

**Association between body mass index status and peripheral airway obstruction in school-age and adolescence  
- a population based cohort study**

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**Online supplement**

## **Definition of asthma symptoms, medication and diagnosis**

Current wheeze: at least one episode of wheeze in the last 12 months (assessed in the 8 year questionnaire and in the adolescent's 16-year questionnaire).

Breathing difficulties during exercise:

At 8 years: wheezing or raspy breathing in connection with physical exertion at 8 years (assessed in the 8 year questionnaire).

At 16 years: wheezy or raspy breathing, difficulty breathing, or troublesome cough in connection with physical exertion (assessed in the adolescent's questionnaire)

Asthma medication: inhaled steroids occasionally or regularly (as steroids only or as a combination of inhaled steroids and long acting beta-agonists) in the last 12 months (assessed in the 8 year questionnaire and in the adolescent's 16-year questionnaire).

Doctor's diagnosis of asthma: a doctor's diagnosis ever in life up to 8 or 16 years, as reported by the parent.

## **Definition of covariates**

Parental allergic disease: doctor's diagnosed asthma and/or hay fever in combination with reported allergy to pollen or pets in one or both parents (assessed in the baseline questionnaire).

Maternal smoking during pregnancy and/or infancy: the mother smoked at least one cigarette per day at any point of time during pregnancy and/or in infancy (assessed in the baseline questionnaire).

Birth weight: obtained from the medical birth register

Gestational age: obtained from the medical birth register

Breastfeeding  $\geq$  4 months: exclusive breastfeeding for at least four months (assessed in the 1-year questionnaire)

Socioeconomic status: parental occupation categorized into six categories with dominance order: unskilled blue-collar workers, skilled blue collar workers, low level white collar workers, intermediate level white collar workers, high level white collar workers and other (student) according to Statistics Sweden "Socioeconomic division (SEI); Reports on Statistical Coordination 1982:4" (assessed in the baseline questionnaire).

Maternal BMI in early pregnancy: maternal body mass index ( $\text{kg}/\text{m}^2$ ) recorded at the first visit to the antenatal-care clinic around week 10 in pregnancy (obtained from the Swedish Medical Birth Register).

Pubertal status: categorized into five categories: pre-pubertal, early pubertal, mid-pubertal, late pubertal or post-pubertal according to a pubertal development scale (1) based on questions on body hair development, linear growth spurt, and pubic hair growth (both males and females); voice change and beard growth (boys only); and breast development and menarche (girls only) (assessed in the adolescent questionnaire at 12 and 16 years).

Physical activity: self-reported amount of vigorous physical activity (hours/week) such as lifting heavy weights, aerobics, or high speed bicycling in the last 12 months. Mean of summer and winter season was calculated (assessed in the adolescent questionnaire at 16 years).

Smoking at 16 years: self-reported smoking at 16 years (assessed in the adolescents questionnaire at 16 years)

**Table S1.** Distribution of selected exposure characteristics among children included and excluded from the study population

	<b>Children included in the study population</b> (n= 2889 <sup>1</sup> )		<b>Children not included in the study population</b> (n=1199 <sup>1</sup> )		<b>p-value<sup>2</sup></b>
	<b>Mean</b>	<b>SD</b>	<b>Mean</b>	<b>SD</b>	
Maternal age (y)	30.8	4.5	30.3	4.5	<0.001
Maternal BMI in early pregnancy <sup>3,4</sup> (kg/m <sup>2</sup> )	22.9	3.2	23.0	3.3	0.28
Birth weight <sup>3</sup> (g)	3531	546	3545	565	0.47
Gestational age <sup>3</sup> (w)	39.5	1.8	39.5	1.9	0.50
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	<b>p-value<sup>5</sup></b>
Male sex	1423	49.3	642	53.5	0.01
Older siblings <sup>3</sup>	1232	43.5	569	48.3	0.005
Exclusive breastfeeding $\geq$ 4 months	2283	80.8	833	76.1	0.001
Maternal smoking during pregnancy and/or infancy	366	12.7	197	16.4	0.002
Parental history of allergic disease	902	31.5	298	25.3	<0.001
Any parent working as a professional worker	2395	84.2	928	79.2	<0.001
Either parent born outside of Scandinavia	449	16.2	94	14.9	0.41

<sup>1</sup> Some variables contain missing

<sup>2</sup> p-values obtained from the *t*-test

<sup>3</sup> Obtained from the medical birth register

<sup>4</sup> Recorded around week 10 in pregnancy

<sup>5</sup> p-values obtained from the chi-square test

**Table S2.** Associations between body mass index status (overweight/obese compared to normal weight) and asthma symptoms, asthma medication and asthma diagnosis at 8 and 16 years

	8 years					
	Girls			Boys		
	N <sup>1</sup> /n <sup>2</sup> (%)	OR <sup>3</sup>	95% CI	N <sup>1</sup> /n <sup>2</sup> (%)	OR <sup>3</sup>	95% CI
<b>Any wheeze at 8 y<sup>4</sup></b>						
Normal weight	911/83(9.1)	Referent		960/121(12.6)	Referent	
Overweight/obesity	261/28(10.7)	1.20	0.76-1.88	228/32(14.0)	1.13	0.74-1.72
<b>Doctor's diagnosis up to 8 y<sup>4</sup></b>						
Normal weight	900/94(10.4)	Referent		950/141(14.8)	Referent	
Overweight/obesity	254/32(12.6)	1.24	0.81-1.90	221/31(14.0)	0.94	0.62-1.42
<b>Any asthma medication at 8 y<sup>4,5</sup></b>						
Normal weight	914/53(5.8)	Referent		965/95(9.8)	Referent	
Overweight/obesity	262/23(8.8)	1.56	0.94-2.60	227/19(8.4)	0.84	0.50-1.40
	16 years					
	Girls			Boys		
	N <sup>1</sup> /n <sup>2</sup> (%)	OR <sup>3</sup>	95% CI	N <sup>1</sup> /n <sup>2</sup> (%)	OR <sup>3</sup>	95% CI
<b>Any wheeze at 16 y<sup>6</sup></b>						
Normal weight	1011/155(15.3)	Referent		891/89(10.0)	Referent	
Overweight/obesity	176/39(22.2)	1.57	1.06-2.33	219/29(13.2)	1.38	0.88-2.15
<b>Breathing difficulties during exercise<sup>6,7</sup></b>						
Normal weight	1034/293(28.3)	Referent		909/191(21.0)	Referent	
Overweight/obesity	179/71(39.7)	1.66	1.20-2.31	224/62(27.7)	1.44	1.03-2.01
<b>Doctor's diagnosis of asthma up to 16 y<sup>4</sup></b>						
Normal weight	1030/145(14.1)	Referent		919/162(17.6)	Referent	
Overweight/obesity	177/38(21.5)	1.67	1.12-2.49	228/51(22.4)	1.35	0.94-1.92
<b>Any asthma medication at 16 y<sup>5,6</sup></b>						
Normal weight	1032/80(7.8)	Referent		915/75(8.2)	Referent	
Overweight/obesity	179/22(12.3)	1.67	1.01-2.75	227/19(8.4)	1.02	0.60-1.73

<sup>1</sup> Number of exposed

<sup>2</sup> Number of exposed cases

<sup>3</sup> Estimates obtained by logistic regression

<sup>4</sup> Based on parental reports

<sup>5</sup> Inhaled steroids occasionally or regularly (as steroids only or as a combination of inhaled steroids and long acting beta-agonist)

<sup>6</sup> Based on adolescents report

<sup>7</sup> Includes breathing difficulties, tightness of the chest, wheezy or raspy breathing

**Table S3.** Association between body mass index status and fractional exhaled nitric oxide (FeNO), blood eosinophils and blood neutrophils at 16 years (n=1035 girls and 1008 boys for FeNO and 1223 girls and 1168 boys for eosinophils/neutrophils).

	<b>Girls</b>			<b>Boys</b>		
<b>FeNO (ppb)</b>	<b><math>\beta^1</math></b>	<b>95% CI</b>	<b>p-value</b>	<b><math>\beta^1</math></b>	<b>95% CI</b>	<b>p-value</b>
Thinness	-0.57	-2.63;1.50	0.59	-1.03	-3.80;1.75	0.47
Normal weight	Referent			Referent		
Overweight	-1.08	-2.79;0.62	0.21	1.48	-0.50;3.45	0.14
Obesity	-1.79	-5.48;1.82	0.34	-2.15	-6.07;1.78	0.28
<b>Blood eosinophils (10<sup>9</sup> cells/L)</b>						
Thinness	0	-0.01;0.01	1.00	0	-0.06;0.06	1.00
Normal weight	Referent			Referent		
Overweight	0	-.0.1;0.01	1.00	0	-0.04;0.0.04	1.00
Obesity	0.1	0.08;0.12	<0.001	0	-0.09;0.09	1.00
<b>Blood neutrophils (10<sup>9</sup> cells/L)</b>						
Thinness	-0.7	-1.03;-0.37	<0.001	0.1	-0.20;0.40	0.51
Normal weight	Referent			Referent		
Overweight	0.3	0.03;0.57	0.03	0.2	-0.01;0.41	0.06
Obesity	0.9	0.24;1.56	0.007	0.3	-0.13;0.73	0.17

<sup>1</sup> Represent the median difference compared to the reference group. Estimates obtained by quantile regression adjusted for smoking at 16 years (FeNO).

**Table S4.** Descriptive results on body mass index among children categorized into groups of overweight (including obesity) from 8 to 16 years. Children with thinness are excluded.

	<b>BMI at 8 years</b>					
	<b>Girls</b>			<b>Boys</b>		
	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>
No overweight at 8 y or 16 y	513	16.4	1.1	480	16.4	1.0
Overweight at 8 y, not at 16 y	98	20.0	1.3	61	19.9	1.1
Overweight at 16 y, not at 8 y	42	17.4	0.8	72	17.5	0.9
Overweight both at 8 and 16 y	60	21.0	1.7	66	21.1	1.7
	<b>BMI at 16 years</b>					
	<b>Girls</b>			<b>Boys</b>		
	<b>N</b>	<b>Mean</b>	<b>SD</b>	<b>N</b>	<b>Mean</b>	<b>SD</b>
No overweight at 8 y or 16 y	595	20.9	1.6	510	20.8	1.6
Overweight at 8 y, not at 16 y	109	22.6	1.4	62	22.4	1.4
Overweight at 16 y, not at 8 y	49	26.0	1.3	78	26.1	1.6
Overweight both at 8 and 16 y	87	27.7	2.8	71	27.7	3.2

**Table S5.** Overweight (including obesity) status between 8 and 16 years and impulse oscillometry at 16 years. Children with thinness are excluded.

	Girls			Boys		
	$\beta^1$	95% CI	p-value	$\beta^1$	95% CI	p-value
<b>FEV<sub>1</sub>, z-score</b> (n=840 girls and 721 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	0.12	-0.06;0.31	0.19	0.26	0.01;0.52	0.04
Overweight at 16 y, not at 8 y	0.19	-0.07;0.46	0.15	0.26	0.03;0.48	0.03
Overweight both at 8 and 16 y	0.32	0.12;0.52	0.002	0.22	-0.02;0.46	0.07
<b>FVC, z-score</b> (n=840 girls and 721 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	0.19	0.01;0.36	0.04	0.42	0.18;0.66	0.001
Overweight at 16 y, not at 8 y	0.29	0.04;0.55	0.03	0.42	0.20;0.64	<0.001
Overweight both at 8 and 16 y	0.58	0.38;0.77	<0.001	0.53	0.30;0.75	<0.001
<b>R<sub>5-20</sub> (Pa·L<sup>-1</sup>·s)</b> (n=928 girls and 924 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	1.7	-7.4;11.0	0.72	3.7	-4.8;12.2	0.39
Overweight at 16 y, not at 8 y	39.5	26.3;52.6	<0.001	22.2	14.0;30.4	<0.001
Overweight both at 8 and 16 y	34.0	23.1;44.9	<0.001	27.6	19.2;36.1	<0.001
<b>AX<sup>0.5</sup> (Pa·L<sup>-1</sup>·s)<sup>0.5</sup></b> (n=928 girls and 923 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	0.2	-0.8;1.2	0.70	-0.1	-1.0;0.8	0.77
Overweight at 16 y, not at 8 y	3.6	2.3;5.0	<0.001	1.3	0.5;2.2	0.003
Overweight both at 8 and 16 y	2.8	1.7;3.9	<0.001	2.0	1.1;2.9	<0.001
<b>FeNO (ppb)</b> (n=762 girls and 776 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	-0.25	-2.32;1.82	0.82	-1.20	-4.20;1.80	0.43
Overweight at 16 y, not at 8 y	-0.50	-3.40;2.40	0.73	1.17	-1.55;3.89	0.40
Overweight both at 8 and 16 y	-1.94	-4.20;0.33	0.09	0.61	-2.27;3.49	0.68
<b>Blood eosinophils (10<sup>9</sup> cells/L)</b> (n=912 girls and 907 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	0	-0.01;0.01	1	-0.1	-0.16;-0.04	<0.001
Overweight at 16 y, not at 8 y	0	-0.02;0.02	1	0	-0.05;0.05	1.0
Overweight both at 8 and 16 y	0	-0.02;0.02	1	0	-0.06;0.06	1.0
<b>Blood neutrophils (10<sup>9</sup> cells/L)</b> (n=912 girls and 907 boys)						
No overweight at 8 or 16 y	Referent			Referent		
Overweight at 8 years, not at 16 y	0.1	-0.21;0.41	0.53	0.2	-0.10;0.50	0.18
Overweight at 16 y, not at 8 y	0.3	-0.14;0.74	0.18	0.2	-0.08;0.48	0.17
Overweight both at 8 and 16 y	0.2	-0.17;0.57	0.28	0.3	0.02;0.58	0.04



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<sup>1</sup> Represent the median difference in outcome compared to the reference group. Estimates obtained by quantile regression adjusted for age and height ( $R_{5-20}$ ,  $AX^{0.5}$ ) and smoking at 16 years (FeNO).

## REFERENCES

1. Petersen AC, Crockett L, Richards M, et al. A self-report measure of pubertal status: Reliability, validity, and initial norms. *J Youth Adolesc* 1988;17(2):117-133