

Supplementary Table S1: Mean %LAA by sex and race				
	Male	Female	Beta (se)	P value
All subjects	13.62 (12.8)	12.19 (12.6)	1.70 (0.37)	<0.001
NHW	14.23 (12.9)	12.9 (12.8)	1.97 (0.42)	<0.001
AA	11.35 (12.5)	9.67 (11.7)	1.40 (0.79)	0.08
Including all subjects with GOLD grade 2-4 COPD. Data are presented as mean (sd). Adjusted for age, pack-years, current smoking status, BMI, CT scanner. "All subjects" additionally adjusted for race.				

Supplementary Table S2: Log %LAA by sex and race, Siemens Definition scanner						
	Male N	Female N	Male	Female	Beta (se)	P value
All subjects	358	301	1.97 (1.4)	1.69 (1.6)	0.30 (0.09)	<0.001
NHW	323	259	2.06 (1.3)	1.79 (1.5)	0.28 (0.05)	<0.001
AA	35	42	1.63 (1.5)	1.31 (1.7)	0.22 (0.10)	0.03
Including all subjects with GOLD grade 2-4 COPD who had chest CT scans performed using the Siemens© Definition scanner. Data are presented as mean (sd). Adjusted for age, pack-years, current smoking status, and BMI. “All subjects” additionally adjusted for race. Beta represents the difference for males compared to female subjects.						

Supplementary Table S3: Multivariate regression comparing -910 HU between COPD subsets				
Subjects	Male	Female	Beta (se)	P value
All subjects	37.61 (18.4)	33.42 (19.2)	4.65 (0.50)	<0.001
Early Onset	37.7 (19.3)	33.8 (20.6)	1.24 (2.30)	0.59
Severe Emphysema	60.82 (7.7)	60.31 (6.4)	1.78 (0.53)	<0.001
Gold 4	53.32 (14.5)	52.23 (14.7)	3.33 (1.01)	0.001
<p>Comparing %LAA -910 between males and females. HU: Hounsfield units; All subjects: COPD GOLD grade II-IV; Early Onset: early-onset COPD (age < 55, GOLD grade > II); Severe Emphysema: %LAA > 25%. Data are presented as mean (sd). Adjusted for age, pack-years, current smoking status, BMI, CT scanner, and race. Beta represents the difference for males compared to female subjects.</p>				

Supplementary Table S4: Smoking controls demographic data						
	Non-Hispanic White			African American		
	Male	Female	P value	Male	Female	P value
N	1284	1297	NA	1036	771	NA
Age	59.4 (8.8)	59.4 (8.7)	0.91	52.4 (5.4)	53.2 (6.6)	0.01
Pack-years	40.8 (21.5)	35.0 (18.7)	<0.001	36.2 (18.9)	36.3 (21.6)	0.92
Current Smoker (%)	552 (43.0)	486 (37.5)	0.005	925 (89.3)	656 (85.0)	0.009
BMI (kg/m ²)	28.91 (4.9)	28.8 (6.1)	0.52	27.69 (5.1)	30.68 (6.9)	<0.001
FEV _{1pp}	96.81 (11.2)	96.7 (10.8)	0.86	99.04 (12.3)	97.75 (12.0)	0.03
FEV ₁ /FVC	0.77 (0.05)	0.78 (0.1)	<0.001	0.80 (0.1)	0.80 (0.1)	0.003
Mean %LAA	2.94 (3.1)	1.90 (2.4)	<0.001	1.68 (2.1)	0.94 (1.4)	<0.001
Log %LAA	0.49 (1.2)	-0.04 (1.2)	<0.001	-0.1 (1.2)	-0.75 (1.2)	<0.001

Data are presented as mean (sd) or N (%). BMI: body-mass index; P value: univariate comparison of NHW and AA males vs females, respectively. "Smoking controls": Current or former smokers with > 10 pack-years smoking history and spirometrically normal lung function.

Supplementary Table S5: %LAA among smoking controls				
A. Mean %LAA among smoking controls				
	Male	Female	Beta (se)	P value
All Subjects	2.38 (2.8)	1.55 (2.2)	0.97 (0.07)	<0.001
NHW	2.94 (3.1)	1.9 (2.4)	1.16 (0.09)	<0.001
AA	1.68 (2.1)	0.94 (1.4)	0.70 (0.09)	<0.001
B. Mean Log %LAA among smoking controls				
All Subjects	0.23 (1.24)	-0.3 (1.27)	0.47 (0.17)	<0.001
NHW	0.49 (1.23)	-0.04 (1.23)	0.64 (0.04)	<0.001
AA	-0.1 (1.17)	-0.75 (1.21)	0.66 (0.05)	<0.001
Smoking controls: Subjects with greater than 10 pack-years smoking and normal lung function. Presenting mean (sd). Adjusted for age, gender, pack-years, BMI, current smoking status, CT scanner. "All subjects" additionally adjusted for race. Beta refers to male subjects compared to female subjects.				

Supplementary Table S6: %LAA per pack year by sex and study population				
	Male	Female	Beta	P value
All GOLD 0	0.08 (0.11)	0.06 (0.1)	0.03 (0.003)	<0.001
NHW GOLD 0	0.1 (0.13)	0.07 (0.12)	0.03 (0.005)	<0.001
AA GOLD 0	0.06 (0.08)	0.03 (0.05)	0.02 (0.003)	<0.001
All COPD	0.30 (0.38)	0.32 (0.41)	0.004 (0.01)	0.74
NHW COPD	0.29 (0.35)	0.31 (0.39)	0.001 (0.01)	0.93
AA COPD	0.32 (0.49)	0.33 (0.50)	-0.03 (0.03)	0.38
Data are presented as mean (sd). Adjusted for age, sex, current smoking status, BMI, CT scanner. Beta represents the difference for male subjects compared to female subjects. GOLD 0: smoking control subjects; COPD: GOLD grade II-IV COPD.				

Supplementary Table S7: Mean %LAA by GOLD grade				
GOLD Grade	Male	Female	Beta (se)	P value
All subjects				
2	7.54 (8.0)	6.59 (7.6)	1.10 (0.32)	<0.001
3	16.42 (12.3)	15.51 (12.8)	1.59 (0.65)	0.01
4	26.55 (14.2)	26.71 (13.9)	2.15(1.03)	0.04
Non-Hispanic whites				
2	8.1 (8.3)	7.08 (7.9)	1.26 (0.39)	0.001
3	16.65 (12.1)	16.19 (12.7)	1.87 (0.71)	0.009
4	27.05 (13.9)	26.73 (14.0)	2.31 (1.11)	0.04
African Americans				
2	15.95 (12.8)	14.56 (12.9)	2.28 (1.09)	0.04
3	15.45 (13.1)	13.07 (12.9)	1.59 (1.59)	0.32
4	17.27 (13.2)	15.18 (14.6)	2.31 (2.20)	0.30
Presenting mean (sd). Adjusted for age, gender, pack-years, BMI, current smoking status, CT scanner. “All subjects” additionally adjusted for race. Beta refers to male subjects compared to female subjects.				

Supplementary Table S8: Mean %LAA among severe COPD subtypes

	Early-onset COPD				Severe Emphysema			
	Males	Females	Beta (se)	P value	Males	Females	Beta (se)	P value
N	130	130			372	255		
Age	51.31 (2.6)	50.96 (2.6)		0.27	65.64 (7.8)	64.71 (7.8)		0.14
Pack-years	48.2 (25.4)	41.0 (20.0)		0.01	56.31 (25.8)	49.11 (22.1)		<0.001
FEV ₁ pp	35.52 (9.8)	35.52 (10.6)		0.99	33.5 (14.1)	32.93 (13.5)		0.61
%LAA	15.49 (14.5)	13.48 (14.4)	0.13 (0.18)	0.46	35.18 (8.0)	35.29 (7.3)	1.05 (0.61)	0.08

Early-onset COPD defined as COPD GOLD grade III and IV and age < 55. Severe emphysema defined as subjects with %LAA greater than 25%. FEV₁pp: FEV₁ percent predicted. %LAA: percent lung attenuation area less than -950Hu. Univariate comparisons performed for age, pack-years and FEV₁pp. %LAA adjusted for age, race, pack-years, smoking status, BMI, and CT scanner.

Supplementary Table S9: Comparison of additional exposures by sex among all subjects with COPD

	Male	Female	P Value
Mean age started smoking	16.2 (4.5)	17.1 (4.3)	<0.001
Second-hand smoke (yrs)	20.1 (17.5)	23.8 (16.4)	<0.001
Smoke exposure at work (yrs)	24.5 (16.1)	16.9 (14.2)	<0.001
Ever work in dusty job (%)	1324 (65.6)	610 (37.3)	<0.001
Currently work in dusty job (%)	137 (6.7)	69 (4.2)	0.001
Ever work with fumes (%)	1349 (65.8)	590 (36.0)	<0.001
Currently work with fumes (%)	152 (7.4)	71 (4.3)	<0.002

Including all (NHW and AA) subjects with GOLD grade II-IV COPD. Data are presented as mean (sd). P value represents result from t-test (continuous) or chi-square (binary). Second-hand smoke: number of years living with someone who smokes, since age 18; Smoke exposure at work: number of years working with someone who smokes; Ever work in dusty job: Did the subject ever work for a year or more in a dusty job; Ever work with fumes: was the subject ever exposed to gas, chemicals, or fumes at work.

Supplementary Table S10: Multivariate regression comparing %LAA by sex additionally adjusting for occupational exposures among COPD subtypes				
Mean %LAA				
COPD subtype	Male	Female	Beta (se)	P value
All subjects	13.62 (12.8)	12.19 (12.6)	1.06 (0.4)	0.009
Early Onset	15.49 (14.5)	13.48 (14.4)	0.55 (2.0)	0.78
Severe Emphysema	35.18 (8.0)	35.29 (7.3)	1.18 (0.64)	0.07
Gold 4	26.55 (14.2)	26.71 (13.9)	2.57 (1.12)	0.02
Log %LAA				
	Male	Female	Beta (se)	P value
All subjects	1.97 (1.4)	1.69 (1.6)	0.26 (0.05)	<0.001
Early Onset	2.06 (1.4)	1.78 (1.6)	0.25 (0.21)	0.20
Severe Emphysema	3.54 (0.2)	3.54 (0.2)	0.03 (0.02)	0.15
Gold 4	3.05 (0.85)	3.03 (0.91)	0.18 (0.07)	0.01
<p>All subjects: COPD GOLD grade II-IV, Early Onset: early-onset COPD (age < 55, GOLD grade > II); Severe Emphysema: %LAA > 25%. Data are presented as mean (sd). Adjusted for age, pack-years, current smoking status, BMI, race, years exposed to smoke at work, ever exposed to fumes at work. Log %LAA additionally adjusted for passive smoking. Beta represents the difference for male compared to female subjects.</p>				

Supplementary Table S11: IRB names and protocol approval for the COPDGene study		
Clinical Center	IRB Protocol #s	IRB Names
Ann Arbor VA Medical Center	2014-060462	Ann Arbor VA IRB
Baylor College of Medicine	H-22209	IRB for Baylor College of Medicine
Brigham and Women's Hospital	2007P000554	Partners Human Research Committee
Columbia Univ. Medical Center	AAAC9324	Columbia University IRB
Duke Univ. Medical Center	Pro00004464	Duke University Health System IRB
Johns Hopkins University	NA_00011524	Johns Hopkins Medicine IRB
L.A. Biomedical Research Inst.	12756-03	John F. Wolf, M.D. Human Subjects Committee
Michael E. DeBakey VAMC	H-22202	Institutional Review Board for Human Subject Research for Baylor College of Medicine and Affiliated Hospitals (BCM IRB)
Minneapolis VA Medical Center	4128-A	Minneapolis VA Health Care System
Minnesota HealthPartners-Twin Cities	07-127	Health Partners IRB
Morehouse School of Medicine	97826	Morehouse School of Medicine IRB
National Jewish Health	1883a	National Jewish Health IRB
Reliant Medical Group (Fallon)	1441	Reliant Medical Group IRB
Temple University	21659	Temple IRB
Univ. of Alabama, Birmingham	F070712014	University of Alabama at Birmingham IRB for Human Use
Univ. of California, San Diego	140070	UCSD Human Research Protections Program
University of Iowa	200710717	University of Iowa IRB
University of Michigan	HUM00014973	University of Michigan Medical School IRB
University of Minnesota	0801M24949	University of Minnesota IRB Human Subjects Committee
University of Pittsburgh	#07120059	Univeristy of Pittsburgh IRB
UTHSC at San Antonio	HSC20070644H	UT Health Science Center San Antonio IRB

