SUPPLEMENTARY INFORMATION

Title**:** Human Airway Branch Variation and Chronic Obstructive Pulmonary Disease

CONENTS

SUPPLEMENTARY INFORMATION TABLES:

Table S1. Characteristics of MESA Participants and Smokers in SPIROMICS.

	MESA participants attending Exam 5		**Smokers in SPIROMICS attending Exam 1[a]**	
	Included in analysis N=3,169	**Not included in analysis** N=1,751	**Included in analysis** N=2,746	**Not included in analysis** N=26
Age – years	69.3±9.2	70.8±9.8	63.5±8.9	63.5±8.9
Male – %	47.7	44.7	53.9	69.2
Height – cm	165.5±9.9	165.0±10.2	169.8±9.5	171.8±11.2
Weight – kg	78.2±17.5	78.1±18.5	80.7±18.0	82.4±15.7
Race-ethnicity – %				
Caucasian American	38.9	46.0	74.1	57.7
African American	27.2	25.2	17.9	34.6
Hispanic American	21.0	20.8	4.6	7.7
Asian American/Other	13.0	8.0	3.4	0.0
Educational attainment – %				
Less than high school	13.7	15.3	11.4	38.5
High school degree	17.8	16.7	26.9	26.9
Some college	28.8	29.6	35.3	19.2
College degree or higher	39.5	38.2	26.2	15.4
Smoking status – %				
Non-smoker	45.6	43.9	0.0	0.0
Former	46.8	47.7	60.5	65.4
Current	7.6	8.4	39.5	34.6
Pack-years among ever smokers	14.5 (3.0, 33.0)	9.0 (1.5, 31.0)	43.0 (31.3, 60.0)	50.0 (26.5, 75.0)
Smoker at home during childhood – %	55.5	46.5	81.3	86.7
Maternal smoking during pregnancy – %	NA	NA	9.1	16.0
Childhood diagnosis of asthma – %	4.2	4.8	23.3	25.0

Values represent mean ± SD, percentages, or median (25^{th}, 75^{th} percentile). [a]SPIROMICS dataset release: 08/01/2016.

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; NA = not available.

Table S2. Clinical Characteristics of Participants with Standard Anatomy and Common Airway Branch Variants in the MESA Lung Study.

	Standard anatomy N=2,329	**Accessory sub-superior airway** N=506	**Absent right medial-basal airway** N=193
Age – years	69.5±9.2	68.7±9.1	69.2±9.3
Male – %	48.5	48.4	42.0
Height – cm	165.5±10.0	166.3±9.7	162.6±9.6
Weight – kg	78.2±17.6	80.2±17.6	74.2±16.2
Race-ethnicity – %			
Caucasian American	37.1	51.2	34.7
African American	27.6	25.3	18.1
Hispanic American	21.2	18.2	25.4
Asian American/Other	14.1	5.3	21.8
Educational Attainment – %			
Less than high school	13.6	12.3	20.3
High school degree	18.1	15.8	17.2
Some College	28.2	30.3	29.2
College degree or higher	39.9	41.6	33.3
Smoking status – %			
Non-smoker	46.2	41.7	53.4
Former	46.8	50.0	35.2
Current	7.0	8.3	11.4
Pack-years among ever smokers	14.0 (2.8, 33.0)	15.5 (5.0, 33.0)	17.8 (1.2, 39.2)
Living with a smoker during childhood – %	55.2	54.2	55.9
Childhood diagnosis of asthma – %	4.3	5.6	2.3
CT lung volume – L			
Upper lobes	2.6±0.7	2.7±0.7	2.5±0.7
Lower lobes	2.2±0.7	2.3±0.7	2.1±0.6

Values represent mean ± SD, percentages, or median (25th, 75th percentile).
Standard anatomy is defined as the presence of right and left superior, anterior-basal, lateral-basal and posterior-basal segmental airways, as well as the right medial-basal segmental airway. Participants with rare (<5% prevalence) airway branch variants such as presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA Lung, n=141).

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

Table S3. Characteristics of MESA Lung Participants with and without Spirometric Assessment for COPD among those Included in Airway Anatomy Prevalence Analysis.

	Participants Included in Airway Anatomy Prevalence Analysis N=3,169	
	Included in COPD analysis N=2,308	**Not included in COPD analysis** N=861
Age – years	67.9±8.9	72.8±9.1
Male – %	47.1	49.4
Height – cm	165.4±9.8	165.5±10.4
Weight – kg	78.7±17.4	76.7±17.6
Race-ethnicity – %		
Caucasian American	36.7	45.0
African American	27.0	27.5
Hispanic American	23.1	15.3
Asian American/Other	13.3	12.2
Educational attainment – %		
Less than high school	13.7	13.8
High school degree	17.2	19.2
Some college	29.5	27.0
College degree	39.4	39.9
Smoking status – %		
Non-smoker	46.0	44.5
Former	46.6	47.2
Current	7.4	8.4
Pack-years among ever smokers	13.5 (2.8, 31.0)	18.0 (4.0, 39.1)
Lower lobe segmental airway anatomy		
Standard anatomy	73.7	71.7
Accessory sub-superior airway	15.5	17.6
Absent right medial-basal airway	5.9	6.7
Rare airway variants[a]	4.9	4.0

Values represent mean ± SD, percentages, or median (25^{th}, 75^{th} percentile). [a]Rare airway branch variants included presence of the left medial-basal airway, or various combinations of the above-mentioned variants.

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; COPD = chronic obstructive pulmonary disease.

Table S4. Characteristics of MESA Lung and SPIROMICS Participants Included in the COPD Analyses According to COPD Status.

	MESA Lung Study		**SPIROMICS**	
	COPD N=243	**No COPD** N=2,065	**COPD** N=1,823	**No COPD** N=923
Age – years	72.3±8.8	67.4±8.8	65.1±8.0	60.2±9.7
Male – %	60.5	45.5	57.2	47.5
Height – cm	168.5±9.7	165.1±9.7	170.1±9.7	169.3±9.3
Weight – kg	78.2±17.2	78.8±17.5	79.4±18.1	83.4±17.6
Race-ethnicity – %				
Caucasian American	50.6	35.0	78.7	65.1
African American	24.7	27.3	14.4	24.8
Hispanic American	17.7	23.7	3.8	6.2
Asian American/Other	7.0	14.0	3.1	3.9
Educational attainment – %				
Less than high school	14.8	13.6	12.0	10.2
High school degree	17.8	17.2	26.7	26.4
Some college	28.4	29.6	35.2	35.3
College degree or higher	39.0	39.4	25.7	27.2
Smoking status – %				
Non-smoker	20.6	49.0	0	0
Former	63.0	44.7	66.0	49.7
Current	16.5	6.3	34.0	50.3
Pack-years among ever smokers	30.0 (14.4, 48.0)	11.3 (2.0, 27.0)	46.0 (35.0, 62.0)	37.0 (30.0, 49.5)
COPD GOLD severity – %				
Mild	54.3	-	22.1	-
Moderate	41.2	-	44.5	-
Severe-to-very severe	4.5	-	33.3	-
CT percent emphysema - %				
Upper lobes	3.6 (1.6, 8.7)	1.3 (0.5, 2.8)	7.6 (2.5, 18.9)	1.0 (0.4, 2.2)
Lower lobes	2.8 (1.0, 5.8)	0.9 (0.4, 1.9)	4.8 (1.6, 12.4)	0.8 (0.4, 1.7)
Lower lobe segmental airway anatomy				
Standard anatomy	67.9	75.0	57.4	65.3
Accessory sub-superior airway	21.8	14.7	30.5	26.0
Absent right medial-basal airway	6.6	5.8	6.7	4.4
Rare airway variant[a]	3.7	4.6	5.4	4.2

Values represent mean ± SD, percentages, or median (25th, 75th percentile). [a]Rare airway branch variants included the presence of the left medial-basal airway, or various combinations of the above-mentioned variants.
Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; GOLD = Global Initiative for Obstructive Lung Disease; COPD = chronic obstructive pulmonary disease; CT= computed tomography.

Table S5. Odds Ratios for $COPD_{LLN}$ by Common Airway Branch Variants in the MESA Lung Study, SPIROMICS and Both Studies Pooled.

	MESA Lung			SPIROMICS			Pooled[a]		
	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**
Participants with COPD	84	35	12	911	488	107	995	523	119
Participants without COPD	1,827	379	149	737	306	56	2,564	685	205
Odds ratios for COPD									
Unadjusted	Ref.	2.01 (1.33 to 3.03) P<0.001	1.75 (0.94 to 3.28) P=0.080	Ref.	1.29 (1.09 to 1.53) P=0.004	1.55 (1.10 to 2.17) P=0.011	Ref.	1.40 (1.19 to 1.64) P<0.001	1.55 (1.15 to 2.08) P=0.004
Model 1: age, gender, height, weight, race-ethnicity	Ref.	1.92 (1.26 to 2.92) P=0.002	2.08 (1.10 to 3.97) P=0.025	Ref.	1.23 (1.03 to 1.47) P=0.023	1.45 (1.03 to 2.04) P=0.036	Ref.	1.31 (1.11 to 1.54) P<0.001	1.55 (1.13 to 2.12) P=0.006
Model 2: model 1 covariates, smoking status, pack-years	Ref.	1.88 (1.22 to 2.90) P=0.004	1.94 (1.00 to 3.79) P=0.051	Ref.	1.21 (1.01 to 1.45) P=0.039	1.46 (1.03 to 2.06) P=0.036	Ref.	1.29 (1.09 to 1.52) P=0.003	1.57 (1.14 to 2.17) P=0.006

Odds ratios for $COPD_{LLN}$ were calculated using logistic regression with standard anatomy as the reference group. [a]Pooled analysis models include a term for study cohort.Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103; SPIROMICS: n=137).

Abbreviations: $COPD_{LLN}$ = chronic obstructive pulmonary disease defined by an FEV_1-to-FVC ratio less than the lower limit of normal; FEV_1 = forced expired volume in one second; FVC = forced vital capacity; = MESA Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study.

Table S6. Odds Ratios for $COPD_{symptoms}$ by Common Airway Branch Variants in the MESA Lung Study, SPIROMICS and Both Studies Pooled.

	MESA Lung			**SPIROMICS**			**Pooled[a]**		
	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**
Participants with $COPD_{symptoms}$	63	18	11	833	452	98	896	470	109
Participants without $COPD_{symptoms}$	1,650	338	125	817	344	65	2,467	682	190
Odds ratios for $COPD_{symptoms}$									
Unadjusted	Ref.	1.40 (0.82 to 2.39) P=0.224	2.31 (1.19 to 4.49) P=0.014	Ref.	1.29 (1.09 to 1.53) P=0.004	1.48 (1.07 to 2.05) P=0.019	Ref.	1.30 (1.11 to 1.53) P=0.002	1.60 (1.18 to 2.17) P=0.002
Model 1: age, gender, height, weight, race-ethnicity	Ref.	1.31 (0.76 to 2.26) P=0.333	2.77 (1.40 to 5.50) P=0.004	Ref.	1.25 (1.05 to 1.49) P=0.011	1.42 (1.01 to 1.98) P=0.041	Ref.	1.26 (1.07 to 1.49) P=0.006	1.57 (1.15 to 2.13) P=0.005
Model 2: model 1 covariates, smoking status, pack-years	Ref.	1.12 (0.63 to 2.00) P=0.700	2.71 (1.33 to 5.54) P=0.006	Ref.	1.25 (1.05 to 1.49) P=0.014	1.43 (1.02 to 2.00) P=0.039	Ref.	1.25 (1.06 to 1.48) P=0.009	1.60 (1.17 to 2.19) P=0.003

Odds ratios for $COPD_{symptoms}$ were calculated using logistic regression with standard anatomy as the reference group. [a]Pooled analysis models include a term for study cohort. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103; SPIROMICS: n=137).

Abbreviations: $COPD_{symptoms}$ = chronic obstructive pulmonary disease defined by an FEV_1-to-FVC ratio below 0.7 and dyspnea or chronic bronchitis symptoms; FEV_1 = forced expired volume in one second; FVC = forced vital capacity; = MESA Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study.

Table S7. Odds Ratios for COPD according to the presence of a tracheal or carinal airway in the MESA Lung Study, SPIROMICS and Both Studies Pooled.

	MESA Lung		**SPIROMICS**		**Pooled[a]**	
	Absence of tracheal or carinal airway	**Presence of tracheal or carinal airway**	**Absence of tracheal or carinal airway**	**Presence of tracheal or carinal airway**	**Absence of tracheal or carinal airway**	**Presence of tracheal or carinal airway**
Participants with COPD	240	3	1,804	19	2,044	22
Participants without COPD	2,050	15	921	2	2,971	17
Odds ratios for COPD						
Unadjusted model: airway branch variant status	Ref.	1.65 (0.47 to 5.77) P=0.432	Ref.	4.38 (0.97 to 19.9) P=0.060	Ref.	2.57 (1.13 to 5.86) P=0.024
Model 1: age, gender, height, weight, race-ethnicity	Ref.	1.32 (0.36 to 4.85) P=0.673	Ref.	3.70 (0.80 to 17.1) P=0.095	Ref.	2.11 (0.90 to 4.91) P=0.086
Model 2: model 1 covariates, smoking status, pack-years	Ref.	1.00 (0.22 to 4.53) P=0.999	Ref.	3.99 (0.84 to 19.0) P=0.081	Ref.	2.04 (0.84 to 4.94) P=0.116

Odds ratios for COPD were calculated using logistic regression with absence of tracheal or carinal airway as the reference group. [a]Pooled analysis models include a term for study cohort.

Abbreviations: COPD = chronic obstructive pulmonary disease; = MESA Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study

Table S8. Chronic Bronchitis and Dyspnea by Common Airway Branch Variants in the MESA Lung Study, SPIROMICS and Both Studies Pooled.

	MESA Lung			**SPIROMICS[a]**			**Pooled[b]**		
	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**
Chronic bronchitis, N	167	35	13	340	191	37	457	226	50
No Chronic bronchitis, N	2,160	321	123	1,263	577	120	2,858	898	243
Odds ratio for chronic bronchitis									
Unadjusted	Ref.	1.49 (1.00 to 2.21) P=0.049	1.44 (0.79 to 2.63) P=0.234	Ref.	1.23 (1.00 to 1.51) P=0.045	1.15 (0.78 to 1.69) P=0.492	Ref.	1.25 (1.04 to 1.50) P=0.017	1.17 (0.85 to 1.64) P=0.330
Model 1: age, gender, height, weight, race-ethnicity	Ref.	1.38 (0.92 to 2.07) P=0.115	1.55 (0.84 to 2.85) P=0.160	Ref.	1.25 (1.02 to 1.54) P=0.033	1.13 (0.76 to 1.67) P=0.540	Ref.	1.25 (1.04 to 1.50) P=0.016	1.15 (0.83 to 1.61) P=0.394
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	1.35 (0.90 to 2.03) P=0.144	1.47 (0.79 to 2.71) P=0.224	Ref.	1.32 (1.07 to 1.62) P=0.010	1.17 (0.78 to 1.75) P=0.442	Ref.	1.31 (1.08 to 1.57) P=0.005	1.16 (0.83 to 1.62) P=0.400
mMRC dyspnea score >0, N	582	134	58	1,108	543	121	1,690	677	179
mMRC dyspnea = 0, N	1,726	369	130	533	240	41	2,259	609	171
Odds ratio for dyspnea									
Unadjusted	Ref.	1.08 (0.87 to 1.34) P=0.507	1.32 (0.96 to 1.83) P=0.089	Ref.	1.09 (0.91 to 1.31) P=0.366	1.42 (0.98 to 2.05) P=0.063	Ref.	1.04 (0.90 to 1.20) P=0.572	1.30 (1.01 to 1.66) P=0.039
Model 1: age, gender, height, weight, race-ethnicity	Ref.	1.07 (0.85 to 1.34) P=0.581	1.37 (0.97 to 1.93) P=0.071	Ref.	1.15 (0.96 to 1.39) P=0.134	1.55 (1.07 to 2.25) P=0.022	Ref.	1.08 (0.93 to 1.25) P=0.314	1.38 (1.07 to 1.78) P=0.014
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	1.05 (0.84 to 1.33) P=0.661	1.34 (0.95 to 1.89) P=0.093	Ref.	1.15 (0.95 to 1.39) P=0.144	1.56 (1.07 to 2.26) P=0.021	Ref.	1.08 (0.93 to 1.25) P=0.311	1.38 (1.07 to 1.78) P=0.014

Odds ratios calculated using logistic regression. [a]SPIROMICS analysis models include a term for COPD status to reflect case-control design. [b]Pooled analysis models include a term indicating study cohort. There was no evidence of effect modification for symptom associations by cohort (p-interaction≥0.457). Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103; SPIROMICS: n=137).

Table S9. Respiratory Health Status by Common Airway Branch Variants in SPIROMICS.

	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**
CAT score	13.9±8.3	14.7±8.4	14.2±7.9
Mean differences in score			
Unadjusted	Ref.	0.8 (0.1 to 1.5) P=0.031	0.3 (-1.0 to 1.7) P=0.626
Model 1: age, gender, height, weight, race-ethnicity	Ref.	0.5 (0.2 to 0.9) P=0.005	0.3 (-0.4 to 1.0) P=0.371
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	1.1 (0.4 to 1.8) P=0.002	0.7 (-0.6 to 2.0) P=0.295
Model 3: Model 2 covariates, COPD status	Ref.	0.9 (0.2 to 1.6) P=0.008	0.1 (-1.2 to 1.4) P=0.892
SGRQ-C score	32.8±20.5	35.1±20.9	34.1±20.2
Mean differences in score			
Unadjusted	Ref.	2.3 (0.5 to 4.1) P=0.012	1.5 (-2.0 to 4.9) P=0.400
Model 1: age, gender, height, weight, race-ethnicity	Ref.	2.9 (1.1 to 4.7) P=0.001	2.1 (-1.2 to 5.6) P=0.210
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	3.0 (1.2 to 4.7) P=0.001	2.3 (-1.1 to 5.6) P=0.181
Model 2: Model 2 covariates, COPD status	Ref.	2.4 (0.8 to 4.0) P=0.004	0.9 (-2.2 to 4.0) P=0.582

Mean difference in respiratory health status scores calculated using linear regression. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (SPIROMICS: n=137).

Abbreviations: SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; COPD = chronic obstructive pulmonary disease; CAT = COPD Assessment Test; SGRC-C St. George Respiratory Questionnaire for COPD.

Table S10. Respiratory Health Status by Common Airway Branch Variants among participants with COPD in SPIROMICS.

	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**
CAT score	15.3±7.9	16.1±8.2	15.1±7.5
Mean differences in score			
Unadjusted	Ref.	0.8 (-0.1 to 1.6) P=0.071	-0.3 (-1.8 to 1.2) P=0.732
Model 1: age, gender, height, weight, race-ethnicity	Ref.	0.4 (0.3 to 1.9) P=0.009	0.0 (-1.5 to 1.4) P=0.947
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	1.2 (0.4 to 2.0) P=0.004	-0.1 (-1.5 to 1.3) P=0.905
SGRQ-C score	37.2±19.7	39.7±20.0	37.3±18.8
Mean differences in score			
Unadjusted	Ref.	2.6 (0.5 to 4.7) P=0.016	0.1 (-3.7 to 3.9) P=0.941
Model 1: age, gender, height, weight, race-ethnicity	Ref.	3.5 (1.6 to 5.5) P<0.001	0.6 (-3.0 to 4.1) P=0.748
Model 2: Model 1 covariates, smoking status, pack-years	Ref.	3.6 (1.6 to 5.5) P<0.001	0.6 (-2.9 to 4.1) P=0.751

Mean difference in respiratory health status scores calculated using linear regression. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (SPIROMICS: n=137).

Abbreviations: SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; COPD = chronic obstructive pulmonary disease; CAT = COPD Assessment Test; SGRC-C St. George Respiratory Questionnaire for COPD.

Table S11. Percent Emphysema by Common Airway Branch Variants in the MESA Lung Study, SPIROMICS and Both Studies Pooled.

	MESA Lung			SPIROMICS			Pooled[a]		
	Standard anatomy	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**	**Standard anatomy**	**Accessory sub-superior airway**	**Absent right medial-basal airway**
Percent emphysema (25^{th}, 75^{th} %ile)	1.2 (0.5, 2.6)	1.3 (0.6, 2.8)	1.2 (0.4, 2.8)	2.8 (0.9, 9.6)	4.0 (1.3, 14.8)	3.9 (1.5, 11.4)	1.8 (0.6, 4.6)	2.8 (1.0, 9.1)	2.2 (0.7, 6.5)
Mean difference in percent emphysema									
Unadjusted	Ref.	0.1 (-0.1 to 0.3) P=0.198	-0.1 (-0.3 to 0.1) P=0.401	Ref.	1.2 (0.7 to 1.8) P<0.001	1.1 (0.3 to 2.1) P=0.008	Ref.	0.6 (0.3 to 0.8) P<0.001	0.3 (-0.1 to 0.6) P=0.101
Model 1: age, gender, height, weight, race-ethnicity, CT model, dose	Ref.	0.1 (0.0 to 0.2) P=0.111	-0.1 (-0.2 to 0.1) P=0.213	Ref.	0.8 (0.4 to 1.2) P<0.001	0.5 (-0.2 to 1.4) P=0.135	Ref.	0.4 (0.2 to 0.6) P<0.001	0.1 (-0.2 to 0.4) P=0.532
Model 2: model 1 covariates, smoking status, pack-years	Ref.	0.1 (0.0 to 0.2) P=0.174	-0.1 (-0.2 to 0.1) P=0.308	Ref.	0.7 (0.3 to 1.1) P<0.001	0.5 (-0.2 to 1.3) P=0.154	Ref.	0.3 (0.2 to 0.5) P<0.001	0.1 (-0.1 to 0.4) P=0.420
Upper and middle lobe percent emphysema (25^{th}, 75^{th} %ile)	1.3 (0.6, 3.1)	1.4 (0.6, 3.1)	1.2 (0.4, 3.0)	3.0 (0.9, 10.5)	4.3 (1.3, 16.2)	4.1 (1.3, 13.1)	2.0 (0.7, 5.2)	3.1 (1.0, 10.0)	2.4 (0.8, 6.6)
Mean difference in upper lobe percent emphysema									
Unadjusted	Ref.	0.1 (-0.1 to 0.3) P=0.255	-0.1 (-0.3 to 0.2) P=0.468	Ref.	1.3 (0.8 to 1.9) P<0.001	1.1 (0.2 to 2.3) P=0.012	Ref.	0.6 (0.4 to 0.9) P<0.001	0.3 (-0.1 to 0.7) P=0.112
Model 1: age, gender, height, weight, race-ethnicity, CT model, dose	Ref.	0.1 (0.0 to 0.2) P=0.121	-0.1 (-0.3 to 0.1) P=0.171	Ref.	0.9 (0.4 to 1.4) P<0.001	0.5 (-0.2 to 1.5) P=0.174	Ref.	0.4 (0.3 to 0.7) P<0.001	0.1 (-0.2 to 0.4) P=0.671
Model 2: model 1 covariates, smoking status, pack-years	Ref.	0.1 (0.0 to 0.2) P=0.180	-0.1 (-0.3 to 0.1) P=0.272	Ref.	0.7 (0.3 to 1.2) P<0.001	0.5 (-0.2 to 1.4) P=0.199	Ref.	0.4 (0.2 to 0.6) P<0.001	0.1 (-0.2 to 0.4) P=0.550

Lower lobe percent emphysema (25th, 75th %ile)	0.9 (0.4, 2.1)	1.0 (0.5, 2.4)	0.8 (0.3, 2.4)	2.2 (0.7, 6.7)	3.1 (1.0, 10.4)	3.0 (1.0, 8.9)	1.4 (0.5, 3.4)	2.2 (0.7, 6.6)	1.7 (0.5, 4.5)
Mean difference in lower lobe percent emphysema									
Unadjusted	Ref.	0.1 (0.0 to 0.3) P=0.121	-0.1 (-0.3 to 0.1) P=0.218	Ref.	0.9 (0.5 to 1.3) P<0.001	0.8 (0.2 to 1.6) P=0.012	Ref.	0.4 (0.3 to 0.6) P<0.001	0.2 (-0.1 to 0.4) P=0.204
Model 1: age, gender, height, weight, race-ethnicity, CT model, dose	Ref.	0.1 (0.0 to 0.2) P=0.128	-0.1 (-0.2 to 0.1) P=0.241	Ref.	0.6 (0.3 to 0.9) P<0.001	0.4 (-0.2 to 1.0) P=0.189	Ref.	0.3 (0.2 to 0.5) P<0.001	0.1 (-0.2 to 0.3) P=0.590
Model 2: model 1 covariates, smoking status, pack-years	Ref.	0.1 (0.0 to 0.2) P=0.195	-0.1 (-0.2 to 0.1) P=0.318	Ref.	0.5 (0.2 to 0.8) P<0.001	0.3 (-0.2 to 0.9) P=0.217	Ref.	0.3 (0.1 to 0.4) P<0.001	0.1 (-0.1 to 0.3) P=0.479

Predicted mean differences calculated using linear regression with log-transformation of percent emphysema variable. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103; SPIROMICS: n=137). [a]Combined logistic regression models include a term for study cohort, and there was no evidence of interaction by study (p-interaction=0.190).

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

Table S12. Characteristics of MESA COPD Participants Included in the Matched Case-Control Comparison of Apparent Diffusion Coefficients between among Common Airway Branch Variants and Standard Anatomy.

	Accessory sub-superior airway cases N=10	**Standard anatomy matched controls** N=10	**Absent right medial-basal cases** N=2	**Standard anatomy matched controls** N=8
Age – years	71.2±4.4	64.6±7.2	66.0±7.1	64.3±6.8
Male – %	60	60	50	50
Height – cm	168.8±12.2	170.5±8.1	165.8±11.0	166.9±8.1
Weight – kg	71.0±12.8	82.9±8.1	73.2±35.6	79.3±9.2
Smoking status – %				
Non-smoker	0.0	0.0	0.0	0.0
Former	90.0	70.0	50.0	50.0
Current	10.0	30.0	50.0	50.0
Pack-years	46.1±16.3	30.9±11.2	30.9±11.2	30.9±11.2
COPD – %	60.0	60.0	0.0	0.0
CT lung volume – L	5.1±1.4	5.3±1.3	4.0±0.3	4.5±1.1
CT percent emphysema – %	1.8 (0.6, 9.3)	2.3 (0.3, 4.1)	0.2 (0.1, 0.2)	0.4 (0.2, 1.8)

Values represent mean ± SD, percentages, or median (25th, 75th percentile). Of 60 MESA COPD participants performing inhaled hyper-polarized Helium-3 magnetic resonance imaging, 10 participants had an accessory sub-superior airway and were matched 1:1 with 10 standard anatomy participants; and two participants had an absent right medial-basal airway and were matched 1:4 with standard anatomy. Participants were matched for gender, height within 5 cm, and COPD status. Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; COPD = chronic obstructive pulmonary disease; CT = computed tomograph.

Table S13. Candidate single nucleotide polymorphisms and associations with common airway branch variants.

Candidate SNP					Absent right medial basal airway				Accessory sub-superior airway			
ID	Chr	Base-pair	Gene	Minor allele	Frequency in cases (n=172)	Frequency in controls (n=2,425)	Odds ratio	P-value	Frequency in cases (n=398)	Frequency in controls (n=2,199)	Odds ratio	P-value
SNP_A-8479304	1	92187060	TGFBR3	A	0.052	0.070	1.00	0.9989	0.069	0.068	0.94	0.7273
SNP_A-2308322	1	92213527	TGFBR3	T	0.227	0.246	0.93	0.7325	0.253	0.243	1.13	0.1870
SNP_A-8393565	1	92250552	TGFBR3	A	0.521	0.496	1.02	0.8669	0.514	0.494	1.07	0.3826
SNP_A-8301470	1	92281991	TGFBR3	A	0.177	0.180	1.18	0.6406	0.202	0.175	0.99	0.9121
SNP_A-8287930	1	92298266	TGFBR3	A	0.035	0.060	0.86	0.6382	0.046	0.061	0.83	0.3105
SNP_A-8582062	2	16082877	MYCN	A	0.398	0.357	1.09	0.4812	0.382	0.356	1.24	0.0101
SNP_A-8322660	2	16086709	MYCN	G	0.195	0.191	1.09	0.7188	0.226	0.185	1.34	0.0038
SNP_A-4230064	2	16086822	MYCN	A	0.343	0.325	1.15	0.2436	0.368	0.318	1.30	0.0019
SNP_A-1972100	3	25246269	RARB	A	0.180	0.212	0.96	0.8683	0.219	0.208	1.09	0.3986
SNP_A-8422094	3	25269521	RARB	C	0.085	0.095	0.89	0.5618	0.082	0.097	0.92	0.7360
SNP_A-8469803	3	25288713	RARB	A	0.067	0.054	1.31	0.2986	0.043	0.057	0.90	0.5766
SNP_A-8458446	3	25288892	RARB	A	0.218	0.241	0.93	0.5938	0.236	0.240	1.03	0.8925
SNP_A-4198192	3	25294831	RARB	G	0.454	0.497	1.00	0.9998	0.494	0.494	0.97	0.8151
SNP_A-1972103	3	25304837	RARB	A	0.317	0.387	0.87	0.3839	0.368	0.385	0.92	0.3425
SNP_A-8547579	3	25308579	RARB	T	0.119	0.118	1.08	0.6954	0.126	0.117	0.93	0.5758
SNP_A-4237352	3	25312406	RARB	A	0.206	0.218	1.07	0.6104	0.215	0.217	0.90	0.3008
SNP_A-8384819	3	25319855	RARB	T	0.201	0.179	1.21	0.3137	0.188	0.179	1.01	0.9570
SNP_A-1972106	3	25324438	RARB	G	0.113	0.136	0.99	0.9472	0.143	0.133	0.92	0.5223
SNP_A-8413380	3	25341148	RARB	C	0.105	0.114	1.03	0.8705	0.129	0.110	0.92	0.5163
SNP_A-8450623	3	25342145	RARB	T	0.172	0.205	1.00	0.9825	0.207	0.202	1.03	0.8530
SNP_A-8617871	3	25356640	RARB	G	0.384	0.404	0.96	0.7973	0.389	0.405	0.89	0.3647
SNP_A-2199859	3	25361022	RARB	C	0.142	0.161	1.02	0.9469	0.160	0.160	0.99	0.9355
SNP_A-2122555	3	25361700	RARB	G	0.052	0.079	0.91	0.6987	0.096	0.074	1.33	0.0417
SNP_A-8588493	3	25365433	RARB	G	0.343	0.335	1.04	0.7400	0.324	0.338	0.93	0.5942
SNP_A-8630435	3	25366352	RARB	G	0.087	0.086	1.03	0.8882	0.077	0.088	0.89	0.4582
SNP_A-8493534	3	25367584	RARB	C	0.122	0.125	1.12	0.5674	0.104	0.129	0.81	0.0981
SNP_A-4263402	3	25389941	RARB	G	0.058	0.083	0.94	0.8080	0.079	0.081	0.92	0.5831

SNP_A-4299684	3	25401979	RARB	C	0.140	0.160	0.98	0.9229	0.145	0.161	0.87	0.2258
SNP_A-4302257	3	25403332	RARB	C	0.047	0.077	0.77	0.3269	0.072	0.075	0.90	0.4801
SNP_A-4249225	3	25414158	RARB	T	0.076	0.131	0.71	0.1641	0.143	0.124	1.10	0.4974
SNP_A-8322291	3	25422607	RARB	T	0.317	0.330	0.90	0.5256	0.310	0.332	0.92	0.4129
SNP_A-2256758	3	25424654	RARB	G	0.128	0.113	0.99	0.9566	0.126	0.112	1.16	0.2195
SNP_A-8484191	3	25428560	RARB	C	0.113	0.134	0.92	0.6591	0.160	0.128	1.06	0.6143
SNP_A-8380804	3	25429670	RARB	C	0.038	0.070	0.62	0.1010	0.065	0.068	0.84	0.2595
SNP_A-8429777	3	25429952	RARB	T	0.361	0.418	0.87	0.3058	0.418	0.413	0.89	0.2377
SNP_A-4253644	3	25430406	RARB	T	0.323	0.350	0.95	0.6829	0.355	0.347	0.94	0.5840
SNP_A-1836266	3	25435600	RARB	T	0.424	0.435	1.00	0.9860	0.396	0.442	0.92	0.3128
SNP_A-8696572	3	25450840	RARB	C	0.076	0.059	1.25	0.3920	0.069	0.058	1.23	0.2104
SNP_A-1956297	3	25450886	RARB	T	0.084	0.077	1.56	0.2896	0.092	0.075	1.16	0.4686
SNP_A-8457815	3	25454782	RARB	G	0.273	0.283	0.88	0.5518	0.250	0.288	0.97	0.8289
SNP_A-8322584	3	25454987	RARB	T	0.137	0.132	1.09	0.6101	0.138	0.131	1.06	0.7068
SNP_A-8307693	3	25455112	RARB	T	0.052	0.053	1.20	0.4723	0.052	0.053	1.13	0.5000
SNP_A-8609948	3	25455648	RARB	T	0.259	0.268	0.95	0.7414	0.283	0.265	1.09	0.3504
SNP_A-8712629	3	25455682	RARB	C	0.381	0.393	0.97	0.7867	0.377	0.395	0.95	0.6263
SNP_A-8650725	3	25466972	RARB	T	0.336	0.311	1.12	0.3638	0.322	0.311	0.93	0.4141
SNP_A-2008549	3	25483432	RARB	A	0.297	0.361	0.81	0.2245	0.391	0.351	1.11	0.1927
SNP_A-8351129	3	25485859	RARB	C	0.247	0.193	1.22	0.1390	0.187	0.198	0.86	0.2394
SNP_A-8580532	3	25491926	RARB	T	0.298	0.260	1.05	0.6971	0.252	0.264	1.06	0.5116
SNP_A-8649631	3	25495306	RARB	C	0.087	0.079	0.88	0.7612	0.080	0.080	1.02	0.9276
SNP_A-8529905	3	25502657	RARB	C	0.390	0.378	0.95	0.6909	0.362	0.382	1.00	0.9740
SNP_A-8376699	3	25507429	RARB	T	0.154	0.218	0.69	0.1203	0.205	0.215	1.02	0.8232
SNP_A-2075948	3	25516574	RARB	A	0.500	0.462	1.09	0.4429	0.480	0.462	0.96	0.7406
SNP_A-2200732	3	25520472	RARB	G	0.076	0.054	1.68	0.0201	0.062	0.054	1.00	0.9987
SNP_A-1924712	3	25521223	RARB	G	0.084	0.135	0.68	0.2581	0.131	0.132	1.15	0.2461
SNP_A-2136180	3	25523735	RARB	C	0.073	0.063	0.93	0.8717	0.069	0.062	1.20	0.5911
SNP_A-8525553	3	25539902	RARB	T	0.078	0.080	1.38	0.1383	0.079	0.080	0.96	0.7667
SNP_A-8464443	3	25543516	RARB	T	0.102	0.113	1.29	0.4402	0.104	0.114	0.78	0.1899
SNP_A-8679869	3	25544885	RARB	G	0.142	0.126	1.10	0.5596	0.129	0.127	1.10	0.4012

SNP_A-2301558	3	25559838	RARB	T	0.140	0.196	0.69	0.2075	0.197	0.192	1.10	0.4691
SNP_A-8398268	3	25573913	RARB	A	0.247	0.272	0.90	0.6370	0.263	0.272	1.06	0.7101
SNP_A-1972114	3	25577736	RARB	G	0.381	0.361	1.11	0.3699	0.327	0.368	0.89	0.1835
SNP_A-2031641	3	25580105	RARB	C	0.077	0.056	1.66	0.0228	0.065	0.056	1.08	0.8078
SNP_A-1892342	3	25580286	RARB	C	0.273	0.252	0.96	0.8330	0.220	0.259	0.88	0.1700
SNP_A-4201754	3	25580890	RARB	C	0.209	0.180	1.03	0.8259	0.161	0.186	0.80	0.3543
SNP_A-8617876	3	25583580	RARB	A	0.094	0.075	1.11	0.5783	0.088	0.074	1.10	0.4913
SNP_A-1972115	3	25586156	RARB	G	0.087	0.096	1.06	0.8158	0.080	0.098	0.90	0.4780
SNP_A-8445018	3	25594924	RARB	G	0.445	0.399	1.20	0.1111	0.390	0.404	0.96	0.6546
SNP_A-4302121	3	25594939	RARB	T	0.154	0.117	1.26	0.1452	0.136	0.116	1.08	0.5296
SNP_A-8602060	3	25595136	RARB	C	0.288	0.272	1.11	0.4248	0.246	0.278	0.90	0.3686
SNP_A-2270367	3	25595237	RARB	A	0.503	0.503	0.90	0.3914	0.511	0.501	1.01	0.9407
SNP_A-1889370	3	25598744	RARB	G	0.090	0.086	1.19	0.5154	0.073	0.088	0.92	0.5998
SNP_A-8429379	3	25605070	RARB	T	0.329	0.289	1.27	0.0512	0.288	0.292	1.05	0.5553
SNP_A-8325698	3	25605535	RARB	G	0.180	0.176	0.99	0.9691	0.173	0.177	0.99	0.9311
SNP_A-2053513	3	25607898	RARB	T	0.192	0.176	1.04	0.7776	0.177	0.177	1.00	0.9872
SNP_A-8305517	3	25624107	RARB	C	0.174	0.146	1.09	0.5710	0.142	0.149	0.93	0.5464
AFFX-SNP_10538716	3	25627507	RARB	G	0.349	0.336	1.12	0.3249	0.336	0.337	1.05	0.5841
SNP_A-1866350	3	41237448	CTNNB1	C	0.398	0.379	1.14	0.2869	0.408	0.375	1.07	0.5009
SNP_A-4206193	3	41268711	CTNNB1	A	0.429	0.447	0.85	0.1651	0.458	0.444	1.03	0.7416
SNP_A-8594543	4	145638960	HHIP	T	0.352	0.372	0.90	0.4883	0.372	0.371	1.01	0.9108
SNP_A-2250194	4	145643418	HHIP	C	0.352	0.285	1.26	0.0530	0.295	0.289	0.95	0.6057
SNP_A-1876176	4	145652902	HHIP	T	0.241	0.238	0.88	0.5410	0.250	0.236	1.09	0.3965
SNP_A-8363286	5	44308353	FGF10	C	0.444	0.359	1.40	0.0126	0.320	0.373	0.81	0.0137
SNP_A-8415986	5	44314920	FGF10	C	0.105	0.134	0.83	0.4318	0.150	0.129	1.03	0.8144
SNP_A-8616840	5	44316591	FGF10	A	0.061	0.100	0.59	0.0292	0.131	0.091	1.24	0.0826
SNP_A-1957063	5	44341272	FGF10	A	0.285	0.229	1.30	0.0464	0.215	0.236	0.90	0.2622
SNP_A-1981468	5	44344655	FGF10	T	0.078	0.059	1.50	0.0587	0.059	0.060	0.87	0.4692
SNP_A-8665560 (rs980510)	5	44354289	FGF10	T	**0.564**	**0.447**	**1.63**	**3.95E-05**	0.411	0.463	0.94	0.6020
SNP_A-8665561 (rs10512844)	5	44374516	FGF10	A	**0.411**	**0.308**	**1.58**	**1.43E-04**	0.297	0.318	0.88	0.1452

SNP_A-2312179	6	43745041	VEGFA	A	0.082	0.106	0.88	0.5648	0.102	0.105	1.14	0.3680
SNP_A-2205423	6	43746614	VEGFA	T	0.090	0.087	0.92	0.6709	0.077	0.090	1.04	0.8143
SNP_A-8553366	10	123258879	FGFR2	C	0.244	0.271	0.90	0.4958	0.261	0.271	0.94	0.4730
SNP_A-8334743	10	123315745	FGFR2	T	0.430	0.407	1.02	0.8871	0.426	0.406	1.08	0.3523
SNP_A-8461231	10	123316636	FGFR2	A	0.535	0.457	1.30	0.0250	0.475	0.460	1.10	0.2414
SNP_A-1863115	10	123328965	FGFR2	C	0.326	0.329	0.97	0.8055	0.384	0.319	1.21	0.0206
SNP_A-8601379	10	123336106	FGFR2	G	0.416	0.464	0.92	0.5486	0.493	0.455	1.22	0.0768
SNP_A-8483184	10	123338345	FGFR2	A	0.195	0.210	1.09	0.6629	0.234	0.205	1.11	0.2734
SNP_A-1925966	10	123344716	FGFR2	G	0.186	0.202	0.83	0.3266	0.210	0.199	1.17	0.1021
SNP_A-1936059	13	22248509	FGF9	A	0.297	0.293	0.94	0.5980	0.314	0.289	1.03	0.7590
SNP_A-8690066	13	22255136	FGF9	T	0.483	0.448	1.07	0.5373	0.438	0.452	1.02	0.8054
SNP_A-8471080	13	22263589	FGF9	C	0.125	0.114	0.93	0.6943	0.097	0.118	0.81	0.1350
SNP_A-8471082	13	22264747	FGF9	G	0.175	0.183	0.96	0.8349	0.218	0.177	1.18	0.2921
SNP_A-1800292	13	22269474	FGF9	G	0.238	0.261	0.93	0.5932	0.284	0.255	0.99	0.9380
SNP_A-8680551	13	22271503	FGF9	C	0.439	0.414	1.02	0.8848	0.388	0.420	0.95	0.5245
SNP_A-8449796	14	76447869	TGFB3	C	0.064	0.069	0.92	0.8700	0.069	0.069	1.06	0.7294
SNP_A-2223781	20	60890723	LAMA5	T	0.044	0.048	0.97	0.9021	0.047	0.048	0.81	0.2656
SNP_A-2306205	20	60899589	LAMA5	A	0.192	0.190	1.20	0.2058	0.195	0.190	1.01	0.9058
SNP_A-8349966	20	60915757	LAMA5	C	0.368	0.375	1.04	0.7383	0.353	0.379	0.91	0.2545
SNP_A-8403925	20	60916487	LAMA5	C	0.244	0.263	0.81	0.3875	0.246	0.265	0.93	0.6445
SNP_A-1860446	20	60932842	LAMA5	A	0.093	0.110	0.82	0.3102	0.120	0.107	1.02	0.8954

Candidate SNPs were selected *a priori* based on their location within genes implicated in airway morphogenesis. Genotyping: Affymetrix 6.0, excluding MAF<0.5, missingness per SNP >0.1, missingness per subject >0.1, and linkage dysequilibrium >0.7. The degree of linkage dysequilibrium below 0.7 is depicted by the r2 color scale. Odds ratios and p-values calculated using logistic regression analyses stratified by race-ethnicity, adjusted for gender, genetic ancestry principle components, and pooled by random effects meta-analysis. Bonferroni p-threshold of significance: 4.59E-04. SNP denotes single nucleotide polymorphism.

Table S14. Replication of FGF10 polymorphism rs980510 and absence of the right medial-basal airway in SPIROMICS.

	Chromosome	SNP	Gene	Minor allele	Frequency	Standard anatomy	Absence of the right medial-basal airway	Odds ratio	p-value
Whites	5	rs980510	FGF10	T	0.382	1,122	73	1.46	0.0096
All race-ethnicities	5	rs980510	FGF10	T	0.366	1,456	95	1.42	0.0086

Genotype data for the SPIROMICS sample was derived from OmniExpress plus Exome GeneChip (Illumina; San Diego, CA). Because this sample was predominantly White, the main analysis was restricted to Whites, adjusting for gender, and principal components of genetic ancestry. Secondary analysis included all race-ethnicities and an additional adjustment term for race.

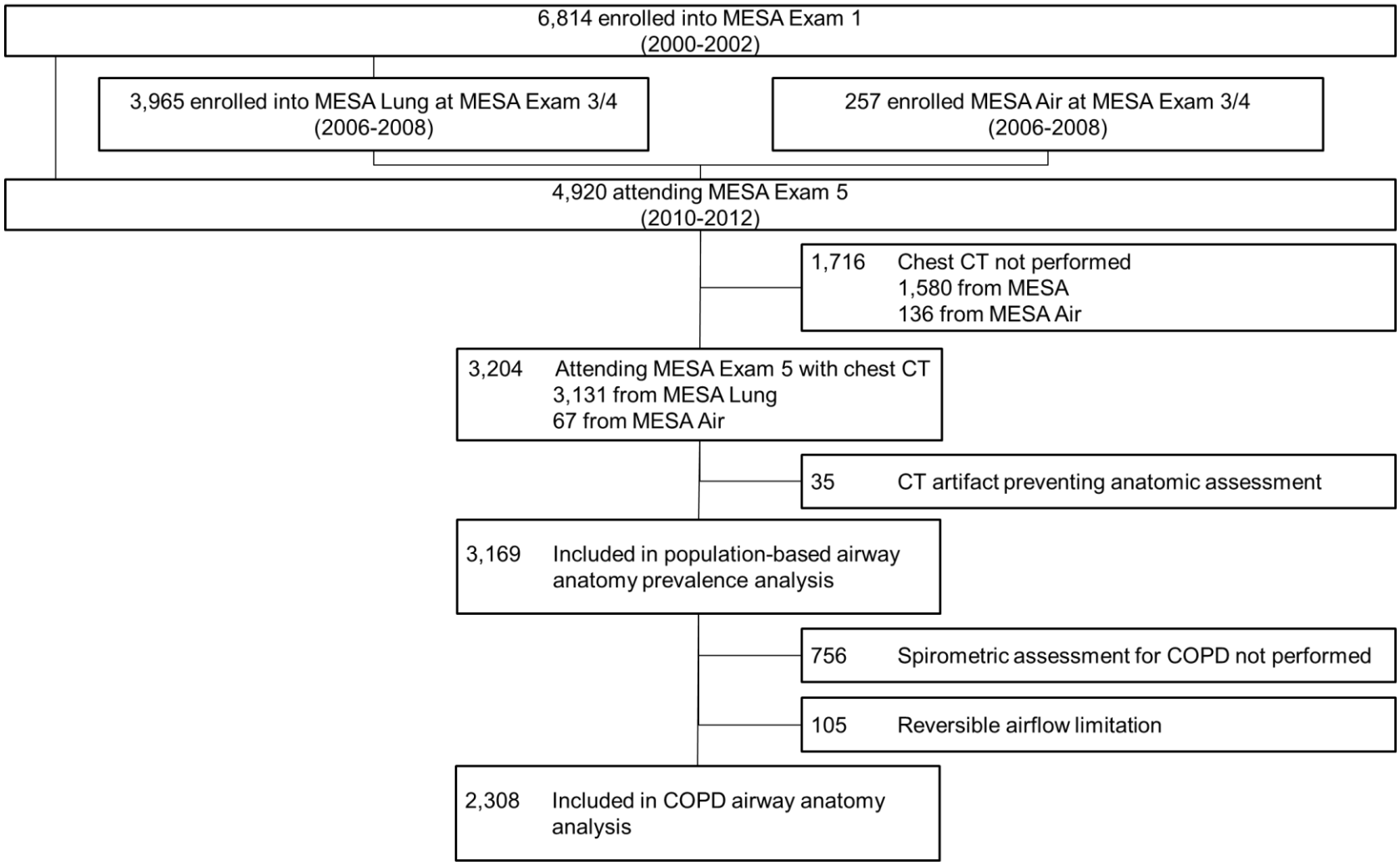
Table S15. Intra-class correlation coefficients for quantitative CT measures in the SPIROMICS Reproducibility Substudy.

	Intra-class correlation coefficient
Percent emphysema	0.99
Segmental airway lumen area	
Right upper lobe	0.97
Right middle lobe	0.63
Right lower lobe	0.90
Left upper lobe	0.92
Left lower lobe	0.94

Replicate scans performed as part of the SPIROMICS Reproducibility Substudy. Ninety six participants were scanned twice with a 2 to 6 week interval. Measures were performed (VIDA Diagnositics) with full blinding of the reading center.[1]

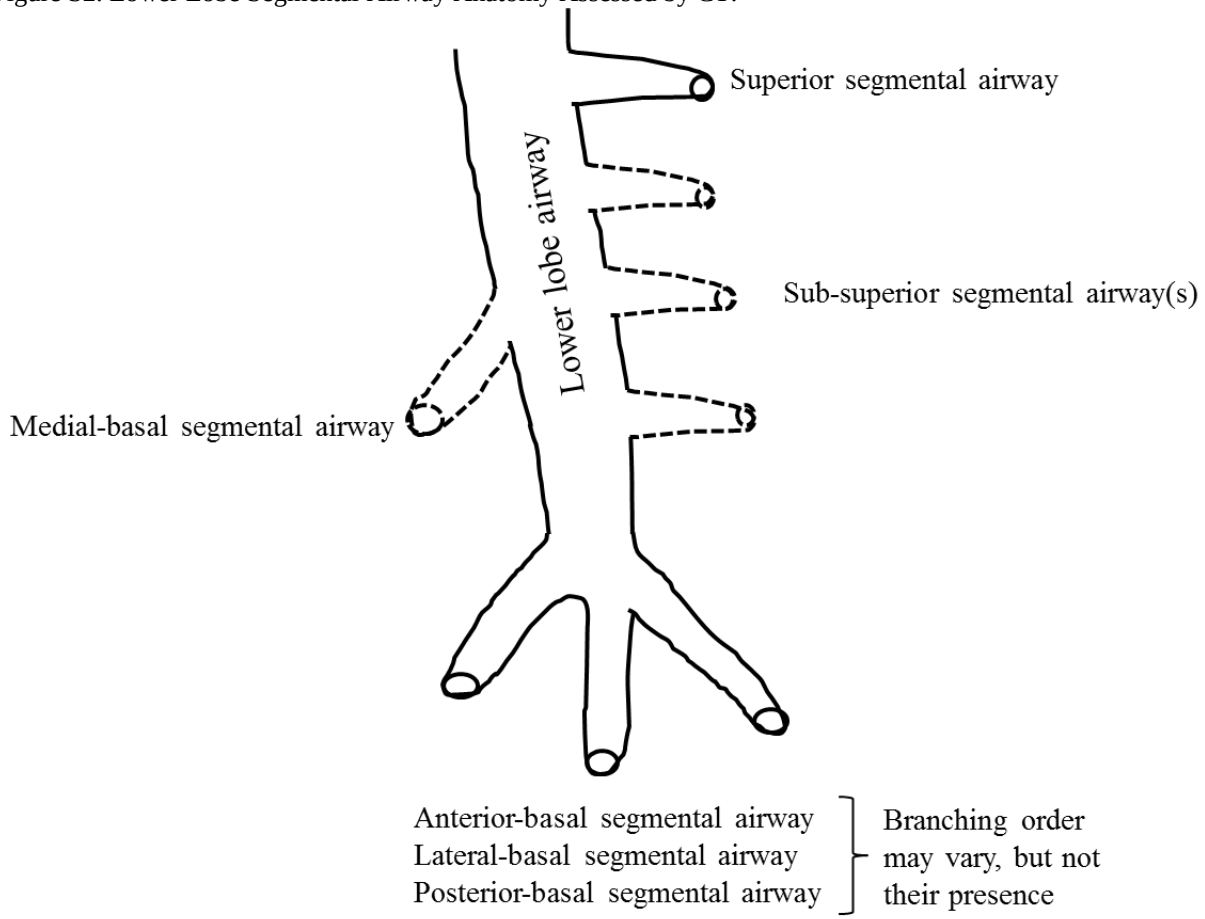
SUPPLEMENTARY INFORMATION FIGURES:

Figure S1. Flowchart of Enrollment and Inclusion in the MESA Lung Airway Anatomy and COPD Prevalence Analyses.



Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

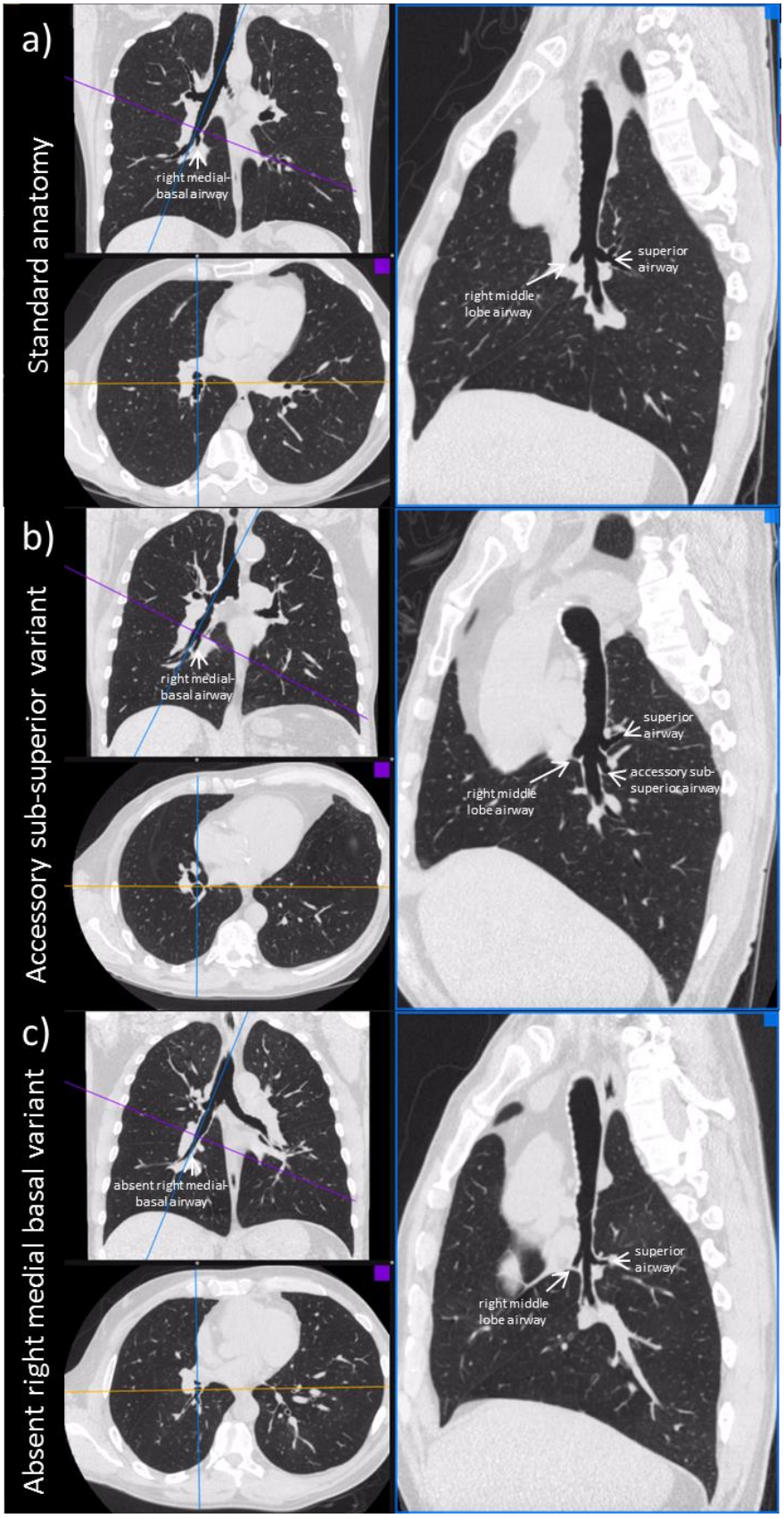
Figure S2. Lower Lobe Segmental Airway Anatomy Assessed by CT.



Medial perspective of right or left lower lobe segmental airways. Standard anatomy was defined as the presence of right and left superior, anterior-basal, lateral-basal, and posterior-basal segmental airways; presence of the right-medial basal segmental airway; absence of the left medial-basal segmental airway; and absence of right or left sub-superior segmental airway. Dashed lines depict common sites of segmental airway variation from the standard anatomy.

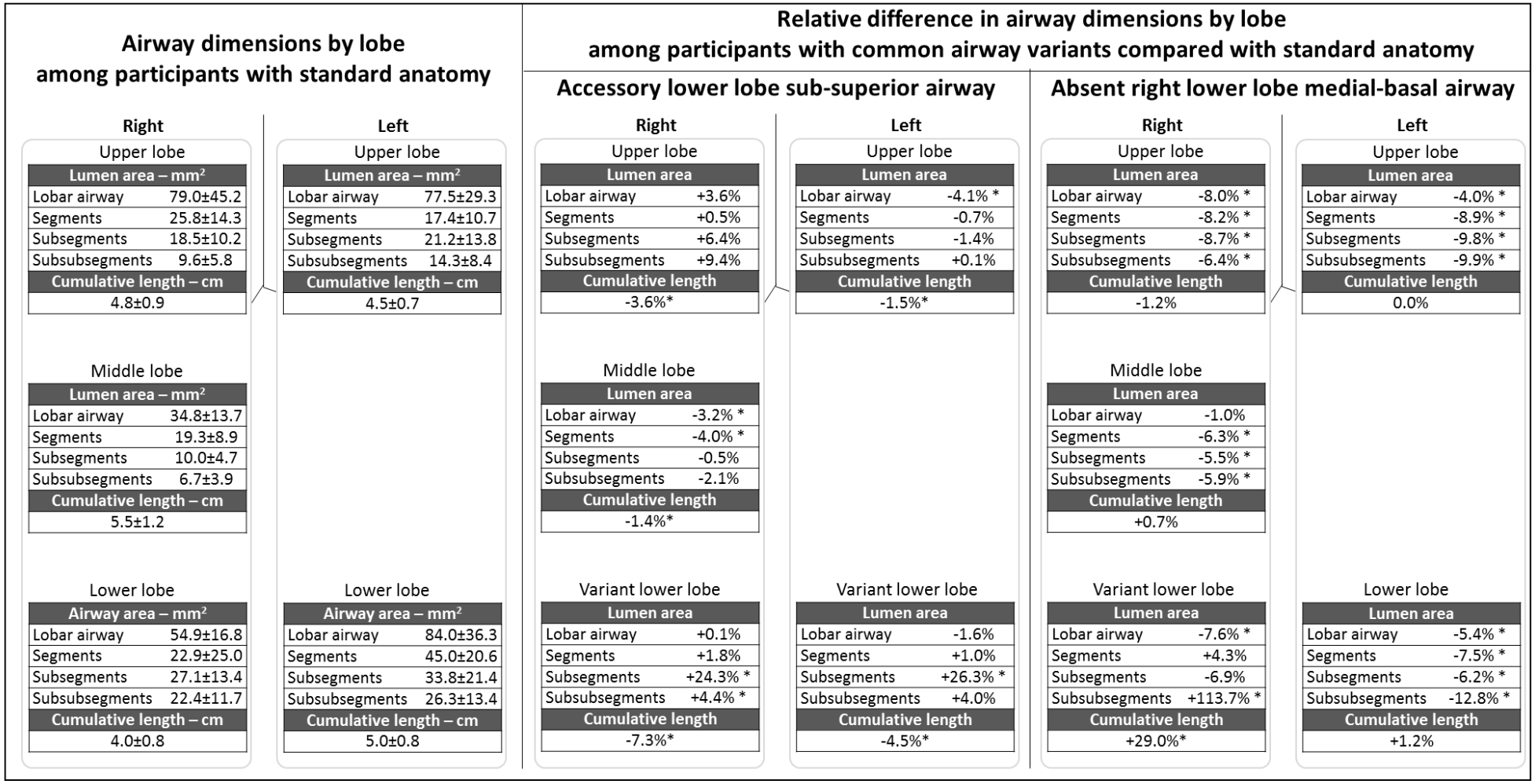
Abbreviations: CT denotes computed tomography.

Figure S3. Multi-Planar Image Assessment of Lower Lobe Segmental Airway Anatomy by Computed Tomography.



Representative multi-planar image assessment of lower segmental airway anatomy for participants with a) standard anatomy; b) an accessory sub-superior airway; and c) an absent right medial-basal airway. In each panel, the colored cross-hair is centered on the lumen of the right lower lobe airway, just inferior to the right middle lobe airway.

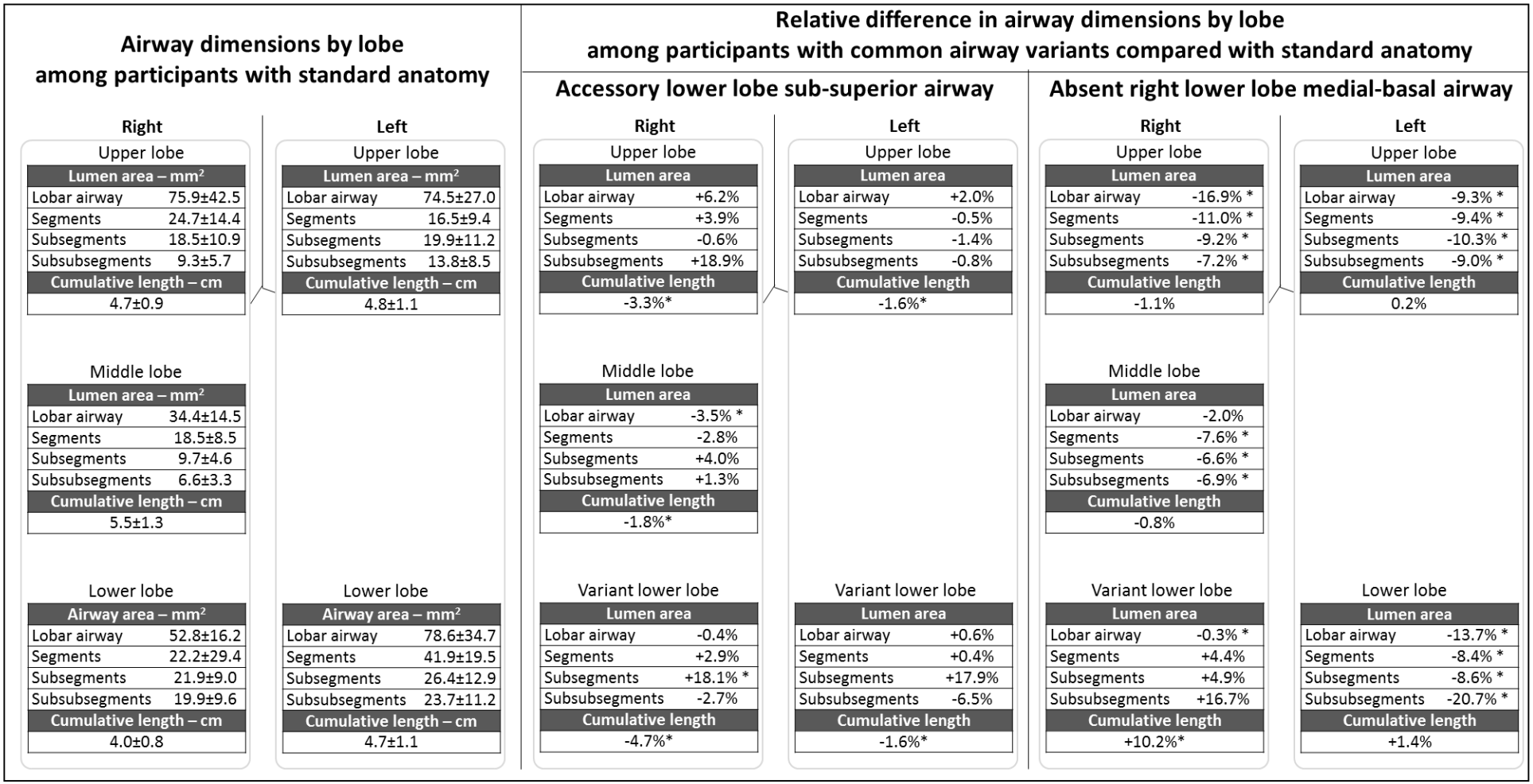
Figure S4. Airway Dimensions by Lobe Among Participants with Standard Anatomy and Common Airway Branch Variant Differences in the MESA Lung Study and SPIROMICS Pooled.



* indicates p<0.05. Mean airway dimensions (+/SD) were calculated for all airways measured from lobar to sub-sub-segmental levels within each lobe. Differences in airway dimensions by common airway branch variant status were calculated using linear regression to adjust for lobar volume, study cohort, and COPD status among SPIROMICS participants to account for the case-control design. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103; SPIROMICS: n=137). See Methods for standard and variant airway anatomy definitions, and airway measures.

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

Figure S5. Airway Dimensions by Lobe Among Participants with Standard Anatomy and Common Airway Branch Variant Differences in the MESA Lung

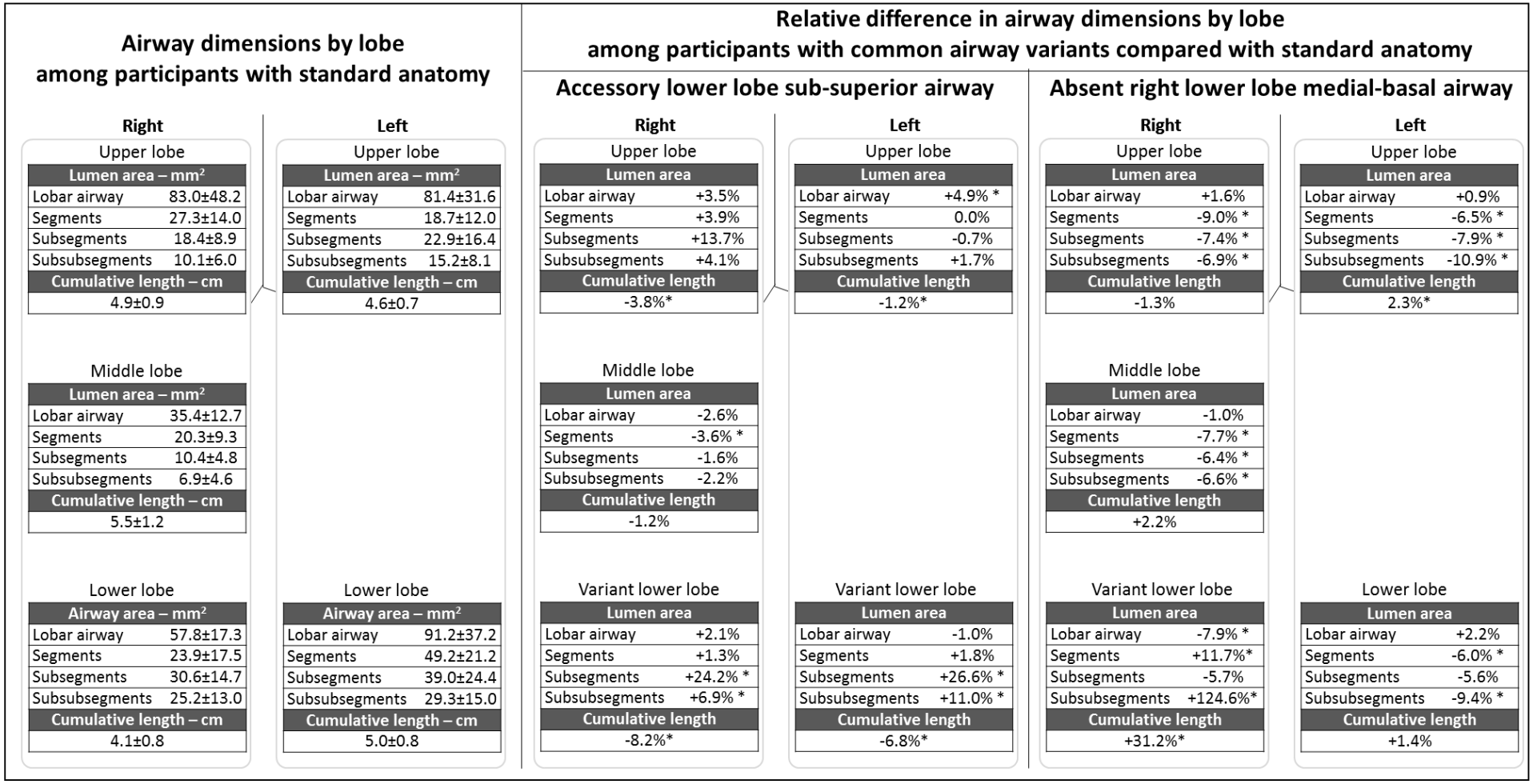


Study.

* indicates $p<0.05$. Mean airway dimensions (+/SD) were calculated for all airways measured from lobar to sub-sub-segmental levels within each lobe. Differences in airway dimensions by common airway branch variant status were calculated using linear regression to adjust for lobar volume. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (MESA: n=103). See Methods for standard and variant airway anatomy definitions, and airway measures.

Abbreviations: MESA = Multi-Ethnic Study of Atherosclerosis; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

Figure S6. Airway Dimensions by Lobe Among Participants with Standard Anatomy and Common Airway Branch Variant Differences in SPIROMICS.



* indicates p<0.05. Mean airway dimensions (+/SD) were calculated for all airways measured from lobar to sub-sub-segmental levels within each lobe. Differences in airway dimensions by common airway branch variant status were calculated using linear regression to adjust for lobar volume, and COPD status to account for the case-control design of SPIROMCIS. Participants with rare airway branch variants consisting of presence of the left medial-basal airway, or combinations of the above-mentioned variants are not shown (SPIROMICS: n=137). See Methods for standard and variant airway anatomy definitions, and airway measures.

Abbreviations: SPIROMICS = Subpopulations and Intermediate Outcome Measures in COPD Study; COPD = chronic obstructive pulmonary disease; CT = computed tomography.

SUPPLEMENTARY INFORMATION REFERENCES:

1. Motahari, A*., et al.* Short term repeatability of CT-derived pulmonary airway and density measures: role of quality control measures in assuring measurement reliability in SPIROMICS. in *American Thoracic Society* A8351 (Washington, D. C., 2017).