

Infancy Weight Gain Predicts Childhood Body Fat and Age at Menarche in Girls

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Context: Rapid postnatal weight gain has been associated with subsequent increased childhood adiposity. However, the contribution of rapid weight gain during specific infancy periods is not clear.

Objective: We aimed to determine which periods of infancy weight gain are related to childhood adiposity and also to age at menarche in UK girls.

Design, Setting, and Participants: A total of 2715 girls from a prospective UK birth cohort study participated in the study.

Main Outcome Measures: Routinely measured weights and lengths at ages 2, 9, and 19 months were extracted from the local child health computer database. Body composition was assessed by dual-energy x-ray absorptiometry at age 10 yr, and age at menarche was assessed by questionnaire (categorized into three groups: <12.0, 12.0–13.0, and >13.0 yr).

Results: Faster early infancy weight gain between 0 and 2 months and also 2 to 9 months were associated with increased body fat mass relative to lean mass at age 10 yr and also with earlier age at menarche. Each +1 unit gain in weight SD score between 0 and 9 months was associated with an odds ratio (95% confidence interval) = 1.48 (1.27–1.60) for overweight (body mass index > 85th centile) at 10 yr, and 1.34 (1.21–1.49) for menarche at less than 12 yr. In contrast, subsequent weight gain between 9 and 19 months was not associated with later adiposity or age at menarche.

Conclusions: In developed settings, rapid weight gain during the first 9 months of life is a risk factor for both increased childhood adiposity and early menarche in girls. (*J Clin Endocrinol Metab* 94: 1527–1532, 2009)

The prevalence of obesity is rising, even in young children. In a study of data from 50,455 children 3 to 4 yr old in Wirral, United Kingdom, mean body mass index (BMI) and risk of overweight increased steadily between 1988 and 2003 (1). Childhood obesity has been shown to track into adult life (2, 3) and to predict later cardiovascular disease events and mortality (4). Long-term strategies to prevent obesity and its related metabolic disorders may therefore benefit from interventions acting very early in life.

Recent systematic reviews have identified consistent associations between postnatal rapid weight gain during the first 1 to 2 yr of life and later obesity in children and adults (5–7). Overall there is a 2- to 3-fold increase in overweight or obesity risk in those individuals whose weight centile crossed upward by at least one major band (e.g. 2nd to 9th centile, or 9th to 25th centile; equivalent to a gain in weight SD score ≥ 0.67) between birth and ages 1 or 2 yr (6). However, there is still debate as to the exact timing of rapid postnatal weight gain that is most detrimental to later obesity risk.

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Abbreviations: BMI, Body mass index; DXA, dual-energy x-ray absorptiometry.

Rapid infancy growth in length has been associated with earlier age at menarche in women (8). However, in that study specific associations with infancy weight gain were not reported. Earlier age at menarche is a robust marker of increased adult obesity risk in women (9–11), and it also predicts adult-onset diabetes (12). However, because girls with earlier menarche are more likely to be overweight even before the onset of puberty (13, 14), the adult disease associations with earlier menarche may actually reflect the effects of rapid weight gain during earlier childhood.

We therefore aimed to determine which specific periods of infancy weight gain are related to childhood adiposity and also age at menarche in UK girls.

Subjects and Methods

Participants

The Avon Longitudinal Study of Parents and Children (ALSPAC) is a prospective study that has been described in detail elsewhere (15) (<http://www.alspac.bris.ac.uk>). Briefly, 14,541 pregnant women living in one of three Bristol-based health districts in the former County of Avon with an expected delivery date between April 1991 and December 1992 were enrolled in the study. Detailed information has been collected using self-administered questionnaires, data extraction from medical notes, and linkage to routine information systems and at research clinics. Ethical approval for the study was obtained from the ALSPAC Law and Ethics Committee and Local Research Ethics Committees.

Infant body size and infancy growth

Birth weight as recorded in the delivery room was obtained from medical records, and birth length was measured by trained ALSPAC staff

within 24 h after birth wherever possible. Body weight and length at around ages 2, 9, and 19 months were available from routinely collected measurements performed by health visitors as part of the infant health surveillance program and were extracted from the local child health database. BMI was calculated as weight (kilograms)/length (meters)². Body weight, length, and BMI at each time point were converted to SD scores (or ‘z-scores’) by comparison with the British 1990 growth reference (16) using gestational age or the actual age at measurement for each individual.

Infancy weight gain and growth (length gain) during specific time periods were calculated as the difference in weight or length SD score between those ages (e.g. weight gain between 2 to 9 months = weight SD score at 9 months minus weight SD score at 2 months). For the purpose of display only, infancy weight gain between 0 and 9 months was categorized into six groups (as shown in Fig. 2).

Anthropometry and body composition

Measurements of anthropometric and body composition variables were taken at a research clinic, to which all ALSPAC children were invited at age 10 yr. Total body fat mass and fat-free mass were assessed by a whole-body dual-energy x-ray absorptiometry (DXA) scan (Prodigy scanner; Lunar Radiation Corp., Madison, WI). At the same visit, height was measured to the last complete millimeter using a Harpenden stadiometer (Holtain Ltd., Crosswell, UK), and weight was measured using a body fat analyzer (model TBF 305; Tanita UK Limited, Viewsley, UK). BMI was calculated as weight (kilograms)/height (meters)². Overweight was defined as BMI above the 85th centile by the British 1990 growth reference (16).

The coefficients of variation for total body fat mass and fat-free mass were 2.3 and 1.1%, respectively. Fat mass index (fat mass/height²) and fat-free mass index (fat-free mass/height²) were calculated to adjust body composition for height, and analyses using these variables were further adjusted for height because this is a recognized confounder of body composition parameters (17). Percentage body fat was calculated as

TABLE 1. Size at birth and at ages 2, 9, and 19 months and 10 yr by girls’ age at menarche

	Age at menarche (yr)			P trend
	<12.0	12.0–13.0	>13.0	
Birth (n)	567	717	1431	
Weight (kg)	3.38 ± 0.02	3.36 ± 0.02	3.42 ± 0.01	0.04
Length (cm)	50.4 ± 0.1	50.3 ± 0.1	50.5 ± 0.1	0.2
BMI (kg/m ²)	13.3 ± 0.1	13.3 ± 0.1	13.4 ± 0.1	0.2
2 months (n)	551	700	1390	
Weight (kg)	4.81 ± 0.02	4.78 ± 0.02	4.81 ± 0.02	0.9
Length (cm)	56.9 ± 0.1	56.7 ± 0.1	56.9 ± 0.1	0.6
BMI (kg/m ²)	14.8 ± 0.1	14.9 ± 0.1	14.9 ± 0.1	0.9
9 months (n)	483	608	1230	
Weight (kg)	8.91 ± 0.04	8.76 ± 0.04	8.73 ± 0.03	<0.001
Length (cm)	71.5 ± 0.1	71.2 ± 0.1	71.2 ± 0.1	0.1
BMI (kg/m ²)	17.5 ± 0.1	17.3 ± 0.1	17.3 ± 0.1	0.007
19 months (n)	452	570	1137	
Weight (kg)	11.58 ± 0.06	11.40 ± 0.06	11.31 ± 0.04	<0.001
Length (cm)	83.0 ± 0.2	83.0 ± 0.2	82.5 ± 0.1	<0.001
BMI (kg/m ²)	16.9 ± 0.1	16.7 ± 0.1	16.7 ± 0.1	0.09
10 yr (n)	499	630	1273	
Weight (kg)	38.6 (33.4–44.0)	34.0 (30.4–39.4)	31.2 (28.2–35.8)	<0.001
Height (cm)	142.5 (138.3–146.8)	139.5 (135.7–144.0)	137.4 (133.4–141.6)	<0.001
BMI (kg/m ²)	18.9 (17.1–21.1)	17.5 (16.0–19.7)	16.5 (15.3–18.3)	<0.001
Fat mass index (kg/m ²) ^a	5.5 (4.2–7.3)	4.6 (3.5–6.3)	3.9 (2.8–5.4)	<0.001
Fat-free mass index (kg/m ²) ^a	12.5 (11.8–13.1)	12.1 (11.5–12.6)	11.9 (11.3–12.4)	<0.001
% Body fat ^a	29.3 (24.2–35.0)	26.7 (21.3–33.1)	23.4 (18.4–29.5)	<0.001
Fat mass to fat-free mass ^{2.10} ratio (kg ^{−1.10}) ^a	1.29 (0.95–1.67)	1.25 (0.91–1.62)	1.08 (0.80–1.44)	<0.001

Data are presented as mean ± SE or median (interquartile range). P trend, Association with trend across the three age at menarche groups, adjusted for age.

^a Further adjusted for height.

100 × total body fat mass/body weight, and these analyses were also adjusted for height. We also calculated the ratio of total fat mass to fat-free massⁿ to produce a measure of fat mass that was completely independent of fat-free mass (18). The value of *n* used was 2.1, which was derived in this sample by regressing log total fat mass on the log of fat-free mass.

Girls' age at menarche

Girls were asked at a research clinic at mean age 12.9 yr (interquartile range = 12.8, 13.0) whether they had started their menstrual periods and, if so, at what age. Of the 3298 girls who attended and provided data at this clinic, 1637 (49.6%) stated that they had not yet started their periods. Of the 1661 (50.3%) who had started their periods, age at start of first period was available for 1550 (93.3%). Some missing data on the age at first menstruation at this clinic were imputed from similar data collected at a research clinic when the girls were aged 11 yr. Age at menarche of the girl was therefore categorized into three groups: less than 12.0 yr, 12.0–13.0 yr, and more than 13.0 (the last category included those who had not yet started menstruation).

Study sample and analyses

We restricted the current analysis to 2715 girls who had available data on age at menarche and who were singleton-born. Compared with all other singleton-born girls in the study (*n* = 3956), our sample was heavier at birth (mean birth weight, 3396 vs. 3301 g; *P* < 0.001) and were less likely to be born preterm (gestation < 37 wk, 3.8 vs. 6.7%), but they showed similar rates of infancy weight gain 0–9 months (*P* > 0.3). Data on both age at menarche and body composition at age 9–10 yr were available for 2402 girls.

Multiple regression models were performed to test the linear associations between infant body size, infant weight gain, and infant growth (length gain) with subsequent body composition or age at menarche. A girl's age at menarche (<12.0, 12.0–13.0, or >13.0 yr) was treated as a continuous variable. The effect of conditional infancy weight gain between birth to 9 months on the categorical outcomes overweight at 10 yr and menarche < 12.0 yr were analyzed by logistic regression models that included birth weight SD score as a covariable.

The mother's highest educational qualification, recorded by questionnaire during pregnancy as an indicator of social-economic status, was included as a potential confounding factor for associations with infant growth, childhood body size, and body composition and age at menarche. We have previously reported in this cohort that faster infancy weight gain and growth are associated with: smoking at 32 wk of pregnancy, first born birth order, and formula-milk vs. breast feeding (19). We therefore also tested the association between these "potentially modifiable" determinants of infant growth and the girl's age at menarche.

Results

Infancy weight and weight gain related to girls' age at menarche

Birth weight was slightly lower in girls with earlier menarche compared with other girls (*P* = 0.04; Table 1). However, no difference in weight was apparent at age 2 months, and girls with earlier menarche had larger body weight and BMI than other girls at ages 9 and 19 months; these girls also had longer body length by age 19 months (Table 1).

Accordingly, girls with earlier menarche showed faster rates of weight gain between ages 0 and 2 months (*P* = 0.006) and 2 and 9 months (*P* < 0.001) than other girls (Fig. 1A) and also had faster rates of growth (length gain) between ages 2–9 months (*P* = 0.006) and 9–19 months (*P* = 0.004; Fig. 1B).

Various previously identified determinants of faster infant weight gain (smoking during pregnancy, first-born birth order,

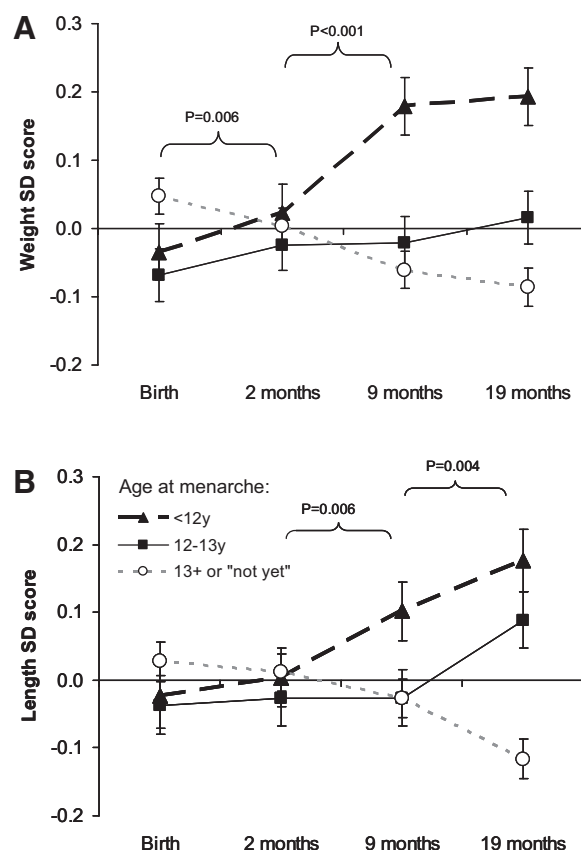


FIG. 1. Age at menarche in girls related to infancy weight gain (A) and infancy growth rates (B). *P* values for trend in weight gain or growth between three groups of age at menarche (<12.0 yr, 12.0–13.0 yr, and >13.0 yr or "not yet").

and formula-milk-feeding) were also associated with earlier age at menarche (see Supplemental Table 1, published as supplemental data on The Endocrine Society's Journals Online web site at <http://jcem.endojournals.org>). After adjusting for these determinants, the associations between earlier menarche showing faster rates of weight gain between ages 0–2 months (*P* = 0.005) and 2–9 months (*P* < 0.001) still persisted.

Infancy weight gain related to childhood body composition

Faster weight gain during all three postnatal periods (0–2, 2–9, and 9–19 months) was positively related to body weight, height, and BMI at age 10 yr (Table 2). However, only earlier infancy weight gains between 0–2 months and 2–9 months were positively related to fat mass index or percentage body fat (*P* = 0.03 to 0.001) and were also associated with, or showed trends toward, a greater fat mass to fat-free mass ratio (*P* = 0.06 to *P* < 0.001; Table 2). Figure 2 shows that these associations were largely linear (*P* value for quadratic model = 0.9). Later infancy weight gain, between 9–19 months, was positively related to fat-free mass index, but not to fat mass index (Table 2).

In logistic regression models, each +1 U gain in weight SD score between 0 and 9 months was associated with a 48% increased risk of overweight at 10 yr (odds ratio, 95% confidence interval: 1.48, 1.27–1.60) and a 34% increased risk for menarche at <12.0 yr (1.34, 1.21–1.49).

TABLE 2. Associations between infancy weight gain and childhood size and body composition at age 10 yr in 2402 girls

Body size and composition at age 10 yr	Weight gain (change in SDS)		
	0 to 2 months	2 to 9 months	9 to 19 months
Weight (kg)	0.99 ± 0.20 (<i>P</i> < 0.001)	0.86 ± 0.16 (<i>P</i> < 0.001)	1.01 ± 0.25 (<i>P</i> < 0.001)
Height (cm)	0.71 ± 0.17 (<i>P</i> < 0.001)	0.83 ± 0.14 (<i>P</i> < 0.001)	0.95 ± 0.21 (<i>P</i> < 0.001)
BMI (kg/m ²)	0.31 ± 0.08 (<i>P</i> < 0.001)	0.24 ± 0.06 (<i>P</i> < 0.001)	0.24 ± 0.09 (<i>P</i> = 0.01)
Fat mass index (kg/m ²) ^a	0.15 ± 0.06 (<i>P</i> = 0.01)	0.09 ± 0.04 (<i>P</i> = 0.001)	0.05 ± 0.07 (<i>P</i> = 0.7)
Fat-free mass index (kg/m ²) ^a	0.06 ± 0.02 (<i>P</i> = 0.008)	0.01 ± 0.02 (<i>P</i> = 0.6)	0.07 ± 0.03 (<i>P</i> = 0.03)
% Body fat ^a	0.45 ± 0.20 (<i>P</i> = 0.03)	0.48 ± 0.17 (<i>P</i> = 0.005)	0.07 ± 0.25 (<i>P</i> = 0.8)
Fat mass to fat-free mass ^{2,10} ratio (kg ^{-1.10}) ^a	0.025 ± 0.013 (<i>P</i> = 0.06)	0.028 ± 0.011 (<i>P</i> < 0.001)	0.001 ± 0.016 (<i>P</i> = 0.9)

Values are regression coefficients (B) ± SE, adjusted for mother's education.

^a Further adjusted for height at age 10 yr.

Infancy weight gain related to infancy growth

Because girls' age at menarche appeared to be related to both earlier infancy weight gain and later infancy growth, we assessed the associations between length gain and earlier weight gain during infancy. Weight gain between 2 and 9 months was positively related to subsequent length gain between 9 and 19 months (*r* = 0.065; *P* = 0.004). In contrast, weight gain between 9 and 19 months was unrelated, or even weakly inversely related, to earlier length gain between 2 and 9 months (*r* = -0.044; *P* = 0.051). Consequently, the apparent associations between infancy length gain and girls' age at menarche shown in Fig. 1 were largely explained by infancy weight gain (see Supplemental Table 2).

Discussion

In this contemporary birth cohort, rapid early infancy weight gain from birth to age 2 months, and also from 2 to 9 months, but not later infancy weight gain between 9 and 19 months, predicted subsequent greater adiposity, assessed by DXA at age 10 yr, and earlier age at menarche in girls. In addition to its psychosocial consequences (20), early menarche is a robust marker of increased obesity risk in adult life (9–12). Therefore, the association with earlier age at menarche suggests that the current observed effects of infancy weight gain over the first 9 months of life on BMI and body fat in childhood are likely to be much longer lasting.

Rapid infancy weight gain has been consistently associated with subsequent obesity risk, based on BMI, in children and adults (6, 7). In addition to increased BMI, which is a poor marker of adiposity, previous smaller studies have also reported that weight gain during early infancy may influence later body composition. In the Stockholm Weight Development Study, a gain in weight of 1 SD score in infancy (0–6 months) or in early childhood (3–6 yr) was associated with an increase in fat mass of 1.8 and 3.4 kg, respectively, and with an increase in lean mass of 1.0 and 1.4 kg, respectively, assessed by whole body plethysmography at age 17 yr (21). German children who showed rapid growth during infancy (0–24 months) achieved a persistently higher level of BMI than other children between ages 2 and 7 yr; furthermore, their percentage body fat assessed by skinfold thicknesses was already higher by age 2 yr, and remarkably this difference progressively increased over the next 5 yr (22). In a

similar study with repeated measures of body composition assessed by DXA, Spanish low birth weight children continued to gain excess total body fat and abdominal fat even after completion of rapid postnatal weight gain (23). Such studies suggest that rapid growth during infancy may not only be accompanied by greater concurrent gains in body fat mass, but may also lead to an ongoing propensity to accumulate fat mass and central fat during childhood. Those observational studies are supported by the long-term follow-up of randomized feeding trials in nasogastric tube-fed preterm infants, which report that greater dietary energy content during the first 4 wk of life has remarkable adverse effects on later body size and metabolic disease risk (24, 25).

In contrast to the above reports, studies from Brazil (26) and India (27) have observed that rapid weight gain during infancy more strongly predicts later lean body mass, rather than fat mass. In those studies, later weight gain occurring after infancy (after age 1 yr) predicted later adiposity. However, in those settings, birth weights and infancy weights were significantly lower compared with UK or international growth references (in the Indian study 53% were underweight at age 2 yr), and both populations caught up in weight in subsequent childhood or adult life (26, 27). It is therefore possible that it is the rapidity, rather than any specific timing, of weight gain that predicts later increased body fat.

An association between greater infancy length and earlier age at menarche was described in the 1946 British National Birth Cohort (8). Earlier menarche has also been related to lower birth weight (28) and the transition from lower birth weight to larger body size at age 8 yr (29, 30). Our current results now demonstrate the specific periods of childhood growth that predict age at menarche; in particular, faster weight gain during the first year of life was associated with both earlier menarche and greater adiposity. In the current birth cohort, we have previously reported that mother's age at menarche predicts faster weight gain and growth during infancy, but not during childhood, in both male and female offspring (31). Therefore, the mechanisms linking faster infancy weight gain and growth to earlier menarche in girls likely include transgenerational factors, such as genetic or epigenetic factors, or familial behaviors. Future studies should examine the effects of specific genetic determinants of age at menarche on early childhood growth and body composition.

We observed that mother's smoking and first-born status predispose to, and breast milk appears to be protective against, earlier menarche in girls. These findings suggest that the predis-

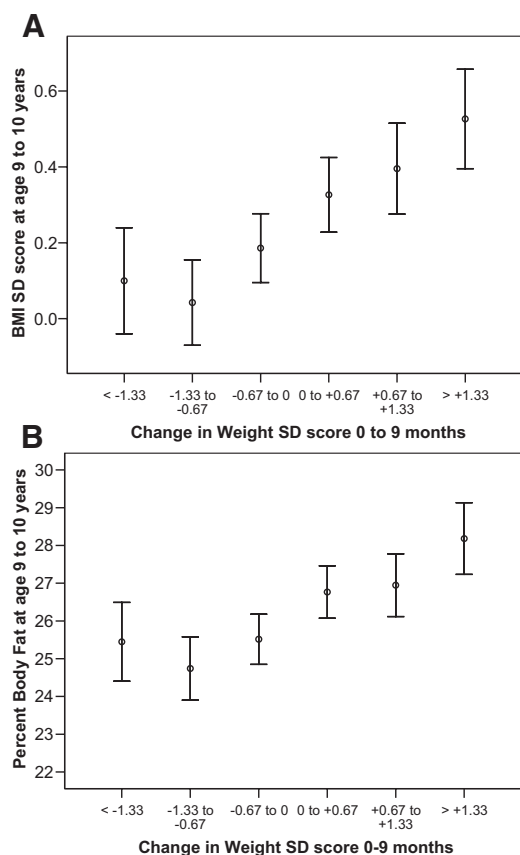


FIG. 2. Infancy weight gain (between 0 and 9 months) related to subsequent BMI (British 1990 SD score) (A) and adiposity (percent body fat by DXA) (B) at age 10 yr. Data represent means \pm 95% confidence interval. Note that 0.67 SD score represents the distance between centile bands on standard weight charts (e.g. 2nd to 9th centile; 9th to 25th, or 25th to 50th, etc.).

position to earlier menarche may be potentially modifiable. Smoking during pregnancy and breast milk feeding have also been related recently to higher and lower levels, respectively, of childhood body fat in this cohort; however, effects of confounding factors could not be fully ruled out (32, 33). In westernized populations, there is a continuing secular trend toward greater infancy weight gain (1). Our findings suggest that these infancy trends could contribute to the childhood trends toward increasing overweight girls (34) and earlier menarche (35). Furthermore, interventions to avoid rapid infancy weight gain could potentially reduce later adiposity and also avoid early menarche in girls.

A limitation of the study was that our data on infant growth and weight gain in the general ALSPAC cohort were derived from routinely collected data from health visitor measurements in various home and clinic settings. The precision and accuracy of these measurements is therefore likely to be highly variable (36), especially at an age when anthropometry may be difficult. This could explain why estimates of effect size on subsequent obesity risks were lower than in other studies (6) and lower than that reported from a subgroup of the same cohort with more detailed research clinic measurements (37). Further studies should also explore whether the current associations between infancy weight gain and timing of puberty are generalizable to boys; however,

self-reported markers of puberty onset and development in males are much less reliable than in girls.

In conclusion, faster infancy weight gain during the first 9 months from birth was associated with greater BMI and adiposity at age 10 yr and with earlier age at menarche in girls. Although transgenerational or heritable factors are likely to be involved (31), potentially modifiable determinants of infancy weight gain were also related to both later adiposity and age at menarche, indicating that interventions to avoid rapid infancy weight gain could potentially reduce later adiposity and also avoid early menarche in girls.

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