



## Longitudinal Growth and Timing of Thelarche and Menarche in Adopted Chinese Girls: Comparison with the China Growth and Pubertal Development References

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Author Details
Dr. Gonzalo Oliván-Gonzalvo
Authors Affiliations
Pediatrics and International Adoption Center, Zaragoza, Spain
Corresponding Author*
<b>Dr. Gonzalo Oliván-Gonzalvo</b>
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**Abstract: Background:** Prospective studies on growth in adopted Chinese girls are scarce and are limited to short-term follow-ups. The objectives of this study were to provide data on the longitudinal growth and timing of thelarche and menarche in girls adopted from China. **Material and Methods:** Prospective cohort study on 30 Chinese girls adopted in Spain between the years 2001-2007 in which growth and pubertal development were controlled after adoption during a 15-year follow-up. Weight, height, and head circumference were measured and recorded in a standardized way, and body mass index (BMI) was calculated. The anthropometric parameter values, and ages at thelarche and menarche, were compared with the China growth and pubertal development references. **Results:** Initial evaluation (1.33 years): weight Z-score, -1.55; height Z-score, -1.4; BMI Z-score, -0.72; head circumference Z-score, -1.1. At 2 years of age, there had been significant catch-up growth in weight and height (Z-score -0.74 and -0.62, respectively). Growth pattern: they weighed less up to 14 years and more between 15-16 years (at 16 years, +0.64 kg); they measured less in all ages (at 16 years, -2.83 cm); BMI was lower between 1.33-2 years and 10-12 years, and higher between 14-16 years; head circumference was lower at all ages (at 6 years, -0.96 cm). There were no statistically significant differences. Mean age at thelarche was 10.08 years (median, 10 years), and at menarche 12.17 years (median, 12.5 years). **Conclusions:** In the cohort of adopted Chinese girls, the growth potential was lower and the pubertal development was slightly later, although without significant differences, compared with the China growth and pubertal development references.

**Keywords:** Female, China, Adoption, Growth, Thelarche, Menarche

### INTRODUCTION

Prospective studies on growth in adopted Chinese girls are very scarce and are limited to short-term follow-ups of less than four years. The main purpose of these studies was to assess the degree of growth retardation upon arrival in the adoptive country and the degree of catch-up growth after adoption.<sup>1-6</sup>

Growth retardation is a common finding in internationally adopted girls. Studies suggest that the cause may be related to phenomena such as malnutrition, stress, and psychosocial deprivation prior to adoption.<sup>7-9</sup>

The drastic change that occurs after adoption usually causes them to experience significant catch-up growth, but this can result in an acceleration of pubertal development. The pathophysiological mechanisms are not clear and possibly involve various endogenous and exogenous factors.<sup>9-12</sup>

China has been the main country of origin for children adopted abroad by Spanish families.<sup>13</sup> China is a very large country in which genetic growth potential can vary between different geographic regions and socioeconomic classes.<sup>14</sup>

### AIMS AND OBJECTIVES

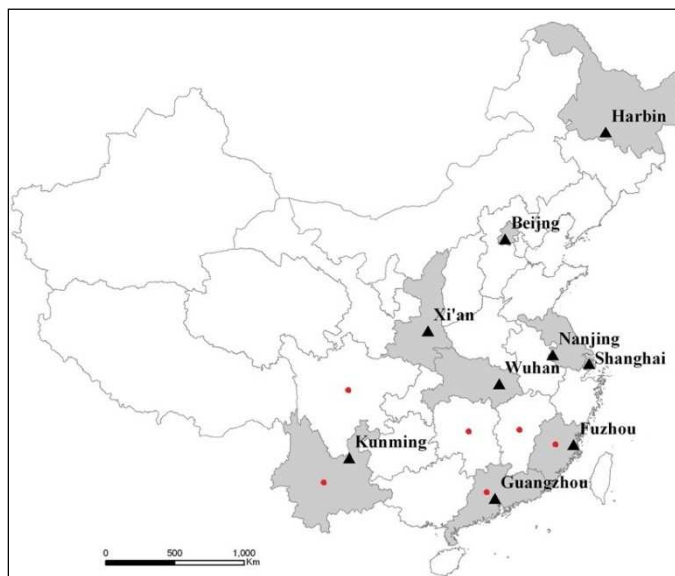
The objectives of this study were to provide data on the longitudinal growth and timing of thelarche and menarche in adopted Chinese girls and comparison with the China growth and pubertal development references.

### MATERIAL AND METHODS

Observational epidemiological study of longitudinal design carried out on a cohort of 30 Chinese girls adopted by Spanish families between the years 2001-2007 in which growth and pubertal development were controlled after adoption during a 15-year follow-up in a specialized center of reference.

The total sample at the beginning of the study was 64 girls. Girls whose growth could not be controlled for 15 years ( $n = 33$ ) and those who showed signs of pubertal development before 7 years of age and were referred to pediatric endocrinology for further evaluation of possible precocious puberty ( $n = 1$ ) were excluded from the study.

The adopted Chinese girls studied had been abandoned for socioeconomic reasons and/or sexual discrimination within a few hours or days of their birth at the doors or near health centers, public buildings, or the orphanages themselves, thereby ensuring a quick reunion, reception, and care. All were institutionalized until their adoption in orphanages in the southeast and southwest provinces of China (Jiangxi, Guangdong, Hunan, Fujian, Yunnan, and Sichuan) (Figure 1).



**Figure 1.** Geographical distribution of the 9 cities (their corresponding provinces are shaded) in China where girls were selected for the China growth references. With a red dot, the provinces of origin of the adopted Chinese girls. Adapted from Zong XN and Li H<sup>15</sup>

The quality of the food and the health and psycho-affective care received during their institutionalization was questionable based on the information collected by the families in the orphanages and by the pre-adoption medical reports issued. Data on the health and nutritional status of the biological mother during pregnancy, gestational age and immediate neonatal period, anthropometric, health, and educational family history, and areas of residence (urban, suburban, or rural) were unknown.

### Measurements

Weight, height, and head circumference were measured and recorded in a standardized way, always by the same professional. The technical equipment used consisted of a Seca 708 electronic platform scale (Max 200 kg;  $d = 0.1$  kg) with a built-in stadiometer for height, GC-1104 children's electronic scale (Max 20 kg;  $d = 10$  g), horizontal board for length (Max 100 cm) for children under 3 years, and a flexible non-stretchable plastic tape measure. The anthropometric parameter values were entered into an Excel sheet with which the arithmetic mean, standard deviation (SD), and body mass index ( $BMI = \text{kg}/\text{m}^2$ ) were calculated. Families were instructed to detect thelarche and menarche and to carry out control after their appearance. The age values were entered into an Excel sheet with which the arithmetic mean, the SD, and the median were calculated. The anthropometric parameters values, and ages at thelarche and menarche, were compared with the China growth and pubertal development references.

The procedures used in the patients were performed after obtaining informed consent from the legal guardian. The data was used in accordance with Organic Law 3/2018 on the Protection of Personal Data and Guarantee of Digital Rights in force in Spain

### Statistical analysis

Through the Social Science Statistics ©2023 operating system, the mean values obtained from the anthropometric parameters were compared with the China growth references for girls<sup>15</sup>, calculating the Z-score and the p-value with a significance level  $< 0.05$ . Significant catch-up growth was defined when the Z-score of the parameter had an increase  $> +0.5$  SD. The graphs were prepared with the Excel calculation program.

## RESULTS

Table 1 shows the values of weight, height, BMI, and head circumference of the adopted Chinese girls obtained at the initial evaluation after the adoption and in the annual controls during a 15-year follow-up.

The mean age at which the initial evaluation was carried out was 1.33 years. The mean age of onset of thelarche (Tanner stage 2) was 10.08 years (median, 10 years). The mean age at menarche presentation was 12.17 years (median, 12.5 years).

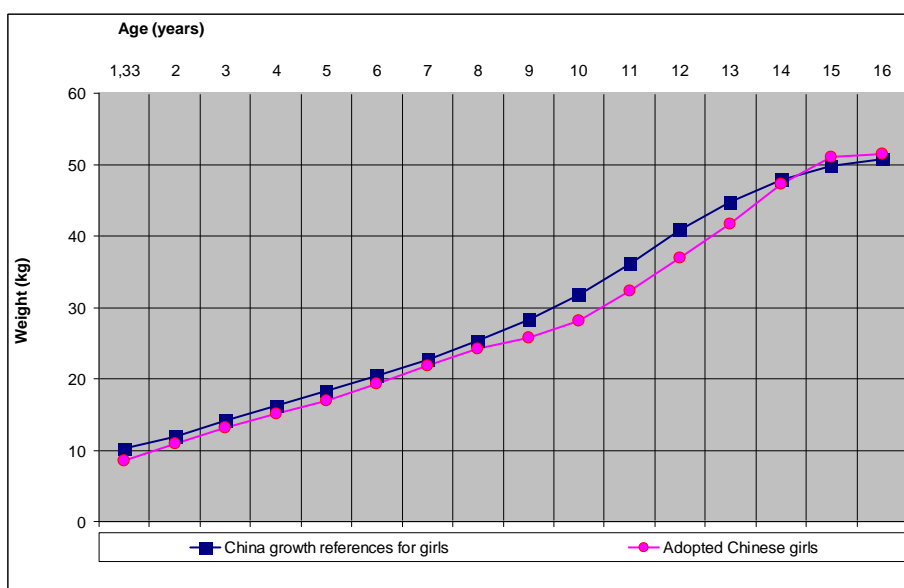
**Table 1.** Values of weight, height, body mass index, and head circumference of adopted Chinese girls (n = 30) at initial evaluation after adoption and during a 15-year follow-up.

Age (years)	Weight (kg)	Height (cm)	BMI (kg/m <sup>2</sup> )	Head circumference (cm)
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
1.33*	8.53 (1.65)	74.45 (6.91)	15.4 (0.3)	44.37 (1.52)
2	10.96 (1.50)	85.05 (5.79)	15.2 (0.1)	46.18 (1.18)
3	13.13 (1.53)	92.58 (5.66)	15.3 (0.1)	47.54 (1.03)
4	15.06 (1.95)	100.02 (5.92)	15.1 (0.3)	48.51 (0.84)
5	16.92 (2.72)	106.26 (6.61)	15.0 (0.7)	49.04 (0.95)
6	19.32 (3.37)	113.12 (6.84)	15.1 (1.0)	49.54 (1.04)
7	21.80 (3.93)	119.61 (6.89)	15.2 (1.1)	50.13 (1.10)
8	24.18 (4.58)	125.49 (7.11)	15.4 (1.4)	50.70 (1.24)
9	25.73 (4.32)	128.87 (5.64)	15.5 (1.4)	51.19 (1.35)
10	28.13 (3.44)	134.44 (4.73)	15.6 (0.9)	51.74 (1.44)
11	32.26 (4.04)	140.92 (5.35)	16.2 (0.9)	52.39 (1.48)
12	36.94 (5.17)	146.95 (5.56)	17.1 (1.2)	52.94 (1.70)
13	41.71 (5.63)	151.36 (4.63)	18.2 (1.4)	53.65 (1.66)
14	47.25 (4.21)	154.64 (4.92)	19.8 (0.6)	54.52 (1.67)
15	51.02 (4.54)	156.55 (5.21)	20.8 (0.5)	55.04 (1.79)
16	51.45 (5.21)	157.27 (5.12)	20.8 (0.8)	55.14 (1.74)

\* Initial evaluation after adoption; BMI: body mass index; SD: standard deviation.

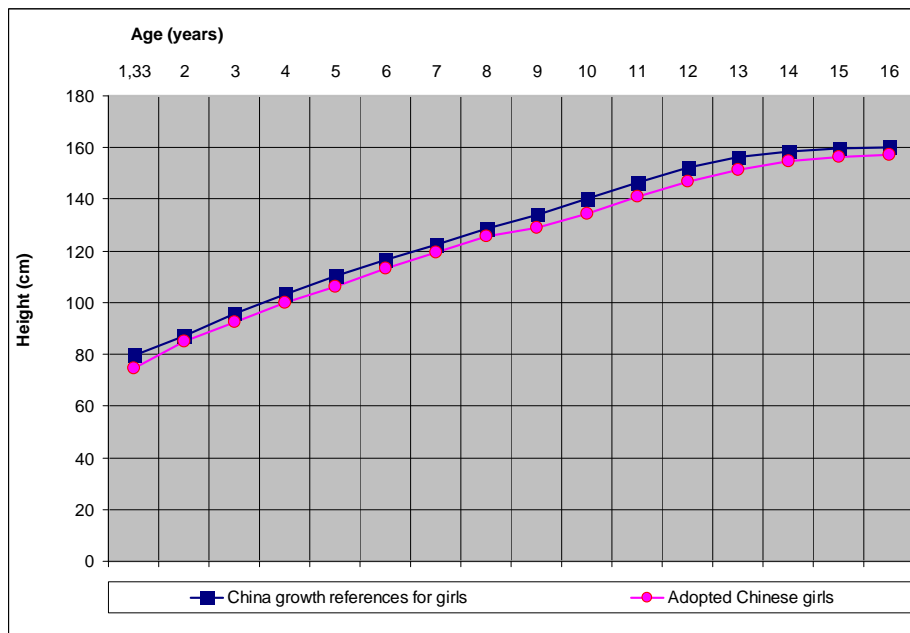
Figures 2 to 5 compare the curves of mean values for the age of weight, height, BMI, and head circumference of Chinese girls adopted with the China growth references for girls.

**Weight-for-age** (Figure 2). At initial evaluation, Z-score was -1.55. At 2 years of age, there had been significant catch-up growth (Z-score -0.74). In longitudinal evolution, adopted Chinese girls weighed less up to 14 years, mainly between 10-12 years, and weighed more between 15-16 years. At 16 years the weight was +0.64 kg. No statistically significant differences were found.



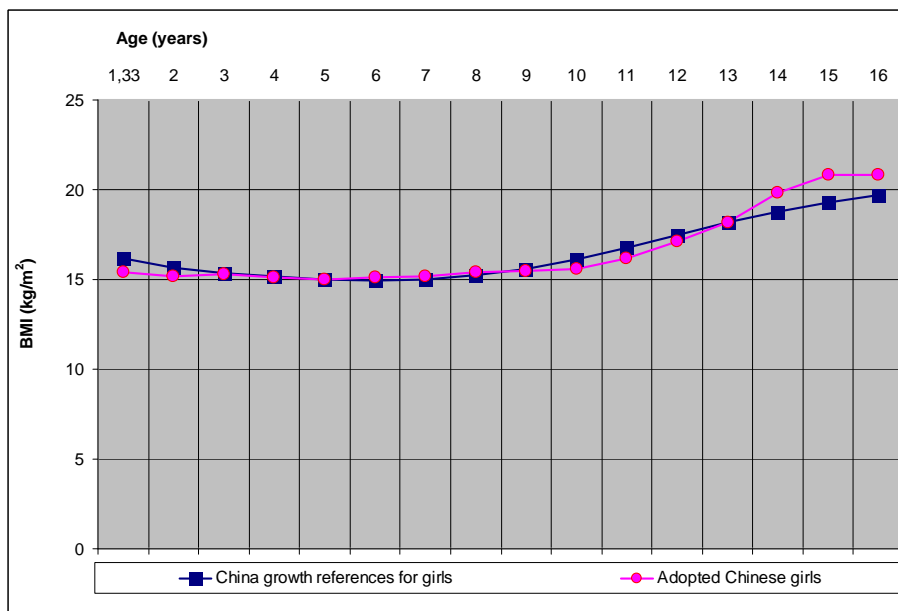
**Figure 2.** Weight-for-age of adopted Chinese girls compared with the China growth references for girls.

**Height-for-age** (Figure 3). At initial evaluation, Z-score was -1.4. At 2 years of age, there had been significant catch-up growth (Z-score -0.62). In longitudinal evolution, adopted Chinese girls were smaller at all ages, mainly between 10-12 years. At 16 years of age, the height was -2.83 cm. No statistically significant differences were found.



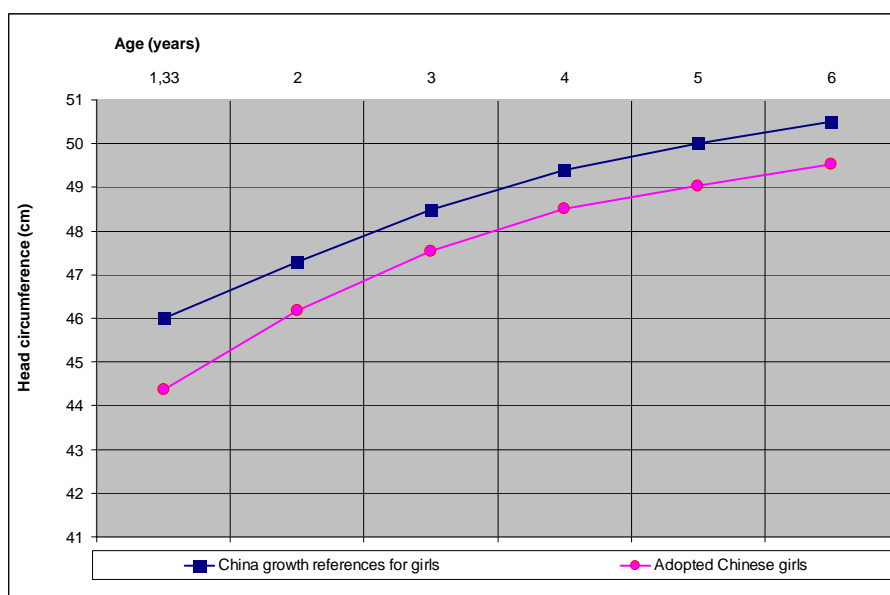
**Figure 3.** Height-for-age of adopted Chinese girls compared with the China growth references for girls.

**BMI-for-age** (Figure 4). At initial evaluation, Z-score was -0.72. At 2 years of age, Z-score was -0.38. In longitudinal evolution, it was lower in adopted Chinese girls between 1.33-2 years and 10-12 years, and higher between 14-16 years. At 16 years of age, the BMI was +1.08 kg/m<sup>2</sup>. No statistically significant differences were found.



**Figure 4.** BMI-for-age of adopted Chinese girls compared with the China growth references for girls.

**Head circumference-for-age** (Figure 5). At initial evaluation, the Z-score was -1.1. At 6 years of age, there had been no significant catch-up growth (Z-score -0.74). In longitudinal evolution, it was lower in adopted Chinese girls at all ages, mainly between 1.33-2 years. At 6 years of age, the head circumference was -0.96 cm. No statistically significant differences were found.



**Figure 5.** Head circumference-for-age of adopted Chinese girls compared with the China growth references for girls.

## DISCUSSION

To our knowledge, this is the first prospective study on long-term growth in adopted Chinese girls with a 15-year follow-up.

The China growth references for girls were developed in 2005 with a sample of 47,213 girls randomly selected from the urban areas of 9 major cities (Beijing, Shanghai, Harbin, Xi'an, Nanjing, Wuhan, Guangzhou, Fuzhou, and Kunming) (Figure 1). The reference sample was representative of a healthy and relatively well-nourished population that was born and raised in good conditions, with high living standards and educational level (80.6-84.4% of mothers and fathers, respectively, of these girls had secondary education or higher; the overall breast-feeding rate was 85.1% and exclusive breastfeeding 47.7%). Exclusion criteria included temporary residents, history of premature birth, birth weight less than 2,500 g, chronic illness, obviously malnourished, physically handicapped, and acute illness within the screening period.<sup>15</sup>

The characteristics of the studied cohort of adopted Chinese girls were previously described, and it is clear that we are comparing a cohort of disadvantaged girls from an early age until their adoption with a national sample of girls privileged from birth.

All short-term prospective studies on growth in adopted Chinese girls observed delayed weight, height, and head circumference at initial post-adoption assessment, with Z-scores between -1 and -2 SD with respect to the reference standards used (World Health Organization or national standards of the adoptive country).<sup>1-6</sup>

Studies with follow-up between 1 and 3 years after adoption have shown significant weight recovery between 6-12 months and height between 12-24 months.<sup>4-6</sup> Van Ijzendoorn, *et al.*<sup>16</sup>, through a meta-analysis study, calculated the differences in rates of stunting between internationally adopted children and reference populations. In adopted children, they observed that at the time of adoption, they presented significant delays in weight, height, and head circumference and that after adoption they showed almost complete recovery of weight and height, but recovery of head circumference was slower and remained incomplete. They concluded that international adoption leads to a substantial recovery of weight and height, but not head circumference, demonstrating the differential plasticity of children's physical growth.

These short-term growth findings were corroborated in our study's cohort of adopted Chinese girls, and with respect to observed delays, no significant differences were found compared with the China growth references.

Regarding the longitudinal growth pattern of the cohort of adopted Chinese girls, although no significant differences were found with the China growth references, the main divergences were as follows. The nutrition level of the adopted Chinese girls was lower than that of the China girls up to the age of 14, from which age the nutrition level was higher. The height level of adopted Chinese girls was lower than that of the China girls at all ages. According to the China growth references for girls, height after age 15 is very close to adult height.<sup>15</sup> The head circumference of the adopted Chinese girls was smaller than that of the China girls at all ages.

Concerning pubertal development, Ma, *et al.*<sup>17</sup>, in a cross-sectional study on a nationally representative sample of 20,654 Chinese girls, determined the median age of thelarche and menarche at 9.20 years and 12.27 years, respectively. Sun, *et al.*<sup>18</sup>, in a cross-sectional study on a nationally representative sample of 15,388 Chinese girls of the Han ethnic group, determined the median age of thelarche and menarche at 9.18 years and 12.43 years, respectively, and that urban girls reached menarche at a much earlier age than rural girls. Liang, *et al.*,<sup>19</sup> in a recent cross-sectional study on a nationally representative sample of 108,343 Chinese girls, determined the median age at thelarche and menarche to be 9.65 years and 12.39 years, respectively. Hayes, *et al.*,<sup>20</sup> in a survey study of parents of 814 Chinese girls adopted in North America, estimated the median age at menarche to be 12.37 years and the pre-10-year prevalence to be 3%. Tan, *et al.*<sup>21</sup> studied 298 Chinese girls with an age range of 7.3-11.1 years, adopted in North America at 1.05 years, and observed that in 3.5% thelarche appeared before the 8 years and 2.3% presented menarche before the age of 11.

In the studied cohort of adopted Chinese girls, compared to the national studies from China, the age of onset of thelarche was slightly later and the age of menarche was similar. In 3.3%, the thelarche appeared before the age of 8, and 6.6% presented menarche before the age of 11. A phenomenon that we do not know how to interpret is the fact that between thelarche and menarche was the period in which the greatest difference was observed, by default, in weight and height with respect to the China growth references (Figures 2 and 3).

It is known that growth and pubertal development are determined by endogenous factors (genetic, epigenetic, metabolic, and neurohormonal) that interact throughout the entire process with a multitude of exogenous factors (food, nutrition, hygiene, medical care, chronic diseases, climate affective, psychosocial environment, stress, environmental variables, etc.). So that the genetic potential is not altered, it is essential that all the factors work correctly and are balanced.<sup>7,8,22-25</sup>

Although we cannot justify it pathophysiologically, we believe that various exogenous factors may be involved in the pattern of growth and pubertal development that we have observed in the cohort of adopted Chinese girls.

## CONCLUSIONS

In the cohort of adopted Chinese girls, the growth potential was lower and the pubertal development was slightly later, although without significant differences, compared with the China growth and pubertal development references.

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