

ONLINE DATA SUPPLEMENT

Title: Percent emphysema is associated with respiratory and lung cancer mortality in the general population: a cohort study

Authors:

Elizabeth C Oelsner, MD MPH

J Jeffrey Carr, MD

Paul Enright, MD

Eric A Hoffman, PhD

Aaron R Folsom, MD MPH

Steven M Kawut, MD MSc

Richard Kronmal, PhD

David J Lederer, MD MSc

Joao AC Lima, MD PhD

Gina S Lovasi, PhD

Benjamin M Smith, MD MS

Steven J Shea, MD MS

R Graham Barr, MD DrPH

FIGURE LEGENDS

Figure E1. Multi-Ethnic Study of Atherosclerosis (MESA) and MESA-Lung Study.

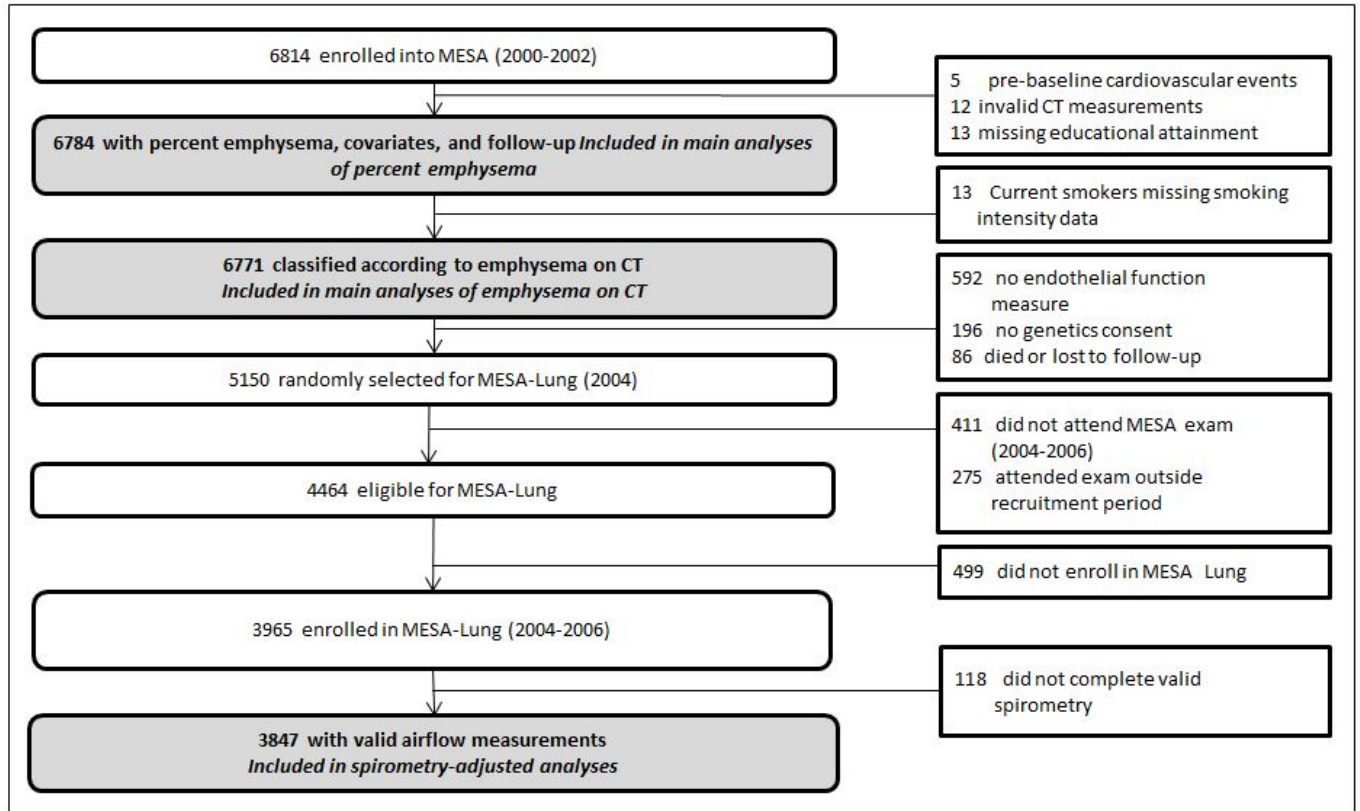


Figure E2. Emphysema on computed tomography and mortality due to lung diseases, by model adjustment and selected strata.

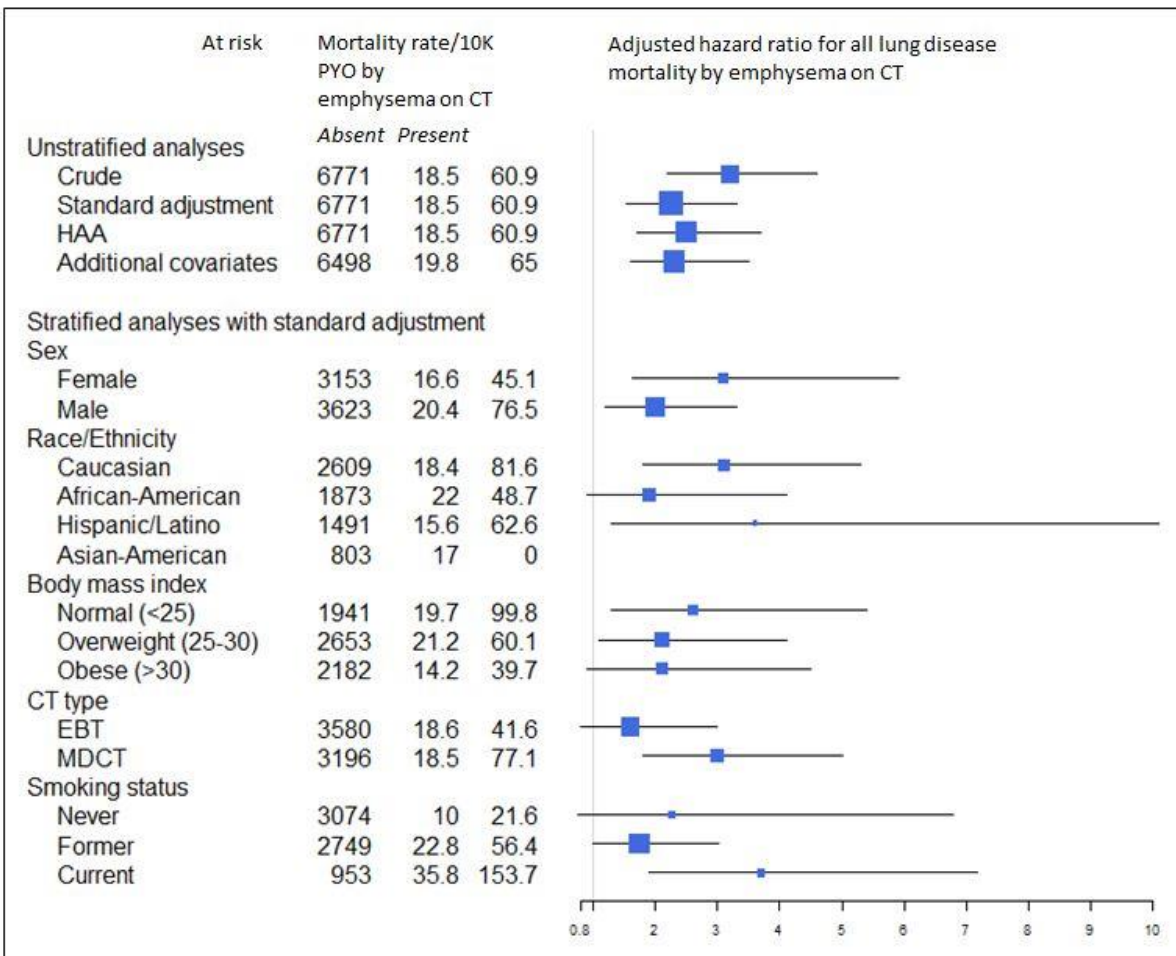


Table E1. Mortality due to diseases of the respiratory system in the Multi-Ethnic Study of Atherosclerosis, 2000-2013.

Underlying cause of death	ICD-10 Code	Number of deaths
Asthma	J45.9	1
Chronic obstructive pulmonary disease with acute lower respiratory infection	J44.0	1
Chronic obstructive pulmonary disease, unspecified	J44.9	30
Emphysema	J43.9	5
Lobar pneumonia, unspecified	J18.1	4
Other interstitial pulmonary diseases with fibrosis	J84.1	12
Pneumoconiosis due to asbestos and other mineral fibers	J61	1
Pneumoconiosis due to other dust containing silica	J62.8	1
Pneumonia due to pseudomonas	J15.1	1
Pneumonia, unspecified	J18.9	19
Pneumonitis due to food and vomit	J69.0	1
Pneumothorax	J93.9	1

Table E2. Associations between emphysema on computed tomography, percent emphysema, and mortality due to lung disease in the Multi-Ethnic Study of Atherosclerosis, 2000-2013, in sequentially adjusted models.

Underlying cause of death		Emphysema on computed tomography (dichotomous)			Percent emphysema (continuous)	
		Absent (N=6,233)	Present (N=538)	P-value	All (N=6,784)	P-value
Respiratory diseases						
Deaths		57	18		77	
	Unadjusted	1.00 (referent)	3.67 (2.16-6.25)	<0.001	1.48 (1.35-1.63)	<0.001
	+ Age	1.00 (referent)	3.67 (2.16, 6.24)	<0.001	1.49 (1.36, 1.64)	<0.001
	+ Sex	1.00 (referent)	3.48 (2.04, 5.94)	<0.001	1.49 (1.35, 1.65)	<0.001
	+ Race	1.00 (referent)	3.45 (2.01, 5.91)	<0.001	1.54 (1.38, 1.72)	<0.001
	+BMI	1.00 (referent)	3.54 (2.06, 6.08)	<0.001	1.54 (1.38, 1.72)	<0.001
	+Site	1.00 (referent)	3.63 (2.10, 6.27)	<0.001	1.55 (1.39, 1.73)	<0.001
	+Smoking status	1.00 (referent)	3.31 (1.92, 5.72)	<0.001	1.54 (1.38, 1.72)	<0.001
	+Pack-years	1.00 (referent)	2.88 (1.64, 5.04)	<0.001	1.49 (1.33, 1.68)	<0.001
	+Coronary artery calcium	1.00 (referent)	2.88 (1.64, 5.06)	<0.001	1.50 (1.34, 1.69)	<0.001
	+Educational attainment	1.00 (referent)	2.94 (1.68-5.15)	<0.001	1.51 (1.35-1.69)	<0.001
	+ HAA	1.00 (referent)	3.36 (1.91-5.93)	<0.001	1.48 (1.32-1.66)	<0.001
	+ Other clinical factors	1.00 (referent)	3.06 (1.70-5.49)	<0.001	1.42 (1.26-1.61)	<0.001
	+ FEV ₁	1.00 (referent)	3.44 (0.88-13.44)	0.076	1.24 (0.80-1.94)	0.340
Chronic lower respiratory diseases						
Deaths		20	17		39	
	Unadjusted	1.00 (referent)	10.11 (5.25-19.46)	<0.001	1.71 (1.55-1.88)	<0.001
	+ Age	1.00 (referent)	10.16 (5.28, 19.55)	<0.001	1.74 (1.57, 1.92)	<0.001
	+ Sex	1.00 (referent)	10.23 (5.28, 19.82)	<0.001	1.80 (1.63, 2.00)	<0.001
	+ Race	1.00 (referent)	10.16 (5.21, 19.81)	<0.001	1.93 (1.72, 2.18)	<0.001
	+BMI	1.00 (referent)	11.31 (5.75, 22.25)	<0.001	1.91 (1.69, 2.16)	<0.001
	+Site	1.00 (referent)	12.46 (6.27, 24.77)	<0.001	1.90 (1.67, 2.15)	<0.001
	+Smoking status	1.00 (referent)	10.67 (5.38, 21.18)	<0.001	1.87 (1.65, 2.12)	<0.001
	+Pack-years	1.00 (referent)	9.49 (4.70, 19.13)	<0.001	1.81 (1.59, 2.06)	<0.001
	+Coronary artery calcium	1.00 (referent)	9.58 (4.74, 19.35)	<0.001	1.83 (1.61, 2.08)	<0.001
	+Educational attainment	1.00 (referent)	9.54 (4.70-19.35)	<0.001	1.78 (1.57-2.03)	<0.001
	+ HAA	1.00 (referent)	8.28 (3.94-17.41)	<0.001	1.82 (1.59-2.09)	<0.001
	+ Other clinical factors	1.00 (referent)	8.27 (3.80-18.01)	<0.001	1.75 (1.51-2.04)	<0.001
	+ FEV ₁	1.00 (referent)	358.93 (1.23+)	0.042	16.74 (1.20-233)	0.036
Lung cancer						
Deaths		76	19		95	
	Unadjusted	1.00 (referent)	2.81 (1.70-4.65)	<0.001	1.35 (1.20-1.52)	<0.001
	+ Age	1.00 (referent)	2.84 (1.72, 4.69)	<0.001	1.35 (1.20, 1.52)	<0.001
	+ Sex	1.00 (referent)	2.64 (1.60, 4.38)	<0.001	1.29 (1.13, 1.48)	<0.001
	+ Race	1.00 (referent)	2.56 (1.54, 4.25)	<0.001	1.30 (1.13, 1.49)	<0.001
	+BMI	1.00 (referent)	2.62 (1.58, 4.36)	<0.001	1.29 (1.12, 1.48)	<0.001
	+Site	1.00 (referent)	2.59 (1.55, 4.32)	<0.001	1.29 (1.13, 1.47)	<0.001
	+Smoking status	1.00 (referent)	2.21 (1.32, 3.69)	0.002	1.27 (1.11, 1.45)	<0.001
	+Pack-years	1.00 (referent)	1.84 (1.09, 3.11)	0.023	1.19 (1.04, 1.36)	0.012
	+Coronary artery calcium	1.00 (referent)	1.81 (1.07, 3.07)	0.027	1.20 (1.05, 1.37)	0.009
	+Educational attainment	1.00 (referent)	1.84 (1.09-3.12)	0.023	1.21 (1.06-1.38)	0.006
	+ HAA	1.00 (referent)	1.99 (1.17-3.38)	0.011	1.22 (1.07-1.38)	0.002
	+ Other clinical factors	1.00 (referent)	1.76 (1.01-3.06)	0.047	1.20 (1.05-1.38)	0.008
	+ FEV ₁	1.00 (referent)	1.65 (0.54-5.02)	0.376	1.37 (1.00-1.87)	0.046
All lung diseases						
Deaths		133	37		172	
	Unadjusted	1.00 (referent)	3.16 (2.20-4.56)	<0.001	1.42 (1.32-1.53)	<0.001
	+ Age	1.00 (referent)	3.19 (2.21, 4.59)	<0.001	1.43 (1.33, 1.54)	<0.001
	+ Sex	1.00 (referent)	2.99 (2.07, 4.31)	<0.001	1.40 (1.29, 1.52)	<0.001
	+ Race	1.00 (referent)	2.92 (2.02, 4.22)	<0.001	1.42 (1.30, 1.54)	<0.001
	+BMI	1.00 (referent)	3.00 (2.07, 4.34)	<0.001	1.41 (1.29, 1.54)	<0.001
	+Site	1.00 (referent)	2.99 (2.06, 4.34)	<0.001	1.41 (1.29, 1.53)	<0.001
	+Smoking status	1.00 (referent)	2.64 (1.82, 3.83)	<0.001	1.39 (1.28, 1.52)	<0.001
	+Pack-years	1.00 (referent)	2.23 (1.52, 3.26)	<0.001	1.32 (1.21, 1.45)	<0.001
	+Coronary artery calcium	1.00 (referent)	2.21 (1.50, 3.24)	<0.001	1.33 (1.22, 1.46)	<0.001
	+Educational attainment	1.00 (referent)	2.25 (1.54-3.30)	<0.001	1.34 (1.23-1.46)	<0.001
	+ HAA	1.00 (referent)	2.49 (1.69-3.67)	<0.001	1.34 (1.23-1.45)	<0.001
	+ Other clinical factors	1.00 (referent)	2.33 (1.56-3.47)	<0.001	1.31 (1.20-1.43)	<0.001
	+ FEV ₁	1.00 (referent)	1.94 (0.87-4.29)	0.103	1.31 (1.03-1.67)	0.028

The endpoints were defined by an underlying cause of death of respiratory disease (J00-J99), lung cancer (C33-C34) and, combining these, all lung disease. We also specifically examined mortality due to chronic lower respiratory

disease (CLRD; J40-47), which was defined as deaths with COPD, emphysema, chronic bronchitis or asthma as the underlying cause, or, in the context of pneumonia as the underlying cause (J12-18), with these diseases (J40-47) recorded as a contributing cause.

CI = confidence interval. HAA = high attenuation areas. FEV₁ = forced expiratory volume in one second.

For percent emphysema, hazard ratios reported per interquartile range (4.5%), which is equivalent to the difference between the third quartile (5.7%) and the first quartile (1.2%) of percent emphysema. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment. Upper limit of normal for percent emphysema defined by reference equations. Other clinical factors are hypertension, hypertension medication, systolic and diastolic blood pressure; diabetes and fasting glucose; high density lipoprotein cholesterol, total cholesterol, and cholesterol medication use; history of cancer; creatinine; and alcohol use.

The numbers of events and numbers at risk are equivalent to those reported in Table 2 except for HRs adjusted for the FEV₁, since spirometry was only performed in a subset, hence the sample size was substantially lower and equivalent to numbers reported in Supplementary Table 3.

Table E3. Associations between upper-lobe and lower-lobe percent emphysema and mortality in the Multi-Ethnic Study of Atherosclerosis, 2000-2013.

Underlying cause of death		Upper-lobe percent emphysema		Basilar percent emphysema	
		All (N=3,835)	P-value	All (N=3,835)	P-value
Diseases of the respiratory system (J00-99)					
	Deaths	20		20	
	Person-years	30,338		30,338	
	Mortality rate per 10,000 person-years	6.7		6.7	
	Hazard Ratio _{crude} (95% CI)	1.37 (1.28-1.47)	<0.001	1.45 (1.32-1.59)	<0.001
	Hazard Ratio _{adjusted} (95% CI)	1.39 (1.28-1.50)	<0.001	1.44 (1.28-1.62)	<0.001
Chronic lower respiratory diseases (J40-47)					
	Deaths	8		8	
	Person-years	30,338		30,338	
	Mortality rate per 10,000 person-years	2.6		2.6	
	Hazard Ratio _{crude} (95% CI)	1.50 (1.38-1.63)	<0.001	1.61 (1.45-1.79)	<0.001
	Hazard Ratio _{adjusted} (95% CI)	1.58 (1.43-1.74)	<0.001	1.78 (1.55-2.04)	<0.001
Cancers of the trachea and lung (C33-C34)					
	Deaths	34		34	
	Person-years	30,338		30,338	
	Mortality rate per 10,000 person-years	11.2		11.2	
	Hazard Ratio _{crude} (95% CI)	1.26 (1.16-1.36)	<0.001	1.29 (1.14-1.45)	<0.001
	Hazard Ratio _{adjusted} (95% CI)	1.20 (1.08-1.33)	<0.001	1.16 (0.99-1.35)	0.061
Any lung disease (J00-99+C33-34)					
	Deaths	54		54	
	Person-years	30,338		30,338	
	Mortality rate per 10,000 person-years	17.8		17.8	
	Hazard Ratio _{crude} (95% CI)	1.31 (1.24-1.38)	<0.001	1.36 (1.27-1.47)	<0.001
	Hazard Ratio _{adjusted} (95% CI)	1.29 (1.21-1.37)	<0.001	1.29 (1.17-1.43)	<0.001
Cardiovascular disease					
	Deaths	250		250	
	Person-years	77,750		77,750	
	Mortality rate per 10,000 person-years	32.2		32.2	
	Hazard Ratio _{crude} (95% CI)	1.11 (1.01-1.22)	0.029	1.10 (0.99-1.23)	0.087
	Hazard Ratio _{adjusted} (95% CI)	1.08 (0.97-1.20)	0.162	1.03 (0.90-1.17)	0.680
Non-lung malignant neoplasms (C00-99, excluding C33-34)					
	Deaths	244		244	
	Person-years	77,750		77,750	
	Mortality rate per 10,000 person-years	4.5		4.5	
	Hazard Ratio _{crude} (95% CI)	0.99 (0.88-1.11)	0.826	0.96 (0.84-1.10)	0.554
	Hazard Ratio _{adjusted} (95% CI)	0.91 (0.80-1.05)	0.206	0.85 (0.72-0.99)	0.039

The endpoints were defined by an underlying cause of death of respiratory disease (J00-J99), lung cancer (C33-C34) and, combining these, all lung disease. We also specifically examined mortality due to chronic lower respiratory disease (CLRD; J40-47), which was defined as deaths with COPD, emphysema, chronic bronchitis or asthma as the underlying cause, or, in the context of pneumonia as the underlying cause (J12-18), with these diseases (J40-47) recorded as a contributing cause. Non-lung disease mortality endpoints were defined as an underlying cause of death of circulatory disease (I00-99) or other cancers (C00-99, excluding C33-34).

Hazard ratios reported per interquartile range. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment.

Table E4. Associations between percent emphysema and mortality due to lung disease in the Multi-Ethnic Study of Atherosclerosis, by pack-years, 2000-2013, in sequentially adjusted models.

Underlying cause of death	0 pack-years (never smoker)		<10 pack-years ever-smoker		>10 pack-years ever-smoker		P-interaction for pack-years
	All (N=3,072)	P-value	All (N=1,028)	P-value	All (N=2,218)	P-value	
Respiratory diseases							
Deaths	21		13		43		0.348
Person-years	35,686		17,274		24,788		
Mortality rate	5.9		7.5		17.4		
Unadjusted	1.14 (0.79, 1.64)	0.49	1.41 (1.00, 2.00)	0.053	1.57 (1.39-1.78)	<0.001	
+ Age	1.14 (0.79, 1.65)	0.49	1.40 (0.99, 1.99)	0.061	1.60 (1.40, 1.82)	<0.001	
+ Sex	1.09 (0.71, 1.67)	0.71	1.56 (1.11, 2.20)	0.011	1.59 (1.40, 1.81)	<0.001	
+ Race	1.07 (0.68, 1.69)	0.78	1.61 (1.12, 2.31)	0.011	1.62 (1.41, 1.85)	<0.001	
+BMI	1.12 (0.70, 1.79)	0.62	1.58 (1.10, 2.28)	0.014	1.57 (1.37, 1.81)	<0.001	
+Site	1.14 (0.72, 1.80)	0.57	1.65 (1.13, 2.39)	0.009	1.57 (1.37, 1.81)	<0.001	
+Smoking status	1.14 (0.72, 1.80)	0.57	1.43 (0.95, 2.15)	0.089	1.61 (1.40, 1.86)	<0.001	
+Pack-years	1.14 (0.72, 1.80)	0.57	1.42 (0.95, 2.14)	0.090	1.55 (1.34, 1.79)	<0.001	
+Coronary artery calcium	1.14 (0.73, 1.80)	0.57	1.44 (0.96, 2.18)	0.081	1.58 (1.37, 1.83)	<0.001	
+Educational attainment	1.18 (0.78-1.77)	0.44	1.74 (1.14, 2.66)	0.011	1.61 (1.39-1.86)	<0.001	
Chronic lower respiratory diseases							
Deaths	5		8		26		0.603
Person-years	35,686		17,274		24,788		
Mortality rate	1.4		4.6		10.5		
Unadjusted	1.29 (0.70, 2.39)	0.68	1.76 (1.26, 2.45)	0.001	1.85 (1.62, 2.12)	<0.001	
+ Age	1.29 (0.70, 2.40)	0.41	1.75 (1.25, 2.44)	0.001	1.94 (1.68, 2.24)	<0.001	
+ Sex	1.43 (0.79, 2.59)	0.23	2.18 (1.48, 3.22)	<0.001	1.97 (1.71, 2.27)	<0.001	
+ Race	1.36 (0.79, 2.37)	0.27	2.16 (1.45, 3.21)	<0.001	1.99 (1.71, 2.31)	<0.001	
+BMI	1.47 (0.85, 2.56)	0.17	2.19 (1.47, 3.26)	<0.001	1.95 (1.65, 2.30)	<0.001	
+Site	1.42 (0.79, 2.53)	0.24	2.30 (1.53, 3.48)	<0.001	1.94 (1.62, 2.32)	<0.001	
+Smoking status	1.42 (0.79, 2.53)	0.24	2.08 (1.29, 3.35)	0.003	2.00 (1.66, 2.41)	<0.001	
+Pack-years	1.42 (0.79, 2.53)	0.24	2.07 (1.28, 3.36)	0.003	1.92 (1.59, 2.32)	<0.001	
+Coronary artery calcium	1.41 (0.78, 2.53)	0.25	2.22 (1.32, 3.75)	0.003	1.95 (1.62, 2.35)	<0.001	
+Educational attainment	1.42 (0.84, 2.40)	0.19	2.36 (1.26, 4.43)	0.008	1.99 (1.63, 2.41)	<0.001	
Lung cancer							
Deaths	17		7		71		0.355
Person-years	35,686		17,274		24,788		
Mortality rate	4.8		4.0		28.6		
Unadjusted	1.23 (0.84, 1.80)	0.28	1.38 (0.82, 2.31)	0.22	1.24 (1.07, 1.44)	0.005	
+ Age	1.24 (0.85, 1.83)	0.27	1.38 (0.81, 2.34)	0.23	1.24 (1.07, 1.44)	0.005	
+ Sex	1.17 (0.74, 1.86)	0.49	1.22 (0.64, 2.30)	0.55	1.23 (1.05, 1.44)	0.009	
+ Race	1.18 (0.82, 1.71)	0.37	1.24 (0.65, 2.35)	0.51	1.24 (1.06, 1.45)	0.008	
+BMI	1.17 (0.80, 1.69)	0.42	1.19 (0.61, 2.32)	0.60	1.23 (1.05, 1.44)	0.010	
+Site	1.17 (0.83, 1.64)	0.37	1.39 (0.68, 2.83)	0.37	1.22 (1.05, 1.42)	0.011	
+Smoking status	1.17 (0.83, 1.64)	0.37	1.40 (0.69, 2.85)	0.35	1.25 (1.07, 1.45)	0.004	
+Pack-years	1.17 (0.83, 1.64)	0.37	1.41 (0.68, 2.90)	0.35	1.18 (1.01, 1.37)	0.032	
+Coronary artery calcium	1.18 (0.84, 1.65)	0.35	1.42 (0.68, 2.94)	0.35	1.18 (1.02, 1.38)	0.030	
+Educational attainment	1.17 (0.81, 1.69)	0.40	1.53 (0.70, 3.31)	0.29	1.19 (1.03, 1.39)	0.022	
All lung diseases							
Deaths	38		20		114		0.738
Person-years	35,686		17,274		24,788		
Mortality rate	10.6		11.6		46.0		
Unadjusted	1.18 (0.91, 1.53)	0.22	1.40 (1.05, 1.87)	0.022	1.39 (1.27, 1.53)	<0.001	
+ Age	1.18 (0.91, 1.54)	0.22	1.39 (1.04, 1.87)	0.026	1.40 (1.27, 1.54)	<0.001	
+ Sex	1.12 (0.82, 1.53)	0.47	1.42 (1.05, 1.92)	0.021	1.40 (1.27, 1.55)	<0.001	
+ Race	1.12 (0.84, 1.49)	0.44	1.40 (1.03, 1.90)	0.031	1.41 (1.28, 1.56)	<0.001	
+BMI	1.15 (0.86, 1.54)	0.34	1.37 (1.00, 1.88)	0.049	1.39 (1.26, 1.54)	<0.001	
+Site	1.17 (0.90, 1.53)	0.24	1.35 (0.97, 1.87)	0.076	1.37 (1.24, 1.52)	<0.001	
+Smoking status	1.17 (0.90, 1.53)	0.24	1.25 (0.90, 1.73)	0.19	1.40 (1.27, 1.55)	<0.001	
+Pack-years	1.17 (0.90, 1.53)	0.24	1.26 (0.91, 1.75)	0.17	1.33 (1.21, 1.47)	<0.001	
+Coronary artery calcium	1.18 (0.90, 1.53)	0.23	1.29 (0.92, 1.80)	0.14	1.34 (1.22, 1.48)	<0.001	
+Educational attainment	1.18 (0.91, 1.53)	0.22	1.43 (1.04, 1.96)	0.028	1.36 (1.23, 1.50)	<0.001	

The endpoints were defined by an underlying cause of death of respiratory disease (J00-J99), lung cancer (C33-C34) and, combining these, all lung disease. We also specifically examined mortality due to chronic lower respiratory disease (CLRD; J40-47), which was defined as deaths with COPD, emphysema, chronic bronchitis or asthma as the

underlying cause, or, in the context of pneumonia as the underlying cause (J12-18), with these diseases (J40-47) recorded as a contributing cause.

Hazard ratios reported per interquartile range (4.5%), which is equivalent to the difference between the third quartile (5.7%) and the first quartile (1.2%) of percent emphysema. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment. P-values for interaction reported for multiplicative interaction terms for percent emphysema and pack-years (continuous) using fully-adjusted models.

Table E5. Associations between percent emphysema and mortality due to lung disease in the Multi-Ethnic Study of Atherosclerosis, by baseline physician diagnosis of lung disease, 2000-2013.

Underlying cause of death	Without baseline physician diagnosis of emphysema		Without baseline physician diagnosis of asthma	
	<i>All (N=6,680)</i>	<i>P-value</i>	<i>All (N=6,122)</i>	<i>P-value</i>
Respiratory diseases				
Deaths	66		64	
Person-years	76,679		70,167	
Mortality rate per 10,000 person-years	8.6		9.1	
Hazard Ratio _{crude} (95% CI)	1.35 (1.18-1.54)	<0.001	1.43 (1.29-1.60)	<0.001
Hazard Ratio _{adjusted} (95% CI)	1.35 (1.15-1.59)	<0.001	1.46 (1.27-1.67)	<0.001
Chronic lower respiratory diseases				
Deaths	29		28	
Person-years	76,679		70,167	
Mortality rate per 10,000 person-years	3.8		4.0	
Hazard Ratio _{crude} (95% CI)	1.58 (1.39-1.80)	<0.001	1.65 (1.48-1.84)	<0.001
Hazard Ratio _{adjusted} (95% CI)	1.72 (1.44-2.05)	<0.001	1.86 (1.59-2.18)	<0.001
Lung cancers				
Deaths	87		86	
Person-years	76,679		70,167	
Mortality rate per 10,000 person-years	11.4		12.3	
Hazard Ratio _{crude} (95% CI)	1.24 (1.06-1.46)	0.008	1.31 (1.14-1.50)	<0.001
Hazard Ratio _{adjusted} (95% CI)	1.13 (0.95-1.35)	0.168	1.22 (1.05-1.43)	0.012
All lung diseases				
Deaths	153		150	
Person-years	76,679		70,167	
Mortality rate per 10,000 person-years	20.0		21.4	
Hazard Ratio _{crude} (95% CI)	1.30 (1.17-1.44)	<0.001	1.38 (1.27-1.50)	<0.001
Hazard Ratio _{adjusted} (95% CI)	1.23 (1.09-1.38)	<0.001	1.31 (1.19-1.45)	<0.001

The endpoints were defined by an underlying cause of death of respiratory disease (J00-J99), lung cancer (C33-C34) and, combining these, all lung disease. We also specifically examined mortality due to chronic lower respiratory disease (CLRD; J40-47), which was defined as deaths with COPD, emphysema, chronic bronchitis or asthma as the underlying cause, or, in the context of pneumonia as the underlying cause (J12-18), with these diseases (J40-47) recorded as a contributing cause.

Hazard ratios reported per interquartile range (4.5%), which is equivalent to the difference between the third quartile (5.7%) and the first quartile (1.2%) of percent emphysema. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment.

Table E6. Effects of spirometry adjustment on associations between percent emphysema and mortality due to lung disease in the persons with valid spirometry measures in the Multi-Ethnic Study of Atherosclerosis Lung Study, 2004-2013.

Underlying cause of death	Percent emphysema as continuous exposure	
	All (N=3,828)	P-value
Respiratory diseases		
Deaths	20	
Person-years	29,261	
Mortality rate per 10,000 person-years	8.8	
Hazard Ratio (95% CI)		
Crude	1.41 (1.01-1.97)	0.041
Adjusted	1.31 (0.89-1.93)	0.169
+ spirometry measures	1.31 (0.84-2.03)	0.179
+ high attenuation areas	1.41 (0.91-2.19)	0.123
Lung cancer		
Deaths	36	
Person-years	29,261	
Mortality rate per 10,000 person-years	15.8	
Hazard Ratio (95% CI)		
Crude	1.42 (1.11-1.80)	0.005
Adjusted	1.20 (0.92-1.58)	0.179
+ spirometry measures	1.08 (0.78-1.51)	0.635
+ high attenuation areas	1.27 (0.91-1.77)	0.157
All lung diseases		
Deaths	56	
Person-years	29,261	
Mortality rate per 10,000 person-years	24.5	
Hazard Ratio (95% CI)		
Crude	1.42 (1.17-1.72)	<0.001
Adjusted	1.22 (0.98-1.53)	0.074
+ spirometry measures	1.17 (0.91-1.77)	0.157
+ high attenuation areas	1.33 (1.02-1.72)	0.032

The endpoints were defined by an underlying cause of death of respiratory disease (J00-J99), lung cancer (C33-C34) and, combining these, all lung disease. We do not report mortality due to chronic lower respiratory disease (CLRD; J40-47) due to very low event rates in this group (N=6 and N=2 in persons with and without airflow limitation, respectively).

Hazard ratios reported per interquartile range (4.5%), which is equivalent to the difference between the third quartile (5.7%) and the first quartile (1.2%) of percent emphysema. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment. The spirometry measures are the forced expiratory volume in one second (FEV1), ratio of the FEV1 to forced expiratory volume (FVC), and absence/presence of a restrictive pattern. The final model is additionally adjusted for log-transformed volume of high attenuation areas.

Table E7. Associations between percent emphysema and mortality due to cardiovascular and non-lung cancers in the Multi-Ethnic Study of Atherosclerosis, 2000-2013.

Underlying cause of death		Percent emphysema as continuous exposure	
		All (N=6,784)	P-value
Circulatory diseases			
	Deaths	250	
	Person-years	77,750	
	Mortality rate per 10,000 person-years	32.2	
	Hazard Ratio _{crude} (95% CI)	1.07 (0.96-1.20)	0.219
	Hazard Ratio _{adjusted} (95% CI)	1.00 (0.88-1.14)	0.945
Adjudicated cardiovascular endpoints			
Cardiovascular death			
	Deaths	194	
	Person-years	77,750	
	Mortality rate per 10,000 person-years	31.4	
	Hazard Ratio _{crude} (95% CI)	1.06 (0.93-1.20)	0.392
	Hazard Ratio _{adjusted} (95% CI)	1.03 (0.90-1.19)	0.655
Coronary heart disease death			
	Deaths	101	
	Person-years	77,750	
	Mortality rate per 10,000 person-years	25.0	
	Hazard Ratio _{crude} (95% CI)	1.14 (0.98-1.34)	0.097
	Hazard Ratio _{adjusted} (95% CI)	1.11 (0.93-1.32)	0.268
Cerebrovascular death			
	Deaths	35	
	Person-years	77,750	
	Mortality rate per 10,000 person-years	13.0	
	Hazard Ratio _{crude} (95% CI)	0.97 (0.70-1.35)	0.870
	Hazard Ratio _{adjusted} (95% CI)	1.11 (0.80-1.54)	0.519
Other cancers			
	Deaths	244	
	Person-years	77,750	
	Mortality rate per 10,000 person-years	4.5	
	Hazard Ratio _{crude} (95% CI)	0.97 (0.70-1.35)	0.600
	Hazard Ratio _{adjusted} (95% CI)	0.86 (0.74-1.01)	0.061

Non-adjudicated mortality endpoints were defined as an underlying cause of death of circulatory disease (I00-99) or other cancers (C00-99, excluding C33-34). Adjudicated cardiovascular endpoints were defined according to MESA Events Committee protocols.

Hazard ratios reported per interquartile range (4.5%), which is equivalent to the difference between the third quartile (5.7%) and the first quartile (1.2%) of percent emphysema. Models adjusted for baseline age, sex, race/ethnicity, body mass index, site, smoking status, pack-years of smoking, coronary artery calcium score, and educational attainment.