Even transient rapid infancy weight gain is associated with higher BMI in young adults and earlier menarche

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Abstract

Background

Early postnatal rapid "catch-up" weight gain has been consistently associated with subsequent higher obesity risk and earlier pubertal development. In many low- and middle-income countries, infancy catch-up weight gain is transient and often followed by growth faltering. We explored the hypothesis that even transient catch-up weight gain during infancy is associated with later obesity risk and earlier puberty.

Methods

2352 (1151 male, 1201 female) black South African children in the Birth to Twenty (Bt20) prospective birth cohort study (Johannesburg-Soweto) underwent serial measurements of body size and composition from birth to age 18 years. At age 18 years, whole-body fat mass and fat-free mass were determined using dual energy x-ray absorptiometry. Pubertal development was assessed by the research team between ages 9 and 10 years, and recorded annually from age 11 years using a validated self-assessment protocol.

Results

Catch-up weight gain from birth to age 1 year, despite being followed by growth faltering between ages 1 and 2 years, was associated greater mid-upper arm circumference ($p=0.04$) and skin fold thickness ($p=0.048$) at age 8 years, and with higher weight ($p<0.001$) and BMI ($p=0.001$) at age 18 years after adjustment for sex, age, smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status. Infancy catch-up weight gain was also associated with younger age at menarche in girls ($p<0.001$). This association persisted after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status ($p=0.005$).

Conclusion

Transient catch-up weight gain from birth to age 1 year among children born in a low-income area of South Africa was associated with earlier menarche and greater adiposity in early adulthood. This observation suggests that modifiable determinants of rapid infancy weight gain may be targeted in order to prevent later obesity and consequences of earlier puberty in girls.

Introduction

Childhood obesity has been shown to track into adult life and confer a higher risk of cardiovascular disease and all-cause mortality [1-4]. Strategies to prevent the development of obesity may therefore benefit from interventions that are implemented in early life. This in turn requires a better understanding of biological factors that underlie the development of childhood overweight and obesity.

In high-resource settings, rapid “catch-up” weight gain during the first two postnatal years has consistently been associated with obesity in children and adults [5-9]. In addition, rapid infancy weight gain has been associated with earlier menarche with younger age at menarche as a robust marker of increased risk of adult obesity [10-18].

However, in many low- and middle-income countries infancy catch-up weight gain is transient and tends to be followed by growth faltering from around the age at weaning due to environmental factors and changes in feeding practice [19-21]. We therefore explored the hypothesis that even transient early postnatal catch-up weight gain is associated with later obesity risk and earlier puberty in a developing middle-income country.

Methods

Study population

Birth to Twenty (Bt20) is a prospective birth cohort study of 3,273 singleton births between late April 1990 and early June 1990, who continued residence within the metropolitan area of Johannesburg-Soweto, South Africa, for at least six months after delivery. At that time, Johannesburg-Soweto covered approximately 100 square miles and had close to 3.5 million inhabitants living in various forms of housing, including 400,000 informal housing units.

Children were enrolled into the Bt20 cohort through public antenatal and delivery clinics and hospitals. No children was excluded based on gestational age or birth weight. Study participants were demographically representative of the study area population for black, Asian and mixed ancestry backgrounds. White subjects were underrepresented as private clinics were not targeted during the recruitment strategy. The recruitment process and cohort characteristics are described in more detail elsewhere [22, 23]. All subjects of the current study were of black South African origin. Ethical approval was obtained from the University of the Witwatersrand Committee for Research and Human Subjects. A parent provided signed consent and verbal assent was obtained from each child.

<u>Assessments of body size, body composition and pubertal development</u>

Birth weight was obtained from hospital records. Birth length data were not available. Experienced research assistants measured weight and length during home visits at age 1 year and 2 years. Weight and standing height were measured by research assistants in a data collection site at ages 4, 5, 8, 13, 15 and 18 years. Mid-upper arm circumference (MUAC) as a general marker of nutritional status and triceps and subscapular skinfold thickness as estimates of fat mass were additional measurements at age 8 years. At age 18 years, dual energy x-ray absorptiometry (DEXA) (Hologic QDR 4500A) was used to measure whole-body fat and fat-free mass. A trained member of the research team assessed pubertal development between ages 9 and 10 years using the Sexual Maturation Scale (SMS) by Tanner [24, 25]. Subsequent determination of pubertal development was based on annual self-assessments according to the SMS and supported by drawings, descriptions and a tutorial. We have previously shown a high concordance between these self-assessments and assessments undertaken by a healthcare professional in the same population [26]. Female subjects and their parents were asked to recall age at menarche in full years on an annual basis from age 8 years.

<u>Calculations</u>

Body mass index (BMI) was calculated as weight/height^2 in kilogram per square metre. Sex- and age-adjusted standard deviation scores (SDS) for weight, height and BMI were calculated as SDS = (subject's measurement - population mean) / (population SD) in the LMSgrowth program version 2.12 (Medical Research Council, UK) using World Health Organization standards. Measurements of triceps and subscapular skinfold thickness were added together to create the sum of skinfolds in millimetres. DEXA-derived measurements of whole-body fat mass were corrected for height (ratio of whole-body fat mass to height) and for whole-body fat-free mass (ratio of whole-body fat mass to fat-free mass). Infancy weight gain was calculated as the change in weight SDS from birth to age 1 year. Gain in weight SDS greater than 0.67 (equivalent to a change in weight e.g from 9th to 25th centile) was taken to indicate catch-up weight gain [27]. Downward change in weight SDS less than -0.67 between birth and age 1 year was defined as "catch-down" weight gain [27]. The remaining children showed "no rapid change" in weight SDS during infancy.

Statistics

Data were analysed for normality using the Kolmogorov-Smirnov test and log-transformed to a normal distribution to allow use of analysis of variance to assess differences between boys and girls and across subjects with different patterns of weight gain during infancy. Post-hoc analyses using the Bonferroni correction were employed to test body size and composition between subjects of different patterns of infancy weight gain. Mean values for body size and composition and age at menarche were adjusted for several covariates as indicated. Weight and height from birth to age 18 years were also assessed using repeated-measures analysis for women stratified according to age at menarche. Significance was set to $p<0.05$. Analyses were performed using SPSS for Windows version 19. Data are means (standard deviation) unless stated otherwise.

Results

Cohort characteristics

Cohort characteristics are summarised in Table 1. The mean gestational age was 38.1 weeks (range 26-44 weeks, 61 subjects with gestational age <33 weeks) and the mean birth weight was 3064 grams (range 1000-4920 grams, 78 subjects with a birth weight <2000 grams). Data on 1613 out of the original 2352 subjects were available at age 18 years. The average birth weight was <0 SDS according to WHO growth standards (Table 1, Figure 1A). Weight gain till age 1 year was relatively fast in both boys and girls (Figure 1A). Girls age 1 year showed a trend towards higher weight SDS than boys ($p=0.06$; Table 1, Figure 1A) whilst height SDS ($p=0.8$; Table 1, Figure 1B) and BMI SDS ($p=0.1$; Table 1, Figure 1C) were similar.

Weight and height gain slowed between ages 1 and 2 years in boys and girls (Figure 1A and 1B). At age 8 years, girls had similar weight SDS ($p=0.3$; Table 1, Figure 1A), BMI SDS ($p=0.9$; Table 1, Figure 1C) and MUAC ($p=0.2$; Table 1), but lower height SDS ($p=0.04$; Table 1, Figure 1B) and greater skin fold thickness ($p<0.001$; Table 1) than boys.

Gender differences in body composition were more marked at age 18 years: girls gained more weight for height than boys during puberty and up to age 18 years (Table 1, Figure 1A-C). Girls age 18 years had higher weight SDS ($p<0.001$; Table 1, Figure 1A), height SDS ($p<0.001$; Table 1, Figure 1B), BMI SDS ($p<0.001$; Table 1, Figure 1C), whole-body fat mass ($p<0.001$; Table 1), percentage fat mass ($p<0.001$; Table 1), whole-body fat mass corrected for height ($p<0.001$; Table 1) and whole-body fat mass to fat-free mass ratio ($p<0.001$; Table 1).

<u>Relation of infancy weight gain to body size and composition from birth to age 18 years</u>

290 (46% male) out of the total of 2352 children showed catch-up weight gain between birth and age 1 year. They were born an average of 1.1 weeks earlier ($p<0.001$; Table 2) and had lower birth weight SDS ($p<0.001$; Table 2; Figure 2A) than children who did not show rapid change in weight or those with catch-down weight gain during infancy. The difference in birth weight persisted after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status ($p<0.001$; Table 2).

By age 4 years, children with infancy catch-up weight gain had similar weight SDS, height SDS and BMI SDS to children without rapid change in weight or catch-down weight gain during infancy (Figure 2A-C). This similarity in body size persisted (Figure 2A-C) albeit lower height SDS at age 8 years in children with infancy catch-up weight gain versus other children after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status ($p=0.02$; Table 2). Children age 8 years with infancy catch-up weight gain also had greater MUAC ($p=0.04$; Table 2) and skin fold thickness ($p=0.048$; Table 2) than children without rapid change in weight during infancy after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status, sex, current age and height.

By at age 18 years, subjects with infancy catch-up weight gain had higher weight SDS ($p<0.001$; Table 2, Figure 2A), BMI SDS ($p=0.001$; Table 2, Figure 2C) and similar height SDS ($p=0.6$; Table 2, Figure 2B) than other subjects after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status. Subjects age 18 years with infancy catch-up weight gain had higher percentage fat mass than subjects without rapid change in weight during infancy (p=0.04; Table 2) and lower fat-free mass than other subjects (p=0.04; Table 2). These differences did not persist after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding, household socio-economic status, sex, current age and height (Table 2). If women are singled out and age at menarche is added as a covariate, the association between infancy catch-up weight gain and higher weight SDS and BMI SDS at age 18 years persists (p=0.005 and p=0.008 respectively). Infancy catch-up weight gain then also shows a trend towards an association with higher DEXA-derived measures of fat mass (p=0.08) and fat to fat-free mass ratio (p=0.08).

Infancy weight gain and age at menarche

Catch-up weight gain from birth to age 1 year was associated with earlier menarche (12.52±0.06 vs. 12.63±0.06 vs. 13.07±0.10 years for catch-up weight gain, no rapid change in weight and catch-down weight gain; p<0.001; Figure 3). This association persisted after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status (p=0.005). Accordingly, girls who were youngest at menarche had higher weight SDS (p=0.001; Figure 4A) and BMI SDS (p=0.008; Figure 4C) during childhood and adolescence. These associations persisted after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding, household socio-economic status (p=0.03 and p=0.02 respectively). Girls who were youngest at menarche also had higher height SDS before age 4 years (p<0.001; Figure 4B). This association persisted for girls youngest versus oldest at menarche after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding, household socio-economic status (p=0.046).

Discussion

We explored the relationship between infancy weight gain, subsequent body size and body composition in boys and girls at ages 8 and 18 years as well as timing of pubertal development in girls in a prospective birth cohort of black children born in a low-income metropolitan area of Johannesburg-Soweto, South Africa. The main findings were the associations between transient catch-up weight gain from birth to age 1 year and higher BMI at age 18 years and earlier menarche.

A debate continues about the timing and tempo of rapid postnatal weight gain that conveys the greatest risk of later obesity. Most studies to date have focussed on growth patterns in the first two postnatal years [5-9], but there are data to suggest that growth trajectories in the first 3-6 months may be more important for determining the risk of later cardio-metabolic disease [28-30]. There are even observational and trial data linking weight gain and nutrition during the first 8-14 days of life to later risks of obesity and insulin resistance [31, 32]. An improved characterisation of the most detrimental features of weight gain in childhood would allow interventions to be directed towards potentially modifiable critical windows that contribute to metabolic functional capacity [33]. In the majority of low- and middle-income countries, catch-up weight gain is transient; it tends to cease by age 1 year and is followed by growth faltering due to the combined effect of poverty, infection, poor hygiene and under-nutrition [19-21]. We observed a similar growth pattern in children of the Bt20 study with catch-up weight gain during infancy but relative loss in weight and height in the following year. Nonetheless, children who showed catch-up weight gain from birth to age 1 year became relatively adipose during adolescence with distinctly higher weight and BMI at age 18 years, even after adjustment for sex, age, height, smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status.

The relationship between weight and onset of puberty, usually assessed by age at menarche in girls, is more complex. Earlier menarche is a robust marker of increased childhood and adult risk of obesity as well as being predictive of adult-onset diabetes [10-12, 15, 34, 35]. However, girls who are younger at menarche are more likely to be overweight before the onset of puberty [36, 37] so that adult disease associations with earlier menarche may simply reflect the effect of rapid weight gain during earlier parts of childhood. The current study confirms these findings in children born into the low-income area of Johannesburg-Soweto amongst whom catch-up weight gain from birth to age 1 year was associated with younger age at menarche, even after adjustment for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status. Earlier menarche could therefore represent a marker of higher risk of obesity in adult life in low-income countries. It is also unclear whether our finding can be extended to timing of puberty in boys, a more challenging undertaking because self-reported markers of puberty onset are less reliable among boys than girls. Nonetheless, we recently reported that the trajectory to earlier sexual maturation in males (time of voice breaking) of the 1946 British Birth Cohort Study was associated with faster weight gain from birth to age 2 years and led to higher adult BMI [17].

A study population of only black children born in one specific area may limit the generalisability of our findings; however, our data are consistent with those in other settings and ethnic groups. We only had access to weight, height, MUAC and skin fold thickness during childhood, which are relatively inaccurate estimates of body composition. We also did not have the means of adjusting the analyses for parental adiposity. At age 18 years, DEXA-derived measures of fat and fat-free mass were available for 1208 out of the original 2352 subjects, which may not have provided enough statistical power to determine differences in body composition despite greater weight and BMI gains in those who showed infancy catch-up weight gain. Our analyses of associations with infancy catch-up weight gain were further limited by not being able to adjust for age at maternal menarche, nutritional factors during childhood and adolescence, stressful psychological and physiological circumstances, objective markers of first- and second-hand smoking, and we did not screen for genetic conditions such as Turner syndrome.

In conclusion, transient catch-up weight gain between birth and age 1 year was common in black children who live in a low-income area of South Africa. Despite being followed by growth faltering between ages 1 and 2 years, this was associated with greater adiposity in early adulthood and with earlier menarche in girls, an observation that may be important for public health policy. Directly modifiable determinants of infancy weight gain such as feeding practices, mother's age at pregnancy and smoking could be targeted in order to prevent later obesity and earlier puberty in the offspring [38]. Given that younger age at menarche in mothers predicts faster weight gain of their offspring during infancy, but not during childhood, in male and female offspring [34], we speculate that mechanisms linking infancy catch-up and subsequent weight gains to earlier menarche may reflect transgenerational factors that include metabolic programming and epigenetic modification.

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Table 1. Body size and composition of male and female subjects from birth to age 18 years. Data are means (SD).

Table 2. Body size and composition from birth to age 18 years for subjects who showed catch-up weight gain, no significant change in weight or catch-down weight gain from birth to age 1 year. Data are unadjusted means (SD) adjusted for smoking during pregnancy, birth order, gestational age, formula-milk feeding and household socio-economic status where indicated. ▲Additional adjustment for sex. •Additional adjustment for age and sex. ■Additional adjustment for age, sex and height. [a]$p<0.05$ for 'catch-up' versus 'no change'. [b]$p<0.05$ for 'catch-up' versus 'catch-down'.

Figure 1. Weight SDS (**A**), height SDS (**B**) and BMI SDS (**C**) in male and female subjects from birth to age 18 years. Data are means ± standard error. ■ = male. ● = female.

Figure 2. Relation of change in weight SDS from birth to age 1 year to weight SDS (**A**), height SDS (**B**) and BMI SDS (**C**) from birth to age 18 years. Data are means ± standard error. ▲ = catch-down weight gain. ■ = no rapid change in weight. ● = catch-up weight gain.

Figure 3. Relationship between change in weight SDS from birth to age 1 year and age at menarche. Data are means ± standard error.

Figure 4. Relation of age at menarche to weight SDS (**A**), height SDS (**B**) and BMI SDS (**C**) from birth to age 18 years. Data are means ± standard error. ● = menarche at age <12 years. ■ = menarche at age 12 or 13 years. ▲ = menarche at age >13 years.

Table 1.

	Male n=1151	**Female** n=1201	**p-value**
Birth			
Weight (kg)	3.11 (0.54)	3.02 (0.50)	*<0.001*
Weight SDS	-0.55 (1.20)	-0.53 (1.19)	0.9
Age 1 year			
Weight (kg)	9.3 (1.2)	9.2 (1.2)	*0.001*
Weight SDS	-0.17 (1.11)	-0.09 (1.04)	0.06
Height (cm)	73.8 (3.0)	73.2 (2.9)	*<0.001*
Height SDS	-0.54 (1.21)	-0.52 (1.12)	0.8
BMI (kg/m^2)	17.2 (1.8)	17.2 (1.8)	0.6
BMI SDS	0.27 (1.24)	0.38 (1.18)	0.1
Age 8 years			
Weight (kg)	24.8 (4.1)	24.3 (4.4)	*0.01*
Weight SDS	-0.49 (1.11)	-0.54 (1.05)	0.3
Height (cm)	124.7 (5.9)	123.7 (6.0)	*0.001*
Height SDS	-0.66 (1.01)	-0.79 (0.97)	*0.04*
BMI (kg/m^2)	15.8 (1.8)	15.8 (2.1)	0.4
BMI SDS	-0.12 (1.02)	-0.12 (0.98)	0.9
MUAC (cm)	17.8 (1.8)	18.0 (2.0)	0.2
Sum of skin folds (mm)	13.7 (4.8)	16.2 (5.8)	*<0.001*
Age 18 years			
Weight (kg)	59.7 (11.7)	58.9 (12.1)	0.1
Weight SDS	-1.05 (1.35)	-0.04 (1.28)	*<0.001*
Height (cm)	167.0 (8.9)	163.3 (8.7)	*<0.001*
Height SDS	-1.17 (1.18)	0.02 (1.28)	*<0.001*
BMI (kg/m^2)	21.4 (4.0)	22.1 (4.6)	*0.001*
BMI SDS	-0.33 (1.24)	0.05 (1.15)	*<0.001*
Fat mass (kg)	8.4 (5.0)	19.1 (7.6)	*<0.001*
Percentage fat mass (%)	13.9 (5.6)	32.4 (6.6)	*<0.001*
Fat mass/height (kg/m)	5.1 (3.0)	11.7 (4.6)	*<0.001*
Fat-free mass (kg)	49.6 (6.1)	38.1 (5.3)	*<0.001*
Fat mass/fat-free mass	0.66 (0.19)	1.04 (0.52)	*<0.001*

Table 2.

	Catch-down n=511	**No change** n=938	**Catch-up** n=903	**Unadjusted p-value**	**Adjusted p-value**
Birth					
Gestational age (weeks)	38.7 (1.3)	38.5 (1.4)	37.5 (2.6)	*<0.001*[a,b]	▲*<0.001*[a,b]
Weight (kg)	3.53 (0.38)	3.15 (0.34)	2.71 (0.50)	*<0.001*[a,b]	*<0.001*[a,b]
Weight SDS	0.48 (0.76)	-0.33 (0.74)	-1.35 (1.23)	*<0.001*[a,b]	*<0.001*[a,b]
Age 1 year					
Weight (kg)	8.4 (0.8)	9.0 (0.8)	9.9 (1.4)	*<0.001*[a,b]	*<0.001*[a,b]
Weight SDS	-0.99 (0.79)	-0.30 (0.72)	0.53 (1.12)	*<0.001*[a,b]	*<0.001*[a,b]
Height (cm)	72.1 (2.6)	73.4 (2.6)	74.5 (3.1)	*<0.001*[a,b]	*<0.001*[a,b]
Height SDS	-1.17 (1.02)	-0.59 (1.02)	-0.14 (1.20)	*<0.001*[a,b]	*<0.001*[a,b]
BMI (kg/m^2)	16.0 (1.3)	16.8 (1.3)	18.1 (2.0)	*<0.001*[a,b]	*<0.001*[a,b]
BMI SDS	-0.49 (1.03)	0.11 (0.92)	0.96 (1.21)	*<0.001*[a,b]	*<0.001*[a,b]
Age 8 years					
Weight (kg)	25.0 (4.5)	24.4 (3.8)	24.5 (4.7)	0.2	0.2
Weight SDS	-0.42 (1.12)	-0.54 (1.00)	-0.55 (1.13)	0.3	0.2
Height (cm)	124.5 (6.2)	124.1 (5.7)	124.1 (6.1)	0.8	*0.01*[b]
Height SDS	-0.71 (1.03)	-0.73 (0.97)	-0.74 (1.00)	0.9	*0.02*[b]
BMI (kg/m^2)	16.1 (2.1)	15.8 (1.6)	15.8 (2.1)	0.1	0.2
BMI SDS	0.00 (1.05)	-0.14 (0.90)	-0.17 (1.07)	0.1[b]	0.2
MUAC (cm)	18.1 (1.9)	17.8 (1.7)	17.8 (2.0)	0.2	■0.1[a]
Sum of skin folds (mm)	15.0 (6.0)	14.7 (4.8)	15.2 (5.8)	0.4	■0.1[a]
Age 18 years					
Weight (kg)	56.6 (10.5)	57.9 (10.0)	62.3 (13.7)	*<0.001*[a,b]	*<0.001*[a,b]
Weight SDS	-0.88 (1.31)	-0.68 (1.34)	-0.15 (1.47)	*<0.001*[a,b]	*<0.001*[a,b]
Height (cm)	164.8 (9.1)	164.6 (9.0)	165.7 (8.8)	0.1[a]	0.6
Height SDS	-0.63 (1.40)	-0.63 (1.38)	-0.42 (1.32)	*0.01*[a,b]	0.6
BMI (kg/m^2)	20.9 (3.9)	21.4 (3.8)	22.7 (4.9)	*<0.001*[a,b]	*<0.001*[a,b]
BMI SDS	-0.43 (1.17)	-0.21 (1.15)	0.12 (1.24)	*<0.001*[a,b]	*0.001*[a,b]
Fat mass (kg)	14.0 (8.7)	13.4 (8.0)	14.4 (8.6)	0.2	■0.3
Percentage fat mass (%)	23.3 (11.2)	22.7 (10.8)	24.2 (11.3)	0.1[a]	■0.3
Fat mass/height (kg/m)	8.6 (5.1)	8.3 (4.9)	8.9 (5.5)	0.2	•0.3
Fat-free mass (kg)	44.4 (8.3)	44.0 (8.3)	43.0 (7.7)	*0.04*[b]	■0.7
Fat mass/fat-free mass	0.86 (0.25)	0.85 (0.25)	0.87 (0.26)	0.3	■0.4

Figure 1A.

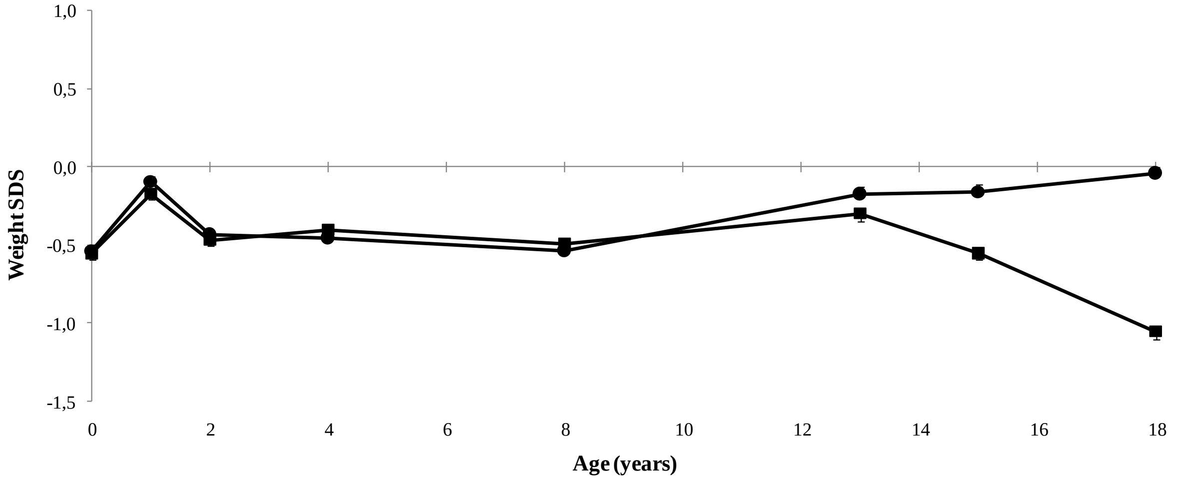


Figure 1B.

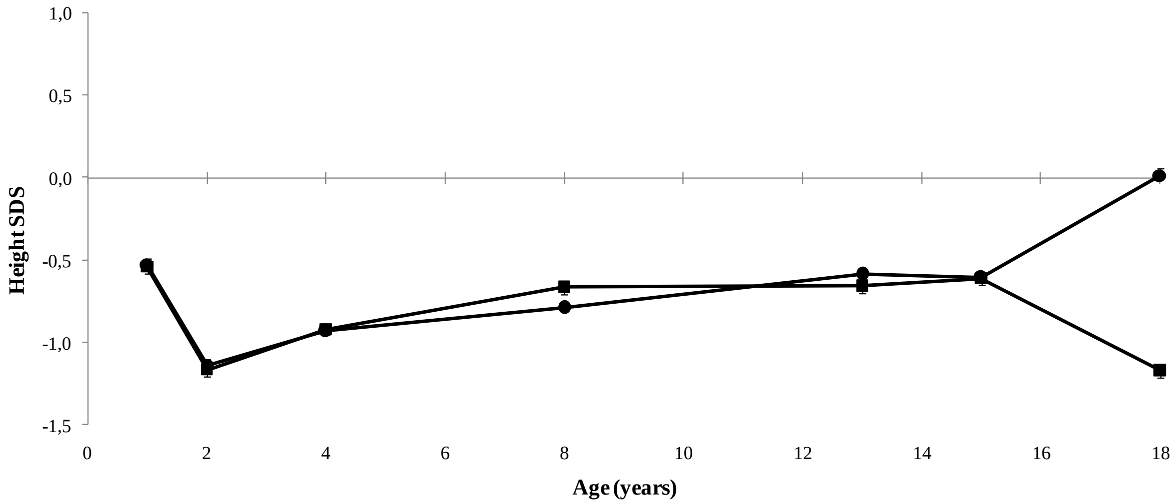


Figure 1C.

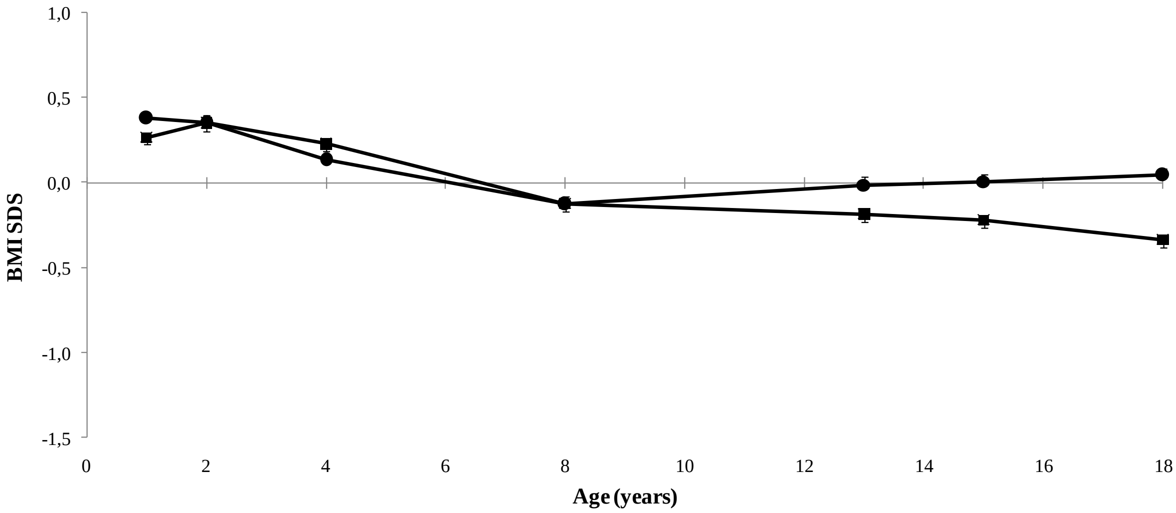


Figure 2A.

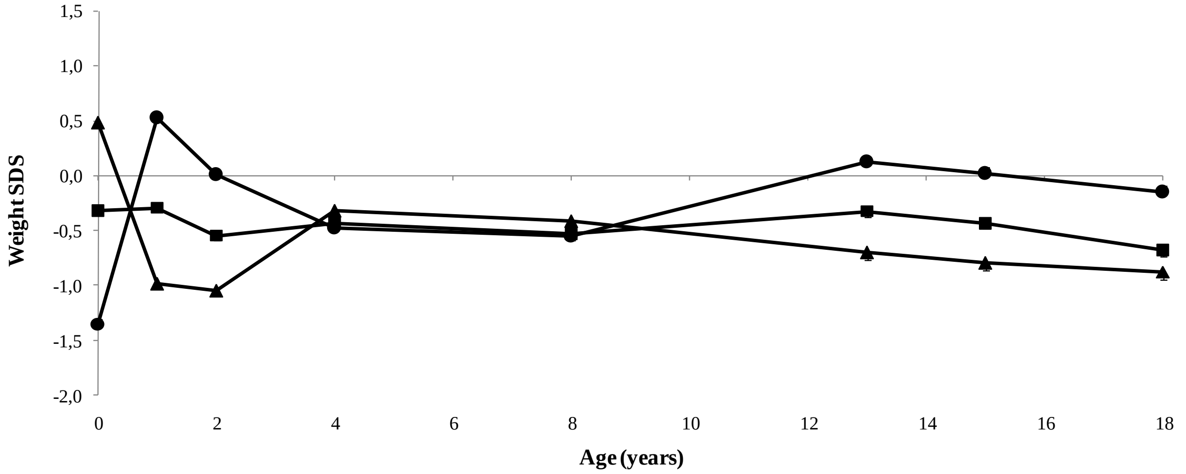


Figure 2B.

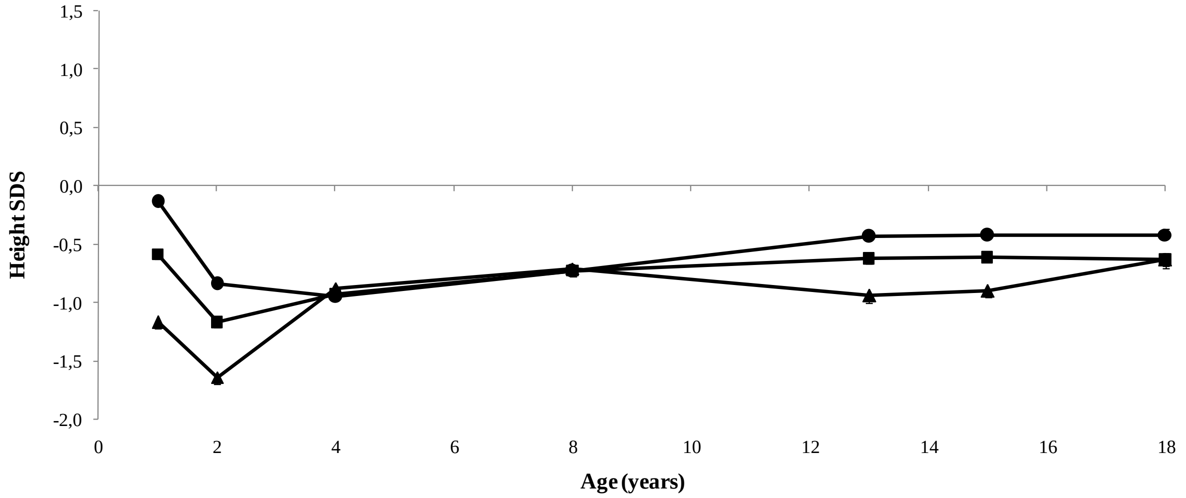


Figure 2C.

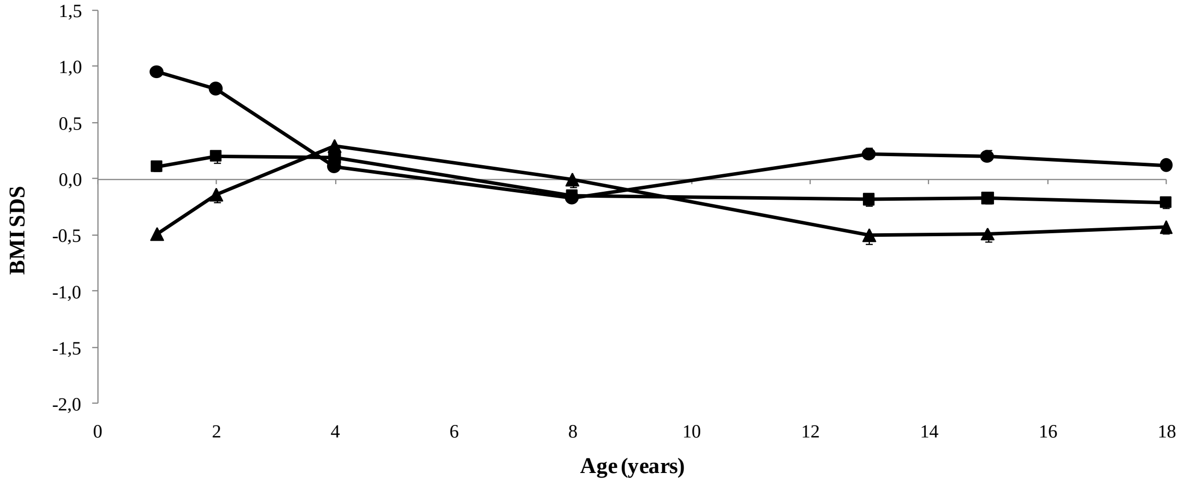
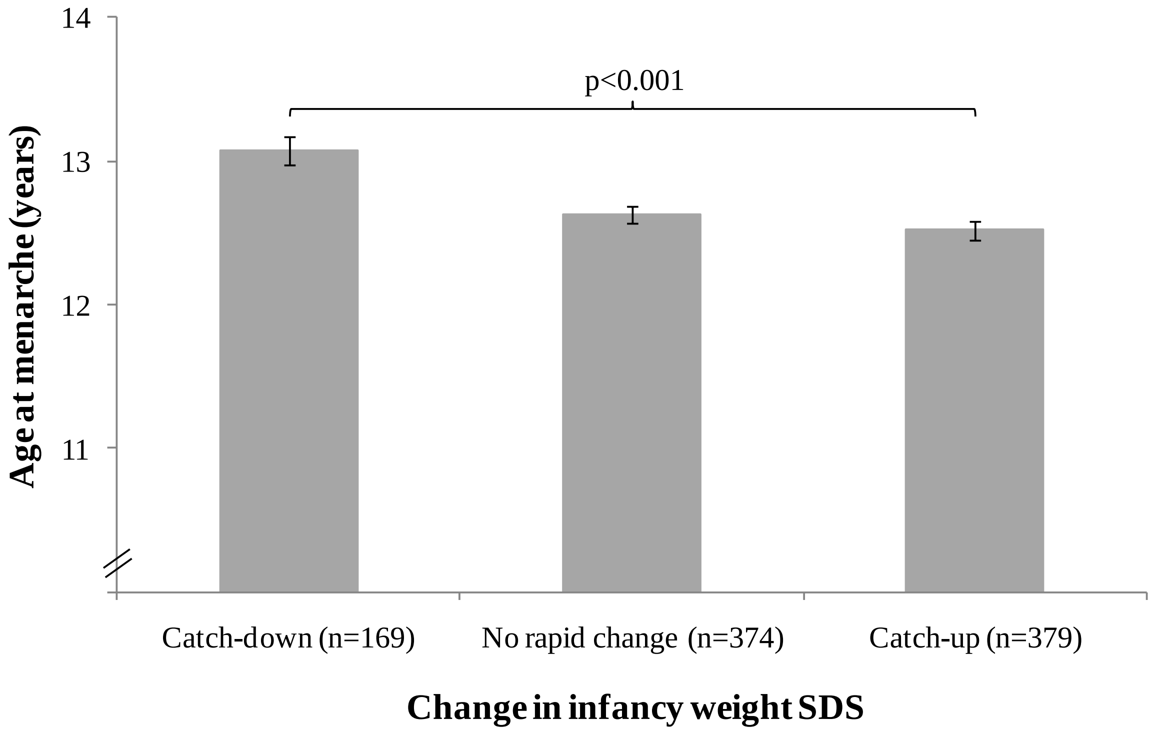


Figure 3.



14
13
12
11
p<0.001
Age at menarche (years)
Catch-down (n=169)
No rapid change (n=374)
Catch-up (n=379)
Change in infancy weight SDS

Figure 4A.

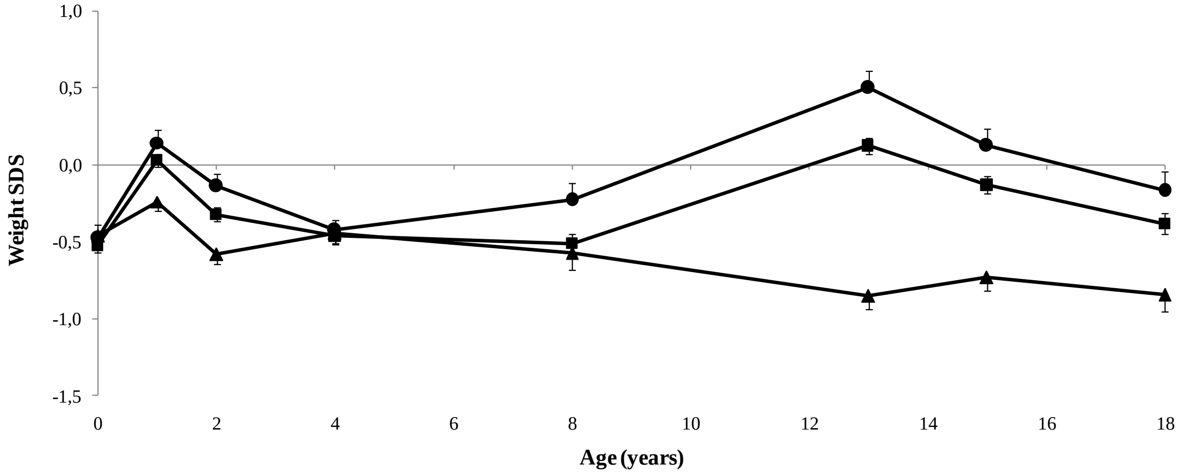


Figure 4B.

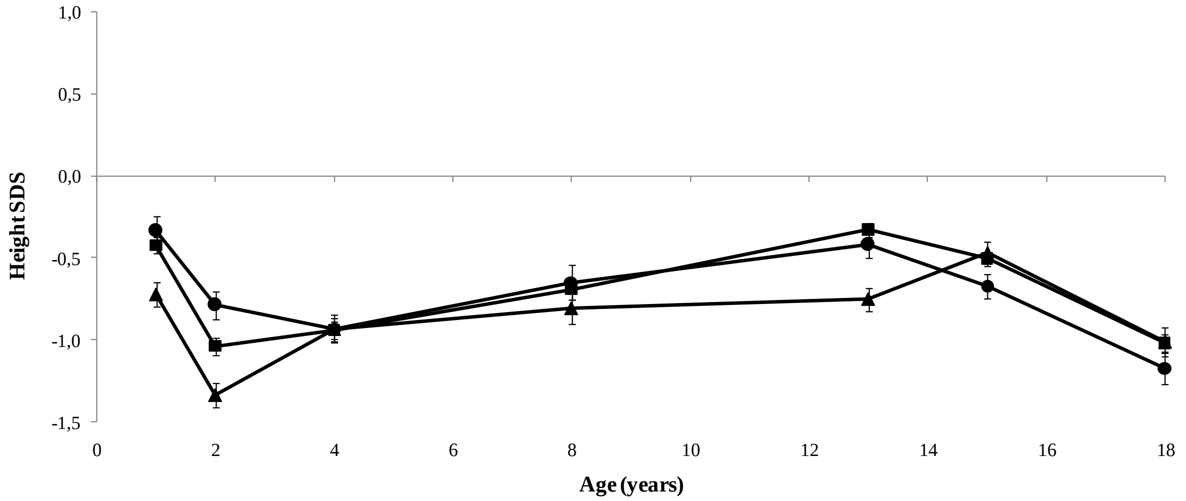


Figure 4C.