Early-growth faltering in post-institutionalized youth and later anthropometric and pubertal development

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Abstract

Background—Early life adversity that increases the risk of growth stunting is hypothesized to increase the risk of obesity and, in girls, early onset puberty. This hypothesis was tested in children adopted from orphanages.

Methods—Post-institutionalized (PI) youth were compared with youth reared in comparable families (non-adopted; NA) on height, weight, pubertal stage, and fat mass (127 PI, 80 female; 156 NA, 85 female, aged 7–14 years). Anthropometrics at adoption were obtained from first US clinic visits.

Results—25% of PIs were height stunted (<3rd percentile) at adoption. Years post adoption, PIs had lower BMI-for-age ($p = .004$); height-for-age ($p < .001$); and less body fat ($p < .001$) than NAs, but did not differ by sex. Pubertal status did not differ by group or sex. The anthropometric findings held when the stunted-at-adoption subset was examined; they were also less likely to be in central puberty than other PI youth.

Conclusion—Early deprived orphanage care increases the risk of growth stunting but not obesity in children adopted into US families and does not independently contribute to early onset puberty for PI girls. The role of the environment following early adversity may modify the impact of early adverse care.

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Clinical Observation

INTRODUCTION

Throughout evolution, humans have experienced periods of feast and famine. There is evidence that early in development, physiological adaptations to deprived environments increases later risks of obesity, early onset puberty in girls and later, metabolic syndrome and cardiovascular disease, particularly if there is a shift over time from resource-poor to resource-rich environments (1–4). Studies of maltreated children and youth reveal that similar effects of childhood adversity on pubertal timing and obesity risk may result even when adversity is psychosocial (5–7). Here it may be that continued adversity, such as low socioeconomic status, enhances risk.

Children adopted from orphanages (post-institutionalized; PI) provide an interesting case to test hypotheses about the sequelae of early adversity. Institutional care early in life typically results in significant delays in height and weight as well as delays in other domains of development (8–11). These delays are correlated with reductions in psychosocial care and are observed even when the nutritional content of feedings is adequate. Propped bottles and stress-impaired absorption of nutrients are also likely contributors to poor growth for institutionalized infants and young children (8, 12). With adoption into families in industrialized countries, these children make a radical shift from conditions of low to high psychosocial and physical resources. They typically experience rapid catch-up growth in height and weight and are typically within normal height and weight ranges within a year or two of adoption (8, 11). Clinically, there is concern that PI children with rapid catch-up growth may be at higher risk for obesity, early onset puberty in girls, and, in adulthood, metabolic syndrome (9).

Research on postnatal growth trajectories in typically-developing children suggest that being small at birth but having a large body mass as an adult is associated with a high risk of disease (13, 14). There is some evidence to suggest that the physiological mechanisms of catch-up growth promote the accumulation of body fat after nutritional deprivation (15). Studies of children in low and middle income (LAMI) countries show that early postnatal catch-up growth is associated with obesity and risk for metabolic syndrome later in life (2, 16). Robust catch-up growth prevalent in children adopted internationally is a risk factor for later obesity and early onset puberty, both of which are risk factors for cardiovascular diseases, type-2 diabetes, and musculoskeletal disorders (17). Early puberty is also associated with sexually transmitted diseases and teenage pregnancy in girls, smoking and aggressive behavior in boys, adolescent alcohol abuse and drug use and early sexual debut in both sexes (18–20).

There is some evidence that clinical concerns for PI children may be substantiated. Girls from India adopted into Sweden were found to have earlier menarche if they were growth stunted at adoption and experienced rapid catch-up growth (21). Looking only at children seen for precocious puberty in Sweden, international adoption after age 2 was associated with a marked increase in risk of precocious puberty (22). The rate of central precocious puberty in the population is 1 in 5,000 to 10,000 children, but is much more common (10 to 1 ratio) in girls than in boys (23) and has an increased incidence (0.8–1.8%) in internationally adopted children (24). However, in at least one study, the risk of precocious

puberty was as great for immigrant children without evidence of early growth stunting from the same regions of the world which suggests the possibility that changes in diet that occur after immigration could influence pubertal status; alternatively, early exposures to endocrine disruptors might be involved (25). In contrast to these studies, a recent study in girls adopted from China into North America found that adopted girls had similar age at menarche to their non-adopted peers (26). Though internet surveys of parents of internationally adopted children have yielded evidence of precocious puberty, accuracy of pubertal stage cannot be determined in such surveys nor can the percentage of families responding be determined (27).

In this study we examined and compared height, weight, and pubertal stage in PI children aged 7 through 14 years to children born into homes comparable in parental education and income to the homes of the PI youth (non-adopted; NA). We also examined the impact of height-stunting at adoption on growth and pubertal status within PI youth. Our goal was to test the hypothesis that a shift from psychosocial and physical deprivation to highly resourced homes would increase the risk of obesity in boys and girls and, for girls, advanced pubertal timing. We predicted that this would be most clearly observed for PI youth who were stunted at adoption.

METHODS

Study Population

PI youth were recruited from a registry of internationally adopting families interested in research participation. NA youth were recruited from a registry of research-interested families with comparable education and income to adoptive families. Both PI and NA youth lived within driving distance of Minneapolis, MN. Exclusion criteria for PI youth was adoption from institutions after 60 months of age, facial indices of fetal alcohol exposure using the FAS Facial Photographic Analysis software, and congenital and endocrine disorders. Comparison children were excluded if they experienced early adversity as determined by early life maltreatment or neglect or had been diagnosed with neurodevelopmental disorders. All procedures were approved by the University's institutional review board. Written informed consent was obtained from parents and written informed assent was obtained from the children.

Measurements and Protocol

Anthropometrics—Height and weight for age at adoption was obtained from PI children's first pediatric visit after entering the US. Parents signed HIPAA release forms and provided their child's providers name and address. As some clinics reported that the early adoption data was missing from their files, 109 of 127 PIs data were obtained. Early life growth faltering (stunting) was defined as a height-for-age equal to or below -2 standard deviations from the mean of the WHO reference group (i.e., < 3rd percentile height-for-age) at adoption (35).

A nurse trained in auxology measured height in triplicate to the nearest 0.1 cm using a calibrated stadiometer (SECA model 216, Seca Co. Hanover, MD) and weight to the nearest

0.1 kg using a calibrated scale (Health-O-Meter Professional 349KLX Professional Medical Weight Scale, Pelstar LLC, McCook, IL). If there was a discrepancy between the measurements in triplicate, the mean score was taken. To compare children of different ages, height and BMI (weight in kg/height in m^2) measurements were converted to z-scores (the difference between the child's measurement and the age mean divided by the standard deviation [SD] for the child's age). We calculated age-sex-adjusted BMI z-score and height-for-age z-score using the 2007 World Health Organization reference data, which is comprised of growth data from widely different ethnic backgrounds and cultural settings around the world (35). Waist and hip circumferences (cm) were measured in triplicate with an anthropometric tape while the participants were wearing light clothing. Waist circumference was measured one inch above the navel. Hip circumference was measured at the maximum protuberance of the buttocks. The waist-to-stature ratio was calculated by dividing the waist (cm) by the height (cm). Body fat percentage was measured in the BOD POD (Life Measurement Instruments, Concord, CA), a 2-chamber air displacement plethysmograph method of determining body fat percentage and body volume through a software-driven automated test (36). The BOD POD was calibrated before each test following the manufacturer's recommendations. Participants wore a tight-fitting swimsuit or biking shorts, and a swim cap, and remained seated in the chamber during the measurement.

Pubertal Development—Study nurses received Tanner stage training from an expert in performing this assessment in clinical trials and a pediatric endocrinologist. A total of 264 participants underwent a nurse's exam for Tanner Staging (range 1–5, M=2.48, SD = 1.51). 6% (n=17) of youth refused the Tanner stage exam and had pubertal development scores estimated from self-reported Petersen Pubertal Development Scale. Three pediatric endocrine nurses conducted a physical exam to measure pubertal stage using Marshal and Tanner criteria (37, 38). Cohen's κ was run to determine if there was agreement between the three nurses' Tanner stage assessment on breast and genital measures in 33 boys and 50 girls. There was almost perfect agreement between the nurses' assessments, κ = .87, p < .001 using Landis and Koch criteria of >.81. In girls, breast and pubic hair stage was determined by visual examination and the nurse palpated breasts to distinguish breast from adipose tissue. In boys, genital and pubic hair stage was determined by visual examination and the nurse determined testicular volume using a Prader orchidometer. Tanner breast stage in girls and genital stage in boys was used to determine entry into central puberty, as these indicators are most indicative of central puberty. Central puberty was therefore defined as Tanner stage 2 in breasts for girls and Tanner stage 2 genital for boys (4mL), using the most developed breast or testicle measured. Central precocious puberty was defined as Tanner breast stage 2 before age 8 years in girls and Tanner genital stage 2 before age 9 years in boys. "Early-onset" puberty was defined as the onset of puberty (Tanner stage 2) in girls between 8 and 10 years of age and in boys between 9 and 11 years of age (24). Delayed puberty was defined as not reaching Tanner breast stage 2 by age 14 for girls and not reaching Tanner genital stage 2 by age 15 for boys (24).

Pubertal status was also assessed using self-report from the child and parent of body changes associated with pubertal using the Pubertal Development Scale (39, 40). For boys, measures included growth in height, body hair, skin changes, deepening of voice, and facial hair. For

girls, measures included growth in height, body hair, skin changes, breast development, and onset of menarche. Responses were 1 = not yet started, 2 = barely started, 3 = definitely started, and 4 = seems complete (39). Menstruation was coded as 4 if it begun and 1 if it had not begun, alongside a self-report of age in months of menarche. This measure yields a mean score from 1 (puberty has not begun) to 4 (puberty is complete).

Data Analysis

Preliminary analysis of missing data from adoption clinic visits with Little's MCAR test indicated that the early growth data was missing at completely at random. Analyses were then conducted in four parts. First, descriptive statistics were examined and independent samples t-tests were conducted to examine group differences in participants' age and growth. Then, a chi-square test was used to determine group differences in early onset puberty compared to typical onset puberty. Fisher's exact test was used to determine the association between group and precocious puberty for PI and NA youth. Fisher's exact test was also used to determine the association between early life height stunting or no early life height stunting in PI youth and Tanner stage 1. Finally, we used a proportional odds model to determine the effect of BMI, age, gender, and group on Tanner stage. We assessed the parallel regressions assumption model by fitting a partial proportional odds model and assessing the change in model fit using a test of a deviance. We found that BMI and age met the parallel regressions assumption but gender and group did not. However, because gender and group were not statistically significantly overall, they were dropped from the model and the model presented in the results section were from the proportional odds model with BMI and age.

RESULTS

Demographic and anthropometric results are shown in Table 1. Study participants were 7 through 14 years ($M = 11.16$, $SD = 2.30$). 127 (80 females) participants were adopted internationally from orphanages (PI) and 156 (85 females) participants were non-adopted (NA) youth. PIs were from 14 countries (54 Russia, 23 China, 16 India, 8 Guatemala, 5 Colombia, 4 Ethiopia, 4 Ukraine, 4 Vietnam, 2 Haiti, 2 Kazakhstan, 2 Solvakia, 1 Ecuador, 1 Nepal, 1 Romania), PIs were also from a range of racial and ethnic backgrounds: 49 Asian, 52 Caucasian, 6 Black/African, 13 Latin American Indian, 4 multiracial, 3 other/unknown. NAs were born in the US (1 Asian, 139 Caucasian, 4 Black, 11 multiracial, 1 other/unknown). Age did not differ between groups. Household income also did not differ between groups with a median household income of $85,001–$100,000 (range $25,000 to > $200, 000).

At adoption ($M = 19.8$ months old, $SD = 12.6$ months), the PIs were below norms on height-for-age (z-score, $M = -1.12$, $SD = 1.46$) and weight-for-age (z-score, $M = -0.92$, $SD = 1.15$), with 43% being below the 10th percentile in height-for-age and 24% being classified as growth stunted (below the 3rd percentile). The PI youth displayed the expected catch-up growth such that, by the time of our assessment, 5% were stunted and 72% were above 1 SD below the mean on height and weight.

Anthropometrics

PIs were shorter than the NAs, on average, at assessment. In contrast to predictions, we found no evidence that PIs were heavier than NAs. Indeed, PIs had lower BMIs than NAs (Figure 1). At Time 1, 11.8% of PI children were overweight (BMI>85th percentile) and 7.9% were obese (BMI>95th percentile). 15.4% of NA children were overweight (BMI>85th percentile) and 7.1% were obese (BMI>95th percentile). Both groups fell below rates of overweight (14.9%) and obese (16.9%) in US children, but were roughly comparable with percentages for their socioeconomic group (28). They also had lower body fat percentages measured by air displacement plethysmography than NAs. This held even when we removed 9 implausible cases with body fat below 3%; $t(271) = -2.82$, $p = .005$.

There was also no evidence that weight was being preferentially stored in the gut, as waist-hip ratios and waist-to-stature ratios did not differ between PIs and NAs. The effect sizes of the differences found between the two groups were large for height-for-age ($d = 0.64$) and moderate for BMI-for-age ($d = 0.35$) and body fat percentage ($d = 0.40$). Additional analyses assessed the data to determine if girls might be showing the early adversity-obesity effects; however, none of the measures were significant significantly different for PI girls. Finally, although some children (5 PI, 4%; 5 NA, 3%) were taking stimulant medication for ADHD which can affect growth and weight gain, adding stimulant use as covariate had no effect on these findings.

Pubertal development

Table 2 shows the results for pubertal stage with the full range of Tanner stages noted for both PIs and NAs. We predicted that PI children as a group would be in later Tanner stages to indicate either earlier onset or a more rapid tempo of pubertal development than NA children. Though one PI girl displayed signs of precocious puberty, there was no statistically significant association between PI status and precocious puberty as assessed by Fisher's exact test, p = .170. No children were in early-onset puberty. Furthermore, no children were in delayed puberty, and a t-test showed no difference in self-reported age at menarche between PI and NA girls.

A proportional odds model was run to determine the effect of group (PI or NA), sex, BMI, and age on pubertal status (Tanner stage). We found a main effect of BMI and age but found no evidence of an effect from sex or group membership. An increase in age (expressed in years) was associated with an increase in the odds of higher Tanner stage, with an odds ratio of 3.418 (95% CI, 2.820 to 4.143), $\chi^2(1) = 156.80$, p < .001 (Figure 2). An increase in BMI was associated with an increase in the odds of higher Tanner stage, with an odds ratio of 1.159 (95% CI, 1.071 to 1.253), $\chi^2(1) = 13.61$, p < .001. The results did not differ when using the WHO-adjusted metric of BMI-for-age, and thus raw BMI is reported for ease of interpretation. As there was no group or sex difference found in pubertal stage, these data were inconsistent with our prediction that PI girls would be more likely to enter puberty earlier than non-adopted peers.

Anthropometric and pubertal development in previously stunted post-institutionalized youth

The 26 children who had been growth stunted at adoption were not different in age at adoption or sex than their non-stunted PI peers. Notably, previously-stunted PI youth had greater height catch-up growth than their non-stunted peers; $t(107) = 6.89$, $p < .001$. Rather than being prone to obesity, previously growth stunted PI youth did not exhibit greater fat mass or BMI-forage. Two youth who were previously stunted at adoption were overweight at follow-up (8%) while 18 non-stunted at adoption PI youth were overweight or obese at follow-up (22%). Previously stunted youth were also still shorter for age than the non-stunted PI youth; $t(107) = 3.05$, $p = .003$.

Of the previously height stunted PI youth, 15 (57.7%) were in Tanner stage 1 compared to all other Tanner stages at follow-up. For previously non-height stunted PI youth, 25 (30.1%) were in Tanner stage 1 compared to all other Tanner stages. There was a statistically significant association between prior height-stunted status and Tanner stage 1 as assessed by Fisher's exact test, $p = .011$. However, linear catch-up growth was not associated with Tanner stage 1.

DISCUSSION

The results of this study provided no support for the hypothesis that significant adversity and growth stunting early in life would increase risk of obesity and, for girls, early onset puberty. Instead of finding greater BMIs, fat mass, and waist-hip ratios in the PI than NA youth, PI youth had lower BMI's and fat mass and did not differ from NAs in waist-hip ratio. No sex by group effects were noted, thus these findings held for both girls and boys. The results for pubertal development also did not support the early adversity-early puberty hypothesis. Similar to a recent study of girls adopted from China, we did not find a difference in the timing of menarche between PI and NA children (26). Our growth data are also similar with those of Walker, Chang, and Powell, who reported that previously stunted Jamaican children remained shorter and had lower BMIs, smaller body fat percentages than non-stunted Jamaican children in late adolescence (29). Although PI children were, on average, shorter and thinner than their non-adopted peers in body fat and BMI measures, the waist-to-stature ratio (WSR) for PI and NA children did not differ significantly. Both group's WSRs were well below the at-risk cut-off of .5 (30).

Our results comparing previously stunted PI children to non-stunted PI children demonstrate that catch-up growth post-adoption was not associated with any measures of pubertal development or early onset puberty. Perhaps the cohort of children adopted internationally in our study, adopted before 5 years of age into highly-resourced homes in the US, were adopted early enough or had medical care or home environments that helped to mitigate risks of rapid catch-up growth. The risk of robust catch-up growth post adoption might not have been captured by our measure of catch-up growth. Rapid catch-up growth is an ill-defined concept in many studies, which further complicates comparison of catch-up growth outcomes between cohorts that are different age ranges and ethnicities (16). A recent twin study found that an obesogenic postnatal environment is more important than the fetal environment for the development of increased adiposity (31) and thus our sample of high

SES families might mitigate any risk for future obesity and early-onset puberty by providing a health-conscious environment for otherwise at-risk PI children. Both PI and NA youth groups had low rates of obesity compared to national standards in the US (28). Early onset of puberty in at-risk youth might be critically related to the obesogenic environment and adiposity levels necessary for pubertal hormones. The work of Addo, et al, shows that postnatal weight gain is a crucial factor in early pubertal development making a lack of post-adoption weight gain one potential reason for the absence of earlier puberty in our previously-stunted study population (32).

Though this study has the strengths of pubertal stage by exam and use of the BodPod to determine growth and pubertal status of PI and NA youth rather than relying upon self or parent report, this study had several limitations. The data were the initial data from a study that will follow children across three annual assessments. Thus, it is possible that more evidence of precocious puberty will emerge as the children progress through the study. Though another definition of delayed puberty is defined as Tanner breast stage 2 with no menarche by age 16, no children in this sample were 16 years old or older and thus delayed puberty defined by menarche could not be established. Future waves of data collection will enable us to better characterize development both in anthropometric measures and pubertal measures over time in the same cohort of children. However, as many have hypothesized that post-institutionalized and stunted children – and especially girl children – will have early onset puberty and greater risk of obesity, this study suggests that stress and growth stunting early in life do not necessarily increase the risk of obesity or early puberty in the context of a major intervention, adoption by highly educated and resourced parents. Although we have only a single case of precocious puberty in our cohort (1 out of 127=0.8%), this is in agreement with previous reports (0.8–1.8%) in internationally adopted children (24) and the association between precocious puberty and PI status was not statistically significant.

We also were unable to collect adoption-age-equivalent growth data for NA youth to compare their outcomes to previously height stunted PI and non-previously height stunted PI youth. However, as the rate of height-stunting is exceedingly low in industrialized countries, we would not expect NA youth from highly-resourced homes to have experienced height-stunting early in life.

Second, for the smallest children, low body fat percent scores might not be accurate due to the Bod Pod's methods of calculating body fat percentage, which is normed to typically-developing children and may over-estimate both the thoracic volume and bone density of children who are smaller in stature to result in unusually low body fat percentage scores. Other means of measuring body fat percentage, such as dual-energy x-ray absorptiometry (DXA), might be needed to further clarify the relationship between early life adversity and body fat percentage. However, even after removing the leanest Bod Pod measurements, the effect size remained between PI and NA children's body fat percentage scores, suggesting that PI children do indeed have lower percentages of body fat. However, cardiovascular risk depends not only on the percent of fat but where the fat is located (33). It is possible that for PI youth, fat is more likely to be concentrated in the gut. This will need to be assessed in future studies, although we should note that the waist-hip ratio was not greater for PI than NA children in this report. Conversely, PI youth might have metabolic abnormalities even in

the face of normal BMI ranges (34). Hence these data do not necessarily argue that the cardiovascular and metabolic risk for PI children is less than for the NAs.

Conclusion

These results suggest that stress and growth stunting early in life do not necessarily result in early onset puberty (for girls) and obesity risk. They raise the possibility that either the early timing of removal from adversity or the later context of rearing in highly resourced homes with highly educated parents may alter and perhaps buffer children from long-term impacts on BMI and early pubertal development. Of course, it will be critical to follow the subsequent waves of data collection on this project to understand growth curves both of body fat and pubertal stage as PI youth progress through adolescence.

Acknowledgments

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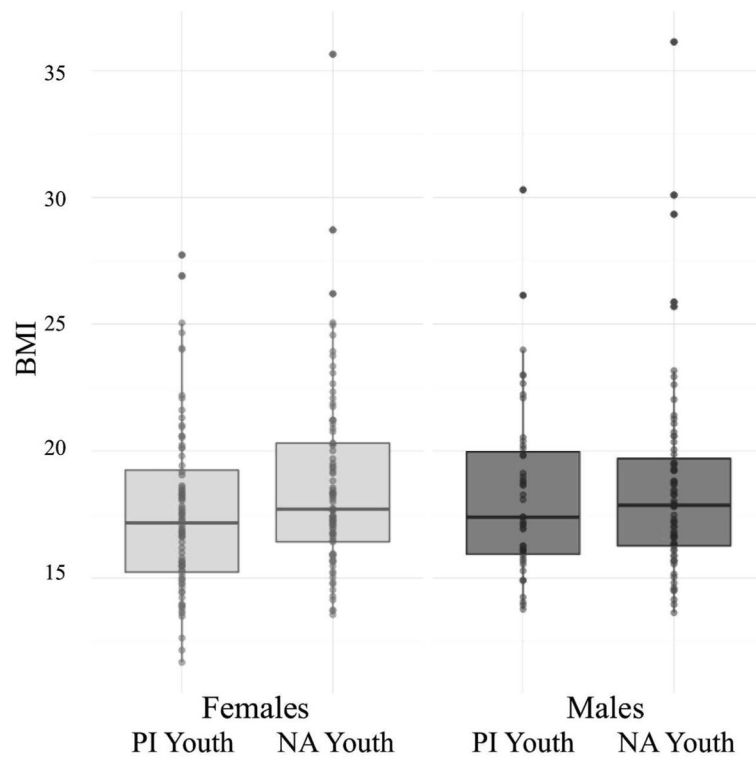
Figure 1.
Body Mass Index (BMI) of Post-Institutionalized (PI) and Comparison (NA) Youth. Female youth are compared in the left panel, while male youth are compared in the right panel. Dark grey boxplots represent NA youth, where light grey boxplots represent PI youth.

Figure 2.
Tanner Stage of Post-Institutionalized (PI) and Comparison (NA) Youth. Female youth are compared in the left panel, while male youth are compared in the right panel. Dark grey boxplots represent NA youth, where light grey boxplots represent PI youth.
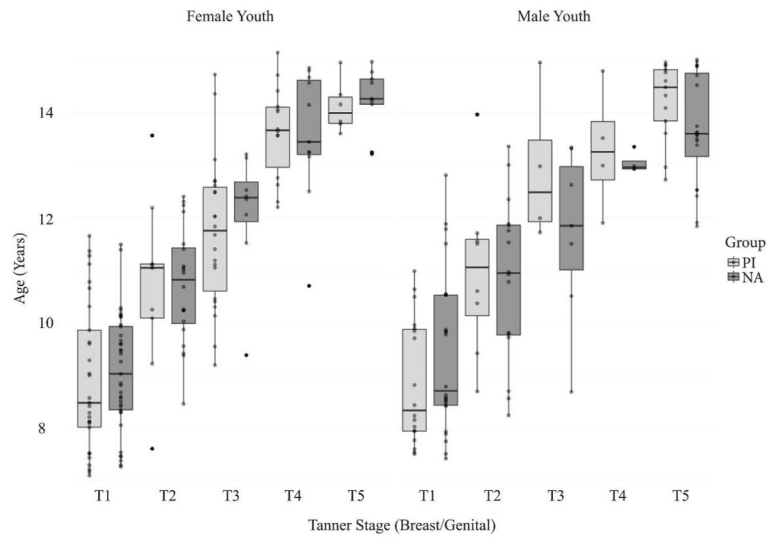
Table 1

Anthropometric and pubertal stage data in PI and NA children at exam 1

Characteristics	Post-Institutionalized; PI (*n* = 127) Mean ± SD	Non-adopted; NA (*n* = 156) Mean ± SD	*P*
Female	*n* = 80 (63%)	*n* = 85 (54.5%)	*.149*
Age (y)	11.24 ± 2.41	11.10 ± 2.22	*.629*
Height (cm)	143.09 ±15.09	146.74 ± 15.43	-
Height-for-age (z-score)	−0.37 ± 1.06	0.30 ± 1.02	.005 **
Weight (kg)	37.53 ± 12.39	41.50 ± 15.55	-
BMI	17.85 ± 3.35	18.64 ± 0.94	-
BMI-for-age (z-score)	−0.08 ± 1.31	0.33 ± 1.08	.005 **
Body fat percentage	15.55 ± 9.15[1]	19.18 ± 9.06	.001 ***
Waist (cm)	61.00 ± 9.44	63.50 ± 10.68	-
Hip (cm)	74.24 ± 10.43	76.70 ± 11.90	-
Waist to hip ratio	0.82 ± 0.07	0.83 ± .07	.393
Waist to stature ratio	0.43 ± 0.05	0.43 ± 0.05	*.362*

*
P ≤ 0.05

**
P ≤ 0.01

***
P ≤ 0.001

[1]
n = 126

Table 2

Anthropometric and pubertal stage data in PI and NA children

Characteristics	Post-Institutionalized; PI (*n* = 127)	Non-adopted; NA (*n* = 156)	
	Mean ± SD Median (range)	Mean ± SD Median (range)	*P*
Tanner Stage	2 (1 – 5)	2 (1 – 5)	*.536*
Number of menarcheal girls	16 (20%)	23 (27%)	*.327*
Age of onset of menstruating (years)	11.70 ± 1.64[1]	12.09 ± 1.29[2]	*.408*

[1] *n* = 16

[2] *n* = 23