Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eMethods

Statistical modeling

The extent of disease at baseline can be likely associated with progression of disease due to the exposure of interest, measured confounders and unmeasured confounding factors. We developed a statistical model to better understand the relationship between long-term air pollution exposure and the progression of the measured outcomes adjusting for a wide number of potential confounders and to avoid bias in the analysis. We fit a longitudinal mixed model with random slopes and intercepts, which jointly models the cross-sectional and longitudinal relationships between long-term exposure to air pollution and the outcomes. This modeled examined the included three components,1) the cross-sectional relationship between the baseline outcome and values of covariates at baseline, 2) the longitudinal relationship to model rate of change, and 3) time-varying "transient" terms that adjust for variables relevant to specific measurements without modification for the slope), as follows:

$$Y_{iv} = [\alpha_0 + X_{i0}\alpha_1 + a_i] + [t_{iv}\beta_0 + W_{iv}t_{iv}\beta_1 + t_{iv}b_i] + [U_{iv}\gamma_1 + \epsilon_{iv}]$$

Where:

Y_{iv} = Outcome measurement for subject *i* at v^{th} follow-up exam

X_{i0} = time-invariant cross-sectional confounders and risk factors at Exam 1 for subject *i*, including mean air pollution exposure during the year of baseline.

W_{iv} = possibly time-varying longitudinal confounders and risk factors at exam *v* for subject *i*, including mean air pollution exposure during the time period between baseline (v = 0) and v^{th} follow-up exam, rounded to the nearest whole year as well as air pollution exposure for the years at baseline exam

U_{iv} = time-varying variables to adjust measurements at exam *v* for subject *i*, primarily CT scanner in the percent emphysema analyses

t_{iv} = time in years from baseline (v = 0) to the v^{th} follow-up exam for subject i

β_0 = Outcome progression (annual rate of change) in average participants in the reference group

β_1 = coefficients for interaction between risk factors and time; this includes the air pollution exposure by time interaction which is interpreted as a rate (association between air pollution and annual progression) and the primary parameter of interest in this study

α_0 = average percent emphysema or lung function measurements at baseline for participants in the reference group

α_1 = coefficients for cross-sectional associations between baseline outcome measurements and risk factors (including baseline air pollution exposure)

γ_1 = coefficients for cross-sectional associations between time-varying variables and outcome measurements at all exams

a_i = subject-specific random intercept, which is nested within a neighborhood-specific intercept (in a sensitivity analysis)

b_i = subject-specific random slope

ε_{iv} = error associated with Y_{iv}

The α_1 characterizes the cross-sectional association between air pollution levels preceding the baseline exam and baseline outcomes. The longitudinal terms model an overall progression rate (β_0), interpreted as the rate of change in outcome for a subject with no additional risk factors (i.e. all terms W_i=0), and incorporate terms which adjust that rate (β_1) according to the association between progression rate and risk factors. β_1 which shows the longitudinal effect of air pollution is the main interest of this study.

eTable 1 Unadjusted annual percent emphysema progression and lung function decline by quartile of O_3 exposure concentrations in the MESA cohort

	N of participants	Quartile of long-term O_3 concentration			
		Q1	Q2	Q3	Q4
Percent emphysema progression/year					
Winston-Salem, NC	1037	0.02 (0.28)	0.04 (0.23)	0.09 (0.31)	0.14 (0.35)
New York, NY	1182	0.07 (0.45)	0.10 (0.32)	0.05 (0.52)	0.09 (0.59)
Baltimore, MD	1054	0.09 (0.48)	0.07 (0.34)	0.09 (0.44)	0.11 (0.40)
St. Paul, MN	1021	0.02 (0.15)	0.07 (0.22)	0.06 (0.29)	0.09 (0.26)
Chicago, IL	1142	0.12 (0.45)	0.07 (0.57)	0.12 (0.66)	0.09 (0.47)
Los Angeles, CA	1424	0.00 (0.61)	0.02 (0.47)	0.01 (0.36)	0.03 (0.41)
All regions[a]	6860	0.05 (0.41)	0.06 (0.46)	0.08 (0.53)	0.09 (0.45)
FEV_1 (ml/year)					
Winston-Salem, NC	498	-18.7 (38.8)	-27.2 (37.2)	-25.2 (38.2)	-30.5 (31.6)
New York, NY	761	-28.2 (24.1)	-29.0 (32.0)	-30.4 (27.5)	-41.3 (38.8)
Baltimore, MD	435	-29.4 (40.7)	-36.0 (35.8)	-36.9 (41.1)	-34.0 (38.0)
St. Paul, MN	507	-36.4 (28.7)	-40.8 (28.3)	-42.6 (35.4)	-29.2 (29.8)
Chicago, IL	666	-22.4 (23.4)	-20.7 (35.8)	-28.9 (29.8)	-30.9 (29.4)
Los Angeles, CA	769	-33.2 (32.9)	-35.6 (26.6)	-38.6 (31.6)	-37.8 (50.6)
All regions[a]	3636	-28.3 (34.5)	-31.3 (35).0	-32.6 (34.1)	-33.9 (33.2)
FVC (ml/year)					
Winston-Salem, NC	498	-19.3 (52.9)	-19.3 (51.2)	-32.2 (46.1)	-29.9 (45.6)
New York, NY	761	-28.6 (31.3)	-33.7 (40.3)	-33.0 (32.0)	-63.9 (70.7)
Baltimore, MD	435	-37.8 (55.1)	-38.6 (50.0)	-28.4 (62.3)	-31.6 (61.8)
St. Paul, MN	507	-44.0 (43.0)	-47.2 (42.5)	-49.1 (45.8)	-43.3 (36.9)
Chicago, IL	666	-19.3 (32.8)	-20.5 (40.3)	-27.8 (49.2)	-25.8 (42.9)
Los Angeles, CA	769	-34.8 (37.8)	-33.3 (42.6)	-35.8 (41.3)	-38.4 (32.1)
All regions[a]	3636	-30.5 (41.7)	-33.6 (43.4)	-34.1 (47.9)	-39.1 (52.2)

[a]O_3 exposure concentrations were centralized to city means.

eTable 2 Descriptive characteristics [mean (SD) or %] of study participants at baseline in 2004-2007 and unadjusted longitudinal outcomes by study areas in the analysis of lung function.

Site	Winston-Salem, NC	New York, NY	Baltimore, MD	St. Paul, MN	Chicago, IL	Los Angeles, CA
N Participants						
Baseline (n=3636)	498	761	435	507	666	769
Follow-up (n=2772)	367	571	318	423	551	542
Baseline age	59.8(10.7)	62.6(10.3)	64.8(9.5)	60.2(9.5)	63.8(9.6)	66.6(9.0)
Female (%)	257 (51.6)	413 (54.3)	211 (48.5)	244 (48.1)	345 (51.8)	382 (49.7)
Race (%)						
White	270 (54.2)	160 (21.0)	211 (48.5)	291 (57.3)	297 (44.5)	65 (8.4)
Chinese	0 (0)	0 (0)	0 (0)	0 (0)	230 (34.6)	359 (46.8)
Black	228 (45.8)	244 (32.1)	224 (51.5)	0 (0)	139 (20.9)	84 (10.9)
Hispanic	0 (0)	357 (46.9)	0 (0)	216 (42.7)	0 (0)	261 (33.9)
Education (%)						
≤ High school	135 (27.2)	336 (44.2)	107 (24.5)	199 (39.2)	99 (14.9)	375 (48.7)
≥Some college	363 (72.8)	425 (55.8)	328 (75.5)	308 (60.8)	567 (85.1)	394 (51.3)
Smoking status (%)						
Never	202 (40.5)	350 (46.0)	180 (41.3)	191 (37.6)	335 (50.4)	453 (58.8)
Former	244 (49.0)	329 (43.2)	215 (49.6)	249 (49.2)	279 (41.9)	267 (34.7)
Current	52 (10.5)	82 (10.8)	40 (9.1)	67 (13.3)	52 (7.8)	49 (6.4)
Pack-years of smoking in ever-smokers, median (q1, q3)	18 (4, 38)	14 (3, 32)	18 (5, 35)	13 (4, 30)	17 (4, 39)	10 (2, 27)
Second hand smoking (%)[a]	307 (61.7)	324 (42.6)	210 (48.2)	312 (61.5)	326 (48.9)	222 (28.9)
Gas exposure (%)	126 (25.3)	145 (19.0)	101 (23.2)	159 (31.4)	73 (11.0)	78 (10.2)
Fume exposure (%)	174 (34.9)	186 (24.4)	148 (34.1)	183 (36.1)	71 (10.7)	92 (11.9)
Current employment at baseline (%)	341 (68.5)	435 (57.2)	274 (63.1)	375 (73.9)	458 (68.8)	384 (49.9)
BMI<30kg/m^2(%)	299 (60.1)	511 (67.1)	261 (60.0)	294 (57.9)	547 (82.2)	593 (77.1)
Air pollution at baseline[b]						
O_3 (ppb)	26.3(2.5)	15.7(2.6)	22.9(1.9)	22.3(1.6)	22.3(2.1)	19.8(2.5)
$PM_{2.5}$ (μg/m^3)	14.2(0.4)	14.6(2.2)	14.6(1)	9.8(0.9)	14.3(1.3)	16.9(1.4)
NOx (ppb)	15.2(5.4)	64.1(20.4)	30.1(10.1)	21.8(5.3)	34.6(7.3)	54.3(13.8)
Black carbon (μg/m^3)	0.5(0.1)	1.2(0.3)	0.7(0.2)	0.4(0.1)	0.6(0.1)	1.2(0.1)
Air pollution over follow-up[c]						
O_3 (ppb)	27.3(2.3)	17.8(2.6)	24.7(1.8)	22.7(1.4)	23.4(1.8)	20.4(2.7)
$PM_{2.5}$ (μg/m^3)	11.5(1.1)	12.5(2)	11.2(1.1)	9.4(0.6)	12.2(1.1)	13.7(1.6)
NOx (ppb)	10.9(3.8)	50.0(17.2)	21.3(7.4)	17.1(3.9)	26.3(6.3)	42.4(11)

FEV_1 (mL)						
Baseline	2463.2 (675.9)	2413.9 (742.3)	2435.2 (672.8)	2731.9 (745.3)	2430.8 (736.7)	2424.3 (724.9)
Change/year	-25.3(36.9)	-32.3(31.5)	-34.1(38.9)	-37.2(31)	-26(30.2)	-36.1(36.9)
FVC (mL)						
Baseline	3306.2 (895.8)	3229.1 (994.7)	3267.7 (939.4)	3660.9 (969.8)	3247.9 (963.3)	3179.9 (918.2)
Change/year	-24.4(49.6)	-40(48.8)	-34.6(57.4)	-45.9(42)	-23.6(41.9)	-35.3(38.3)
FEV_1/FVC (%)						
Baseline	74.7 (7.7)	75.2 (8.0)	75.4 (9.5)	74.8 (7.7)	76.5 (7.7)	76.5 (7.7)
Change/year	-0.2(0.8)	-0.1(0.7)	-0.3(1.4)	-0.1(0.7)	-0.3(0.7)	-0.3(1.1)

[a]Second hand smoking was determined as participants including never and ever smokers, who contacted other people smoking at home, in car or work in the past year.
[b]Baseline exposures were assessed as pollutant concentration for the year of the baseline exam in 2004-07 or for the years of 2006-08 (for black carbon).
[c]Exposure over follow-up was the mean exposures for each participant aggregated from the year of the baseline exam to that of the follow-up clinic exam within the years from 2004 to 2018.

eTable 3 Pearson correlation coefficients between predicted air pollution exposures at the MESA participants' homes within the MESA cities (N=6860)

	O_3	$PM_{2.5}$	NO_x	Black carbon[a]
Exposure at baseline				
O_3	1	-0.36	-0.42	-0.29
$PM_{2.5}$	-0.36	1	0.62	0.43
NO_x	-0.42	0.62	1	0.61
Black carbon	-0.29	0.43	0.61	1
Exposure over follow-up				
O_3	1	-0.32	-0.42	-
$PM_{2.5}$	-0.32	1	0.69	-
NO_x	-0.42	0.69	1	-
Exposure at baseline vs over follow-up	0.78	0.53	0.82	-

[a]Average concentration between 2006-08.

eTable 4 Main and sensitivity analyses of effect estimates (95% CIs) of air pollution concentrations, assessed at baseline in 2000, with longitudinal changes of percent emphysema on CT, per 10 years from staged models.

Model	Description	Number of participants	O_3 (3 ppb)	$PM_{2.5}$ (2 μg/m^3)	NO_x (10 ppb)	Black carbon (0.2 μg/m^3)[a]
	Main analysis					
1	Base	6860	0.12 (0.02, 0.23)	0.13 (0.05, 0.21)	0.08 (0.03, 0.14)	0.12 (0.03, 0.21)
2	Primary	6860	0.13 (0.03, 0.24)	0.11 (0.03, 0.19)	0.06 (0.01, 0.12)	0.10 (0.01, 0.18)
3	Extended	6860	0.14 (0.03, 0.24)	0.11 (0.03, 0.18)	0.05 (0.00, 0.10)	0.07 (-0.02, 0.15)
	Sensitivity analysis					
4	Adjust for all the other pollutants	6860	0.23 (0.10, 0.36)	0.08 (0.01, 0.15)	0.05 (-0.04, 0.13)	0.05 (-0.07, 0.17)
5	Log-transformed outcome[b]	6860	4.27 (0.58, 8.08)	2.67 (0.06, 5.34)	2.48 (0.63, 4.37)	2.13 (0.00, 4.26)
6	Exclude low volume CT scan[c]	5759	0.13 (0.02, 0.23)	0.09 (0.01, 0.17)	0.06 (0.01, 0.12)	0.06 (-0.03, 0.15)
7	Include spatial cluster	6860	0.12 (0.01, 0.23)	0.11 (0.03, 0.20)	0.07 (0.01, 0.12)	0.10 (0.01, 0.19)
8	HMMF as outcome[d]	4231	0.12 (0.02, 0.22)	-0.01 (-0.12, 0.11)	0.01 (-0.07, 0.09)	0.11 (-0.02, 0.23)
9	PD15 as outcome[e]	6861	-0.64 (-1.27, -0.01)	-0.29 (-0.57, -0.01)	-0.10 (-0.44, 0.23)	-0.23 (-0.78, 0.32)
10	Exclude single exam subjects	5780	0.14 (0.03, 0.25)	0.10 (0.02, 0.18)	0.06 (0.00, 0.11)	0.09 (0.00, 0.18)
11	Subjects with lung function	3636	0.15 (0.03, 0.28)	0.13 (0.04, 0.22)	0.08 (0.01, 0.14)	0.09 (-0.01, 0.19)

Model 1 adjusted for baseline age, gender, race, study region and air pollutant and time-varying height, weight, CT scanners, pixel size, milliamperes (mAs);
Model 2 (primary model)= Model 1 + physical activity, income, employment status, NSES index, and NSES*study region, time varying smoking status, second hand smoking, pack years, cigarettes per day, BMI, education, temperature;
Model 3 = Model 2 + high-attenuation areas on CT;
Model 4 = Model 2 + all the other pollutants (i.e. O_3, NOx, $PM_{2.5}$, Black carbon);
Model 5 = Same as Model 2;
Model 6 = Same as Model 2 without low lung volume CT-scans;
Model 7 = Same as Model 2 with additional random effect accounting for census tract;
Model 8-9 = Same as Model 2 with different outcomes;
Model 10 = Same as Model 2 without subjects with single examination;
Model 11 = Same as Model 2 with subset present in both cohorts;
[a]Average concentration between 2006-08.
[b]Log-transformed percent emphysema (-950HU). Results interpret as percent increase in percent emphysema over ten years.
[c]Exclude low volume CT scan: we excluded scans with inspiratory levels less than 80% of the subject's maximum lung volume on scans.
[d]a novel approach to the measurement of percent emphysema uses a hidden modified Markov field (HMMF). For more details please see the method section.
[e]PD15 unit is g/L; A lower PD15 value indicates more emphysema.

eTable 5 Main and sensitivity analyses of effect estimates (95% CIs) of long-term air pollution concentrations, assessed during follow-up, with longitudinal change of percent emphysema on CT over 10 years from staged models.

Model	Description	Number of participants	O_3 (3 ppb)	$PM_{2.5}$ (2 μg/m^3)	NOx (10 ppb)
	Main analysis				
1	Base	6860	0.19 (0.09, 0.29)	0.02 (-0.10, 0.14)	0.14 (0.07, 0.22)
2	Primary	6860	0.18 (0.08, 0.28)	-0.04 (-0.15, 0.08)	0.12 (0.04, 0.19)
3	Extended	6860	0.18 (0.08, 0.28)	-0.04 (-0.16, 0.07)	0.10 (0.03, 0.18)
	Sensitivity analysis				
4	Adjust for all the other pollutants	6860	0.21 (0.10, 0.32)	-0.24 (-0.50, 0.02)	0.29 (0.18, 0.40)
5	Log-transformed outcome[a]	6860	6.83 (3.28, 10.51)	-1.90 (-5.56, 1.91)	11.12 (2.65, 20.27)
6	Exclude low volume CT scan[b]	5759	0.21 (0.10, 0.31)	-0.04 (-0.16, 0.07)	0.12 (0.04, 0.20)
7	Include spatial cluster	6860	0.18 (0.07, 0.28)	-0.05 (-0.17, 0.07)	0.14 (0.06, 0.22)
8	HMMF as outcome[c]	4231	0.15 (0.00, 0.30)	-0.08 (-0.23, 0.08)	-0.01 (-0.11, 0.09)
9	PD15 as outcome[d]	6861	-0.74 (-1.43, -0.05)	0.67 (-0.21, 1.55)	-0.42 (-0.81, -0.03)
10	Exclude single exam subjects	5780	0.19 (0.09, 0.29)	-0.05 (-0.16, 0.07)	0.10 (0.02, 0.18)
11	Subjects with lung function	3636	0.20 (0.09, 0.32)	0.00 (-0.14, 0.13)	0.11 (0.02, 0.20)

Model 1 adjusted for baseline age, gender, race, study region and air pollutant and time-varying height, weight, CT scanners, pixel size, milliamperes (mAs);
Model 2 (primary model) = Model 1 + physical activity, income, employment status, NSES index, and NSES*study region, time varying smoking status, second hand smoking, pack years, cigarettes per day, BMI, education, temperature;
Model 3 = Model 2 + high-attenuation areas on CT;
Model 4 = Model 2 + all the other pollutants (i.e. O_3, NOx, $PM_{2.5}$);
Model 5 = Same as Model 2;
Model 6 = Same as Model 2 without low lung volume CT-scans;
Model 7 = Same as Model 2 with additional random effect accounting for census tract;
Model 8-9 = Same as Model 2 with different outcomes;
Model 10 = Same as Model 2 without subjects with single examination;
Model 11 = Same as Model 2 with subset present in both cohorts;
[a]Log-transformed percent emphysema (-950HU). Results interpret as percent increase in percent emphysema over ten years.
[b]Exclude low volume CT scan: we excluded scans with inspiratory levels less than 80% of the subject's maximum lung volume on scans.
[c]a novel approach to the measurement of percent emphysema uses a hidden modified Markov field (HMMF). For more details please see the method section.
[d]PD15 unit is g/L; A lower PD15 value indicates more emphysema.

eTable 6 Effect estimates (95% CIs) for the associations between air pollutant exposures at baseline or over follow-up and progression of percent emphysema in single-pollutant, multiple-pollutant and linear combination models, per IQR increment for O_3 (3 ppb), $PM_{2.5}$ (2 μg/m^3), NOx (10 ppb) and black carbon (BC; 0.2 μg/m^3).

Health models	Exposure at baseline[a]	Exposure over follow-up[b]
Single-pollutant model[c]		
O_3	0.13 (0.03, 0.24)	0.18 (0.08, 0.28)
$PM_{2.5}$	0.11 (0.03, 0.19)	-0.04 (-0.15, 0.08)
NO_x	0.06 (0.01, 0.12)	0.12 (0.04, 0.19)
BC	0.10 (0.01, 0.18)	
Multiple-pollutant model[d]		
O_3	0.23 (0.10, 0.36)	0.21 (0.10, 0.32)
$PM_{2.5}$	0.08 (0.01, 0.15)	-0.24 (-0.50, 0.02)
NO_x	0.05 (-0.04, 0.13)	0.29 (0.18, 0.4)
BC	0.05 (-0.07, 0.17)	
Linear combination model[e]		
O_3+$PM_{2.5}$+NO_x+BC	0.41 (0.20, 0.62)	
O_3+$PM_{2.5}$+NO_x	0.36 (0.17, 0.55)	0.25 (0.06, 0.44)
O_3+ $PM_{2.5}$+BC	0.36 (0.14, 0.58)	
O_3+ NO_x +BC	0.33 (0.14, 0.52)	
$PM_{2.5}$+ NO_x +BC	0.18 (0.05, 0.30)	
O_3+ $PM_{2.5}$	0.31 (0.13, 0.49)	-0.03 (-0.23, 0.17)
O_3+ NO_x	0.28 (0.11, 0.45)	0.50 (0.32, 0.67)
O_3+BC	0.28 (0.10, 0.47)	
$PM_{2.5}$+ NO_x	0.13 (0.02, 0.23)	0.04 (-0.08, 0.17)
$PM_{2.5}$+BC	0.13 (-0.03, 0.29)	
NO_x +BC	0.10 (-0.01, 0.21)	

[a]Baseline air pollution exposures were calculated in 2000 or for the years of 2006-08 (for black carbon) in 18902 samples

bFollow-up air pollution exposures were aggregated from the year of the baseline exam to that of the follow-up clinic exam from 2000 to 2018 in 18574 samples

[c]Results of single-pollutant model derived from main analyses for the associations between each of the air pollutants and progression of percent emphysema (percentage of lung pixels less than -950 Hounsfield unit).

[d]Multi-pollutant model presented the associations of the fully-adjusted model when all the air pollutants were modelled simultaneously.

[e]Linear combination models were implemented by combining the associations from any pairs of the air pollutants, based on associations from the multi-pollutant model which included all the pollutants simultaneously.

eTable 7 Longitudinal changes in percent emphysema (95% CI) per over ten years per increase of O_3, $PM_{2.5}$, NO_x and black carbon, assessed at baseline between 2000 and 2007, stratified by potential effect modifiers

Effect modification	N	O_3 (3 ppb)	P-value[a]	$PM_{2.5}$ (2 µg/m^3)	P-value[a]	NOx (10 ppb)	P-value[a]	Black carbon (0.2 µg/m^3)[b]	P-value[a]
Gender			<0.01		<0.01		<0.01		<0.01
Male	3224	0.27 (0.16, 0.38)		0.07 (-0.02, 0.15)		-0.02 (-0.08, 0.04)		-0.03 (-0.12, 0.07)	
Female	3636	0.01 (-0.10, 0.13)		0.17 (0.08, 0.25)		0.13 (0.07, 0.18)		0.18 (0.08, 0.27)	
Baseline age			0.31		0.19		0.15		0.50
<65	3859	0.16 (0.05, 0.27)		0.09 (0.00, 0.17)		0.05 (0.00, 0.11)		0.08 (-0.01, 0.17)	
⩾65	3001	0.12 (-0.01, 0.24)		0.13 (0.05, 0.22)		0.09 (0.02, 0.16)		0.11 (0.01, 0.21)	
Race			0.02		0.04		0.00		<0.01
White	2707	0.23 (0.11, 0.35)		0.00 (-0.11, 0.11)		-0.03 (-0.10, 0.04)		-0.08 (-0.19, 0.03)	
Chinese	784	0.14 (-0.11, 0.39)		0.15 (0.04, 0.25)		0.18 (0.07, 0.29)		0.21 (0.00, 0.41)	
Black	1879	0.07 (-0.06, 0.20)		0.19 (0.07, 0.32)		0.10 (0.03, 0.18)		0.15 (0.05, 0.25)	
Hispanic	1490	0.06 (-0.10, 0.21)		0.10 (0.01, 0.20)		0.07 (0.00, 0.13)		0.11 (0.00, 0.22)	
Smoking status			0.01		0.16		0.43		0.76
Never	3113	0.17 (0.05, 0.28)		0.10 (0.02, 0.18)		0.06 (0.00, 0.12)		0.09 (0.00, 0.19)	
Former	2799	0.16 (0.05, 0.28)		0.12 (0.03, 0.21)		0.06 (0.00, 0.12)		0.08 (-0.02, 0.18)	
Current	948	-0.08 (-0.26, 0.09)		0.23 (0.09, 0.37)		0.12 (0.02, 0.22)		0.14 (-0.01, 0.29)	
BMI			0.41		0.08		0.04		0.27
< 30	4621	0.12 (-0.01, 0.25)		0.16 (0.07, 0.25)		0.11 (0.04, 0.17)		0.12 (0.02, 0.23)	
⩾ 30	2239	0.16 (0.05, 0.27)		0.10 (0.01, 0.18)		0.05 (-0.01, 0.10)		0.08 (-0.01, 0.17)	
Airflow obstruction[c]			0.04		0.04		0.03		0.01
No	2818	0.12 (0.00, 0.25)		0.10 (0.01, 0.20)		0.09 (0.02, 0.15)		0.12 (0.02, 0.23)	
Yes	818	0.25 (0.09, 0.41)		0.21 (0.09, 0.33)		0.00 (-0.09, 0.09)		-0.01 (-0.14, 0.11)	
NSES disadvantage[d]			<0.01		0.03		0.01		0.00

Yes	3473	0.08 (-0.04, 0.21)		0.13 (0.05, 0.22)		0.08 (0.02, 0.13)		0.11 (0.02, 0.20)	
No	3387	0.21 (0.10, 0.32)		0.06 (-0.03, 0.14)		0.00 (-0.06, 0.07)		-0.01 (-0.11, 0.09)	
Study regions			0.24		0.53		0.65		0.76
Winston-Salem, NC	1037	0.23 (0.05, 0.42)		0.14 (-0.27, 0.56)		0.05 (-0.23, 0.33)		0.16 (-0.44, 0.76)	
New York, NY	1182	-0.06 (-0.37, 0.25)		0.31 (0.11, 0.51)		0.08 (-0.01, 0.17)		0.12 (0.02, 0.22)	
Baltimore, MD	1054	0.05 (-0.18, 0.27)		0.11 (-0.17, 0.40)		-0.03 (-0.16, 0.11)		-0.05 (-0.26, 0.17)	
St. Paul, MN	1021	0.34 (-0.01, 0.69)		0.05 (-0.19, 0.3)		0.00 (-0.27, 0.26)		0.10 (-0.42, 0.62)	
Chicago, IL	1142	0.21 (-0.05, 0.48)		0.12 (-0.05, 0.29)		0.14 (-0.02, 0.30)		0.21 (-0.17, 0.59)	
Los Angeles, CA	1424	0.01 (-0.21, 0.23)		0.09 (-0.01, 0.19)		0.09 (0.00, 0.18)		0.16 (-0.17, 0.49)	
Scanner manufacturer			0.22		0.15		0.43		0.33
GE	4679	0.12 (-0.07, 0.31)		0.08 (-0.13, 0.30)		0.05 (-0.01, 0.11)		0.08 (-0.02, 0.18)	
Siemens	2181	0.07 (-0.05, 0.20)		0.17 (-0.02, 0.37)		0.08 (0.00, 0.17)		0.11 (-0.01, 0.24)	

All models adjust for age, gender, race, baseline O_3 or $PM_{2.5}$, physical activity, income, employment status, education, SES index, study region and SES*study region, height, weight, temperature, smoking status, second hand smoking, pack years, cigarettes per day, BMI, interactions of these variables with time, CT scanners, pixel size;

[a]P-value for the F-test of the three-way interaction between air pollutant, follow-up time, and stratification variable;

[b]Average concentration between 2006-08.

[c]Presence of airflow obstruction for FEV_1 and FVC is defined as a pre-bronchodilator FEV1/FVC ratio less than 0.7;

[d]Neighborhood Socio-economic Status (NSES) index was constructed by factor analysis of indicators of neighborhood-level SES (wealth, income, education, employment and occupation). It was included as continuous variable (range: -24 to 11) with higher value indicating more socioeconomic disadvantage. A cut-off point at 0 was considered in the analysis of the effect modification.

eTable 8 Longitudinal changes in percent emphysema (95% CI) over ten years per increase of long-term O_3, $PM_{2.5}$ and NO_x concentration, assessed during following, stratified by potential effect modifiers

Effect modification	N	O_3 (3 ppb)	P-value[a]	$PM_{2.5}$ (2 µg/m^3)	P-value[a]	NOx (10 ppb)	P-value[a]
Gender			<0.01		<0.01		<0.01
Male	3224	0.31 (0.20, 0.43)		-0.15 (-0.28, -0.02)		0.00 (-0.09, 0.09)	
Female	3636	0.06 (-0.05, 0.17)		0.06 (-0.07, 0.19)		0.21 (0.12, 0.29)	
Baseline age			0.85		0.14		0.52
<65	3859	0.18 (0.07, 0.29)		-0.07 (-0.19, 0.05)		0.11 (0.03, 0.19)	
≥65	3001	0.19 (0.06, 0.32)		0.02 (-0.12, 0.17)		0.13 (0.04, 0.23)	
Race			0.05		0.63		0.06
White	2707	0.27 (0.15, 0.39)		-0.06 (-0.21, 0.10)		0.04 (-0.06, 0.14)	
Chinese	784	0.21 (-0.06, 0.47)		-0.09 (-0.27, 0.09)		0.19 (0.02, 0.35)	
Black	1879	0.10 (-0.04, 0.24)		0.05 (-0.14, 0.23)		0.18 (0.07, 0.28)	
Hispanic	1490	0.06 (-0.11, 0.23)		-0.02 (-0.17, 0.13)		0.11 (0.02, 0.21)	
Smoking status			0.22		0.66		0.82
Never	3113	0.16 (0.04, 0.28)		-0.03 (-0.16, 0.09)		0.11 (0.02, 0.19)	
Former	2799	0.22 (0.10, 0.33)		-0.05 (-0.19, 0.08)		0.12 (0.03, 0.21)	
Current	948	0.03 (-0.19, 0.26)		0.04 (-0.18, 0.26)		0.15 (0.01, 0.30)	
BMI			0.10		0.45		0.71
< 30	4621	0.22 (0.11, 0.33)		-0.02 (-0.15, 0.10)		0.12 (0.03, 0.20)	
≥ 30	2239	0.12 (0.00, 0.25)		-0.07 (-0.22, 0.07)		0.10 (0.01, 0.19)	
Airflow obstruction[b]			0.01		0.07		0.24
No	2818	0.15 (0.03, 0.27)		-0.04 (-0.18, 0.09)		0.12 (0.03, 0.21)	
Yes	818	0.35 (0.18, 0.51)		0.12 (-0.07, 0.31)		0.06 (-0.07, 0.18)	
NSES disadvantage[c]			0.03		0.74		0.22
Yes	3473	0.12 (-0.01, 0.24)		-0.05 (-0.18, 0.08)		0.12 (0.04, 0.21)	
No	3387	0.25 (0.14, 0.36)		-0.07 (-0.20, 0.06)		0.07 (-0.02, 0.17)	
Study regions			0.08		0.05		0.04
Winston-Salem, NC	1037	0.33 (0.08, 0.58)		-1.15 (-2.29, -0.01)		-0.41 (-0.85, 0.03)	
New York, NY	1182	0.20 (-0.06, 0.46)		-0.01 (-0.22, 0.21)		0.08 (-0.03, 0.19)	
Baltimore, MD	1054	0.11 (-0.10, 0.31)		0.35 (0.07, 0.63)		0.12 (-0.07, 0.31)	
St. Paul, MN	1021	0.42 (0.06, 0.78)		-0.75 (-1.46, -0.04)		-0.20 (-0.60, 0.20)	
Chicago, IL	1142	-0.12 (-0.37, 0.12)		0.82 (0.57, 1.07)		0.71 (0.50, 0.91)	
Los Angeles, CA	1424	0.19 (-0.02, 0.40)		-0.27 (-0.56, 0.03)		0.01 (-0.12, 0.15)	
Scanner manufacturer			0.63		0.15		0.09
GE	4679	0.12 (0.03, 0.21)		0.04 (-0.17, 0.26)		0.05 (-0.07, 0.17)	

Siemens	2181	0.11 (-0.02, 0.23)		0.09 (-0.09, 0.28)		0.13 (0.01, 0.26)	

All models adjust for age, gender, race, baseline O_3 or $PM_{2.5}$, physical activity, income, employment status, education, SES index, study region and SES*study region, height, weight, temperature, smoking status, second hand smoking, pack years, cigarettes per day, BMI, interactions of these variables with time, CT scanners, pixel size;

[a]P-value for the F-test of the three-way interaction between air pollutant, follow-up time, and stratification variable;

[b]Presence of airflow obstruction for FEV_1 and FVC is defined as a pre-bronchodilator FEV1/FVC ratio less than 0.7;

[c]Neighborhood Socio-Economic Status (NSES) index was constructed by factor analysis of indicators of neighborhood-level SES (wealth, income, education, employment and occupation). It was included as continuous variable (range: -24 to 11) with higher value indicating more socioeconomic disadvantage. A cut-off point at 0 was considered in the analysis of the effect modification.

eTable 9 Multiplicative interactions between air pollutant exposures for effect of air pollution on progression of percent emphysema over ten years (N=6860)

Multiplicative Interaction[a]	Exposure at baseline	P-value	Exposure over follow-up	P-value
O_3* $PM_{2.5}$	0.00 (-0.04, 0.05)	0.86	-0.02 (-0.08, 0.04)	0.52
O_3* NOx	-0.01 (-0.04, 0.02)	0.43	0.02 (-0.02, 0.05)	0.37
O_3*Black carbon	-0.04 (-0.10, 0.02)	0.16	-	-
$PM_{2.5}$*NO_x	0.01 (-0.01, 0.03)	0.32	-0.03 (-0.06, 0.01)	0.10
$PM_{2.5}$*Black carbon	0.03 (-0.01, 0.08)	0.17	-	-
NO_x*Black carbon	0.02 (0.00, 0.04)	0.05	-	-

[a]changes over ten years per 3 ppb increase of O_3, 2 µg/m^3 of $PM_{2.5}$, 10ppb of NO_x and 0.2 µg/m^3 of black carbon. Black carbon: average concentration between 2006-08.

eTable 10 Main and sensitivity analyses of effect estimates (95% CIs) of long-term air pollution concentrations, assessed during following with longitudinal changes of lung function over 10 years from staged models

Model	Description	N	O_3 (3 ppb)	$PM_{2.5}$ (2 μg/m^3)	NOx (10 ppb)
FEV_1 (ml)					
1	Base	3636	-17.04 (-32.96, -1.12)	11.22 (-5.5, 27.94)	1.84 (-10.08, 13.75)
2	Primary	3636	-18.15 (-34.71, -1.59)	12.82 (-4.98, 30.63)	2.88 (-10.08, 15.84)
3	Extended	3631	-17.53 (-34.11, -0.95)	12.31 (-5.47, 30.10)	3.27 (-9.69, 16.22)
4	Multi -pollutant	3636	-15.95 (-31.29, -0.60)	18.66 (-6.64, 43.95)	-7.46 (-26.12, 11.20)
FVC (ml)					
1	Base	3636	-37.38 (-58.94, -15.81)	10.36 (-11.94, 32.66)	-0.29 (-16.2, 15.63)
2	Primary	3636	-40.19 (-62.49, -17.88)	17.80 (-5.95, 41.56)	3.46 (-13.87, 20.79)
3	Extended	3631	-37.86 (-60.20, -15.51)	17.61 (-6.18, 41.39)	3.51 (-13.85, 20.87)
4	Multi -pollutant	3636	-31.44 (-57.86, -5.02)	25.42 (-3.78, 54.62)	-16.94 (-35.26, 1.37)
FEV_1/FVC (%)					
1	Base	3636	0.27 (-0.27, 0.82)	0.11 (-0.26, 0.49)	0.09 (-0.20, 0.36)
2	Primary	3636	0.31 (-0.27, 0.88)	0.03 (-0.38, 0.44)	0.06 (-0.20, 0.36)
3	Extended	3631	0.29 (-0.27, 0.86)	0.02 (-0.38, 0.43)	0.07 (-0.20, 0.37)
4	Multi -pollutant	3636	0.27 (-0.42, 0.94)	-0.22 (-0.80, 0.35)	0.11 (-0.30, 0.54)

Model 1 adjusted for baseline age, gender, race, study region and air pollutant and tine-varying height and weight
Model 2 = Model 1 +, physical activity, income, employment status, occupational exposure to gases and fume, SES index, SES*study region, time-varying smoking status, pack years, cigarettes per day, second hand smoking, education, BMI, temperature;
Model 3 = Model 2 + emphysema, cold, flu, or sore throat in past two weeks, bronchitis in past two weeks, asthma before the age of 45, and pneumonia in past two weeks;
Model 4 = Model 2 + all the other pollutants (i.e. O_3, NOx, $PM_{2.5}$,);

eTable 11 Longitudinal changes in lung function (95% CI) per 3 ppb increase of O_3 assessed during following over 10 years stratified by personal factors

Effect modification[a]	N	FEV_1 (ml)	P-value[b]	FVC (ml)	P-value[b]
Gender			0.42		0.43
Male	1843	-15.03 (-33.51, 3.45)		-36.02 (-60.90, -11.14)	
Female	1796	-21.48 (-40.13, -2.83)		-44.62 (-69.74, -19.49)	
Baseline Age			0.15		0.37
<65	1735	-13.04 (-31.22, 5.13)		-35.75 (-60.22, -11.28)	
≥65	1901	-24.71 (-43.68, -5.74)		-45.50 (-71.03, -19.97)	
Race			0.99		0.94
White	1321	-17.91 (-40.04, 4.22)		-34.73 (-64.64, -4.81)	
Chinese	583	-13.74 (-50.17, 22.69)		-40.54 (-89.02, 7.93)	
Black	923	-19.87 (-42.29, 2.55)		-43.16 (-73.40, -12.92)	
Hispanic	809	-19.53 (-46.71, 7.65)		-44.57 (-81.06, -8.07)	
Smoking status			<0.01		0.02
Never	1695	-12.36 (-31.17, 6.46)		-33.57 (-58.87, -8.28)	
Former	1597	-18.89 (-37.38, -0.39)		-40.55 (-65.47, -15.64)	
Current	342	-66.16 (-102.28, -30.03)		-101.45 (-149.81, -53.09)	
BMI			0.99		0.73
< 30	2509	-16.85 (-33.10, -0.60)		-39.63 (-63.01, -16.26)	
≥ 30	1127	-16.96 (-37.38, 3.47)		-35.67 (-63.22, -8.13)	
Airflow obstruction[c]			0.05		0.30
No	2810	-13.22 (-30.49, 4.05)		-35.24 (-58.41, -12.06)	
Yes	826	-27.06 (-49.44, -4.68)		-48.73 (-78.72, -18.74)	
NSES advantage[d]			0.54		0.20
No	1844	-18.40 (-35.15, -1.65)		-40.93 (-63.48, -18.38)	
Yes	1792	-16.81 (-34.07, 0.46)		-36.47 (-59.72, -13.23)	
Study regions			0.93		0.11
Winston-Salem, NC	498	-22.51 (-60.91, 15.9)		-25.07 (-77.16, 27.02)	
New York, NY	761	-28.72 (-56.74, -0.69)		-81.13 (-119.82, -42.44)	
Baltimore, MD	435	-4.60 (-70.59, 61.39)		-28.69 (-117.74, 60.35)	
St. Paul, MN	507	-6.87 (-74.99, 61.25)		-13.09 (-104.61, 78.42)	
Chicago, IL	666	-1.45 (-54.88, 51.98)		30.29 (-40.79, 101.36)	
Los Angeles, CA	769	-14.47 (-48.07, 19.12)		-35.40 (-80.40, 9.61)	

All models adjust for baseline age, gender, race, baseline O_3, physical activity, income, employ status, occupational exposure, BMI, SES index, study region, SES*study region, height, weight, temperature, smoking status, pack years, cigarettes per day, second hand smoking, education, and interactions of these variables with time;

[b]P-value for the F-test of the three-way interaction between O_3, follow up time, and stratification variable;

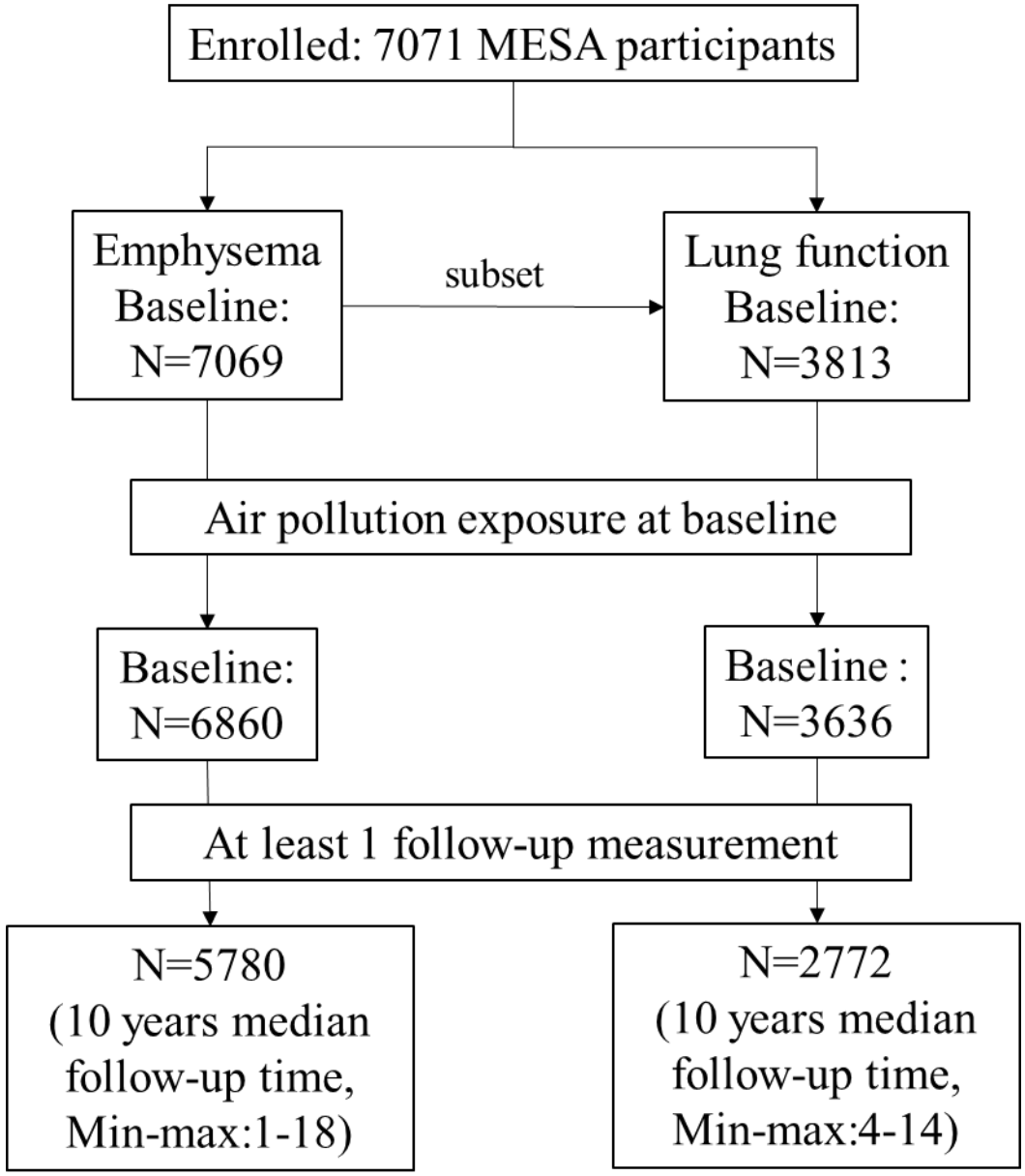
[c]Presence of airflow obstruction for FEV_1 and FVC is defined as a pre-bronchodilator FEV1/FVC ratio less than 0.7;

[d]Neighborhood Socio-Economic Status (NSES) index was constructed by factor analysis of indicators of neighborhood-level SES (wealth, income, education, employment and occupation). It was included as continuous variable (range: -11 to 24) with lower value indicating more socioeconomic disadvantage. A cut-off point at 0 was considered in the analysis of the effect modification.

eTable 12 Main and sensitivity analyses of effect estimates (95% CIs) of exposure to air pollution concentrations assessed at baseline in 2000 with longitudinal changes of lung function over 10 years from staged models

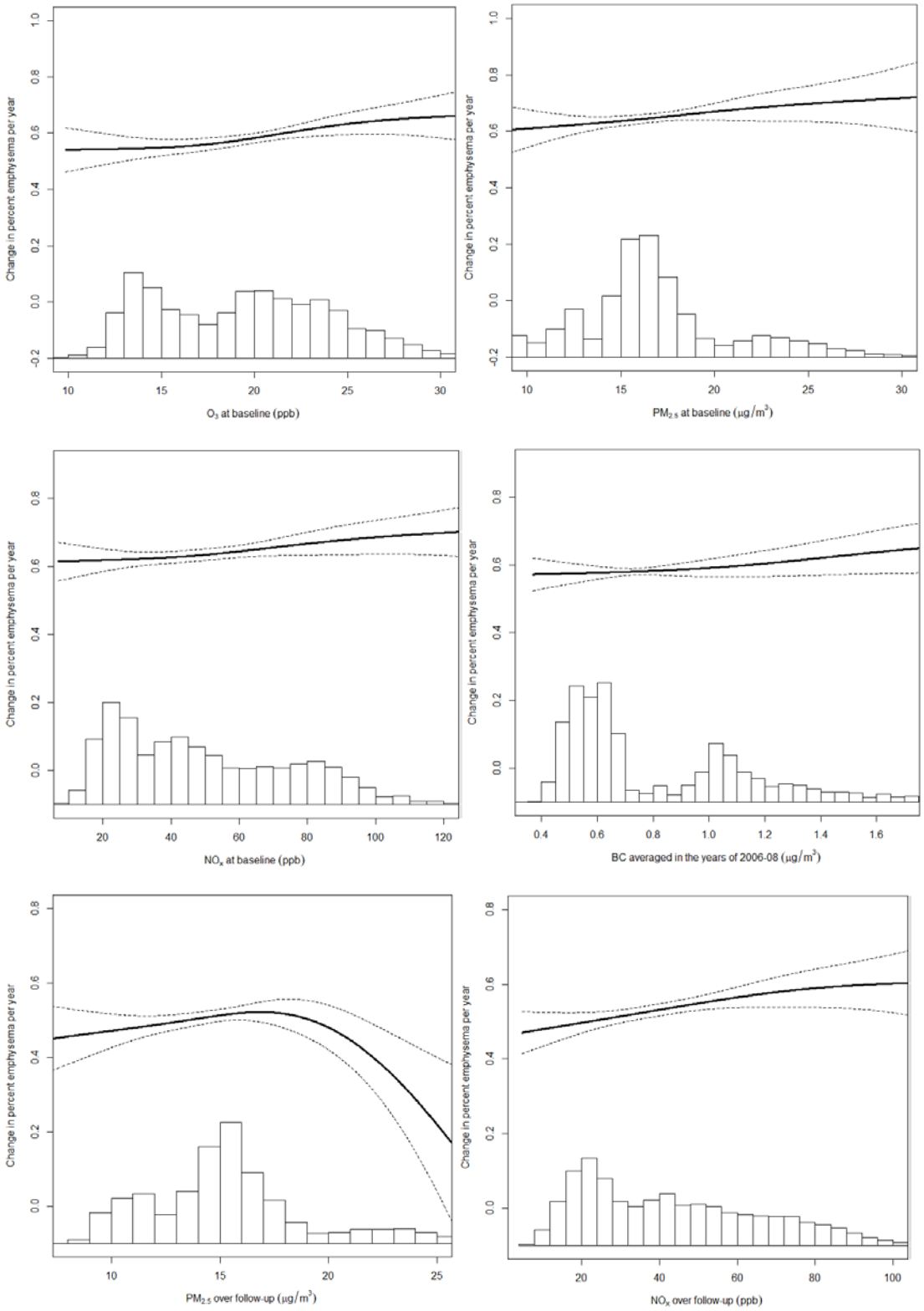
Model	Description	N	O_3 (3 ppb)	$PM_{2.5}$ (2 μg/m^3)	NOx (10 ppb)	Black carbon (0.2 μg/m^3)[a]
FEV_1 (ml)						
1	Base	3636	-15.31 (-30.13, -0.50)	-2.19 (-17.03, 12.66)	-7.87 (-15.68, -0.07)	-2.08 (-15.71, 11.54)
2	Primary	3636	-13.41 (-26.11, -0.71)	4.91 (-11.03, 20.84)	-8.15 (-17.33, 1.03)	-2.79 (-17.34, 11.77)
3	Extended	3631	-12.55 (-24.65, -0.45)	5.03 (-10.90, 20.96)	-7.92 (-17.09, 1.26)	-2.80 (-17.34, 11.75)
4	Multi -pollutant	3636	-18.64 (-36.38, -0.91)	9.92 (-15.77, 35.62)	-13.66 (-32.58, 5.26)	1.83 (-18.60, 22.27)
FVC (ml)						
1	Base	3636	-27.19 (-48.18, -6.20)	-1.16 (-21.11, 18.79)	-7.04 (-17.56, 3.47)	0.22 (-18.14, 18.59)
2	Primary	3636	-28.09 (-49.46, -6.72)	6.02 (-15.44, 27.47)	-5.74 (-18.13, 6.66)	-1.13 (-20.79, 18.52)
3	Extended	3631	-26.56 (-47.94, -5.18)	6.94 (-14.52, 28.41)	-5.55 (-17.94, 6.85)	-1.20 (-20.85, 18.45)
4	Multi -pollutant	3636	-24.09 (-47.43, -0.76)	12.12 (-22.93, 47.17)	-10.72 (-36.52, 15.08)	-0.87 (-28.55, 26.80)
FEV_1/FVC (%)						
1	Base	3636	0.27 (-0.27, 0.82)	0.04 (-0.30, 0.38)	-0.06 (-0.20, 0.12)	-0.04 (-0.35, 0.27)
2	Primary	3636	0.31 (-0.27, 0.88)	0.12 (-0.24, 0.49)	-0.08 (-0.30, 0.13)	-0.04 (-0.37, 0.30)
3	Extended	3631	0.29 (-0.27, 0.86)	0.10 (-0.26, 0.46)	-0.08 (-0.30, 0.13)	-0.05 (-0.39, 0.28)
4	Multi-pollutant	3636	0.27 (-0.42, 0.94)	0.29 (-0.20, 0.78)	-0.20 (-0.50, 0.11)	0.00 (-0.47, 0.47)

Model1 adjusted for baseline age, gender, race, study region and air pollutant and time-varying height and weight;
Model 2 = Model 1 +, physical activity, income, employment status, occupational exposure to gases and fume, SES index, SES*study region, time-varying smoking status, pack years, cigarettes per day, second hand smoking, education, BMI, temperature;
Model 3 = Model 2 + emphysema, cold, flu, or sore throat in past two weeks, bronchitis in past two weeks, asthma before the age of 45, pneumonia in past two weeks;
Model 4 = Model 2 + all the other pollutants (i.e. O_3, NOx, $PM_{2.5}$, Black carbon);
[a]Average concentration between 2006-08.

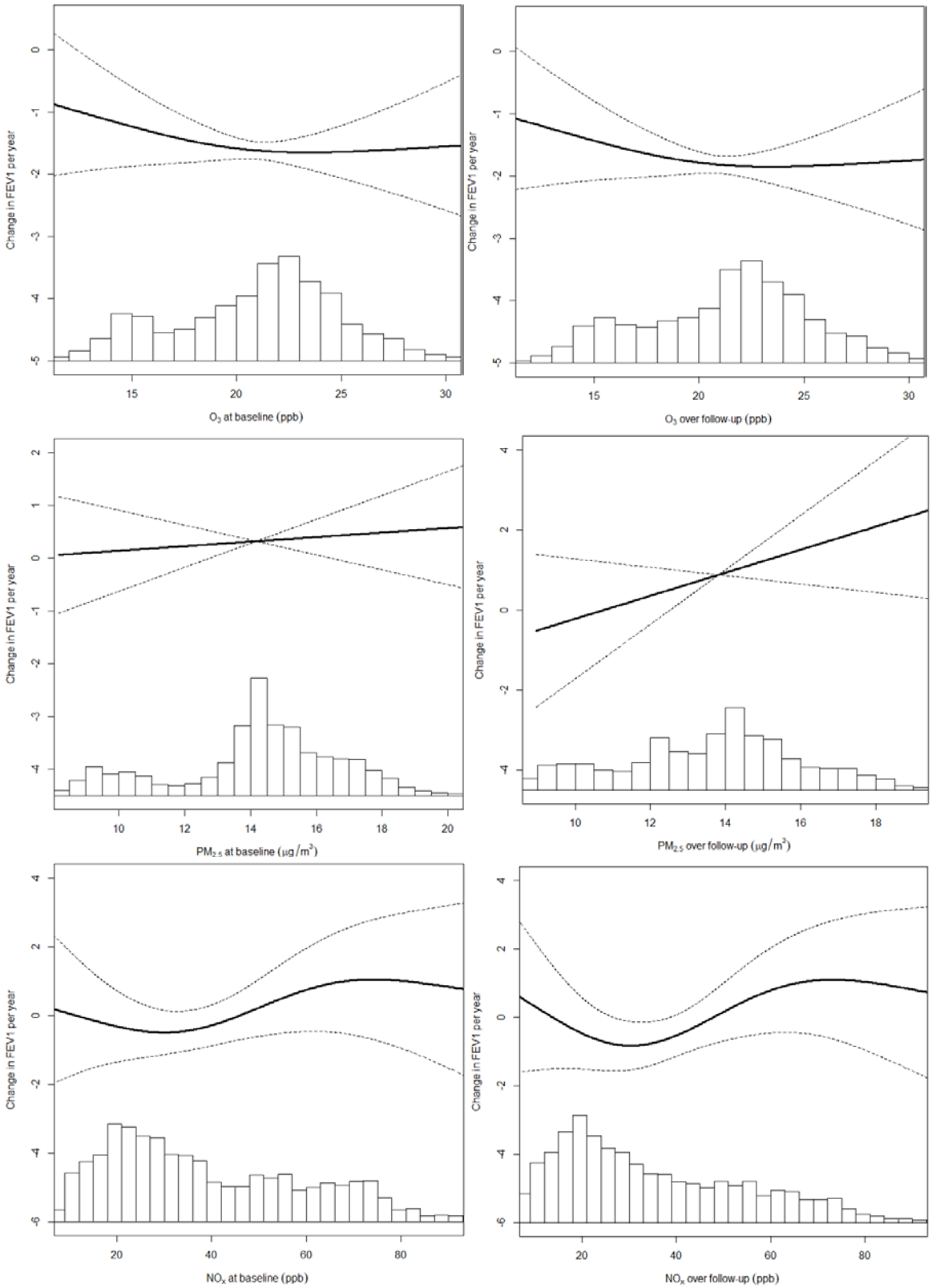


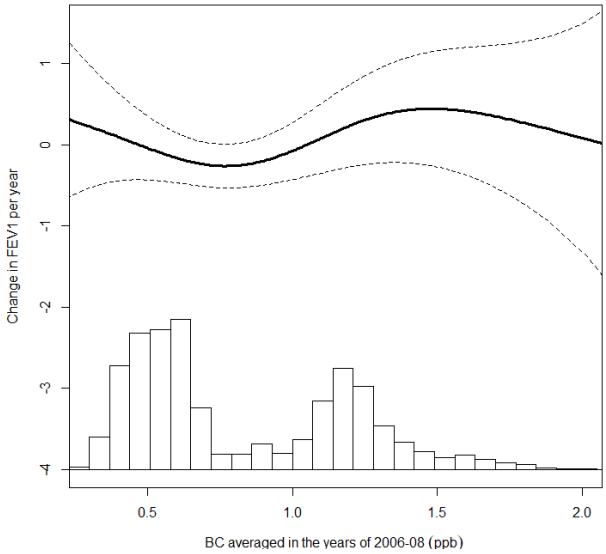
MESA Exam Year	1 (2000-02)	2 (2002-04)	3 (2004-05)	4 (2005-07)	5 (2010-11)	6 (2016-18)
Emphysema	6812	5703		1559	3197	2308
Lung function			3813		2539	1672

eFigure 1 Participant recruitment, retention, and flow of outcome testing in the analysis of percent emphysema and lung function in the Multi-Ethnic Study of Atherosclerosis.

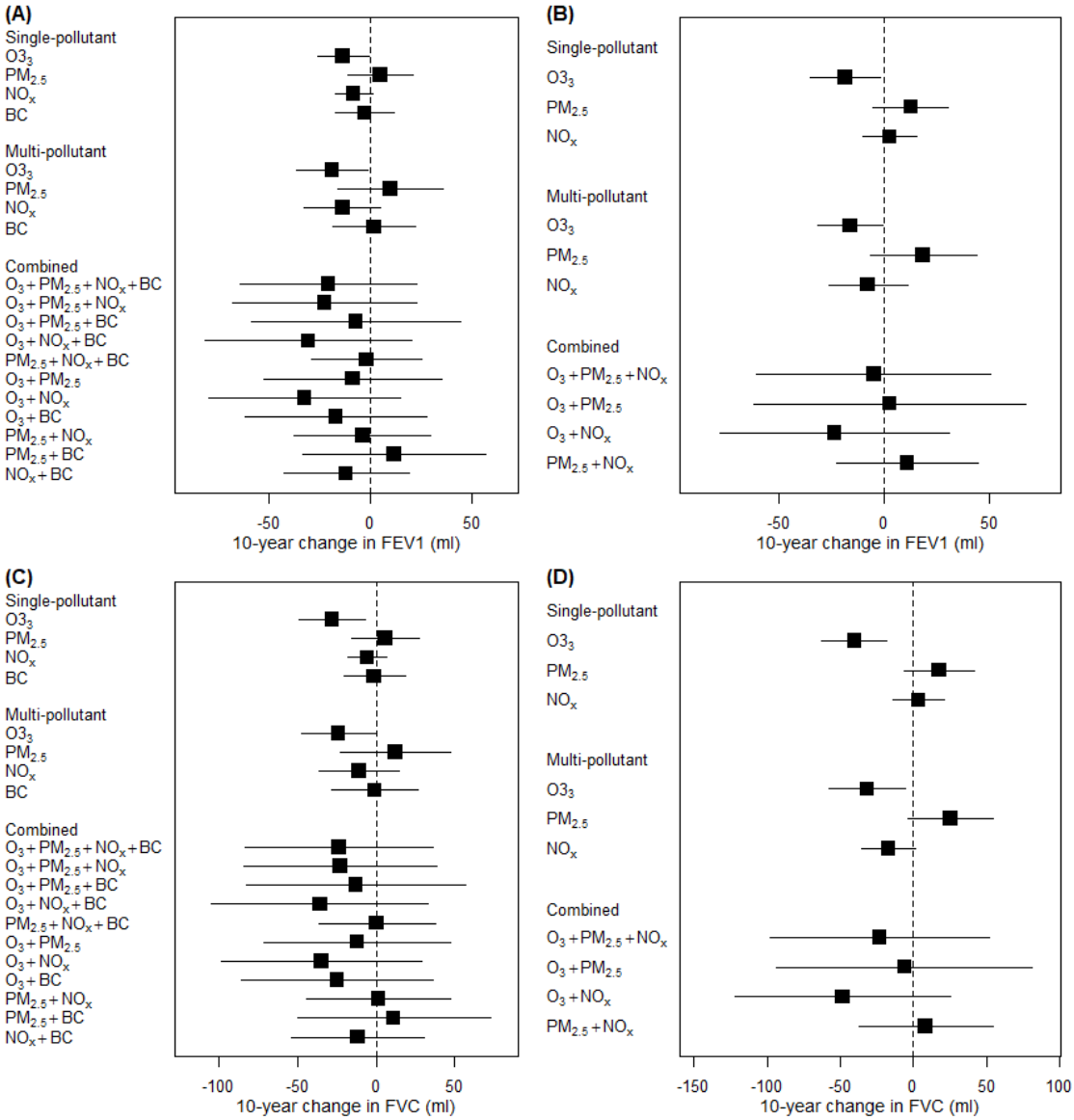


eFigure 2 Concentration-response curves with 95%CI for the overall change of percent emphysema progression rate associated with air pollution concentrations, assessed at baseline in 2000 and over follow-up (N=6860).





eFigure 3 Concentration-response curve with 95%CI for the change of FEV1 associated with air pollution concentrations, assessed at baseline in 2000 and over follow-up (N=3636).



eFigure 4 Effect estimates for the associations between air pollutants and lung function decline (N=3636). Results from single-pollutant model, multiple-pollutant model and linear combination model for the effect estimates of multiple air pollutant exposures (A: at baseline for FEV1, B: over follow-up for FEV1, C: at baseline for FVC, and D: over follow-up for FVC), from multi-pollutant models.