Pubertal onset with adulthood lung function mediated by height growth in adolescence

Liang Li[1], Hongmei Zhang[1*], John W. Holloway[2], A. John Henderson[3], Susan Ewart[4], Caroline L. Relton[5], S. Hasan Arshad[6,7], Wilfried Karmaus[1]

Affiliations: [1] Division of Epidemiology, Biostatistics, and Environmental Health, School of Public Health, University of Memphis, Memphis, TN, USA. [2] Human Development and Health, Faculty of Medicine, University of Southampton, Southampton, UK. [3] Population Health Sciences, University of Bristol, Bristol, BS8 2BN, UK. [4] College of Veterinary Medicine, Michigan State University, East Lansing, MI, USA. [5] MRC Integrative Epidemiology Unit, University of Bristol, Bristol, BS8 2BN, UK. [6] Clinical and Experimental Sciences, Faculty of Medicine, University of Southampton, Southampton, SO16 6YD, UK. [7] The David Hide Asthma and Allergy Research Centre, St Mary's, Hospital, Parkhurst Road, Newport, Isle of Wight PO30 5TG, UK.

***Correspondence:** Hongmei Zhang, Division of Epidemiology, Biostatistics, and Environmental Health, School of Public Health, University of Memphis, Memphis, TN, USA. E-mail: hzhang6@memphis.edu

Supplementary materials

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S. 1. Sample sizes at each follow-up for the study variables.

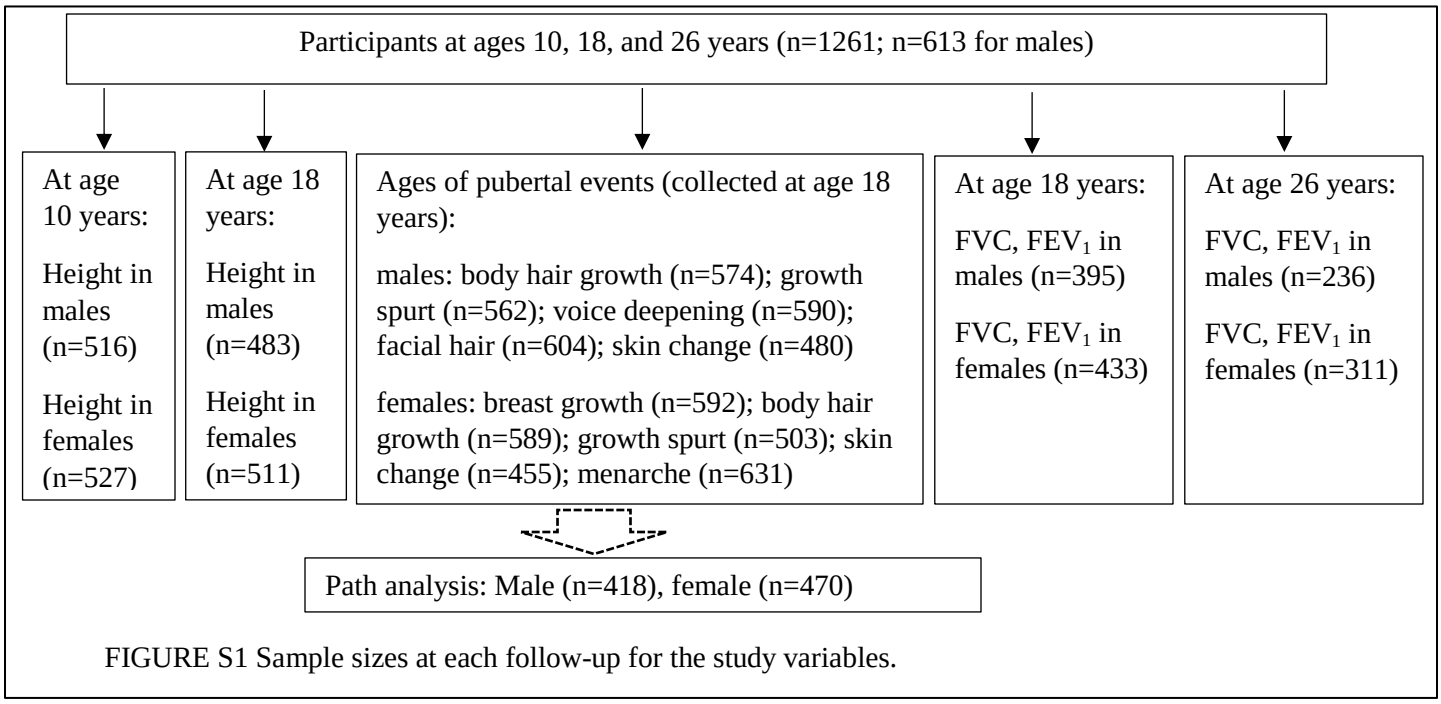

FIGURE S1 Sample sizes at each follow-up for the study variables.

S. 2. Identification of pubertal events and lung function parameters to be included in path analyses (Figure 1 in the main text).

To identify pubertal events and lung function parameters to be included in path analyses, we examined the association of ages at pubertal events onset with height growth during adolescence as well as their associations with three lung function parameters, FVC, FEV_1 at ages 18 and 26, using data in the IOW cohort. Statistical significance is set at 0.05.

For each gender, ages at five pubertal events were tested (Table S1) and our data showed statistically significant positive associations between ages of pubertal events and height growth for all the pubertal events in both genders. That is, the later the age of puberty, the larger the height growth between ages 10 and 18 years.

TABLE S1 The association of age of pubertal events and height growth from ages 10 to 18 years in the IOW cohort. Potential confounders adjusted in the model including asthma status at age 10 years, height

at age 10 years, BMI at age 10 years, SES at age 10 years, birth weight status, maternal smoking during pregnancy (Figure 1 in the main text)

Female			Male		
Pubertal events	Coeff. Estimate[#]	p-value	Pubertal events	Coeff. Estimate[#]	p-value
Breast growth	0.007	$\mathbf{7.57\times10^{-12}}$	Body hair growth	0.005	$\mathbf{2.13\times10^{-4}}$
Body hair growth	0.006	$\mathbf{2.25\times10^{-6}}$	Growth spurt	0.004	$\mathbf{1.34\times10^{-4}}$
Growth spurt	0.007	$\mathbf{8.79\times10^{-9}}$	Voice deepening	0.005	$\mathbf{1.04\times10^{-4}}$
Skin changes	0.005	$\mathbf{1.50\times10^{-4}}$	Facial hair	0.004	$\mathbf{8.37\times10^{-3}}$
Menarche	0.011	$\mathbf{1.34\times10^{-17}}$	Skin changes	0.003	$\mathbf{4.06\times10^{-2}}$

[#]: Coeff. Estimate: Regression coefficient estimates.

We next examined ages of these pubertal events on their associations with lung function parameters at ages 18 and 26 years in the IOW cohort.

In females, for lung function parameters measured at age 18 years, the associations of age at menarche with FVC and FEV_1 were statistically significant (Table S2). For age 26 years lung function parameters, ages of body hair growth and menarche onset showed statistically significant associations with FVC and FEV_1 (Table S3). For males, ages of body hair growth, growth spurt, voice deepening, and appearance of facial hair growth were associated with FVC at age 26 years. No other statistically significant associations were identified at these two ages.

Lung function parameters at ages 18 or 26 years and pubertal events showing statistically significant associations were included in path analyses. Specifically, FVC, FEV_1ages at body hair growth and menarche for females, and ages at body hair growth, growth spurt, voice deepening, and appearance of facial hair growth for males were included in subsequent path analyses (Tables S2 and S3).

TABLE S2 Estimated regression coefficients for the association of age of pubertal events onset with lung function at age 18 years in the IOW cohort. Potential confounders adjusted in the model including Asthma status at age 10 years, height at age 10 years, BMI at age 10 years, SES at age 10 years, birth weight status, maternal smoking during pregnancy (Figure 1 in the main text)

Female				Male		
Lung function	Pubertal events	Coeff. Estimate[#]	p-value	Pubertal events	Coeff. Estimate[#]	p-value
FVC	Breast growth	0.000	0.998	Body hair growth	0.017	0.546
	Body hair growth	0.030	0.096	Growth spurt	0.013	0.607
	Growth spurt	0.017	0.327	Voice deepening	0.016	0.601
	Skin changes	0.021	0.280	Facial hair growth	0.054	0.096
	Menarche	0.046	**0.014**	Skin changes	0.025	0.411
FEV_1	Breast growth	0.007	0.605	Body hair growth	0.020	0.402
	Body hair growth	0.022	0.152	Growth spurt	0.013	0.535
	Growth spurt	0.018	0.225	Voice deepening	0.018	0.471
	Skin changes	0.008	0.611	Facial hair growth	0.030	0.285
	Menarche	0.033	**0.040**	Skin changes	0.007	0.782

[#]: Coeff. Estimate: Regression coefficient estimates, and the unit presented in litres(L).

TABLE S3 Estimated regression coefficients for the association of age of pubertal events with lung function at age 26 years in the IOW cohort. Potential confounders adjusted in the model including Asthma status at age 10 years, height at age 10 years, BMI at age 10 years, SES at age 10 years, birth weight status, maternal smoking during pregnancy, and smoking at age 18 years. (Figure 1 in the main text)

Female				Male		
Lung function	Pubertal events	Coeff. Estimate[#]	p value	Pubertal events	Coeff. Estimate[#]	p value
FVC	Breast growth	0.042	0.056	**Body hair growth**	0.099	**0.020**
	Body hair growth	0.055	**0.022**	**Growth spurt**	0.086	**0.021**
	Growth spurt	0.038	0.070	**Voice deepening**	0.115	**0.016**
	Skin changes	0.035	0.161	**Facial hair growth**	0.111	**0.029**
	Menarche	0.077	**0.001**	Skin changes	0.052	0.299
FEV_1	Breast growth	0.020	0.249	Body hair growth	0.052	0.171
	Body hair growth	0.044	**0.019**	Growth spurt	0.041	0.223
	Growth spurt	0.025	0.121	Voice deepening	0.055	0.205
	Skin changes	0.032	0.103	Facial hair growth	0.031	0.492
	Menarche	0.067	**0.000**	Skin changes	0.035	0.447

[#]: Coeff. Estimate: Regression coefficient estimates, and the unit presented in litres(L).

S. 3. Results on the mediation effects of height growth on the associations of age at pubertal events onset with lung function parameters in the IOW cohort, along with testing results in the ALSPAC cohort.

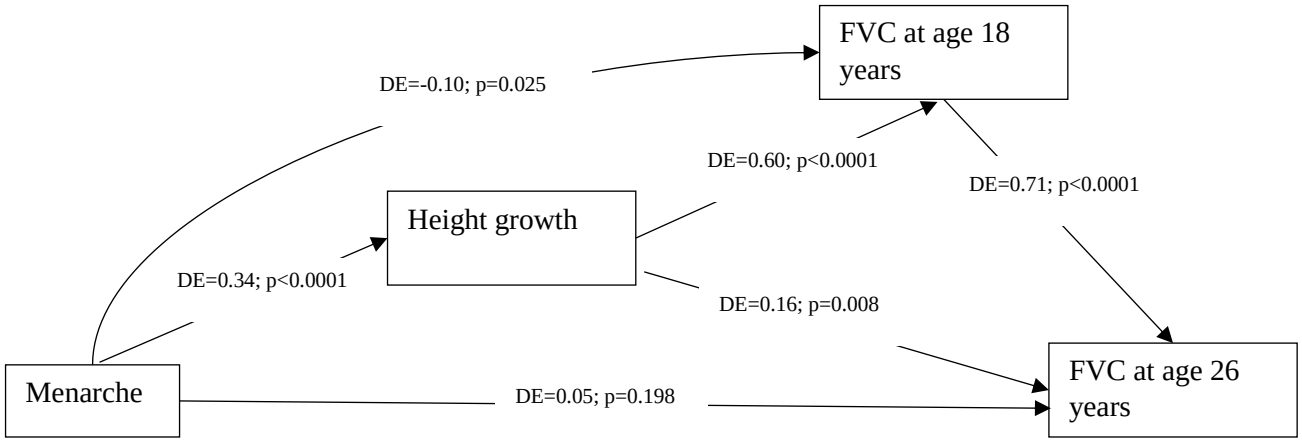

FIGURE S2 Estimated direct effects of each path (IOW), age at menarche and lung function parameter FVC.

The Principe of path (or mediation) analysis is to analyze that an initial variable X may influence an outcome variable Y through a mediating variable M or multiple mediators, such as M1, M2, et.al.
In our study, the X is age of onset of puberty; Y is lung function parameters at age 26 years; and M1 is height growth and M2 is lung function at age 18 years.

Direct effect assesses the effect of one variable (independent variable or exogenous variable) to another variable (dependent variable or endogenous variable) evaluated using a regression model. For example, the direct effect of age at menarche on FVC at age 26 is assessed by regressing FVC at age 26 years on age at menarche and the regression coefficient represents the direct effect.
Indirect effect is the effect of one variable on another variable through one or more variables in between (i.e., mediators). For instance, age of menarche indirectly affects FVC at age 26 through height growth and/or FVC at age 18 years.

Conceptually, a total effect is the sum of direct and indirect effects. In our study, the total effect of age at menarche on FVC at age 26 years is the sum of all the direct and indirect effects explained above.
We give an example to interpret indirect effect. The indirect coefficient (IEC) of 0.13 for age at menarche means that, with other factors kept constant, one year delay in the onset of menarche was associated with a 0.13 Liter increase in FVC at age 26 years. One of such indirect paths was later menarche → larger height growth → higher lung function FVC at age 18 years → higher lung function FVC at age 26 years (the estimated effect was 0.34*0.60*0.71=0.14). The second indirect path is later menarche →larger height growth → higher lung function FVC at age 26 years (the estimated effect was 0.34*0.16=0.054), and the third path is through FVC at 18 years (-0.10*0.71=-0.071). Adding all portions of indirect effects up, we have IEC= -0.10*0.71+0.34*0.60*0.71+0.34*0.16=0.13 for age at menarche.

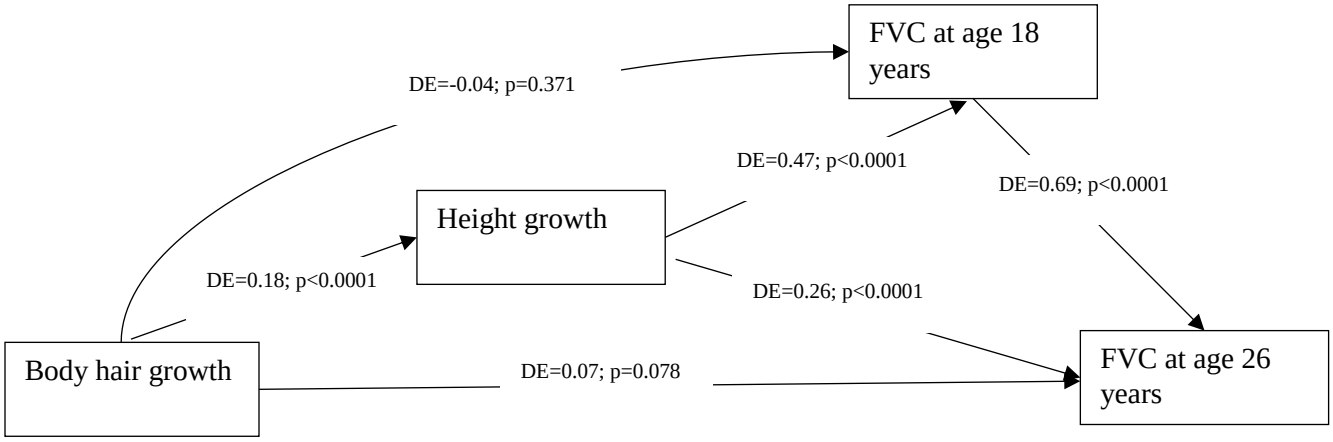

FIGURE S3 Estimated direct effects of each path (IOW), age at body hair growth and lung function parameter FVC in males.

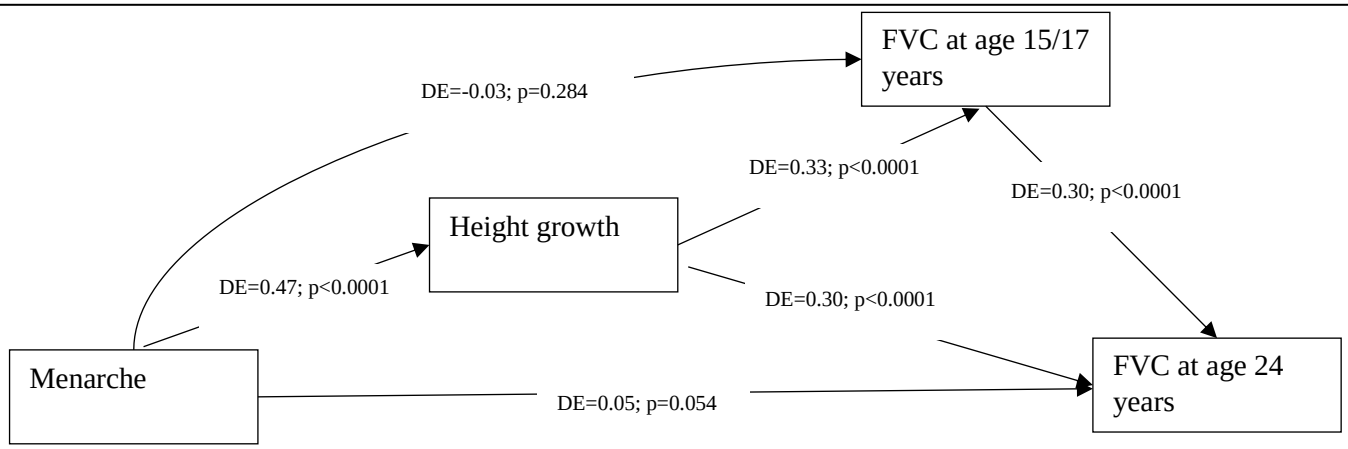

FIGURE S4 Estimated direct effects of each path (ALSPAC), age at menarche and lung function parameter FVC in females.

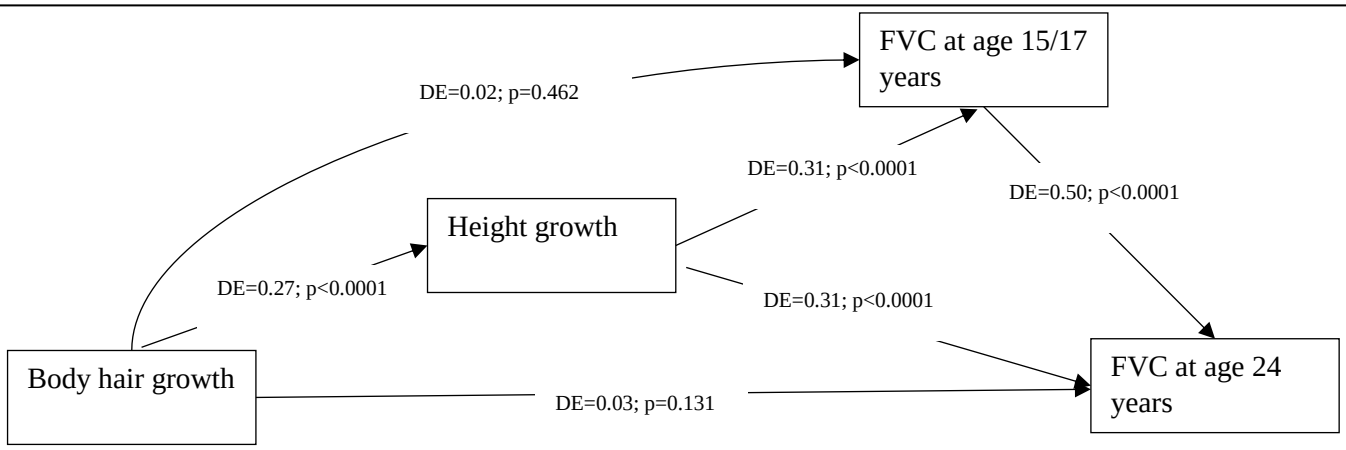

FIGURE S5 Estimated direct effects of each path (ALSPAC), age at body hair growth and lung function parameter FVC in females.

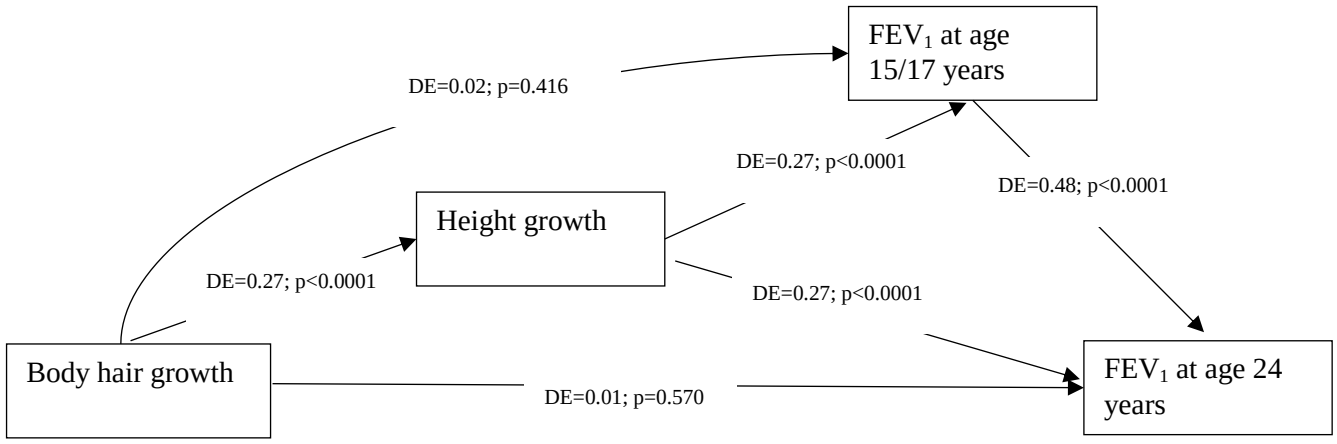

FIGURE S6 Estimated direct effects of each path (ALSPAC), age at body hair growth and lung function parameter FEV_1 in females.