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Birth size and adult size in same-sex siblings discordant for fetal growth in the Early Determinants of Adult Health study

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Abstract

Many studies have reported on relations between birth size and adult size but the findings to date are hard to compare due to the lack of uniform measures across studies. Interpretation of findings is also hampered by potential confounding by ethnic, socioeconomic and family factors. The purpose of this study is to explore these relationships in a comprehensive fashion, with multiple measures of birth size and adult size, using same-sex sibling controls discordant in birth weight to address potential confounding at the family level. Study subjects include pregnant women enrolled during 1959–1966 in the Child Health and Development Study in Oakland, CA and the Boston, MA, and providence, RI, sites of the Collaborative Perinatal Project in New England, currently combined into the New England Family Study. We assessed 392 offspring (mean age 43 years), the great majority as sibships as available. Our analyses confirm the positive association between birth weight and adult length reported in other studies, with a change in adult height of 1.25 cm (95% CI: 0.79 to 1.70 cm) for each quintile change in standardized birth weight. No associations were seen between birth weight and adult fatness for which findings in other studies are highly variable. As adult weight is likely to reflect recent variations in the adult nutritional environment rather than the early environment, it may be more useful for studies of birth size and adult size to focus on adult length rather than weight measures in evaluating the role of early influences on adult health.

Keywords

adult height and weight; birth size; birth weight and length; prenatal factors; sibling control study

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Introduction

Low birth size and high adult body mass index (BMI) are associated with increased cardiovascular disease risk and diabetes. Understanding the causal pathways that may underlie these associations requires knowledge of the associations between birth size and adult size. The associations between birth size and adult size remain unclear, however, especially for adult BMI and other fatness-related adult outcomes, with findings across studies[1-9] that are hard to compare for several reasons given below.

First, the variability in the reported measures of birth size, including birth weight, birth weight adjusted for gestation, birth length and birth length adjusted for weight (using BMI in kg/m^2 or Ponderal index[10] in kg/m^3), as well as various combinations of these. Second, the limited measurement of adult size, with most studies relying only upon BMI to measure fatness-related outcomes, and reporting total adult height but not specific components of height such as trunk length and leg length. Third, the variability in the quality of the measures of birth size and adult size, ranging from retrospective self-report to detailed physical examinations using specified protocols. Fourth, the associations may vary across populations, and at the same time, may be race and gender specific. Fifth, the varying degree of control for confounding factors across studies. Few studies have been able to rigorously control for confounders at the family level, which is especially important when associations are modest and potential biases arising from family confounding are substantial. This is often the case for studies examining the associations between birth size and adult size.

The purpose of this study is to provide more complete growth measures than previously available, including prospective data collected during pregnancy and birth and full anthropometric assessments in adulthood, and achieving rigorous control of confounding at the family level through the use of same-sex sibling controls who are discordant on birth size but not on gestational age. We can thereby systematically explore relationships between size at birth and adult size and minimize potential biases due to family-level confounders. As discordant sibling pairs represent the majority, but not all of the assessed subjects, we examined the associations between birth size and adult size with an analytic strategy that can be applied to the full sample as well as to the sibling pairs alone, and report results of both analyses.

Materials and methods

Study sample

The data for these analyses derive from the Early Determinants of Adult Health (EDAH) study described in detail in Susser *et al.* (this issue). Briefly, for the core EDAH sample, we selected study subjects from the New England Family Study (NEFS) and from the parallel Child Health and Development Study (CHDS) in Oakland, CA, USA. The NEFS comprises the Boston and providence cohorts of the Collaborative Perinatal Project, which have now been coalesced as the NEFS for follow-up studies (see Susser *et al.*, this issue). We recruited participants from same-sex sibling sets where two or more members were discordant on birth weight, adjusted for gestational age and gender. Sibling-pair designs are increasingly used in epidemiology for control of family-level confounding in studies of early determinants of child and adult health and have been very effective in ruling out or detecting confounding in similar contexts to this study.[11-13] In the NEFS, the low birth weight proband was below the lowest 20th percentile of the gender-specific birth weight for gestational age distribution and the higher birth weight sibling was at or above the 20th percentile and at least 10 or more percentile points higher. These criteria applied to approximately half of the CHDS sibling sets; the remainder included sibling sets in which the two siblings differed by at least 10 percentile points on the birth weight for gestational age distribution, but where the lower birth weight sibling was not in the lowest quintile of the birth weight for gestational age distribution. Further, both siblings had to be between 38 and 43 completed weeks of gestation. Siblings were not recruited for the study if they did not live within commuting distance of the clinics in Boston and Oakland where the assessments were done.

Although there are standards of birth weight for gestational age that pertain to the birth dates of the subjects,[14] the EDAH study used the percentile measure of birth weight, adjusted for gestational age and gender, from recent nationwide US births[15] as these allow for the approximately continuous scaling of fetal growth in relation to gestation. This provides greater precision than scaling by broader percentile categories from older tables. Individual study subjects from eligible sibling sets were all retained in the analysis, even if it was not possible to examine both (or all) members of the sibling set.

Data collection

Prenatal and birth information—In both the NEFS and CHDS, pregnancy information and measures of infant birth size were based on direct measurements and maternal reports at exam visits (for further detail, see Susser *et al.*, this issue). Information on mothers and their pregnancies (mother's self-reported race, marital status, age at delivery, child birth order and date of last menstrual period) were collected during prenatal visits. Maternal height and birth characteristics including birth weight and birth length were measured using calibrated scales and standardized procedures. In this report we use the term 'birth size' as a common denominator for birth weight, birth weight for gestation, birth weight for gestation adjusted for sex, birth length or BMI at birth. We use the term 'birth weight' for that measure alone.

Assessment of adult outcomes—Study assessments were performed as part of a clinic visit that took approximately 4–5 h. During the visit, the men were administered a questionnaire to obtain data on social and demographic characteristics and health history of self and first-degree relatives (women had been administered these questions via computer assisted telephone interview as part of a related project (see Susser *et al.* and Terry *et al.*, this issue).

We here report on anthropometric outcomes in relation to body size at birth and selected maternal and pregnancy characteristics in this study population. We collected standing measures (height, weight, waist circumference, subscapular skinfolds, triceps skinfolds) and sitting measures (sitting height). All anthropometric measures were obtained by research nurses who were provided specific training and retraining sessions by one of us (LHL). We measured both leg length and trunk length in view of the reported inverse association between leg length and atherosclerosis in the Atherosclerosis Risk in Communities Study[16] and between leg length and coronary heart disease or type 2 diabetes mellitus in the British Women's Heart and Health Study, the Whitehall II study, and the Caerphilly study.[17-20] Leg length is of special interest as a shorter leg length in relation to trunk length may be a reflection of a poorer diet in early childhood. This may affect leg length more than trunk length.[21]

Participants were measured without shoes wearing only socks, lightweight undergarments and a lightweight gown. Standing height was measured to the nearest 1 mm using a portable stadiometer (SECA, Hamburg, Germany), and seated height was obtained to the nearest 1 mm with the participant seated on a hard stool of known height (Teak Step Stool, no. 563361, www.smithandhawken.com). Weight was obtained to the nearest 100 g with the participant standing on a portable digital scale (SECA). Two measures were taken for height and weight with the mean value taken for analysis. If height differed by more than 0.5 cm or weight by more than 0.1 kg, a third and fourth measure was taken and the mean of the three closest measures was taken for analysis. Trunk length was calculated by subtracting the height of a sitting stool (18″) from seated height, and leg length was obtained by subtracting trunk length from standing height. BMI was calculated as weight (kg)/height (m)^2. Waist circumference was measured to the nearest 1 mm using a non-stretch measuring tape (Seritex, Hoboken, NJ, USA) with a leading blank segment at the level of the iliac crest and intersection with the mid-axillary line using the protocol used in National Health and Nutrition Examination Survey-III.[22] Two readings were taken and averaged unless the readings were more than 1 cm apart in which case a third and fourth readings were taken and the three closest values were averaged. Subscapular and triceps skinfolds were measured to the nearest 0.2 mm using skinfold calipers with a maximal spread of 44 mm (Holtain, Dyfed, Wales, UK). The first two measures were averaged unless they differed by more than 1.0 mm in which case a third and fourth measures were taken and the three closest measures were averaged. Skinfold thicknesses that exceeded the capacity of the calipers were seen in 10% of those examined and were coded as 44 with an annotation to that effect. Body fat percentage was estimated by generalized regression equations from body density (D) and the Brozek formula.[23,24] The trunk-to-extremity skinfold thickness ratio was calculated as measure of central distribution of body fat. This ratio classifies individuals by the ratio of subcutaneous fat present on the trunk [subscapular (mm) skinfold] to subcutaneous fat on the limb [triceps (mm) skinfold]. We used the ratio as a measure of centripetal *v.* peripheral fat deposition.[25]

Data analysis

We compared demographic characteristics of the mothers from the two study sites and compared the distributions by *t*-tests or χ^2-tests as appropriate.

Birth weight percentiles (standardized for gestation and gender) and adult body size measures were then analyzed separately for men and women adjusting for study site, and by study site adjusting for gender. In these analyses, we evaluated for each 20 percentile unit change in a measure of birth size (e.g. birth weight for gestational age, birth length) the associated change in the measures of adult size (e.g. standing height, BMI, trunk-to-extremity thickness ratio). For convenience, we will refer to a 20-unit percentile change as a quintile change.

We first conducted the analysis using all study participants (including subjects with no, one, two or three study siblings), and then using the subset of sibling pairs only (i.e. only subsets with one sibling). To use all available data in this population with sibships of size 1, 2, 3 and 4 and to take clustering within siblings in to account we used a multilevel linear regression mixed model known as the linear random intercept regression model, with family-level random intercepts.[26] These analyses were repeated for the subset of sibling pairs (i.e. sibship size 2). After adjusting for study site and gender, we evaluated the effect of further adjustments: first for age at examination; then for mother's race, marital status, age at delivery and child birth order; and then for mother's height.

Analyses were performed with the SPSS v.10 (Chicago, IL, USA) and STATA v.11 (College Station, TX, USA) statistical packages. We used the STATA xtree command for parameter estimations of the random intercept linear regression models described above.

Results

We examined 149 members of the NEFS cohort and 243 members of the CHDS cohort. Of the 392 offspring, 137 had no sibling in the study, 123 had one, two had two and one had three. Among the total sample, 376 (95.9%) had anthropometric data on all measures.

Table 1 shows the characteristics of mothers and offspring from the archived data of the NEFS and CHDS cohorts. Mothers in the NEFS study were more likely to be younger compared to mothers in the CHDS, with mother's age at delivery being 24 years or less in 58% *v.* 41% of women. NEFS mothers were also more likely to be white (93% *v.* 61%), married (95% *v.* 73%) and to smoke in pregnancy (52% *v.* 39%) compared to CHDS women. They were on average also somewhat shorter compared to CHDS women (160.0 *v.* 162.8 cm). A lower proportion of mothers in the NEFS had been educated beyond high school compared to CHDS women (60% *v.* 78%). As per our study inclusion criteria, all offspring were born at full term or later, and offspring in the NEFS study were more likely to include infants at the lower centiles of birth weight for gestational age. This is also reflected in distributions of offspring birth weight and birth length.

Table 2 shows the adult body size measurements from the EDAH follow-up, by gender, maternal race and study site. Height, trunk length, leg length, weight and waist circumference in men were larger compared to women (all at $P < 0.001$), but men and women showed no statistical difference in BMI (29.9 *v.* 28.9 kg/m^2; $P = 0.18$). The estimated body fat percentage in women was 4.9% higher compared to men (35.6% *v.* 30.7%; 95% CI: 3.7 to 6.0; $P = 0.001$). Height, trunk length, leg length and weight (but not BMI or body fat percentage) were also independently associated with mother's race and study site ($P = 0.01$ for main effects gender, race and study site in a three-way ANOVA; data not shown).

Table 3 exhibits the relationships between selected measures of birth weight (standardized for gestation and gender) and measures of adult body size for the full study population. Relations are given separately for men and women adjusting for study site, for site adjusting for gender and for all study participants combined, adjusting for site and gender. For each quintile change in birth size, we tabulated the associated change in adult standing height, trunk height, leg length, weight, BMI, waist circumference, body fat percentage and the trunk-to-extremity thickness ratio. A quintile change in birth size was significantly related to increases in linear growth outcomes (1.25 cm in adult height (95% CI: 0.79 to 1.70), 0.65 cm in trunk length (95% CI: 0.41 to 0.89) and 0.57 cm in leg length (95% CI: 0.26 to 0.88); it showed a non-significant trend for an association with adult weight (0.71 kg; 95% CI: −0.94 to 2.36 kg); and showed no appreciable associations with BMI, waist circumference or the trunk-to-extremity thickness ratio ($P > 0.25$ for all measures). There was an inverse, rather than positive association with the estimated body fat percentage (change of −0.53%; 95% CI: −0.98 to −0.10).

Table 4 shows these relationships for both the full study population and for the sibling pairs alone with additional adjustment for age at examination. The observed patterns were the same as in Table 3. With respect to estimates of effect size, the regression coefficients among the sibling subset were, ~30% smaller relative to estimates including all study subjects. As an example, a quintile change in birth weight for gestation, adjusted for study site, gender and age at examination, using all study subjects and regression adjustment for clustering, was associated with a 1.24-cm change (95% CI: 0.79 to 1.70) in adult height; using only the sibling pairs and regression adjustment for clustering it was associated with a 1.08-cm change in height (95% CI: 0.52 to 1.65). By contrast, quintile changes in birth weight were not associated with BMI changes in adults, using either all study subjects (−0.22 BMI unit change; 95% CI: −0.77 to 0.34) or only the sibling pairs (0.30 BMI unit change; 95% CI: −0.43 to 1.03).

Table 4 also shows the results after additional adjustment: first for mother's race, marital status, age at delivery and child birth order; and then for mother's height.

These adjustments had little effect on the observed relationships. Further adjustments for mother's education (data not shown) also had no appreciable effect.

In Table 5, we compare the associations of three additional measures of size at birth (birth weight standardized for gestation and sex, birth length and BMI) with the measures of adult body size. Birth length shows a consistent statistical association with the linear growth measures of height, trunk length and leg length at age 43 years, but not with fatness-related outcomes such as weight, adult BMI or waist circumference. As an example, a 1-cm change in birth length is associated with an adult height change of 0.72 cm (95% CI: 0.46 to 0.98), but only with a BMI change of 0.16 units (95% CI: −0.16 to 0.48). When birth weight for gestation and birth length are evaluated jointly in one model, both show a strong statistical association with linear growth at age 43 years, although in that case the effect size estimates for each unit change in birth weight or length are diminished by 30–50%. Infant BMI only shows weak associations with adult body size, which do not reach statistical significance.

Discussion

In this study, we found robust positive associations between birth weight for gestational age in term babies and measures of adult length at age 43 years, but not with measures of adult fatness such as BMI, waist circumference, body fat percentage or body fat distribution. We found no associations between weight for height (BMI) at birth and measures of adult body size. These associations were confirmed in analyses limited to same-sex sibling pairs discordant on birth weight. The relations also persisted with further adjustments for age at examination and for maternal characteristics.

Our findings of a positive association between birth weight for gestational age and adult height are in general agreement with previous reports, although some of these reports have suggested that birth length may be a better predictor of adult height than birth weight.[4,6,7] In our overall study group, birth weight (adjusted for gestational age and sex) and birth length were independently associated with adult length, alone or in combination. The change in adult length associated with a quintile change in birth weight was somewhat smaller after additional adjustment for birth length, but the change in adult length per unit change in birth length was similarly diminished after additional adjustment for birth weight. This pattern was the same in the subset of sibling pairs.

We found no association, however, between various indicators of birth size and fatness-related outcomes. The association between birth size and fatness-related outcomes is unclear from previous studies. Most studies use only adult BMI as the outcome measures and results have been quite variable.[1-9] Among Danish and Swedish conscripts, for example, birth weight was positively associated with BMI.[2,9] An Icelandic study of a high birth weight population also suggested that there may be a relationship between size at birth and adult BMI.[3] In the 1958 British birth cohort, on the other hand, birth weight and adult BMI showed a weak positive association that was largely explained by maternal weight.[5] In the Jerusalem Perinatal Study, results were somewhat inconclusive, with a modest relation between being above average birth weight and being overweight as an adult.[8]

We think there is a plausible explanation for our findings that indicators of birth size are related to adult length (confirming most other studies of this question) but not to adult weight (on which other studies give inconsistent results). These findings may reflect the fact that adult weight is particularly sensitive to changes in the adult nutritional environment, irrespective of early influences. And this adult environment is likely to be specific to every study setting. For studies of early influences on adult health, adult measures of weight and fatness may therefore not be the most sensitive outcomes.

With respect to trunk length and leg length, our study provides no evidence that birth weight for gestation or other indicators of birth size are related more to one or the other length measure. Previous studies have reported that leg length shows a stronger relation to cardiovascular risk than trunk length, but the relation with size at birth was not evaluated.[17-19] Our results suggest that if leg length is indeed more strongly related to cardiovascular disease, this is unlikely to be explained by a differential effect of nutritional or other exposures on growth in leg *v.* trunk length prior to birth.

In this study, subjects were classified by birth weight percentiles, adjusted for gestational age and gender.[15] Such classifications may be problematic at preterm gestations where the number of fetuses that are still *in utero* may greatly exceed the number of births at a particular gestation week and cause significant bias.[27] Our study population only includes infants born at term so that these issues do not arise.

In our statistical analyses, we used a multilevel mixed model known as the linear random intercept regression model, with family-level random intercepts.[26] This model fully uses the information of our study population that includes families of size 1, 2, 3 and 4 subjects. Because the average cluster size was small in the overall population (~1.5) it is not possible to accurately estimate the cluster-level effect.[28] Our goal, however, was to obtain best estimates of the individual-level effects, and this was achieved by adjusting for family-level effects with these methods.

In summary, our findings among the overall cohort and among sibling pairs confirm associations between birth weight and adult length as also reported in other studies. They do not show an association between birth weight and adult fatness for which findings in other studies are highly variable, probably reflecting variations in the adult nutritional environment rather than the early environment. We therefore suggest that it may be more useful for studies of birth size and adult size to use adult length measures rather than adult weight measures in evaluating the role of early influences on adult health.

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Table 1

EDAH study – mother's demographic and infant's birth characteristics, by study site

	NEFS (*n* = 149)	CHDS (*n* = 243)	*P*-value
Mother's race			
White	138 (93)	148 (61)	<0.001
Black	11 (7)	55 (23)	
Other	–	40 (17)	
Mother's height (cm)			
Mean (S.D.)	160.0 (7.6)	162.8 (6.7)	<0.001
Marital status			
Married	141 (95)	178 (73)	
Other/unknown	8 (5)	65(27)	<0.001
Mother's age at delivery (years)			
≤19	19 (13)	14 (6)	0.007
20–24	67 (45)	86 (35)	
25–29	33 (22)	73 (30)	
30–34	23 (15)	45 (19)	
35 +	7 (5)	25 (10)	
Birth order			
First	35 (23)	43 (18)	0.31
Second	37 (25)	71 (29)	
Third of fourth	46 (31)	88 (36)	
Fifth or more	31 (21)	41 (17)	
Mother's education			
No high school	59 (40)	53 (22)	<0.001
High school	71 (49)	81 (33)	
Over high school	17 (11)	109 (45)	
Mother's smoking during pregnancy			
No	72 (48)	148 (71)	0.01
Yes or unknown[a]	77 (52)	95 (39)	
Infant's gender			
Male (%)	44	49	0.77
Gestation (completed weeks)			
37	3 (2)	3 (1)	
38–41	130 (87)	214 (88)	0.84
42+	16 (11)	26 (11)	
Birth weight (g)			
<2499	3 (2)	5 (2)	0.002
2500–1999	43 (29)	45 (19)	
3000–3499	75 (50)	109 (45)	
3500–2999	27 (18)	67 (28)	
4000 +	1 (1)	17 (7)	

	NEFS (*n* = 149)	CHDS (*n* = 243)	*P*-value
Birth weight centile adjusted for gestation and infant sex			
1–20th	69 (46)	67 (28)	0.001
21–40th	33 (22)	57 (24)	
4l–60th	29 (19)	49 (20)	
61–80th	12 (8)	42 (17)	
81–100th	6 (4)	28 (12)	
Birth length (cm)			
≤49	46 (31)	34 (14)	0.001
50	23 (15)	27 (11)	
51	34 (23)	57 (24)	
52	25 (17)	40 (17)	
≥53	20 (13)	85 (35)	
Infant's BMI (kg/m^2)			
9.1–11.6	33 (22)	46 (19)	0.49
11.6–12.2	29 (19)	47 (919)	
12.2–12.8	25 (17)	59 (24)	
12.8–13.4	28 (19)	39 (16)	
13.4–15.9	33 (22)	52 (21)	

EDAH, Early Determinants of Adult Health; NEFS, New England Family Study; CHDS, Child Health and Development Study.

[a]Smoking status in pregnancy unknown in twelve subjects. Values are represented as number (%) for the categorical variables, mean (s.d.) for the continuous variable, mother's height, and as the percentage of all subjects for the variable infant's gender. Variable categories may not sum to 100% due to rounding.

Table 2

EDAH study – body size measures at age ~ 43 years, by gender, maternal race and study site

Study category	Height (cm)	Trunk length (cm)	Leg length (cm)	Weight (kg)	BMI (kg/m^2)	Waist circumference (cm)	Body fat percentage	Trunk-to-extremity thickness ratio	*n* [a]
Men									
White									
NEFS	174.7	92.1	82.6	91.2	29.9	101.9	31.4	1.23	59
CHDS	180.0	94.8	85.3	94.1	29.0	98.6	29.1	1.41	72
Black									
NEFS	173.8	87.7	86.2	96.0	31.9	103.0	31.8	1.27	6
CHDS	179.7	92.1	87.5	104.0	32.0	104.1	31.9	1.63	26
Other									
NEFS	–	–	–	–	–	–	–	–	0
CHDS	174.9	92.8	82.1	89.6	29.2	98.0	33.5	1.35	15
All men	177.6 (7.2)	93.1 (3.5)	84.5 (5.0)	94.3 (19.9)	29.9 (6.0)	100.6 (14.1)	30.7 (6.5)	1.38 (0.61)	178
Women									
White									
NEFS	163.1	86.0	77.1	74.5	28.0	90.2	34.7	0.95	77
CHDS	164.9	88.5	76.3	80.0	29.4	96.0	36.0	0.88	68
Black									
NEFS	163.7	83.7	80.0	70.9	26.3	92.7	34.5	1.05	5
CHDS	166.0	86.4	79.6	86.1	31.0	97.1	37.8	0.93	27
Other									
NEFS	–	–	–	–	–	–	–	–	0
CHDS	158.7	86.3	72.4	71.8	28.6	95.6	35.2	0.89	21
All women	163.6 (5.9)	86.9 (3.2)	76.8 (4.2)	77.6 (22.3)	28.9 (7.9)	93.8 (16.3)	35.6 (4.8)	0.92 (0.23)	198

EDAH, Early Determinants of Adult Health; BMI, body mass index; NEFS, New England Family Study; CHDS, Child Health and Development Study.

Values in parentheses indicate S.D.

[a] Table includes the 376 subjects with complete data in all adult body size measures. Height, trunk length, leg length and weight are independently associated with gender, mother's race and study site ($P < 0.01$ for all main effects by three-way ANOVA) but BMI is not ($P > 0.12$ for all main effects). Body fat percentage is only independently associated with gender ($P < 0.01$).

Table 3

EDAH study – changes in selected body size measures at age ~ 43 years for each birth weight quintile change[a] by gender and study site

Study category	Height (cm)	Trunk length (cm)	Leg length (cm)	Weight (kg)	BMI (kg/m^2)	Waist circumference (cm)	Body fat percentage	Trunk-to-extremity thickness ratio
Men and women (adjusted for site)								
Men	1.38	0.66	0.70	0.46	−0.26	0.02	−1.00	0.71
	0.66 to 2.10	0.29 to 1.03	0.20 to 1.20	−1.76 to 2.69	−0.93 to 0.41	−1.58 to 1.62	−1.70 to −0.29	0.03 to 1.39
	0.000	0.000	0.01	0.68	0.45	0.98	0.006	0.04
Women	1.10	0.67	0.42	1.06	−0.03	0.60	−0.05	−0.27
	0.53 to 1.66	0.36 to 0.98	0.03 to 0.81	−1.37 to 3.49	−0.91 to 0.84	−1.21 to 2.40	−0.58 to 0.48	−0.53 to −0.02
	0.000	0.000	0.04	0.39	0.94	0.52	0.84	0.04
New England and California study sites (adjusted for gender)								
NEFS	0.62	0.48	0.09	0.82	0.14	−0.07	0.06	0.14
	−0.09 to 1.33	0.04 to 0.92	−0.35 to 0.52	−1.62 to 3.52	−0.70 to 0.98	−2.07 to 1.94	−0.68 to 0.80	−0.22 to 0.49
	0.09	0.03	0.69	0.51	0.74	0.95	0.88	0.45
CHDS	1.53	0.73	0.79	0.71	−0.32	0.47	−0.78	0.14
	0.94 to 2.12	0.45 to 1.02	0.37 to 1.21	−1.49 to 2.91	−1.05 to 0.41	−1.05 to 1.99	−1.33 to −0.23	−0.38 to 0.66
	0.000	0.000	0.000	0.53	0.39	0.55	0.005	0.60
All categories combined (adjusted for study site and gender)	1.25	0.65	0.57	0.71	−0.23	0.17	−0.53	0.20
	0.79 to 1.70	0.41 to 0.89	0.26 to 0.88	−0.94 to 2.36	−0.79 to 0.32	−1.04 to 1.39	−0.98 to −0.10	−0.15 to 0.56
	0.000	0.000	0.000	0.40	0.41	0.28	0.02	0.26

EDAH, Early Determinants of Adult Health; BMI, body mass index; NEFS, New England Family Study; CHDS, Child Health and Development Study.

[a]Birth weight quintiles standardized for gestation and infant's sex. *β*-Coefficients with 95% CI and *P*-values from multilevel linear regression models with random intercept adjustment for clustering within families. Body fat percentage estimated by generalized regression equations from body density (D) that was estimated from the sum of the subscapular and triceps skinfolds and the Brozek conversion formula as outlined in the 'Materials and methods' section. Trunk-to-extremity skinfold thickness ratio: ratio of subscapular skinfold (mm) to triceps skinfold (mm). Overall study population: 392 participants including 136 with no siblings, 123 with one sibling, two with two siblings and one with three siblings. Sibling pairs' subset includes 123 participants with one sibling. A total of 376 subjects with complete data were used for this analysis.

Table 4

EDAH – study changes in selected body size measures at age ~ 43 years for each birth weight quintile change[a] by availability of sibling controls

Study population	Height (cm)	Trunk length (cm)	Leg length (cm)	Weight (kg)	BMI (kg/m^2)	Waist circumference (cm)	Body fat percentage	Trunk-to-extremity thickness ratio
All study subjects								
Adjusted for study site, gender and age at examination	1.24	0.65	0.57	0.76	−0.22	0.15	−0.57	0.24
	0.79 to 1.70	0.41 to 0.89	0.25 to 0.88	−0.90 to 2.41	−0.77 to 0.34	−1.07 to 1.37	−1.00 to −0.13	−0.12 to 0.59
	0.000	0.000	0.000	0.37	0.45	0.81	0.01	0.19
Adjusted for mother's and pregnancy characteristics[b]	1.13	0.60	0.51	0.83	−0.15	0.20	−0.48	0.21
	0.68 to 1.59	0.36 to 0.83	0.20 to 0.83	−0.84 to 2.50	−0.71 to 0.42	−1.03 to 1.44	−0.92 to −0.04	−0.12 to 0.59
	0.000	0.000	0.001	0.33	0.61	0.75	0.03	0.20
Adjusted for mother's height	0.95	0.46	0.49	0.85	−0.03	0.37	−0.42	0.24
	0.48 to 1.43	0.20 to 0.71	0.15 to 0.84	−1.01 to 2.72	−0.61 to 0.59	−1.01 to 1.75	−0.92 to 0.07	−0.17 to 0.65
	0.000	0.000	0.005	0.37	0.90	0.60	0.10	0.25
Sibling pairs only								
Adjusted for study site, gender and age at examination	1.08	0.57	0.50	2.21	0.30	1.15	−0.17	0.10
	0.52 to 1.65	0.27 to 0.86	0.12 to 0.90	0.05 to 4.36	−0.43 to 1.03	−0.43 to 2.74	−0.71 to 0.36	−0.33 to 0.55
	0.000	0.000	0.01	0.05	0.42	0.15	0.53	0.63
Adjusted for mother's and pregnancy characteristics[b]	1.05	0.56	0.48	2.32	0.36	1.21	−0.11	0.10
	0.48 to 1.62	0.27 to 0.85	0.08 to 0.87	0.16 to 4.49	−0.37 to 1.10	−0.38 to 2.81	−0.64 to 0.43	−0.35 to 0.55
	0.000	0.000	0.01	0.04	0.34	0.14	0.69	0.66

EDAH, Early Determinants of Adult Health; BMI, body mass index.

[a]Birth weight quintiles standardized for gestation and infant's sex. β-Coefficients with 95% CI and *P*-values from multilevel linear regression models with random intercept adjustment for clustering within families. Sibling pairs subset includes 123 participants with one sibling.

[b]Mother's and pregnancy characteristics include mother's race, marital status, age at delivery and child birth order.

Table 5

EDAH study – changes in selected body size measures at age ~ 43 years for changes in selected measures of birth size[a], by availability of sibling controls

Measure of birth size	Height (cm)	Trunk length (cm)	Leg length (cm)	Weight (kg)	Adult BMI (kg/m^2)	Waist	Body fat percentage	Trunk-to-extremity thickness ratio
All study subjects								
Birth weight for gestation (quintile)	1.25	0.65	0.57	0.71	−0.23	0.17	−0.53	0.20
	0.79 to 1.70	0.40 to 0.89	0.26 to 0.88	−0.94 to 2.36	−0.79 to 0.32	−1.04 to 1.39	−0.98 to −0.10	−0.15 to 0.56
	0.000	0.000	0.000	0.40	0.41	0.78	0.02	0.26
Birth length (cm)	0.72	0.38	0.34	0.29	−0.16	−0.14	−0.24	0.13
	0.46 to 0.98	0.24 to 0.52	0.16 to 0.52	−0.67 to 1.25	−0.48 to 0.16	−0.84 to 0.56	−0.50 to 0.01	−0.08 to 0.33
	0.000	0.000	0.000	0.56	0.33	0.70	0.06	0.23
Birth weight for gestation (quintile)	0.78	0.41	0.35	0.64	−0.10	0.51	−0.45	0.12
	0.22 to 1.35	0.11 to 0.70	−0.04 to 0.74	−1.44 to 2.73	−0.81 to 0.60	−1.03 to 2.05	−1.00 to 0.10	−0.33 to 0.57
	0.007	0.008	0.08	0.55	0.77	0.52	0.11	0.61
Birth length (cm)	0.45	0.24	0.22	0.06	−0.12	−0.32	0.09	0.09
	0.12 to 0.78	0.06 to 0.41	−0.01 to 0.44	−1.15 to 1.27	−0.53 to 0.28	−1.20 to 0.57	−0.41 to 0.23	−0.17 to 0.35
	0.007	0.008	0.06	0.92	0.55	0.48	0.60	0.52
BMI (kg/m^2)	0.48	0.22	0.24	0.02	−0.21	0.26	−0.45	−0.02
	−0.04 to 1.00	−0.06 to 0.49	−0.11 to 0.59	−1.83 to 1.87	−0.83 to 0.42	−1.10 to 1.61	−0.94 to 0.04	−0.41 to 0.38
	0.07	0.12	0.18	0.98	0.52	0.71	0.07	0.94
Sibling pairs only								
Birth weight for gestation (quintile)	1.08	0.57	0.51	2.21	0.30	1.14	−0.17	0.11
	0.52 to 1.65	0.27 to 0.86	0.12 to 0.90	0.05 to 4.36	−0.43 to 1.03	−0.44 to 2.72	−0.71 to 0.36	−0.33 to 0.55
	0.000	0.000	0.01	0.05	0.42	0.16	0.14	0.63
Birth length (cm)	0.55	0.33	0.23	0.73	0.05	0.24	−0.14	0.09
	0.23 to 0.87	0.17 to 0.50	0.004 to 0.45	−0.48 to 1.95	−0.36 to 0.46	−0.64 to 1.12	−0.44 to 0.16	−0.16 to 0.33
	0.001	0.000	0.05	0.24	0.81	0.60	0.36	0.50
Birth weight for gestation (quintile)	0.78	0.31	0.43	2.40	0.44	1.56	−0.02	0.02
	0.04 to 1.52	−0.08 to 0.70	−0.08 to 0.94	−0.49 to 5.30	−0.55 to 1.42	−0.58 to 3.69	−0.73 to 0.70	−0.58 to 0.62
	0.04	0.12	0.10	0.10	0.39	0.15	0.97	0.95

Measure of birth size	Height (cm)	Trunk length (cm)	Leg length (cm)	Weight (kg)	Adult BMI (kg/m^2)	Waist	Body fat percentage	Trunk-to-extremity thickness ratio
Birth length (cm)	0.27	0.22	0.07	−0.16	−0.11	−0.34	−0.13	0.08
	−0.15 to 0.69	0.01 to 0.44	−0.22 to 0.36	−1.79 to 1.46	−0.66 to 0.44	−1.52 to 0.85	−0.73 to 0.70	−0.25 to 0.41
	0.21	0.05	0.63	0.84	0.69	0.58	0.51	0.64
BMI (kg/m^2)	0.49	0.16	0.29	1.35	0.22	1.03	−0.17	−0.20
	−0.17 to 1.15	−0.19 to 0.51	−0.15 to 0.74	−1.17 to 3.86	−0.63 to 1.07	−0.81 to 2.87	−0.79 to 0.45	−0.71 to 0.31
	0.15	0.37	0.20	0.29	0.62	0.27	0.58	0.44

EDAH, Early Determinants of Adult Health; BMI, body mass index.

[a] Birth size adjusted for study site and gender. *β*-Coefficients with 95% CI and *P*-values from multilevel linear regression models with random intercept adjustment for clustering within families. Sibling pairs subset includes 123 participants with one sibling.