

Figure S1

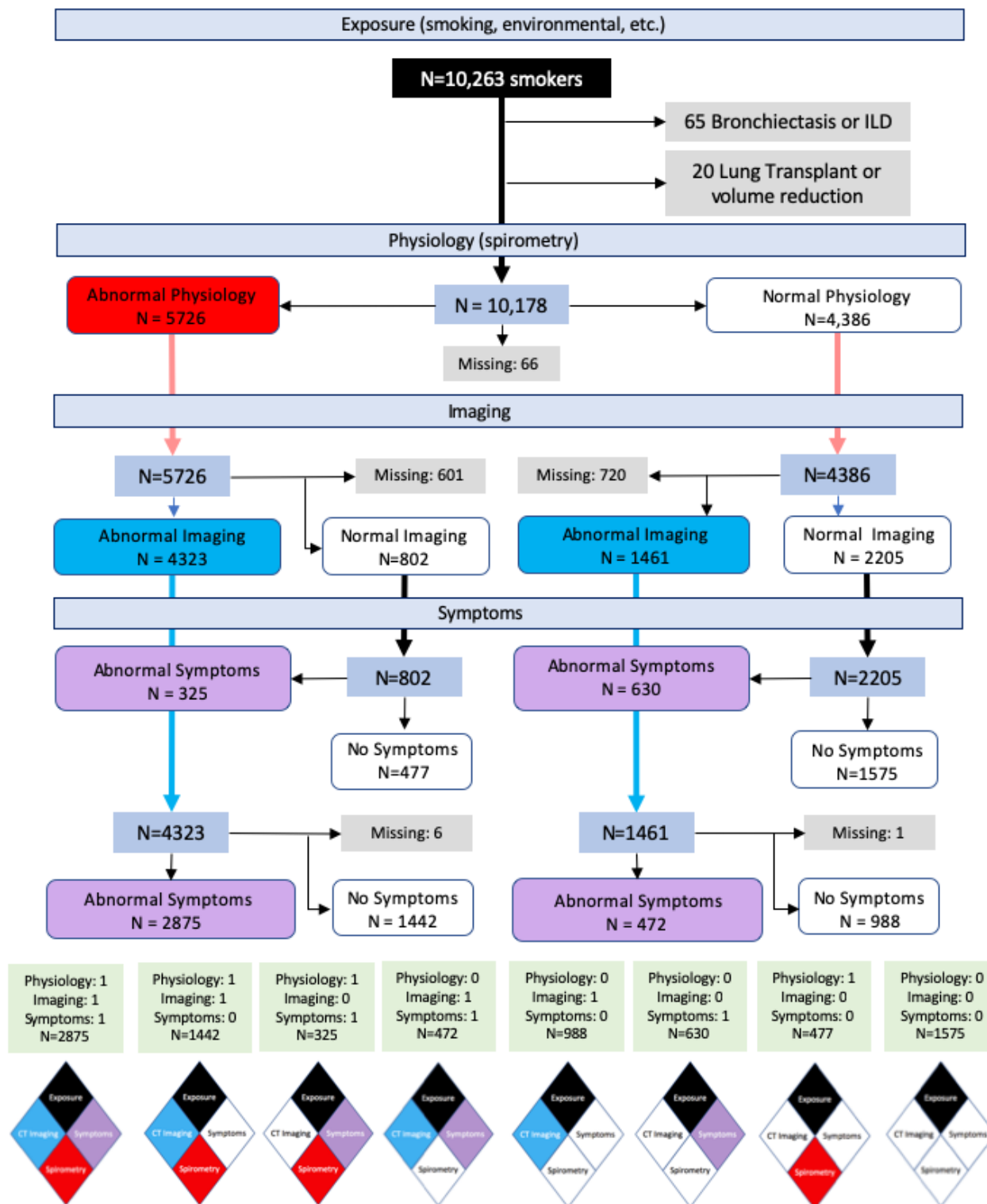


Figure S1: Consort diagram showing how each classification category is formed through a combination of exposure, spirometry, imaging, and symptoms. The diagram also demonstrates how many participants are in each category. To ease identification of categories, each disease aspect is identified by a different color. Exposure is represented by black, abnormal spirometry (FEV1, < 80% predicted and/or FEV1/FVC < 0.70) is represented by red, abnormal CT imaging (emphysema $\geq 5\%$, gas-trapping $\geq 15\%$, and/or Pi10 ≥ 2.55 mm) is represented by blue, and symptoms (chronic bronchitis or MMRC dyspnea ≥ 2) are represented by purple.

Table S1. Demographics, Spirometry and Symptoms of the Individuals Included in this Analysis and Those Excluded Due to Missing Data as Shown in Supplement Figure S1.

	Included Individuals	Excluded Individuals Due to Missing Data
n	8784	1394
Sex (% Male)	53.5%	53.3%
Race (%NHW)	51%	69%
Age	59.8 (9.1)	57.9 (8.8)
Body Mass Index	28.8 (6.2)	29.0 (6.8)
Pack Years	44.6 (25.0)	41.4 (24.3)
Current Smokers	51.8%	61.9%
Spirometry		
FEV ₁ % predicted	75.8 (25.6)	80.3 (24.2) [†]
FVC % predicted	87.0 (18.2)	86.8 (18.4) [†]
FEV ₁ /FVC	0.66 (0.16)	0.71 (0.14) [†]
Symptoms		
SGRQ Total Score	27.4 (22.9)	27.1 (23.3)
Distance walked (feet)	1359 (398)	1296 (397)
mMRC ≥ 2	41.9%	43.1%
Chronic Bronchitis	19.5%	17.1%
Severe Exacerbations	12.0%	11.2%

[†] Sample size is 1328

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score

Table S2-A. Characteristics of Individuals Included in Category A in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are separately listed. All data are from the baseline visit (i.e., Phase 1).

Category A				
N=1575				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	999	503	73	1
Sex (% Male)	45.2%	57.3%	74.0%	100%
Race (% NHW)	71.7%	58.4%	53.4%	0%
Age (yrs)	57.6 (8.2)	54.7 (7.6)	57.7 (8.5)	53.6
BMI (Kg/m ²)	28.9 (5.2)	28.6 (5.4)	28.2 (5.5)	21.42
Pack years	34.9 (19.5)	35.03 (17.4)	36.91 (16.7)	29
Current Smoker	45.2%	64.0%	74.0%	100%
Spirometry				
FEV ₁ % predicted	98.2 (11.3)	98.8 (11.3)	95.8 (10.6)	95.2
FVCP% predicted	96.2 (11.4)	97.1 (11.7)	93.8 (10.8)	91.4
FEV ₁ /FVC	0.79 (0.05)	0.8 (0.05)	0.79 (0.05)	0.82
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	1.30 (1.22)	1.15 (1.16)	1.11 (1.07)	0.4
Gas Trapping (LAA% ≤ -856 HU)	6.56 (3.98)	6.03 (4.03)	6.44 (3.79)	10.25
Pi10, mm	1.87 (0.27)	1.91 (0.28)	1.86 (0.31)	1.39
Symptoms				
SGRQ Total Score	8.22 (9.23)	9.18 (10.32)	11.65 (11.00)	20.7
Distance walked (feet)	1617 (332)	1554 (333)	1507 (303)	861
mMRC ≥2	0%	0%	0%	0%
Chronic bronchitis	0%	0%	0%	0%
Severe Exacerbation	1.0%	1.4%	2.7%	0%
*Cause of death was adjudicated for 88% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-B: Characteristics of Individuals Included in Category B in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category B				
N=988				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	652	286	50	2
Sex (% Male)	60.4%	65.0%	78.0%	100%
Race (% NHW)	75.8%	49.0%	60.0%	50.0%
Age (yrs)	60.2 (8.8)	56.2 (9.1)	59.0 (10.0)	66.2 (7.5)
BMI (Kg/m ²)	28.2 (5.4)	27.4 (4.8)	27.3 (5.0)	26.1 (9.0)
Pack years	37.4 (20.4)	37.3 (18.6)	40.0 (19.0)	28.3 (16.6)
Current Smoker	36.7%	67.8%	64.0%	0%
Spirometry				
FEV ₁ % predicted	98.4 (12.0)	97.8 (11.9)	95.9 (10.9)	90.6 (14.6)
FVCPP % predicted	98.5 (12.5)	98.6 (11.9)	96.7 (10.9)	92.2 (10.9)
FEV ₁ /FVC	0.77 (0.05)	0.78 (0.05)	0.76 (0.05)	0.74 (0.03)
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	4.46 (4.00)	2.84 (3.10)	3.51 (4.14)	16.36 (11.76)
Gas Trapping (LAA% ≤ -856 HU)	18.41 (9.61)	16.18 (9.50)	15.92 (9.42)	26.9 (20.7)
Pi10, mm	2.03 (0.56)	2.31 (0.62)	2.23 (0.60)	1.85 (0.37)
Symptoms				
SGRQ Total Score	8.31 (9.86)	10.19 (11.49)	12.47 (12.51)	8.82 (12.47)
Distance walked (feet)	1569 (323)	1462 (346)	1489 (305)	1332 (482)
mMRC ≥2	0%	0%	0%	0%
Chronic bronchitis	0%	0%	0%	0%
Severe Exacerbation	0.9%	3.1%	4.0%	0%
*Cause of death was adjudicated for 78% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-C. Characteristics of Individuals Included in Category C in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category C				
N=630				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	356	236	38	3
Sex (% Male)	37.4%	47.9%	47.4%	100%
Race % NHW)	49.7%	44.5%	63.2%	100%
Age (yrs)	55.5 (7.6)	53.3 (6.8)	59.3 (9.7)	66.8 (14.3)
BMI (Kg/m ²)	30.6 (6.4)	30.2 (6.4)	30.6 (7.7)	26.4 (3.7)
Pack years	38.6 (20.5)	39.7 (20.5)	41.5 (25.6)	25.1 (5.7)
Current Smoker	74.2%	83.1%	71.1%	0%
Spirometry				
FEV ₁ % predicted	96.5 (11.0)	97.2 (11.3)	96.8 (13.8)	93.1 (7.9)
FVCPP % predicted	94.8 (11.2)	96.2 (11.8)	94.7 (14.8)	84.2 (4.2)
FEV ₁ /FVC	0.80 (0.05)	0.80 (0.05)	0.79 (0.05)	0.82 (0.06)
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	0.94 (1.06)	0.90 (1.05)	1.07 (1.12)	0.65 (0.43)
Gas Trapping (LAA% ≤ -856 HU)	6.10 (4.15)	5.60 (3.95)	6.69 (4.26)	3.78 (0.64)
Pi10, mm	1.94 (0.26)	1.96 (0.27)	1.97 (0.26)	1.69 (0.09)
Symptoms				
SGRQ Total Score	32.1 (18.5)	36.2 (18.7)	37.6 (17.5)	38.1 (15.1)
Distance walked (feet)	1383 (335)	1380 (311)	1259 (303)	1300 (400)
mMRC ≥2	74.7%	75.8%	76.3%	33.3%
Chronic bronchitis	42.1%	44.9%	50.0%	66.7%
Severe Exacerbation	8.7%	9.7%	10.5%	66.7%
*Cause of death was adjudicated for 95% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-D. Characteristics of Individuals Included in Category D in Figure 2. Participants included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category D				
N=477				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	295	153	29	1
Sex (% Male)	47.8%	55.6%	69.0%	100%
Race (% NHW)	79.3%	58.8%	72.4%	100%
Age (yrs)	59.9 (8.2)	57.1 (8.8)	63.5 (8.7)	66.0
BMI (Kg/m ²)	29.3 (5.6)	28.9 (5.3)	28.5 (5.9)	25.6
Pack years	40.6 (22.5)	38.6 (17.7)	52.4 (25.5)	52.0
Current Smoker	49.2%	71.2%	55.2%	100%
Spirometry				
FEV ₁ % predicted	77.3 (10.7)	77.6 (11.4)	75.1 (11.8)	77.0
FVCP% predicted	85.0 (16.0)	84.2 (16.4)	79.6 (15.5)	75.8
FEV ₁ /FVC	0.71 (0.08)	0.73 (0.08)	0.72 (0.06)	0.76
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	1.37 (1.25)	1.09 (1.06)	1.37 (1.13)	0.60
Gas Trapping (LAA% ≤ -856 HU)	7.63 (4.09)	7.12 (3.96)	8.48 (4.30)	1.55
Pi10, mm	2.06 (0.25)	2.10 (0.25)	2.12 (0.19)	2.26
Symptoms				
SGRQ Total Score	10.77 (10.71)	13.30 (11.47)	9.46 (8.65)	18.57
Distance walked (feet)	1535 (295)	1461 (326)	1314 (362)	1310
mMRC ≥2	0%	0%	0%	0%
Chronic bronchitis	0%	0%	0%	0%
Severe Exacerbation	2.4%	2.0%	3.4%	0%
*Cause of death was adjudicated for 83% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-E. Characteristics of Individuals Included in Category E in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category E				
N=472				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	256	180	36	1
Sex (% Male)	50.0%	52.2%	69.4%	0%
Race (% NHW)	53.1%	42.2%	47.2%	100%
Age (yrs)	55.9 (7.9)	53.8 (7.0)	57.3 (10.2)	48.6
BMI (Kg/m ²)	30.5 (6.6)	30.6 (6.9)	27.7 (6.06)	27.2
Pack years	41.3 (22.1)	39.5 (20.1)	48.7 (26.6)	51.9
Current Smoker	69.1%	80.6%	80.6%	100%
Spirometry				
FEV ₁ % predicted	94.2 (11.1)	95.8 (11.3)	96.1 (10.6)	103.3
FVCP% predicted	95.1 (11.8)	96.1 (12.2)	98.0 (11.5)	104.5
FEV ₁ /FVC	0.78 (0.05)	0.79 (0.06)	0.76 (0.05)	0.79
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	2.44 (3.15)	2.62 (3.60)	2.19 (2.31)	0.18
Gas Trapping (LAA% ≤ -856 HU)	13.94 (9.18)	14.34 (10.55)	17 (10.16)	1.69
Pi10, mm	2.39 (0.60)	2.52 (0.65)	2.44 (0.65)	3.01
Symptoms				
SGRQ Total Score	34.95 (18.95)	36.27 (18.35)	37.49 (19.72)	70.15
Distance walked (feet)	1324 (357)	1321 (364)	1254 (291)	1003
mMRC ≥2	76.2%	79.4%	69.4%	100%
Chronic bronchitis	40.2%	40.6%	50.0%	100%
Severe Exacerbation	11.3%	15.0%	16.7%	0%
*Cause of death was adjudicated for 81% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-F. Characteristics of Individuals Included in Category F in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category F				
N=325				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	173	113	39	5
Sex (% Male)	42.8%	42.5%	51.3%	40.0%
Race (% NHW)	72.8%	56.6%	69.2%	100%
Age (yrs)	58.8 (7.8)	56.1 (7.5)	60.9 (8.9)	62.0 (6.9)
Body Mass Index (Kg/m ²)	32.1 (7.2)	30.6 (6.6)	30.1 (6.8)	29.6 (6.3)
Pack years	41.0 (19.9)	46.4 (25.8)	51.2 (26.6)	58.5 (35.9)
Current Smoker	57.8%	77.0%	56.4%	60.0%
Spirometry				
FEV ₁ % predicted	73.1 (10.5)	75.7 (12.5)	71.8 (8.1)	73.0 (11.1)
FVCP % predicted	79.0 (14.4)	83.5 (19.3)	77.0 (10.2)	77.2 (19.0)
FEV ₁ /FVC	0.72 (0.07)	0.72 (0.09)	0.72 (0.08)	0.74 (0.08)
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	1.17 (1.15)	1.15 (1.15)	1.19 (1.16)	1.34 (1.36)
Gas Trapping (LAA% ≤ -856 HU)	7.55 (4.14)	7.25 (4.22)	8.18 (3.95)	6.87 (2.93)
Pi10, mm	2.15 (0.24)	2.14 (0.24)	2.18 (0.24)	2.39 (0.08)
Symptoms				
SGRQ Total Score	36.79 (19.00)	39.28 (17.85)	42.71 (18.64)	44.5 (19.2)
Distance walked (feet)	1315 (360)	1293 (351)	1194 (318)	1172 (129)
mMRC ≥2	79.8%	79.6%	87.2%	100%
Chronic bronchitis	41.6%	41.6%	41.0%	40.0%
Severe Exacerbation	12.1%	15.0%	23.1%	20.0%
*Cause of death was adjudicated for 90% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-G. Characteristics of Individuals Included in Category G in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category G				
N=1442				
CATEGORY	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	898	403	141	31
Sex (% Male)	58.2%	57.6%	58.2%	48.4%
Race (% NHW)	78.5%	69.2%	78.0%	71.0%
Age (yrs)	63.2 (8.6)	60.8 (9.6)	65.3 (9.1)	69.5 (8.5)
BMI (Kg/m ²)	27.7 (5.4)	27.9 (5.5)	26.8 (5.7)	24.0 (4.5)
Pack years	46.2 (23.4)	45.6 (25.2)	50.8 (29.9)	45.7 (21.5)
Current Smoker	43.4%	57.6%	42.6%	12.9%
Spirometry				
FEV ₁ % predicted	71.5 (17.3)	70.3 (15.8)	61.9 (19.8)	45.9 (15.3)
FVCP% predicted	89.0 (18.2)	85.9 (16.1)	82.6 (17.5)	80.0 (18.5)
FEV ₁ /FVC	0.62 (0.11)	0.63 (0.11)	0.57 (0.13)	0.43 (0.11)
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	7.75 (8.40)	5.84 (7.27)	10.12 (10.51)	17.6 (11.62)
Gas Trapping (LAA% ≤ -856 HU)	28.14 (15.96)	24.25 (15.95)	33.24 (18.61)	48.64 (15.36)
Pi10, mm	2.47 (0.55)	2.65 (0.62)	2.61 (0.58)	2.60 (0.45)
SGRQ Total Score	14.93 (12.76)	16.90 (13.63)	20.55 (14.75)	27.87 (16.48)
Symptoms				
Distance walked (feet)	1481 (319)	1403 (356)	1250 (344)	1152 (326)
mMRC ≥2	0%	0%	0%	0%
Chronic bronchitis	0%	0%	0%	0%
Severe Exacerbation	5.5%	8.4%	12.8%	29.0%
*Cause of death was adjudicated for 85% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units

Table S2-H. Characteristics of Individuals Included in Category H in Figure 2. Individuals included in the analysis of FEV₁ decline are listed as those with a Phase 2 visit and FEV₁ measured. Data for missing individuals are shown for those who were alive but did not have a Phase 2 visit with FEV₁ measured and those who died and did not have a Phase 2 visit. Deaths due to respiratory death are also listed. All data are from the baseline visit (i.e., Phase 1).

Category H N=2875				
Characteristic	Visit 2 FEV₁	No Visit 2 FEV₁	No Visit 2 & Died	Respiratory Death*
N	1296	807	772	326
Sex (% Male)	51.6%	52.0%	59.8%	58.3%
Race (% NHW)	73.0%	73.0%	80.2%	82.2%
Age (yrs)	61.5 (8.6)	60.9 (8.9)	65.3 (8.6)	66.2 (8.0)
BMI (Kg/m ²)	29.5 (6.9)	29.3 (7.0)	27.0 (6.6)	26.0 (6.5)
Pack years	51.9 (27.1)	51.3 (25.8)	59.4 (32.0)	59.6 (32.9)
Current Smoker	45.1%	48.0%	37.3%	27.0%
Spirometry				
FEV ₁ % predicted	55.4 (18.3)	53.6 (19.7)	40.4 (19.8)	31.3 (14.1)
FVCP % predicted	78.7 (17.4)	76.3 (18.4)	69.6 (19.9)	64.4 (19.4)
FEV ₁ /FVC	0.54 (0.14)	0.54 (0.15)	0.43 (0.15)	0.37 (0.11)
CT Metrics				
Emphysema (LAA% ≤ -950 HU)	11.32 (11.53)	11.43 (12.55)	19.24 (15.04)	24.45 (14.71)
Gas Trapping (LAA% ≤ -856 HU)	34.72 (19.55)	34.69 (21.68)	47.54 (21.42)	55.32 (18.34)
Pi10, mm	2.76 (0.60)	2.86 (0.59)	2.87 (0.53)	2.89 (0.49)
Symptoms				
SGRQ Total Score	44.66 (18.4)	49.60 (18.97)	52.62 (17.48)	56.45 (15.8)
Distance walked (feet)	1206 (353)	1120 (365)	942 (390)	848 (361)
mMRC ≥2	87.2%	89.4%	94.8%	97.2%
Chronic bronchitis	38.5%	39.4%	37.6%	35.9%
Severe Exacerbation	20.9%	26.8%	32.1%	38.3%
*Cause of death was adjudicated for 85% of deaths.				

Results shown are mean (SD) or percent (%) as indicated. NHW – Non-Hispanic White, SGRQ – St. George’s Respiratory Questionnaire, mMRC – modified Medical Research Council Dyspnea Score, Pi10 – Square root of airway wall area for a standardized airway of 10 mm internal perimeter. %LAA – Percent Low attenuation area, HU – Hounsfield Units