Puberty

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Pubertal Growth Assessment

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Puberty · Pre-pubertal height · Height growth · Infancy-childhood-puberty (ICP) growth model · Prediction models · Children

Abstract
Almost all available sets of height growth reference values are constructed in a cross-sectional manner, except for a few studies in which longitudinal sampling was used. Such reference values are, however, flawed because of considerable individual variation in the timing of puberty, especially among children with early or late pubertal maturation. An additional complicating factor is that the magnitude of the total pubertal growth spurt is significantly larger among those individuals with early pubertal maturation, compared with late maturation. Based on the growth records of 145 healthy Swedish children followed longitudinally, this study introduces a pre-pubertal standard for the assessment of pre-pubertal height for children with late onset of puberty. By plotting the height values of a child in a chart containing pre-pubertal reference values, the onset of the pubertal growth spurt can be identified by a change in the pre-pubertal height standard deviation score values of 0.3 standard deviations or more over a period of 1 year. Once the pubertal onset is established, a highly accurate final height prediction method can be applied to the data, as described in this article, in which height and age at pubertal onset are the only two measures required. The r^2 value of the prediction model was over 0.80 for both sexes. Finally, a method for assessing total pubertal height gain is presented. The method adjusts for the timing of puberty and is based on the height and age at pubertal onset, plus the observed final height.

Introduction

Pubertal growth can be assessed by pubertal stages, for example, breast and pubic hair development in girls, and testis size and pubic hair development in boys. There is, however, often more of an interest in growth in height, prior to, during and after puberty. For an accurate evaluation, we need access to longitudinal height measurements of the individuals to be assessed, but at present, almost all available sets of height growth reference values are constructed in a cross-sectional manner, even in the few studies that used longitudinal sampling. Many researchers have shown that such reference values are flawed because of considerable individual variations in the timing of

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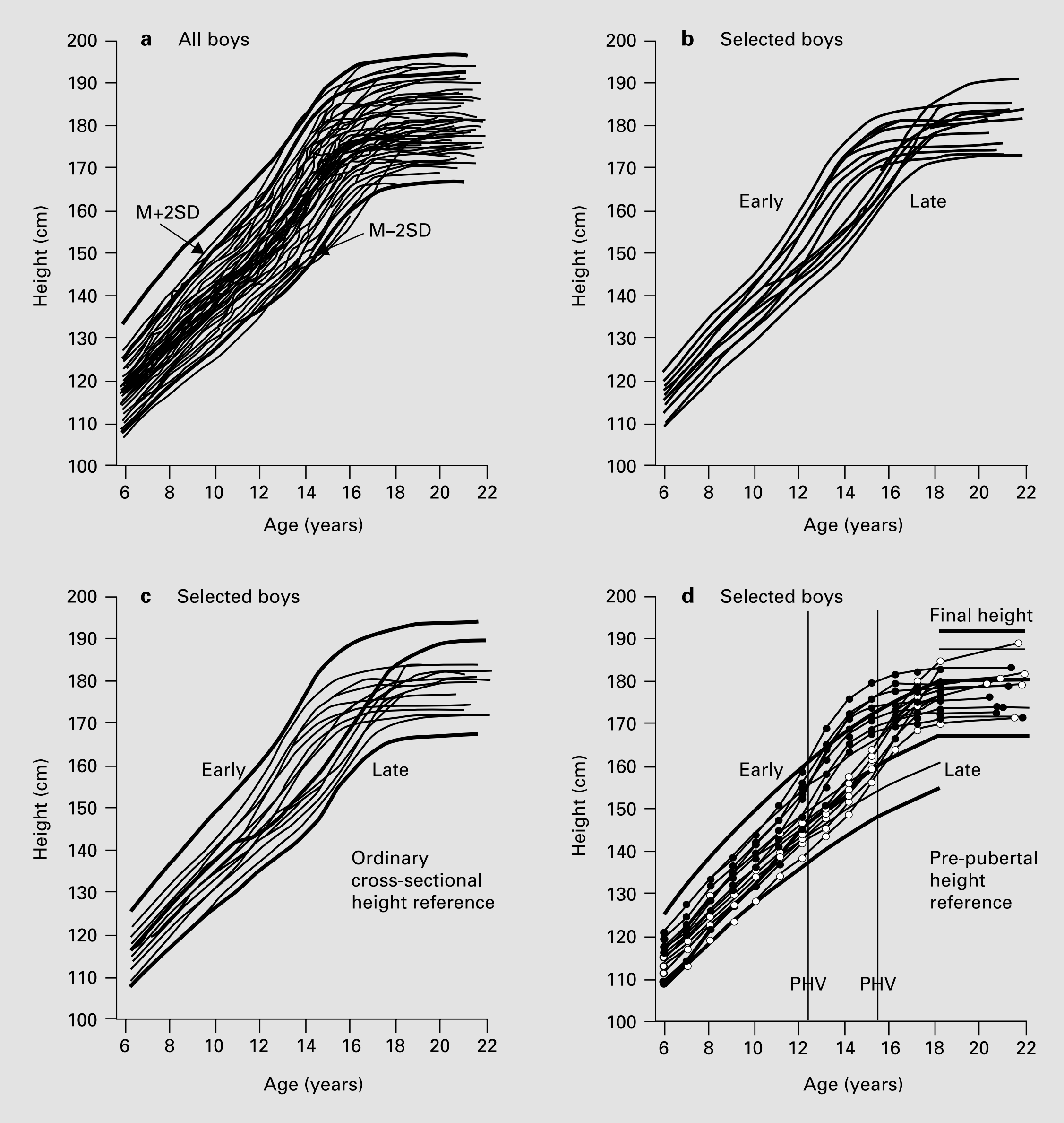

Fig. 1. a The growth pattern of all boys (n = 81) in the Swedish longitudinal study (mean ± 2 SD). **b–d** A subset of the data, i.e. the boys with the earliest and latest timing of the pubertal growth spurt. The mean and SD are given in the usual cross-sectional manner in **c** and for the pre-pubertal (ICP) height reference values (table 1) in **d**.

puberty, especially among children with an early or late pubertal maturation, as illustrated in figure 1 [1–3]. This seems logical, and the question of how more realistic reference values might be constructed is central to this discussion. An additional complicating factor, when aiming to produce realistic reference values over the full range of pubertal ages, is that the magnitude of the total pubertal growth spurt is significantly larger for those individuals with early pubertal maturation compared with late maturation [1, 4, 5].

So far, the most widely accepted solution to the problem of assessing height during adolescence has been the infancy-childhood-puberty (ICP) growth model [4–7]. In this mathematical model, linear growth during the first 3 years of life is represented by the combination of a sharply decelerating infancy component and a slowly decelerating childhood component – the latter emerging from the second half of the first post-natal year. From around the age of 3 years to maturity, linear growth is represented by the combination of the continuing childhood component and a sigmoid puberty component that operates throughout adolescence. The mean additional growth, contributed by the puberty phase of growth, is aligned with the timing of an individual, thus producing realistic, individual pubertal reference values for height [5, 7]. The computation is quite extensive, however, and sophisticated computer software is required to make full use of this method.

In this article, the ability of the ICP model to describe and evaluate individual growth patterns for linear growth in healthy children from 3 years of age to maturity, merely by using the reference values of the childhood component for height and disregarding the contribution of the puberty component, is assessed. The data were partially refitted to produce user-friendly reference values for assessment of the height of an individual during adolescence. The use of these reference values to evaluate pre-pubertal growth and determine the age of pubertal onset will also be discussed, as well as a new method for assessing the magnitude of the pubertal growth spurt and predicting final height.

The ICP Growth Model

Data Source

The data are from the Swedish part of an International Longitudinal Growth Study of healthy children conducted in Sweden, the UK, Switzerland and France [8]. The material consists of the longitudinal records of 81 boys and 64 girls. Annual examinations were made from 3 to 18 years of age, with a final examination at the age of 21 years. Among these children, mid-parental height (the mean height of both parents) was available for 59 boys and 46 girls.

Measurements Derived from the ICP Growth Model

The ICP model was sequentially fitted to the individual growth curves, from birth to maturity, for the children in the Swedish study [4, 5]. The infancy component is represented by an exponential function, the childhood component by a simple second-degree polynomial function, and the puberty component by a logistic function, with all the functional values presented elsewhere [4, 5]. Standard deviations (SD) for measured attained size are also represented by mathematical functions [5]. This work also presents an additional curve-fitting result so that values from the childhood phase can be more easily computed from the age of 3 years onwards. A second-degree polynomial function was fitted to the sum of the mean infancy and mean childhood component (omitting the contribution of the puberty component) from 3 years onwards, thus providing a single function representing the childhood values from 3 years of age throughout childhood and adolescence into maturity. This height reference is known as the pre-pubertal (ICP) reference [5, 7].

For each individual, the age at maximum growth velocity during puberty – peak height velocity (PHV) – was determined mathematically and visually as described elsewhere. Based on this analysis, the age at the onset of puberty could be reliably defined as being 2.0 years before the age when PHV occurs [4, 5, 7]. The height at the age when puberty begins was computed by means of interpolation using the individually-fitted mathematical ICP growth model functions [4, 5, 7].

Results

Figure 1a includes all the individual height curves for the 81 boys. Figure 1b depicts the height curves for selected boys with the earliest and the latest age at PHV, illustrating the striking difference in height gain during adolescence. Figure 1c shows the difficulties in using cross-sectional height reference values for assessing pre-pubertal growth in height in the group of boys who reached maturation late and for assessing pubertal growth in both groups of boys.

The new functional pre-pubertal reference values that are valid from the age of 3 years onwards are presented in table 1. The SD around the mean childhood values [5], and the mean and SD of final height, mid-parental height and the age at PHV for girls and boys [7] are also included in table 1. The mean values, and 1 and 2 SD around the mean are shown for the pre-pubertal phase and for final height in figure 1d for boys.

Growth before the Onset of Puberty

The childhood height reference values are constructed to represent the pre-pubertal path of growth. As illustrated in figure 1d, the individual height growth curves continue to follow this pre-pubertal growth pattern until approximately 2 years prior to the age at PHV, which is of particular importance for the group reaching maturation late.

All height measurements for both sexes were converted into standard deviation scores (SDS) based on the pre-

Table 1. Mean and SD for the childhood component (valid from the age of 3 years onwards) of the ICP growth model, age at PHV, mid-parental height and final height for boys (n = 81) and girls (n = 64)

Sex	Measure	Value/function by age (years)
Girls	Mean pre-pubertal values (cm)	$69.855536 + 8.934107 \times age - 0.215179 \times age^2$
	SD for pre-pubertal values (cm)	$1.820381 + 0.532667 \times age - 0.016139 \times age^2$
	Mean final height (cm)	165.82
	SD of final height (cm)	6.25
	Mean age at PHV (years)	11.88
	SD of age at PHV (years)	0.92
	Mean mid-parental height (cm)	169.72*
	SD of mid-parental height (cm)	4.85
Boys	Mean pre-pubertal values (cm)	$71.886012 + 8.533750 \times age - 0.180298 \times age^2$
	SD for pre-pubertal values (cm)	$1.814919 + 0.514192 \times age - 0.014683 \times age^2$
	Mean final height (cm)	179.65
	SD of final height (cm)	6.51
	Mean age at PHV (years)	13.97
	SD of age at PHV (years)	1.05
	Mean mid-parental height (cm)	169.95**
	SD of mid-parental height (cm)	4.34

* n = 46; ** n = 59.

pubertal reference values (table 1). The SDS values are plotted in figures 2a and b in relation to the age at PHV for each individual child. Note that the mean – the smoothed curve in figure 2 – is zero or close to zero up to 2 years prior to the age at PHV for both sexes. Figures 2c and d also show the change in childhood height SDS values (delta SDS) over a 1-year period; the values were plotted in relation to the age at PHV using the age in the middle between two consecutive ages. The pre-pubertal delta SDS values were not correlated ($r < 0.1$) with the age at the onset of puberty, implying that children with a late pubertal maturation follow the path of the childhood height reference values before puberty.

Onset of the Pubertal Growth Spurt

The onset of the pubertal growth spurt is usually defined as a clear increase in growth rate. One possible means of detecting such a deviation, independent of the timing of puberty, is to refer the pattern of growth for an individual child to those reference values representing the childhood phase of growth (fig. 1d). The analysis revealed, however, that an increase of 0.3 SDS or more is seldom observed during the 1-year period up to 1.5 years before the age at PHV. Only 3.0% (7 of 233) of the annual height delta SDS values plotted in figure 2c positioned 1.5 years prior to the age at PHV for girls reached a value of 0.3 SDS, or higher. The corresponding figure for boys was 4.7% (14 of 305). However, 81.5% (75 of 92) of the annual height delta SDS values between 1.5 years before the age at PHV and the age at PHV reached a value of more than 0.3 SDS for girls; the corresponding figure for boys was 88.9% (120 of 135).

Not until the start of puberty do increases of 0.3 SDS or more occur on a substantial scale, indicating the onset of puberty. Using the graph depicted in figure 1d to show the pre-pubertal pattern of growth, an increase in height of 0.3 SD or more over 1 year can be used to demonstrate the onset of puberty for an individual child. An example of a boy with an age of 12.3 years at PHV is provided in figure 3a. Height follows the pre-pubertal reference curve up to 10 years of age. Between the ages of 10 and 11 years, there is an increase in height SDS based on the pre-pubertal and childhood height reference values with a 0.32 SDS, thus implying the onset of puberty during this interval. Although an increase in the childhood height SDS value of 0.3 or more can be noted over a year of observation, we are still not in a position to define the exact age at pubertal onset based on growth data only. A proper assessment of the age at PHV can only be made after another 1–2 years of follow-up observations. The age at PHV is indicated in figure 3 as a vertical line and the age at pubertal onset, which is defined here as 2 years prior to the estimated age at PHV, is also shown. In addition, figure 3 includes another three individual growth curves illustrating a clear increase in the childhood SDS values corresponding to pubertal onset.

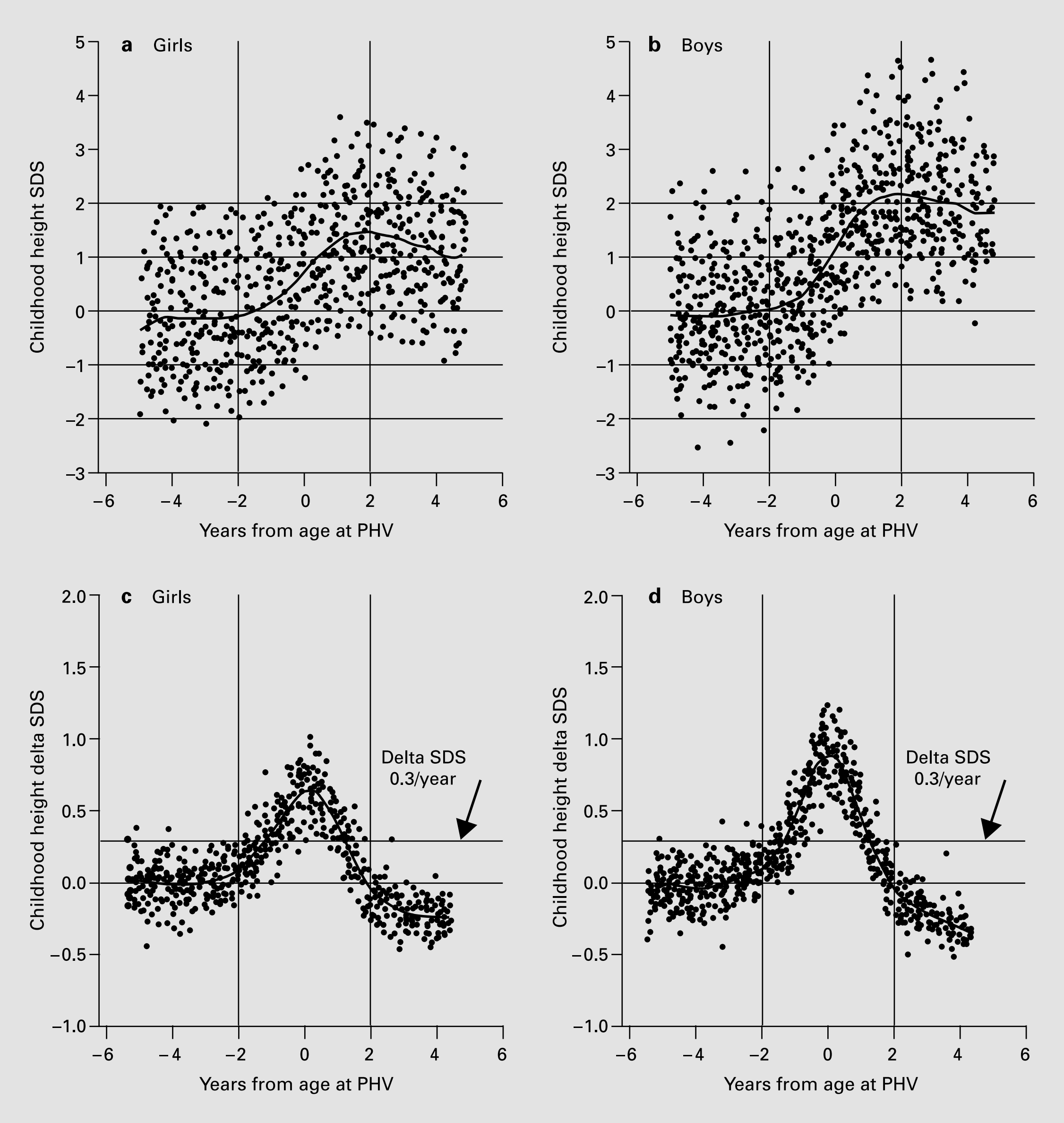

Fig. 2. The individual values for the childhood SDS values adjusted according to the timing of the age at PHV of each child (**a** for girls, **b** for boys). The changes in the childhood SDS values over 1 year (delta SDS) are included in **c** and **d** and are adjusted according to the timing of the age at PHV for each child (**c** for girls, **d** for boys); in addition, a horizontal line representing the cut-off point of +0.3 delta SDS is included. A spline function was used to draw the mean curve.

Prediction of Final Height

The results of different linear regression models of final height prediction based on height and age at pubertal onset, together with parental height, both in isolation and in combination, are presented in table 2. The models are given for both sexes separately and for height expressed in cm, as well as in SDS based on childhood reference values. It should be noted that the r^2 values are virtually the same when height at pubertal onset is given in either cm or SDS units. Neither mid-parental height nor age at the onset of puberty, alone or in combination, give a good final height prediction as indicated by the relatively low r^2 values and high residual SD values. However, the model including the height and age at pubertal onset gives an r^2

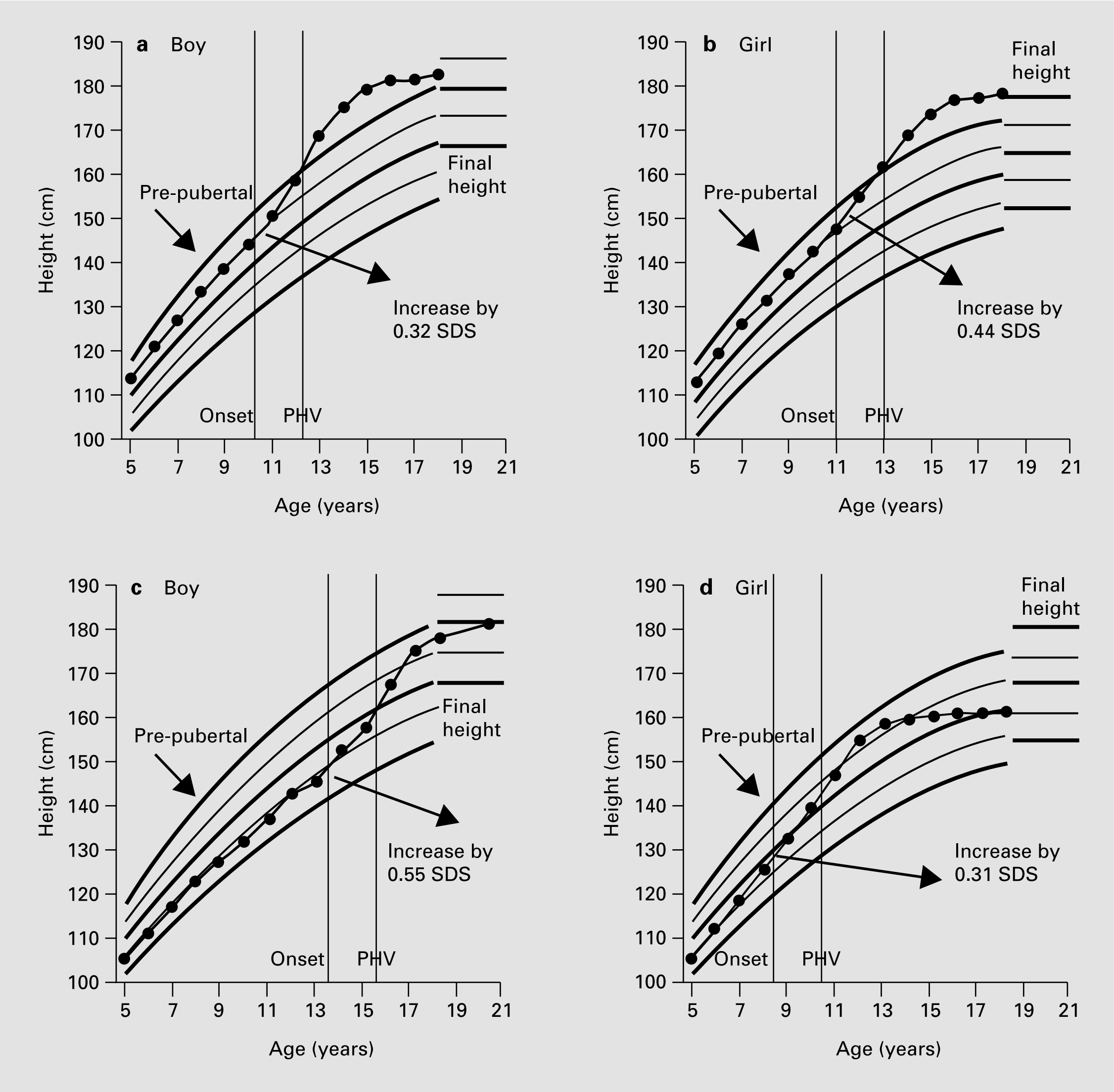

Fig. 3. Four typical growth patterns for various timings of puberty in two boys (**a**, **c**) and two girls (**b**, **d**). The charts include the mean ± 1, 2 and 3 SD for both the pre-pubertal ICP-based height reference values and for final height. The interval with a delta SDS value over 0.3 SDS is indicated for each child. The age at PHV for each child is shown as a vertical line (PHV) and the pubertal onset (i.e. 2 years prior to the age at PHV) is also shown as a vertical line (onset).

value of 0.83 for girls and 0.82 for boys. Only a marginally increased r^2 value is noted when mid-parental height is introduced into this latter model, and the slope for mid-parental height is only significant ($p < 0.05$) for boys.

Assessment of the Magnitude of the Pubertal Growth Spurt

The regression lines in table 2 are not only useful for an appropriate prediction of final height, but they can also be used to evaluate the total pubertal growth spurt of an individual (or for groups of individuals) following disease intervention. This is achieved by examining the observed final height in relation to predicted final height, based on the height and age at pubertal onset.

An alternative and more direct method, however, is illustrated in figure 4, in which the total gain from the onset of puberty (i.e. 2 years before the age at PHV) is plotted along the y-axis and the age at pubertal onset along the x-axis. The two linear regression lines (one for girls and one for boys) have negative slope values of 1.9–2.5 (table 3). This means that pubertal growth gain decreases by ~1.9–2.5 cm for each year of delay in the onset of

Table 2. Linear regression analysis with final height as the dependent measure, and the height at pubertal onset (onset height) both in cm and in childhood height SDS units, the age at pubertal onset (onset age) and mid-parental height as the independent measures

Unit/sex	n	r^2	Residual SD	Intercept	Onset height slope	Onset age (years) slope	Mid-parental height (cm) slope
Onset height (cm)							
Girls	64	0.72	3.35	50.1029	**0.8431**		
	64	0.01	6.27	58.8475		0.7000	
	46	0.39	5.04	26.4871			**0.8235**
	46	0.41	5.00	19.1852		0.9891	**0.8088**
	46	0.78	3.07	14.7842	**0.7124**		**0.3137**
	64	0.83	2.62	51.0147	**1.0216**	**–2.5723**	
	46	0.86	2.47	27.9609	**0.9592**	**–2.3341**	0.1718
Onset height (SDS)							
Girls	64	0.73	3.30	165.4681	**5.1506**		
	64	0.01	6.27	158.8475		0.7000	
	46	0.39	5.04	26.4871			**0.8235**
	46	0.41	5.00	19.1852		0.9891	**0.8088**
	46	0.76	3.24	118.4560	**4.6661**		**0.2772**
	64	0.83	2.62	143.2584	**5.6425**	**2.2461**	
	46	0.86	2.51	115.5497	**5.3253**	**2.1539**	**0.1680**
Onset height (cm)							
Boys	81	0.76	3.17	54.1800	**0.8429**		
	81	0.05	6.26	163.5592		**1.3592**	
	59	0.29	5.32	49.7806			**0.7648**
	59	0.31	5.27	47.0866		0.9294	**0.7156**
	59	0.76	3.09	23.1850	**0.7569**		**0.2589**
	81	0.83	2.70	53.5748	**0.9948**	**–1.8414**	
	59	0.85	2.50	21.2491	**0.9810**	**–2.0491**	**0.2175**
Onset height (SDS)							
Boys	81	0.68	3.63	178.7878	**5.3914**		
	81	0.05	6.26	163.5592		**1.3592**	
	59	0.29	5.32	49.7806			**0.7648**
	59	0.31	5.27	47.0866		0.9294	**0.7156**
	59	0.73	3.31	114.8720	**5.0433**		**0.3762**
	81	0.82	2.73	151.1530	**5.8265**	**2.3039**	
	59	0.85	2.52	117.7908	**5.7282**	**2.0428**	**0.2153**

Statistically significant ($p < 0.05$) slope values are shown in bold.

Table 3. Linear regression analysis with pubertal height gain (cm) as the dependent measure and the height at pubertal onset (onset height), the age at pubertal onset (onset age) and mid-parental height as the independent measures

Sex	n	r^2	Residual SD	Intercept	Onset height (cm) slope	Onset age (years) slope	Mid-parental height (cm) slope
Girls	64	0.45	2.60	53.2962		**–2.5030**	
	46	0.52	2.45	28.3346		**–2.4756**	0.1447
	46	0.52	2.47	27.9609	–0.0408	**–2.3341**	0.1718
Boys	81	0.35	2.71	53.4048		**–1.8970**	
	59	0.47	2.54	22.5694		**–2.1576**	**0.2003**
	59	0.47	2.50	21.2491	–0.0190	**–2.0491**	**0.2175**

Statistically significant ($p < 0.05$) slope values are shown in bold.

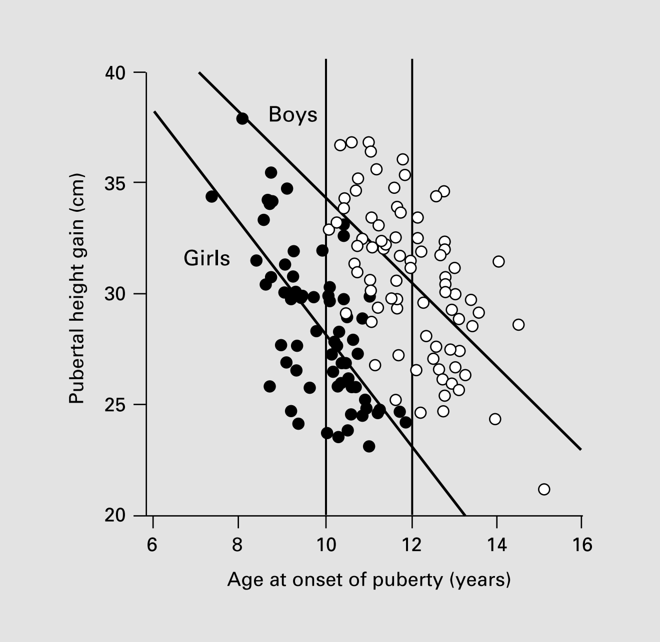

Fig. 4. The total pubertal gain from the age at onset of puberty to final height, and the age at pubertal onset is plotted for girls (closed circle) and boys (open circle). A simple linear regression has been fitted to the values (table 3); pubertal height gain = 53.2962 – 2.5030 × onset-age for girls and pubertal height gain = 53.4048 – 1.8970 × onset-age for boys.

puberty. The details of the curve fitting are presented in table 3, showing that the height at pubertal onset is not significantly associated with the total gain during puberty and that mid-parental height is only of importance ($p < 0.05$) for the total pubertal gain for boys. The functions in table 3 allow reference values to be calculated for the total pubertal gain adjusted for the onset of puberty; the function allows calculation of the predicted gain, and the residual SD can be used to compute SDS in the usual way.

Discussion

In contrast to other mathematical models for human growth, the ICP model covers the whole post-natal growth period and is analytical rather than descriptive. Most importantly, its subcomponent structure is linked to the hormonal regulation of development [4, 5]. A further point of difference is that the model provides reference values for both total growth and individual components. In this paper, ICP-constructed reference values for pre-pubertal growth have been shown to agree with those derived directly from the data. Reference values based on the ICP approach appear to have a number of advantages. Pre-pubertal growth and pubertal onset can be assessed in a more satisfactory way using the ICP model than using ordinary cross-sectional standards. The reference values involved, referred to as the pre-pubertal ICP standard, continue into adolescence, excluding the contribution of the pubertal component. The path of the curve follows a second-degree polynomial function, or a parabola that slowly decreases in its power over the years of adolescence. A similar pattern is also observed in girls with Turner syndrome who do not have a spontaneous pubertal growth spurt, thus providing strong evidence for the existence of a decelerating pre-pubertal curve up to 20–21 years of age in girls [9].

As demonstrated in this paper, the pre-pubertal ICP standard offers a novel way of assessing pre-pubertal height for children with late onset of puberty. In addition, by plotting the height values of a child on a chart containing the pre-pubertal ICP reference values, the onset of the pubertal growth spurt can be identified by means of a change in the pre-pubertal height SDS values of 0.3 SD or more. Once the onset of puberty is identified, a highly accurate final height prediction method can be applied to the data, as described in this paper, with height and age at pubertal onset being the only two measures required. The r^2 value of the prediction model was over 0.80 and only minor improvements were added to the regression by introducing additional information such as mid-parental height. There are, of course, already several methods for predicting height using pre-pubertal measures. The results presented here suggest, however, that the intermediate step of predicting pubertal onset and thereafter final height is also a fruitful approach. The concept was first published in 1987 [7] and has been evaluated independently using a series of data from Israel [10]. The authors concluded that use of height and age at pubertal onset alone resulted in more accurate predictions of adult height than predictions made by methods requiring bone age determination, e.g. the Bayley-Pinneau and Tanner-Whitehouse methods [10]. The final height prediction method presented in this article can also be useful in the clinic for predicting final height of a pre-pubertal child for various hypothetical times of pubertal onset. For example, the method offers support for decision-making regarding induction of puberty as may be needed with extremely tall individuals.

Differences in pubertal maturation can be taken into account when setting standards during puberty, and the

ICP growth model appears to be the first model to offer a solution to this problem [5, 7]. It should be emphasised that this angle has not been fully explored in this paper because it requires complex computations and is only assessable using specific computer software. This work does, however, describe more clearly than before new analytical tools used to assess height during puberty in an individual child, or for a group of children, under study. The method considers both the difference in the timing of puberty and the negative relationship between the size of the pubertal gain and the age at PHV. All of this permits the construction of an appropriate continuous method for height assessment during adolescence which can accommodate any pattern of maturation, whether it be early, normal or late. First, the age at PHV should be identified by observing the pubertal velocity curve; the age at onset of puberty is thereafter computed as being 2.0 years before the age at PHV. The second step is to estimate the height at pubertal onset by interpolation or by carrying forward the last pre-pubertal height SDS value to the age at pubertal onset. This latter method has been shown to be reliable [10] and the SDS value at pubertal onset can be converted into centimetres by using the functions of the mean and SD for the pre-pubertal/childhood values as provided in table 1. The total pubertal gain can be converted into SDS based on the linear regression function using the age at onset of puberty (table 3). The method is simple and offers a useful means of analysing data from pubertal growth studies. Similar standard values can be developed for other series of normal children and for disease-specific growth data. The methods should, however, if possible, be tested on other series before they are generally adopted.

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