Association of age at menarche with cardiovascular risk factors, vascular structure, and function in adulthood: the Cardiovascular Risk in Young Finns study¹–³

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ABSTRACT

Background: It is unclear whether age at menarche is an independent determinant of future cardiovascular risk.

Objective: We aimed to determine whether menarcheal age is an independent predictor of body mass index (BMI) and a wide range of cardiovascular risk factors in adolescence and adulthood.

Design: We examined the associations of menarcheal age with BMI (in kg/m²) and other cardiovascular risk factors in adolescence and adulthood in a population-based sample of 794 female adolescents aged 9–18 y at baseline. Their age at first menstruation was requested at baseline and again 3 and 6 y later. Cardiovascular risk factors were assessed at baseline and at age 30–39 y.

Results: A 1-y decrease in menarcheal age was associated with 0.81 (95% CI: 0.53, 1.08) higher adult BMI as well as greater waist circumference and waist-to-hip ratio, elevated systolic blood pressure, higher insulin resistance, and greater risk of metabolic syndrome (P < 0.05 for all). In multivariable analysis in which these adult risk factors were mutually adjusted for, only the inverse association between age at menarche and adult BMI remained. However, this inverse association was lost after adjustment for premenarcheal BMI (β: −0.16; 95% CI −0.55, 0.23; P = 0.42). Higher premenarcheal BMI predicted earlier menarche, and the strong association between premenarcheal BMI and adult BMI was robust to adjustment for age at menarche.

Conclusions: These findings suggest that early menarche is only a risk marker. Greater childhood BMI seems to contribute to earlier age at menarche and, because of tracking, greater adult BMI and associated cardiovascular risk. An independent effect of early menarche on adult adiposity cannot be excluded, but it is likely to be small at best. Am J Clin Nutr 2008;87:1876–82.

INTRODUCTION

Many studies show that girls with earlier age at menarche tend to have worse cardiovascular risk factor levels in adulthood than those who underwent menarche at a later age (1–11). The most consistent evidence relates to higher adult body mass index (BMI; in kg/m²) in women who had on average earlier menarche (1, 2, 6–8, 10, 12), but an inverse association of menarcheal age has also been reported with blood pressure (6), glucose intolerance (6), and risk of ischemic heart disease and stroke (4, 5, 13, 14). Whether early menarche is an independent predictor of adverse adult outcomes or only a marker of other risk factors remains unclear.

It has been hypothesized that having an earlier age at menarche causes important differences in postpubertal growth and development of greater adiposity (1, 12, 15). This view emphasizes the importance of targeting girls with earlier menarche for antidiabetes interventions (1, 6). However, if the associations are largely driven by prepubertal risk factors, such targeting would not result in public health benefit. The latter is plausible because it is known that greater adiposity in childhood and factors that promote the accumulation of body fat are associated with an earlier age at menarche (8, 16–19) and that greater adiposity tracks from childhood to adulthood (11). Thus, children with greater BMI would be expected to have on average earlier menarche and would be expected to have greater BMI and its associated risk factors in adulthood. Other exposures occurring before puberty that are associated both with younger age at menarche and greater adult adiposity (eg, familiar socioeconomic adversity and intrauterine influences) may also result in such spurious associations (20–23).

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To date at least 7 studies have taken account of potential early risk factors in assessing this association. The Northern Finland birth cohort for 1966 (2), a cohort of individuals born in Aberdeen, Scotland, in the 1950s (7), and the Fels longitudinal study of white girls aged 8–21 y (6) showed that the association of earlier age at menarche with greater BMI in adulthood was not explained by other factors measured. In contrast, in a study of Philadelphia high school girls, the inverse association of age at menarche with variations in BMI 1 y after menarche was mostly explained by earlier BMI (24), and similar results were found for the association of age at menarche with adult BMI in the Bogalusa Heart study (8), the 1958 British Birth Cohort (11), and the Newton Girls study (10) (the association was largely driven by childhood BMI in these studies). Methodologic problems in all of these previous studies may have contributed to the conflicting results: in 5 of the studies, measurement of adult BMI only extended up to age 21 (6, 24) or was completely or partially based on self-reported height and weight (2, 7, 10), in 2 of the studies there was large loss to follow-up (ie, >40%) (7, 8), in 1 study the baseline measurement was assessed over a 50-y period and therefore included many birth cohorts in whom age at menarche and adiposity distributions are likely to be heterogeneous (6), and in 1 study age at menarche was assessed retrospectively in late adulthood (11). None of these studies examined adult cardiovascular outcomes other than adiposity.

We have measurements of age at menarche in adolescence and prospective information on childhood and adult BMI determined by standard research measurements and a range of adult cardiovascular risk factors [fasting glucose, insulin, lipids, blood pressure, and carotid intima-media thickness (IMT)] for a subsample of the Young Finns study. The aim of the present study was to determine whether menarcheal age is an independent predictor of BMI and a wide range of cardiovascular risk factors in adolescence and adulthood.

SUBJECTS AND METHODS

Study population

The first clinical examination in the population-based Cardiovascular Risk in Young Finns Study (25, 26) was conducted for age cohorts of 3, 6, 9, 12, 15, and 18 y in 1980, with the participation rate being 83%, ie, 3596 (1832 female and 1764 male) of the 514 girls who participated in more than one examination after menarche, 83% of the recalled ages at menarche differed by ≤1 y and for those women who reported their age at first menstruation on all 3 occasions different reports were highly correlated (Cronbach α = 0.92 for all assessments), indicating high reproducibility of our measure. Mean difference in recalled menarcheal age between the first and second measurements was <0.03 (SD: 0.81) y and Bland-Altman plots (27) did not show any evidence that the differences varied in any systematic way over the range of measurement (correlation between difference and mean scores for reported age at menarche over 2 examinations: r = 0.01, P = 0.72). The differences in reported menarcheal age between the examinations were not associated with premenarcheal BMI (Pearson r = 0.05, P = 0.53), postmenarcheal BMI before age 18 (r = 0.08, P = 0.12), or BMI at adulthood (r = −0.03, P = 0.96), and the plots for difference by average menarcheal age over the 2 examinations were similar for high and low BMI at baseline and follow-up. In all analyses we used the first report of the date of menarche for each woman, because errors in recalling age at menarche are likely to increase with the duration of time.

Assessment of age at menarche

Age at menarche was assessed by an interview on 3 occasions—baseline (1980), 1983, and 1986. Participants were asked age at their first menses (in y and mo). The 9- and 12-y-olds were interviewed with their parents. Among the 514 girls who participated in more than one examination after menarche, 83% of the recalled ages at menarche differed by ≤1 y and for those women who reported their age at first menstruation on all 3 occasions different reports were highly correlated (Cronbach α = 0.92 for all assessments), indicating high reproducibility of our measure. Mean difference in recalled menarcheal age between the first and second measurements was <0.03 (SD: 0.81) y and Bland-Altman plots (27) did not show any evidence that the differences varied in any systematic way over the range of measurement (correlation between difference and mean scores for reported age at menarche over 2 examinations: r = 0.01, P = 0.72). The differences in reported menarcheal age between the examinations were not associated with premenarcheal BMI (Pearson r = 0.05, P = 0.53), postmenarcheal BMI before age 18 (r = 0.08, P = 0.12), or BMI at adulthood (r = −0.03, P = 0.96), and the plots for difference by average menarcheal age over the 2 examinations were similar for high and low BMI at baseline and follow-up. In all analyses we used the first report of the date of menarche for each woman, because errors in recalling age at menarche are likely to increase with the duration of time.

Assessment of risk factors

For those included in our analyses, birth weight (g) and birth height (cm) were reported by the mothers who were asked to bring with them the booklet from the well baby center in which these information was recorded in 1983. Other childhood and adolescence risk factors were assessed in 1980 at the age of 9–18 y and adulthood risk factors were assessed in 2001–2002 at the age of 30–39 y (26). Several cardiovascular risk factors were assessed at both time points. Socioeconomic position was measured by parental occupational status as classified by Statistics Finland (28) and categorized as manual versus nonmanual (29). If socioeconomic position differed between parents, data on the parent with the higher occupational status were used. The participant’s own adult socioeconomic position was measured by occupational status and categorized as for parental socioeconomic position. Physical measurements of weight (kg) and height (mm) and in 2001 also waist circumference (mm, measured in duplicate at the level of the twelfth rib or level with the navel in thin subjects) and hip circumference (mm) were obtained to calculate BMI and waist-to-hip ratio. Blood pressure was measured with a standard mercury sphygmomanometer in
1980 and with a random-zero sphygmonanometer in 2001 (30). The average of 3 measurements was used in statistical analysis. Fasting blood samples were taken in both 1980 and 2001. All measurements of lipid concentrations were performed in duplicate in the same laboratory. Standard enzymatic methods were used for measuring concentrations of serum total cholesterol, HDL cholesterol, and triglyceride. LDL cholesterol was calculated by the Friedewald formula (31). Interassay CVs were 2.0% in 1980 and 2.2% in 2001 for serum cholesterol, 2.0% and 2.3% for HDL cholesterol, and 4.7% and 3.8% for serum triglyceride concentrations (32, 33).

In 2001, serum insulin was measured by a microparticle enzyme immunoassay kit (Abbott Laboratories, Diagnostic Division, Dainabot, Tokyo, Japan). Details of these methods have been described previously (34, 35). Insulin resistance was estimated according to the homeostasis model (36) as the product of fasting glucose and insulin divided by the constant 22.5. The metabolic syndrome was defined according to the International Diabetes Federation criteria (37) as abdominal obesity and ≥2 of the following criteria: waist ≥94 cm in men and ≥80 cm in women, fasting plasma glucose ≥5.6 mmol/L, hypertriglyceridemia ≥1.695 mmol/L and HDL cholesterol concentrations <1.036 mmol/L in men and <1.295 mmol/L in women, and blood pressure ≥130/85 mmHg or treatment. Information on number of children, use of contraceptives, adult smoking, and alcohol consumption (units/wk) was obtained by questionnaire in 2001. One unit of alcohol (12 g) was equal to a glass of wine, a single 4-cl shot of spirits, or a 33-cl bottle of beer (29).

In 2001–2002, ultrasound studies were performed with use of Sequoia 512 ultrasound mainframes (Acuson, Mountain View, CA) to measure carotid IMT and brachial artery flow-mediated dilation (26, 38). In brief, the image was focused on the posterior (far) wall of the left carotid artery. A minimum of 4 measurements of the common carotid far wall were taken ∼10 mm proximal to the carotid bifurcation to derive mean carotid IMT. The between-visit CV for the IMT measurements was 6.4% (26). To assess brachial artery flow-mediated dilation, the left brachial artery diameter was measured both at rest and during reactive hyperemia. The vessel diameter from scans after reactive hyperemia was expressed as the percentage relative to the diameter from the resting scan. The 3-mo between-visit CV was 3.2% for the brachial artery diameter measurements and 26.0% for the flow-mediated dilation measurements (38).

### Statistical analysis

We examined the association between age at menarche and risk factors in childhood and adulthood with linear regression models including menarcheal age as a continuous variable. To determine primary adult risk outcomes, we tested linear associations of menarcheal age with each adult risk factor in a model adjusting for age at the time of the adult clinical examination and other adult risk factors.

For childhood and adolescent risk factors, we constructed z scores (z; 0, SD: 1) of these risk factors, standardizing for age at the time of clinical examination to take account of the association of age with risk factor distributions (12, 39). We determined whether the assessment of risk factors between the ages of 9 and 18 y was before or after menarche and tested whether age-at-examination-standardized risk factor z scores after menarche were more strongly associated with menarcheal age than age-at-examination-standardized risk factor z scores before menarche by including an interaction term, age at menarche × timing of risk factor measurement, in a model including main effects. A stronger association between menarcheal age and postmenarcheal risk factor levels than between menarcheal age and premenarcheal risk factor levels would be consistent with the hypothesis that elevated risk factor levels are a consequence rather than a determinant of menarcheal age. We used multivariable linear regression models to further examine whether age at menarche is an independent predictor of premenarcheal risk factors. The first step involved a series of models in which we tested age-adjusted associations of menarcheal age and premenarcheal risk factor z scores with adult risk factors. The second step entered these predictors together into the same model.

In each analysis, participants with missing values were excluded. All of the data analysis was performed by using SAS software (version 9.1; SAS Institute Inc, Cary, NC). In all tests, statistical significance was inferred at a 2-tailed P < 0.05.

### RESULTS

Sample characteristics are presented in Table 1 and Table 2. We assessed menarcheal age on average at the age of 14.4 y for girls who had their first menses before age 12 y and at the age of 16.1 y for those with menarche at age 14 y or older (Table 1). Higher BMI in childhood and adolescence was associated with early menarche with a slightly stronger association for BMI measured before rather than after menarche. Other baseline risk factors were not associated with menarcheal age.

Early menarche predicted greater BMI, waist circumference, and waist-to-hip ratio, elevated systolic blood pressure, higher insulin concentrations and insulin resistance, and marginally greater prevalence of metabolic syndrome in adulthood (Table 2). In multivariable analysis in which we mutually adjusted adult risk factors for each other, only the association between age at menarche and adult BMI remained, suggesting that age-adjusted associations with other risk factors were fully explained by the association of age at menarche with adult BMI (Table 3). This association remained after additional adjustment for use of contraceptives and the number of pregnancies and when adjusted for years after menarche instead of age. Analyses with age-at-examination-standardized z scores replicated these findings (data not shown). Thus, subsequent analyses relate to menarcheal age and BMI only.

An independent effect of age at menarche on subsequent BMI would be supported if age at menarche was more strongly associated with subsequent BMI than premenarche BMI was associated with age at menarche. Analysis of BMI z scores between the ages 9 and 18 y provided no such evidence (Table 4). If anything, the association between premenarcheal BMI and age at menarche was stronger than the association between age at menarche and postmenarcheal BMI, although the formal test failed to confirm a difference in the magnitude of these associations (P for interaction age at menarche × timing of BMI measurement = 0.08).

BMI in childhood and adolescence predicted adult BMI, waist circumference, waist-to-hip ratio, systolic and diastolic blood pressure, HDL cholesterol concentrations, glucose and insulin concentrations, insulin resistance and metabolic syndrome, carotid IMT, and brachial artery flow-mediated dilation (all P < 0.05). If there was an independent association between age at menarche and adult BMI, this association should be robust to controlling for...
### TABLE 1
Levels of childhood and adolescence risk factors in all participants and by age at menarche

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Subjects</th>
<th>Value</th>
<th>≤11.9 (n = 108)</th>
<th>12–12.9 (n = 231)</th>
<th>13–13.9 (n = 266)</th>
<th>≥14 (n = 189)</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth height (cm)</td>
<td>672</td>
<td>1.0</td>
<td>67.2</td>
<td>1.0</td>
<td>67.2</td>
<td>1.0</td>
<td>67.2</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>672</td>
<td>0.1</td>
<td>67.2</td>
<td>0.1</td>
<td>67.2</td>
<td>0.1</td>
<td>67.2</td>
</tr>
</tbody>
</table>

BMI before menarche. However, among the 341 women with the baseline measurement of BMI before menarche, the age-adjusted association between age at menarche and adult BMI was almost completely lost after adjustment for premenarcheal BMI, indicating that age at menarche had no independent effect on adult BMI (Table 5). In contrast, the strong effect of premenarcheal BMI on adult BMI remained largely unchanged when adjusted for age at menarche. The same was true for the association between postmenarcheal BMI assessed at age 18 y or earlier and adult BMI.

### TABLE 2
Adult risk factors in all participants and by age at menarche

<table>
<thead>
<tr>
<th>Risk factor in adulthood</th>
<th>Subjects</th>
<th>Value</th>
<th>≤11.9</th>
<th>12–12.9</th>
<th>13–13.9</th>
<th>≥14</th>
<th>P for trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>794</td>
<td>13.6±3.2</td>
<td>14.4</td>
<td>15.1</td>
<td>15.9</td>
<td>16.1</td>
<td>N/A</td>
</tr>
<tr>
<td>Age at menarche (y)</td>
<td>794</td>
<td>13.1±1.2</td>
<td>11.3</td>
<td>12.4</td>
<td>13.3</td>
<td>14.7</td>
<td>N/A</td>
</tr>
<tr>
<td>Parental SEP (% of manual)</td>
<td>766</td>
<td>40.9</td>
<td>37.5</td>
<td>42.6</td>
<td>40.0</td>
<td>41.8</td>
<td>0.56</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>687</td>
<td>3428±251</td>
<td>3479</td>
<td>3433</td>
<td>3414</td>
<td>3409</td>
<td>0.43</td>
</tr>
<tr>
<td>Birth height (cm)</td>
<td>672</td>
<td>50.0±2.3</td>
<td>50.2</td>
<td>50.1</td>
<td>50.0</td>
<td>49.8</td>
<td>0.31</td>
</tr>
<tr>
<td>BMI (in kg/m²)</td>
<td>792</td>
<td>19.0±2.9</td>
<td>19.7</td>
<td>19.4</td>
<td>18.9</td>
<td>18.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pre-menarche</td>
<td>349</td>
<td>17.1±2.4</td>
<td>17.7</td>
<td>17.9</td>
<td>16.8</td>
<td>16.5</td>
<td>0.0008</td>
</tr>
<tr>
<td>Post-menarche</td>
<td>443</td>
<td>20.4±2.4</td>
<td>20.7</td>
<td>20.5</td>
<td>20.5</td>
<td>19.9</td>
<td>0.06</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>792</td>
<td>155.5±12.7</td>
<td>155.2</td>
<td>155.6</td>
<td>155.9</td>
<td>155.0</td>
<td>0.40</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>794</td>
<td>115.1±9.9</td>
<td>115.6</td>
<td>115.6</td>
<td>114.8</td>
<td>114.5</td>
<td>0.80</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>794</td>
<td>69.4±9.2</td>
<td>69.5</td>
<td>69.2</td>
<td>69.5</td>
<td>69.2</td>
<td>0.88</td>
</tr>
<tr>
<td>Total cholesterol (mmol/L)</td>
<td>789</td>
<td>5.13±0.8</td>
<td>5.17</td>
<td>5.13</td>
<td>5.08</td>
<td>5.18</td>
<td>0.52</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/L)</td>
<td>793</td>
<td>1.52±0.28</td>
<td>1.50</td>
<td>1.51</td>
<td>1.51</td>
<td>1.54</td>
<td>0.11</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/L)</td>
<td>793</td>
<td>3.32±0.74</td>
<td>3.37</td>
<td>3.32</td>
<td>3.27</td>
<td>3.35</td>
<td>0.88</td>
</tr>
</tbody>
</table>

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1 N/A, not applicable; SEP, socioeconomic position. All risk factors were measured in 1980. Age at menarche was measured in 1980, 1983, and 1986 (the first report of the date of menarche for each woman was used).  
2 T ± SD (all such values).  
3 Participant’s age when menarcheal age was assessed.
null after adjustment for adult BMI. Rather than supporting independent effects of earlier menarche on adult adiposity, these findings are in agreement with the hypothesis that menarcheal age is only a risk marker; greater childhood BMI may contribute to earlier age at menarche and, because of tracking, greater adult BMI. Adult BMI itself is related to other adult cardiovascular risk factors explaining the association of early menarche with these factors.

The Cardiovascular Risk in Young Finns Study is based on 6 birth cohorts with each randomly chosen in 5 areas of Finland from the national register (25). We excluded the 2 youngest birth cohorts aged 3 and 6 y at baseline as few of them reported experiencing their first menses during the 6 subsequent years when menarcheal age was assessed, but exclusion of these whole birth cohorts should not introduce any selection bias. In addition, we excluded 9% of those eligible (ie, at age ≥9 y at baseline) because of missing data on menarcheal age and a further 27% because of lack of adulthood outcomes assessed 21 y after the baseline. It is not possible to determine whether this moderate loss of data caused selection bias but to do so and reverse our findings would have to mean that those excluded had a strong association of age at menarche with adult BMI that was independent of childhood BMI; ie, the excluded women would have to have one or more of following: weaker association between childhood and adult BMI than those included; weaker associations of age at menarche with childhood BMI than those included; or stronger association of age at menarche with adult BMI than those included. Because the likelihood of responding to a question about age at menarche is unlikely to be affected by future BMI and there was no evidence that attending a follow-up clinic was determined by age at menarche, a major selection bias because of these missing data seems unlikely.

This study was based on a smaller sample than the largest studies in the field (7, 11), but it had the advantage of reports of age at menarche close to time of menarche in adolescence and objective measures of height and weight both in childhood or adolescence and in adulthood. This data collection reduces the risk for artificial inflation of associations between age at menarche and adult BMI attributable to common method bias that may arise if age at menarche was reported many years later in

These results suggest that premenarcheal BMI largely explains the association of age at menarche with adult BMI. A multivariable model including all premenarcheal cardiovascular factors as predictors of adult BMI provided little evidence for additional confounding by premenarcheal blood pressure, lipid concentrations, or parental socioeconomic position (β for age at menarche: −0.16; P = 0.42 in a model adjusted for age and premenarcheal BMI and −0.15; P = 0.47 in a model additionally adjusted for other premenarcheal cardiovascular risk factors among the 334 women with no missing data on premenarcheal risk factors).

**DISCUSSION**

This population-based study suggests that age at menarche is associated with adult BMI and associated risk factors, but we obtained no support for the interpretation that these associations would reflect an independent effect of early menarche on worse cardiovascular risk factor levels in adulthood. We found that greater premenarcheal BMI was associated with earlier age at menarche and that they both were associated with greater adult BMI. In multivariate models the association of age at menarche with adult BMI was essentially completely lost after adjustment for BMI assessed before menarche and its association with other adult cardiovascular risk factors, such as blood pressure, glucose, insulin resistance, and metabolic syndrome and attenuated to the

**TABLE 4**

Age-adjusted and multivariate models on the association between age at menarche and adult risk factors

<table>
<thead>
<tr>
<th>Adulthood outcome</th>
<th>Change in outcome per 1-y increase in menarcheal age</th>
<th>Mutually adjusted model</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\beta$ 95% CI $P$</td>
<td>$\beta$ 95% CI $P$</td>
</tr>
<tr>
<td>BMI (in kg/m$^2$)</td>
<td>$-0.81$ $-1.08$, $-0.53$ $&lt;0.0001$ $-0.10$ $-0.19$, $-0.01$ $0.03,^7$</td>
<td></td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>$-17.77$ $-24.77$, $-10.77$ $&lt;0.0001$ $-0.52$ $1.24$, $2.29$ $0.56$</td>
<td></td>
</tr>
<tr>
<td>Waist-to-hip ratio</td>
<td>$-0.006$ $-0.010$, $-0.002$ $0.003$ $-0.000$ $-0.002$, $0.002$ $0.86$</td>
<td></td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>$-1.07$ $-1.87$, $-0.28$ $0.008$ $-0.24$ $-0.99$, $0.50$ $0.52$</td>
<td></td>
</tr>
<tr>
<td>Insulin (mU/L)</td>
<td>$-0.600$ $-0.925$, $-0.275$ $0.0003$ $0.001$ $-0.059$, $0.061$ $0.96$</td>
<td></td>
</tr>
<tr>
<td>Insulin resistance (HOMA index)</td>
<td>$-0.155$ $-0.238$, $-0.072$ $0.0003$ $-0.002$ $-0.017$, $0.013$ $0.78$</td>
<td></td>
</tr>
<tr>
<td>Metabolic syndrome$^4$</td>
<td>$-0.022$ $-0.043$, $0.001$ $0.04$ $0.008$ $-0.010$, $0.026$ $0.37$</td>
<td></td>
</tr>
</tbody>
</table>

$^1$ Since BMI z score before menarche (before vs after menarche), $P = 0.08$. 

$^2$ Analysis performed in 334 women with no missing data on premenarcheal risk factors.

$^3$ Adjusted for age and all other outcomes presented in the table.

$^4$ Interaction between BMI z score before and after menarche at age 9–18 y

$^5$ This association remained after additional adjustment for use of contraceptives and the number of pregnancies and when adjusted for years after menarche

$^6$ Binary variable.
older adulthood and BMI was determined on the basis of self-reported height and weight. Imprecision in reports of age at menarche can lead to underestimation of associations. In analysis, we used the first report of the date of menarche for each woman to minimize recall bias, but data on 3 repeated measurements enabled tests regarding the validity of the measure. Cronbach α reliability >0.9 across the measurements, a mean difference between repeated measurements of <0.03 years, and Bland-Altman plots suggested that our indicator of age at menarche was reproducible and reliable. Any inconsistencies in repeated measurements of menarcheal age were independent of pre- and postmenarcheal adiposity, providing evidence against systematic error. In addition to adult BMI, we assessed waist circumference and waist-to-hip ratio in adulthood, but they may all be imperfect measures of adiposity. This would bias our conclusion regarding the role of menarcheal age as a marker of premenarcheal influence only if the use of an imperfect proxy measure for adiposity led to substantially greater underestimation of the association of age at menarche with postmenarcheal adiposity than that with premenarcheal adiposity.

Our findings confirm several earlier studies with weaknesses that were overcome in this study. For example, the Bogalusa Heart Study found that adult obesity was more strongly related to childhood BMI than menarcheal age, but that study was limited by >60% loss of participants to follow-up and a reproducibility of assessment of age at menarche that was “somewhat lower than in other studies” (8, p. 8). Investigators of the British 1958 Birth Cohort Study reported an association between early menarche and adult obesity but did not provide an estimate of the association after adjustment for premenarcheal BMI (40), the Newton Girls study suggested an association of childhood risk factors with early menarche, but the findings were based on a small nonrepresentative sample (10), and the Philadelphia high school studies were limited to only 1-year follow-up (24).

In contrast to our findings, the UK Aberdeen study found that early menarche was an independent predictor of adult BMI (7). In that study, childhood BMI was measured but adult BMI was derived from self-reported weight and height and age at menarche recalled at 42.5 years of age. Common method bias in the cross-sectional association between age at menarche and adult BMI combined with a low tracking correlation between childhood BMI at age 4–7 and adult BMI (r = 0.19) may have contributed to a false impression of independent effects of early menarche. In our study, for example, the tracking correlation is much higher (r = 0.52) among those whose BMI was measured at 9 years of age with the use of BMI z scores similar to those in the Aberdeen study. The investigators of the Fels Longitudinal Study reported that early menarcheal age was related to increases in both adiposity and lean tissue and adversely affected cardiovascular risk factor changes, such as elevated blood pressure and glucose intolerance, independent of body composition (6). However, the serial analyses of repeated measures from 8–18 years of age did not explicitly test reverse causality because risk factor trends before and after menarche were not distinguished and a cohort effect due to extensive variation in timing of baseline measurements that occurred between 1929 and 1983 may also have introduced bias.

In conclusion, although the possibility of an independent effect of early menarche on adult adiposity cannot be excluded, our study combined with other evidence suggests that the effect is at best small and of minor importance compared with the effects of premenarcheal BMI that tracks on adult BMI. The present study suggests that preventing obesity in girls before puberty rather than focusing on early menarche would result in greater public health benefits.

The authors’ responsibilities were as follows—MK with DAL, GDS, ME, MJK, J-AV, and OTR: designed the hypothesis, analyzed the data, and wrote the manuscript. None of the authors had a personal or financial conflict of interest.

REFERENCES


### TABLE 5

| TABLE 5 | Associations of BMI z score at age 9–18 y and menarcheal age with BMI at age 30–39 y by timing of age-at-exam—standardized BMI z score measured at age 9–18 y

| Age-adjusted model | Mutually adjusted model
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>BMI before menarche (n=341)</strong></td>
<td><strong>BMI after menarche (n=129)</strong></td>
</tr>
<tr>
<td><strong>BMI z score</strong></td>
<td>2.18</td>
</tr>
<tr>
<td><strong>Menarcheal age (y)</strong></td>
<td>−0.80</td>
</tr>
<tr>
<td><strong>BMI z score</strong></td>
<td>2.12</td>
</tr>
<tr>
<td><strong>Menarcheal age (y)</strong></td>
<td>−0.16</td>
</tr>
</tbody>
</table>

1 BMI was measured in kg/m². Interaction between BMI z score and timing of the BMI assessment (before vs after menarche) on adult BMI, P = 0.31.

2 Model includes age, BMI z score between ages 9 and 18 y, and menarcheal age as predictors of adult BMI.