Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

eTable 1.	Characteristics	of the Cohorts	Included in the	NHLBI Po	ooled Cohort	s Study
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Cohort	Sites	Enrollment year	Major eligibility criteria	Self-reported fixed categories for race or race/ethnicity	Censoring year for events / Median follow-up in years (Q1, Q3)
Atherosclerosis Risk in	Forsyth County, NC	1987-89	Age 45 -64 years	American Indian	2018
(ARIC)	Jackson, MS			Black East Asian/Pacific Islanders	26.5
	Minneapolis, MN	_		White	(18.5, 28.1)
	Washington County, MD	_			
Coronary Artery Risk	Chicago, IL	1985-1986	Age 18 – 30	Black	2018
Adults Study (CARDIA)	Oakland, CA	_	years	White	29.3
	Birmingham, AL				(28.2, 30.0)
	Minneapolis, MN				
Cardiovascular Health	Pittsburgh, PA	1989-90 1992-93 (African American	Age 65 + years	American Indian	2018
Study (CHS)	Winston-Salem, NC			Black East Asian/Pacific Islanders White	13.2
	Sacramento, CA				(7.8, 18.1)
	Hagerstown, MD	cohort)		Others	
Framingham Offspring Cohort (FOC)	Framingham, MA	1971–1975	Offspring of the Framingham heart Study- Original Cohort and their spouses	The FOC study was conducted in offspring of the original Framingham Heart Study cohort, which was exclusively non-Hispanic White race. No question separate question regarding race/ethnicity was administered at enrollment.	2018 21.8 (17.0, 26.2)
Health, Aging, and	Pittsburgh, PA	1997-98	Age 70 – 79	Black	2014
(Health ABC) Study	Memphis, TN		years	East Asian/Pacific Islanders	12.5
(·····································	San Francisco, CA			White	(7.8, 16.4)

Cohort	Sites	Enrollment year	Major eligibility criteria	Self-reported fixed categories for race or race/ethnicity	Censoring year for events / Median follow-up in years (Q1, Q3)
Hispanic Community Health Study/ Study of Latinos (HCHS/SOL)	San Diego, CA Chicago, IL Bronx, NY Miami, FL	2008-11	Age 18 – 74 years	Two separate questions were administered at the enrollment describing Hispanic/Latino heritage and race: 1. Hispanic/Latino heritage: i) Dominican/ Dominican descent ii) Central American/ Central American descent iii) Cuban/ Cuban descent iv) Mexican/ Mexican descent v) Puerto Rican/ Puerto Rican descent vi) South American/ South American descent vii) More than one heritage viii) Other 2) Race: i) White ii) Black or African American iii) Asian iv) American Indian/Alaskan Native v) Native Hawaiian/ Pacific Islander vi) More than one race For the purposes of this paper, all participants were considered to be of Hispanic/Latino race/ethnicity.	Data not available

Cohort	Sites	Enrollment year	Major eligibility criteria	Self-reported fixed categories for race or race/ethnicity	Censoring year for events / Median follow- up in years (Q1, Q3)
Jackson Heart Study (JHS)	Jackson, MS	2000-04	Age 20 – 95 years	The JHS was conducted exclusively in Black participants. No question separate question regarding race/ethnicity was administered at enrollment.	2016 13.8 (13.1, 14.5)
Multi-Ethnic Study of	Winston-Salem, NC	2000-02	Age 45-84 years	Black	2018
(MESA)	Upper Manhattan/Bronx, NY		required to be	East Asian (Chinese)/Pacific Islanders	11.2
	Los Angeles, CA		cardiovascular	White	(0.9, 12.1)
	Baltimore, MD		disease.		
	Chicago, IL	-			
	Minneapolis, MN	-			
Strong Heart Study	Phoenix, AZ	1989-91	Age 45 – 74	The SHS was conducted	2016
(SHS)	Southwestern OK	-	years	exclusively in participants of	10.2
	Western and central ND and SD			question separate question regarding race/ethnicity was administered at enrollment.	(10.5, 22.1)

eTable 2.	Classification	of Coronary	Heart Disease	(CHD) and	Respiratory	[•] Mortality	and Events
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Events	Definitions
CHD	Coronary heart disease (CHD) events data were available in all cohorts
hospitalizations/	excent HCHS/SOI
mortality	 In all cohorts, all potential clinical CHD events were reviewed and adjudicated by the physicians in the endpoints review committee.
	 Participants were diagnosed as having developed CHD if upon review of
	 the case the review committee agrees on one of the following definite manifestations of CHD: myocardial infarction, coronary insufficiency, angina pectoris, sudden death from CHD, non-sudden death from CHD. For hospitalized events, a diagnosis of definite, probable, or silent myocardial infarction (MI) was made by trained abstractors or physician reviewers based on presenting symptoms, cardiac enzymes tests, and electropartiegrame (ECCa)
	 Out-of-hospital deaths, including deaths in emergency room, were investigated by death certificates and by interview with next-of-kin, and guestionnaire completed by the patient's physicians.
	 Incident cases had at least one of the following newly developed manifestations: Fatal MI defined as definite MI within previous 4 weeks of death and no known non-atherosclerotic or non-cardiac atherosclerotic process or event that was likely to have been lethal.
	 Fatal coronary heart disease defined based on combinations of: (1) no known non-atherosclerotic or non-cardiac atherosclerotic process or event that was likely to have been lethal, (2) presence of chest pain, (3) history of CHD (MI or angina), and/or (4) ICD-9 codes410-414, 427.5, 429.2 and/or 799 from death certificate; definite and probable MI identified by chest pain, ECG and/or enzymes; silent MI identified by ECG.
Respiratory-related events	 Respiratory–related events were defined as hospitalizations or deaths for which chronic lower respiratory disease was classified as a primary, underlying, or contributing cause
	 Respiratory-related events data were available in 4 cohorts- ARIC, CHS, HABC, and MESA.
	 In three cohorts (ARIC, CHS, and MESA), events were classified using International Classification of Diseases, Ninth Revision (ICD-9) and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision (ICD-10) diagnosis codes for COPD [ICD-9: 496; ICD-10: J44], chronic bronchitis [ICD-9: 490-1; ICD-10; J40-2], and emphysema [ICD-9: 492; ICD-10: J43].
	 In FABC, events were prospectively ascertained and adjudicated for COPD hospitalizations.
Respiratory mortality	Respiratory mortality data were available in 6 cohorts- ARIC, CHS, CARDIA, HABC, MESA, and SHS.
	Respiratory disease–related deaths were defined by adjudication or administrative criteria (ICD-10: J1-J99).

eTable 3. Comparison Between Nonimputed and Imputed Datasets for All-Cause Mortality Analyses

	Non-imputed	Imputed
Ν	53,701	53,701
Age, mean (SD)	53.2 (15.8)	53.2 (15.8)
Missing	0	
Sex, N (%)		
Female	30,288 (56.4)	30,288 (56.4)
Male	23,413 (43.6)	23,413 (43.6)
Missing	0	
Race, N (%)		
American Indian	1,779 (3.3)	1,779 (3.3)
Black / African American	11,672 (21.7)	11,672 (21.7)
East Asian / Pacific Islander	659 (1.2)	659 (1.2)
Hispanic / Latino	14,597 (27.2)	14,597 (27.2)
Non-Hispanic White	24,979 (46.5)	24,979 (46.5)
Other ^a	15 (0.03)	15 (0.03)
Missing	0	
Education, N (%)		
Less than high school	7,806 (14.5)	7,856 (14.6)
High school	14,499 (27.0)	14,739 (27.5)
Some college	8,366 (15.6)	8,543 (15.9)
College or more	22,311 (41.6)	22,563 (42.0)
Missing	719 (1.3)	
Smoking Status, N (%)		
Never	25,956 (48.3)	26,048 (48.5)
Former	16,602 (30.9)	16,664 (31.0)
Current	10,953 (20.4)	10,989 (20.5)
Missing	190 (0.4)	
Pack-years among ever smokers, median (Q1, Q3)	15.6 (4.5, 34.0)	15.4 (4.5, 34.0)
Missing	943	
Body Mass Index, mean (SD)	28.1 (5.8)	28.1 (5.8)
Missing	105	
Co-morbidities, N (%)		
Hypertension		
Yes	22,516 (41.9)	22,528 (42.0)
No	31,167 (58.0)	31,173 (58.0)
Missing	18 (0.03)	

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	Non-imputed	Imputed
Diabetes ^c		
Yes	7,729 (14.4)	7,736 (14.4)
No	45,944 (85.6)	45,965 (85.6)
Missing	28 (0.1)	
Coronary heart disease ^d		
Yes	2,849 (5.3)	2,886 (5.4)
No	50,621 (94.3)	50,815 (94.6)
Missing	231 (0.4)	
Heart failure ^d		
Yes	3,107 (5.8)	3,133 (5.8)
No	50,425 (93.9)	50,568 (94.2)
Missing	169 (0.3)	
Stroke ^d		
Yes	859 (1.6)	945 (1.8)
No	49,970 (93.1)	52,756 (98.2)
Missing	2,872 (5.4)	
Asthma ^e		
Yes	4,521 (8.4)	4,567 (8.5)
No	48,838 (90.9)	49,134 (91.5)
Missing	342 (0.6)	
Chronic lower respiratory disease ^f		
Yes	6,042 (11.3)	6,059 (11.3)
No	47,474 (88.4)	47,642 (88.7)
Missing	185 (0.3)	
eGFR ^g , mean (SD)	83.3 (239.2)	82.7 (213.2)
Missing	11,179	
eGFR ^g categories, N (%)		
60 + mL/min/1.73m ²	35,465 (66.0)	44,669 (83.2)
30-59 mL/min/1.73m ²	6,773 (12.6)	8,686 (16.2)
<30 mL/min/1.73m ²	284 (0.5)	346 (0.6)
Missing	11,179 (20.8)	

^a "Other" race category includes self-identified "other" or self-identified mixed race individuals

^b Self-reported hypertension or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or use of antihypertensive medications

° Self-reported diabetes or fasting blood sugar level ≥ 126 mg/dl or use of oral hypoglycemic agents or insulin

^d Data on comorbidities at baseline, including coronary heart disease, congestive heart failure (HF), and stroke were selfreported. If missing, data was obtained from hospitalization records prior to baseline spirometry. In JHS, neither selfreported information on HF nor hospitalization records prior to baseline spirometry were available. Therefore, baseline HF was defined as HF events occurring within 5 years of baseline spirometry.

^e Self-reported physician diagnosed asthma

^fSelf-reported physician diagnosed chronic obstructive pulmonary disease, chronic bronchitis, or emphysema

⁹ For baseline eGFR, measurements obtained at baseline spirometry visit were used. If missing, first available eGFR measurements were used.

	Number of	Median follow-	10	DR/1,000 person-y	ears	Difference in IDR /1,000 person-years		
	events /	up in years		(95% CI) ^a		(95% CI)		
	at risk	(Q1, Q3)			p-value			
	(Cum. Inc.)		PRISm	Obstructive	Normal	PRISm vs Normal	PRISm vs Obstructive	
				Spirometry	Spirometry	Spirometry	Spirometry	
ARIC	14,843 /	26.5	30.4	25.2	17.8	12.6	5.2	
	6,928	(18.5, 28.1)	(27.8, 32.9)	(24.0, 26.4)	(17.2, 18.3)	(10.0, 15.2)	(2.4, 8.0)	
	(46.7)					<.001	<.001	
CARDIA	4,994 /	29.3	7.0	3.4	2.4	4.5	3.6	
	373	(28.2, 30.0)	(4.6, 9.4)	(1.9, 4.9)	(2.2, 2.7)	(2.1, 7)	(0.8, 6.4)	
	(7.5)					<.001	0.012	
CHS	4,812 /	13.2	72.9	69.2	51	21.9	3.7	
	3.786	(7.8, 18.1)	(64.8, 81)	(65.8, 72.5)	(48.5, 53.4)	(13.5, 30.4)	(-5, 12.5)	
	(78.7)					<.001	0.41	
FOC	3,894 /	21.8	23.6	14.7	12.7	10.9	9	
	1,131	(17.0, 26.2)	(19.1, 28.1)	(13, 16.3)	(11.7, 13.7)	(6.3, 15.5)	(4.2, 13.8)	
	(29.0)					<.001	<.001	
HABC	2,578 /	12.5	79.5	65.2	45	34.6	14.3	
	1,575	(7.8, 16.4)	(66.9, 92.2)	(59, 71.5)	(42.1, 47.9)	(21.6, 47.5)	(0.2, 28.4)	
	(61.1)					<.001	0.046	
JHS	2,498 /	13.8	14	13.4	6.7	7.4	0.7	
	261	(13.1, 14.5)	(9, 19.1)	(7.2, 19.5)	(5.7, 7.7)	(2.2, 12.6)	(-7.3, 8.7)	
	(10.4)					0.005	0.87	
MESA	4,463 /	11.2	22.8	18.1	12.8	10	4.7	
	632	(6.9, 12.1)	(17.2, 28.4)	(15.6, 20.5)	(11.3, 14.2)	(4.2, 15.8)	(-1.4, 10.8)	
	(14.2)					<.001	0.13	
SHS	1,754 /	19.2	55.7	39.2	31.6	24.1	16.5	
	975	(10.5, 22.1)	(35.5, 75.8)	(33.2, 45.2)	(29.1, 34)	(3.8, 44.4)	(-4.6, 37.5)	
	(55.6)					0.02	0.13	

eTable 4. Age and Smoking-Adjusted Absolute Incidence Rates for Respiratory Mortality, Stratified by Cohort

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

^a Using the direct method and the observed age distribution across all 9 cohorts, age- and smoking-adjusted absolute incidence density rates, and their differences were calculated per 1,000 person-years for each lung function category.

	Number of events / at risk	Median follow- up in years (Q1, Q3)	IDR/1,000 person-years (95% CI)ª		Difference in IDR /1,000 person-years (95% CI) p-value		
	(Cum. Inc.)		PRISm	Obstructive Spirometry	Normal Spirometry	PRISm vs Normal spirometry	PRISm vs Obstructive spirometry
ARIC	472 / 13,398 (3.5)	25.8 (17.7, 28.0)	1.6 (1.0, 2.2)	3.3 (2.9, 3.7)	0.7 (0.6, 0.8)	0.9 (0.3, 1.6) 0.003	-1.7 (-2.4, -1) <.001
CARDIA ^b	14 / 4,994 (0.3)	29.3 (28.2, 30.0)	-	0.5 (-0.2, 1.1)	0.1 (0, 0.1)	-	-
CHS	402 / 4,812 (8.4)	13.2 (7.8, 18.1)	7.1 (4.6, 9.7)	9.3 (8.1, 10.5)	3.7 (3.1, 4.4)	3.4 (0.7, 6.1) 0.012	-2.2 (-5.0, 0.6) 0.13
HABC	94 / 2,578 (3.7)	12.5 (7.8, 16.4)	5.6 (2.1, 9.1)	6.7 (4.9, 8.6)	1.3 (0.9, 1.8)	4.3 (0.7, 7.8) 0.019	-1.1 (-5.1, 2.8) 0.58
MESA	28 / 4,462 (0.6)	11.2 (6.9, 12.1)	1.6 (0.0, 3.2)	1.1 (0.5, 1.6)	0.3 (0.1, 0.6)	1.2 (-0.4, 2.9) 0.13	0.5 (-1.2, 2.2) 0.55
SHS	90 / 1,754 (5.1)	19.2 (10.5, 22.1)	2.7 (0.8, 4.6)	4.5 (2.7, 6.3)	2.7 (2, 3.5)	0.0 (-2.1, 2.0) 0.97	-1.8 (-4.4, 0.8) 0.17

eTable 5. Age and Smoking-Adjusted Absolute Incidence Rates for Respiratory Mortality, Stratified by Cohort

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

^a Using the direct method and the observed age distribution across all 9 cohorts, age- and smoking-adjusted absolute incidence density rates, and their differences were calculated per 1,000 person-years for each lung function category.

^b No respiratory deaths reported in individuals with PRISm.

	Number of events / at risk	Median follow- up in years (Q1, Q3)	1	DR/1,000 person-y (95% CI)ª	ears	Difference in ID (0R /1,000 person-years 95% CI) p-value
	(Cum. Inc.)		PRISm	Obstructive Spirometry	Normal Spirometry	PRISm vs Normal Spirometry	PRISm vs Obstructive Spirometry
ARIC	623 / 14,843 (4.2)	26.5 (18.5, 28.1)	4.1 (3.2, 5.1)	2.0 (1.7, 2.3)	1.6 (1.4, 1.7)	2.6 (1.6, 3.5) <.001	2.2 (1.2, 3.1) <.001
CARDIA	16 / 4,994 (0.3)	29.3 (28.2, 30.0)	0.7 (-0.1, 1.4)	0.5 (-0.1, 1.1)	0.1 (0.0, 0.1)	0.6 (-0.2, 1.4) 0.13	0.1 (-0.8, 1.1) 0.77
CHS	942 / 4,812 (19.6)	13.2 (7.8, 18.1)	17.5 (13.6, 21.4)	17.6 (15.9, 19.3)	12.6 (11.4, 13.8)	4.9 (0.8, 9.0) 0.02	-0.1 (-4.4, 4.2) 0.95
FOC	108 / 3,894 (2.8)	21.8 (17.0, 26.2)	3.5 (1.9, 5.2)	1.0 (0.6, 1.5)	1.3 (1.0, 1.6)	2.3 (0.6, 4.0) 0.01	2.5 (0.8, 4.2) 0.004
HABC	346 / 2,578 (13.4)	12.5 (7.8, 16.4)	17.8 (11.9, 23.8)	12.6 (9.9, 15.3)	10.4 (9.0, 11.7)	7.5 (1.4, 13.6) 0.02	5.2 (-1.3, 11.7) 0.12
JHS⁵	9 / 2,291 (0.4)	13.8 (13.1, 14.5)	0.8 (0.0, 1.6)	-	0.3 (0.0, 0.5)	0.5 (-0.3, 1.4) 0.21	-
MESA	68 / 4,462 (1.5)	11.2 (6.9, 12.1)	2.7 (0.8, 4.7)	1.5 (0.8, 2.1)	1.5 (1.0, 2.0)	1.2 (-0.8, 3.2) 0.24	1.2 (-0.8, 3.3) 0.24
SHS	240 / 17,54 (13.7)	19.2 (10.5, 22.1)	12.5 (8.6, 16.5)	8.0 (5.3, 10.8)	7.9 (6.7, 9.1)	4.6 (0.5, 8.8) 0.028	4.5 (-0.3, 9.3) 0.07

eTable 6. Age and Smoking-Adjusted Absolute Incidence Rates for Coronary Heart Disease (CHD) Mortality, Stratified by Cohort

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

^a Using the direct method and the observed age distribution across all 9 cohorts, age- and smoking-adjusted absolute incidence density rates, and their differences were calculated per 1,000 person-years for each lung function category.

^b No CHD deaths reported in individuals with Obstructive spirometry.

	Number of	Median	1[DR/1,000 person-	years	Difference in ID	R /1,000 person-years
	events /	follow-up in		(95% CI) ^a		(95% CI)	
	at risk	years				ļ p	o-value
	(Cum. Inc.)	(Q1, Q3)	PRISm	Obstructive	Normal	PRISm vs Normal	PRISm vs Obstructive
				Spirometry	Spirometry	Spirometry	Spirometry
ARIC	2,476 /	21.3	12.3	18.1	5.7	6.6	-5.9
	13,373	(13.5, 26.3)	(10.6, 13.9)	(17.1, 19.2)	(5.3, 6.1)	(4.9, 8.2)	(-7.8, -3.9)
	(18.5)					<.001	<.001
CHS	1,172 /	11.9	16.8	33.1	10.7	6.2	-16.2
	4,756	(6.4, 18.1)	(13, 20.6)	(30.7, 35.5)	(9.5, 11.8)	(2.2, 10.1)	(-20.8, -11.7)
	(24.6)					0.002	<.001
HABC	288 /	12.2	12.6	23.9	4.7	7.9	-11.3
	2,567	(7.0, 16.3)	(7.9, 17.4)	(20.1, 27.8)	(3.7, 5.7)	(3.1, 12.8)	(-17.4, -5.2)
	(11.2)					0.001	<.001
MESA	165 /	11.2	7.3	7.7	2.1	5.2	-0.4
	4,384	(6.7, 12.0)	(4.1, 10.5)	(6, 9.3)	(1.5, 2.6)	(2.0, 8.5)	(-4, 3.2)
	(3.8)					0.002	0.83

eTable 7. Age and Smoking-Adjusted Absolute Incidence Rates for Respiratory-Related Events, Stratified by Cohort

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

^a Using the direct method and the observed age distribution across all 9 cohorts, age- and smoking-adjusted absolute incidence density rates, and their differences were calculated per 1,000 person-years for each lung function category.

eTable 8. Age and Smoking-Adjusted Absolute Incidence Rates for Coronary Heart Disease (CHD)-Related Events, Stratified by Cohort

	Number of events / at risk	Median follow- up in years (Q1, Q3)	IDR/1,000 person-years (95% CI)ª			Difference in IDR /1,000 person-years (95% CI) p-value		
	(Cum. Inc.)		PRISm	Obstructive Spirometry	Normal Spirometry	PRISm vs Normal Spirometry	PRISm vs Obstructive Spirometry	
ARIC	2,454 / 14,830 (16.6)	26.5 (18.5, 28.1)	13.2 (11.4, 14.9)	8.7 (8.0, 9.5)	6.7 (6.4, 7.1)	6.4 (4.7, 8.2) <.001	4.4 (2.6, 6.3) <.001	
CARDIA	102 / 4,993 (2.0)	29.3 (28.2, 30.0)	1.7 (0.5, 2.9)	0.7 (0.0, 1.3)	0.7 (0.6, 0.8)	1.0 (-0.2, 2.2) 0.10	1.0 (-0.3, 2.4) 0.14	
CHS	1,452 / 3,829 (37.9)	14.2 (8.5, 18.5)	34.1 (27.7, 40.5)	35.9 (33.0, 38.9)	27.7 (25.7, 29.8)	6.3 (-0.4, 13.0) 0.06	-1.9 (-8.9, 5.2) 0.60	
FOC	483 / 3,680 (13.1)	21.9 (17.5, 26.5)	10.0 (7.1, 12.9)	6.5 (5.2, 7.8)	6.4 (5.7, 7.1)	3.6 (0.6, 6.6) 0.02	3.5 (0.3, 6.7) 0.03	
HABC	341 / 2,347 (14.5)	12.5 (7.8, 16.4)	18.7 (12.2, 25.2)	14.0 (11.0, 17.0)	11.4 (9.9, 12.9)	7.3 (0.6, 14.0) 0.03	4.7 (-2.4, 11.9) 0.20	
JHS	64 / 2,291 (2.8)	13.8 (13.1, 14.5)	3.0 (1.4, 4.6)	4.8 (-0.1, 9.8)	2.1 (1.5, 2.8)	0.9 (-0.9, 2.6) 0.33	-1.8 (-7.1, 3.4) 0.49	
MESA	185 / 4,401 (4.2)	11.2 (6.9, 12.1)	8.6 (5.1, 12.1)	4.6 (3.2, 5.9)	4.1 (3.3, 4.9)	4.5 (0.9, 8.1) 0.02	4.0 (0.2, 7.8) 0.04	
SHS	471 / 1,697 (27.8)	19.6 (10.6, 22.1)	21.3 (15.7, 27.0)	17.8 (13.4, 22.1)	18.9 (16.9, 20.9)	2.5 (-3.6, 8.5) 0.42	3.6 (-3.6, 10.7) 0.33	

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

^a Using the direct method and the observed age distribution across all 9 cohorts, age- and smoking-adjusted absolute incidence density rates, and their differences were calculated per 1,000 person-years for each lung function category.

	Total	PRISm-LLN	Obstructive Spirometry-LLN	Normal
		(FEV₁/FVC ≥	FEV ₁ /FVC < LLN	Spirometry-
		LLN		LLN
		& FEV ₁ < LLN)		(FEV₁/FVC ≥
N (row %)	53 701	3 065 (5 7)	7 720 (14 4)	42 916 (79 9)
Age mean (SD)	53 2 (15 8)	54 9 (14 2)	63.0 (12.0)	50 7 (15 9)
Age group, N (%)				
< 30 years	6.558 (12.2)	372 (12.1)	663 (8.6)	5.523 (12.9)
30-39 years	3,493 (6.5)	174 (5.7)	279 (3.6)	3,040 (7.1)
40-49 years	8,599 (16.0)	533 (17.4)	979 (12.7)	7,087 (16.5)
50-59 years	15,358 (28.6)	897 (28.3)	2,334 (30.2)	12,127 (28.3)
60-69 years	10,714 (20.0)	569 (18.6)	2,012 (26.1)	8,133 (19.0)
70-79 years	7,311 (13.6)	430 (14.0)	1,178 (15.3)	5,703 (13.3)
>80 years	1,668 (3.1)	90 (2.9)	275 (3.6)	1,303 (3.0)
Sex, N (%)				
Female	30,288 (56.4)	1,832 (59.8)	3,746 (48.5)	24,710 (57.6)
Male	23,413 (43.6)	1,233 (40.2)	3,974 (51.5)	18,206 (42.4)
Race, N (%)				
American Indian / Alaskan Native	1,779 (3.3)	106 (3.5)	231 (3.0)	1,442 (3.4)
Black	11,672 (21.7)	1,844 (60.2)	1,336 (17.3)	8,492 (19.8)
East Asian / Pacific Islander	659 (1.2)	52 (1.7)	75 (1.0)	532 (1.2)
Hispanic/Latino	14,597 (27.2)	543 (17.7)	1,129 (14.6)	12,925 (30.1)
non-Hispanic White	24,979 (46.5)	519 (16.9)	4,948 (64.1)	18,512 (45.5)
Other	15 (0.03)	1 (0.03)	1 (0.03)	13 (0.03)
Education, N (%) ^a				
Less than high school	7,856 (14.6)	513 (16.7)	1,229 (15.9)	6,117 (14.3)
High school	14,739 (27.5)	762 (24.9)	2,180 (28.2)	11,803 (27.5)
Some college	8,543 (15.9)	478 (15.6)	1,158 (15.0)	6,919 (16.1)
College or more	22,563 (42.0)	1,312 (42.8)	3,153 (40.8)	18,076 (42.1)

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	Total	PRISm-LLN (FEV1/EVC >	Obstructive spirometry-LLN FEV4/EVC < LLN	Normal Spirometry-
				LLN
		& FEV ₁ < LLN)		(FEV₁/FVC ≥
		,		LLN
				& FEV₁≥ LLN)
Smoking Status, N (%) ^a				
Never	26,048 (48.5)	1,478 (48.2)	2,057 (26.6)	22,513 (52.5)
Ever	27,653 (51.5)	1,588 (51.7)	5,663 (73.4)	20,403 (47.5)
Current smokers among ever smokers	10,989 (39.7)	784 (49.4)	2,843 (50.2)	7,364 (36.1)
Pack-years among ever smokers,	15.4 (4.5, 34.0)	18.0 (6.0, 36.2)	30.9 (13.2, 48.0)	12.0 (3.5, 29.0)
median (Q1,Q3)				
Redy Mass Index, mean (SD) a	20.1 (5.0)	20.9.(7.6)	26.6.(5.2)	29.2 (5.7)
Body Mass Index, mean (SD) ^a	20.1 (0.0)	30.0 (7.0)	20.0 (5.2)	20.2 (3.7)
EEV ₁ % predicted mean (SD)	97.0 (18.2)	75 1 (9 4)	80.6 (20.4)	103 4 (13 4)
FVC % predicted mean (SD)	102 1 (17 1)	78.1 (11.4)	100.3(20.4)	105.4(13.4)
	102.1 (17.1)	70.1(11.4)	100.3 (20.1)	100.4 (14.4)
Co-morbidities. N (%) ^a				
Hypertension ^b	22,528 (42.0)	1,828 (59.6)	3,477 (45.0)	17,225 (40.1)
Diabetes ^c	7,736 (14.4)	757 (24.7)	856 (11.1)	6,123 (14.3)
Chronic lower respiratory disease ^d	6,059 (11.3)	510 (16.6)	1,822 (23.6)	3,737 (8.7)
Asthma ^e	4,567 (8.5)	387 (12.6)	1,268 (16.4)	2,922 (6.8)
Heart failure ^f	3,133 (5.8)	251 (8.2)	788 (10.2)	2,094 (4.9)
Coronary heart disease ^f	2,886 (5.4)	252 (8.2)	608 (7.9)	2,025 (4.7)
Stroke ^f	945 (1.8)	124 (4.0)	177 (2.4)	639 (1.5)
eGFR ^g (mL/min/1.73m ²)				
≥60	44,669 (83.2)	2,636 (86.0)	6,098 (79.0)	35,824 (83.5)
30-59	8,686 (16.2)	387 (12.6)	1,562 (20.2)	6,835 (15.9)
<30	364 (0.6)	42 (1.4)	60 (0.8)	258 (0.6)
	Total	PRISm-LLN	Obstructive spirometry-LLN	Normal

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		(FEV₁/FVC ≥ LLN & FEV₁< LLN)	FEV1/FVC < LLN	Spirometry- LLN (FEV₁/FVC ≥ LLN & FEV₁≥ LLN)
Cohort, N (row %)				
ARIC	14,944	693 (4.6)	3,044 (20.4)	11,207 (75)
HCHS/SOL	13,625	506 (3.7)	1,044 (7.7)	12,075 (88.6)
CARDIA	5,004	353 (7.1)	578 (11.6)	4,073 (81.4)
CHS	4,814	261 (5.4)	1,069 (22.2)	3,484 (72.4)
MESA	4,585	305 (6.7)	587 (12.8)	3,693 (80.5)
FOC	3,898	85 (2.2)	768 (19.7)	3,045 (78.1)
HABC	2,578	149 (5.8)	284 (11.0)	2,145 (83.2)
JHS	2,498	609 (24.4)	121 (4.8)	1,768 (70.8)
SHS	1,755	104 (5.9)	225 (12.8)	1,426 (81.3)

Data is represented as N (column %), or mean SD (standard deviation, SD), or median (interquartile range, denoted as Q1, Q3) unless otherwise noted FEV₁ = Forced expiratory volume in one second; FVC = Forced vital capacity; eGFR = estimated glomerular filtration rate

ARIC = Atherosclerosis Risk in Communities study; CARDIA = Coronary Artery Risk Development in Young Adults study; CHS = Cardiovascular Health Study; FOC = Framingham Offspring cohort; HABC = Health ABC study; HCHS/SOL = Hispanic Community Health Study / Study of Latinos; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; SHS = Strong Heart Study

"Other" race category includes self-identified "other" race and individuals of mixed-race.

Lung function categories were defined as: PRISm-LLN = FEV₁/FVC≥LLN, FEV₁<LLN; Obstructive Spirometry-LLN = FEV₁/FVC<LLN; Normal Spirometry-LLN= FEV₁/FVC≥LLN, FEV₁≥LLN. **Based on GLI equations for "Other" race.**

All P-value for comparison between PRISm and normal spirometry from Student's t-test or Wilcoxon rank sum test for continuous variables as appropriate and Chisquared test for categorical variables were <.001.

^a Values represent average over 10 imputed datasets

^b Self-reported hypertension or systolic blood pressure ≥ 140 mmHg or diastolic blood pressure ≥ 90 mmHg or use of anti-hypertensive medications

° Self-reported diabetes or fasting blood sugar level ≥ 126 mg/dl or use of oral hypoglycemic agents or insulin

^d Self-reported physician diagnosed chronic obstructive pulmonary disease, chronic bronchitis, or emphysema

^e Self-reported physician diagnosed asthma

^f Data on comorbidities at baseline, including coronary heart disease, congestive heart failure (HF), and stroke were self-reported. If missing, data was obtained from hospitalization records prior to baseline spirometry. In JHS, neither self-reported information on HF nor hospitalization records prior to baseline spirometry were available. Therefore, baseline HF was defined as HF events occurring within 5 years of baseline spirometry.

⁹ For baseline eGFR, measurements obtained at baseline spirometry visit were used. If missing, first available eGFR measurements were used.

eTable 10. Associations Between Lung Function Category Defined Using GLI Equations for Lower Limit of Normal (LLN), All-Cause, Respiratory, and Coronary Heart Disease (CHD) Mortality, as Well as Respiratory-Related and CHD-Related Hospitalizations and Mortality

	At risk	Median Follow-Up in	Events	Incidence	Lung Function	HR [95% CI]
		Years	(Cumulative	density rate	Category	
		(IQR)	Incidence)	/1,000	(reference: Normal	
				person-	Spirometry-LLN)	
				years		
All-cause mortality ^a	39,835	19.4 (12.1, 27.6)	15,661 (39.3)	21	PRISm-LLN	1.59 [1.49, 1.70]
					Obstructive	1.44 [1.39, 1.50]
					Spirometry-LLN	
Respiratory Mortality ^b	31,998	19.6 (11.5, 27.8)	1,100 (3.4)	2	PRISm-LLN	2.18 [1.63, 2.91]
					Obstructive	4.05 [3.56, 4.61]
					Spirometry-LLN	
CHD mortality ^a	39,628	19.6 (12.1, 27.6)	2,352 (5.9)	3	PRISm-LLN	1.51 [1.29, 1.78]
					Obstructive	1.17 [1.05, 1.30]
					Spirometry-LLN	
Respiratory-related	25,080	14.3 (8.9, 22.9)	4,101 (16.4)	11	PRISm-LLN	2.36 [2.07, 2.70]
events ^c					Obstructive	3.40 [3.17, 3.63]
					Spirometry-LLN	
CHD-related events ^a	38,068	20.4 (12.3, 27.7)	5,552 (14.6)	8	PRISm-LLN	1.29 [1.15, 1.44]
					Obstructive	1.09 [1.02, 1.17]
					Spirometry-LLN	- •

Lung function categories were defined as: PRISm-LLN = FEV₁/FVC≥LLN, FEV₁<LLN; Obstructive Spirometry-LLN = FEV₁/FVC<LLN; Normal Spirometry-LLN= FEV₁/FVC≥LLN, FEV₁≥LLN. **Based on GLI equations for "Other" race.**

Cox proportional hazards models were was adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable. ^a Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

^b Cohorts included: ARIC, CHS, CARDIA, Health ABC, MESA, SHS

^c Cohorts included: ARIC, CHS, Health ABC, MESA

eTable 11. Associations Between Lung Function Category, All-Cause, Respiratory, and Coronary Heart Disease (CHD) Mortality, as Well as Respiratory-Related and CHD-Related Hospitalizations and Mortality, Additionally Adjusting for Baseline FEV1:FVC

	At risk	Median Follow-Up in Years (IQR)	Events (Cumulative Incidence)	Incidence density rate /1,000 person- years	Lung Function Category (reference: Normal Spirometry)	HR [95% CI]
All-cause mortality ^a	39,835	19.4 (12.1, 27.6)	15,661 (39.3)	21	PRISm	1.47 [1.39, 1.55]
					Obstructive Spirometry	1.10 [1.04, 1.16]
Respiratory mortality ^b	31,998	19.6 (11.5, 27.8)	1,100 (3.4)	2	PRISm	1.79 [1.41, 2.27]
					Obstructive	0.99 [0.83, 1.19]
					Spirometry	
CHD mortality ^a	39,628	19.6 (12.1, 27.6)	2,352 (5.9)	3	PRISm	1.54 [1.35, 1.76]
					Obstructive	1.11 [0.97, 1.27]
					Spirometry	
Respiratory-related	25,080	14.3 (8.9, 22.9)	4,101 (16.4)	11	PRISm	1.82 [1.62, 2.04]
events ^c					Obstructive	1.49 [1.36, 1.64]
					Spirometry	
CHD-related events ^a	38,068	20.4 (12.3, 27.7)	5,552 (14.6)	8	PRISm	1.29 [1.18, 1.42]
					Obstructive	1.13 [1.03, 1.24]
					Spirometry	

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive Spirometry = FEV₁/FVC<0.7; Normal Spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, estimated glomerular filtration rate, and baseline FEV1/FVC; cohort was treated as a stratum variable.

^a Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

^b Cohorts included: ARIC, CHS, CARDIA, Health ABC, MESA, SHS

^c Cohorts included: ARIC, CHS, Health ABC, MESA

eTable 12. Associations Between Lung Function Category, Mortality, CHD Events, and Respiratory-Related Events, Complete Case Analysis

	At risk	Median Follow-Up in Years (IQR)	Events (Cumulative Incidence)	Incidence density rate /1,000 person- years	Lung Function Category (reference: Normal Spirometry)	HR [95% CI]
All-cause mortality ^a	26,994	17.5 (11.9, 28.0)	8,105 (30.0)	16	PRISm	1.47 [1.36, 1.59]
					Obstructive Spirometry	1.32 [1.25, 1.39]
Respiratory mortality ^b	20,871	17.6 (11.2, 28.4)	616 (3.0)	2	PRISm	1.83 [1.35, 2.50]
					Obstructive	2.73 [2.28, 3.27]
					Spirometry	
CHD mortality ^a	26,790	17.7 (11.9, 28.0)	1,521 (5.7)	3	PRISm	1.35 [1.13, 1.61]
					Obstructive	1.16 [1.04, 1.31]
					Spirometry	
Respiratory-related	15,424	12.8 (8.4, 21.9)	1,986 (12.9)	9	PRISm	1.78 [1.50, 2.12]
events ^c					Obstructive	3.04 [2.75, 3.36]
					Spirometry	
CHD-related events ^a	25,504	18.8 (12.1, 28.2)	3,258 (12.8)	7	PRISm	1.13 [0.99, 1.28]
					Obstructive	1.06 [0.98, 1.16]
					Spirometry	

Lung function categories were defined as: PRISm = FEV1/FVC≥0.7, FEV1<80%; Obstructive Spirometry = FEV1/FVC<0.7; Normal Spirometry = FEV1/FVC≥0.7, FEV1≥80%.

Cox proportional hazards models were was adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable. ^a Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

^b Cohorts included: ARIC, CHS, CARDIA, Health ABC, MESA, SHS

^c Cohorts included: ARIC, CHS, Health ABC, MESA



Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Hispanic Community health Study/Study of Latinos (HCHS/SOL) Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

eFigure 2. Residual Plot for Checking the Proportional Hazards Assumption for PRISm and Mortality, CHD Events, and Respiratory-Related Events







eFigure 4. Unadjusted Cumulative Incidence of Respiratory- and Coronary Heart Disease (CHD) Mortality, and Respiratory-Related and CHD-Related Hospitalizations and Mortality by Lung Function Category



eFigure 5. Effects of Omitting Covariates From the Fully Adjusted Model for All-Cause Mortality on the Hazard Ratio for PRISm vs Normal Spirometry



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

* Cox proportional hazards full model was adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease (CHD), congestive heart failure (CHF), stroke, and estimated glomerular filtration rate (eGFR); cohort was treated as a stratum variable. Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

eFigure 6. Forest Plot of Stratified Subgroup Analyses (PRISm vs Normal Spirometry) for All-Cause Mortality

Group	<u>Sub-group</u>	<u>At risk</u>	<u>Events</u>	<u>Cum. Inc.</u>	į		P-Interaction
Pooled analysis		39,835	15,661	39.3			
Age group					1		
	< 45 years	6,756	498	7.4			<.001
	45-65 years	21,832	8,299	38.0			
	65+ years	11,248	6,864	61.0			
Sex							
	Women	21,967	7,628	34.7			0.31
	Men	17,869	8,033	45.0	1		
Race							
	White	24,921	10,742	43.1	1		0.14
	Black	11,529	3,700	32.1			
	Others	3,386	1,219	36.0	i —		
Education status					1		
Le	ss than high school	4,587	2,492	54.3	i		0.97
	High school	11,125	4,509	40.5	1	—— — —	
Мо	re than high school	24,117	8,663	35.9	1		
					1		
Obesity							
	Yes	10,861	4,467	41.1	1	_ 	0.05
	No	28,975	11,194	38.6			
Smoking status							
	Never	17,721	5,481	30.9	1		<.001
	Former	13,827	6,203	44.9	i I	_ 	
	Current	8.288	3.977	48.0			
Hypertension					i i		
	Yes	18.455	9.620	52.1			<.001
	No	21.381	6.041	28.3	i		
Diabetes		,	-,- · ·		1	—	
	Yes	5,168	3.187	61.7	i	_	<.001
	No	34.668	12.474	36.0	1	_ _	
CVD*		0 1,000	,	00.0	i	-	
	Yes	5 427	3 617	66 6	1		0.61
	No	3/ /09	12 044	35.0	i		0.01
eGER (ml/min/1 73	(m2)	54,405	12,044	55.0	1	-	
	60+	31 398	11 463	36.5			0.24
	30-50	8 124	3 973	18.9	1		0.24
	~20 -09	31/	225	71 7			
Healthy**	~30	514	220	(1.1	-		
nearing	Voc	3 376	161	13.7			
	No	36 460	404	/1 7	1		×.001
		30,400	10,197	41./	I I		
					0.00	0.50	1.00
						Log of Hazards Ratio	

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable.

Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

*Cardio-vascular disease, which includes coronary heart disease, congestive heart failure, and stroke

eFigure 7. Forest Plot of Stratified Subgroup Analyses (PRISm vs Normal Spirometry) for Respiratory Mortality

Group Sub-group	<u>At risk</u> Events	<u>s Cum. Inc.</u>		<u>P-Inte</u>
Pooled analysis	31,998 1,100	3.4		
Age group				
< 45 years	5,005 16	0.3	Not estimable	<
45-65 years	16,604 517	3.1	_	
65+ years	10,390 567	5.5	_	
Sex				
Women	17,396 532	3.1		
Men	14,603 568	3.9	_	
Race				
White	19,916 830	4.2	_	C
Black	8,704 169	1.9	_	
Others	3,379 101	3.0		
Education status	-			
Less than high school	4,073 195	4.8		
High school	8,910 291	3.3		
More than high school	19,016 614	3.2		
	,		_	
Obesity				
Yes	8 365 244	29		C
No	23 634 856	36		-
Smoking status	20,001 000	0.0	-	
Never	13 893 241	17		<
Former	11 244 436	3.0		
Current	6 962 422	5.9 6.2		
Hyportonsion	0,002 420	0.2	-	
Vec	15 366 635	11		
Tes	10,300 035	4.1		
Dishataa	10,035 405	2.0		
Diabetes	4 407 464	2.6		
Yes	4,427 101	3.0		<
NO NO	21,012 939	3.4		
CVD"	4 000 004	6.6	_	
Yes	4,839 321	0.0		(
	27,160 779	2.9		
eGFR (ml/min/1./3m2)	05 007 700	0.4		-
60+	25,697 798	3.1		C
30-59	6,027 291	4.8		
<30	275 11	4.0	Not estimable	
Healthy**				_
Yes	2,848 20	0.7		
No	29,151 1,080	3.7		
		-0.50	0.00 0.50 1.00 1.50 2.00	-
			Log of Hazarda Datio	

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable.

Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Health, Aging, and Body Composition (Health ABC), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

"Other" race category includes Hispanic, East Asian, and individuals of mixed race.

*Cardio-vascular disease, which includes coronary heart disease, congestive heart failure, and stroke

eFigure 8. Forest Plot of Stratified Subgroup Analyses (PRISm vs Normal Spirometry) for CHD Mortality Events

<u>Group</u> <u>Sub-group</u>	<u>At risk</u>	Events	<u>Cum. Inc.</u>	_	P-Interaction
Pooled analysis	39,628	2,352	5.9		
Age group	6 714	27	0.4	_	0.0055
	0,714	27	0.4		0.0055
45-65 years	21,701	860	4.0		
65+ years	11,214	1,465	13.1		
Sex	04.040	070	4.5		0.4077
Women	21,840	973	4.5		0.1877
Men	17,789	1,379	7.8		
Race					
White	24,921	1,606	6.4		0.4049
Black	11,322	473	4.2	i ∎	
Others	3,386	273	8.1 -		
Education status					
Less than high school	4,576	385	8.4 -		0.488
High school	11,092	655	5.9	_	
More than high school	23,961	1,312	5.5	_	
Obesity					
Yes	10,750	706	6.6	_	0.9162
No	28,879	1,646	5.7		
Smoking status				1 1	
Never	17,603	833	4.7 -		0.1404
Former	13,781	1.059	7.7		
Current	8 245	460	56		
Hypertension	0,210		0.0		
Yes	18 314	1 719	94		0 4551
No	21 315	633	3.0		0.1001
Diabetes	21,010	000	0.0	-	
Ves	5 1 1 2	678	12.2		0.0079
No	34 517	1 674	13.5		0.0079
CVP*	54,517	1,074	4.0		
CVD	5 000	705	45.0		0.0700
Yes	5,296	/95	15.0		0.6733
NO	34,333	1,557	4.5		
eGFR (ml/min/1.73m2)				·	
60+	31,211	1,644	5.3		0.4315
30-59	8,109	669	8.3		
<30	309	39	12.6		
Healthy**					
Yes	2,848	20	0.7		0.0018
No	36,263	2,314	6.4	— — —	
			-0.50	0.50 1.50	2.50
				Log of Hazards R	Ratio

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry = FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable.

Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

"Other" race category includes Hispanic, East Asian, and individuals of mixed race.

*Cardio-vascular disease, which includes coronary heart disease, congestive heart failure, and stroke

eFigure 9. Forest Plot of Stratified Subgroup Analyses (PRISm vs Normal Spirometry) for Respiratory-Related Events

Group Sub Pooled analysis	o-group	<u>At risk</u> 25,080	<u>Events</u> 4,101	<u>Cum. Inc.</u> 16.4						<u>P-Interacti</u>
< 4 < 4	5 vears	29	5	17.2						0.74
45-6	5 vears	15,235	2.482	16.3						
65	+ vears	9.817	1.614	16.4						
Sex	<i>j</i> = = =	-,	.,			_				
	Women	13.531	1.895	14.0			_			0.41
	Men	11,550	2,206	19.1						
Race		,	_,							
	White	17.365	3.303	19.0	!					0.83
	Black	6 111	727	11.9						
	Others	1 605	71	4 4	<u> </u>		_			
Education status	0	.,	••				-			
Less than high	school	3,192	770	24.1			_			0.58
Hink	school	6 876	1 243	18.1						0.00
More than high	school	15 013	2 088	13.9			_			
wore than high	1 3011001	10,010	2,000	10.0		-				
Obesity										
	Yes	6,744	996	14.8		_				0.009
	No	18,337	3,105	16.9	i					
Smoking status										
	Never	10,588	683	6.5						<.001
	Former	9,779	1,612	16.5			_			
	Current	4,714	1,806	38.3						
Hypertension										
	Yes	13,735	2,408	17.5						0.56
	No	11,346	1,693	14.9						
Diabetes										
	Yes	3.517	592	16.8						0.04
	No	21.564	3,509	16.3						
CVD*		,••	-,		i	_				
-	Yes	4.688	1.207	25.7						0.016
	No	20,393	2.894	14.2						0.010
eGFR (ml/min/1.73m	2)	20,000	_,			_				
	60+	19,172	3.007	15.7	i					0.33
	30-59	5 682	1 050	18.5	-					0.00
	<30-	-227	-44	-19.4						
Healthy**	-00		(T	10.7		-				
	Yes	1 348	62	46 —					_	< 001
	No	23 733	4 039	 17.0	-		1			001
	110	20,100	4,039	17.0						
				-0.50	0.00	0.50	1.00	1.50	2.00	2.50
							Log	of Hazards Ratio		
							LOG			

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry = FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable.

Cohorts included: Atherosclerosis Risk in Communities (ARIC), Cardiovascular Health Study (CHS), Health, Aging, and Body Composition (Health ABC), and Multi-Ethnic Study of Atherosclerosis (MESA)

"Other" race category includes Hispanic, East Asian, and individuals of mixed race.

*Cardio-vascular disease, which includes coronary heart disease, congestive heart failure, and stroke

eFigure 10. Forest Plot of Stratified Subgroup Analyses (PRISm vs Normal Spirometry) for CHD-Related Events

<u>Group</u> <u>Sub-group</u> Pooled analysis	<u>At risk</u> 38,068	<u>Events</u> 5,552	<u>Cum. Inc.</u> 14.6			P-Interaction
Age group						
< 45 years	6,704	183	2.7			<.001
45-65 years	21,495	3,176	14.8			
65+ years	9,870	2,193	22.2	-		
Sex						
Women	21,196	2,483	11.7		_ _	<.001
Men	16,873	3,069	18.2		i — B —	
Race						
White	23,658	3,899	16.5			0.07
Black	11,113	1,102	9.9		_	
Others	3,298	551	16.7			
Education status						
Less than high school	4,329	857	19.8		_	0.81
High school	10,652	1,631	15.3			
More than high school	23,088	3,064	13.3		_	
Obesity						
Yes	10.373	1.711	16.5			0.08
No	27 696	3 841	13.9			
Smoking status	21,000	0,011	10.0		-	
Never	17 068	1 928	11.3			0 19
Former	12 942	2 262	17.5			0.10
Current	8 059	1 362	16.9			
Hyportonsion	0,000	1,002	10.5		-	
Vec	17 054	3 510	20.6			0.28
les	21 015	2 042	20.0			0.28
Diabatos	21,015	2,042	5.1		-	
Voc	1 756	1 204	27.4			< 001
Tes	4,750	1,304	27.4			<.001
NO NO	33,313	4,248	12.8			
	4 4 0 0	4 4 2 4	00.0		_	0.00
Yes	4,198	1,131	26.9			0.68
NO	33,871	4,421	13.1		_ _	
eGFR (mi/min/1./3m2)			40.0		_	
60+	30,273	4,004	13.2			0.32
30-59	7,523	1,466	19.5			
<30	273	82	30.0 —			
Healthy**					_	
Yes	3,358	140	4.2			<.001
No	34,711	5,412	15.6			
				-0.50 0	00 0.50 1.00	1.50
					Log of Hazards Ratio	

Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate; cohort was treated as a stratum variable.

Cohorts included: Atherosclerosis Risk in Communities (ARIC), Coronary Artery Risk Development in Young Adults (CARDIA), Cardiovascular Health Study (CHS), Framingham Offspring Cohort (FOC), Health, Aging, and Body Composition (Health ABC), Jackson Heart Study (JHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Strong Heart Study (SHS)

"Other" race category includes Hispanic, East Asian, and individuals of mixed race.

*Cardio-vascular disease, which includes coronary heart disease, congestive heart failure, and stroke

eFigure 11. Forest Plot of Cohort-Stratified Analyses (PRISm vs Normal Spirometry) for All-Cause Mortality



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

ARIC = Atherosclerosis Risk in Communities study; CARDIA = Coronary Artery Risk Development in Young Adults study; CHS = Cardiovascular Health Study; FOC=Framingham Offspring Cohort; HABC = Health ABC study; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; SHS = Strong Heart Study

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate.

eFigure 12. Forest Plot of Cohort-Stratified Analyses (PRISm vs Normal Spirometry) for Respiratory Mortality



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

ARIC = Atherosclerosis Risk in Communities study; CARDIA = Coronary Artery Risk Development in Young Adults study; CHS = Cardiovascular Health Study; HABC = Health ABC study; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; SHS = Strong Heart Study

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate

eFigure 13. Forest Plot of Cohort-Stratified Analyses (PRISm vs Normal Spirometry) for CHD Mortality



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

ARIC = Atherosclerosis Risk in Communities study; CARDIA = Coronary Artery Risk Development in Young Adults study; CHS = Cardiovascular Health Study; FOC=Framingham Offspring Cohort; HABC = Health ABC study; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; SHS = Strong Heart Study

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate.

eFigure 14. Forest Plot of Cohort-Stratified Analyses (PRISm vs Normal Spirometry) for Respiratory-Related Events



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

ARIC = Atherosclerosis Risk in Communities study; CHS = Cardiovascular Health Study; HABC = Health ABC study; MESA = Multi-Ethnic Study of Atherosclerosis

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated glomerular filtration rate.

eFigure 15. Forest Plot of Cohort-Stratified Analyses (PRISm vs Normal Spirometry) for CHD-Related Events



Lung function categories were defined as: PRISm = FEV₁/FVC≥0.7, FEV₁<80%; Obstructive spirometry = FEV₁/FVC<0.7; Normal spirometry= FEV₁/FVC≥0.7, FEV₁≥80%.

ARIC = Atherosclerosis Risk in Communities study; CARDIA = Coronary Artery Risk Development in Young Adults study; CHS = Cardiovascular Health Study; FOC=Framingham Offspring Cohort; HABC = Health ABC study; JHS = Jackson Heart Study; MESA = Multi-Ethnic Study of Atherosclerosis; SHS = Strong Heart Study

Cox proportional hazards models were adjusted for age, gender, race/ethnicity, education, body mass index, smoking status, medical comorbidities such as, hypertension, diabetes, coronary heart disease, congestive heart failure, stroke, and estimated