exhibit a significant association with PRISm compared to the low score group. In the health factor score group, the moderate and high score groups exhibited a significant association with PRISm across all models.

The associations between PRISm and each component of LE8 score was shown in Supplementary Table S3. Only the BMI and glucose score groups showed a significant association with PRISm across all models.

The linear relationship between the LE8 score with PRISm

A restricted cubic spline model was used to define the nonlinear relationship between the LE8 score and PRISm, as shown in Fig. 2. A linear relationship was observed between the LE8 score and PRISm (p overall = 0.000, p for

Variables	Total (n = 2,869, Weighted%)	PRISm	Normal	P-value
		N = 316	N = 2,553	
Age, years(S.E)	44.09(0.44)	47.61(1.03)	43.78(0.51)	0.002
Sex, n(%)				0.180
Female	1403(48.68)	169(52.48)	1234(48.35)	
Male	1466(51.32)	147(47.52)	1319(51.65)	
Race, n(%)				< 0.001
Non-Hispanic white	1350(71.86)	82(47.20)	1268(74.03)	
Non-Hispanic black	497(9.25)	152(33.24)	345(7.14)	
Mexican American	482(8.09)	18(3.01)	464(8.54)	
Other	540(10.80)	64(16.55)	476(10.29)	
Marital status, n(%)				0.010
Married/ With partner	1826(66.95)	185(61.68)	1641(67.41)	
Never married	566(19.65)	64(18.81)	502(19.73)	
Divorced/ Separated	362(10.62)	48(12.96)	314(10.41)	
Widowed	115(2.78)	19(6.55)	96(2.45)	
Education, n(%)				< 0.001
High school/GED/AA	1268(43.94)	157(48.44)	1111(43.55)	
College and above	840(36.95)	66(23.07)	774(38.17)	
≤ 12th grade	761(19.11)	93(28.49)	668(18.28)	
PIR, n(S.E)	3.19(0.06)	2.75(0.14)	3.22(0.06)	0.001
PIR status, n(%)				0.020
< 1	512(12.10)	57(14.42)	455(11.89)	
1–4	1497(47.56)	179(56.01)	1318(46.82)	
> 4	860(40.34)	80(29.57)	780(41.29)	
BMI, n(S.E)	27.97(0.18)	30.18(0.44)	27.78(0.18)	< 0.001
BMI status, n(%)				< 0.001
Under & health weight	893(34.22)	78(26.19)	815(34.92)	
Overweight	1025(35.72)	103(28.68)	922(36.34)	
Obese	951(30.06)	135(45.13)	816(28.74)	
Smoking status, n(%)				0.260
Never	1679(58.31)	180(54.42)	1499(58.65)	
Former	686(25.23)	66(24.59)	620(25.28)	
Current	504(16.46)	70(20.99)	434(16.06)	
Alcohol user, n(%)				< 0.001
Mild	993(39.01)	95(36.60)	898(40.78)	
Moderate	445(16.54)	49(15.86)	396(17.27)	
Heavy	619(21.57)	55(15.07)	564(23.01)	
Former	403(11.85)	50(15.69)	353(11.98)	
Never	288(7.48)	57(16.78)	231(6.96)	
Hypertension, n(%)				0.002
No	1904(69.89)	174(58.41)	1730(70.90)	
Yes	965(30.11)	142(41.59)	823(29.10)	
Diabetes, n(%)				< 0.001
DM	453(10.99)	90(26.35)	363(9.74)	
IFG	230(7.97)	26(9.86)	204(7.88)	
IGT	245(7.53)	28(7.15)	217(7.64)	
No	1915(72.64)	169(56.64)	1746(74.74)	
LE8 score, n(S.E)	70.54(0.45)	64.02(0.98)	71.11(0.44)	< 0.001
Health behavior score, n(S.E)	71.40(0.41)	67.76(1.17)	71.72(0.42)	0.002
HEI-2015 diet score, n(S.E)	39.57(0.45)	36.95(1.20)	39.80(0.48)	0.040
PA score, n(S.E)	93.83(0.35)	91.00(1.41)	94.08(0.36)	0.020
Smoke score, n(S.E)	67.22(1.13)	62.81(3.62)	67.61(1.12)	0.190
Sleep score, n(S.E)	84.99(0.56)	80.27(1.42)	85.41(0.59)	0.002
Health factor score, n(S.E)	69.67(0.66)	60.28(1.54)	70.50(0.65)	< 0.001
BMI score, n(S.E)	65.98(1.03)	54.98(2.20)	66.95(1.01)	< 0.001
Non-HDL score, n(S.E)	64.78(0.94)	62.08(2.04)	65.01(0.97)	0.170
Continued				

Variables	Total (n= 2,869, Weighted%)	PRISm	Normal	P-value
		N= 316	N= 2,553	
Glucose score, n(S.E)	72.27(0.97)	57.26(2.85)	73.59(0.96)	< 0.001
BP score, n(S.E)	75.65(0.93)	66.79(2.10)	76.43(0.98)	< 0.001
LE8 score level, n(%)				< 0.001
Low	252(6.87)	54(17.49)	198(5.94)	
Moderate	1959(67.19)	230(72.34)	1729(66.74)	
High	658(25.94)	32(10.18)	626(27.32)	

Table 1. Characteristic of all study participants. *PRISm* preserved ratio impaired spirometry, *AA* Associate of Arts, *GED* general educational development, *BMI* body mass index, *PIR* Poverty-to-income ratio, *DM* diabetes mellitus, *IFG* compromised impaired fasting glycemia, *IGT* impaired glucose tolerance, *LE8* life’s essential 8.

Variables	Model 1 OR (95% CI)	P value	Model 2 OR (95% CI)	P value	Model 3 OR (95% CI)	P value
LE8 score	0.96(0.95,0.97)	< 0.001	0.96(0.95,0.97)	< 0.001	0.97(0.96,0.98)	< 0.001
LE8 score level						
Low (0–49)	Ref		Ref		Ref	
Moderate (50–79)	0.37(0.24,0.57)	< 0.001	0.38(0.25,0.57)	< 0.001	0.42(0.27,0.64)	< 0.001
High (80–100)	0.13(0.08,0.20)	< 0.001	0.13(0.08,0.21)	< 0.001	0.18(0.11,0.32)	< 0.001
Per 10-point increase	0.67(0.60,0.74)	< 0.001	0.68(0.60,0.75)	< 0.001	0.73(0.64,0.83)	< 0.001
Health behavior score	0.98(0.97,0.99)	0.002	0.98(0.97,0.99)	0.001	0.98(0.97,1.00)	0.027
Health behavior score level						
Low (0–49)	Ref		Ref		Ref	
Moderate (50–79)	0.55(0.31,1.00)	0.051	0.52(0.29,0.95)	0.033	0.60(0.30,1.20)	0.145
High (80–100)	0.44(0.25,0.77)	0.005	0.42(0.24,0.74)	0.004	0.52(0.26,1.01)	0.053
Per 10-point increase	0.83(0.73,0.93)	0.002	0.81(0.72,0.92)	0.001	0.85(0.73,0.98)	0.027
Health factor score	0.98(0.97,0.98)	< 0.001	0.98(0.97,0.98)	< 0.001	0.98(0.98,0.99)	< 0.001
Health factor score level						
Low (0–49)	Ref		Ref		Ref	
Moderate (50–79)	0.46(0.31,0.68)	< 0.001	0.48 (0.33,0.70)	< 0.001	0.55(0.37,0.82)	0.005
High (80–100)	0.33(0.23,0.46)	< 0.001	0.36(0.26,0.50)	< 0.001	0.51(0.35,0.75)	0.001
Per 10-point increase	0.80(0.75,0.85)	< 0.001	0.80(0.76,0.85)	< 0.001	0.85(0.80,0.91)	< 0.001

Table 2. Weighted ORs (95% CIs) for the association between LE8 score and PRISm. *Ref* reference, *OR* odds ratio, *CI* confidence interval, *LE8* life’s essential 8, *PRISm* preserved ratio impaired spirometry. Model1: unadjusted model. Model2: adjustment for age, sex. Model3: adjustment for age, gender, race, marital status, education, alcohol consumption, PIR.

nonlinear = 0.881) (Fig. 2A). In addition, there was significant association between the health behavior score (p overall = 0.009, p for nonlinear = 0.835) (Fig. 2B), health factor score (p overall < 0.001, p for nonlinear = 0.233) (Fig. 2C), and PRISm, the restricted cubic spline model suggested a linear relationship.

Subgroup analysis stratified by covariates

The subgroup analysis investigated the association between the LE8 score and PRISm, as presented in Fig. 3. Significant effect modification was found between the LE8 score and PIR status on PRISm risk (interaction *p* < 0.05). The association between a higher LE8 score and lower odds of PRISm was more pronounced among individuals with higher income.

Discussion

In this nationally representative cross-sectional study of 2,869 participants from 2007 to 2012 in NHANES, we revealed a negative correlation between the LE8 score, its health factor score, and behavior score with PRISm among individuals. We found a notable linear dose-response relationship between the LE8 score, its health behavior score, and health factor score with PRISm. This study indicated that higher LE8 score levels correspond to a reduced risk of PRISm. Furthermore, subgroup analyses indicated enhanced inverse LE8-PRISm associations among individuals with higher income.

Fan et al.¹⁹ explored the relationship between the American Heart Association’s “Life’s Simple 7” (LS7) metrics and lung function in both COPD and non-COPD subjects, finding that a higher LS7 score is linked with better lung function. Compared to LS7, LE8 not only incorporates sleep health as a pivotal factor but also enhances the

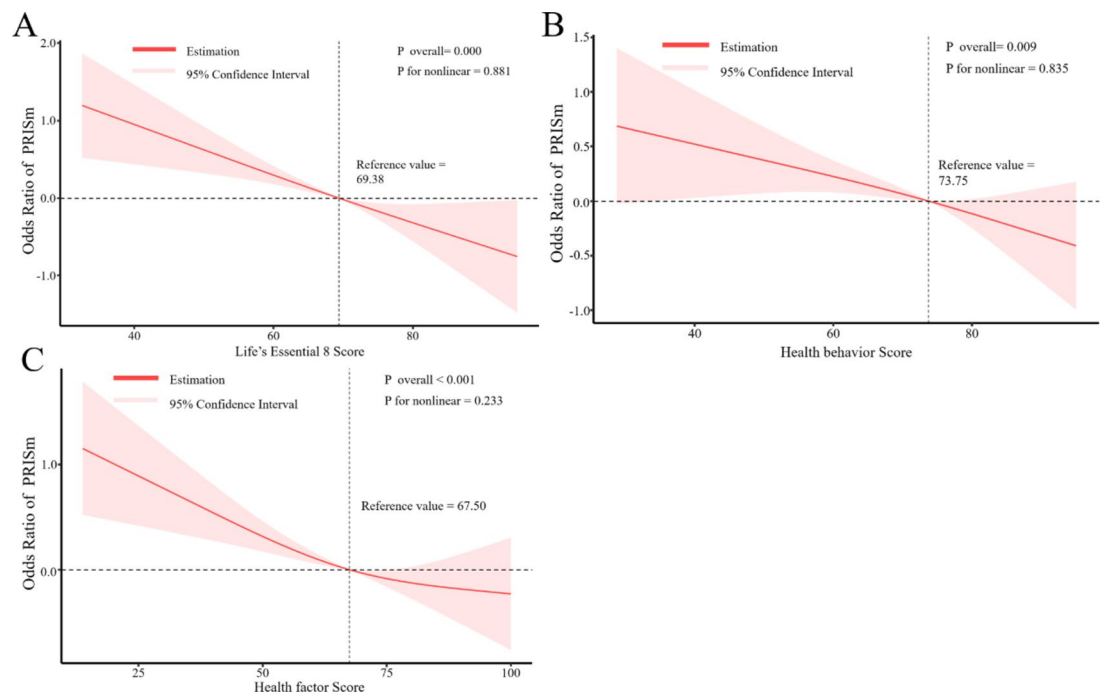


Fig. 2. The linear association between LE8 and its sub-scores with PRISm. (A) the relationship between LE8 score and PRISm; (B) the relationship between health behavior score and PRISm; (C) the relationship between health factor score and PRISm. Adjusted for age, gender, race, marital status, education, alcohol consumption, PIR.

algorithm, reevaluating cardiovascular health on a more continuous scale^{18,31}. Our study is first to examine the association between the LE8 score and PRISm, aiming to offer preventive strategies targeting PRISm.

PRISm is a newly discovered phenotype of lung function impairment that can transition to obstructive or restrictive spirometry over time. It also increased the risks of multiple adverse outcomes, including respiratory symptoms, hypertension, diabetes, cardiovascular disease, frailty, and all-cause mortality^{6,12,14,25,32–34}. Our study revealed a significant negative correlation between LE8 score, its health factor score, and behavior score with PRISm. Additionally, we discovered a linear pattern in the associations between the LE8 score, its health factor score, and behavior score with PRISm. The mechanisms underlying the association between the LE8 score and PRISm may reflect the composite metric's ability to capture metabolic disturbances and unhealthy behaviors implicated in PRISm. This highlights the potential for interventions focused on improving health behaviors and factors, as measured by the LE8 score, to reduce the risk of PRISm.

Smoking is a crucial etiological factor in the development of PRISm, as it can induce oxidative stress, inflammation, an imbalance between protease and anti-protease activity, and small airway disease^{10,35,36}. These effects can directly damage lung function and increase the risk of developing PRISm^{36,37}. Higher diet quality has been linked to a reduced prevalence of restrictive lung disease, COPD, and improved FEV₁ and FVC^{38–40}. The mechanism connecting diet and lung function is hypothesized to involve the antioxidant properties of certain nutrients such as vitamins A, C, and E, beta-carotene, and omega-3 fatty acids^{41–43}. Maintaining a healthy diet pattern is necessary for individuals with PRISm. Previous studies have indicated that healthy dietary behaviors can protect lung function and prevent or improve COPD^{28,44}. Additionally, several studies have demonstrated positive associations between physical activity and lung function, highlighting the beneficial effects of physical activity on lung function^{45–49}. A UK biobank cohort study found that lower physical grip strength and potentially reduced cardiovascular fitness over time are associated with accelerated lung function decline⁵⁰. Moreover, a previous study indicated that PRISm affects a significant portion of general population, with more than half being physically inactive⁵¹. It found that adherence to a minimum of 150 min per week of physical activity was associated with a 2/3 reduction in all-cause mortality. Therefore, recommending appropriate physical activity to individuals with PRISm may yield significant health benefits. Sleep plays a crucial role in maintaining overall health. Sleep quality has been shown to be a predictor of the severity of day times symptoms, COPD-hospitalization, mortality, and health-related quality of life in COPD subjects^{52,53}. COPD subjects frequently report impaired sleep, which can exacerbate the complex effects on the respiratory systems^{54,55}. A cross-section study found that both short and long sleep durations were significantly associated with reduced lung function⁵⁶. PRISm is perceived as a transitional state to COPD, individuals with PRISm may be particularly vulnerable to developing COPD. Maintaining healthy behaviors may improve respiratory symptoms and decrease the risk of developing COPD.

The factors contributing to PRISm are multifaceted, including smoking, an abnormal BMI, air pollution, age, female sex, and a history of asthma^{36,37,57–59}. Additionally, PRISm is significantly associated with a myriad of

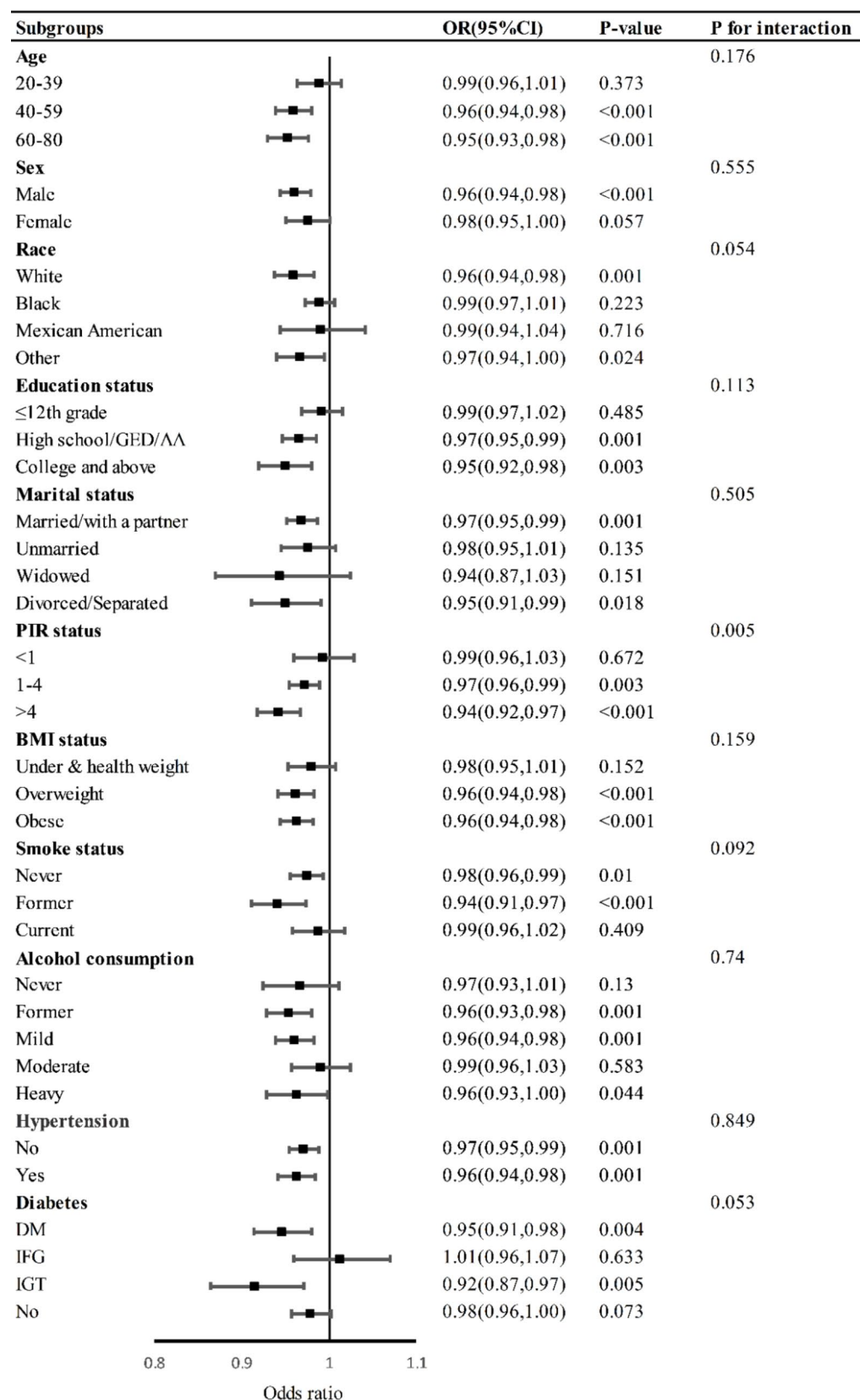


Fig. 3. Subgroup analysis for association between LE8 score and PRISm. Note: Adjusted for age, sex, race, education status, marital status, alcohol consumption, PIR, except for subgroup variable.

health concerns, including advanced age, obesity, hypertension, and diabetes^{14,32}. Furthermore, lung function is closely linked to various physiological and pathological states.

An abnormal BMI (underweight and severely obese) is a significant factor that increases the risk of PRISm^{57,58}. Obesity directly alters the mechanical properties of lungs and chest wall through fat accumulation in the mediastinum and within the abdominal and thoracic cavities, which cause pleural pressure to increase and functional residual capacity to decrease^{60,61}. Both FEV₁ and FVC decrease linearly with increasing obesity, while the FEV₁/FVC ratio remains unchanged^{60,62,63}. In addition to mechanical factors, adipocytes and infiltrating macrophages in obese individuals produces inflammatory cytokines and hormones that can contribute to a poor lung function^{63–65}. Epidemiological and clinical studies consistently indicated that diabetes and various anomaly indices (such as fasting insulin, fasting glucose, and hemoglobin A1c levels) have long been associated with poor lung function^{66–69}, potentially increasing the risk for PRISm. In this study, we observed that in the DM subgroup, the association between LE8 score and PRISm was significantly negative in IGT group. Dyslipidemia may influence respiratory disease and lung function⁶³. A previous study explored the relationship between lipids and lung function, finding that low-density lipoprotein was negatively associated with FEV₁, while high-density lipoprotein was positively associated with FEV₁⁷⁰. COPD and cardiovascular diseases frequently coexist⁷¹. Previous studies have identified an association between lung function and hypertension^{72–75}. However, whether hypertension can cause a reduction in lung function and trigger PRISm remains unknown.

As a composite score, LE8 indicates the overall effect of LE8 metrics in association with PRISm. Elevated LE8 scores may reduce the risk of PRISm by enhancing health behaviors and factors. We observed linear patterns in the associations between the LE8 score in PRISm. The management of PRISm is currently lacking, and lifestyle intervention may be an important cornerstone for its management. LE8 is a comprehensive and easy-to-use tool for assessing health behaviors and factors, and it could extend to monitoring and promoting a new paradigm focusing on pulmonary health. Our study suggests that adherence to ideal LE8 metrics could be an effective strategy for the prevention and management of PRISm. In addition, individuals with mild PRISm are more likely to revert to normal lung function, while those with severe PRISm tend to progress to more advanced stage of COPD^{9,15}. Whether adherence to LE8 health metrics changes the outcomes for individuals with PRISm is unknown. Therefore, prospective studies should be conducted to validate this.

This study exhibits several strengths. Firstly, it is the first investigation of the relationship between LE8 and PRISm, presenting new evidence supporting the role of LE8 in the prevention and management of PRISm. Secondly, the use of a nationally representative sample of American adults enhances the generalizability of the study findings to a broader population.

Nonetheless, this study also has several limitations. Firstly, due to the inherent nature of the cross-sectional design, we could not make causal inferences between LE8 and PRISm. Consequently, large-scale prospective studies are essential to establish causality. Secondly, self-reported health behaviors indicators may introduce reporting biases. Thirdly, we used pre-bronchodilator spirometry values because of sample size limitations for post-bronchodilator data. While some research has found a non-significant discrepancy between the use of pre-bronchodilator and post-bronchodilator values for diagnosing air obstruction^{76,77}, GOLD standards recommend the use of post-bronchodilator data.

Conclusions

Our findings indicated a robust inverse association between the LE8 score and PRISm. Specifically, a higher LE8 score is associated with a reduced likelihood of PRISm. Additionally, an independent linear association between LE8 score, its health factor score, and behavior score with PRISm were observed. These findings underscore the significance of adhering to LE8 health metrics and its potential utility in the prevention and management of PRISm. Future prospective investigations should explore the causal relationship and whether PRISm could be prevented through the promotion of healthy behaviors and factors.

Data availability

The datasets used and analysed during the current study are available from: <http://www.cdc.gov/nchs/nhanes.htm>.

Received: 8 August 2024; Accepted: 12 February 2025

Published online: 10 March 2025

References

- Christenson, S. A., Smith, B. M., Bafadhel, M. & Putcha, N. Chronic obstructive pulmonary disease. *Lancet Lond. Engl.* **399**, 2227–2242 (2022).
- Agusti, A. et al. Global Initiative for Chronic Obstructive Lung Disease 2023 Report: GOLD Executive Summary. *Eur. Respir. J.* **61**, 2300239 (2023).
- Wan, E. S. The clinical spectrum of PRISm. *Am. J. Respir. Crit. Care Med.* **206**, 524–525 (2022).
- Wan, E. S. et al. Epidemiology, genetics, and subtyping of preserved ratio impaired spirometry (PRISm) in COPDGene. *Respir. Res.* **15**, 89 (2014).
- Wan, E. S. et al. Longitudinal phenotypes and mortality in preserved ratio impaired spirometry in the COPDGene Study. *Am. J. Respir. Crit. Care Med.* **198**, 1397–1405 (2018).
- He, D. et al. Preserved ratio impaired spirometry and COPD accelerate Frailty Progression: evidence from a prospective cohort study. *Chest* **165**, 573–582 (2024).
- Washio, Y. et al. Risks of mortality and airflow limitation in Japanese individuals with preserved ratio impaired spirometry. *Am. J. Respir. Crit. Care Med.* **206**, 563–572 (2022).
- Guerra, S. et al. Morbidity and mortality associated with the restrictive spirometric pattern: a longitudinal study. *Thorax* **65**, 499–504 (2010).

9. He, D. et al. Different risks of mortality and longitudinal transition trajectories in new potential subtypes of the preserved ratio impaired spirometry: evidence from the English Longitudinal Study of Aging. *Front. Med.* **8**, 755855 (2021).
10. Marott, J. L., Ingebrigtsen, T. S., Çolak, Y., Vestbo, J. & Lange, P. Trajectory of preserved ratio impaired spirometry: natural history and long-term prognosis. *Am. J. Respir. Crit. Care Med.* **204**, 910–920 (2021).
11. Wan, E. S. et al. Significant spirometric transitions and preserved ratio impaired Spirometry among ever smokers. *Chest* **161**, 651–661 (2022).
12. Wijnant, S. R. A. et al. Trajectory and mortality of preserved ratio impaired spirometry: the Rotterdam Study. *Eur. Respir. J.* **55**, 1901217 (2020).
13. Heo, I. R., Kim, H. C. & Kim, T. H. Health-Related Quality of Life and related factors in persons with preserved ratio impaired spirometry: data from the Korea National Health and Nutrition Examination Survey. *Med. Kaunas Lith.* **57**, 4 (2020).
14. Wan, E. S. et al. Association between preserved ratio impaired spirometry and clinical outcomes in US adults. *JAMA* **326**, 2287–2298 (2021).
15. Huang, J. et al. Preserved ratio impaired spirometry (PRISm): A Global Epidemiological Overview, Radiographic characteristics, Comorbid associations, and differentiation from Chronic Obstructive Pulmonary Disease. *Int. J. Chron. Obstruct Pulmon Dis.* **19**, 753–764 (2024).
16. Yang, S., Liao, G. & Tse, L. A. Association of preserved ratio impaired spirometry with mortality: a systematic review and meta-analysis. *Eur. Respir. Rev.* **32**, 230135 (2023).
17. Zheng, J. et al. Preserved ratio impaired Spirometry in Relationship to Cardiovascular outcomes: a large prospective cohort study. *Chest* **163**, 610–623 (2023).
18. Lloyd-Jones, D. M. et al. Life's essential 8: updating and enhancing the American Heart Association's construct of Cardiovascular Health: a Presidential Advisory from the American Heart Association. *Circulation* **146**, e18–43 (2022).
19. Fan, W., Lee, H., Lee, A., Kieu, C. & Wong, N. D. Association of lung function and chronic obstructive pulmonary disease with American Heart Association's life's simple 7 cardiovascular health metrics. *Respir. Med.* **131**, 85–93 (2017).
20. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the global burden of Disease Study 2019. *Lancet Lond. Engl.* **396**, 1204–1222 (2020).
21. Krebs-Smith, S. M. et al. Update of the healthy eating index: HEI-2015. *J. Acad. Nutr. Diet.* **118**, 1591–1602 (2018).
22. Wang, L. et al. Association between dietary live microbe intake and Life's essential 8 in US adults: a cross-sectional study of NHANES 2005–2018. *Front. Nutr.* **11**, 1340028 (2024).
23. Shen, R. & Zou, T. The association between cardiovascular health and depression: results from the 2007–2020 NHANES. *Psychiatry Res.* **331**, 115663 (2024).
24. Hankinson, J. L., Odencrantz, J. R. & Fedan, K. B. Spirometric reference values from a sample of the General U.S. Population. *Am. J. Respir. Crit. Care Med.* **159**, 179–187 (1999).
25. Cadham, C. J. et al. The prevalence and mortality risks of PRISm and COPD in the United States from NHANES 2007–2012. *Respir. Res.* **25**, 208 (2024).
26. Vollmer, W. M. et al. Comparison of spirometry criteria for the diagnosis of COPD: results from the BOLD study. *Eur. Respir. J.* **34**, 588–597 (2009).
27. Ford, E. S. et al. Trends in the prevalence of obstructive and restrictive lung function among adults in the United States: findings from the National Health and Nutrition Examination surveys from 1988–1994 to 2007–2010. *Chest* **143**, 1395–1406 (2013).
28. Chen, C., Yang, T. & Wang, C. The Dietary Inflammatory Index and early COPD: results from the National Health and Nutrition Examination Survey. *Nutrients* **14**, 2841 (2022).
29. Tang, M., Liu, M., Zhang, Y. & Xie, R. Association of family income to poverty ratio and vibration-controlled transient elastography quantified degree of hepatic steatosis in U.S. adolescents. *Front. Endocrinol.* **14**, 1160625 (2023).
30. Rattan, P. et al. Inverse Association of Telomere length with Liver Disease and Mortality in the US Population. *Hepatol. Commun.* **6**, 399–410 (2021).
31. Liu, P. et al. Lowering the risk of hyperuricemia and gout is associated with ideal cardiovascular health. *J. Health Popul. Nutr.* **43**, 167 (2024).
32. Higbee, D. H., Granell, R., Davey Smith, G. & Dodd, J. W. Prevalence, risk factors, and clinical implications of preserved ratio impaired spirometry: a UK Biobank cohort analysis. *Lancet Respir. Med.* **10**, 149–157 (2022).
33. Kogo, M. et al. Longitudinal Changes and Association of Respiratory Symptoms with preserved ratio impaired spirometry (PRISm): the Nagahama Study. *Ann. Am. Thorac. Soc.* **20**, 1578–1586 (2023).
34. Kadier, K. et al. Maintaining ideal cardiovascular health is associated with higher serum anti-aging protein klotho in the middle-aged and older populations. *J. Nutr. Health Aging.* **28**, 100224 (2024).
35. Lei, J. et al. Heterogeneities and impact profiles of early chronic obstructive pulmonary disease status: findings from the China Pulmonary Health Study. *Lancet Reg. Health West. Pac.* **45**, 101021 (2024).
36. Shiraishi, Y. et al. The prevalence and physiological impacts of centrilobular and paraseptal emphysema on computed tomography in smokers with preserved ratio impaired spirometry. *ERJ Open. Res.* **8**, 00063–2022 (2022).
37. Lugg, S. T., Scott, A., Parekh, D., Naidu, B. & Thickett, D. R. Cigarette smoke exposure and alveolar macrophages: mechanisms for lung disease. *Thorax* **77**, 94–101 (2022).
38. Ducharme-Smith, K. et al. Lung function, COPD and Alternative Healthy Eating Index in US adults. *ERJ Open. Res.* **7**, 00927–2020 (2021).
39. Garcia-Larsen, V. et al. Dietary intake of flavonoids and ventilatory function in European adults: a GA²LEN study. *Nutrients* **10**, 95 (2018).
40. Scoditti, E., Massaro, M., Garbarino, S. & Toraldo, D. M. Role of Diet in Chronic Obstructive Pulmonary Disease Prevention and Treatment. *Nutrients* **11**, 1357 (2019).
41. Hanson, C., Rutten, E. P. A., Wouters, E. F. M. & Rennard, S. Diet and vitamin D as risk factors for lung impairment and COPD. *Transl. Res. J. Lab. Clin. Med.* **162**, 219–236 (2013).
42. Hu, G. & Cassano, P. A. Antioxidant nutrients and pulmonary function: the Third National Health and Nutrition Examination Survey (NHANES III). *Am. J. Epidemiol.* **151**, 975–981 (2000).
43. Kelly, Y., Sacker, A. & Marmot, M. Nutrition and respiratory health in adults: findings from the health survey for Scotland. *Eur. Respir. J.* **21**, 664–671 (2003).
44. Catalin, R-E. et al. Mediterranean Diet and lung function in adults current smokers: a cross-sectional analysis in the MEDISTAR Project. *Nutrients* **15**, 1272 (2023).
45. Bédard, A. et al. Physical activity and lung function—cause or consequence? *PLoS ONE*. **15**, e0237769 (2020).
46. Garcia-Aymerich, J., Lange, P., Benet, M., Schnohr, P. & Antó, J. M. Regular physical activity modifies smoking-related lung function decline and reduces risk of chronic obstructive pulmonary disease: a population-based cohort study. *Am. J. Respir. Crit. Care Med.* **175**, 458–463 (2007).
47. Hopkinson, N. S. & Polkey, M. I. Does physical inactivity cause chronic obstructive pulmonary disease? *Clin. Sci. Lond. Engl.* **1979**, 118, 565–572 (2010).
48. Luzak, A. et al. Association of physical activity with lung function in lung-healthy German adults: results from the KORA FF4 study. *BMC Pulm. Med.* **17**, 215 (2017).
49. Pelkonen, M. et al. Delaying decline in pulmonary function with physical activity: a 25-year follow-up. *Am. J. Respir. Crit. Care Med.* **168**, 494–499 (2003).

50. Li, L. K. et al. The longitudinal association between physical activity, strength and fitness, and lung function: a UK Biobank cohort study. *Respir Med.* **220**, 107476 (2023).
51. Shu, C.-C., Tsai, M. K., Lee, J. H., Su, T.-C. & Wen, C. P. Mortality risk in patients with preserved ratio impaired spirometry: assessing the role of physical activity. *QJM Mon J. Assoc. Physicians.* **117**, 436–444 (2024).
52. Nunes, D. M. et al. Impaired sleep reduces quality of life in chronic obstructive pulmonary disease. *Lung* **187**, 159–163 (2009).
53. Omachi, T. A. et al. Disturbed sleep among COPD patients is longitudinally associated with mortality and adverse COPD outcomes. *Sleep. Med.* **13**, 476–483 (2012).
54. Marques, R. D. et al. Sleep quality and architecture in COPD: the relationship with lung function abnormalities. *J. Bras. Pneumol.* **47**, e20200612 (2021).
55. McNicholas, W. T. Impact of sleep in COPD. *Chest* **117**, 48S–53S (2000).
56. Yang, G. et al. Sleep duration, current asthma, and lung function in a nationwide study of U.S. adults. *Am. J. Respir. Crit. Care Med.* **200**, 926–929 (2019).
57. Tang, X. et al. The relationship between BMI and lung function in populations with different characteristics: a cross-sectional study based on the enjoying breathing program in China. *Int. J. Chron. Obstruct Pulmon Dis.* **17**, 2677–2692 (2022).
58. Grigsby, M. R. et al. Low body Mass Index is Associated with higher odds of COPD and lower lung function in low- and Middle-Income Countries. *COPD* **16**, 58–65 (2019).
59. Godfrey, M. S. & Jankowich, M. D. The vital capacity is vital: epidemiology and clinical significance of the restrictive spirometry pattern. *Chest* **149**, 238–251 (2016).
60. Jones, R. L. & Nzekwu, M.-M.-U. The effects of body mass index on lung volumes. *Chest* **130**, 827–833 (2006).
61. Watson, R. A. et al. Reduction of total lung capacity in obese men: comparison of total intrathoracic and gas volumes. *J. Appl. Physiol. Bethesda Md.* **1985**, **108**, 1605–1612 (2010).
62. Forno, E., Han, Y.-Y., Mullen, J. & Celedón, J. C. Overweight, obesity, and lung function in children and Adults-A Meta-analysis. *J. Allergy Clin. Immunol. Pract.* **6**, 570–581e10 (2018).
63. Peters, U., Suratt, B. T., Bates, J. H. T. & Dixon, A. E. Beyond BMI. *Chest* **153**, 702–709 (2018).
64. Hegewald, M. J. Impact of obesity on pulmonary function: current understanding and knowledge gaps. *Curr. Opin. Pulm Med.* **27**, 132 (2021).
65. Kawai, T., Autieri, M. V. & Scalia, R. Adipose tissue inflammation and metabolic dysfunction in obesity. *Am. J. Physiol. Cell. Physiol.* **320**, C375–C391 (2021).
66. Klein, O. L., Krishnan, J. A., Glick, S. & Smith, L. J. Systematic review of the association between lung function and type 2 diabetes mellitus. *Diabet. Med. J. Br. Diabet. Assoc.* **27**, 977–987 (2010).
67. Walter, R. E., Beiser, A., Givelber, R. J., O'Connor, G. T. & Gottlieb, D. J. Association between glycemic state and lung function: the Framingham Heart Study. *Am. J. Respir. Crit. Care Med.* **167**, 911–916 (2003).
68. Zaigham, S., Nilsson, P. M., Wollmer, P. & Engström, G. The temporal relationship between poor lung function and the risk of diabetes. *BMC Pulm Med.* **16**, 75 (2016).
69. Zhu, J. et al. Genetic Correlation and Bidirectional Causal Association between Type 2 diabetes and pulmonary function. *Front. Endocrinol.* **12**, 777487 (2021).
70. Cirillo, D. J., Agrawal, Y. & Cassano, P. A. Lipids and pulmonary function in the Third National Health and Nutrition Examination Survey. *Am. J. Epidemiol.* **155**, 842–848 (2002).
71. Ramalho, S. H. R. & Shah, A. M. Lung function and cardiovascular disease: a link. *Trends Cardiovasc. Med.* **31**, 93–98 (2021).
72. Engström, G., Hedblad, B., Valind, S. & Janzon, L. Increased incidence of myocardial infarction and stroke in hypertensive men with reduced lung function. *J. Hypertens.* **19**, 295–301 (2001).
73. Enright, P. L. et al. Reduced vital capacity in elderly persons with hypertension, coronary heart disease, or left ventricular hypertrophy. *Cardiovasc. Health Study Chest.* **107**, 28–35 (1995).
74. Margretardottir, O. B. et al. Hypertension, systemic inflammation and body weight in relation to lung function impairment-an epidemiological study. *COPD* **6**, 250–255 (2009).
75. Wu, Y. et al. Relationship between lung function and blood pressure in Chinese men and women of Beijing and Guangzhou. PRC-USA Cardiovascular and Cardiopulmonary Epidemiology Research Group. *Int. J. Epidemiol.* **27**, 49–56 (1998).
76. Smith, L. J. Postbronchodilator reference values: should they be the norm? *Am. J. Respir. Crit. Care Med.* **208**, 356–357 (2023).
77. Mannino, D. M., Diaz-Guzman, E. & Buist, S. Pre- and post-bronchodilator lung function as predictors of mortality in the Lung Health Study. *Respir Res.* **12**, 136 (2011).

Author contributions

Yuxin Lai and Xiaomei Zhang conceptualized and designed the study. Yuxin Lai performed the data and drafted the manuscript, Tianshu Yang contributed significantly to analysis and manuscript preparation. Mengqian Li contributed to collecting, analyzing, and interpreting the data. All authors read and approved the final version of the manuscript.

Funding

This research article was funded by the Beijing University of Chinese Medicine reveal the main project (2024-JYB-JBZD-009). The funding sources were not involved in study design or in the collection, analysis or interpretation of data or in the writing of the report or in the decision to submit the article for publication.

Declarations

Ethics approval and consent to participate

This study followed the institutional guidelines of the “Declaration of Helsinki Ethical Principles” for all procedures involving human participants and was approved by the National Center for Health Statistics Ethics Committee. (NHANES - NCHS Research Ethics Review Board Approval (cdc.gov))

Competing interests

The authors declare no competing interests.

Additional information

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1038/s41598-025-90381-w>.

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