

ERJ-00477-2019: Supplementary file

Title: Association of asthma and smoking with lung function impairment in adolescence and early adulthood; the Isle of Wight Birth Cohort Study

Authors:

S. Hasan Arshad^{a,b,c} (sha@soton.ac.uk)

Claire Hodgekiss^a (claire.hodgekiss@gmail.com)

John W. Holloway^d (J.W.Holloway@soton.ac.uk)

Ramesh Kurukulaarachy^{a,b,c} (Rjk1s07@soton.ac.uk)

Wilfried Karmaus^e (karmaus1@memphis.edu)

Hongmei Zhang^e (hzhang6@memphis.edu)

Graham Roberts^{a,b,c} (G.C.Roberts@soton.ac.uk)

From:

a The David Hide Asthma and Allergy Research Centre, Isle of Wight, UK.

b Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, UK.

c Respiratory Biomedical Centre, University Hospital Southampton, UK.

d Human Development and Health, Faculty of Medicine, University of Southampton, UK.

e Division of Epidemiology, Biostatistics, and Environmental Health, School of Public Health, University of Memphis, TN, USA.

Corresponding Author:

Professor S Hasan Arshad DM, FRCP

sha@soton.ac.uk

MP: 810, South Block, Southampton General Hospital, Tremona Road, Southampton, UK

Tel: +44 (01983) 534373, +44 (02381)203366

Table S1. Demographic and clinical disease details of the participants

	All (n=1030)	Non-smokers without asthma (n=600)	Non-smokers with asthma (n=108)	Smokers without asthma (n=270)	Smokers with asthma (n=52)
At birth					
Male sex	470 (45.6%)	283 (47.2%)	41 (38.0%)	124 (46.0%)	22 (42.3%)
Mother smokes	379 (25.0%)	119 (20.0%)	17 (15.7%)	73 (27.3%)	14 (28.0%)
Father smokes	572 (38.4%)	180 (69.9%)	33 (31.1%)	116 (44.1%)	28 (54.9%)
Maternal doctor diagnosed asthma	112 (10.9%)	60 (10.0%)	13 (12.0%)	25 (9.3%)	14 (26.9%)
Maternal eczema	124 (12.0%)	67 (11.2%)	11 (10.2%)	33 (12.2%)	13 (25.0%)
Maternal hayfever	210 (20.4%)	115 (19.2%)	29 (26.9%)	52 (19.3%)	154 (26.9%)
Paternal doctor diagnosed asthma	88 (8.5%)	51 (8.5%)	11 (10.2%)	19 (7.0%)	7 (13.5%)
Paternal eczema	73 (7.1%)	47 (7.8%)	6 (5.6%)	18 (6.7%)	2 (3.9%)
Paternal hayfever	150 (14.6%)	90 (15.0%)	16 (14.8%)	40 (14.8%)	4 (7.7%)
At 26 years					
Mean BMI, Kg/m ²	26.1 (6.0)	25.8 (5.7)	26.9 (6.6)	26.2 (6.2)	28.4 (7.3)
Atopic	254 (45.7%)	128 (40.4%)	44 (67.7%)	55 (38.5%)	27 (87.1%)
Employed	847 (82.5%)	506 (84.5%)	92 (85.0%)	208 (77.6%)	41 (78.8%)
Current smoking	322 (31.3%)	0 (0.0%)	0 (0.0%)	270 (100.0%)	52 (100.0%)
Smoking ever	641 (62.2%)	170 (28.3%)	33 (30.6%)	270 (100.0%)	52 (100.0%)
For smokers ever, median duration, years	9 (6,11)	5 (3,8)	7 (4,8)	11 (8,12)	11 (9,13)
Other householder smoker	268 (26.0%)	87 (15.5%)	22 (20.4%)	134 (49.6%)	25 (48.1%)
Wheeze ever	441 (42.8%)	171 (28.5%)	101 (93.5%)	117 (43.3%)	52 (100.0%)
Wheeze in last year at 26 years	237 (23.0%)	52 (8.7%)	89 (82.4%)	44 (16.3%)	52 (100.0%)
Ever had asthma	325 (31.6%)	109 (18.2%)	108 (100.0%)	56 (20.7%)	52 (100.0%)
Physician diagnosed asthma	318 (30.9%)	106 (17.7%)	108 (100.0%)	52 (19.3%)	52 (100.0%)
Median duration of asthma by 26 years, years	5 (3,9)	-	6.5 (4,11)	-	4 (2,7)
Rhinitis symptoms ever	486 (47.2%)	245 (40.8%)	75 (69.4%)	128 (47.4%)	38 (73.1%)
Rhinitis symptoms in last year	435 (42.2%)	220 (36.7%)	69 (63.9%)	110 (40.7%)	36 (69.2%)
<i>Also conjunctivitis</i>	<i>278 (64.0%)</i>	<i>120 (54.5%)</i>	<i>56 (81.2%)</i>	<i>70 (64.2%)</i>	<i>32 (91.4%)</i>
Hay fever ever	474 (46.0%)	243 (40.5%)	74 (68.5%)	120 (44.4%)	37 (71.2%)
Recurrent itchy rash ever	232 (22.5%)	123 (20.5%)	33 (30.6%)	53 (19.6%)	23 (44.2%)
Recurrent itchy rash in last year	170 (16.5%)	89 (14.8%)	25 (23.2%)	36 (13.3%)	20 (38.5%)
<i>Affected folds of the elbows behind knees, ankles</i>	<i>104 (61.5%)</i>	<i>53 (60.2%)</i>	<i>15 (60.0%)</i>	<i>21 (58.3%)</i>	<i>15 (75.0%)</i>
Eczema ever	296 (28.7%)	154 (25.7%)	49 (45.4%)	66 (24.4%)	27 (51.9%)

Note: Figures represent mean (standard deviation) or median (25th and 75th quartiles). Data are raw data from baseline (birth) and 26 year questionnaires. Further information can be found below.

Additional information for table S1

Variable	Questionnaire question
Ever household smoker	Does anyone else in your household smoke?
Wheeze ever	Have you ever had wheezing or whistling in the chest at any time in the past?
Wheeze in last year at 26 years	Have you had wheezing or whistling in the chest in the last 12 months?
Ever had asthma	Have you ever had asthma?
Physician diagnosed asthma	If you have ever had asthma was it physician diagnosed?
Rhinitis symptoms ever	Have you ever had a problem with sneezing or a runny or blocked nose when you did not have a cold?
Rhinitis symptoms in last year	In the past 12 months have you had a problem with sneezing or a runny or blocked nose when you did not have a cold?
Also conjunctivitis	In the past 12 months has this nose problem been accompanied by itchy watery eyes?
Hay fever ever	Have you ever had hay fever?
Recurrent itchy rash ever	Have you ever had an itchy rash which comes and goes for at least 6 months?
Recurrent itchy rash in last year	Have you had this itchy rash at any time in the last 12 months?
Affected folds of the elbows behind knees, ankles	Has this rash at any time affected the folds of the elbows behind knees, ankles?
Eczema ever	Have you ever had eczema?

Questions used to generate the variables in Table S1.

Table S2. Characteristics of participants in the analysis data set

Variable	All (N=1456)	Analysis population (N=1030)	Participants with LFT at 10 years (N=980)	Participants with LFT at 18 years (N=839)	Participants with LFT at 26 years (N=547)
Male sex	735 (50.5%)	470 (45.6%)	488 (49.8%)	396 (47.2%)	236 (43.2%)
Mean BMI, Kg/m ²	26.1 (6.0)	26.1 (6.0)	26.1 (6.0)	26.0 (6.0)	26.2 (6.0)
Employed at 26 years	847 (82.4%)	847 (82.4%)	621 (83.4%)	589 (84.3%)	464 (85.0%)
LFT at 10 years	980	745	745	589	458
LFT at 18 years	839	699	589	699	454
LFT at 26 years	547	547	458	454	457
Ever asthma at 26 years	325 (31.6%)	325 (31.6%)	238 (31.9%)	216 (30.9%)	182 (33.3%)
Wheeze in last year at 26 years	237 (23.0%)	237 (23.0%)	177 (23.7%)	152 (21.7%)	141 (25.8%)
Hay fever ever at 26 years	474 (46.0%)	474 (46.0%)	353 (47.4%)	329 (56.2%)	258 (47.2%)
Eczema ever at 26 years	296 (28.7%)	296 (28.7%)	219 (29.4%)	197 (28.2%)	171 (31.3%)
Smoking at 26 years	322 (31.3%)	322 (31.3%)	243 (32.6%)	208 (29.8%)	172 (31.4%)

Figures represent mean (standard deviation) or median (25th and 75th quartiles). Data are crude data from baseline (birth) and 26 year questionnaires. LFT = lung function testing

Participants who attended the Centre for lung function measurements (n=547) were compared to cohort members who participated at 26 years assessment and provided any data (Table S2). There were no significant differences indicating that the subgroup who was assessed for lung function was representative of the overall cohort. .

Table S3. Spirometry at 10, 18 and 26 years of age in male and female participants

	Male			Female		
	10 years	18 years	26 years	10 years	18 years	26 years

FEV₁ (L)	2.06 (0.30)	4.62 (0.62)	4.61 (0.72)	2.00 (0.29)	3.47 (0.45)	3.42 (0.43)
FEV₁ percent predicted	98.9% (11.5)	106.75% (13.48)	98.85% (12.71)	98.1% (11.0)	100.74% (12.36)	100.79% (10.88)
Post-FEV₁ (L)		4.83 (0.64)	4.81 (0.72)		3.64 (0.46)	3.55 (0.44)
Post-FEV₁ percent predicted		106.75% (13.48)	103.22% (12.24)		100.74% (12.36)	104.26% (10.84)
FVC	2.35 (0.34)	5.35 (0.72)	5.85 (0.82)	2.24 (0.33)	3.96 (0.53)	4.24 (0.54)
FVC percent predicted	101.2 (10.7)	112.9 (15.7)	104.3 (11.7)	100.0 (9.5)	107.0 (15.0)	106.5 (11.3)
FEV₁/FVC	0.88 (0.06)	0.87 (0.07)	0.79 (0.07)	0.90 (0.06)	0.88 (0.07)	0.81 (0.06)
FEV₁/FVC percent predicted	101.18% (6.94)	101.08% (8.60)	94.33% (8.59)	104.09% (6.51)	101.38% (8.84)	94.27% (7.41)
Post- FEV₁/FVC		0.89 (0.07)	0.83 (0.06)		0.91 (0.06)	0.85 (0.06)
Post- FEV₁/FVC percent predicted		104.17% (7.75)	98.73% (7.78)		104.62% (8.21)	98.39% (6.92)
FEF₂₅₋₇₅ (L)	2.38 (0.56)	4.99 (1.16)	4.37 (1.24)	2.48 (0.56)	3.95 (0.87)	3.44 (0.84)
FEF₂₅₋₇₅ percent predicted	95.23% (21.21)	110.82% (25.91)	90.42% (24.74)	104.76% (22.75)	102.39% (32.80)	89.83% (21.68)
Post-FEF₂₅₋₇₅ (L)		5.51 (1.11)	5.08 (1.30)		4.40 (0.89)	4.00 (0.88)
Post-FEF₂₅₋₇₅ (L) percent predicted		123.98% (25.50)	105.19% (25.44)		114.95% (34.51)	104.29% (22.52)

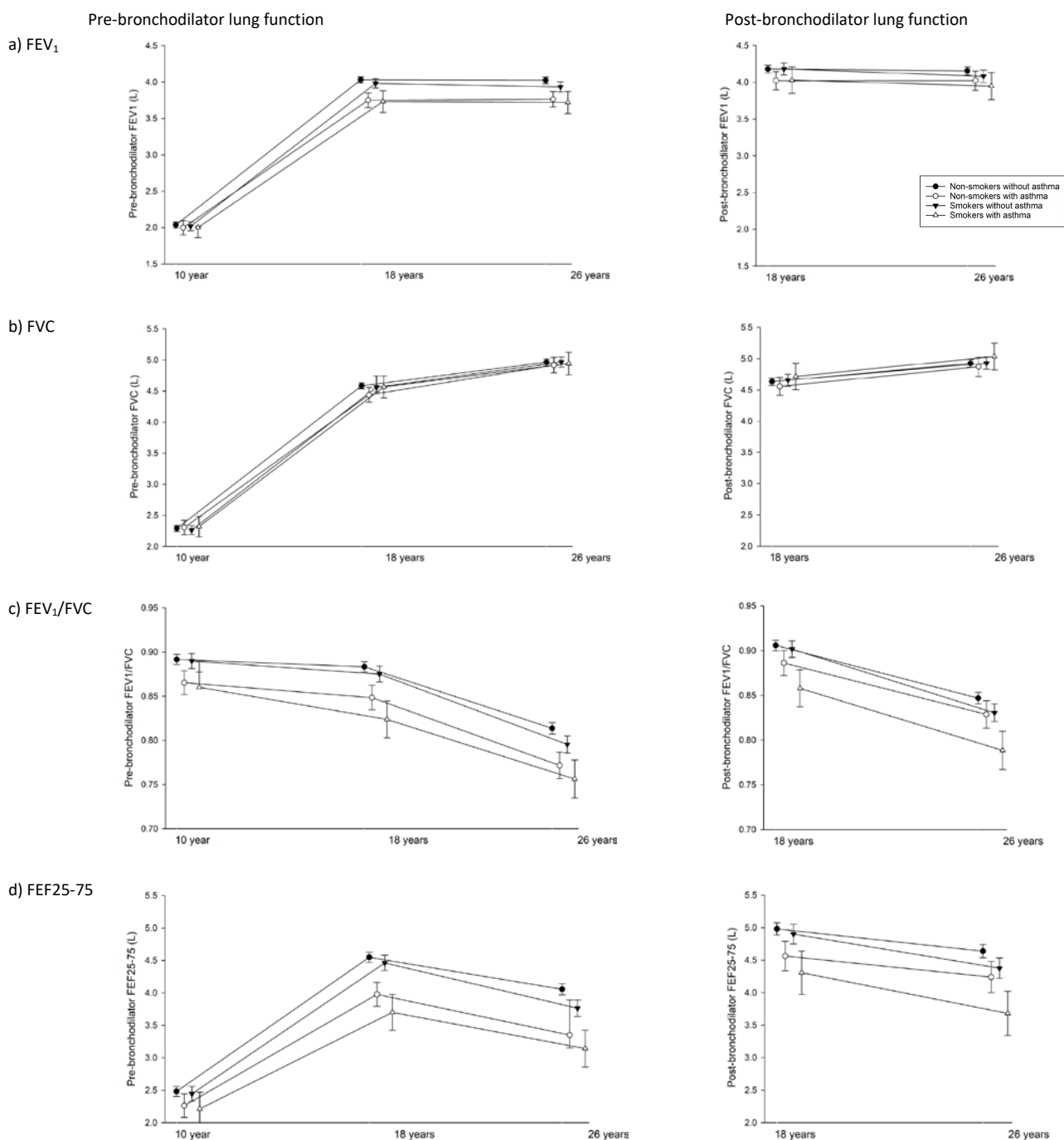
Figures are means (standard deviations). Data represent crude data. Lung function was only repeated after bronchodilator at 18 and 26 year assessments.

Table S4. Lung function at 26 year by parental smoking at birth

	Parental smoking at birth					No parental smoking at birth			
Pre-bronchodilator									
	FEV ₁	FEV ₁ /FVC	FEF ₂₅₋₇₅	FVC		FEV ₁	FEV ₁ /FVC	FEF ₂₅₋₇₅	FVC
Non-smokers without asthma	3.98 (3.89, 4.07)	0.810 (0.798, 0.822)	3.96 (3.79, 4.13)	4.94 (4.83, 5.04)		4.03 (3.96, 4.09)	0.816 (0.807, 0.824)	4.09 (3.96, 4.21)	4.96 (4.88, 5.04)
Non-smokers with asthma	3.46 (3.23, 3.69)	0.755 (0.724, 0.786)	2.96 (2.62, 3.40)	4.61 (4.33, 4.88)		3.85 (3.71, 4.00)	0.777 (0.758, 0.796)	3.47 (3.19, 3.74)	4.99 (4.82, 5.17)
Smokers without asthma	3.83 (3.71, 3.95)	0.788 (0.773, 0.804)	3.63 (3.40, 3.85)	4.89 (4.75, 5.03)		4.02 (3.92, 4.13)	0.801 (0.787, 0.815)	3.89 (3.68, 4.09)	5.04 (4.91, 5.17)
Smokers with asthma	3.63 (3.40, 3.87)	0.770 (0.739, 0.801)	3.16 (2.71, 3.60)	4.73 (4.45, 5.01)		3.90 (3.62, 4.18)	0.737 (0.700, 0.773)	3.12 (2.60, 3.65)	5.33 (5.00, 5.67)
Post-bronchodilator									
Non-smokers without asthma	4.13 (4.03, 4.22)	0.845 (0.834, 0.856)	4.55 (4.37, 4.72)	4.90 (4.79, 5.01)		4.16 (4.09, 4.23)	0.847 (0.839, 0.855)	4.68 (4.55, 4.81)	4.93 (4.84, 5.00)
Non-smokers with asthma	3.69 (3.43, 3.95)	0.802 (0.771, 0.833)	3.54 (3.06, 4.03)	4.63 (4.33, 4.92)		4.12 (3.97, 4.27)	0.839 (0.821, 0.856)	4.47 (4.20, 4.75)	4.93 (4.75, 5.10)
Smokers without asthmas	3.95 (3.83, 4.08)	0.822 (0.808, 0.837)	4.14 (3.92, 4.37)	4.83 (4.69, 4.97)		4.20 (4.09, 4.32)	0.838 (0.824, 9.851)	4.60 (4.39, 4.81)	5.02 (4.89, 5.15)
Smokers with asthma	3.84 (3.60, 4.08)	0.798 (0.769, 0.826)	3.64 (3.19, 4.09)	4.84 (4.56, 5.11)		4.10 (3.81, 4.39)	0.763 (0.730, 0.797)	3.61 (3.07, 4.14)	5.40 (5.06, 5.74)

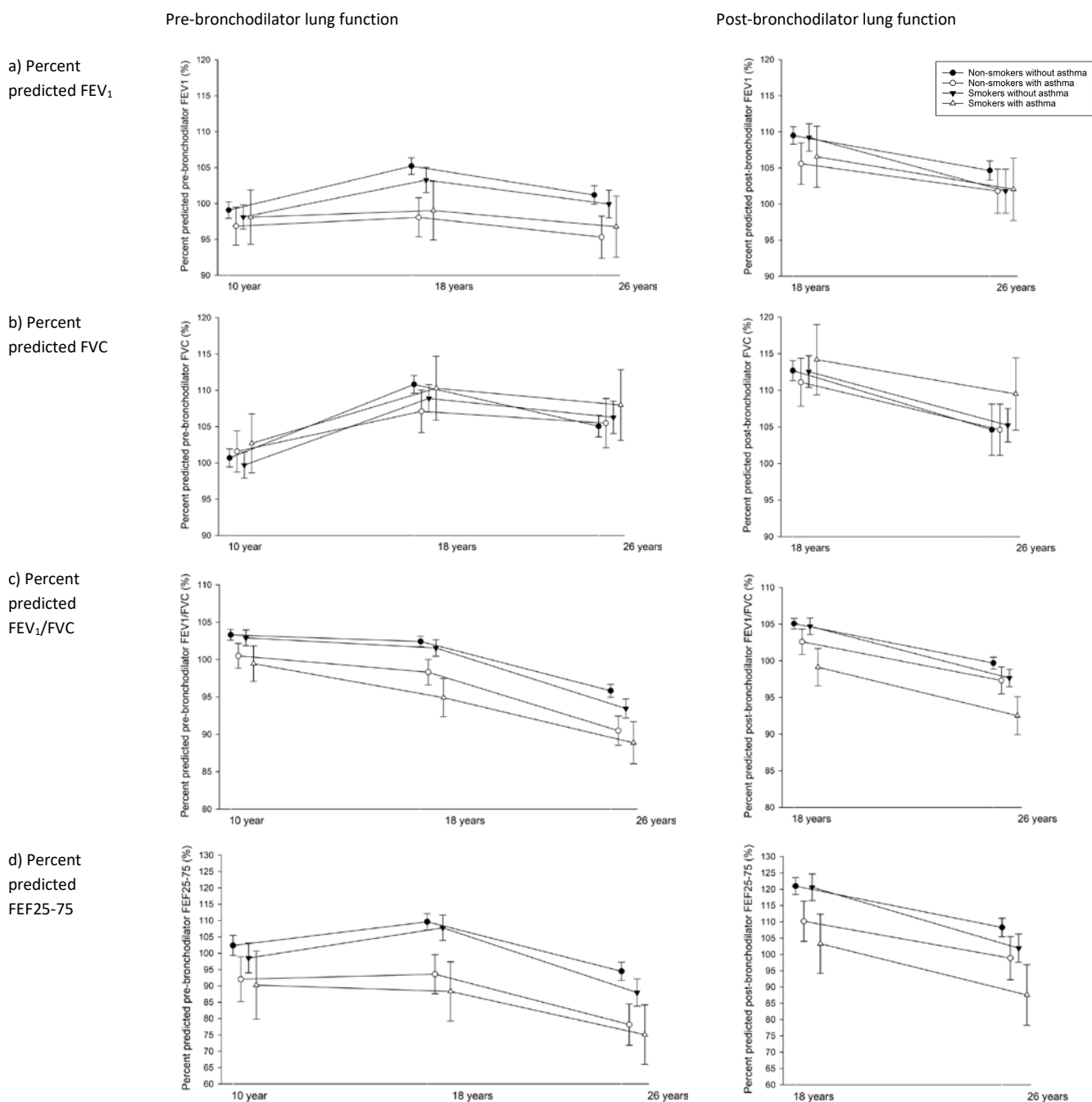
Figures describe the mean value of each lung function parameter at 26 years of age in smokers with asthma (open triangle), non-smokers with asthma (open circles), Smokers without asthma (closed triangle) and non-smokers without asthma (closed circles) from longitudinal models. Data are split between those who were and were not exposure to parental smoking in early life. Data generated from a GEE longitudinal model with parameters adjusted for sex. Values represent means (95% confidence intervals). Data from 454 participants; post-bronchodilator results available for 428 participants.

Figure S1: Lung Function Parameters at 10, 18 and 26 years of age by asthma and smoking status



Figures describe the mean value of each lung function parameter at 10, 18 and 26 years of age in Smokers with asthma (open triangle), Non-smokers with asthma (open circles), Smokers without asthma (closed triangle) and Non-smokers without asthma (closed circles). Data generated from a GEE longitudinal model with parameters adjusted for sex. Points represent means with 95% confidence intervals. Post-bronchodilator parameters only available at 18 and 26 years. Data from 10 to 26 years represents results available for 401 participants with data at each point; post-bronchodilator results available for 428 participants.

Figure S2: Percent predicted lung function parameters at 10, 18 and 26 years of age by asthma and smoking status



Figures describe the mean value of each percent predicted lung function parameter at 10, 18 and 26 years of age in Smokers with asthma (open triangle), Non-smokers with asthma (open circles), Smokers without asthma (closed triangle) and Non-smokers without asthma (closed circles). Data generated from a GEE longitudinal models. Points represent means with 95% confidence intervals. Post-bronchodilator parameters only available at 18 and 26 years. Data from 10 to 26 years represents results available for 401 participants with data at each point; post-bronchodilator results available for 428 participants.