HHS Public Access

Author manuscript

Int J Obes (Lond). Author manuscript; available in PMC 2011 June 01.

Published in final edited form as:

Int J Obes (Lond). 2010 December ; 34(12): 1766–1771. doi:10.1038/ijo.2010.104.

Mother's age at menarche and offspring size

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Abstract

Objective—An individual's growth trajectory is, at least in part, inherited. Mother's early age at menarche has been associated with taller offspring height and greater body mass index (BMI) at age 9 years, suggesting that mother's age at menarche may be an intergenerational marker of growth. We examined the association between mother's age at menarche and childhood size at birth, and at the ages 1, 3, 4, 7, and 8 years in the Collaborative Perinatal Project (CPP).

Subjects—We examined 128,636 measurements from 31,474 Black and White children. We transformed the original measurements into z-scores. Child size was examined in mixed models, adjusted for center, child sex, race, socioeconomic index, child's exact age at measurement (in months), mother's age at recruitment and, depending on which measure was the outcome in the specific model, mother's height, pre-pregnancy weight, or BMI.

Results—Compared with children whose mother had menarche at age 15 or later, children whose mothers had age at menarche before age 12 were taller from age 1 and had higher BMI at ages 7 and 8 (0.17 and 0.19 z, respecively).

Conclusions—Mother's age at menarche is a modest predictor of their children's growth trajectory. The mechanism is likely to be heritable, although other explanations are possible.

Keywords

Age at menarche; Body Mass Index; Growth trajectory

An individual's growth trajectory is, at least in part, inherited. In 2007, Ong and colleagues reported that mother's age at menarche before 12 years predicted offspring who were taller and had a higher BMI at age 9 compared with children whose mothers had menarche at 15 years of age or later. Similar patterns were seen in boys and girls, and the authors suggested that mother's age at menarche was an intergenerational marker of a faster growth tempo1.

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Conflict of interest

None of the authors has any conflict of interest in connection with this manuscript.

Evidence suggests that rapid early childhood weight gain, insulin resistance, and timing of puberty are interrelated and may recur in consecutive generations2. Rapid growth in infancy or early childhood is itself a predictor of higher body mass index (BMI) in later childhood and young adulthood, although this has not been observed in all populations3–6. A study of pedigrees suggested that the significant associations between age at menarche and obesity phenotypes were mainly attributable to shared genetic rather than environmental factors7, and age at menarche appears to have a strong heritable component8–10.

BMI before age 13 appears to have a limited value in predicting adult BMI on an individual basis11, but a correlation exists at a population level. Mother's age at menarche will be an even weaker predictor of adult BMI, but it is of interest to identify heritable markers that may interact with environmental determinants of overweight. In this paper, we examined whether the association between mother's age at menarche and offspring growth was present in a large population of US Black and White children born from 1959 to 1966 in the Collaborative Perinatal Project.

Methods

The Collaborative Perinatal Project was a prospective pregnancy cohort of 58,760 pregnancies in 48,197 women who gave birth between 1959 and 1966. Women were enrolled in 12 U.S. academic medical centers during pregnancy (Baltimore, Boston, Buffalo, Memphis, Minneapolis, New Orleans, New York Columbia, New York Metropolitan, Philadelphia, Portland, Providence, and Richmond) and were followed through delivery, while their children were followed up to 7 years of age in all centers, and up to 8 years of age in approximately half the centers12. Mothers self-reported their height and pre-pregnancy weight. Children were measured according to standardized procedures by trained personnel. Length/height was measured to the nearest 0.5 cm, in a supine position through 20 months age, and standing thereafter. Scales were calibrated at least semi-annually 13.

We included the first singleton live birth contributed by each woman during the study enrollment period (not necessarily her first child) with non-missing data on baby's sex, birth weight, and mother's age at menarche (n=43,037). We excluded women with race other than Black or White (n=3,553), infants with major malformations (n=3,266), and those with unlikely birth weight (n=35). Among the remaining 36,183, 4,531 children had no further weight measurements (beyond birth), thus leaving 31,652 eligible children. Finally, we excluded 3 records with mother's age at menarche recorded as having been less than 7 years, and 175 mothers whose age at menarche was within 2 years of age at recruitment. We excluded these mothers because we wanted to be sure that menstruation had been fully established by the time of conception. As we only had age in completed years for age at recruitment, a 2 year difference was chosen to guarantee this. The final sample included 31,474 children with valid birth weight and at least one later weight measurement, with 128,636 measurements in total. Some analyses, however, include fewer individuals due to missing length/height in children or missing weight or height in mothers, as mother's anthropometry was included as a covariate in the models. Sample size varied also by age of the children, depending on how many were measured at each point in time.

We examined the association between mother's age at menarche and child length/height, weight, and body mass index (BMI) at birth and ages 1, 3, 4, 7, and 8 years (±2 months) using linear mixed models. Due to the relatively small number of measurement times and the nonlinear nature of child growth, we modeled age as a step function with different intercepts and different menarche slopes for each age at measurement. We also included a continuous covariate accounting for the month of measurement in each year (children could, however, be only ±2 months younger or older than the nominal age, otherwise the observation was excluded).

We considered the data both in their original scale and as z-scores calculated from the whole CPP cohort. As the z-score was sex- and age-specific, it is not influenced by age,14 which allowed us to easily compare the relative effects at different ages. Here, we present the results based on the z-score.

In our primary models, we categorized mother's age at menarche as ≤11, 12, 13, 14, and 15 years or older. The categorical treatment provided us with a non-parametric assessment of the age at menarche-child size relations, which is consistent with the approach of Ong and colleagues1. However, to determine if there was a significant linear relation between age at menarche and child size at different ages, we also treated age at menarche as continuous, with values, in completed years, in the range 11–15, with <11 coded as 11, and >15 coded as 15. Regardless of how we treated age at menarche, we always allowed the effect to change with child's age in order to test for a menarche-by-year interaction.

For each measurement, our primary model (ignoring covariates) was as follows:

$$y_{it}=\beta_{0t}+\beta_{1t}\,(\mathrm{q}_{1i})+\beta_{2t}\,(\mathrm{q}_{2i})+\beta_{3t}\,(\mathrm{q}_{3i})+\beta_{4t}\,(\mathrm{q}_{4i})+\beta_{5t}\,(\mathrm{age}_{it}-t)+\varepsilon_{it},$$

where y_{it} is the measurement (height, weight, or BMI) for child i at year t, q_{ki} is an indicator variable that equals 1 if the age at menarche of the child's mother was in the k^{th} category (k = 1, 2, 3, 4 with menarche at 15+ serving as the reference category); age_{it} is the age of the child at time of measurement in year t, β_{0t}, β_{1t}, β_{2t}, β_{3t}, β_{4t}, and β_{5t} are the year-specific intercept and slopes, and ε_{it} is the residual error. An unstructured covariance matrix was used to model the variances and correlations between the errors from the same child at different years. We used the Kenward-Roger method15 to calculate the degrees of freedom for tests of menarche effects and menarche-by-year interactions, assuming an unstructured covariance matrix for measurements obtained from the same child at different years.

We first tested whether there were significant interactions between mother's age at menarche and children's sex and race on their body size. We used age at menarche as a continuous variable to have a more sensitive test. When using the z-score, there was no interaction with a $p<0.10$, and we thus present the results for Blacks and Whites and boys and girls together (stratified results are shown in the online appendix). When using the measurements in the original scale, for weight there was a significant interaction between mother's age at menarche and race (we present these results in the online appendix). Estimates were adjusted for center, race (Black or White), child sex, socioeconomic index (3 levels, plus a separate category for the 3% with missing values), child's exact age at

measurement (in months), mother's age at recruitment and, depending on which measure was the outcome in the specific model, mother's height, pre-pregnancy weight, or BMI. We adjusted for mother's anthropometry to evaluate whether an effect of age at menarche was present beyond that due to correlation with the size of the mother. In a further analysis, however, we also ran models not adjusted for mother's anthropometry, using the total available sample (i.e., including the women with missing height and weight).

We did not treat mother's smoking as a confounder, because smoking is likely to have started after menarche. However, because a previous analysis showed that mother's smoking during pregnancy was associated with higher BMI in their children16, we checked whether including smoking in the models had an impact on our estimates. SAS 9.1 (SAS Institute Inc., Cary, NC) was used for statistical analyses.

Results

As expected, women with age at menarche ≤11 were, on average, shorter and more frequently overweight than women with menarche at later ages (table 1). Table 2 shows mean length/height, weight, and BMI of the children at different ages, according to mother's age at menarche. Especially at ages 7 and 8, children whose mother's age at menarche was ≤11 years were slightly taller and had a higher BMI compared with children whose mother's age at menarche was later, particularly 15 or older.

Offspring anthropometry differed according to mother's age at menarche. Although the association between age at menarche and offspring anthropometry was statistically significant at several ages in the adjusted models, the largest and most consistent association was seen when the children were aged 7 and 8 (appendix table 1, contrasts). Figure 1 shows the difference in length/height, weight, and BMI (expressed as *z* scores) at the various ages as a function of mother's age at menarche (children whose mother had menarche at ≥ 15 years constitute the reference category). There was a small difference in birth length with mother's age, and the trend became stronger with age, with children born to mothers with age at menarche before 12 years being taller than children whose mothers had menarche at an older age, particularly 15+. Babies born to mothers with early age at menarche tended to be slightly lighter at birth, but the pattern reversed at 1 year and thereafter resembled the trend seen with height. The results for BMI were similar to those for weight, although a clear trend of increasing BMI among children born to women with early menarche is not seen until age 4. For reference, at age 7, a difference of 0.2 z corresponded to about 1 cm (<1% of the mean height), 0.8 kg (3% of the mean weight), and 0.4 kg/m^2 (approximately 2.5% of the mean BMI), respectively. (Appendix figures 1 and 2 show the results for the analogous models, stratified by sex and race, for height and BMI).

Table 3 shows the linear coefficients from the mixed models when age at menarche is treated continuously (as described above). Although the effect of each increment in mother's age at menarche on offspring size is small, all estimates (except that for BMI at age 3) were significant ($p<.05$).

We saw similar results in the models where mother's anthropometry was not included as a covariate. However, the association of age at menarche with child's height was slightly attenuated by omitting mother's height in the model, while the association with child's BMI was strengthened when mother's BMI was omitted. (Appendix figure 3 shows the results with and without adjustment).

The results were virtually identical when we further adjusted for mother's smoking (never, former, current, and missing), and also when we reintroduced the 175 women excluded because their age at menarche was within two years of their age at enrolment (not shown).

The results were also very similar when we used the measurements in the original scale instead of the *z*-score (not shown). However, the relation between mother's age at menarche and child weight in the original scale showed statistical evidence of varying according to race (p=0.052). We thus report the results for weight stratified by race (appendix figure 4).

Discussion

In this large cohort of US children born from 1959 to 1966, we saw that children whose mothers had menarche at 11 years or younger appeared to have a faster growth trajectory than children born to mothers with later age at menarche. We saw similar results in Blacks and Whites, and in boys and girls, and we present the combined results. The estimated effects were small in absolute terms, but consistent in showing that children of women with early age at menarche were, on average, taller and had a higher BMI at ages 7 and 8 than women with later age at menarche. Our estimates were adjusted, among other factors, for mother's anthropometry (mother's height when child's length/height was the outcome, etc), because we wanted to assess whether there was an association beyond that due to the mother's own size. When we omitted mother's anthropometry in the analysis, the results were attenuated for height and strengthened for weight and BMI. We were particularly interested in examining the effect of age at menarche on BMI. As mothers with early age at menarche were themselves heavier, we included their BMI in the model to see whether any effect remained following adjustment. The fact that inclusion of height in the models strengthened the association, rather than attenuate it, is due to the fact that mothers with earlier age at menarche were shorter than mothers with late age at menarche, while their children were taller in the age range of this study.

The larger size of children born to mothers with early menarche was more apparent at ages 4 and, especially, 7 and 8 than in earlier childhood –but such a pattern was detectable in infancy for length/height and weight. Children of mothers with menarche at ≤11 years, although taller at age 8, are likely to end up being shorter adults, since their vertical growth stops earlier1.

Girls with a high BMI for their age have a tendency to experience menarche earlier17 and to have higher BMI as adults18. In a study based on 597 mother-daughter pairs from the CPP with complete menstrual history available, Keim et al reported that a maternal BMI of 25 or higher predicted earlier age at menarche in their daughters, a finding symmetrical to ours19. Terry et al20 reported that, among 262 women who had been born to mothers enrolled in the

CPP, higher percentile change in weight between 4 months and 1 year of age was associated with earlier age at menarche, after adjustment for mother's age at menarche. Garn and colleagues have speculated that the same factors cause both fatness and early maturation18 and these factors may in part be genetic7.

Early age at mother's menarche predicted larger size in both boys and girls, suggesting that it may be one of many markers related to programming of overall growth, rather than being specific to female development.

Our results indicate that, when accounting for the mother's own height, children born to mothers who had early menarche tend to be slightly taller from infancy and, by age 7, these children are taller and have higher weight and BMI than children born to mothers with later age at menarche. Although trends were, for the most part, linear, the largest difference was mostly between children born to women with menarche at age 11 or earlier and those born to women with age at menarche of 15 or older. It has been suggested that rapid growth in infancy may have a programming effect on later body composition21. While this may be true, the finding of a relation between mother's age at menarche and more rapid growth suggests that a tendency to faster growth is, at least in part, inherited. Rapid early postnatal growth, childhood adiposity, and earlier age at puberty may all have shared genetic determinants2,22, and heritability of age at menarche has been estimated to be between 0.5 and 0.78–10. It is, however, also possible that mothers' age at menarche is associated with non-genetic characteristics, such as nutritional status or physical activity, that also influence their children's growth. Mothers with younger age at menarche were generally younger, tended to be of higher social class, and were more likely to be smokers (appendix table 2). We adjusted for age and socioeconomic index in our analyses, but we cannot rule out that other correlates of age at menarche, such as diet, could have produced our findings.

Adair23 reports that girls who were relatively long and thin at birth tended to have earlier menarche. An earlier age at first conception24 and higher social class 23 had been previously reported among women with early menarche. Along similar lines, our results suggest that women with early menarche give birth to slightly longer and thinner babies.

Our study has several strengths and limitations. The cohort was large, and children were measured at various ages by trained personnel, although not all ages were equally well represented. Furthermore, we were able to adjust for several covariates, and we had a large number of Blacks. The fact that maternal age at menarche and pre-pregnancy anthropometry were self-reported constitutes a limitation of this study, as well as the absence of any information about the father's height or age at puberty (although indicators of puberty in males are difficult to recollect). However, we saw the expected relation between mother's age at menarche and her height and BMI. We used BMI as an outcome for infants, which may not be the best measure to assess adiposity at such an early age. Most of the influence of mother's age at menarche was, however, observed at ages 7 and 8. Missingness of the child's measurements at some ages was weakly associated with body size (based on the non-missing measurements). However, the estimates from the mixed model are unbiased as long as missingness is not related to the unobserved measurements. If the children's body size determined, in some instances, their willingness to take part in later measurements, and if

these children were more likely to have mothers who themselves had a higher BMI, we may have underestimated the relation between mother's age at menarche and children size.

Our findings, based on data collected 30 years before those in the ALSPAC Cohort, corroborate those reported by Ong et al 1, and indicate that mothers' age at menarche is a modest predictor of their children's size at age 7 and 8. This mechanism is likely to be heritable, although other explanations are possible.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This research was supported by the Intramural program of the NIH, National Institute of Environmental Health Sciences (Z01 ES049021). The authors wish to thank Xuguang Guo for substantial help with statistical analysis, Clarice R Weinberg and Lea Cupul Uicab for suggestions on an earlier draft.

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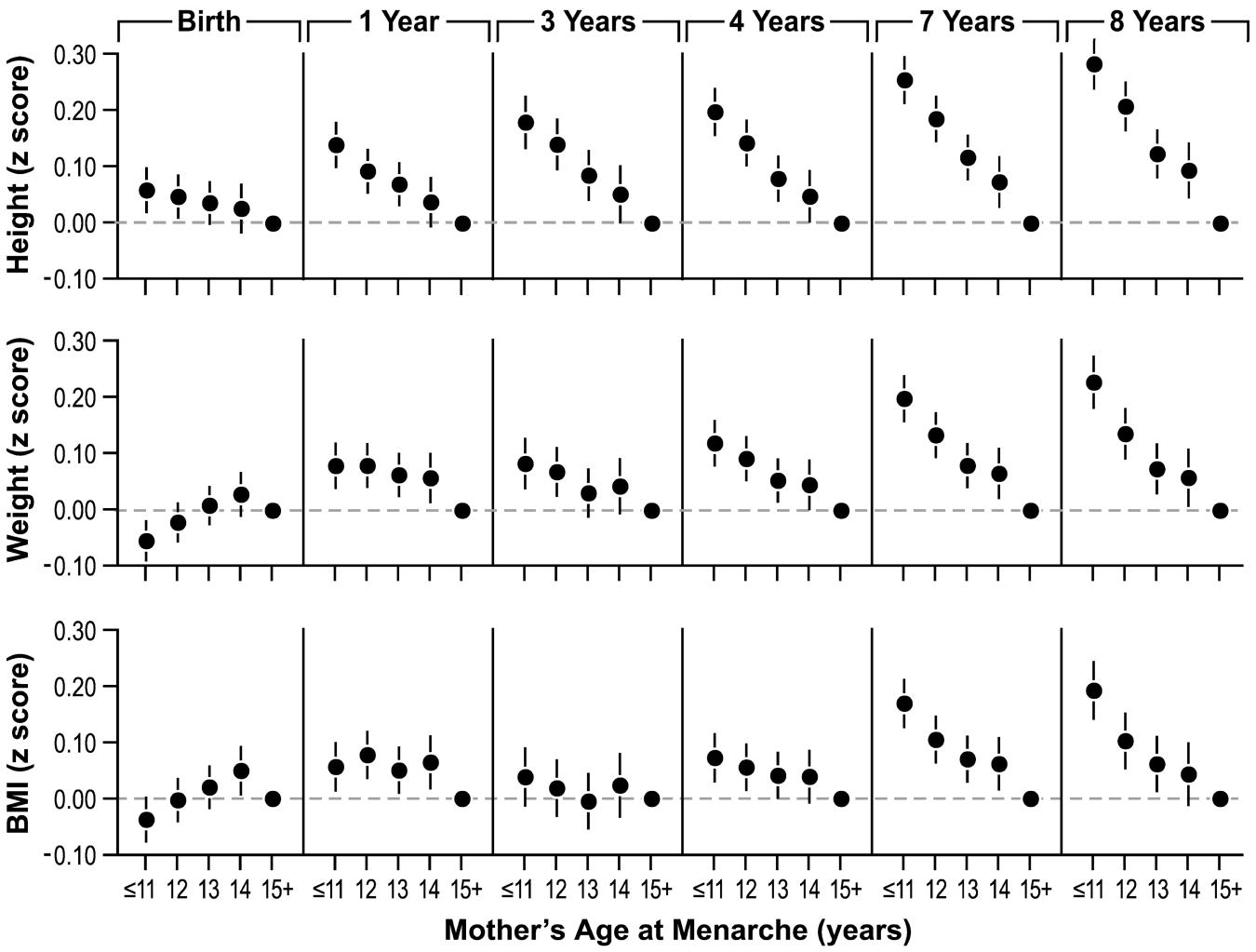

Figure 1.

Mean length/height (95% CI), weight, and BMI at birth, 1, 3, 4, 7, and 8 years of age in children as a function of mother's age at menarche. Estimates are adjusted differences from children born to women with menarche at age 15 obtained from mixed models1,2.

[1]Adjusted for study center, race, child's sex, socioeconomic index, child's age at measurement, mother's age at recruitment, and mother's height (in the length/height model), weight (in the weight model) or BMI (in the BMI model).

[2]All p-values for a linear trend were <0.05, except for BMI at age 3.

Table 1

Mother's anthropometry in relation to her self-reported age at menarche

	Length/Height, cm			Weight, kg			BMI, kg/m^2			
Age at menarche	**No.**	**Mean**	**SD**	**No.**	**Mean**	**SD**	**No.**	**Mean**	**SD**	**% ≥ 25**
≤11 yrs	6357	160.64	6.63	6608	60.49	12.52	6296	23.49	4.72	27.5
12 yrs	7535	161.33	6.68	7837	59.23	11.51	7450	22.79	4.28	21.3
13 yrs	8166	161.77	6.60	8536	58.71	11.28	8086	22.46	4.17	19.6
14 yrs	4041	162.00	6.75	4186	58.25	11.19	3997	22.25	4.07	18.2
≥15 yrs	3371	162.17	6.99	3504	58.40	11.43	3331	22.21	4.12	18.1

Table 2

Mean length/height, weight, and BMI in children as a function of their mother's age at menarche.

		Child's age (yrs)																	
	Age at menarche	**Birth**			**1**			**3**			**4**			**7**			**8**		
		N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.	N	Mean	S.D.
Length/	≤11 yrs	6674	49.9	2.70	6026	74.3	3.18	2688	94.6	3.86	4476	101.9	4.46	5068	121.7	5.38	2595	128.0	5.54
height(cm)	12 yrs	7937	49.9	2.69	7186	74.3	3.17	3226	94.5	3.90	5234	101.8	4.45	5965	121.5	5.32	3139	127.7	5.58
	13 yrs	8624	50.0	2.66	7829	74.3	3.23	3647	94.4	3.98	5749	101.5	4.45	6578	121.2	5.39	3481	127.3	5.50
	14 yrs	4222	49.9	2.61	3806	74.2	3.21	1677	94.4	3.96	2763	101.5	4.47	3216	120.9	5.46	1615	127.2	5.80
	≥15 yrs	3536	49.9	2.64	3209	74.2	3.31	1373	94.2	4.08	2349	101.4	4.44	2663	120.7	5.47	1322	126.8	5.72
Weight	≤11 yrs	6778	3.2	0.53	6046	9.8	1.20	2708	14.4	1.76	4485	16.6	2.32	5071	24.0	4.24	2598	27.0	5.01
(kg)	12 yrs	8068	3.2	0.52	7206	9.8	1.20	3251	14.3	1.82	5250	16.5	2.24	5970	23.6	4.04	3143	26.5	4.77
	13 yrs	8742	3.2	0.52	7847	9.8	1.20	3681	14.2	1.77	5766	16.4	2.19	6579	23.4	3.94	3486	26.2	4.64
	14 yrs	4288	3.2	0.52	3826	9.7	1.20	1695	14.2	1.82	2771	16.4	2.24	3220	23.2	3.93	1617	26.0	4.63
	≥15 yrs	3598	3.2	0.53	3223	9.7	1.23	1382	14.1	1.88	2352	16.3	2.29	2665	23.0	3.92	1324	25.8	5.04
BMI	≤11 yrs	6674	12.7	1.60	6026	17.7	1.68	2688	16.1	1.43	4476	16.0	1.57	5068	16.1	2.07	2595	16.4	2.25
(kg/m^2)	12 yrs	7937	12.7	1.55	7186	17.7	1.68	3226	16.0	1.43	5234	15.9	1.52	5965	15.9	1.95	3139	16.2	2.13
	13 yrs	8624	12.7	1.46	7829	17.7	1.69	3647	15.9	1.39	5749	15.9	1.52	6578	15.9	1.93	3481	16.1	2.11
	14 yrs	4222	12.7	1.46	3806	17.7	1.76	1677	15.9	1.44	2763	15.8	1.52	3216	15.8	1.90	1615	16.0	2.05
	≥15 yrs	3536	12.7	1.49	3209	17.6	1.77	1373	15.9	1.55	2349	15.8	1.58	2663	15.7	1.92	1322	15.9	2.21

Int J Obes (Lond). Author manuscript; available in PMC 2011 June 01.

Table 3

Estimated effect of continuous mother's age at menarche (in completed years) on children's size from birth to age 8[1].

	Height, cm				Weight, kg				BMI, kg/m^2			
Age	**Estimate**	**SE**	**DF**	**p**	**Estimate**	**SE**	**DF**	**p**	**Estimate**	**SE**	**DF**	**p**
Birth	−0.013	0.0045	28131	0.00280	0.018	0.0041	30843	0.00000	0.015	0.0045	28995	0.00060
1	−0.033	0.0045	27515	0.00000	−0.016	0.0046	29974	0.00030	−0.011	0.0049	27250	0.02320
3	−0.045	0.0052	21609	0.00000	−0.020	0.0050	25091	0.00010	−0.008	0.0058	18297	0.14580
4	−0.050	0.0047	25560	0.00000	−0.029	0.0046	28746	0.00000	−0.016	0.0048	24921	0.00120
7	−0.063	0.0047	25430	0.00000	−0.047	0.0046	28081	0.00000	−0.039	0.0048	25773	0.00000
8	−0.069	0.0050	23890	0.00000	−0.055	0.0052	24224	0.00000	−0.046	0.0057	19831	0.00000

[1] Adjusted for study center, race, child's sex, socioeconomic index, child's age at measurement, mother's age at recruitment, and mother's height (in the length/height model), weight (in the weight model) or BMI (in the BMI model)..