

SUPPLEMENTARY MATERIAL

e-Table 1: Outcomes studied in present analysis.				
Outcome	Abbreviation	Definition	Nature of data, direction indicating adverse effect (continuous only)	Regression used for analysis
Clinical outcomes- subjective (symptoms, health status, quality of life)				
St. George's Respiratory Questionnaire	SGRQ	Questionnaire assessing respiratory disease-specific quality of life	Continuous, higher score indicates worse QOL	Linear
Medical Outcomes Short-form 12 item questionnaire	SF-12	Questionnaire assessing general quality of life	Continuous, lower score indicates worse QOL	Linear
COPD Assessment Test	CAT	Questionnaire assessing health status specific to COPD	Continuous, higher score indicates worse health status	Linear
Modified Medical Research Council questionnaire	MMRC	Dyspnea severity score, ranging from 0-4.	Continuous, higher score indicates worse dyspnea	Linear
Ease of cough and sputum questionnaire	Ease of cough and sputum score	Questionnaire assessing difficulty with cough and sputum experienced by the participant over the past day.	Continuous, higher score indicates more difficulty	Linear
Chronic cough	NA	Reported "usual" cough production in past day as assessed by American Thoracic Society-Division of Lung Diseases (ATS-DLD) questionnaire	Dichotomous	Logistic
Chronic productive cough	NA	Reported "usual" cough and phlegm production in past day as assessed by ATS-DLD questionnaire	Dichotomous	Logistic
Clinical outcomes (healthcare utilization)				
Exacerbations reported in past year	Exacerbation risk	Reported number of events in the past year in which the participant had to make medication changes, dose adjustments, or had unscheduled contact with their physician,	Dichotomous	Logistic

		emergency room, or hospitalization due to worsening of respiratory symptoms due to COPD.		
Severe exacerbations reported in past year	Severe exacerbation risk	Reported number of events in the past year in which the participant had to go to the emergency room or required hospitalization due to worsening of respiratory symptoms requiring escalation of treatment for COPD.	Dichotomous	Logistic
Clinical outcomes (physiologic)				
Six minute walk distance	6MWD	Measure of exercise capacity in which the distance that a patient can walk quickly on a flat surface in 6 minutes is measured in meters	Continuous, lower value indicates worse exercise capacity	Linear
Forced Expiratory Volume in 1 second, percent predicted	FEV1 % predicted	Percent predicted of post-bronchodilator spirometry value, predicted values calculated using NHANES III reference values[CITATION]	Continuous, lower value indicates worse lung function	Linear
Computed Tomography (CT) outcomes				
Square root of wall area of a hypothetical airway with an internal perimeter of 10 mm	Pi10	A measure of airway wall thickness, calculated using all airways detected by CT to regress square-root wall area on internal perimeter to predict the square-root wall area of a single hypothetical airway with internal perimeter of 10mm	Continuous, higher value indicates greater airway wall thickness relative to internal perimeter	Linear
Airway wall thickness	Wall diameter	A measure of the cross-sectional airway wall diameter.	Continuous, higher value indicates greater diameter	Linear
Airway wall area	Wall area	A measure of the cross-sectional airway wall area.	Continuous, higher value indicates greater area	Linear
Airway lumen diameter	Lumen diameter	A measure of the cross-sectional airway lumen diameter.	Continuous, higher value indicates greater diameter	Linear
Airway lumen area	Lumen area	A measure of the cross-sectional airway lumen area.	Continuous, higher value indicates greater area	Linear
Airway wall area percentage	Wall area percentage	A measure of airway wall thickness relative to the total airway area.	Continuous, higher value	Linear

			indicates greater airway wall thickness relative to total airway size.	
Percent emphysema	% emphysema	Percent of total voxels in the field < - 950 Hounsfield units at total lung capacity	Continuous, higher value indicates more emphysema	Linear
Percent gas trapping	% gas trapping	Percent of total voxels in the field <- 856 Hounsfield units at residual volume	Continuous, higher value indicates more gas trapping	Linear

e-Table 3: Associations of quartiles of years of SHS exposure in the home with outcomes in participants with COPD in SPIROMICS			
Years of SHS smoke quartiles (1st REF)	β	95% CI	p-value
2nd			
3rd			
4th			
6MWD, meters	21.65	(-11.51, 54.81)	0.200
	5.91	(-17.45, 29.27)	0.620
	-3.04	(-26.30, 20.22)	0.797
FEV1 % predicted	0.47	(-3.10, 4.04)	0.553
	0.17	(-2.38, 2.72)	0.313
	1.36	(-1.20, 3.91)	0.291
SGRQ score*	-5.51	(-9.80, -1.22)	0.012
	-2.30	(-5.29, 0.68)	0.131
	-0.34	(-3.37, 2.69)	0.823
SF12 GH score	0.69	(-2.00, 3.38)	0.614
	0.64	(-1.25, 2.52)	0.508
	0.26	(-1.62, 2.14)	0.788
Total CAT score	-1.65	(-3.41, 0.11)	0.066
	-1.27	(-2.52, -0.01)	0.048
	-0.14	(-1.41, 1.13)	0.825
MMRC score	-0.07	(-0.31, 0.17)	0.559
	-0.07	(-0.24, 0.10)	0.432
	-0.06	(-0.23, 0.11)	0.472
Ease of cough/sputum	-0.91	(-1.73, -0.09)	0.029
	-0.67	(-1.24, -0.10)	0.022
	-0.38	(-0.96, 0.19)	0.190
	OR	95% CI	p-value
Frequent exacerbator	1.15	(0.54, 2.45)	0.722
	0.91	(0.53, 1.57)	0.736
	1.30	(0.77, 2.20)	0.325
Nocturnal symptoms	0.64	(0.35, 1.18)	0.152
	0.82	(0.55, 1.22)	0.324
	0.88	(0.59, 1.31)	0.523
Any wheezing	0.84	(0.49, 1.44)	0.538
	1.02	(0.69, 1.49)	0.915
	1.08	(0.74, 1.59)	0.678
Chronic cough	0.83	(0.48, 1.43)	0.507
	0.73	(0.50, 1.07)	0.103
	0.82	(0.56, 1.21)	0.325

Chronic productive cough	0.76 0.65 0.63	(0.42, 1.39) (0.43, 0.98) (0.41, 0.94)	0.376 0.040 0.026
Exacerbation risk in past year	0.93 1.31 1.18	(0.51, 1.68) (0.88, 1.96) (0.78, 1.77)	0.809 0.182 0.431
Severe exacerbation risk in past year	0.51 1.14 0.76	(0.21, 1.22) (0.71, 1.83) (0.45, 1.27)	0.130 0.591 0.290
% emphysema	-0.98 -1.07 -0.03	(-3.25, 1.30) (-2.72, 0.57) (-1.65, 1.60)	0.401 0.200 0.972
% gas-trapping	1.02 0.05 1.57	(-2.27, 4.31) (-2.32, 2.43) (-0.78, 3.92)	0.542 0.964 0.190
Pi10 (normalized)	-0.13 -0.22 -0.12	(-0.37, 0.12) (-0.40, -0.05) (-0.30, 0.05)	0.309 0.014 0.170
>median % emphysema, OR	0.90 0.78 1.14	(0.50, 1.62) (0.50, 1.20) (0.74, 1.75)	0.715 0.252 0.563
> median % gas-trapping, OR	0.87 0.76 0.99	(0.50, 1.51) (0.51, 1.14) (0.66, 1.47)	0.631 0.187 0.949
	RR	95% CI	p-value
Exacerbations experienced over follow-up	0.83 0.89 0.94	(0.47, 1.44) (0.66, 1.19) (0.70, 1.28)	0.501 0.430 0.711
Severe exacerbations experienced over follow-up	0.82 0.83 0.91	(0.29, 2.29) (0.52, 1.33) (0.57, 1.45)	0.705 0.442 0.697
Adjusted for age, gender, race, severity of COPD (GOLD 1-2 vs GOLD 3-4), education level, current smoking status, pack-years smoked. Refer to Table 2 legend for all abbreviations. Poisson models of exacerbations and severe exacerbations over follow-up additionally adjusted for follow-up time. *Likelihood ratio test for contribution of years of SHS to nested models p<0.047. Results for similar testing from all other outcomes did not reach statistical significance.			

e-Table 4: Associations of SHS exposure in past week with outcomes in SPIROMICS, stratum 1 (healthy nonsmokers).			
Hours of SHS smoke in the past 7 d	β	95% CI	p-value
0-1 Hr (REF)			
2+ hours			
6MWD, meters	12.06	(-33.22, 57.35)	0.600
SGRQ score	0.65	(-4.33, 5.64)	0.796
SF12 GH score	-0.27	(-3.35, 2.80)	0.861
CAT score	0.68	(-2.03, 3.40)	0.619
MMRC score	0.03	(-0.21, 0.27)	0.792
Ease of cough and sputum score	-0.49	(-1.61, 0.63)	0.388
Pi10 (normalized)	0.44	(0.03, 0.86)	0.038
Nocturnal symptoms	1.79	(0.44, 7.32)	0.419
Any wheezing	3.07	(0.62, 15.28)	0.171
Living with a smoker	β	95% CI	p-value
6MWD, meters	5.65	(-37.00, 48.30)	0.794
FEV1 % predicted	2.82	(-1.82, 7.45)	0.232
SGRQ score	0.79	(-4.29, 5.86)	0.760
SF12 GH score	-5.47	(-8.41, -2.53)	<0.001
CAT score	1.74	(-0.95, 4.44)	0.204
MMRC score	0.11	(-0.13, 0.35)	0.365
Ease of cough and sputum score	-0.45	(-1.56, 0.66)	0.426
% emphysema	0.11	(-0.60, 0.81)	0.764
% gas-trapping	-0.58	(-7.17, 6.00)	0.862
PI 10 (normalized)	-0.02	(-0.46, 0.41)	0.920
Nocturnal symptoms	1.52	(0.37, 6.24)	0.558
Any wheezing	0.58	(0.07, 5.15)	0.629
Chronic cough	0.32	(0.04, 2.80)	0.301
Adjusted for age, gender, race, FEV1% predicted, education level. SPIROMICS- subpopulations and intermediate outcomes of COPD Study COPD- Chronic Obstructive Pulmonary Disease β- coefficient for modeled estimate 6MWD- six-minute walk distance FEV1- forced expiratory volume in 1 second SGRQ- St George's Respiratory Questionnaire SF12 GH- Medical outcomes short form-12 item questionnaire general health score CAT- COPD assessment test MMRC- modified medical research council questionnaire			

e-Table 5: Associations of SHS exposure in past week with outcomes in SPIROMICS, stratum 2 (“healthy” current and former smokers).

Hours of SHS smoke in the past 7 d	β	95% CI	p-value
0-2 Hr (REF)			
2+ hours			
6MWD, meters	-4.14	(-21.43, 13.14)	0.638
SGRQ score	3.57	(0.35, 6.78)	0.030
SF12 GH score	-0.75	(-2.08, 0.57)	0.264
CAT score	0.60	(-0.82, 2.02)	0.410
MMRC score	0.11	(-0.03, 0.25)	0.129
Ease of cough and sputum score	0.69	(0.10, 1.27)	0.022
PI 10 (normalized)	0.17	(-0.001, 0.35)	0.052
Nocturnal symptoms	1.41	(0.94, 2.13)	0.097
Any wheezing	1.58	(1.06, 2.37)	0.024
Living with a smoker	β	95% CI	p-value
6MWD, meters	-14.86	(-31.58, 1.85)	0.081
FEV1 % predicted	-0.52	(-2.94, 1.91)	0.674
SGRQ score	2.94	(-0.15, 6.03)	0.062
SF12 GH score	-0.55	(-1.82, 0.72)	0.398
CAT score	1.10	(-0.28, 2.48)	0.118
MMRC score	0.18	(0.04, 0.32)	0.012
Ease of cough and sputum score	0.66	(0.09, 1.23)	0.024
% emphysema	0.11	(-0.22, 0.45)	0.504
% gas-trapping	-1.11	(-4.14, 1.91)	0.471
Pi10 (normalized)	0.19	(0.02, 0.36)	0.029
Nocturnal symptoms	0.95	(0.64, 1.41)	0.806
Any wheezing	1.19	(0.81, 1.74)	0.386
Chronic cough	1.03	(0.70, 1.52)	0.875

Adjusted for age, gender, race, FEV1% predicted, education level.

SPIROMICS- subpopulations and intermediate outcomes of COPD Study

COPD- Chronic Obstructive Pulmonary Disease

β - coefficient for modeled estimate

6MWD- six-minute walk distance

FEV1- forced expiratory volume in 1 second

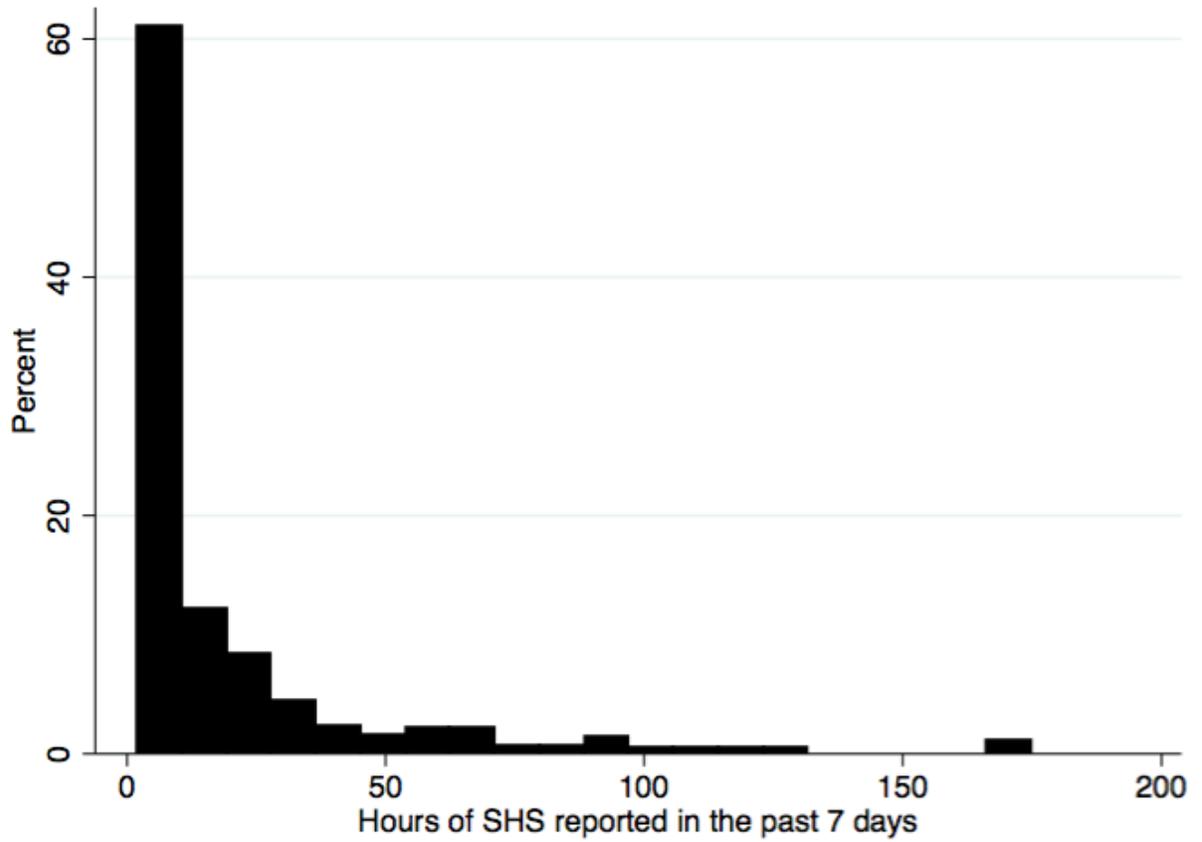
SGRQ- St George’s Respiratory Questionnaire

SF12 GH- Medical outcomes short form-12 item questionnaire general health score

CAT- COPD assessment test

MMRC- modified medical research council questionnaire

e-Figure 1: Distribution of hours of secondhand smoke exposure reported over the past 7 days among individuals reporting 2 or more hours of exposure.



Supplementary Material for Text:**Methods section, study population:**

Current and former smokers with (strata 3-4) and without COPD (stratum 2) were recruited, as were healthy, lifelong nonsmokers (stratum 1). We studied individuals in SPIROMICS strata 3 (post-bronchodilator FEV₁≥50% predicted) and 4 (FEV₁<50% predicted), which included mild through severe COPD (GOLD spirometry grade 1-4) in primary analysis, based upon post-bronchodilator FEV₁/FVC of <70%, enrolled prior to October, 2014. Secondary analyses also incorporated individuals from strata 1-2. Exclusion criteria were non-COPD obstructive lung disease (except asthma), BMI >40 kg/m², history of lung surgery, or intolerance to bronchodilators. Participants were enrolled in the study and consented to study procedures at the first study visit and then followed annually for up to 3 years (with current ongoing follow-up).

Methods section, CT measures:

Percent emphysema was defined as percent of total voxels in the field < -950 Hounsfield units at total lung capacity. Percent gas-trapping was defined as percent of total voxels in the field < -856 Hounsfield units at residual volume. Pi10, a measure of airway wall thickness, was calculated using all airways by regressing the square-root wall area on internal perimeter of airways to predict the square-root wall area of a single hypothetical airway with internal perimeter of 10mm, as previously described. [1] We also studied airway dimensions including area and diameter of walls and lumens of airways in generations 1-6 using techniques as previously described.[1] We calculated differences in wall and lumen area and diameter measurements, and also in wall area percent, a measure of airway wall thickness relative to total airway size.

Methods section, covariate selection:

Unadjusted tabulations of the differences between individuals reporting 0-1 hours and 2+ hours of recent SHS exposure were performed to help determine what factors would be included as covariates in adjusted analyses. In addition to those factors felt to *a priori* be potential confounders, we included variables which were significantly different between groups with and without SHS exposure at the $p < 0.05$ level with the exception of household income (due to inclusion of educational attainment as an adjustment for socioeconomic status), GOLD categories (due to adjustment for FEV₁ % predicted), % gas-trapping and emphysema (as both were analyzed as outcome variables).

Methods section, statistical modeling:

Because all data except exacerbations over follow-up was cross-sectional, all models were linear or logistic regression models (in which coefficients and log odds were the modeled effects) with the exception of analyses of longitudinal exacerbations and severe exacerbations over follow-up, which were analyzed as count data using adjusted Poisson regression with robust standard errors (in which relative risk was the modeled effect, with log link function), controlling additionally for time to follow-up which varied between individuals. Recent SHS exposure (past week) was only analyzed for association with shorter term outcomes (outcomes assessing status in the last 3 months or less: SGRQ, 6-minute walk distance, SF12 general score, CAT score, MMRC, Ease of cough and sputum, nocturnal symptoms and wheezing) in addition to airway wall thickness which may partly represent airway inflammation[2]. Models of recent SHS exposure were additionally adjusted for markers of disease severity including FEV₁ percent predicted and oxygen use (a positive response to question "Do you use supplemental oxygen prescribed by your doctor at home?", not including those indicating use only at night). Given the possible influences from occupational exposures as shown in previous work in this cohort,[3] models of

SHS exposure in the past week were additionally adjusted for self-report of exposure to vapors, dusts, gases or fumes in the longest held job. We additionally used likelihood ratio testing of nested models with and without terms for years of SHS exposure (modeled as quartiles) to determine if the overall contribution of years of SHS exposure was significantly informative. Finally, in addition to analyzing CT metrics of Pi10 and percent emphysema and gas-trapping, we used generalized estimating equations (GEE) to calculate mean differences in airway wall and lumen area and diameter as well as wall area percent for generation 1 to 6[1], controlling for the same factors as listed above in addition to total lung volume achieved at CT. GEE was utilized in the case of airways analyses because multiple measurements were obtained for each individual in the many generations of airways, therefore analyses with GEE accounted for the within-person correlation of these measurements.

References for supplement:

1. Smith BM, Hoffman EA, Rabinowitz D, et al. Comparison of spatially matched airways reveals thinner airway walls in COPD. *The Multi-Ethnic Study of Atherosclerosis (MESA) COPD Study and the Subpopulations and Intermediate Outcomes in COPD Study (SPIROMICS)*. 2014;**69**(11):987-96 doi: 10.1136/thoraxjnl-2014-205160[published Online First: Epub Date]].
2. O'Donnell RA, Peebles C, Ward JA, et al. Relationship between peripheral airway dysfunction, airway obstruction, and neutrophilic inflammation in COPD. *Thorax* 2004;**59**(10):837-42 doi: 10.1136/thx.2003.019349[published Online First: Epub Date]].
3. Paulin LM, Diette GB, Blanc PD, et al. Occupational exposures are associated with worse morbidity in patients with chronic obstructive pulmonary disease. *American journal of respiratory and critical care medicine* 2015;**191**(5):557-65 doi: 10.1164/rccm.201408-1407OC[published Online First: Epub Date]].