SUPPLEMENTAL METHODS

Impaired lung function, lung disease and risk of incident dementia

Spirometry measurements

Pulmonary function was assessed at baseline using a water-sealed Collins Survey II volume displacement spirometer (Collins Medical, Braintree, MA) and PULMO-SCREEN II software (PDS Healthcare Products, Louisville, CO). Spirometry was conducted using American Thoracic Society guidelines,(1) using a protocol standardized across the four field centers, with training and certification of pulmonary technicians and extensive quality assurance throughout the study.(2) For each participant, at least three acceptable spirograms were sought from a minimum of five forced expirations. At least two were required to be reproducible (volumes within +/-5%). A best reading was then selected by computer software and confirmed by a technician using American Thoracic Society criteria for acceptability. Spirometry measures used in this analysis are FEV1, FVC, and the FEV1/FVC ratio. Each measure as a percentage of age-, race-, and sex-specific predicted values and lower limit of normal (LLN) values of each metric were calculated using equations published by Hankinson et al.(3) Bronchodilator (beta2-agonist) response was not evaluated.

Covariates & Potential Effect Modifiers

Covariate information was obtained at baseline, concurrent with exposure measurement. Questionnaires were used to ascertain age, sex, education, race-center, cigarette smoking, pack-years of smoking, physical activity, and prevalent coronary heart disease, stroke and heart

failure. Participants were asked to bring all medications taken in the two weeks prior to the exam; all medication names were recorded. Height and weight were measured, body mass index calculated as height (m)/weight $(kg)^2$. Sitting blood pressure was measured with a random-zero sphygmomanometer after a five minute rest. A total of three measurements were taken, the mean of the latter two was used in analysis.

Fasting serum and plasma samples were drawn and stored at −80°C. Total plasma cholesterol and triglycerides were determined by enzymatic methods. HDL-C was measured after dextran-magnesium precipitation, and the Friedewald equation(4) was used to calculate LDL-C in participants. Diabetes was defined as a fasting blood glucose ≥126 mg/dL, non–fasting blood glucose ≥200 mg/dL, a self-reported physician diagnosis of diabetes, or current use of antidiabetic medication. Methods for the measurement and classification of the APOE ε4 risk allele have been described elsewhere.(5)

Dementia adjudication

For the 6,471 participants who underwent a detailed neurocognitive assessment, an expert panel adjudicated syndromic dementia and MCI based on a full neuropsychological assessment plus a functional activities questionnaire (FAQ), a clinical dementia rating (CDR) interview (administered separately to the participant and the informant) and a neuropsychiatric inventory (NPI) interview (administered to the informant only). Interviews were conducted using standardized protocols and by certified staff, and quality control of interviewer performance was monitored via review of audiotaped recordings. For individuals who were seen in-person and given diagnoses of dementia or MCI, etiologic diagnoses were assigned by a panel of physicians and neuropsychologists.(6) The panel was required to designate one

etiology as primary, though they were allowed to diagnose more than one etiology. Diagnosis of dementia or MCI due to AD etiology followed criteria from the National Institute on Aging-Alzheimer's Association (NIA-AA) workgroups,(7, 8) and was based on the presence of a cognitive syndrome that is not of abrupt onset and includes memory or non-memory (e.g. language or visuospatial) presentations, and the absence of features of other specific diagnoses sufficient to cause the cognitive impairment. Cardiovascular disease-related MCI and dementia was defined by an algorithm based in the National Institute of Neurological Disorders and Stroke-Association Internationale pour la Recherche et l'Enseignement en Neurosciences criteria.(9) For the present analysis we did not specifically evaluate dementia and MCI attributed to other etiologies (e.g. Lewy body disease) due to the low prevalence of these conditions in our sample.

IPW Weights

Inverse probability weighting (IPW) was used to adjust for attrition due to either death or failure to attend the follow-up neurocognitive exam (censoring). For each individual we separately modeled estimated probabilities of i) being alive at the time of the follow-up neurocognitive exam and ii) participating in the follow-up neurocognitive exam, conditional on being alive at the time of the follow-up neurocognitive exam. Weights were calculated as the inverse of estimates probabilities. Stabilized weights as the ratio of two probabilities were used. Values of the stabilized weights beyond the extreme 1st and 99th percentiles were winsorized to the values at the 1st and 99th percentiles.

Logistic models for IPW weights included the following variables measured at visit 1: age, sex, education, race-center, APOE, cigarette smoking, pack-years of smoking, physical activity, body mass index, systolic blood pressure, antihypertensive medications, diabetes, HDL cholesterol, LDL cholesterol, lipid lower medication, prevalent coronary heart disease, stroke, heart failure, lung function impairment, the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), the FEV1/FVC ratio, FEV1% predicted, FVC% predicted, FEV1/FVC% predicted, global z-score for three cognitive tests (Delayed Word Recall Test, Digit Symbol Substitution Test, and Word Fluency Test), and incident dementia. Logistic models for estimates of the numerators of the stabilized weights included age, gender, education, race-center, APOE, cigarette smoking, and pack-years of smoking.

The c-statistics for visit 5 participation and survival were 0.694 and 0.816, respectively.

Weights mean (SD) by Visit 5 status

Visit 5 attendee: 2.26 (1.65); min = 1.20, max = 11.94

Visit 5 nonattendee: 5.19 (3.83); min = 1.20, max = 11.94

Stabilized weights mean (SD) by Visit 5 status

Visit 5 attendee: 0.98 (0.37); min = 0.46, max = 3.09

Visit 5 nonattendee: 1.41 (0.83); min = 0.46, max = 3.09

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SUPPLEMENTAL TABLES

Impaired lung function, lung disease and risk of incident dementia

Supplemental Table 1.
Baseline characteristics (1987-1989) stratified by neurocognitive study (2011-2013) participation status[a]: The Atherosclerosis Risk in Communities (ARIC) study.

Supplemental Table 2

Baseline characteristics according to forced vital capacity (FVC) percent of predicted: The Atherosclerosis Risk in Communities (ARIC) study, 1987-1989

Supplemental Table 3

Lung function disease categories, objective indices of lung function, and risk of incident dementia among nonsmokers: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

Supplemental Table 4

Lung function disease categories, objective indices of lung function, and risk of incident dementia among blacks and whites: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

Supplemental Table 5

Objective indices of lung function and risk of incident dementia according to follow-up time*: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

Supplemental Table 6

Weighted* odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories and objective lung function measures with dementia or MCI among never smokers: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 7

Race-stratified weighted* odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories, FEV1% predicted, FVC% predicted and FEV1/FVC% predicted with dementia or MCI: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 8 – FEV1/FVC% predicted & adjudicated outcomes

Inverse-probability weighted odds ratios (OR) and 95% confidence intervals (CI) of FEV1/FEC percent of predicted quartile categories with dementia, mild cognitive impairment (MCI), Alzheimer's disease and cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 9

Odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 10

Odds ratios (ORs) and 95% confidence intervals (CI) of FEV1 percent predicted quartile with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 11

Odds ratios (ORs) and 95% confidence intervals (CI) of FVC percent predicted quartile with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

Supplemental Table 1.

Baseline characteristics (1987-1989) stratified by neurocognitive study (2011-2013) participation status[a]: The Atherosclerosis Risk in Communities (ARIC) study.

	N	Participant 5,889	Nonparticipant still alive 3,087	Nonparticipant due to death 5,208
Demographics				
Age, years		52.1 (5.2)	53.7 (5.6)	56.8 (5.4)
Female, %		59.3	63.5	45.9
African American, %		22.8	24.8	30.1
Education level, %				
<High school		15.0	22.9	33.3
High school graduate		41.6	44.0	38.3
College/Graduate school		43.4	33.1	28.3
Behaviors				
Smoking status, %				
Current		17.7	22.7	37.0
Former		32.8	30.1	31.4
Never		49.5	47.2	31.6
Pack-years*		13.4 (7.5, 31.0)	15.7 (9.7, 34.0)	24.7 (17.2, 45.0)
Physical activity**		2.5 (0.8)	2.4 (0.8)	2.4 (0.8)
Respiratory Indicators				
FEV1%, pred		97.3 (14.3)	95.9 (15.1)	87.7 (19.3)
FVC%, pred		100.9 (13.1)	99.7 (13.6)	94.0 (15.7)
FEV1/FVC %, pred		95.8 (7.9)	95.6 (8.4)	92.3 (12.3)
FEV1, Liter		3.0 (0.7)	2.8 (0.7)	2.6 (0.8)
FVC, Liter		3.9 (1.0)	3.8 (1.0)	3.6 (1.0)
FEV1/FVC		75.8 (6.4)	75.5 (6.8)	72.0 (9.9)
Self-reported symptoms, %				
Cough		8.0	10.8	18.3
Phlegm		6.2	8.2	14.3
Dyspnea		4.6	7.4	12.6
Self-reported MD diagnosis, %				
Bronchitis		6.6	7.6	10.8
Emphysema		0.6	0.7	3.6
Asthma		5.1	5.8	6.9
Lung disease categories, %				
COPD pattern		12.4	14.1	25.5
Restrictive impairment pattern		4.1	4.9	8.5
Respiratory symptoms with normal spirometric results		33.4	34.6	33.0
Normal		50.1	46.5	33.1

Other Physiologic Characteristics			
Body mass index, kg/m^2	27.2 (4.9)	27.6 (5.3)	28.3 (5.8)
Systolic blood pressure, mmHg	116.6 (16.0)	120.2 (17.2)	126.3 (20.5)
Antihypertensive medications, %	17.6	23.5	33.7
Prevalent diabetes, %	5.9	8.0	19.4
HDL cholesterol, mg/dL	53.4 (16.8)	53.2 (16.9)	49.3 (16.8)
LDL cholesterol, mg/dL	134.3 (38.1)	138.9 (39.5)	140.5 (40.0)
Lipid lowering medication, %	2.1	3.0	3.5
Prevalent CHD, %	1.8	3.7	6.4
Prevalent HF, %	2.5	3.5	7.5
Prevalent Stroke, %	3.7	3.7	6.4
APOE, %			
e4/e4	2.2	2.3	3.3
e2/e4 or e3/e4	26.4	27.4	30.0
Other	71.4	70.3	66.7

Data shown as mean (SD) or percentage except for *geometric mean (interquartile range)
*among smokers
**Score on the sport index of the Baecke physical activity questionnaire[1]
[a]Neurocognitive study attendance status defined as attending ARIC visit 5 and not missing dementia status

Supplemental Table 2

Baseline characteristics according to forced vital capacity (FVC) percent of predicted: The Atherosclerosis Risk in Communities (ARIC) study, 1987-1989

		FVC%, predicted				
		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5
		<86.7	86.7-94.9	95.0-101.7	101.8-109.8	>109.8
	N	2,836	2,838	2,835	2,839	2,836
Demographics						
Age, years		55.1 (5.7)	54.2 (5.7)	54.0 (5.6)	53.7 (5.8)	53.8 (5.9)
Female, %		55.0	51.8	55.5	55.5	58.7
African American, %		25.3	22.9	23.8	24.9	32.6
Education level, %						
<High school		31.7	22.1	22.5	20.3	20.6
High school graduate		39.6	43.5	40.7	41.5	39.5
College/Graduate school		28.8	34.5	36.8	38.2	40.0
Behaviors						
Smoking status, %						
Current		39.4	28.0	23.3	20.3	18.3
Former		29.2	32.7	30.4	34.1	32.3
Never		31.4	39.4	46.4	45.6	49.4
Pack-years*		25.6 (18.8, 45.0)	20.4 (13.5, 41.0)	17.3 (10.0, 37.9)	15.1 (8.4, 33.0)	12.5 (6.8, 30.0)
Physical activity		2.3 (0.8)	2.4 (0.8)	2.5 (0.8)	2.5 (0.8)	2.5 (0.8)
Respiratory Indicators						
FEV1%, pred		72.0 (14.4)	87.4 (9.0)	94.9 (8.5)	101.2 (8.6)	111.9 (10.7)
FVC%, pred		77.6 (8.6)	91.1 (2.3)	98.4 (1.9)	105.5 (2.3)	117.9 (7.3)
FEV1/FVC %, pred		91.8 (14.3)	95.3 (9.5)	95.8 (8.4)	95.3 (7.9)	94.4 (7.8)
FEV1, Liter		2.2 (0.6)	2.7 (0.6)	2.9 (0.6)	3.1 (0.7)	3.3 (0.8)
FVC, Liter		3.0 (0.7)	3.6 (0.8)	3.8 (0.8)	4.1 (0.9)	4.4 (1.0)
FEV1/FVC		72.1 (11.6)	74.8 (7.7)	75.4 (6.8)	75.0 (6.5)	74.5 (6.4)
Self-reported symptoms						
Cough, %		22.0	12.5	10.7	8.8	8.0

Phlem, %	17.5	9.5	8.3	6.6	6.1
Dyspnea, %	16.6	8.1	6.9	5.2	3.9
Self-reported MD diagnosis					
Bronchitis, %	14.1	9.4	6.9	6.0	5.3
Emphysema, %	4.6	1.4	1.2	0.6	0.9
Asthma, %	10.2	5.9	5.0	4.3	4.1
Other Physiologic Characteristics					
Body mass index, kg/m^2	28.9 (6.2)	28.0 (5.5)	27.6 (5.3)	27.1 (4.8)	26.7 (4.6)
Systolic blood pressure, mmHg	124.5 (20.2)	121.1 (18.3)	120.8 (19.0)	119.8 (17.2)	118.5 (17.4)
Antihypertensive medications, %	33.0	25.9	25.4	21.1	18.7
Prevalent diabetes, %	18.2	12.3	10.1	9.3	6.6
HDL cholesterol, mg/dL	48.8 (16.3)	50.3 (16.5)	51.8 (16.6)	52.7 (16.9)	55.7 (17.5)
LDL cholesterol, mg/dL	137.8 (39.7)	138.1 (38.6)	138.5 (39.5)	137.8 (39.1)	135.7 (39.3)
Lipid lowering medication, %	3.1	3.2	2.3	2.7	2.6
Prevalent CHD, %	9.0	4.8	4.1	3.4	1.8
Prevalent HF, %	9.3	4.3	3.9	2.9	2.4
Prevalent Stroke, %	6.1	5.5	4.5	3.6	3.6
APOE, %					
e4/e4	2.4	2.4	2.6	3.1	2.5
e2/e4 or e3/e4	28.1	27.3	27.7	28.5	28.3
Other	69.5	70.3	69.7	68.4	69.2

Data shown as mean (SD) or percentage except for *geometric mean (interquartile range)

Supplemental Table 3

Lung function disease categories, objective indices of lung function, and risk of incident dementia <u>among nonsmokers</u>: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

		Lung Function Category			
		Normal	Respiratory symptoms with normal spirometric results	Restrictive impairment pattern	COPD pattern
	N	3,301	1,920	294	503
Dementia cases, *n*		335	229	34	62
Person-years		71,727	40,457	5,724	10,654
Incident Rate*		4.7	5.7	5.9	5.8
Hazard ratio (95% CI)					
Model 1		1	1.18 (1.00, 1.40)	1.45 (1.02, 2.08)	1.41 (1.07, 1.85)
Model 3		1	1.07 (0.90, 1.28)	1.12 (0.78, 1.62)	1.31 (0.99, 1.72)

		FEV1%, predicted					
		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)
	N	654	1,058	1,291	1,429	1,586	
Dementia cases, *n*		80	129	112	149	190	
Person-years		12,873	22,374	27,706	31,014	34,595	
Incident Rate*		6.2	5.8	4.0	4.8	5.5	
Hazard ratio (95% CI)							
Model 1		1.38 (1.06, 1.80)	1.14 (0.91, 1.43)	0.83 (0.65, 1.05)	0.98 (0.79, 1.22)	1	1.13 (1.03, 1.25)
Model 3		1.13 (0.86, 1.48)	1.03 (0.82, 1.29)	0.72 (0.57, 0.92)	0.90 (0.72, 1.12)	1	1.05 (0.97, 1.17)

		FVC%, predicted					
		Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)
	N	891	1,117	1,315	1,294	1,401	

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)
Dementia cases, *n*	113	129	116	145	157	
Person-years	17,756	23,490	28,390	28,077	30,848	
Incident Rate*	6.4	5.5	4.1	5.2	5.1	
Hazard ratio (95% CI)						
Model 1	1.44 (1.13, 1.84)	1.16 (0.92, 1.46)	0.95 (0.75, 1.21)	1.14 (0.91, 1.43)	1	1.14 (1.04, 1.23)
Model 3	1.15 (0.89, 1.49)	1.08 (0.85, 1.37)	0.81 (0.64, 1.04)	1.08 (0.86, 1.36)	1	1.06 (0.99, 1.16)

	FEV1/FVC%, predicted					
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)
N	621	1,114	1,305	1,422	1,556	
Dementia cases, *n*	76	89	136	158	201	
Person-years	13,185	24,186	28,036	30,382	32,772	
Incident Rate*	5.8	3.7	4.9	5.2	6.1	
Hazard ratio (95% CI)						
Model 1	1.03 (0.79, 1.34)	0.70 (0.54, 0.90)	0.89 (0.72, 1.11)	0.91 (0.74, 1.13)	1	0.98 (0.89, 1.08)
Model 3	1.02 (0.78, 1.34)	0.74 (0.57, 0.96)	0.93 (0.74, 1.16)	0.94 (0.76, 1.16)	1	0.99 (0.89, 1.09)

*Per 1,000 person-years
Model 1: Cox regression adjusted for age, sex, center, education level, and race-center (5-level variable)
Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking
Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

Supplemental Table 4

Lung function disease categories, objective indices of lung function, and risk of incident dementia among blacks and whites: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

	Lung Function Category				
	Normal	Respiratory symptoms with normal spirometric results	Restrictive impairment pattern	COPD pattern	p-race interaction
Blacks					
Dementia cases, *n*	208	176	19	68	
Person-years	34,058	25,185	2,969	9,367	
Incident Rate*	6.1	7.0	6.4	7.3	
Hazard ratio (95% CI)					
Model 1	1	1.20 (0.98, 1.47)	1.32 (0.82, 2.12)	1.40 (1.06, 1.85)	P=0.64
Model 2	1	1.21 (0.98, 1.48)	1.32 (0.82, 2.12)	1.43 (1.07, 1.92)	P=0.54
Model 3	1	1.14 (0.92, 1.41)	1.23 (0.76, 1.98)	1.31 (0.98, 1.76)	P=0.49
Whites					
Dementia cases, *n*	408	307	60	161	
Person-years	96,045	71,529	12,516	36,645	
Incident Rate*	4.2	4.3	4.8	4.4	
Hazard ratio (95% CI)					
Model 1	1	1.05 (0.91, 1.22)	1.34 (1.02, 1.75)	1.17 (0.97, 1.41)	
Model 2	1	0.99 (0.85, 1.15)	1.19 (0.90, 1.57)	0.99 (0.81, 1.20)	
Model 3	1	0.92 (0.79, 1.07)	0.93 (0.70, 1.23)	0.99 (0.82, 1.21)	

	FEV1%, predicted						
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)	p-race interaction
Blacks							
Dementia cases, *n*	79	92	78	89	133		

	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)	p-race interaction
Person-years	10,737	12,666	13,668	14,750	19,757		
Incident Rate*	7.4	7.3	5.7	6.0	6.7		
Hazard ratio (95% CI)							
Model 1	1.39 (1.05, 1.85)	1.16 (0.89, 1.52)	0.82 (0.62, 1.09)	0.94 (0.72, 1.23)	1	1.11 (1.00, 1.21)	0.58
Model 2	1.41 (1.06, 1.89)	1.16 (0.88, 1.52)	0.83 (0.63, 1.10)	0.94 (0.72, 1.24)	1	1.11 (1.00, 1.23)	0.87
Model 3	1.24 (0.92, 1.67)	1.03 (0.78, 1.36)	0.71 (0.54, 0.95)	0.87 (0.66, 1.14)	1	1.07 (0.97, 1.17)	0.83
Whites							
Dementia cases, *n*	196	190	168	201	181		
Person-years	39,894	44,436	45,731	45,365	41,308		
Incident Rate*	4.9	4.3	3.7	4.4	4.4		
Hazard ratio (95% CI)							
Model 1	1.37 (1.12, 1.69)	1.11 (0.91, 1.36)	0.98 (0.79, 1.20)	1.15 (0.94, 1.41)	1	1.15 (1.07, 1.23)	
Model 2	1.17 (0.94, 1.45)	1.02 (0.75, 1.15)	0.93 (0.75, 1.15)	1.14 (0.93, 1.39)	1	1.07 (1.00, 1.17)	
Model 3	1.06 (0.85, 1.32)	0.97 (0.79, 1.20)	0.91 (0.73, 1.12)	1.12 (0.92, 1.38)	1	1.03 (0.95, 1.11)	

	FVC%, predicted						
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)	p-race interaction
Blacks							
Dementia cases, *n*	97	81	85	94	114		
Person-years	12,543	12,294	13,078	14,421	19,242		
Incident Rate*	7.7	6.6	6.5	6.5	5.9		
Hazard ratio (95% CI)							
Model 1	1.50 (1.14, 1.97)	1.19 (0.89, 1.58)	1.12 (0.84, 1.49)	1.16 (0.88, 1.52)	1	1.09 (1.00, 1.17)	0.26
Model 2	1.49 (1.13, 1.97)	1.18 (0.89, 1.58)	1.12 (0.84, 1.48)	1.16 (0.88, 1.53)	1	1.09 (1.00, 1.17)	0.44
Model 3	1.27 (0.95, 1.69)	1.17 (0.88, 1.57)	0.96 (0.72, 1.28)	1.10 (0.83, 1.45)	1	1.04 (0.96, 1.14)	0.97
Whites							
Dementia cases, *n*	186	211	172	203	164		
Person-years	39,528	44,530	45,665	45,439	41,572		
Incident Rate*	4.7	4.7	3.8	4.5	3.9		

Hazard ratio (95% CI)							
Model 1	1.42 (1.15, 1.76)	1.33 (1.08, 1.63)	1.09 (0.88, 1.35)	1.30 (1.06, 1.59)	1	1.16 (1.08, 1.25)	
Model 2	1.29 (1.04, 1.60)	1.26 (1.02, 1.54)	1.06 (0.86, 1.32)	1.29 (1.05, 1.58)	1	1.12 (1.04, 1.21)	
Model 3	1.06 (0.85, 1.33)	1.18 (0.96, 1.46)	1.02 (0.82, 1.26)	1.23 (1.00, 1.51)	1	1.04 (0.97, 1.12)	

	FEV1/FVC%, predicted						
	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	Trend (per 1 SD decrease)	p-race interaction
Blacks							
Dementia cases, *n*	76	75	81	112	127		
Person-years	11,821	13,072	14,201	15,312	17,173		
Incident Rate*	6.4	5.7	5.7	7.3	7.4		
Hazard ratio (95% CI)							
Model 1	1.05 (0.79, 1.39)	0.88 (0.66, 1.17)	0.89 (0.67, 1.17)	0.89 (0.67, 1.17)	1	1.03 (0.93, 1.14)	0.91
Model 2	1.04 (0.77, 1.39)	0.89 (0.67, 1.18)	0.89 (0.67, 1.18)	1.22 (0.95, 1.58)	1	1.03 (0.93, 1.14)	0.83
Model 3	0.99 (0.73, 1.33)	0.95 (0.71, 1.26)	0.86 (0.65, 1.14)	1.29 (1.00, 1.67)	1	1.03 (0.92, 1.14)	0.94
Whites							
Dementia cases, *n*	181	172	185	175	223		
Person-years	41,013	45,250	44,924	44,068	41,479		
Incident Rate*	4.4	3.8	4.1	4.0	5.4		
Hazard ratio (95% CI)							
Model 1	0.93 (0.77, 1.14)	0.80 (0.65, 0.98)	0.80 (0.66, 0.98)	0.77 (0.63, 0.93)	1	1.03 (0.96, 1.11)	
Model 2	0.77 (0.63, 0.95)	0.73 (0.60, 0.90)	0.77 (0.63, 0.93)	0.74 (0.61, 0.91)	1	0.96 (0.89, 1.04)	
Model 3	0.88 (0.71, 1.09)	0.80 (0.65, 0.98)	0.86 (0.70, 1.05)	0.79 (0.64, 0.96)	1	0.99 (0.92, 1.07)	

*Per 1,000 person-years

Model 1: Cox regression adjusted for age, sex, center, education level, and race-center (5-level variable)

Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking

Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

Supplemental Table 5

Objective indices of lung function and risk of incident dementia <u>according to follow-up time</u>*: The Atherosclerosis Risk in Communities (ARIC) study, 1996-2013

	FEV1%, predicted					Trend (per 1-SD decrease)
	Q1	Q2	Q3	Q4	Q5	
Before the median follow up cutpoint*						
Dementia cases, n	202	170	135	159	167	
Person-years	49,426	55,277	57,450	58,093	58,979	
Incident Rate (per 1000 person-years)	4.1	3.1	2.3	2.7	2.8	
Hazard Ratio (95% CI)						
Model 1	1.65 (1.34, 2.04)	1.25 (1.01, 1.55)	0.94 (0.75, 1.18)	1.07 (0.86, 1.33)	1	1.21 (1.13, 1.29)
Model 2	1.49 (1.20, 1.86)	1.19 (0.96, 1.48)	0.91 (0.73, 1.15)	1.06 (0.85, 1.32)	1	1.17 (1.07, 1.25)
Model 3	1.32 (1.06, 1.65)	1.09 (0.87, 1.36)	0.85 (0.68, 1.07)	1.02 (0.82, 1.27)	1	1.11 (1.03, 1.19)
After the median follow up cutpoint*						
Dementia cases, n	73	112	111	131	147	
Person-years	1,206	1,825	1,950	2,022	2,087	
Incident Rate (per 1000 person-years)	60.5	61.4	56.9	64.8	70.4	
Hazard Ratio (95% CI)						
Model 1	0.91 (0.68, 1.21)	0.95 (0.74, 1.21)	0.87 (0.68, 1.12)	1.07 (0.84, 1.36)	1	0.98 (0.90, 1.09)
Model 2	0.85 (0.63, 1.15)	0.92 (0.71, 1.18)	0.86 (0.70, 1.10)	1.06 (0.84, 1.35)	1	0.97 (0.87, 1.07)
Model 3	0.79 (0.58, 1.06)	0.85 (0.66, 1.10)	0.81 (0.63, 1.05)	1.02 (0.80, 1.29)	1	0.93 (0.84, 1.03)

FVC%, predicted

	Q1	Q2	Q3	Q4	Q5	Trend (per 1-SD decrease)
Before the median follow up cutpoint*						
Dementia cases, n	187	191	146	162	147	
Person-years	50,699	55,019	56,869	57,903	58,736	
Incident Rate (per 1000 person-years)	3.7	3.5	2.6	2.8	2.5	
Hazard Ratio (95% CI)						
Model 1	1.72 (1.38, 2.14)	1.59 (1.28, 1.98)	1.14 (0.90, 1.43)	1.26 (1.01, 1.58)	1	1.23 (1.14, 1.32)
Model 2	1.60 (1.28, 1.99)	1.53 (1.23, 1.91)	1.11 (0.88, 1.40)	1.25 (1.00, 1.57)	1	1.19 (1.12, 1.28)
Model 3	1.31 (1.05, 1.65)	1.44 (1.15, 1.79)	1.01 (0.80, 1.28)	1.17 (0.93, 1.46)	1	1.14 (1.06, 1.23)
After the median follow up cutpoint*						
Dementia cases, n	96	101	111	135	131	
Person-years	1,373	1,805	1,875	1,957	2,079	
Incident Rate (per 1000 person-years)	69.9	56.0	59.2	69.0	63.0	
Hazard Ratio (95% CI)						
Model 1	1.10 (0.85, 1.44)	0.93 (0.72, 1.21)	1.03 (0.80, 1.33)	1.23 (0.97, 1.57)	1	0.99 (0.90, 1.08)
Model 2	1.07 (0.82, 1.40)	0.92 (0.71, 1.20)	1.02 (0.79, 1.32)	1.23 (0.97, 1.57)	1	0.97 (0.89, 1.06)
Model 3	0.95 (0.72, 1.26)	0.89 (0.68, 1.15)	0.94 (0.73, 1.22)	1.19 (0.93, 1.51)	1	0.94 (0.85, 1.03)

*Follow-up stratified at the median follow-up for events, which was 23.0 years

Supplemental Table 6

Weighted* odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories and objective lung function measures with dementia or MCI <u>among never smokers</u>: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

		Lung Disease Category			
		Normal	Respiratory symptoms with normal spirometric results	Restrictive impairment pattern	COPD pattern
	N	1679	894	103	239
Dementia or MCI, n		402	247	38	76
Model 1		1	1.24 (1.02, 1.52)	2.10 (1.30, 3.39)	1.65 (1.19, 2.28)
Model 3		1	1.17 (0.96, 1.44)	1.69 (1.04, 2.76)	1.72 (1.23, 2.40)

		FEV1%, predicted			
		Quartile 1	Quartile 2	Quartile 3	Quartile 4
	N	580	712	761	862
Dementia or MCI, n		193	164	181	225
Model 1		1.58 (1.22, 2.05)	0.97 (0.75, 1.25)	0.90 (0.71, 1.16)	1
Model 3		1.43 (1.10, 1.87)	0.91 (0.70, 1.18)	0.84 (0.66, 1.09)	1

		FVC%, predicted			
		Quartile 1	Quartile 2	Quartile 3	Quartile 4
	N	628	778	735	774
Dementia or MCI, n		187	201	183	192
Model 1		1.43 (1.10, 1.87)	1.20 (0.93, 1.54)	1.13 (0.88, 1.46)	1
Model 3		1.29 (0.98, 1.69)	1.11 (0.86, 1.43)	1.07 (0.83, 1.39)	1

		FEV1/FVC%, predicted			
	N	556	740	784	835
Dementia or MCI, n		156	169	196	242
Model 1		1.07 (0.83, 1.40)	0.79 (0.62, 1.02)	0.87 (0.68, 1.12)	1
Model 3		1.11 (0.85, 1.46)	0.81 (0.62, 1.04)	0.87 (0.68, 1.11)	1

*Inverse-probability weighting was used.

Model 1: Logistic regression adjusted for age, sex, center, education level, and race-center (5-level variable)
Model 3: Model 1 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

Supplemental Table 7

Race-stratified weighted* odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories, FEV1% predicted, FVC% predicted and FEV1/FVC% predicted with dementia or MCI: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

	Lung Disease Category					
	Normal	Respiratory symptoms with normal spirometric results	Restrictive impairment pattern	COPD pattern	Type III p-value	Effect Modification by Race
Blacks						
Dementia or MCI, n	180	133	11	51		
Model 1	1	0.97 (0.71, 1.31)	0.88 (0.36, 2.11)	1.57 (1.02, 2.42)	0.20	P=0.04
Model 2	1	1.02 (0.75, 1.38)	0.89 (0.35, 2.26)	1.76 (1.13, 2.74)	0.12	P=0.04
Model 3	1	1.13 (0.82, 1.54)	0.80 (0.32, 1.99)	2.13 (1.34, 3.40)	0.03	P=0.04
Whites						
Dementia or MCI, n	541	385	76	161		
Model 1	1	1.22 (1.03, 1.44)	2.32 (1.65, 3.26)	1.26 (1.01, 1.59)	<.0001	
Model 2	1	1.20 (1.01, 1.42)	2.23 (1.58, 3.15)	1.19 (0.94, 1.52)	0.0003	
Model 3	1	1.11 (0.93, 1.31)	1.79 (1.27, 2.54)	1.21 (0.96, 1.54)	0.01	

	FEV1%, predicted					
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Type III p-value	Effect Modification By Race
Blacks						
Dementia or MCI, n						
Model 1	1.72 (1.20, 2.46)	1.12 (0.77, 1.63)	0.94 (0.64, 1.38)	1	0.016	P=0.66
Model 2	1.82 (1.26, 2.63)	1.21 (0.83, 1.76)	0.99 (0.67, 1.45)	1	0.011	P=0.60
Model 3	1.82 (1.24, 2.69)	1.18 (0.80, 1.75)	0.92 (0.62, 1.36)	1	0.008	P=0.49
Whites						
Dementia or MCI, n						
Model 1	1.33 (1.08, 1.64)	1.01 (0.82, 1.25)	0.92 (0.75, 1.14)	1	0.004	
Model 2	1.27 (1.02, 1.57)	0.99 (0.80, 1.23)	0.92 (0.74, 1.14)	1	0.02	
Model 3	1.17 (0.94, 1.45)	0.95 (0.76, 1.18)	0.88 (0.71, 1.10)	1	0.06	

	FVC%, predicted					
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Type III p-value	Effect Modification By Race
Blacks						
Dementia or MCI, n						
Model 1	1.68 (1.18, 2.39)	0.99 (0.67, 1.47)	0.94 (0.65, 1.36)	1	0.01	P=0.26
Model 2	1.67 (1.17, 2.39)	0.98 (0.66, 1.46)	0.92 (0.64, 1.33)	1	0.01	P=0.26
Model 3	1.74 (1.20, 2.52)	0.91 (0.60, 1.37)	0.92 (0.63, 1.34)	1	0.006	P=0.12
Whites						
Dementia or MCI, n						
Model 1	1.38 (1.11, 1.70)	1.23 (1.00, 1.51)	1.13 (0.91, 1.40)	1	0.02	
Model 2	1.32 (1.07, 1.64)	1.21 (0.98, 1.49)	1.12 (0.90, 1.39)	1	0.06	
Model 3	1.17 (0.94, 1.45)	1.13 (0.91, 1.39)	1.08 (0.87, 1.34)	1	0.53	

	FEV1/FVC%, predicted					
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Type III p-value	Effect Modification By Race
Blacks						
Dementia or MCI, n						
Model 1	1.10 (0.76, 1.59)	0.66 (0.44, 0.99)	0.97 (0.67, 1.38)	1	0.07	P=0.60
Model 2	1.20 (0.82, 1.75)	0.70 (0.46, 1.05)	0.99 (0.69, 1.42)	1	0.07	P=0.52
Model 3	1.26 (0.85, 1.87)	0.70 (0.46, 0.97)	1.02 (0.70, 1.47)	1	0.06	P=0.60
Whites						
Dementia or MCI, n						
Model 1	0.98 (0.80, 1.20)	0.82 (0.67, 1.01)	1.01 (0.82, 1.24)	1	0.17	
Model 2	0.91 (0.74, 1.12)	0.80 (0.65, 0.99)	1.00 (0.81, 1.23)	1	0.13	
Model 3	1.02 (0.83, 1.27)	0.85 (0.69, 1.05)	1.04 (0.85, 1.29)	1	0.22	

*Inverse-probability weighting was used.

Model 1: Logistic regression adjusted for age, sex, center, education level, and race-center (5-level variable)

Model 3: Model 1 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

Supplemental Table 8 – FEV1/FVC% predicted & adjudicated outcomes

Inverse-probability weighted odds ratios (OR) and 95% confidence intervals (CI) of FEV1/FEC percent of predicted quartile categories with dementia, mild cognitive impairment (MCI), Alzheimer's disease and cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

	FEV1/FVC%, predicted				
	Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend (per 1 SD decrease)
N	1472	1473	1471	1473	
Dementia/MCI, n	397	329	388	424	
Odds ratio (95% CI)					
Model 1	1.00 (0.83, 1.19)	0.78 (0.65, 0.94)	0.99 (0.83, 1.19)	1	1.00 (0.93, 1.06)
Model 2	0.96 (0.80, 1.16)	0.77 (0.64, 0.93)	0.98 (0.82, 1.18)	1	0.98 (0.92, 1.05)
Model 3	1.05 (0.87, 1.27)	0.80 (0.67, 0.97)	1.01 (0.84, 1.22)	1	1.01 (0.95, 1.09)
Dementia, n	73	60	74	91	
Odds ratio (95% CI)					
Model 1	0.92 (0.63, 1.33)	0.75 (0.50, 1.10)	0.95 (0.66, 1.38)	1	0.93 (0.80, 1.07)
Model 2	0.85 (0.58, 1.25)	0.73 (0.50, 1.08)	0.93 (0.65, 1.35)	1	0.89 (0.77, 1.03)
Model 3	0.92 (0.61, 1.38)	0.74 (0.49, 1.12)	0.94 (0.64, 1.38)	1	0.92 (0.78, 1.08)
MCI, n	324	269	314	333	
Odds ratio (95% CI)					
Model 1	1.04 (0.86, 1.26)	0.80 (0.66, 0.97)	1.02 (0.84, 1.23)	1	1.02 (0.95, 1.10)
Model 2	1.02 (0.84, 1.24)	0.79 (0.65, 0.97)	1.01 (0.84, 1.22)	1	1.02 (0.94, 1.09)
Model 3	1.12 (0.92, 1.36)	0.83 (0.68, 1.01)	1.04 (0.86, 1.26)	1	1.05 (0.97, 1.13)
Alzheimer's disease, n	239	212	265	288	
Odds ratio (95% CI)					
Model 1	0.86 (0.70, 1.06)	0.72 (0.58, 0.90)	0.98 (0.79, 1.20)	1	0.94 (0.87, 1.02)
Model 2	0.86 (0.69, 1.07)	0.72 (0.58, 0.90)	0.97 (0.79, 1.19)	1	0.94 (0.86, 1.02)
Model 3	0.93 (0.75, 1.16)	0.75 (0.60, 0.93)	1.00 (0.81, 1.23)	1	0.97 (0.89, 1.06)
Cerebrovascular disease, n	42	43	47	56	
Odds ratio (95% CI)					
Model 1	1.01 (0.64, 1.60)	0.83 (0.53, 1.30)	1.13 (0.72, 1.78)	1	1.06 (0.89, 1.26)
Model 2	0.84 (0.53, 1.33)	0.78 (0.49, 1.25)	1.08 (0.69, 1.67)	1	0.99 (0.82, 1.18)

Model 3	1.00 (0.63, 1.60)	0.86 (0.54, 1.37)	1.10 (0.70, 1.72)	1	1.05 (0.88, 1.26)

Model 1: Logistic regression adjusted for age, sex, center, education level, and race-center (5-level variable)

Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking

Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

1.   Baecke JA, Burema J, Frijters JE. A short questionnaire for the measurement of habitual physical activity in

epidemiological studies. The American Journal of Clinical Nutrition. 1982;36(5):936-942. doi: 10.1093/ajcn/36.5.936.

Supplemental Table 9

Odds ratios (ORs) and 95% confidence intervals (CI) of lung disease categories with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

		Lung Disease Category		
		Respiratory symptoms with normal spirometric results	Restrictive impairment pattern	COPD pattern
	Normal			
N	2,953	1,967	239	730
Dementia or MCI, n	721	518	87	212
Model 1	1	1.12 (0.98, 1.28)	1.87 (1.40, 2.49)	1.27 (1.05, 1.53)
Model 2	1	1.12 (0.98, 1.29)	1.85 (1.39, 2.48)	1.26 (1.04, 1.53)
Model 3	1	1.09 (0.94, 1.25)	1.63 (1.21, 2.19)	1.30 (1.07, 1.59)
Model 4	1	1.08 (0.94, 1.24)	1.59 (1.18, 2.15)	1.29 (1.06, 1.57)
Dementia, n	147	94	15	42
Model 1	1	0.97 (0.73, 1.29)	1.50 (0.81, 2.78)	1.19 (0.81, 1.75)
Model 2	1	0.95 (0.71, 1.27)	1.43 (0.77, 2.65)	1.15 (0.77, 1.71)
Model 3	1	0.93 (0.69, 1.26)	1.08 (0.57, 2.06)	1.20 (0.79, 1.81)
MCI, n	574	424	72	170
Model 1	1	1.15 (1.00, 1.34)	1.91 (1.41, 2.58)	1.28 (1.05, 1.56)
Model 2	1	1.16 (1.00, 1.35)	1.91 (1.41, 2.60)	1.29 (1.05, 1.59)
Model 3	1	1.13 (0.97, 1.31)	1.73 (1.27, 2.36)	1.33 (1.08, 1.64)
AD dementia or MCI, n	474	344	59	127
Model 1	1	1.13 (0.97, 1.33)	1.92 (1.39, 2.67)	1.16 (0.93, 1.45)
Model 2	1	1.15 (0.98, 1.35)	1.96 (1.41, 2.72)	1.19 (0.94, 1.49)
Model 3	1	1.12 (0.95, 1.31)	1.78 (1.27, 2.49)	1.23 (0.97, 1.55)
Cerebrovascular dementia or MCI, n	88	62	12	26
Model 1	1	1.08 (0.77, 1.52)	2.11 (1.09, 4.07)	1.31 (0.83, 2.07)
Model 2	1	1.06 (0.75, 1.49)	1.99 (1.03, 3.88)	1.22 (0.75, 1.97)
Model 3	1	1.00 (0.70, 1.43)	1.58 (0.80, 3.12)	1.33 (0.81, 2.16)

Model 1: Logistic regression adjusted for age, sex, education level, and race-center (5-level variable)
Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking
Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary

heart disease, heart failure, stroke and APOE genotype
Model 4: Model 3 + fibrinogen

Supplemental Table 10

Odds ratios (ORs) and 95% confidence intervals (CI) of FEV1 percent predicted quartile with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

		FEV1%, predicted			
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	Trend (per 1 SD decrease)
	N	1,473	1,471	1,472	1,473	
Dementia or MCI, n		450	364	346	378	
Model 1		1.30 (1.09, 1.53)	0.99 (0.84, 1.18)	0.91 (0.77, 1.09)	1	1.12 (1.05, 1.19)
Model 2		1.28 (1.08, 1.53)	0.99 (0.83, 1.19)	0.91 (0.77, 1.09)	1	1.11 (1.05, 1.19)
Model 3		1.24 (1.04, 1.48)	0.97 (0.81, 1.15)	0.89 (0.75, 1.06)	1	1.10 (1.04, 1.18)
Model 4		1.23 (1.03, 1.47)	0.96 (0.81, 1.15)	0.88 (0.74, 1.05)	1	1.10 (1.03, 1.17)
Dementia, n		87	59	69	83	
Model 1		1.19 (0.84, 1.67)	0.81 (0.56, 1.17)	0.92 (0.65, 1.31)	1	1.06 (0.94, 1.20)
Model 2		1.13 (0.79, 1.60)	0.79 (0.55, 1.15)	0.93 (0.65, 1.32)	1	1.04 (0.92, 1.18)
Model 3		1.02 (0.70, 1.47)	0.74 (0.50, 1.09)	0.89 (0.62, 1.28)	1	1.01 (0.89, 1.15)
MCI, n		363	305	277	295	
Model 1		1.32 (1.10, 1.58)	1.04 (0.87, 1.25)	0.92 (0.76, 1.11)	1	1.13 (1.06, 1.21)
Model 2		1.32 (1.10, 1.59)	1.04 (0.87, 1.26)	0.92 (0.76, 1.11)	1	1.13 (1.06, 1.21)
Model 3		1.29 (1.07, 1.57)	1.02 (0.85, 1.24)	0.90 (0.75, 1.09)	1	1.13 (1.05, 1.21)
AD dementia or MCI, n		284	223	237	260	
Model 1		1.19 (0.98, 1.45)	0.89 (0.73, 1.09)	0.90 (0.74, 1.11)	1	1.07 (1.00, 1.15)
Model 2		1.20 (0.98, 1.47)	0.89 (0.73, 1.10)	0.91 (0.74, 1.11)	1	1.08 (1.00, 1.16)
Model 3		1.19 (0.97, 1.47)	0.89 (0.72, 1.09)	0.89 (0.73, 1.10)	1	1.08 (1.00, 1.16)
Cerebrovascular dementia or MCI, n		57	53	35	43	
Model 1		1.59 (1.05, 2.43)	1.39 (0.91, 2.13)	0.89 (0.56, 1.42)	1	1.26 (1.09, 1.46)
Model 2		1.51 (0.98, 2.33)	1.37 (0.89, 2.09)	0.89 (0.56, 1.42)	1	1.24 (1.07, 1.44)
Model 3		1.41 (0.90, 2.19)	1.30 (0.84, 2.01)	0.85 (0.53, 1.36)	1	1.22 (1.04, 1.42)

Model 1: Logistic regression adjusted for age, sex, center, education level, and race-center (5-level variable)
Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking
Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications,

prevalent coronary heart disease, heart failure, stroke and APOE genotype
Model 4: Model 3 + fibrinogen

Supplemental Table 11

Odds ratios (ORs) and 95% confidence intervals (CI) of FVC percent predicted quartile with dementia, mild cognitive impairment (MCI), AD-type dementia or MCI, and dementia or MCI due to cerebrovascular disease: The Atherosclerosis Risk in Communities (ARIC) study, 1987-2013

		FVC%, predicted			
					Trend
		Quartile 1	Quartile 2	Quartile 3	Quartile 4	(per 1 SD decrease)
	N	1,472	1,473	1,471	1,473	
Dementia or MCI, n		434	381	361	362	
Model 1		1.30 (1.09, 1.54)	1.09 (0.92, 1.30)	1.03 (0.87, 1.23)	1	1.14 (1.07, 1.21)
Model 2		1.28 (1.08, 1.52)	1.08 (0.91, 1.29)	1.03 (0.87, 1.23)	1	1.13 (1.06, 1.20)
Model 3		1.21 (1.01, 1.44)	1.03 (0.87, 1.23)	1.01 (0.84, 1.20)	1	1.10 (1.04, 1.18)
Model 4		1.21 (1.01, 1.44)	1.04 (0.87, 1.24)	1.01 (0.84, 1.20)	1	1.10 (1.03, 1.17)
Dementia, n		80	69	71	78	
Model 1		1.13 (0.80, 1.61)	0.98 (0.69, 1.41)	1.06 (0.74, 1.50)	1	1.11 (0.98, 1.26)
Model 2		1.08 (0.76, 1.54)	0.95 (0.66, 1.36)	1.06 (0.74, 1.50)	1	1.09 (0.97, 1.23)
Model 3		0.95 (0.66, 1.38)	0.84 (0.58, 1.22)	1.00 (0.70, 1.44)	1	1.04 (0.91, 1.18)
MCI, n		354	312	290	284	
Model 1		1.33 (1.11, 1.60)	1.12 (0.93, 1.34)	1.03 (0.85, 1.24)	1	1.14 (1.07, 1.22)
Model 2		1.32 (1.10, 1.59)	1.11 (0.92, 1.34)	1.03 (0.85, 1.24)	1	1.14 (1.07, 1.22)
Model 3		1.26 (1.04, 1.53)	1.08 (0.89, 1.30)	1.02 (0.84, 1.23)	1	1.12 (1.05, 1.20)
AD dementia or MCI, n		284	237	238	245	
Model 1		1.25 (1.03, 1.53)	1.00 (0.82, 1.23)	1.00 (0.81, 1.22)	1	1.12 (1.04, 1.20)
Model 2		1.26 (1.03, 1.53)	1.00 (0.81, 1.22)	1.00 (0.82, 1.22)	1	1.12 (1.04, 1.20)
Model 3		1.22 (1.00, 1.50)	0.98 (0.80, 1.20)	0.98 (0.80, 1.20)	1	1.10 (1.03, 1.19)
Cerebrovascular dementia or MCI, n		57	52	43	36	
Model 1		1.84 (1.18, 2.85)	1.65 (1.06, 2.57)	1.32 (0.83, 2.09)	1	1.31 (1.13, 1.53)
Model 2		1.76 (1.13, 2.75)	1.61 (1.03, 2.52)	1.32 (0.83, 2.09)	1	1.29 (1.11, 1.51)
Model 3		1.54 (0.97, 2.43)	1.44 (0.92, 2.28)	1.28 (0.80, 2.04)	1	1.22 (1.04, 1.43)

Model 1: Logistic regression adjusted for age, sex, center, education level, and race-center (5-level variable)
Model 2: Model 1 + additional adjustment for cigarette smoking and pack-years of smoking
Model 3: Model 2 + additional adjustment for physical activity, body mass index, systolic blood pressure, blood pressure medication use, diabetes, HDL cholesterol, LDL cholesterol, lipid lowering medications, prevalent coronary heart disease, heart failure, stroke and APOE genotype

Model 4: Model 3 + fibrinogen