Factors associated with changes in lung function between one month and 18 years of age

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Supplementary material

STATISTICAL METHODS

Initially univariate models were fitted for each variable maternal asthma (yes or no), flow limitation (yes or no), maternal smoking (yes or no), atopic infant (yes or no) and gender (male or female) followed by a multivariable model including all variables as fixed effects alongside time. Random effects included patient and patient*time to allow for varying slopes and intercepts for each participant. Finally a model was produced which included all variables as main effects and their interactions with time. This allowed us to see if the variable influenced the profile of lung function over time. The estimate statement in SAS provided estimates of difference between groups at particular ages including interaction terms. All models were based on 242 participants due to missing data for flow limitation (10 participants) and maternal smoking (1 participant); due to missing data for asthma ever (82 participants), results are presented with and without this variable.

	Change in % V'maxFRC/FEV$_1$ associated with variable (univariate analysis)	Change in % V'maxFRC/FEV$_1$ associated with variable (multivariable analysis)	Change in % V'maxFRC/FEV$_1$ associated with variable (multivariable analysis including asthma history term)
Maternal asthma	-5.1 [-9.5, -0.8] *p=0.019*	-5.7 [-9.9, -1.4] *p=0.008*	-5.4 [-9.8, -0.9] *p=0.020*
Flow limitation	-2.9 [-9.7, +4.0] *p=0.411*	-3.7 [-10.2, +2.9] *p=0.271*	-0.5 [-7.7, +6.7] *p=0.900*
Infant atopy	-6.3 [-11.4, -1.2] *p=0.015*	-6.9 [-11.8, -2.0] *p=0.006*	-6.0 [-11.1, -0.9] *p=0.021*
Maternal smoker during pregnancy	-4.5 [-8.9, -0.2] *p=0.040*	-4.5 [-8.7, -0.3] *p=0.034*	-4.6 [-9.1, -0.1] *p=0.047*
Male Sex	+4.5 [+1.0,+8.0] *p=0.011*	+3.9 [+0.5, +7.3] *p=0.024*	+4.5 [+1.0,+8.1] *p=0.012*
Asthma ever	-3.2 [-6.9, +0.5] *p=0.090*		-2.5 [-6.2, +1.2] *p=0.177*

Table E1. Mean change [95% confidence interval] in % predicted lung function measured at ages one, six and twelve months and six twelve and eighteen years associated with variables listed in the left hand column. This model included FEV$_1$ as the spirometric measurements made after infancy. Models in the second column were univariate, models in the third column were multivariable (excluding asthma ever where data were missing in 81 individuals) whilst those in the fourth right hand column included all variables.

	Change in % V'maxFRC/FVC associated with variable (univariate analysis)	Change in % V'maxFRC/ FVC associated with variable (multivariable analysis)	Change in % V'maxFRC/FVC associated with variable (multivariable analysis including asthma history term)
Maternal asthma	-2.8 [-7.0, +1.4] *p=0.188*	-3.2 [-7.3, +0.8] *p=0.114*	-3.1 [-7.4, +1.2] *p=0.154*
Flow limitation	-3.7 [-10.3, +2.9] *p=0.268*	-4.1 [-10.4, +2.2] *p=0.205*	-2.1 [-9.0, +4.9] *p=0.557*
Infant atopy	-4.9 [-9.8, -0.0] *p=0.049*	-5.2 [-10.0, -0.6] *p=0.028*	-4.4 [-9.3, +0.4] *p=0.075*
Maternal smoker during pregnancy	-4.2, [-8.4, -0.1] *p=0.047*	-4.0 [-8.0, +0.0] *p=0.052*	-4.0 [-8.3, -0.4] *p=0.076*
Male Sex	+5.9 [+2.6, +9.2] *p<0.001*	+5.3 [+2.0, +8.5] *p=0.002*	+6.1 [+2.7,+9.5] *p<0.001*
Asthma ever	-1.9 [-5.5, +1.7] *p=0.303*		-1.3 [-4.9, +2.2] *p=0.471*

Table E2. Mean change [95% confidence interval] in % predicted lung function measured at ages one, six and twelve months and six twelve and eighteen years associated with variables listed in the left hand column. This model included FVC as the spirometric measurements made after infancy. Models in the second column were univariate, models in the third column were multivariable (excluding asthma ever where data were missing in 81 individuals) whilst those in the fourth right hand column included all variables.

	Effect size (95% confidence intervals) on percentage of predicted lung function measurements made between one month and eighteen years						p value for interaction term with time
	One month (V'maxFRC)	Six months (V'max FRC)	Twelve months (V'MaxFRC)	Six years (FEV$_1$)	Twelve years (FEV$_1$)	Eighteen years (FEV$_1$)	
Maternal asthma	-10.1 [-20.5, +0.3]	-9.9 [-20.1, +0.3]	-9.8 [-19.6, +0.1]	-8.1 [-14.7, -1.5]	-6.2 [-10.4, -1.9]	-4.2 [-9.8, +1.5]	0.386
Flow limitation	-43.8 [-58.3, -29.3]	-42.5 [-56.6, -28.4]	-40.8 [-54.4, -27.1]	-23.9 [-33.1, -14.7]	-3.6 [-10.1, +2.8]	+16.6 [+7.4, +26.4]	<0.001
Infant atopy	-15.3 [-27.7, -2.8]	-15.0 [-27.1, -2.8]	-14.7 [-26.4, -2.9]	-11.3 [-19.2, -3.4]	-7.2 [-12.2, 2.3]	-3.2 [-9.4, +3.4]	0.138
Maternal smoker during pregnancy	-16.9 [-26.5, -7.4]	-16.5 [-25.8, -7.2]	-16.0 [-25.0, -7.0]	-10.9 [-17.0, -4.8]	-4.8 [-8.9, -0.7]	+1.3 [-4.4, +6.9]	0.005
Male Sex	-10.2 [-18.6, -1.7]	-9.7 [-18.0, -1.5]	-9.2 [-17.1, -1.2]	-3.6 [-8.9, +1.8]	+3.2 [-0.2, +6.6]	+9.9 [+5.4, +14.5]	0.0003

TableE3. Estimate [95% confidence interval] of effect of maternal asthma, flow limitation, infant atopy, maternal smoking and male sex on measurements of lung function (maximal flow at functional residual capacity in infancy, V'maxFRC, and FEV$_1$ in childhood) made between ages one month and eighteen years.

	Effect size (95% confidence intervals) on percentage of predicted lung function measurements made between one month and eighteen years						P value for interaction term with time
	One month (V'maxFRC)	Six months (V'max FRC)	Twelve months (V'MaxFRC)	Six years (FVC)	Twelve years (FVC)	Eighteen years (FVC)	
Maternal asthma	-10.1 [-20.5, +0.3]	-9.9 [-20.0, +0.2]	-9.6 [-19.4, +0.1]	-6.9 [-13.3, -0.5]	-3.7 [-7.7, +0.4]	-0.4 [-6.3, +5.5]	0.171
Flow limitation	-42.8 [-57.2, -28.3]	-41.5 [-55.5, -27.4]	-39.8 [-53.4, -26.2]	-23.1 [-32.1, -14.1]	-3.1 [-9.4, +3.1]	+16.9 [+7.4, +26.3]	<0.001
Infant atopy	-15.5 [-28.0, -3.1]	-15.2 [-27.3, -3.1]	-14.8 [-26.5, -3.1]	-10.6 [-18.3, -2.9]	-5.5 [-10.2, -0.8]	-0.4 [-7.3, +6.4]	0.074
Maternal smoker during pregnancy	-17.1 [-26.6, -7.5]	-16.6 [-25.9, -7.3]	-16.0 [-25.0, -7.1]	-10.6 [-16.5, -4.7]	-4.0 [-8.0, 0]	+2.6 [-3.3, +8.4]	0.003
Male Sex	-10.3 [-18.7, -1.8]	-9.8 [-18.0, -1.6]	-9.1 [-17.0, -1.2]	-2.8 [-8.0, +2.5]	+4.9 [+1.6, +8.1]	+12.5 [+7.8, +17.3]	<0.001

TableE4. Estimate [95% confidence interval] of effect of maternal asthma, flow limitation, infant atopy, maternal smoking and male sex on measurements of lung function (maximal flow at functional residual capacity in infancy, V'maxFRC, and FVC in childhood) made between ages one month and eighteen years.

	Flow limited at one month	Not flow limited at one month
Mean height (SD), cm	176 (11) n=9	173 (9) n=126
Mean age (SD), years	19.1 (1.1) n=13	18.8 (1.2) n=130
Mean FEV_1 (SD), l	4.6 (0.8) n=9	4.2 (0.9) n=125
Mean % FEV_1 (SD)	*109 (12)*	*104 (12)*
Mean FVC (SD), l	5.4 (0.9) n=9	4.9 (1.1) n=125
Mean % FVC (SD)	*107 (9)*	*103 (12)*
Mean FEF_{25-75}(SD), l/s	4.9 (1.1) n=9	4.6 (1.2) n=125
Mean % FEF_{25-75} (SD)	*109 (25)*	*106 (24)*
Skin prick positive	44% (4/9)	48% (61/126)
Wheeze in the past 12 months	50% (6/12)*	23% (30/130)
Doctor diagnosed asthma	31% (4/13)	12% (15/130)
Current smoker	33% (4/12)	23% (29/129)

Table E5. Comparison of outcomes at eighteen years of age in individuals with expiratory flow limitation at one month of age with other cohort members.*p<0.05 compared to those without flow limitation.

	Effect size (95% confidence intervals) on percentage of predicted lung function measurements made between one month and eighteen years						P value for interaction term with time
	One month (V'maxFRC)	Six months (V'maxFRC)	Twelve months (V'maxFRC)	Six years (FEF$_{25-75}$)	Twelve years (FEF$_{25-75}$)	Eighteen years (FEF$_{25-75}$)	
Maternal asthma	-8.8 [-22.0, +4.4]	-8.8 [-21.7, +4.1]	-8.8 [-21.4, +3.7]	-8.8 [-18.1, +0.4]	-8.9 [-16.4, -1.3]	-8.9 [-18.3, +0.6]	0.995
Flow limitation	-43.0 [-61.6, -24.4]	-41.8 [-59.9, -23.7]	-40.2 [-57.9, -22.7]	-25.0 [-38.1, -11.9]	-6.7 [-18.0, +4.7]	+11.7 [-3.3, +26.7]	<0.001
Infant atopy	-13.9 [-28.5, +0.6]	-13.8 [-28.1, +0.4]	-13.7 [-27.6, +0.1]	-12.6 [-22.8, -2.3]	-11.2 [-19.6, -2.7]	-9.8 [-20.4, +0.8]	0.655
Maternal smoker during pregnancy	-21.1 [-34.4, -7.9]	-20.7 [-33.6, -7.8]	-20.1 [-32.7, -7.6]	-14.4 [-23.6, -5.1]	-7.4 [-15.0, +0.2]	+0.5 [-10.0, +9.0]	0.016
Male Sex	-13.0 [-23.7, -2.4]	-12.6 [-22.9, -2.2]	-12.0 [-22.1, -1.9]	-6.4 [-13.8, +1.1]	+0.4 [-5.6, +6.4]	+7.2 [-0.3, +14.7]	0.003
Asthma ever	-9.4 [-20.1, +1.4]	-9.3 [-19.8, +1.2]	-9.1 [-19.3, +1.1]	-7.6 [-15.1, -0.1]	-5.8 [-11.9, +0.4]	-3.9 [-11.7, +3.9]	0.428

Table E6. Estimate [95% confidence interval] of effect of maternal asthma, flow limitation, infant atopy, maternal smoking, male sex and a history of asthma ever on measurements of lung function (maximal flow at functional residual capacity in infancy, V'maxFRC, and FEF$_{25-75}$ in childhood) made between ages one month and eighteen years. This analysis is based on 172 individuals in whom asthma ever was determined.

	Effect size (95% confidence intervals) on percentage of predicted lung function measurements made between one month and eighteen years						P value for interaction term with time
	One month (V'maxFRC)	Six months (V'max FRC)	Twelve months (V'MaxFRC)	Six years (FEF $_{25-75}$)	Twelve years (FEF $_{25-75}$)	Eighteen years (FEF $_{25-75}$)	
Highest 23 V'maxFRC values at one month	+64.1 [+50.5, +77.8]	+62.5 [+49.2, +75.8]	+60.5 [+47.5, +73.5]	+40.3 [+30.4, +50.3]	+16.1 [+7.1, +25.1]	-8.1 [-19.6, +3.4]	<0.001

TableE7. Estimate [95% confidence interval] for lung function (maximal flow at functional residual capacity in infancy, V'maxFRC, and FEF $_{25-75}$ in childhood) over time among individuals with the highest 23 values of V'maxFRC at one month compared to other non-flow limited individuals.