Published in final edited form as:

Arch Womens Ment Health. 2014 December ; 17(6): 511–518. doi:10.1007/s00737-014-0435-6.

Early and late menarche and risk of depressive symptoms in young adulthood

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Abstract

Purpose—We investigated whether girls experiencing early menarche have an increased risk of depression during young adulthood.

Methods—This study used data collected in the Growing Up Today Study (N=9,039), an ongoing prospective cohort of the daughters of women enrolled in the Nurses' Health Study II. After excluding girls who were postmenarcheal at baseline in 1996, <20 years or ≥26 years old in 2007, or missing data on key covariates, the final sample size was 3,711. Self-reported age at menarche was collected annually. Depressive symptomatology was measured in 2007 using the 10-item Center for Epidemiologic Studies Depression (CES-D-10) score.

Results—Sixteen-percent of girls (N=596) reported high levels of depressive symptoms (CES-D-10 ≥14) in 2007. Neither early nor late menarche was associated with high depressive symptoms (for early vs. normative menarche: odds ratio (OR)=1.08, 95% confidence interval (CI): 0.85–1.38; for late v. normative menarche: OR=0.91, 95% CI: 0.70–1.18) or with differences in continuous CES-D-10 score in young adulthood.

Conclusions—Although previous studies suggest that girls with early menarche suffer from increased risk of adolescent depression, this does not appear to persist into young adulthood.

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Ethical standards: GUTS was approved by the Institutional Review Board of the Brigham and Women's Hospital/Partners Healthcare (Boston, MA). Parents provided written informed consent for their child's participation.

Conflict of interest: The authors declare that they have no conflict of interest.

Keywords

depression; Growing Up Today Study; menarche; puberty

Introduction

Depression is the leading cause of years lost to disability in women (IHME 2010). Indeed, approximately 16% of U.S. women experience depression at some point in their lifetime, with the highest rates of depression observed in young women (Kessler et al. 2003). Depression is more prevalent among females than males, a trend that begins in adolescence and persists through menopause (Angold and Costello 2006; Angold and Worthman 1993; Ge et al. 2001). This timing suggests that puberty may play a causal role in the etiology of depression.

Puberty is a multi-dimensional process, with physical, social, and emotional elements, any or all of which could mediate the role of puberty on depression. In their review article, Angold and Costello (2006) outline alternative mechanisms by which puberty may influence the risk and timing of depression. One hypothesis is that normal puberty, possibly through the associated changes in circulating sex steroids, is itself a risk factor for depression. Following this logic, early-maturing girls would initially have higher rates of depression relative to later-maturing girls, with the difference in risk of depression disappearing after all girls have completed puberty and attained similar hormonal profiles. Alternatively, the association between puberty and depression may be attributed to the socio-emotional complexities of puberty rather than its physical manifestations, in which case girls progressing through puberty out of sync with their peers might suffer the highest rates of depression. Under this scenario, we may expect increased rates of depression to persist past the point at which all girls have undergone puberty.

Many studies have reported positive associations between early menarche or other markers of pubertal timing and adolescent depression (Black and Klein 2012; Lien et al. 2010; Deng et al. 2011; Ge et al. 2001; Joinson et al. 2011). However, these studies often measured depression around the time of menarche only, limiting their insight into the potential mechanisms described above. Studies investigating the association of early menarche and depression post-puberty have yielded mixed findings (Boden et al. 2011; Copeland et al. 2010; Deng et al. 2011; Graber et al. 2004; Natsuaki et al. 2009). Some of these studies were conducted internationally, in China (Deng et al. 2011), New Zealand (Boden et al. 2011), and Norway (Lien et al. 2010), and it is uncertain if their results can be applied to U.S. girls due to the potential for culture-specific stressors. Further, the three prospective studies conducted in the U.S (Copeland et al. 2010; Graber et al. 2004; Natsuaki et al. 2009) are limited by small sample size (Graber et al. 2004), limited national generalizability (Copeland et al. 2010; Graber et al. 2004), and questionable outcome validity (Natsuaki et al. 2009). Therefore, in the present study, we prospectively investigated the association between early and late menarche and risk of depression during early adulthood in a large cohort of U.S. girls followed through 25 years of age and assessed with a standard depression measure for population based studies.

Materials and Methods

Study population

The Growing Up Today Study (GUTS) is a prospective cohort study composed of the children of women enrolled in the Nurses' Health Study II cohort (Rockett et al. 2001). At baseline in 1996, the 16,771 participants (9,039 girls) were aged 9 to 14 years. Questionnaires, completed annually by the participants, asked about health indicators, as well as life experiences and health behaviors. Follow-up is ongoing. GUTS was approved by the Institutional Review Board of the Brigham and Women's Hospital/Partners Healthcare (Boston, MA).

Follow-up for the present study began in 1996 and ended in 2007, when data on depressive symptoms were collected. In order to collect data on covariates, including body mass index (BMI), measured before menarche, we excluded girls who were postmenarcheal at baseline (N=3,155). Participants were further excluded if they never reported their age at menarche (N=481), failed to return the 2007 questionnaire (N=1,431), were missing more than one item on the Center for Epidemiologic Studies Depression (CES-D-10) scale (N=59), were younger than 20 years or 26 years or older in 2007 (N=22), or were missing data on key covariates (N=180). This left 3,711 girls eligible for analysis. Compared with ineligible participants, included participants were younger, had a later menarche, a lower baseline BMI, and were more likely to have a father present in the home (Supplemental Table 1). Eligible girls appeared to have higher CES-D-10 scores than those who were ineligible; however, CES-D-10 scores were missing for over one-half of excluded participants (N=2,964 or 55.6%).

Assessment of menarcheal status and age at menarche

Participants were asked, "Have you started having menstrual periods?" on each questionnaire. In 2005, postcards were mailed to girls who had failed to report their age at menarche. When menarche was reported, participants were prompted to report their age in years and calendar month at attainment. To reduce misclassification, we used only the first reported age at menarche. If a girl reported her age at menarche after one or more years of non-report, age at menarche was retrospectively assigned based on later report. If month at menarche was never reported, it was imputed as 6 months later than the reported integer age at menarche. Although age at menarche has not been validated in GUTS, other studies have reported excellent recall, especially when the recall interval was less than one year (Koo and Rohan 1997).

We categorized age at menarche into three groups: early menarche (-1 standard deviation (SD) below the sample mean; <12.0 years), normative menarche (within 1 SD of the sample mean; 12.0 – 14.3 years), and late menarche ($+1$ SD above the sample mean; >14.3 years).

Assessment of depressive symptoms

The 2007 questionnaire included a 10-item version of the CES-D scale, which was developed to capture symptoms relevant to the criteria for Major Depressive Disorder and has been demonstrated to be valid and reliable in young adults (Radloff 1977, 1991).

Depressive symptoms over the past week were reported using a frequency-based four-point Likert scale. After reverse coding two items that were inconsistent with a state of depression (“I felt hopeful about the future” and “I was happy”), we calculated a total CES-D-10 score by summing responses to the individual items. Scores had a possible range of 0–30, with higher scores corresponding with increased type or frequency of symptoms. For participants missing only one CES-D-10 item (N=103), we imputed the value of the missing item as the mean score of the completed items. Girls with a CES-D-10 ≥ 1 SD above the sample mean (i.e., ≥ 14) were considered to have high depressive symptomatology. As an alternative to classifying the cut-point for high depressive symptoms based on the CES-D-10 distribution in the study population, we also used performed analyses using a standard cutpoint for depression, a CES-D-10 score of 11 (Roberts et al. 2013). Lastly, to capture a dimensional measure of depression or distress, we modeled the CES-D-10 as a continuous variable.

Assessment of other variables

Presence of the father or stepfather in the home and race/ethnicity were self-reported at baseline. Children reported their race/ethnic group by marking one or more of six options (white, black, Hispanic, Asian or Pacific Islander, American Indian/Alaskan Native, other). Birth weight was reported by the mother in 1997. Using annually reported data on height and weight, we defined premenarcheal BMI (kg/m^2) as that reported on the questionnaire immediately preceding the year menarche was initially reported. When BMI was missing for this visit (N=279), we instead used BMI from the previous visit. BMI varies by age; therefore, we calculated age-specific BMI z-scores using the 2000 Centers for Disease Control and Prevention reference data (Kuczmarski et al. 2002).

In 2007, the survey included eight items measuring childhood abuse occurring at age 11 years or earlier. Two items assessing emotional bullying were adapted from the Child Trauma Questionnaire (Bernstein et al. 2003), and four items assessing physical bullying were adapted from the Conflict Tactics scale (Straus et al. 1996). Emotional and physical bullying items had a Likert format, with responses ranging from “never” to “very often.” Two items assessing sexual abuse asked (a) “were you touched in a sexual way by an adult or older child or were you forced to touch an adult or an older child in a sexual way when you did not want to” and (b) “did an adult or older child force you or attempt to force you into any sexual activity by threatening you, holding you down or hurting you in some way when you did not want to.” Sexual abuse was measured as never, once, or more than once. A participant was considered as reporting any trauma if she responded in any of the following ways: physical trauma, “sometimes or more often;” emotional trauma, “often and very often;” and sexual abuse, “any.”

Statistical analysis

We used logistic regression to estimate the odd ratios (OR) and 95% confidence intervals (CI) for the association of early or late menarche with high depressive symptomatology, with normative menarche considered the reference group. We used linear regression to assess differences in continuous CES-D-10 scores between girls with early or late menarche and those with normative menarche. For all models, generalized estimating equations (GEE)

assuming constant correlation were used to account for non-independent observations due to sibling clusters (246 sisters).

The following variables are known or suspected predictors of age at menarche or depression in young adulthood and were therefore included in multivariable models: age (in 2007, in years), premenarcheal BMI (continuous z-score), birth weight (quintiles), race (white, nonwhite), family composition (father present, stepfather present, neither father nor stepfather present), and history of childhood abuse before age 11 (never, any) (Boynton-Jarrett and Harville 2012; Boynton-Jarrett et al. 2013; Brown et al. 1999; Chumlea et al. 2003; Costello et al. 2007; James-Todd et al. 2010; Kaplowitz 2008; Sanchez-Villegas et al. 2013).

The association between early or late menarche and depression may be stronger at younger ages. To explore this, we stratified analyses by age at the time of CES-D-10 completion in 2007 (20–22 years, 23–25 years). Some vulnerable subgroups of girls, such as those who have been abused, may be more likely to suffer depression as the result of undergoing puberty out of sync with their peers. Therefore, we additionally stratified by history of abuse (any, none).

Results

Mean age at menarche in the study population was 13.1 years (SD=1.1 years). Girls with normative menarche had a lower premenarcheal BMI and were more likely to have a father present than girls with early menarche, but when compared to girls with late menarche they had a higher premenarcheal BMI and were slightly less likely to have a father present (Table 1). Girls with late menarche tended to be older at the time they reported their depressive symptoms, and reported somewhat lower CES-D-10 scores than girls with early or normative menarche.

For our primary approach, we classified girls with a CES-D-10 score ≥ 1 SD from the study mean as having high depressive symptomatology. Using this outcome metric, we found that neither early nor late age at menarche predicted high depressive symptomatology, after adjusting for predictors of menarche and depression (for early vs. normative menarche: OR=1.08, 95% CI: 0.85–1.38; for late vs. normative menarche: OR=0.91, 95% CI: 0.70–1.18) (Table 2). We observed similar findings when we alternatively modeled depressive symptomatology as a continuous variable (for early vs. normative menarche: adjusted mean difference=0.10, 95% CI: –0.35–0.56; for late vs. normative menarche: adjusted mean difference =0.03, 95% CI: –0.41–0.47) (Table 3). Additional adjustment for premenarcheal BMI z-scores did not alter our findings.

Next, we explored the association between age at menarche and depressive symptomatology during young adulthood in several subgroups of girls. Compared to the total population, effect estimates were not meaningfully different in girls 20–22 years of age in 2007, who reported abuse before age 11, or who were classified as overweight or obese in 2007 (Table 2). We also conducted several sensitivity analyses to test the robustness of our findings. We obtained similar findings when we alternatively defined girls with a CES-D-10 ≥ 11 as

having high depressive symptomatology or used a cutoff for early menarche of 11 years (data not shown). Our findings were unchanged when we did not restrict eligibility to girls who were premenarcheal at baseline (data not shown). Lastly, results were unchanged when we adjusted for individual types of abuse rather than a composite measure (data not shown).

Discussion

In this prospective cohort of U.S. girls, we did not detect an association between early or late menarche and depressive symptomatology in young adulthood. While early menarche has been previously associated with increased risk of depression throughout adolescence (Black and Klein 2012; Lien et al. 2010; Deng et al. 2011; Ge et al. 2001; Joinson et al. 2011), we observed no association between timing of menarche and risk of high depressive symptomatology even among the youngest women in our sample (i.e., ages 20–22 years). Our findings are consistent with four previous prospective studies reporting no association between early menarche and depression during young adulthood (Boden et al. 2011; Lien et al. 2010; Copeland et al. 2010; Graber et al. 2004). Two other studies, however, have reported positive findings. In a large cross-sectional study of Chinese girls and women, Deng et al. (2011) found that early-maturing girls had an elevated risk of depression during both adolescence and early adulthood. Similarly, in the U.S. National Longitudinal Study of Adolescent Health, Natsuaki et al. (2009) report an increased risk of depression among early-maturing girls throughout both adolescence and young adulthood.

While the Great Smoky Mountains Study reported no overall association between early menarche and depression at ages 19 to 21, they did report that, only among girls with adolescent conduct disorder, early menarche predicted an increased risk of depression (Copeland et al. 2010). Thus, we hypothesized that early menarche may trigger an increased risk of depression during young adulthood only for certain vulnerable subgroups. We explored the possibility that girls with a history of childhood abuse were more susceptible to the stresses of early menarche; however, findings in this subgroup were similar to those of the total study population. It remains possible that early menarche increases the risk of depression among a different, yet unidentified vulnerable population, or that the increased risk of depression observed in such vulnerable populations subsides with time, such as was observed in the Iowa Youth and Families Project among girls experiencing recent negative life events (Ge et al. 2001).

Our findings are compatible with several of the potential mechanisms linking puberty and depressive symptomatology in females. First, if puberty is stressful enough to result in concurrent depression for some girls, regardless of the age at which puberty occurs, then we would expect findings similar to what we have observed: similar rates of depression across groups of girls with early, normative, and late menarche once all girls have completed puberty (i.e., early adulthood). Second, during adolescence, higher rates of depression in girls with early menarche may be explained by socio-emotional factors associated with puberty more so than the physiological ones (Black and Klein 2012; Deng et al. 2011; Ge et al. 2001; Joinson et al. 2011). In other words, rather than girls with normative or late menarche “catching up” to the rate of depression observed among girls with early menarche, the risk of depression in those with early menarche may decrease over time. Girls younger

than 12 years old at menarche likely have fewer emotional tools and a weaker available social network to help them navigate the stresses of puberty relative to girls with normative or late menarche. As these girls make emotional and social advances with age, their risk of depression is once again comparable to that of their peers. Indeed, rates of depression are highest between girls 15 and 16 years of age, after which they begin to decline (although never returning to childhood levels) (Angold and Costello 2006; Kessler and Walters 1998; Natsuaki et al. 2009). Lastly, early-maturing girls may have an increased risk of depression because they a unique set of stressors (e.g., sexual harassment) at the time of puberty relative to later-maturing girls. Under this hypothesis, we may expect for the increased risk of depression observed in early-maturing girls to persist from adolescence to adulthood. However, this was not observed in this cohort.

Strengths and limitations

The primary limitation of the present study was that a different instrument was used to measure depression during adolescence, making meaningful comparisons of adolescent and young adulthood depression difficult. Because we were unable to calculate rates of depression for early- and later-maturing girls at the time of adolescence, we cannot distinguish whether the association between early menarche and risk of depression decreased between adolescence and young adulthood or if the risk of depression increased among girls with normative and late menarche.

The GUTS participants are mostly white and from middle to upper income level households. More racially and socioeconomically diverse populations would be expected to experience earlier menarche (Chumlea et al. 2003; James-Todd et al. 2010); thus, our study may not be generalizable to such populations. Likewise, in order to measure potential confounders occurring before menarche, we excluded girls who were postmenarcheal at baseline, limiting our ability to generalize to girls with the earliest menarche. Although we observed similar effect estimates when we defined early menarche using a cutoff of 11 years, only 61 girls met this cutoff, and we may therefore have been underpowered to detect an association. Thus, if only girls with the earliest menarche were at increased risk of depression during young adulthood, this effect may have been missed.

Depressive symptomatology was assessed using the CES-D-10, a shortened version of the widely validated and frequently used 20-item CES-D (Radloff 1977, 1991). A CES-D-10 specific cutoff for high depressive symptoms has not been evaluated in this age group; however, we obtained similar findings when we classified girls with a CES-D-10 score 1 SD above the sample mean or a CES-D-10 score >11 (Roberts et al. 2013) as having high depressive symptomatology. We additionally modeled CES-D-10 scores as a continuous measure in order to investigate absolute differences in symptomatology. We did not detect an association with age at menarche modeling CES-D-10 scores using any of these methods, which supports that our findings were not an artifact of the selected definition of high depressive symptomatology.

Despite these limitations, our study has many unique strengths. The current study has the largest study sample used to explore the link between early menarche and depression in young adulthood. The data were collected as part of a prospective cohort study with

participants from around the United States, making differential misclassification of age at menarche unlikely and supporting generalizability to a large proportion of U.S. girls. Additionally, our study was the first to adjust for history of abuse, a potentially important confounder given the strong association between childhood abuse and depression (Brown et al. 1999) and recent evidence of an association of age at menarche with childhood physical and sexual abuse (Boynton-Jarrett et al. 2013).

Conclusions

The current study investigated whether early or late menarche was associated with risk of depression in young adulthood. Given previous literature supporting an association between early menarche and adolescent depression, we suggest that, in a clinical setting, girls with early menarche should be evaluated for depressive symptomatology. However, our study and others (Boden et al. 2011; Copeland et al. 2010; Graber et al. 2004) suggest that early menarche predicts only a temporally proximal increase in risk of depression.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

The Growing Up Today Study is supported by grant R03 CA 106238. JC was supported by the Breast Cancer Research Foundation; Training Grant T32ES007069 in Environmental Epidemiology from the National Institute of Environmental Health Sciences, National Institutes of Health; and Training Grant T32HD060454 in Reproductive, Perinatal and Pediatric Epidemiology from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health.

We thank the participants of the Growing Up Today Study.

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Table 1

Characteristics and history of childhood abuse by age at menarche among 3,711 female participants in the Growing Up Today Study, 1996–2007

	Early menarche ^a (N=591)	Normative menarche ^a (N=2,537)	Late menarche ^a (N=583)
	Mean (SD)	Mean (SD)	Mean (SD)
Age at menarche (years)	11.5 (0.4)	13.1 (0.6)	14.9 (0.7)
Age in 2007 (years)	21.6 (0.9)	22.4 (1.2)	23.1 (1.5)
1996 BMI (kg/m ²)	19.0 (3.1)	18.2 (3.1)	17.2 (3.0)
Birth weight (grams)	3381.8 (548.0)	3439.3 (523.9)	3450.8 (510.4)
Sum CES-D-10 Score	8.6 (5.1)	8.3 (5.1)	8.2 (4.8)
	N (%)	N (%)	N (%)
White	546 (92.4)	2396 (94.4)	552 (94.7)
Father present	524 (88.7)	2295 (90.5)	539 (92.5)
Stepfather present	16 (2.7)	59 (2.3)	14 (2.4)
High depressive symptomatology (CES-D-10 14) ^b	105 (17.8)	408 (16.1)	83 (14.2)
High depressive symptomatology (CES-D-10 11)	184 (31.1)	721 (28.4)	151 (25.9)
Any abuse ^c	158 (26.7)	638 (25.2)	138 (23.7)
Physical abuse (sometimes or more often) ^c	82 (13.9)	364 (14.4)	77 (13.2)
Emotional abuse (often or very often) ^c	87 (14.7)	363 (14.3)	92 (15.8)
Sexual abuse (any) ^c	61 (10.3)	192 (7.6)	39 (6.7)

^a Age at menarche categorized as early (<12.0 years), normative (>12.0–14.3 years), and late (>14.3 years).

^b 1 SD above the sample mean

^c Before age 11 years.

Abbreviations: BMI, Body Mass Index; CES-D-10, 10-item Center for Epidemiologic Studies-Depression; SD, standard deviation

Odds ratios (95% confidence intervals) for high depressive symptomatology^a for early, normative, and late menarche among 3,711 female participants in the Growing Up Today Study, 1996–2007

Table 2

Odds Ratio (95% CI)					
	Events/N	Model 1: Age-adjusted	Model 2: Age and covariate-adjusted ^b	Model 3: Model 2 + BMI ^c	
Age 20–22 years in 2007	Early menarche ^d	105/591	1.09 (0.85–1.38)	1.08 (0.85–1.38)	0.99 (0.77–1.27)
	Normative menarche ^d	408/2,537	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Late menarche ^d	83/583	0.90 (0.69–1.16)	0.91 (0.70–1.18)	1.00 (0.76–1.31)
	Early menarche	101/549	1.15 (0.90–1.48)	1.15 (0.89–1.48)	1.03 (0.79–1.34)
	Normative menarche	274/1,671	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Late menarche	43/283	0.92 (0.65–1.30)	0.94 (0.66–1.34)	1.05 (0.73–1.52)
Age 23–25 years in 2007	Early menarche	4/42	0.55 (0.19–1.58)	0.57 (0.20–1.67)	0.55 (0.19–1.63)
	Normative menarche	134/866	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Late menarche	40/300	0.88 (0.59–1.32)	0.89 (0.60–1.35)	0.95 (0.63–1.44)
	Early menarche	62/433	1.08 (0.79–1.46)	1.06 (0.78–1.44)	0.94 (0.69–1.28)
	Normative menarche	246/1,899	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Late menarche	50/445	0.88 (0.63–1.22)	0.87 (0.63–1.22)	0.99 (0.71–1.39)
Any abuse	Early menarche	43/158	1.06 (0.71–1.58)	1.08 (0.72–1.62)	1.03 (0.68–1.57)
	Normative menarche	162/638	1.0 (Reference)	1.0 (Reference)	1.0 (Reference)
	Late menarche	33/138	0.95 (0.61–1.48)	0.98 (0.62–1.53)	1.03 (0.65–1.62)

^a High depressive symptomatology is defined as a CES-D-10 score 1 SD above the mean

^b Logistic regression model adjusted for age in 2007 (years), birth weight (quintiles), race (white, nonwhite), 1996 family composition (father present, stepfather present, no father/stepfather present), abuse before age 11 (never, any).

^c Additionally adjusted for premenarcheal BMI z-score.

^d Age at menarche categorized as early (<12.0 years), normative (>12.0–14.3 years), and late (>14.3 years).

^e Emotional, physical, or sexual abuse.

Abbreviations: CI, confidence interval

Table 3

Mean differences (95% confidence intervals) in depressive symptomatology^a by early, normative, and late menarche among 3,711 female participants in the Growing Up Today Study, 1996–2007.

	N	β (95% CI)		
		Model 1: Age-adjusted	Model 2: Age-and covariate-adjusted ^b	Model 3: Model 2 + BMI ^c
Early menarche ^d	591	0.13 (−0.34–0.60)	0.10 (−0.35–0.56)	−0.06 (−0.53–0.41)
Normative menarche ^d	2,537	0.0 (Reference)	0.0 (Reference)	0.0 (Reference)
Late menarche ^d	583	0.00 (−0.44–0.45)	0.03 (−0.41–0.47)	0.21 (−0.24–0.65)

^aDepressive symptomatology measured on using CES-D-10 as a continuous scale

^bLinear regression model adjusted for age in 2007 (years), birth weight (quintiles), race (white, nonwhite), 1996 family composition (father present, stepfather present, no father/stepfather present), abuse before age 11 (never, any).

^cAdditionally adjusted for premenarcheal BMI z-score.

^dAge at menarche categorized as early (<12.0 years), normative (>12.0–14.3 years), and late (>14.3 years).

Abbreviations: CI, confidence interval