ONLINE DATA SUPPLEMENT

Combined Impact of Smoking and Early Life Exposures on Adult Lung Function Trajectories

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Table E1: Relationship between infant lower respiratory infection, sex, birth weight and other early life exposures among 2172 participants included in adult lung function modelling

A: Prevalence of infant lower respiratory tract infection (0-2 years) according to sex, father's occupational class (at 4 years), home overcrowding (at 2 years) and pollution exposure (0-2 years). B: Mean birth weight according to occurrence of a lower respiratory infection. 95%CI = 95% Confidence Interval.

A

				Prevalence of Infant Lower Respiratory Infection (0-2 years)		
				%	95% CI	P value*
OVERALL		**(n=2172)**	(100%)	**25.8**	**23.9 to 27.6**	-
Sex	Female	(n=1140)	(52%)	24.7	22.2 to 27.2	0.24
	Male	(n=1032)	(48%)	26.9	24.2 to 29.6	
Father's Occupational Class (at 4 years)	Non-Manual	(n=938)	(43%)	20.2	17.6 to 22.7	<0.001
	Manual	(n=1234)	(57%)	30.1	27.5 to 32.6	
Home Overcrowding (at 2 years)	No	(n=1239)	(57%)	21.6	19.3 to 23.8	<0.001
	Yes	(n=933)	(43%)	31.4	28.4 to 34.4	
Pollution Exposure (0-2 years)	Low	(n=1101)	(51%)	21.5	19.1 to 24.0	<0.001
	High	(n=1071)	(49%)	30.2	27.4 to 32.9	

*Chi Square test

B

				Birth weight		
				Mean (g)	95% CI	P value**
OVERALL		**(n=2172)**	**(100%)**	**3404**	**3383 to 3426**	-
Infant Lower Respiratory Infection	No	(n=1612)	(74%)	3398	3373 to 3423	0.94
	Yes	(n=560)	(26%)	3400	3358 to 3442	

**independent sample T-test.

Table E2: Prevalence of ever-smoking up to age 60-64 years according to sex and early life exposures among 2172 participants included in adult lung function modelling

95%CI = 95% Confidence Interval.

			Ever-Smoker		
			Prevalence (%)	95% CI	P-value*
OVERALL	**(n=2172)**		**59.8**	**57.7 to 61.9**	-
Sex	**Female**	**(n=1140)**	54.5	51.6 to 57.4	<0.001
	Male	**(n=1032)**	65.7	62.8 to 68.6	
Infant Lower Respiratory Infection (0-2 years)	**Absent**	**(n=1612)**	58.6	56.2 to 61.0	0.06
	Present	**(n=560)**	63.2	59.2 to 67.2	
Father's Occupational Class (at 4 years)	**Non-Manual**	**(n=938)**	55.5	52.4 to 58.7	<0.001
	Manual	**(n=1234)**	63.0	60.4 to 65.7	
Home Overcrowding (at 2 years)	**No**	**(n=1239)**	58.2	55.4 to 60.9	0.08
	Yes	**(n=933)**	62.0	58.8 to 65.1	
Pollution Exposure (0-2 years)	**Low**	**(n=1101)**	58.9	55.9 to 61.8	0.36
	High	**(n=1071)**	60.8	57.9 to 63.7	

*Chi Square test

Table E3: The influence of early life exposures upon inclusion within the current analyses.

In the sample of 3903 individuals providing complete early life data, Chi-square tests for differences in early life exposures (infant lower respiratory infection occurrence, father's occupational class, home overcrowding and pollution exposure) between those included versus not included in the current analysis.

(N=3903)			Number of cohort members	Inclusion within current analysis	
				%	P-value*
Early Life	Infant Lower Respiratory Infection (0-2 years)	No	2913	55.3	0.51
		Yes	990	56.6	
	Father's occupational class (at 4 years)	Non-Manual	1618	58.0	0.01
		Manual	2285	54.0	
	Home Overcrowding (at 2 years)	No	2091	59.3	<0.001
		Yes	1812	51.5	
	Pollution Exposure (0-2 years)	Low	1915	57.5	0.02
		High	1988	53.9	

*Chi-square Test

Table E4: A comparison of the characteristics of ever versus never-smokers included within lung function analyses.

A: Prevalence of male sex, mean weight at age 43, mean height at age 43, prevalence of early life exposures and mean birth weight of ever versus never-smokers included within FEV_1 models. Consistent with prior studies, ever-smokers were more commonly male and from manual socioeconomic households. Differences in other early life exposures were small in magnitude and not statistically significant. There was no difference in height or weight according to ever-smoker status among females or males respectively. Both male and female smokers recorded higher birth weights than their never-smoker counterparts perhaps reflecting poor early life health reducing the likelihood of starting to smoke. These differences are unlikely to explain our main lung function findings, especially as our final models were fully adjusted for all these factors.

B: The estimated associations between ever versus never-smoker status and both FEV_1 and FVC at age 43, Multilevel models adjusted for age only (95% Confidence Interval). When males and females are considered separately, FEV_1 at age 43 was lower among ever-smokers than never smokers and a similar trend was seen in relation to FVC. Arguably, the smaller impairments associated with ever-smoking, shown within this table, compared to those within the fully adjusted models (within the main manuscript) highlights the importance of accounting for the dose and duration of smoking rather than simply binary ever versus never smoking.
95 %CI = 95% Confidence Interval.

Table 4E

A

	OVERALL (n=2172)			Females (n=1140)			Males (n=1032)		
	Ever-smoker (n=1299)	Never-Smoker (n=873)	P value	Ever-smoker (n=621)	Never-Smoker (n=519)	P value	Ever-smoker (n=678)	Never-Smoker (n=354)	P value
% Male Sex*	52.2	40.5	<0.001	n/a	n/a	n/a	n/a	n/a	n/a
Mean (95% CI) weight at age 43 years (kg)**	72.4 (71.8 to 73.0)	71.1 (70.5 to 71.7)	0.02	65.9 (65.3 to 66.4)	66.4 (65.9 to 67.0)	0.44	78.5 (77.9 to 79.0)	77.9 (77.4 to 78.3)	0.43
Mean (95% CI) height at age 43 years (cm)**	169.1 (168.7 to 169.5)	167.4 (167.0 to 167.7)	<0.001	162.3 (162.1 to 162.6)	162.1 (161.8 to 162.3)	0.50	175.3 (175.0 to 175.6)	175.1 (174.8 to 175.4)	0.70
% With lower respiratory tract infection during early life*	27.3	23.6	0.06	25.6	23.7	0.46	28.8	23.4	0.07
% From manual socioeconomic household during early life*	59.9	52.2	<0.001	60.2	55.9	0.14	59.6	46.9	<0.001
% Living in an overcrowded home during early life*	44.5	40.7	0.08	43.2	41.0	0.47	45.7	40.1	0.08
% Exposed to high pollution during early life*	50.1	48.1	0.36	51.9	45.1	0.02	48.5	52.5	0.22
Mean (95% CI) birth weight (g)**	3441.7 (3419.7 to 3463.7)	3334.1 (3312.9 to 3355.3)	<0.001	3373.4 (3352.0 to 3394.7)	3293.0 (3272.4 to 3313.7)	0.01	3504.3 (3482.0 to 3526.5)	3394.3 (3372.5 to 3416.1)	0.001

P values calculated using *Chi Square tests and **Independent sample T-tests respectively

B

	OVERALL			Females			Males		
	Ever-smoker	Never-Smoker	P value	Ever-smoker	Never-Smoker	P value	Ever-smoker	Never-Smoker	P value
FEV_1 at age 43 years (95% CI) (n=2712)	3014.4 (2976.0 to 3052.8)	3018.5 (2971.9 to 3065.1)	0.89	2534.0 (2498.8 to 2569.2)	2632.3 (2593.9 to 2670.8)	<0.001	3456.4 (3409.4 to 3503.4)	3579.3 (3515.5 to 3643.1)	0.002
FVC at age 43 years (n=1960)	3660.5 (3608.7 to 3712.3)	3570.4 (3508.9 to 3632)	0.02	3075.7 (3029.5 to 3121.8)	3124.2 (3074.9 to 3173.5)	0.13	4227.2 (4160.4 to 4294.1)	4284.4 (4196.3 to 4372.5)	0.27

Comparison between FEV_1 and FVC at 43 years among smokers versus never-smokers analysed using multievel models adjusted for age and including 2172 and 1960 individuals respectively

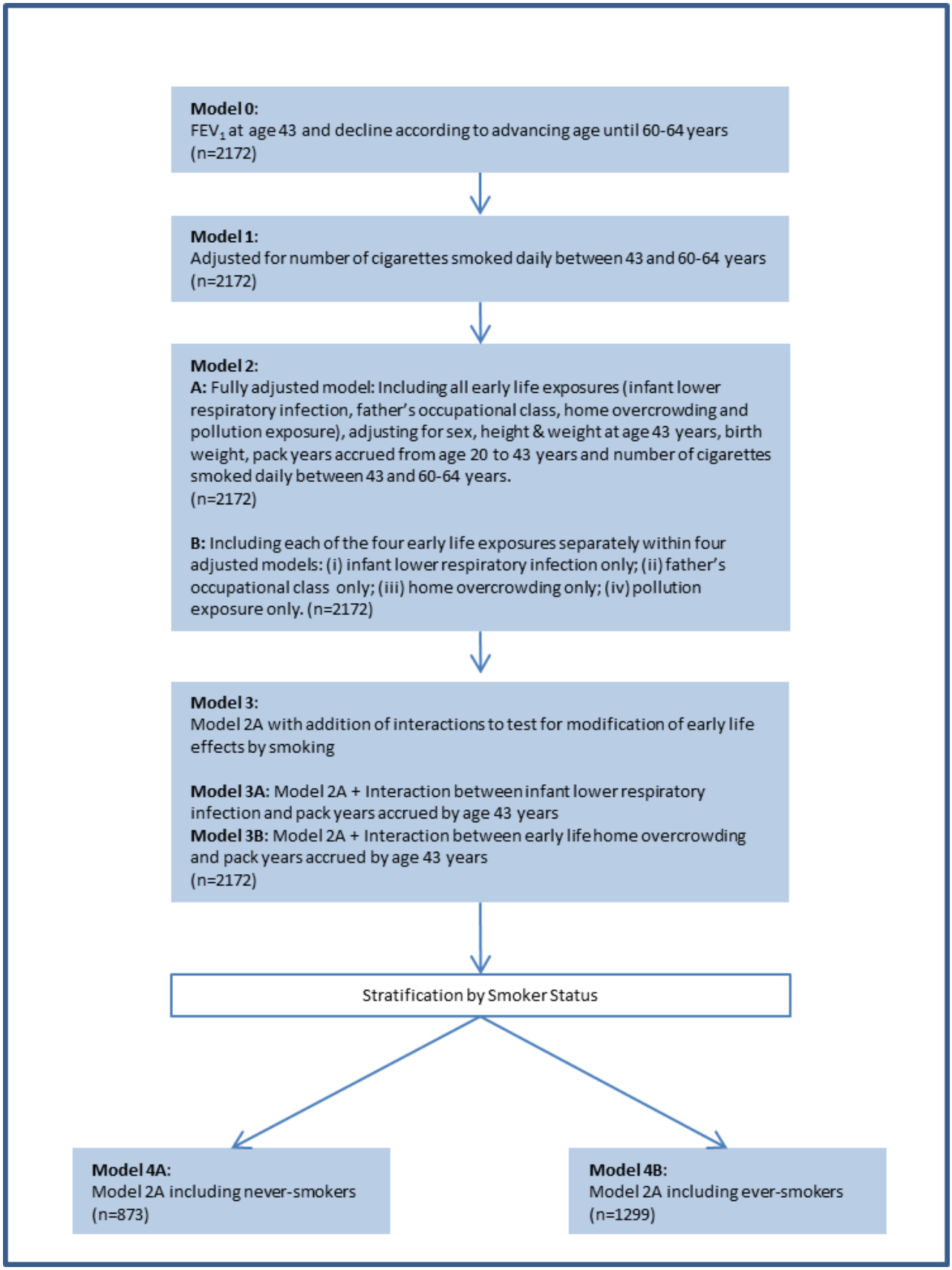
Figure E1: Multilevel models estimating adult FEV_1 decline trajectory between ages 43 and 60-64 years

(i) Characteristics of the 2172 individuals included within the multilevel model

% Males sex	47.5	
Mean (SD) weight at age 43 years (kg)	71.9	(13.7)
Mean (SD) height at age 43 years (cm)	168.4	(9.1)
% With infant lower respiratory infection (0-2 years)	25.8	
% With father from manual occupational class (at 4 years)	56.8	
% Living in an overcrowded home (at 2 years)	43.0	
% Exposed to high pollution (0-2 years)	49.3	
Mean (SD) birth weight (g)	3398	(508)
% Ever smoker	59.8	
- Median (IQR) pack years ever-smokers accrued between by age 43 years	9.6	(3.1 to 19.6)

SD = standard deviation; IQR = interquartile range

(i) Flowchart indicating the Multilevel Model building process used for analysis with FEV_1 decline between ages 43 and 60-64 years (models 0-4)



(ii) Models 0 to 2

Model 0: (N=2172)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	3016.0	2985.8 to 3046.3	-	-24.8	-26.0 to -23.6	<0.001

Model 1: (N=2172)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	3017.2	2985.2 to 3049.2	-	-23.8	-25.1 to -22.5	<0.001
Smoking 43 and 64 years (per cigarette smoked daily)	0.2	-1.9 to 2.3	0.85	-0.5	-0.7 to -0.3	<0.001

Model 2A: (N=2172)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2234.9	-2745.3 to -1724.4	-	-15.9	-24.4 to -7.5	<0.001
Male sex	576.1	517.7 to 634.5	<0.001	-0.7	-3.1 to 1.7	0.59
Height at 43 years (per cm)	30.0	26.7 to 33.3	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.1	-3.8 to -0.4	0.02	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-74.5	-123.2 to -25.9	0.003	-1.0	-3.8 to 1.8	0.49
Father's occupational class at 4 years (manual vs non-manual)	-55.0	-100.3 to -9.8	0.02	-2.0	-4.5 to 0.5	0.11
Home overcrowding at 2 years (yes vs no)	-60.3	-105.1 to -15.5	0.01	2.3	-0.2 to 4.8	0.08
High pollution exposure 0-2 years (yes vs no)	15.7	-26.6 to 58.1	0.47	0.7	-1.7 to 3.1	0.56
Birth weight (per gram)	0.07	0.02 to 0.11	0.003	-0.002	-0.004 to 0.0003	0.09
Pack years accrued between ages 20 and 43 years (per pack year)	-12.0	-14.3 to -9.8	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.7	0.5 to 4.9	0.02	-0.5	-0.7 to -0.3	<0.001

Model 2B: (N=2172)

(i) Infant lower respiratory infection only

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Infant lower respiratory infection 0-2 years (yes vs no)	-84.3	-132.5 to -36.0	0.001	-0.9	-3.7 to 1.8	0.50

(ii) Father's occupational class only

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Father's occupational class at 4 years (manual vs non-manual)	-78.2	-121.7 to -34.6	<0.001	-1.5	-3.9 to 0.9	0.21

(iii) Home overcrowding only

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Home overcrowding at 2 years (yes vs no)	-81.8	-125.0 to -38.6	<0.001	1.6	-0.8 to 4.0	0.19

(iv) Pollution exposure only

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
High pollution exposure 0-2 years (yes vs no)	10.1	-32.2 to 52.5	0.64	0.7	-1.7 to 3.1	0.57

(iii) Models 3A and 3B

Model 3A: Model with interaction between infant lower respiratory infection and pack years accrued by 43 years. (N=2172)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2240.4	-2750.4 to -1730.4	-	-15.9	-24.4 to -7.5	<0.001
Male sex	575.8	517.5 to 634.2	<0.001	-0.7	-3.1 to 1.7	0.59
Height at 43 years (per cm)	30.0	26.7 to 33.4	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.2	-3.9 to -0.5	0.01	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-40.7	-99.5 to 18.0	0.17	-1.1	-3.9 to 1.7	0.45
Father's occupational class at 4 years (manual vs non-manual)	-54.8	-100 to -9.5	0.02	-2.0	-4.5 to 0.5	0.11
Home overcrowding at 2 years (yes vs no)	-60.1	-104.9 to -15.2	0.01	2.3	-0.2 to 4.8	0.08
High pollution exposure 0-2 years (yes vs no)	15.0	-27.3 to 57.3	0.49	0.7	-1.7 to 3.1	0.56
Birth weight (per gram)	0.07	0.02 to 0.11	0.003	-0.002	-0.004 to 0.0004	0.10
Pack years accrued between ages 20 and 43 years (per pack year)	-10.8	-13.3 to -8.3	<0.001	-	-	-
Interaction: Infant lower respiratory infection (yes vs no) X Pack years accrued between ages 20 and 43 years (per pack year)	-3.9	-7.7 to -0.1	0.04	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.7	0.5 to 4.9	0.02	-0.5	-0.7 to -0.3	<0.001

Model 3B: Model with interaction between early life home overcrowding and pack years accrued by 43 years. (N=2172)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2226.3	-2735.9 to -1716.6	-	-15.9	-24.4 to -7.5	<0.001
Male sex	578.2	519.9 to 636.5	<0.001	-0.7	-3.1 to 1.7	0.59
Height at 43 years (per cm)	29.9	26.5 to 33.2	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.1	-3.8 to -0.4	0.01	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-73.6	-122.1 to -25.0	0.003	-1.0	-3.8 to 1.8	0.49
Father's occupational class at 4 years (manual vs non-manual)	-56.3	-101.5 to -11.2	0.02	-2.1	-4.6 to 0.4	0.11
Home overcrowding at 2 years (yes vs no)	-23.8	-76.3 to 28.7	0.38	2.2	-0.3 to 4.7	0.09
High pollution exposure 0-2 years (yes vs no)	15.8	-26.5 to 58.0	0.47	0.7	-1.7 to 3.1	0.55
Birth weight (per gram)	0.07	0.02 to 0.11	0.003	-0.002	-0.004 to 0.0004	0.10
Pack years accrued between ages 20 and 43 years (per pack year)	-9.6	-12.5 to -6.6	<0.001	-	-	-
Interaction: Early Life home overcrowding at 2 years (yes vs no) X Pack years accrued between ages 20 and 43 years (per pack year)	-4.7	-8.2 to -1.2	0.009	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.8	0.6 to 5.0	0.01	-0.5	-0.6 to -0.3	<0.001

(iv) Models 4A and 4B

Model 4A: Ever-smokers (N=1299)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2305.1	-2952.8 to -1657.5	-	-17.3	-29.4 to -5.1	0.001
Male sex	586.3	511.7 to 660.9	<0.001	-1.6	-5.0 to 1.8	0.34
Height at 43 years (per cm)	31.0	26.8 to 35.3	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.9	-5.1 to -0.7	0.01	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-108.2	-170.1 to -46.3	0.001	-1.2	-5.2 to 2.7	0.53
Father's occupational class at 4 years (manual vs non-manual)	-71.6	-130.1 to -13.2	0.02	-1.8	-5.3 to 1.8	0.32
Home overcrowding at 2 years (yes vs no)	-89.2	-147.0 to -31.5	0.002	1.8	-1.8 to 5.3	0.33
High pollution exposure 0-2 years (yes vs no)	27.0	-27.8 to 81.7	0.33	1.7	-1.7 to 5.1	0.32
Birth weight (per gram)	0.07	0.01 to 0.12	0.02	-0.002	-0.005 to 0.002	0.28
Pack years accrued between ages 20 and 43 years (per pack year)	-12.7	-15.4 to -10.0	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.1	-0.3 to 4.6	0.09	-0.4	-0.6 to -0.2	<0.001

Model 4B: Never-smokers (N=873)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2089.8	-2916.4 to -1263.2	-	-15.8	-27.4 to -4.3	0.007
Male sex	561.6	468.6 to 654.7	<0.001	1.4	-1.8 to 4.7	0.39
Height at 43 years (per cm)	28.7	23.4 to 34.1	<0.001	-	-	-
Weight at age 43 years (per kg)	-1.6	-4.3 to 1.0	0.23	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-15.9	-94.0 to 62.2	0.69	-1.2	-4.9 to 2.6	0.54
Father's occupational class at 4 years (manual vs non-manual)	-39.1	-110.0 to 31.9	0.28	-2.2	-5.6 to 1.1	0.20
Home overcrowding at 2 years (yes vs no)	-13.7	-84.3 to 56.8	0.70	2.8	-0.6 to 6.2	0.10
High pollution exposure 0-2 years (yes vs no)	-0.4	-66.4 to 65.7	0.99	-0.7	-3.8 to 2.5	0.69
Birth weight (per gram)	0.06	-0.01 to 0.13	0.09	-0.002	-0.005 to 0.001	0.26
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-

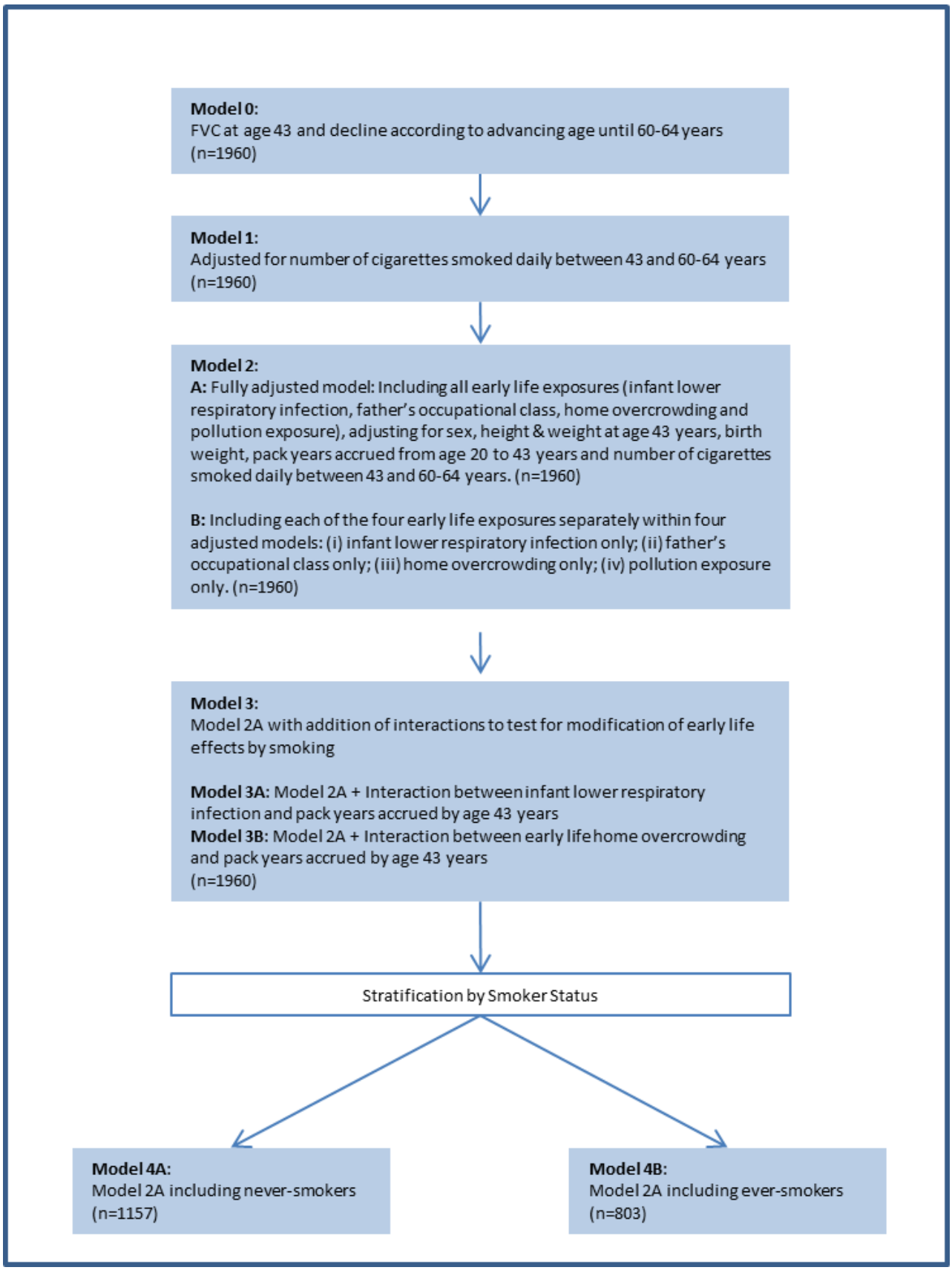
Figure E2: Multilevel models estimating adult FVC decline trajectory between ages 43 and 60-64 years

(ii) Characteristics of the 1960 individuals included within the multilevel model

% Males sex	47.0	
Mean (SD) weight at age 43 years (kg)	71.9	(13.8)
Mean (SD) height at age 43 years (cm)	168.3	(9.2)
% With infant lower respiratory infection (0-2 years)	25.8	
% With father from manual occupational class (at 4 years)	56.4	
% Living in an overcrowded home (at 2 years)	43.2	
% Exposed to high pollution (0-2 years)	49.6	
Mean (SD) birth weight (g)	3399	(509)
% Ever smoker	59.4	
- Median (IQR) pack years ever-smokers accrued between by age 43 years	9.6	(2.7 to 19.6)

SD = standard deviation; IQR = interquartile range

(iii) Flowchart indicating the Multilevel Model building process used for analysis with FVC decline between ages 43 and 60-64 years (models 0-4)



(iv) Models 0 to 2

Model 0: (N=1960)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	3622.8	3581.8 to 3663.8	-	-21.7	-23.6 to -19.8	<0.001

Model 1: (N=1960)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	3631.2	3587.7 to 3674.7	-	-21.7	-23.7 to -19.6	<0.001
Smoking 43 and 64 years (per cigarette smoked daily)	-1.7	-4.9 to 1.5	0.30	-0.1	-0.4 to 0.2	0.39

Model 2A: (N=1960)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3729.3	-4374 to -3084.6	-	-14.2	-27.2 to -1.3	0.03
Male sex	674.3	596.4 to 752.2	<0.001	3.3	-0.4 to 7.0	0.08
Height at 43 years (per cm)	43.7	39.5 to 47.9	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.4	-8.6 to -4.3	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-80.0	-147.7 to -12.2	0.02	1.4	-2.9 to 5.7	0.53
Father's occupational class at 4 years (manual vs non-manual)	-68.4	-131.3 to -5.5	0.03	-1.6	-5.4 to 2.3	0.42
Home overcrowding at 2 years (yes vs no)	-74.8	-137.2 to -12.5	0.02	1.0	-2.9 to 4.8	0.62
High pollution exposure 0-2 years (yes vs no)	23.1	-35.8 to 81.9	0.44	2.4	-1.3 to 6.0	0.20
Birth weight (per gram)	0.09	0.03 to 0.15	0.002	-0.003	-0.007 to 0.001	0.12
Pack years accrued between ages 20 and 43 years (per pack year)	-10.4	-13.3 to -7.4	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.9	-2.4 to 4.2	0.61	-0.2	-0.4 to 0.1	0.18

Model 2B: (N=1960)

(i) Infant lower respiratory infection only

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Infant lower respiratory infection 0-2 years (yes vs no)	-93.3	-160.4 to -26.2	0.006	1.5	-2.7 to 5.7	0.48

(ii) Father's occupational class only

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Father's occupational class at 4 years (manual vs non-manual)	-98.2	-158.5 to -37.9	0.001	-1.2	-4.9 to 2.5	0.52

(iii) Home overcrowding only

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
Home overcrowding at 2 years (yes vs no)	-100.1	-160.1 to -40.2	0.001	0.7	-3.0 to 4.4	0.72

(iv) Pollution exposure only

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
High pollution exposure 0-2 years (yes vs no)	17.9	-41.0 to 76.8	0.55	2.6	-1.1 to 6.2	0.17

(v) Models 3A and 3B

Model 3A: Interaction between infant lower respiratory infection and pack years accrued by 43 years. (N=1960)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3732.6	-4376.7 to -3088.6	-	-14.3	-27.2 to -1.3	0.03
Male sex	674.5	596.6 to 752.3	<0.001	3.3	-0.4 to 7	0.08
Height at 43 years (per cm)	43.7	39.5 to 47.9	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.5	-8.7 to -4.4	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-32.5	-111.9 to 46.8	0.42	1.2	-3.1 to 5.5	0.59
Father's occupational class at 4 years (manual vs non-manual)	-67.6	-130.5 to -4.7	0.04	-1.5	-5.4 to 2.3	0.43
Home overcrowding at 2 years (yes vs no)	-74.1	-136.4 to -11.7	0.020	1.0	-2.9 to 4.8	0.62
High pollution exposure 0-2 years (yes vs no)	22.0	-36.8 to 80.9	0.46	2.3	-1.3 to 6	0.21
Birth weight (per gram)	0.09	0.03 to 0.15	0.002	-0.003	-0.007 to 0.001	0.12
Pack years accrued between ages 20 and 43 years (per pack year)	-8.6	-11.9 to -5.3	<0.001	-	-	-
Interaction: Infant lower respiratory infection (yes vs no) X Pack years accrued between ages 20 and 43 years (per pack year)	-5.6	-10.5 to -0.7	0.02	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.9	-2.4 to 4.2	0.61	-0.2	-0.5 to 0.1	0.15

Model 3B: Interaction between early life overcrowded home and pack years accrued between ages by 43 years. (N=1960)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3718.6	-4363.0 to -3074.1	-	-14.3	-27.2 to -1.3	0.03
Male sex	675.8	597.9 to 753.7	<0.001	3.3	-0.4 to 7.0	0.08
Height at 43 years (per cm)	43.6	39.4 to 47.8	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.4	-8.6 to -4.3	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-78.8	-146.6 to -11.1	0.02	1.4	-2.9 to 5.7	0.53
Father's occupational class at 4 years (manual vs non-manual)	-69.3	-132.2 to -6.5	0.03	-1.6	-5.4 to 2.2	0.41
Home overcrowding at 2 years (yes vs no)	-49.9	-121.1 to 21.3	0.17	0.9	-3.0 to 4.7	0.66
High pollution exposure 0-2 years (yes vs no)	23.5	-35.3 to 82.3	0.43	2.3	-1.3 to 6.0	0.21
Birth weight (per gram)	0.09	0.03 to 0.15	0.002	-0.003	-0.007 to 0.0008	0.12
Pack years accrued between ages 20 and 43 years (per pack year)	-8.6	-12.4 to -4.8	<0.001	-	-	-
Interaction: Early Life home overcrowding at 2 years (yes vs no) X Pack years accrued between ages 20 and 43 years (per pack year)	-3.3	-7.9 to 1.3	0.16	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.9	-2.5 to 4.2	0.61	-0.2	-0.4 to 0.1	0.18

(vi) Models 4A and 4B

Model 4A: Ever-smokers (N=1157)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3802.6	-4633.7 to -2971.5	-	-12.6	-30.2 to 4.9	0.16
Male sex	701.7	601.0 to 802.3	<0.001	1.9	-3.1 to 6.9	0.46
Height at 43 years (per cm)	45.0	39.5 to 50.4	<0.001	-	-	-
Weight at age 43 years (per kg)	-7.1	-10.0 to -4.2	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-117.3	-204.7 to -29.8	0.009	0.4	-5.4 to 6.2	0.89
Father's occupational class at 4 years (manual vs non-manual)	-80.6	-163.1 to 1.9	0.06	-2.4	-7.6 to 2.8	0.36
Home overcrowding at 2 years (yes vs no)	-93.1	-174.6 to -11.5	0.03	2.4	-2.8 to 7.6	0.37
High pollution exposure 0-2 years (yes vs no)	44.4	-32.7 to 121.5	0.26	2.3	-2.6 to 7.3	0.36
Birth weight (per gram)	0.08	0.005 to 0.16	0.04	-0.003	-0.008 to 0.002	0.18
Pack years accrued between ages 20 and 43 years (per pack year)	-12.8	-16.2 to -9.4	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.9	-2.6 to 4.5	0.60	-0.1	-0.4 to 0.1	0.34

Model 4B: Never-smokers (N=803)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3583.9	-4605.5 to -2562.3	-	-17.7	-37.3 to 1.9	0.08
Male sex	627.4	504.1 to 750.7	<0.001	5.9	0.3 to 11.6	0.04
Height at 43 years (per cm)	42.3	35.8 to 48.8	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.0	-9.3 to -2.8	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-18.9	-126.1 to 88.2	0.73	2.9	-3.5 to 9.2	0.38
Father's occupational class at 4 years (manual vs non-manual)	-58.4	-155.6 to 38.9	0.24	0.2	-5.5 to 5.9	0.94
Home overcrowding at 2 years (yes vs no)	-40.4	-137.0 to 56.2	0.41	-1.4	-7.2 to 4.3	0.63
High pollution exposure 0-2 years (yes vs no)	-0.6	-91.4 to 90.2	0.99	2.2	-3.2 to 7.5	0.43
Birth weight (per gram)	0.09	0.001 to 0.19	0.05	-0.002	-0.008 to 0.004	0.48
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-

Figure E3: Multilevel Models for FEV_1 and FVC decline stratified according to smoking behaviour (Model 4) with additional adjustment for childhood asthma

(i) FEV_1 decline models (N=2172)

The analyses presented include individuals with missing information on childhood asthma (N=46) as not having childhood asthma. Exclusion of these individuals from analyses did not significantly change the results)

Model 4A: Ever-smokers (N=1299)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2308.0	-2953.1 to -1663.0	-	-17.4	-29.5 to -5.3	0.005
Male sex	587.3	513.1 to 661.6	<0.001	-1.7	-5.1 to 1.7	0.34
Height at 43 years (per cm)	31.1	26.8 to 35.3	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.8	-5.1 to -0.6	0.01	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-103.9	-165.5 to -42.2	0.001	-1.3	-5.2 to 2.6	0.51
Father's occupational class at 4 years (manual vs non-manual)	-68.4	-126.5 to -10.2	0.02	-1.9	-5.4 to 1.7	0.30
Home overcrowding at 2 years (yes vs no)	-93.9	-151.5 to -36.4	0.001	1.9	-1.6 to 5.5	0.28
High pollution exposure 0-2 years (yes vs no)	21.3	-33.3 to 75.8	0.45	1.9	-1.5 to 5.3	0.27
Birth weight (per gram)	0.07	0.01 to 0.12	0.01	-0.002	-0.005 to 0.001	0.27
Pack years accrued between ages 20 and 43 years (per pack year)	-12.8	-15.5 to -10.2	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.1	-0.4 to 4.5	0.10	-0.4	-0.6 to -0.2	<0.001
Childhood Asthma	-275.0	-436.8 to -113.1	0.001	6.6	-3.8 to 16.9	0.21

Model 4B: Never-smokers (N=873)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2160.9	-2980.0 to -1341.8	-	-16.0	-27.6 to -4.4	0.007
Male sex	572.1	479.7 to 664.6	<0.001	1.6	-1.7 to 5	0.33
Height at 43 years (per cm)	29.2	23.9 to 34.5	<0.001	-	-	-
Weight at age 43 years (per kg)	-1.8	-4.5 to 0.8	0.17	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-2.2	-80.0 to 75.7	0.96	-1.0	-4.7 to 2.8	0.61
Father's occupational class at 4 years (manual vs non-manual)	-44.8	-115.3 to 25.7	0.21	-2.3	-5.7 to 1.1	0.18
Home overcrowding at 2 years (yes vs no)	-11.7	-81.7 to 58.3	0.74	2.8	-0.6 to 6.2	0.11
High pollution exposure 0-2 years (yes vs no)	1.8	-63.7 to 67.3	0.96	-0.7	-3.9 to 2.5	0.66
Birth weight (per gram)	0.06	0.004 to 0.13	0.06	-0.002	-0.005 to 0.001	0.28
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-
Childhood Asthma	-294.4	-452.4 to -136.3	<0.001	-1.9	-9.2 to 5.3	0.60

(ii) FVC decline models (N=1960)

The analyses presented include individuals with missing information on childhood asthma (N=40) as not having childhood asthma. Exclusion of these individuals from analyses did not significantly change the results)

Model 4A: Ever-smokers (N=1157)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3800.4	-4631.0 to -2969.7	-	-12.7	-30.2 to 4.9	0.16
Male sex	703.0	602.4 to 803.6	<0.001	1.9	-3.1 to 6.8	0.46
Height at 43 years (per cm)	45.0	39.5 to 50.4	<0.001	-	-	-
Weight at age 43 years (per kg)	-7.0	-9.9 to -4.1	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-114.8	-202.2 to -27.3	0.01	0.3	-5.5 to 6.1	0.92
Father's occupational class at 4 years (manual vs non-manual)	-77.9	-160.4 to 4.6	0.06	-2.5	-7.7 to 2.7	0.34
Home overcrowding at 2 years (yes vs no)	-96.5	-178.2 to -14.9	0.02	2.5	-2.7 to 7.8	0.34
High pollution exposure 0-2 years (yes vs no)	40.6	-36.6 to 117.8	0.30	2.4	-2.5 to 7.4	0.33
Birth weight (per gram)	0.08	0.01 to 0.16	0.04	-0.003	-0.008 to 0.002	0.17
Pack years accrued between ages 20 and 43 years (per pack year)	-12.9	-16.3 to -9.5	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.9	-2.6 to 4.5	0.61	-0.1	-0.4 to 0.1	0.34
Childhood Asthma	-161.1	-387.1 to 64.9	0.16	6.1	-10.1 to 22.4	0.46

Model 4B: Never-smokers (N=803)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3617.6	-4637.8 to -2597.3	-	-17.6	-37.2 to 2.0	0.08
Male sex	635.5	512.1 to 758.8	<0.001	5.8	0.1 to 11.4	0.05
Height at 43 years (per cm)	42.6	36.1 to 49.0	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.2	-9.4 to -2.9	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-9.8	-117.2 to 97.6	0.86	2.7	-3.7 to 9.0	0.41
Father's occupational class at 4 years (manual vs non-manual)	-61.9	-159.0 to 35.2	0.21	0.3	-5.4 to 6.1	0.91
Home overcrowding at 2 years (yes vs no)	-37.4	-133.9 to 59.1	0.45	-1.6	-7.3 to 4.2	0.59
High pollution exposure 0-2 years (yes vs no)	3.2	-87.6 to 93.9	0.95	2.0	-3.4 to 7.3	0.47
Birth weight (per gram)	0.10	0.003 to 0.19	0.04	-0.002	-0.008 to 0.004	0.47
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-
Childhood Asthma	-203.6	-425.5 to 18.4	0.07	4.9	-8.7 to 18.6	0.48

Figure E4: Multilevel Models for FEV_1 and FVC decline stratified according to smoking behaviour (Model 4) after exclusion of those with childhood asthma

(i) FEV_1 decline models (N=2097)

Model 4A: Ever-smokers (N=1263)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2353.0	-2993.2 to -1712.8	-	-17.1	-29.4 to -4.7	0.007
Male sex	587.0	513.2 to 660.8	<0.001	-1.5	-5.0 to 1.9	0.39
Height at 43 years (per cm)	31.5	27.2 to 35.7	<0.001	-	-	-
Weight at age 43 years (per kg)	-3.2	-5.4 to -1.0	0.004	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-100.1	-161.9 to -38.3	0.001	-1.6	-5.6 to 2.4	0.44
Father's occupational class at 4 years (manual vs non-manual)	-69.7	-127.8 to -11.7	0.02	-2.0	-5.6 to 1.6	0.28
Home overcrowding at 2 years (yes vs no)	-103.5	-160.8 to -46.1	<0.001	1.9	-1.7 to 5.5	0.30
High pollution exposure 0-2 years (yes vs no)	13.4	-41.1 to 67.9	0.63	2.2	-1.2 to 5.7	0.21
Birth weight (per gram)	0.07	0.02 to 0.13	0.01	-0.002	-0.005 to 0.001	0.25
Pack years accrued between ages 20 and 43 years (per pack year)	-13.1	-15.7 to -10.4	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.0	-0.5 to 4.5	0.12	-0.4	-0.6 to -0.2	<0.001

Model 4B: Never-smokers (N=834)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2160.9	-2980.0 to -1341.8	-	-15.3	-27.1 to -3.6	0.01
Male sex	591.5	502.4 to 680.6	<0.001	2.1	-1.2 to 5.4	0.20
Height at 43 years (per cm)	28.5	23.4 to 33.5	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.8	-5.3 to -0.2	0.03	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-24.7	-101.0 to 51.6	0.53	-0.8	-4.6 to 3.0	0.67
Father's occupational class at 4 years (manual vs non-manual)	-47.4	-115.6 to 20.8	0.17	-1.3	-4.7 to 2.0	0.44
Home overcrowding at 2 years (yes vs no)	-6.5	-74.1 to 61.0	0.85	2.3	-1.1 to 5.7	0.18
High pollution exposure 0-2 years (yes vs no)	-12.8	-76.4 to 50.9	0.69	-0.1	-3.3 to 3.1	0.94
Birth weight (per gram)	0.06	-0.002 to 0.13	0.06	-0.002	-0.006 to 0.001	0.18
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-

(ii) FVC decline models (N=1889)

Model 4A: Ever-smokers (N=1123)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3904.0	-4737.2 to -3070.8	-	-13.1	-30.9 to 4.8	0.15
Male sex	691.5	590.5 to 792.5	<0.001	1.7	-3.3 to 6.8	0.51
Height at 43 years (per cm)	45.8	40.4 to 51.3	<0.001	-	-	-
Weight at age 43 years (per kg)	-7.4	-10.4 to -4.4	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-104.1	-192.7 to -15.6	0.02	-0.1	-6 to 5.8	0.97
Father's occupational class at 4 years (manual vs non-manual)	-81.3	-164.5 to 1.9	0.06	-2.6	-7.9 to 2.7	0.33
Home overcrowding at 2 years (yes vs no)	-102.7	-184.9 to -20.4	0.01	2.6	-2.7 to 7.9	0.34
High pollution exposure 0-2 years (yes vs no)	35.7	-42.2 to 113.6	0.37	2.7	-2.3 to 7.8	0.29
Birth weight (per gram)	0.08	0.01 to 0.16	0.03	-0.003	-0.008 to 0.002	0.19
Pack years accrued between ages 20 and 43 years (per pack year)	-13.2	-16.7 to -9.8	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	0.7	-3.0 to 4.3	0.72	-0.1	-0.4 to 0.2	0.38

Model 4B: Never-smokers (N=766)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3422.7	-4425.6 to -2419.8	-	-15.6	-35.6 to 4.4	0.13
Male sex	654.1	532.2 to 776.0	0.000	6.1	0.4 to 11.9	0.04
Height at 43 years (per cm)	41.6	35.2 to 48.0	0.000	-	-	-
Weight at age 43 years (per kg)	-6.8	-9.9 to -3.6	0.00	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-16.7	-124.8 to 91.4	0.76	2.2	-4.4 to 8.7	0.52
Father's occupational class at 4 years (manual vs non-manual)	-58.9	-155.3 to 37.4	0.23	0.01	-5.8 to 5.8	1.00
Home overcrowding at 2 years (yes vs no)	-41.8	-137.4 to 53.8	0.39	-1.5	-7.3 to 4.4	0.62
High pollution exposure 0-2 years (yes vs no)	-4.7	-95.0 to 85.7	0.92	1.5	-4.0 to 7.0	0.59
Birth weight (per gram)	0.10	0.01 to 0.19	0.04	-0.003	-0.008 to 0.003	0.38
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-

Figure E5: Details of the studies included in Figure 4 (main manuscript):

Barker et al 1991(1): Study of 825 mean from the Hertfordshire cohort born between 1920 and 1930. History of respiratory tract infections, recorded between birth and one year, was associated with FEV_1 deficit of 170ml when measured at age 59-67 years. 85% of those included were ever-smokers.

Shaheen 1994 (2): Study of 650 men and woman from the Derbyshire cohort born between 1917 and 1922. History of pneumonia recorded between birth and two years, was associated with FEV_1 deficits of 650mls amongst men and 190ml amongst woman at age 67-74 years. 41% of woman and 88% of men were ever-smokers.(3)

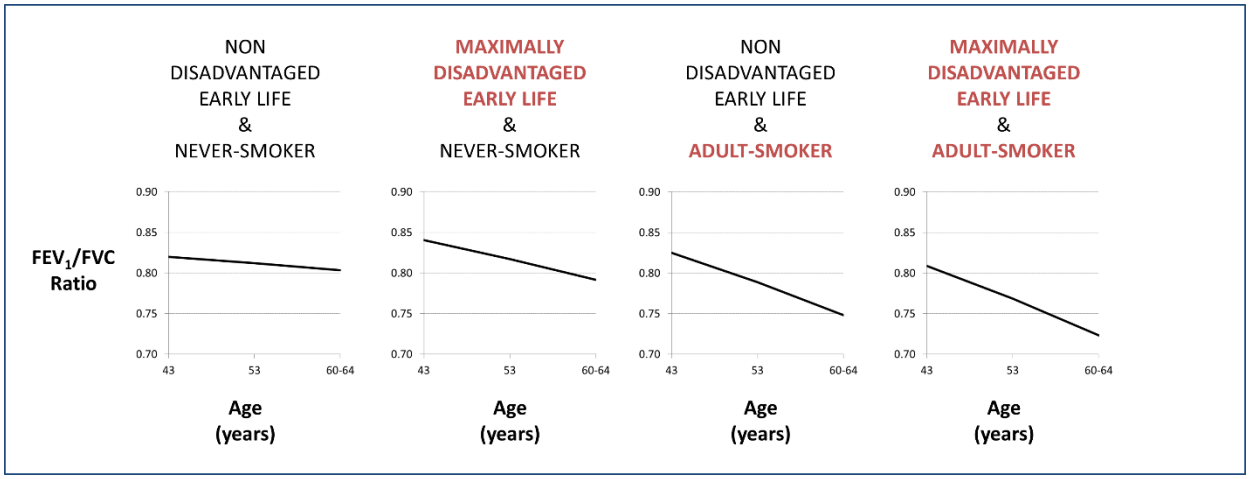
Shaheen 1998 (4): Study of 239 surviving mean and woman from the St Andrew's birth cohort born between 1921 and 1935. History of pneumonia and history of bronchitis recorded between birth and two years was associated with FEV_1 deficits of 390mls and 130mls respectively at mean age 58 years. 69% of those included were ever-smokers.

Johnston et al 1998 (5): Study of 1392 men and woman within the British National Child Development Study 1958 cohort (born in March 1958). History of pneumonia, recorded at age seven years, was associated with a FEV_1 deficit of 91mls at ages 34-35 years. 36% of those included were ever-smokers.

Chan et al 2015 (6): Study of 646 men and woman within the Tuscon Children's Respiratory Study (born between 1980 and 1984). History of pneumonia and history of lower respiratory infection, recorded within the first three years of life, were associated with FEV_1 deficits of 117mls and 63mls respectively at age 26 years. Ever-smoking prevalence by age 26 years within this cohort is reported as 35% (Guerra et al(7)).

NSHD (current study): Study of 2172 men and woman within the MRC National Survey of Health and Development 1946 birth cohort born within one week in March 1946. History of lower respiratory tract infection, recorded at age 2 years, was associated with a FEV_1 deficit of 75mls at age 43 years. 60% of those included were ever-smokers (Figure E1: Model 2A).

Figure E6: Adult FEV_1/FVC ratio plots according to early life exposures and subsequent smoking behaviour calculated using FEV_1 and FVC estimates presented within Figure 3 (main manuscript).



A comparison of the patterns of FEV_1/FVC between ages 43 and 60-64 years decline calculated from FEV_1 and FVC estimates within Figure 3 (estimates for males of average height at age 43 years (175cm), average weight at age 43 years (78 kg) and average birth weight (3.5kg)) according to adult smoking behaviour and early life disadvantage.

Never-smoker = never smoked up to age 60-64 years. *Adult-smoker* = smoking 20 cigarettes per day from age 20 years until 60-64 years. *Non-disadvantaged early life* = no lower respiratory infection, non-manual social class, non-overcrowded home and low pollution exposure during early life. *Maximally disadvantaged early life* = lower respiratory infection present, manual social class, overcrowded home and high pollution exposure during early life.

Appendix 1: Parental smoking as a potential confounder

Introduction

Parental smoking during childhood, being associated with social background and future smoking behaviour, represents a potential confounder within our study. Parental smoking data were not recorded at the instigation of this study in 1946, potentially reflecting that during this era less importance was attached to smoking as a determinant of current and future health. Throughout our main manuscript, we consistently emphasise the value of prospectively recorded data when investigating the relationship between infant and adult lung health. Parental smoking data were recorded during the sixth decade of this study and not from every individual included within the lung function analyses within our main manuscript. Although our parental smoking data were incomplete and retrospective in nature we have sought to investigate whether parental smoking may account for the relationship between early life exposures and adult lung function among smokers.

Methods

At 53 years of age participants were asked "Did either of your parents smoke cigarettes, cigars or pipes when you lived with them as a child?". If an individual had not lived with their parents, they were asked about the people they had lived with. Individuals were classified as either having a parent who had smoked or not.

Among the 2172 individuals (48% male) included within our FEV_1 models who also provided parent smoking data at age 53 years, Chi-square tests were used to investigate ever-smoker, early life exposures and male sex association with parental smoking. Independent t-tests were used to investigate the association between parental smoking and birth weight, weight at age 43 years and height at age 43 years. We also investigated the effect of adjusting the final lung function models discussed in our main manuscript (Table 1 and 2) for parental smoking.

Results

From the 2172 individuals included within our lung function analysis, 1931 (89%) provided data at age 53 years regarding the smoking behaviour of their parents. 1657 (86%) of these 1931 individuals reported that during their childhood, one or both parents had smoked during. Appendix 1 Table 1 shows that those recalling that their parents had smoked, were more likely to have come from a manual socioeconomic household, have been exposed to overcrowding and have been exposed to high pollution during early life. Individuals recalling their parents had smoked were more likely to be smokers themselves relative to those who did not recall their parents smoking (60.1% versus 51.8%; P=0.01). 1931 individuals and 1775 individuals providing parental smoking data were included in FEV_1 and FVC models respectively (Appendix 1 Table 2 and Appendix 1 Table 3). Inclusion of parental smoking within our lung function models did not substantially alter the associations between early life exposures and was not independently associated with lower FEV_1 or FVC at age 43 years, either among ever or never-smokers. We did find that amongst never-smokers only, the recollection that during their childhood a parent

smoked was associated with an accelerated FEV_1 decline between 43 and 60-64 years (-4.5 ml/yr (95% CI: -8.8 to -0.2; P=0.04).

Discussion

The majority (86%) recalled that one or other of their parent smoked reflecting the higher smoking prevalence of previous eras, even compared to the individuals included within this study. However, our finding of an association between early life exposures exposure with regards to adult lung function among smokers only, appears unaltered after adjustment for parental smoking and therefore parental smoking, as measured within this study, does not adequately explain this finding.

The retrospective collection of parental smoking data potentially introduces recall bias, for example those with poor respiratory health in adulthood might be more likely to recall being exposed to parental smoking earlier in life. This might explain why never-smoking adults who remembered their parent smoking appeared to be experiencing steeper FEV_1 decline. Furthermore, our parental smoking data lacks detail regarding the timing, intensity and duration of exposures. Crucially, prenatal and perinatal maternal smoking was not recorded, perhaps reflecting a lack of awareness in 1946 as to the adverse effects of in-utero smoking exposure. Additionally, the majority of our study sample appears to have been exposed to parental smoking during childhood and the small size of the non-exposed reference group may weaken our ability to detect the consequences of parental smoking exposure.

Therefore, although parental smoking exposure appears an unlikely explanation for our findings, the adverse effects of parental smoking may be better demonstrated by studies providing more detailed, prospectively collected parental smoking data.

Appendix 1 Table 1: A comparison of the characteristics of 1931 individuals included within lung function analyses according to whether or not they recalled that at least one parent had smoked during their childhood. 95%CI = 95% Confidence Interval.

Appendix 1 Table 1

	OVERALL (n=1931)	**Parent(s) smoked (n=1657)**	**No parent smoked (n=274)**	P value
% Male sex	46.3	46.5	45.6	0.79
Mean (95% CI) weight at age 43 years (kg)**	71.8 (71.3 to 72.2)	72.0 (71.5 to 72.4)	70.4 (70.0 to 70.9)	0.08
Mean (95% CI) height at age 43 years (cm)**	168.3 (168 to 168.6)	168.3 (168 to 168.6)	168.5 (168.2 to 168.8)	0.67
% With lower respiratory tract infection during early life*	25.1	25.9	20.4	0.05
% From manual socioeconomic household during early life*	56.7	58.9	43.1	<0.001
% Living in an overcrowded home during early life*	42.7	44.7	30.7	<0.001
% Exposed to high pollution during early life*	49.2	50.5	41.6	0.01
Mean (95% CI) birth weight (g)**	3397.4 (3380.5 to 3414.3)	3393.2 (3376.2 to 3410.1)	3423.2 (3407.0 to 3439.3)	0.36
% Ever-smoker*	59.1	60.3	51.8	0.01

P values calculated using *Chi Square tests and **Independent sample T-tests respectively

APPENDIX 1 TABLE 2

A: Ever-smokers (N=1141)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2305.1	-2952.8 to -1657.5	-	-17.3	-29.4 to -5.1	0.001
Male sex	586.3	511.7 to 660.9	<0.001	-1.6	-5.0 to 1.8	0.34
Height at 43 years (per cm)	31.0	26.8 to 35.3	<0.001	-	-	-
Weight at age 43 years (per kg)	-2.9	-5.1 to -0.7	0.01	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-108.2	-170.1 to -46.3	0.001	-1.2	-5.2 to 2.7	0.53
Father's occupational class at 4 years (manual vs non-manual)	-71.6	-130.1 to -13.2	0.02	-1.8	-5.3 to 1.8	0.32
Home overcrowding at 2 years (yes vs no)	-89.2	-147.0 to -31.5	0.002	1.8	-1.8 to 5.3	0.33
High pollution exposure 0-2 years (yes vs no)	27.0	-27.8 to 81.7	0.33	1.7	-1.7 to 5.1	0.32
Birth weight (per gram)	0.07	0.01 to 0.12	0.02	-0.002	-0.005 to 0.002	0.28
Pack years accrued between ages 20 and 43 years (per pack year)	-12.7	-15.4 to -10.0	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	2.1	-0.3 to 4.6	0.09	-0.4	-0.6 to -0.2	<0.001
At least one parent smoked	-28.9	-118.9 to 61.2	0.53	2.1	-3.4 to 7.6	0.45

B: Never-smokers (N=790)

	FEV_1 Intercept (ml) at Age 43 years			FEV_1 Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-2156.6	-3021.4 to -1291.8	-	-11.5	-23.7 to 0.8	0.07
Male sex	571.7	473.7 to 669.7	<0.001	1.4	-1.9 to 4.8	0.41
Height at 43 years (per cm)	28.4	22.8 to 33.9	<0.001	-	-	-
Weight at age 43 years (per kg)	-1.8	-4.6 to 1.0	0.22	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-17.6	-100.2 to 65.0	0.68	-1.1	-4.9 to 2.7	0.56
Father's occupational class at 4 years (manual vs non-manual)	-40.9	-115.3 to 33.5	0.28	-1.6	-5.1 to 1.8	0.35
Home overcrowding at 2 years (yes vs no)	-15.8	-90.0 to 58.3	0.68	2.8	-0.6 to 6.3	0.11
High pollution exposure 0-2 years (yes vs no)	-12.5	-81.8 to 56.8	0.72	0.1	-3.1 to 3.3	0.95
Birth weight (per gram)	0.08	0.01 to 0.16	0.02	-0.002	-0.006 to 0.001	0.19
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-
At least one parent smoked	62.8	-29.4 to 155	0.18	-4.5	-8.8 to -0.2	0.04

APPENDIX 1 TABLE 3

A: Ever-smokers (N=1037)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3698.7	-4578.8 to -2818.6	-	-19.7	-39.4 to -0.1	0.05
Male sex	716.7	610.8 to 822.7	<0.001	1.4	-3.7 to 6.6	0.59
Height at 43 years (per cm)	44.8	39.1 to 50.6	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.9	-10.0 to -3.9	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-99.3	-192.5 to -6.2	0.04	0.1	-5.8 to 6.1	0.97
Father's occupational class at 4 years (manual vs non-manual)	-105.5	-193.1 to -18.0	0.02	-1.6	-7.0 to 3.8	0.57
Home overcrowding at 2 years (yes vs no)	-80.7	-167.1 to 5.6	0.07	1.5	-3.9 to 6.8	0.60
High pollution exposure 0-2 years (yes vs no)	63.2	-18.1 to 144.5	0.13	1.8	-3.3 to 6.9	0.49
Birth weight (per gram)	0.08	0.003 to 0.16	0.06	-0.003	-0.008 to 0.002	0.23
Pack years accrued between ages 20 and 43 years (per pack year)	-12.8	-16.4 to -9.3	<0.001	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	1.5	-2.2 to 5.2	0.42	-0.2	-0.5 to 0.1	0.28
At least one parent smoked	-93.2	-220.9 to 34.5	0.15	7.6	-0.6 to 15.8	0.07

B: Never-smokers (N=738)

	FVC Intercept (ml) at Age 43 years			FVC Linear Change per Year (ml/yr) Between Ages 43 and 60-64 years		
	Coefficient	95% CI	P value	Coefficient	95% CI	P value
constant	-3552.3	-4617.4 to -2487.3	-	-10.5	-31.5 to 10.5	0.33
Male sex	654.9	526.2 to 783.6	<0.001	6.0	0.2 to 11.9	0.04
Height at 43 years (per cm)	41.2	34.5 to 47.9	<0.001	-	-	-
Weight at age 43 years (per kg)	-6.4	-9.7 to -3.0	<0.001	-	-	-
Infant lower respiratory infection 0-2 years (yes vs no)	-25.0	-137.3 to 87.2	0.66	3.5	-3.1 to 10	0.30
Father's occupational class at 4 years (manual vs non-manual)	-52.4	-153.9 to 49.2	0.31	0.4	-5.5 to 6.3	0.90
Home overcrowding at 2 years (yes vs no)	-51.8	-152.8 to 49.1	0.31	-1.3	-7.2 to 4.6	0.67
High pollution exposure 0-2 years (yes vs no)	13.3	-81.3 to 107.9	0.78	1.8	-3.7 to 7.4	0.52
Birth weight (per gram)	0.12	0.02 to 0.22	0.02	-0.003	-0.009 to 0.003	0.33
Pack years accrued between ages 20 and 43 years (per pack year)	-	-	-	-	-	-
Smoking 43 and 64 years (per cigarette smoked daily)	-	-	-	-	-	-
At least one parent smoked	83.5	-43.5 to 210.6	0.20	-5.2	-12.5 to 2	0.16

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