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Relationships between age of puberty onset and height at age 18 years in girls and boys

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Background: **Changes during puberty may influence final adult height. Height is related to multiple health conditions, including lung function. We investigated the association between the age of onset of five puberty events and height at age 18 years, analyzing boys and girls separately.**

Methods: **Of 1456 children recruited into the Isle of Wight birth cohort (1989-1990), 1313 were followed up at age 18 years. Height was measured, and age of pubertal onset was collected at age 18 years. Cluster analysis was performed on the five puberty events in boys and girls and linear regression was applied with the clusters predicting height at age 18 years. Individual linear regression analyses assessed the age of onset of each pubertal event as a potential predictor for height at age 18 years.**

Results: **Of the 1313 children followed up at age 18 years, 653 were males and 660 were females. All puberty variables had high internal consistency. In girls, earlier age of menarche, breast development, and growth spurt were related to shorter height. In boys, earlier age of growth spurt and slower progression through puberty were related to taller height at age 18 years.**

Conclusions: **Given that boys and girls may have opposing associations between pubertal timing and adult height and that height is an important predictor of lung function, the effect of pubertal timing on respiratory health should be explored.**

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Introduction

Puberty, a series of biological processes that occur in the transition between childhood to adulthood, is a pivotal stage in an individual's growth. The developmental changes that occur during puberty may influence adult health outcomes such as obesity and breast and testicular cancers.[1-3] On a fundamental note, it is important to investigate the effect of different pubertal events on final adult height. Height is an objective measure that can be easily obtained and has been independently linked to adult socioeconomic status, cardiovascular health, and pulmonary diseases in both men and women.[4]

Height is of particular importance when respiratory illnesses are considered because it is related to lung growth and respiratory obstruction.[5-8] A few studies suggested that adult height may be influenced by the timing of pubertal events, particularly age at menarche and age of onset of pubertal growth spurt. Early age of menarche has been associated with short adult stature.[9] In a longitudinal study that did not separately analyze boys and girls, pubertal growth spurt was associated with shorter leg length but was not associated with overall height.[10] Age of menarche is often used as a marker for pubertal onset in girls[11, 12] even though it is a relatively later event in puberty and breast development is known to occur first. Furthermore, there are fewer pubertal studies on boys because the age of onset of the first pubertal event, testicular enlargement, is difficult to ascertain in large scale studies. Instead, age of pubertal growth spurt (or peak height velocity) is used as a proxy marker for pubertal onset in boys and sometimes as a common indicator when studying puberty in both sexes.[10,13] Since girls enter puberty earlier and tend to be shorter than boys,[14] separate analyses should be performed when evaluating the effect of pubertal timing on adult height.

Puberty tempo may also be important in conceptualizing the effect of pubertal timing on adult height. The time span between breast development and peak height velocity was found to be longer for early maturers than it was for late and average maturers.[15] Despite this finding, no relationship was found between puberty duration and final adult height. However, the oldest age of follow-up maturation tempo was 16.1 years so the participants may not have yet reached their final adult height. The effect of puberty duration on adult height therefore needs further examination.

In this study, we investigated pubertal onset patterns for boys and girls in the Isle of Wight Birth Cohort and their relationship with height at age 18 years.

Methods

Study population

Between January 1989 and February 1990, 1536 children born on the Isle of Wight (IOW), UK were recruited and interviewed with 1456 available for further follow-up in a longitudinal study. The local research ethics committee approved the study and informed written parental consent was obtained from all participants at recruitment and subsequently at each follow-up. The IOW birth cohort has been described in detail elsewhere.[16,17] Briefly, upon delivery, birth weight was measured and data from birth records and extensive questionnaires were collected, including information on maternal smoking during pregnancy and maternal height. Children were followed up at the ages of 1 (n=1167, 80.2%), 2 (n=1174, 80.6%), 4 (n=1218, 83.7%), 10 (n=1373, 94.3%) and 18 years (n=1313, 90.2%).

Height at age 18 years was reported via the standard height measurement used at the allergy clinic. When a visit to the clinic was not possible for a height measurement, a telephone or postal questionnaire was completed by the study participant.

Puberty measurements

The study used the National Institute of Child and Human Development (NICHD) questionnaire from the Study of Early Child Care and Youth Development,[18] which is based on the Pubertal Development Scale (PDS) method. The PDS method uses self-reports of children on their development using five markers of pubertal growth with both genders being asked about their growth spurt, body hair growth, and skin changes. In addition, changes to voice and growth of facial hair are requested in boys and breast development and age of menarche in girls. At age 18 years, children in the IOW study were first asked to identify the puberty characteristics of interest and then recall the age of the first onset. In our study the questions asked of boys were as follows: 1. How old were you when you noticed that you had started to spurt in height? 2. How old were you when you noticed that your body hair started to grow? 3. How old were you when you noticed changes in your skin? 4. How old were you when you noticed your voice deepening? 5. How old were you when you noticed your facial hair starting to grow? Girls were asked the following questions: 1. How old were you when you noticed that you had started to spurt in height? 2. How old were you when you noticed that your body hair started to grow? 3. How old were you when you noticed changes in your skin? 4. How old were you when you noticed your breasts beginning to grow? 5. How old were you when you started to menstruate?

Statistical analyses

Puberty information gathered in boys and girls was assessed separately. We created a variable to represent the time span of the progression of pubertal onset by subtracting the oldest age of onset by the youngest age of onset. For the sake of brevity, we will henceforth refer to this variable as the progression of puberty onset. Minimum age of puberty was ascertained as the minimum age when the first pubertal event was experienced. Spearman's correlation coefficients of the age of onset described associations between different puberty events. In addition, Cronbach's alpha quantified internal consistency or the average correlation of items in this survey. According to Nunnally et al,[19] a Cronbach's alpha coefficient of 0.7 or higher is a good measure of reliability between variables.

To determine if there was a particular trend in the timing of the five pubertal events in each gender, we conducted cluster analysis using the k-means approach. In cluster analysis, variables are classified into groups so that those individuals within a cluster are highly associated with each other (based on a set of variables) and those between clusters are weakly associated with each other.[20] In the k-means method (least squares estimation), this classification is based on the Euclidean distance between subjects across a number of variables (in our case, age of onset of puberty events). Each observation is initially designated to its own individual cluster, and then clusters are merged to reduce the least squares criterion until convergence is achieved. There is no concrete rule as to the number of clusters that should be assigned. The goal is to find clusters that are the most informative in showing a set of patterns within and between the cluster groups. To that end, we compared results after 50 iterations that consisted of three to eight clusters and found that with five clusters we could observe a pattern whereby homogeneous ages of pubertal events were grouped together to form discrete clusters. For example, when looking at five clusters in girls, all of the girls in the first cluster happened to have the youngest age of onset for all puberty events (this is more clearly illustrated in the results).

We ran linear regression analysis of the clusters predicting height at age 18 years. To do this, we needed to assign one cluster as the reference. Our choice of the reference group for each sex was based on two criteria: the reference cluster that is in the midpoint of all clusters and the cluster that has the largest sample sizes. In girls, the ages in the clusters ranged from 9 to 14 years, leaving the median age to be 11.5 years. This left the "ages 11-14" cluster or the "ages 12-13 cluster". The latter cluster had larger sample sizes for all of the pubertal events, leading us to choose that as the reference group. In boys, the cluster ages ranged from 10 to 15 years, leaving 13 years to be the median point. This led us to the "ages 13-15" cluster which also had the largest sample size, resulting in that cluster being chosen as the reference group in girls.

Lastly, we considered each puberty event by running individual linear regression analyses with each age of onset of pubertal event as a potential predictor for height at age 18 years, controlling for maternal smoking during pregnancy, maternal height, and birth weight. All statistical analyses were performed using SAS 9.2.

Results

Population characteristics

There was no statistically significant difference between the 1313 offsprings (90% of the original birth cohort) who were followed up at age 18 years and the 994 children who had available information on measured height at age 18 years with respect to socioeconomic status, maternal smoking during pregnancy (Yes/No), maternal body mass index (BMI, kg/m^2), birth weight (kg), BMI at age of 10 and 18 years (kg/m^2), height at age of 10 and 18 years (cm), and sex (data not shown). Of those followed up at age 18 years, 653 were males and 660 were females. Boys and girls had similar characteristics regarding maternal height, birth weight, and maternal smoking during pregnancy (Table 1).

The puberty event most frequently recalled was age of facial hair growth in boys (n=602) and age of menarche in girls (n=631, Tables 2, 3). On average, girls started puberty 1.6 years earlier than their male counterparts. The range of progression of puberty onset was also shorter for girls (2 years, Table 3) than for boys (3 years, Table 2), indicating that girls progressed through puberty faster.

All puberty variables had high internal consistency; overall raw Cronbach's alpha coefficient was 0.80 in boys and 0.86 in girls. Age of onset of different puberty events was significantly correlated among boys and girls (Tables 2, 3). On average, male pubertal events had the following sequence: body hair growth, growth spurt, skin changes, voice deepening, and facial hair growth. Female events occurred in the following order: body hair growth, breast development, growth spurt, menarche, and skin

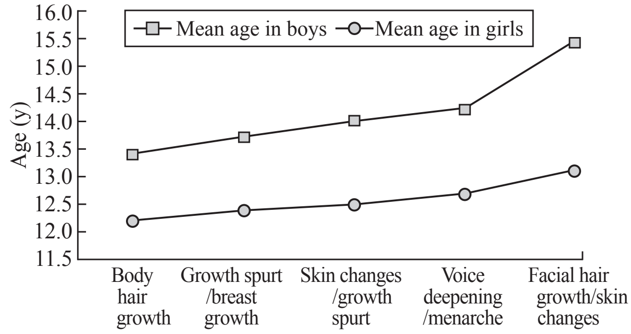

Fig. Sequential order of mean age of pubertal events in boys and girls.

Table 1. Population characteristics

Boys				Girls			
Variables	n	Median	5%, 95%	Variables	n	Median	5%, 95%
Maternal height (cm)	599	162.0	[153, 172]	Maternal height (cm)	580	163.0	[153, 173]
Birth weight (kg)	774	3.5	[2.6, 4.2]	Birth weight (kg)	737	3.4	[2.5, 4.2]
Body hair growth (y)	574	13.0	[11.0, 16.0]	Body hair growth (y)	589	12.0	[10.0, 15.0]
Facial hair growth (y)	604	16.0	[13.0, 17.0]	Breast growth (y)	592	12.0	[10.0, 15.0]
Voice deepening (y)	590	14.0	[12.0, 16.0]	Menarche (y)	631	13.0	[12.6, 12.8]
Skin changes (y)	480	14.0	[12.0, 16.0]	Skin changes (y)	455	13.0	[11.0, 16.0]
Growth spurt (y)	562	14.0	[13.6, 13.9]	Growth spurt (y)	503	13.0	[10.0, 15.0]
Age of first pubertal event (y)	621	13.0	[10.0, 15.0]	Age of first pubertal event (y)	640	12.0	[9.0, 14.0]
Height at age 18 years (cm)	483	178.0	[167.0, 189.9]	Height at age 18 years (cm)	511	164.0	[154.5, 175.0]
		N	%			N	%
Maternal smoking during pregnancy (Yes)		196	25.2	Maternal smoking during pregnancy (Yes)		188	25.3

All years refer to age of onset.

changes (Fig.).

In boys, the later the age of onset of the first pubertal event, the shorter the time window (progression of puberty events) in which all puberty events occurred (Table 2). This inverse correlation was also observed in girls: age at the first pubertal event was correlated with progression of puberty onset (ρ= -0.44, P<0.0001) (Table 3).

Age clusters and height at age 18 years

The five clusters (each in boys and girls) were characterized by similarities in timing of pubertal events within clusters and differences in timing between clusters (Table 4). For example, girls in the first cluster happened to experience the pubertal events at a younger age than girls in the fifth cluster. The cluster results do not emphasize specific individual pubertal events but rather focus on their timing. However, the clusters for both boys and girls suggest that the older the age of onset of puberty, the shorter the time span of onset of all puberty events (Table 4). For example, the youngest age cluster in boys had a range of 5 years, while the oldest group had a range of 1 year. The same pattern was observed between the youngest and oldest age

Table 2. Spearman's correlation of dependent variables for boys

	Median (p5, p95)	Facial hair growth (y)	Voice deepening (y)	Skin changes (y)	Growth spurt (y)	Age at first pubertal event (y)	Progression of puberty onset (y)
Body hair growth (y)	13.0 (11.0, 16.0)	0.45 <0.0001 565	0.53 <0.0001 557	0.49 <0.0001 457	0.48 <0.0001 529	0.80 <0.0001 574	-0.46 <0.0001 574
Facial hair growth (y)	16.0 (13.0, 17.0)		0.50 <0.0001 577	0.45 <0.0001 471	0.38 <0.0001 549	0.41 <0.0001 604	0.29 <0.0001 604
Voice deepening (y)	14.0 (12.0, 16.0)			0.52 <0.0001 465	0.47 <0.0001 537	0.56 <0.0001 590	0.29 <0.0001 604
Skin changes (y)	14.0 (12.0, 16.0)				0.40 <0.0001 436	0.60 <0.0001 480	-0.23 <0.0001 480
Growth spurt (y)	14.0 (11.0, 16.0)					0.70 <0.0001 562	-0.34 <0.0001 562
Age at first pubertal event (y)	13.0 (10.0, 15.0)						-0.67 <0.0001 621
Progression of puberty onset (y)	3.0 (0, 9.0)						

The values in the Spearman's correlation columns represent the following (from top to bottom): Spearman's correlation, P value, and sample size used in that correlation calculation.

Table 3. Spearman's correlation of dependent variables for girls

	Median (p5, p95)	Breast growth (y)	Menarche (y)	Skin changes (y)	Growth spurt (y)	Age at first pubertal event (y)	Progression of puberty onset (y)
Body hair growth (y)	12.0 (10.0, 15.0)	0.64 <0.0001 576	0.58 <0.0001 582	0.50 <0.0001 442	0.50 <0.0001 489	0.76 <0.0001 589	-0.18 <0.0001 589
Breast growth (y)	12.0 (10.0, 15.0)		0.61 <0.0001 586	0.47 <0.0001 445	0.50 <0.0001 489	0.70 <0.0001 592	-0.06 0.17 592
Menarche (y)	13.0 (11.0, 15.0)			0.46 <0.0001 450	0.58 <0.0001 582	0.62 <0.0001 631	0.06 0.15 631
Skin changes (y)	13.0 (11.0, 16.0)				0.42 <0.0001 378	0.70 <0.0001 503	0.21 <0.0001 455
Growth spurt (y)	13.0 (10.0, 15.0)					0.70 <0.0001 503	-0.09 0.06 503
Age at first pubertal event (y)	12.0 (9.0, 14.0)						-0.44 <0.0001 640
Progression of puberty onset (y)	2.0 (0, 7.0)						

The values in the Spearman's correlation columns represent the following (from top to bottom): Spearman's correlation, P value, and sample size used in that correlation calculation.

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cluster in girls.

Clusters of age at puberty onset as predictors for height at age 18 years

In the linear regression analysis, clusters with earlier or later age of puberty onset were associated with shorter adult height in girls (Table 5). Girls in the 9-11-year-old, 11-12-year-old, and 13-14-year-old clusters tended to be shorter [adjusted means of 162.40 cm (160.56 cm, 164.24 cm), 163.73 cm (162.60 cm, 164.85 cm), and 164.24 cm (162.92 cm, 165.56 cm) respectively, data not shown] compared to the reference 12-13-year-old cluster [adjusted mean of 166.05 cm (165.01 cm, 167.07 cm), data not shown] by 3.64 cm, 2.32 cm and 1.81 cm, respectively (Table 5).

The association was opposite in boys. Earlier onset of puberty was associated with greater adult height: the youngest age cluster (age 10-15 years) was 4.0 cm taller at age 18 years than the 13-15 years age cluster (Table 4). The adjusted mean for the 10-15 years age group was 181.2 cm (178.9 cm, 183.4 cm) while the adjusted mean for the reference group (the 13-15 years age cluster) was 177.8 cm (176.7 cm, 178.1 cm) (data not shown).

Individual pubertal markers as predictors for height at age 18 years

In girls, the linear regression analysis of pubertal ages as predictors for height at age 18 years revealed that later onset of breast development and menarche is associated with taller adult height (Table 5). On average, for every one year increase in age of breast development and menarche, height at age 18 years increased by 0.46 cm (*P*=0.01) and 0.59 cm (*P*=0.004), respectively. In

Table 4. Puberty age clusters of five pubertal events in boys and girls

	Female age clusters														
Pubertal events	Ages 9-11			Ages 11-12			Ages 11-14			Ages 12-13			Ages 13-14		
	n	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%
Breast growth, y	47	9.6	[8.0, 11.0]	141	11.6	[10.0, 13.0]	142	11.9	[11.0, 13.0]	160	13.1	[12.0, 15.0]	102	14.5	[13.0, 16.0]
Body Hair growth, y	47	9.7	[8.0, 11.0]	141	11.4	[10.0, 13.0]	141	12.2	[11.0, 13.0]	158	12.8	[12.0, 14.0]	102	13.9	[12.0, 15.0]
Growth spurt, y	37	9.9	[8.0, 12.0]	117	11.3	[9.0, 13.0]	122	13.0	[12.0, 15.0]	137	12.6	[10.0, 14.0]	90	14.5	[13.0, 16.0]
Skin changes, y	41	11.4	[10.0, 13.0]	117	12.0	[11.0, 13.0]	100	14.1	[12.5, 16.0]	123	13.0	[11.0, 14.0]	74	14.7	[13.0, 16.0]
Menarche, y	57	10.8	[9.0, 13.0]	148	11.9	[11.0, 13.0]	143	12.3	[11.0, 14.0]	174	13.4	[12.0, 15.0]	109	14.2	[13.0, 16.0]
	Male age clusters														
Pubertal events	Ages 9-11			Ages 11-12			Ages 11-14			Ages 12-13			Ages 13-14		
	n	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%	*n*	Mean	5%, 95%
Body hair growth, y	43	12.3	[10.0, 14.0]	64	11.7	[10.0, 13.0]	197	13.1	[12.0, 14.0]	177	13.6	[12.0, 15.0]	93	15.3	[14.0, 16.0]
Facial hair growth, y	47	15.6	[14.0, 17.0]	68	13.4	[12.0, 15.0]	209	15.1	[14.0, 16.0]	187	15.8	[15.0, 17.0]	93	16.5	[16.0, 17.0]
Voice deepening, y	45	13.8	[12.0, 15.0]	64	12.5	[11.0, 14.0]	205	13.8	[12.0, 15.0]	182	14.7	[14.0, 16.0]	94	15.6	[14.0, 17.0]
Growth spurt, y	36	10.2	[7.0, 12.0]	61	12.2	[10.0, 14.0]	200	13.2	[12.0, 15.0]	173	14.7	[14.0, 16.0]	92	15.3	[13.0, 17.0]
Skin change, y	33	13.2	[11.0, 15.0]	55	12.3	[11.0, 14.0]	173	13.6	[12.0, 15.0]	146	14.3	[13.0, 16.0]	73	15.9	[15.0, 18.0]

Table 5. Association between age clusters and height at age 18 years and association between puberty events and height at age 18 years

Boys				Girls			
Variables	Effect on height (cm/y)	SD	*P* value	Variables	Effect on height (cm/y)	SD	*P* value
Male clusters for age of pubertal onset				Female clusters for age of pubertal onset			
Intercept	177.76	0.97	<0.0001	Intercept	166.04	0.52	<0.0001
Reference: Age 13-15 cluster	0.00	-	-	Reference: Age 12-13 years cluster	0.00	-	-
Age 10-15 cluster	3.40	1.27	0.008	Age 9-11 y cluster	-3.64	1.08	0.0008
Age 11-13 cluster	-0.67	1.11	0.55	Age 11-12 y cluster	-2.32	0.78	0.003
Age 14-15 cluster	0.39	0.79	0.62	Age 11-14 y cluster	-1.50	0.79	0.059
Age 15-16 cluster	0.44	0.99	0.65	Age 13-14 y cluster	-1.81	0.85	0.035
Male linear regression				Female linear regression			
Age of growth of body hair (y)	-0.10*	0.26	0.71	Age of breast growth (y)	0.46	0.18	0.01
Age of facial hair growth (y)	0.26†	0.29	0.37	Age of body hair growth (y)	0.24§	0.21	0.25
Age of voice deepening (y)	-0.13†	0.28	0.64	Age of growth spurt (y)	0.30‡	0.18	0.09
Age of growth spurt (y)	-0.46*	0.19	0.02	Age of skin changes (y)	0.11†	0.21	0.61
Age of skin changes (y)	-0.27‡	0.25	0.28	Age of menarche (y)	0.59‖	0.20	0.004

*: adjusted for birth weight, maternal height, and maternal smoking during pregnancy; †: adjusted for birth weight and maternal height; ‡: adjusted for birth weight; §: adjusted for maternal height; ||: adjusted for maternal height and maternal smoking during pregnancy. SD: standard errors.

Table 6. Mean ages of onset of pubertal events in published studies (Tanner Stage 2)

Boys				
Growth spurt	Body hair (P2)	Voice changes /deepening	Skin changes	Facial hair
11[24]	12.02[25]	13.90[26]	12[27]	
	11.90[28]	13.37[29]	16[30]	14.45[29]
	12.38[31]			
Girls				
Growth spurt	Breast development (B2)	Body hair (P2)	Skin changes	Menarche
9[24]	10.16[25]	10.57[25]	11[27]	13.10[26]
	11.20[32]	11.90[32]	13.2[32]	13.30[32]
	10.25[28]	11.07[28]		
	10.15[33]	10.48[33]	13[34]	14.54[33]
	9.20[35]	11.16[35]		12.27[35]
	10.71[36]	10.46[36]		12.44[36]
	10.19[37]	10.95[37]		
	9.74[38]	10.49[38]		12.68[38]
	10.20[39]	11.70[39]		
	10.50[40]	10.60[40]		11.90[40]
	10.72[41]			12.42[41]

All units are in years. Values taken only from populations in developed countries in recent years (year 2000 and onward).

boys, the age of growth spurt was inversely associated with height (Table 5). For every year earlier of onset of growth spurt, height increased by 0.46 cm (P=0.02). This inverse association between growth spurt and height at age 18 years is also reflected in the significant association between the youngest age cluster and greater height. Lastly, the progression of puberty onset was not significantly associated with height at age 18 years in either boys or girls after controlling for potential confounders (data not shown).

Discussion

In boys, both cluster and linear regression analyses reveal that earlier age of puberty (specifically growth spurt in linear analysis) is related to taller height at age 18 years. Meanwhile, in girls, cluster analysis suggests that earlier and later puberty is related to shorter height, while linear regression analysis points to earlier puberty being associated with shorter height at age 18 years (particularly early age of menarche and onset of breast development). This suggests that when height and clusters of ages of pubertal onset are considered, boys and girls should be analyzed separately. Furthermore, given that taller height has a number of health advantages such as decreased mortality from pulmonary diseases[4] and decreased risk for intracerebral hemorrhage,[21] early age of puberty in girls and later age in boys may be considered as possible origins of health disparities in adulthood.

The IOW is an unselected whole population cohort with subjects who were recruited at birth. The high proportion of follow up minimizes potential selection biases. Regarding information biases, with the exception of maternal smoking during pregnancy and recall of puberty events, all other information reflected the current status at the point of follow-up. Maternal smoking involved a 9-month recall while information on puberty covered a longer recall period, which may influence the reliability and validity of the puberty variables. Nevertheless, the data collection has yielded puberty markers that have high construct validity (Cronbach's alpha >0.8). Regarding the age of onset of individual events, some variables were more frequently answered than others, suggesting ease of recall.

Another way to assess recall is to compare the order of events in our study to the order reported in other recent investigations. To our knowledge, few studies have assessed all five puberty variables in both genders at once. Aside from the original Tanner study,[22] we found only one other study performed by Lee et al.[23] Focusing on populations in developed countries after 1999, the combined studies have found the order of pubertal events in girls to be growth spurt, breast development and body hair growth occurring at the same time, skin changes, and then menarche (Table 6). We found an order of breast development and body hair growth occurring at the same time, followed by growth spurt, then menarche, and lastly, skin changes. Given that breast development occurs before menarche, it may be more directly and immediately influenced by endocrine changes during puberty and should also be used when investigating timing of pubertal onset. In boys, sequences reported in other studies were as follows: growth spurt and body hair growth, voice deepening, skin changes, and facial hair growth (Table 6). In our study, we found the following order: body hair growth, growth spurt, skin changes, voice deepening, and facial hair growth. Therefore, the timing of growth spurt reported by boys in the IOW study is consistent with those of other studies (Table 6).

Of concern is the lack of differentiation between age at take-off (ATO) and age at peak height velocity (APHV) when determining the age of onset of growth spurt. ATO occurs first and is the event that our questionnaire is targeting. However, it is possible that some children in our study may have reported APHV instead. Despite this limitation, our method of identifying the onset of growth spurt is the best option for large scale epidemiological studies. The two alternatives are using the Tanner Sexual Maturation Scale (SMS) or creating a growth curve. Many studies use the Tanner method, whereby a status of maturation (between scales of 1 to 5) is assigned to the child at one point in time. This is problematic because there is no way to ascertain

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if that child who is in the middle of their growth spurt experienced ATO a year earlier, therefore preventing a differentiation between ATO and APHV. Creating a growth spurt allows for the estimation of ATO and APHV,[42] but it requires repeated measurements of height from age of 5 years for boys and from age of 6 years for girls. To have the best estimation, one would have to take repeated measurements frequently, particularly near the age of take off. This is less feasible for large scale epidemiological studies. Therefore, while the pubertal development scale is retrospective and therefore imperfect, for large studies, it is the best option currently available.

In addition to being a better option of determining the onset of growth spurt, the PDS method is optimal for the ascertainment of the other pubertal events and is less prone to misclassification as compared to the established Tanner method. If measurements are not taken repeatedly in the Tanner method, the measurement only provides a snapshot of pubertal stage at one age, while PDS provides a more comprehensive picture of pubertal onset. Furthermore, SMS has been found to result in more missing data (13%) than the PDS method (4%).[43]

Surprisingly, in the cluster analysis for girls, earlier and later than average puberty onset was associated with shorter adult height. The reason for this is not known, although pre-pubertal factors such as birth weight and infant and early childhood weight gain may be contributing factors.[44,45] It is possible that girls who start puberty very late may be malnourished, resulting in a shorter adult height. In our study, there was a significant difference between the puberty age clusters in boys and in girls with respect to body mass index (BMI) at age of 10 years (P=0.01 in boys and P=0.003 in girls; data not shown). In both sexes, those in the youngest age clusters had the highest BMI at age of 10 years. This could reflect the minimum weight hypothesis for the initiation of puberty, which proposes that a minimum weight is required for the initiation of puberty, particularly in girls.[46] However, it is not possible to know the directionality of the association between higher BMI and early onset of puberty in our data.

In clusters for boys, we noticed that because the "10-15" years age group has a wide range, some of the pubertal variables in that group were older than those in the reference group (the "13-15" years age group). We therefore ran the analysis using a different reference group, "14-15 years", in which all puberty events on average occurred at a later age than those in the 10-15 years age group. The results using this new reference group showed that those in the 10-15 years age group still had a taller height (by 3.0 cm) at age 18 years compared to those in the older "14-15 years" age group. Whereas most pubertal events follow a linear age effect, the "10-15 years age group" seems to present a specific group in boys with a longer progression through puberty not seen in girls.

A limitation of our study is that we have a Caucasian population. Since age of pubertal onset and duration vary with respect to secular trends[47-50] as well as distinctions in race, ethnicity, socioeconomic background, and paternal and maternal history of adolescent development,[51-56] our observations might be limited to Caucasian populations.

The opposite trends observed between boys and girls with regards to early puberty and adult height may be explained by the mechanism responsible for epiphyseal plate closure. In boys, testosterone causes the rise of gonadotropin-releasing hormone (GnRH) levels, whereas in girls, the precursor is estradiol. Although estradiol is also a product of testosterone metabolism in males, the levels of estradiol rise later and more slowly in boys than they do in girls.[57] Therefore, the initiation of puberty in boys seems not to be associated with a rise in estradiol sufficient to initiate epiphyseal plate closure, whereas the opposite seems to be true in girls.[57] In addition, the male growth spurt also starts later and advances more slowly. Growth spurt in boys therefore lasts longer before epiphysis.[57]

When considering adult health associated with height, it is uncertain whether height is on the causal pathway or if pubertal timing is directly associated with these outcomes. For instance, a study found no association between age of attainment of final height and pre-menopausal breast cancer, while a positive relative risk was observed with respect to adult height and invasive breast cancer.[58] On the other hand, other studies have found that women with earlier age of menarche had higher estrogen levels throughout puberty and their adult lives,[59,60] possibly contributing to increased risk of breast cancer incidence.[61,62] Our findings suggest that the timing and tempo of puberty should be more closely examined when addressing adult health outcomes.

This is an epidemiological investigation that is ultimately interested in respiratory outcomes. Height is an important predictor of lung volume and the sex differential association between pubertal timing and adult height sheds insight onto puberty's influence on lung function (since taller adult height may be an indicator of better lung growth). Given evidence that the timing of pubertal onset may play a role in adult health outcomes, pubertal data for pediatric research should more closely document the age of onset of these events (adrenarche, thelarche, menarche, and growth spurt) in boys and in girls.

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