Procedure to derive peak height and weight velocities and adiposity peak

Peak height and weight velocities Peak height velocity (PHV) and peak weight

velocity (PWV) were derived from postnatal growth data using the Reed1 model for

boys and girls separately using the previously described procedure (1, 2). The Reed1

model was chosen since it showed a better fit to the early growth data than the Kouchi,

Carlberg, and Count models, and it showed an equally good fit to the Reed2 model

which has one more parameter than the Reed1 model (3). The difference compared with

the simpler models, for example, the Count model, is that the Reed1 model allows the

velocity to peak after birth, whereas other models force it to peak at birth. In the first

couple of weeks after birth, weight may drop up to 10% in normal individuals. The

PWV is thus usually not in the first weeks after birth, but slightly later. Therefore, the

Reed1 model is more realistic (especially for weight) and more flexible. The Reed1

model was fitted by sex on all height and weight measurements taken at 0-3 years of

age, including birth weight. We assumed both a fixed and a random component for all

our parameters in the model. For each person, the first derivative of the fitted distance

curve was taken to obtain the height and weight velocity curves. Subsequently, the

maximum of these curves was taken to obtain the PHV and the PWV in infancy. The

Reed1 model is a four-parameter extension of the three-parameter Count model and its

functional form is (3, 4): $Y = A + Bt + C\ln(t) + D/t$

Since this model is not defined at birth (t=0), it was modified for this study in the same

way as in Simondon et al.: $Y = A + Bt + C\ln(t+1) + D/(t+1)$ where t, postnatal age; Y,

height or weight reached at age t and A, B, C, and D the function parameters. Of the

function parameters, A is related to the baseline height or weight at birth, B to the linear

component of the growth velocity over time, and D to the inflection point that allows growth velocity to peak after birth rather than exactly at birth. The Reed1 model is linear and its constants. Having two measurements was inadequate to capture the shape of the growth curve, and therefore, we restricted all association analyses to those with a minimum of three measurements per person.

Adiposity peak For body mass index at adiposity peak (BMIAP), a cubic mixed effects model was previously fitted on log(BMI) from 14 days to 1.5 years, using sex as a covariate (2). Modelization of body mass index growth was performed from the age of 14 days onward, since, as mentioned before, children may lose up to 10% of their body weight in the first 2 weeks of life. When fitting the model, age was centralized to 0.75 years. In addition to fixed effects, we included random effects for the constant and the slope in the model. An autoregressive within person correlation structure between measurements was assumed. Then, body mass index was derived for each individual at the point where the curve reaches its maximum, i.e. at infant adiposity peak.
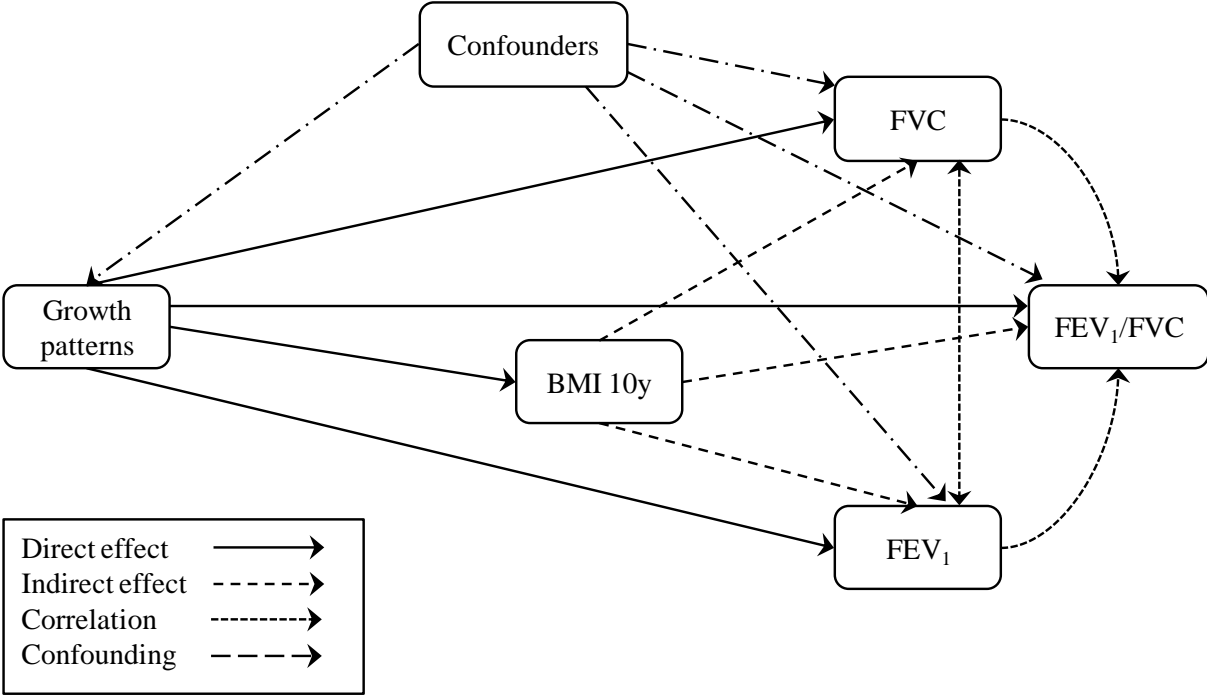
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Supplementary File Figure S1 Diagram showing the association of early childhood growth patterns and lung function and current asthma, including the potential confounders, effect modifiers, and potential mediators (dashed lines)
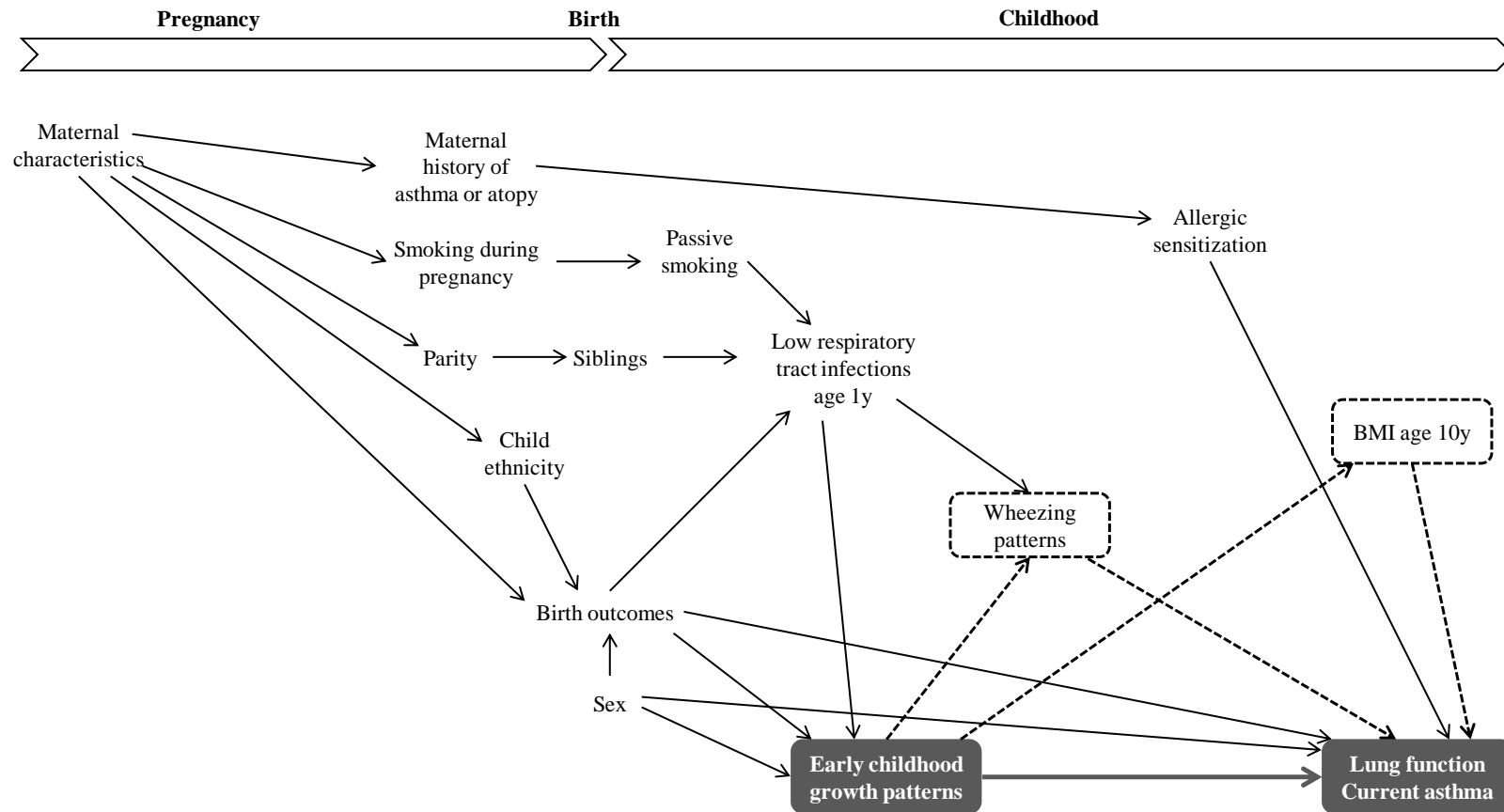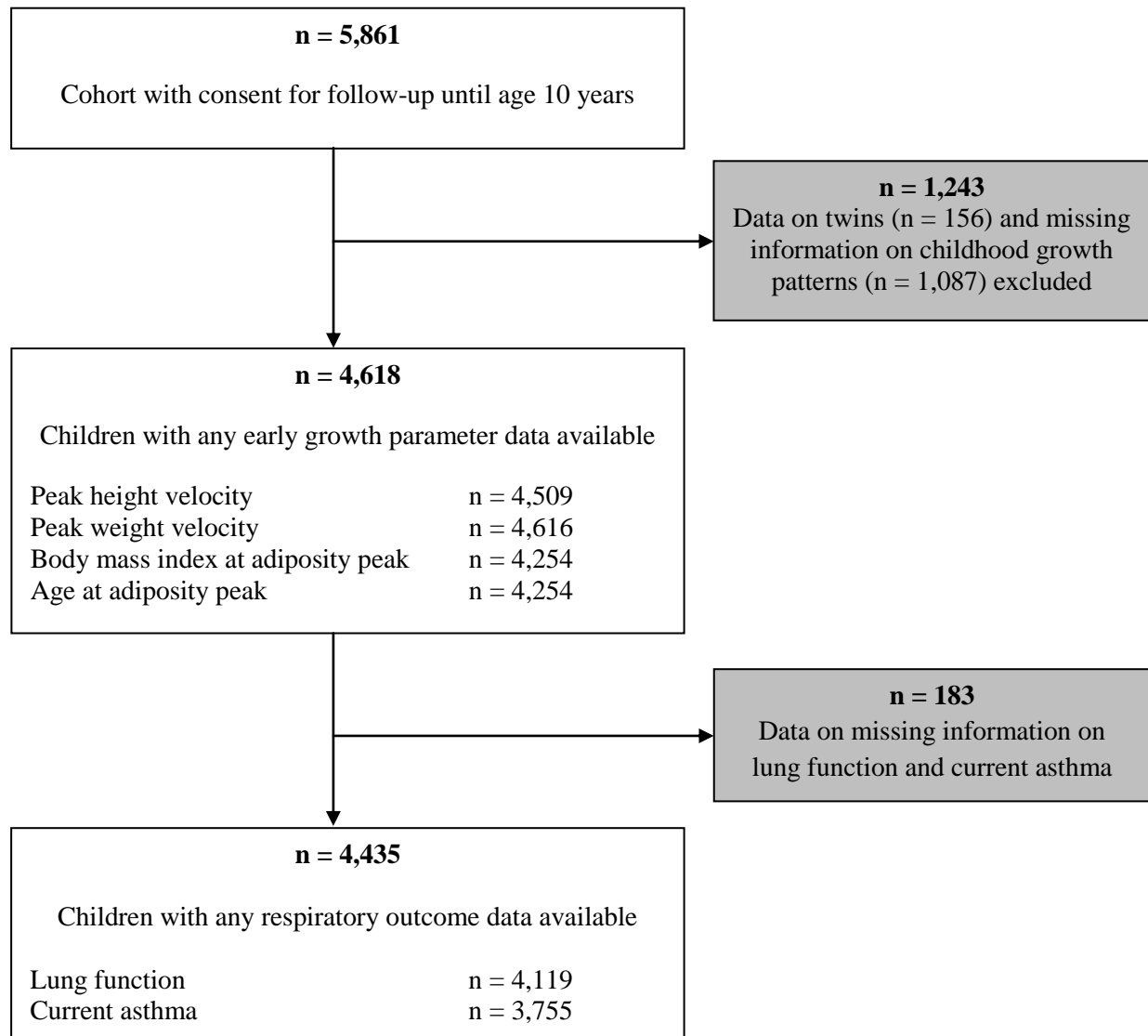

Maternal characteristics include: age at enrolment, pre-pregnancy body mass index, educational level, pet keeping, psychological distress during pregnancy, gestational diabetes, and gestational hypertensive disorders.

Supplementary File Figure S2 Structural equation model of the association of early

childhood growth patterns with lung function parameters

Supplementary File Figure S3 Flow chart of participants included for analysis

n = 5,861 Cohort with consent for follow-up until age 10 years	
↓ →	**n = 1,243** Data on twins (n = 156) and missing information on childhood growth patterns (n = 1,087) excluded
n = 4,618 Children with any early growth parameter data available	

n = 4,618

Children with any early growth parameter data available

Peak height velocity	n = 4,509
Peak weight velocity	n = 4,616
Body mass index at adiposity peak	n = 4,254
Age at adiposity peak	n = 4,254

n = 183
Data on missing information on lung function and current asthma

n = 4,435

Children with any respiratory outcome data available

Lung function	n = 4,119
Current asthma	n = 3,755

Supplementary File Table S1 Difference in characteristics between subjects included and not included in the study

	Included n = 4,435	Not included n = 1,426	*P*-value differences
Maternal characteristics			
Age at enrolment (years)	31.4 (4.7)	29.8 (5.5)	<0.01
Pre-pregnancy body mass index (kg/m^2)	24.4 (4.2)	25.5 (4.6)	<0.01
Educational level			
Primary or secondary	44.8	66.4	<0.01
Higher	55.2	33.6	
History of asthma or atopy, yes	44.9	45.0	0.98
Pet keeping, yes	33.3	33.4	0.95
Psychological distress during pregnancy, yes	7.2	13.0	<0.01
Parity, multiparous	42.0	46.0	0.01
Smoked during pregnancy, yes	22.6	27.1	<0.01
Gestational hypertensive disorders, yes	4.1	4.5	0.61
Gestational diabetes, yes	0.7	2.2	<0.01
Infant characteristics			
Sex, female	50.3	49.9	0.77
Gestational age (weeks)[1]	40.1 (26.7-43.4)	39.9 (26.3-43.6)	<0.01
Birth weight (g)	3456 (543)	3262 (640)	<0.01
Ethnicity, non-European	28.5	45.1	<0.01
Breastfeeding, never	7.6	7.2	0.75
Day care attendance age 1 year, yes	63.2	50.3	<0.01
Lower respiratory tract infections age 1 year, yes	13.2	16.0	0.14
Passive smoking age 1 year, yes	16.1	18.0	0.32
Child characteristics			
Age at the time of respiratory outcomes (years)	9.8 (0.3)	9.8 (0.5)	<0.01
Body mass index at age 10 years (z-score)	0.2 (1.0)	0.4 (1.1)	<0.01

Values are percentages for categorical variables and means (SD) or median (range)[1] for continuous variables. Non-imputed data. *P*-value (included vs. excluded) was estimated by using One-Way Anova, Wilcoxon, or Chi-square tests.

Supplementary File Table S2 Effect modification by child's sex, maternal history of asthma or atopy, preterm birth, small for gestational age, and inhalant allergic sensitization of the association of early childhood growth patterns with lung function and current asthma

	Child's sex p-value for interaction	Maternal history of asthma or atopy p-value for interaction	Preterm birth p-value for interaction	Small for gestational age p-value for interaction	Child's inhalant allergic sensitization p-value for interaction
FVC					
PHV	0.557	0.907	0.871	0.024	0.413
PWV	0.251	0.906	0.687	0.041	0.544
BMIAP	0.053	0.833	0.978	0.095	0.849
AGEAP	0.001	0.417	0.726	0.641	0.440
FEV$_1$					
PHV	0.352	0.947	0.455	0.084	0.692
PWV	0.215	0.322	0.825	0.275	0.724
BMIAP	0.041	0.867	0.994	0.330	0.534
AGEAP	<0.001	0.409	0.239	0.319	0.597
FEV$_1$/FVC					
PHV	0.530	0.777	0.561	0.477	0.344
PWV	0.869	0.098	0.938	0.146	0.680
BMIAP	0.943	0.754	0.988	0.229	0.264
AGEAP	0.578	0.839	0.312	0.031	0.789
FEF$_{75}$					
PHV	0.684	0.857	0.503	0.996	0.322
PWV	0.711	0.147	0.680	0.248	0.296
BMIAP	0.543	0.747	0.700	0.495	0.152
AGEAP	0.164	0.567	0.471	0.014	0.518
Current asthma					
PHV	0.437	0.236	0.991	0.204	0.844
PWV	0.536	0.105	0.430	0.773	0.299
BMIAP	0.657	0.031	0.336	0.730	0.129
AGEAP	0.033	0.535	0.291	0.624	0.002

PHV, peak height velocity; PWV, peak weight velocity; BMIAP, body mass index at adiposity peak; AGEAP, age at adiposity peak.

Supplementary File Table S3 Sequential adjustment of the association of early childhood growth patterns with lung function and current asthma in the overall population

	Minimally adjusted model	+ Maternal characteristics	+ Socioeconomic characteristics	+ Maternal history of asthma or atopy	+ Maternal psychological distress during pregnancy	+ Birth outcomes	+ Child characteristics - Fully adjusted model
FVC							
PHV	-0.00 (-0.01, -0.00)	-0.00 (-0.01, 0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)
PWV	0.04 (0.02, 0.05)	0.04 (0.02, 0.05)	0.03 (0.01, 0.04)	0.03 (0.01, 0.04)	0.03 (0.01, 0.04)	0.03 (0.02, 0.05)	0.03 (0.02, 0.05)
BMIAP	0.18 (0.15, 0.22)	0.18 (0.14, 0.22)	0.17 (0.13, 0.20)	0.17 (0.13, 0.20)	0.17 (0.13, 0.20)	0.14 (0.10, 0.18)	0.15 (0.11, 0.19)
AGEAP	-0.03 (-0.07, 0.01)	-0.03 (-0.07, 0.01)	-0.00 (-0.05, 0.04)	-0.00 (-0.05, 0.04)	-0.00 (-0.05, 0.04)	0.02 (-0.02, 0.07)	0.02 (-0.02, 0.06)
FEV1							
PHV	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)
PWV	0.01 (-0.01, 0.02)	0.01 (-0.01, 0.02)	-0.00 (-0.02, 0.01)	-0.00 (-0.02, 0.01)	-0.00 (-0.02, 0.01)	0.00 (-0.01, 0.02)	0.00 (-0.01, 0.02)
BMIAP	0.12 (0.08, 0.16)	0.11 (0.07, 0.15)	0.10 (0.06, 0.14)	0.10 (0.06, 0.14)	0.10 (0.05, 0.14)	0.06 (0.02, 0.10)	0.06 (0.02, 0.10)
AGEAP	-0.00 (-0.05, 0.04)	0.01 (-0.04, 0.05)	0.03 (-0.01, 0.08)	0.03 (-0.01, 0.08)	0.03 (-0.01, 0.08)	0.07 (0.02, 0.11)	0.07 (0.02, 0.11)
FEV1/FVC							
PHV	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)	-0.00 (-0.01, 0.00)
PWV	-0.05 (-0.07, -0.03)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.03)
BMIAP	-0.11 (-0.15, -0.07)	-0.13 (-0.17, -0.09)	-0.13 (-0.17, -0.09)	-0.13 (-0.17, -0.09)	-0.13 (-0.17, -0.09)	-0.15 (-0.19, -0.10)	-0.15 (-0.19, -0.10)
AGEAP	0.03 (-0.01, 0.08)	0.05 (0.00, 0.09)	0.06 (0.01, 0.10)	0.06 (0.01, 0.10)	0.06 (0.01, 0.10)	0.06 (0.02, 0.11)	0.06 (0.02, 0.11)
FEF75							
PHV	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, -0.00)	-0.01 (-0.01, 0.00)
PWV	-0.04 (-0.05, -0.02)	-0.04 (-0.05, -0.02)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.07, -0.04)	-0.05 (-0.06, -0.03)	-0.05 (-0.06, -0.03)
BMIAP	-0.05 (-0.08, -0.01)	-0.06 (-0.10, -0.02)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.07 (-0.11, -0.03)	-0.10 (-0.14, -0.06)	-0.09 (-0.13, -0.05)

AGEAP	0.02 (-0.02, 0.06)	0.04 (-0.00, 0.08)	0.07 (0.02, 0.11)	0.07 (0.02, 0.11)	0.07 (0.02, 0.11)	0.08 (0.04, 0.12)	0.08 (0.04, 0.12)
Current asthma							
PHV	1.01 (0.99, 1.02)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)	1.00 (0.99, 1.02)	1.00 (0.98, 1.01)	1.00 (0.98, 1.01)
PWV	1.03 (0.97, 1.10)	1.03 (0.96, 1.09)	1.01 (0.95, 1.08)	1.02 (0.96, 1.09)	1.02 (0.96, 1.09)	1.01 (0.95, 1.08)	1.00 (0.94, 1.07)
BMIAP	1.14 (0.97, 1.34)	1.12 (0.95, 1.33)	1.11 (0.94, 1.32)	1.13 (0.96, 1.34)	1.14 (0.96, 1.34)	1.12 (0.94, 1.34)	1.09 (0.91, 1.30)
AGEAP	0.85 (0.71, 1.01)	0.86 (0.72, 1.03)	0.88 (0.73, 1.05)	0.88 (0.73, 1.06)	0.88 (0.73, 1.06)	0.88 (0.73, 1.06)	0.88 (0.73, 1.07)

PHV, peak height velocity; PWV, peak weight velocity; BMIAP, body mass index at adiposity peak; AGEAP, age at adiposity peak. Values represent differences in odds-ratios with their 95% confidence intervals (CI) per standard deviation score increase in childhood growth patterns and were obtained from linear or logistic regression models. One s.d.s of PHV equals 8.4 cm/year, of PWV 2.1 kg/year, of BMIAP 0.8 kg/m^2, and of AGEAP 0.7 months (around 21 days). Models were adjusted for child's sex, age at the time of respiratory outcomes (Minimally adjusted model), maternal age at enrolment, pre-pregnancy BMI, parity (+ Maternal characteristics); maternal educational level, child's ethnicity, smoking during pregnancy (+ Socioeconomic characteristics); maternal history of asthma or atopy; maternal psychological distress during pregnancy; birth weight, gestational age (+ Birth outcomes); day care attendance, lower respiratory tract infections, and passive smoking at 1 year (+ Child characteristics – Fully adjusted model. This model is the one showed in Figure 1 of the main manuscript for the overall population).

Supplementary File Table S4 Associations of early childhood growth patterns with lung function and current asthma in the overall population, in boys, and in girls.

	Overall population			Boys			Girls		
	N	β (95% CI)	p-value	N	β (95% CI)	p-value	N	β (95% CI)	p-value
FVC									
PHV	4027	-0.00 (-0.01, 0.00)	0.253	1991	-0.00 (-0.01, 0.00)	0.267	2036	-0.00 (-0.01, 0.01)	0.832
PWV	4117	0.03 (0.02, 0.05)	<0.001	2036	0.03 (0.01, 0.05)	0.012	2081	0.04 (0.02, 0.06)	0.001
BMIAP	3795	0.15 (0.11, 0.19)	<0.001	1875	0.11 (0.06, 0.17)	<0.001	1920	0.18 (0.12, 0.24)	<0.001
AGEAP	3795	0.02 (-0.02, 0.06)	0.379	1875	0.09 (0.03, 0.15)	0.005	1920	-0.06 (-0.12, 0.01)	0.080
FEV1									
PHV	4027	-0.00 (-0.01, 0.00)	0.159	1991	0.00 (-0.01, 0.00)	0.103	2036	-0.00 (-0.01, 0.01)	0.919
PWV	4117	0.00 (-0.01, 0.02)	0,634	2036	-0.00 (-0.03, 0.02)	0.740	2081	0.01 (-0.01, 0.04)	0.247
BMIAP	3795	0.06 (0.02, 0.10)	0.004	1875	0.02 (-0.04, 0.08)	0.545	1920	0.10 (0.05, 0.16)	<0.001
AGEAP	3795	0.07 (0.02, 0.11)	0.005	1875	0.16 (0.09, 0.22)	<0.001	1920	-0.03 (-0.09, 0.03)	0.358
FEV1/FVC									
PHV	4027	-0.00 (-0.01, 0.00)	0.424	1991	-0.00 (-0.01, 0.00)	0.211	2036	0.00 (-0.01, 0.01)	0.917
PWV	4117	-0.05 (-0.07, -0.03)	<0.001	2036	-0.05 (-0.07, -0.03)	<0.001	2081	-0.05 (-0.07, -0.03)	<0.001
BMIAP	3795	-0.15 (-0.19, -0.10)	<0.001	1875	-0.16 (-0.22, -0.09)	<0.001	1920	-0.14 (-0.20, -0.08)	<0.001
AGEAP	3795	0.06 (0.02, 0.11)	0.007	1875	0.08 (0.02, 0.15)	0.016	1920	0.05 (-0.02, 0.11)	0.151
FEF75									
PHV	4027	-0.01 (-0.01, 0.00)	0.003	1991	-0.01 (-0.01, 0.00)	0.009	2036	-0.00 (-0.01, 0.00)	0.125
PWV	4117	-0.05 (-0.06, -0.03)	<0.001	2036	-0.05 (-0.07, -0.03)	<0.001	2081	-0.04 (-0.07, -0.02)	<0.001
BMIAP	3795	-0.09 (-0.13, -0.05)	<0.001	1875	-0.11 (-0.17, -0.05)	<0.001	1920	-0.08 (-0.13, -0.02)	0.009
AGEAP	3795	0.08 (0.04, 0.12)	<0.001	1875	0.11 (0.05, 0.17)	<0.001	1920	0.05 (-0.01, 0.11)	0.135

PHV	3688	1.00 (0.98, 1.01)	0.818	1816	1.00 (0.98, 1.02)	0.940	1872	0.99 (0.95, 1.02)	0.496
PWV	3753	1.00 (0.94, 1.07)	0.973	1844	0.98 (0.91, 1.06)	0.658	1909	1.04 (0.93, 1.17)	0.476
BMIAP	3501	1.09 (0.91, 1.30)	0.343	1725	1.14 (0.91, 1.43)	0.262	1776	1.05 (0.78, 1.40)	0.760
AGEAP	3501	0.88 (0.73, 1.07)	0.214	1725	0.75 (0.59, 0.96)	0.022	1776	1.15 (0.83, 1.59)	0.414

PHV, peak height velocity; PWV, peak weight velocity; BMIAP, body mass index at adiposity peak; AGEAP, age at adiposity peak. Values represent changes in z-scores with their 95% confidence intervals (CI) per standard deviation (s.d.s) increase in childhood growth patterns, and were obtained from linear or logistic regression models. One s.d.s of PHV equals 8.4 cm/year, of PWV 2.1 kg/year, of BMIAP 0.8 kg/m^2, and of AGEAP 0.7 months (around 21 days). Models were adjusted for maternal age at enrolment, pre-pregnancy BMI, educational level, history of asthma or atopy, psychological distress during pregnancy, parity, smoking during pregnancy, and child's sex (only the overall population models), gestational age, birth weight, ethnicity, day care attendance, lower respiratory tract infections, and passive smoking at 1 year, and age at the time of respiratory outcomes. Effect estimates are the same as in Figure 1.