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Menarche and Time to Cycle Regularity Among Individuals Born Between 1950 and 2005 in the US

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Abstract

IMPORTANCE Early menarche is associated with adverse health outcomes. Trends toward earlier menarche have been observed in the US, but data remain limited on differences by sociodemographic factors and body mass index (BMI). Time from menarche to cycle regularity is another understudied early-life characteristic with health implications.

OBJECTIVES To evaluate the temporal trends and disparities in menarche and time to regularity and explore early-life BMI as a mediator.

DESIGN, SETTING, AND PARTICIPANTS This ongoing cohort study enrolled participants from an ongoing mobile application–based US cohort from November 14, 2019, to March 20, 2023.

EXPOSURES Birth year (categorized as 1950-1969, 1970-1979, 1980-1989, 1990-1999, and 2000-2005).

MAIN OUTCOMES AND MEASURES Main outcomes were age at menarche and time to regularity, which were self-recalled at enrollment. In addition, early (aged <11 years), very early (aged <9 years), and late (aged ≥16 years) age at menarche was assessed.

RESULTS Among the 71 341 female individuals who were analyzed (mean [SD] age at menarche, 12.2 [1.6] years; 2228 [3.1%] Asian, 3665 [5.1%] non-Hispanic Black, 4918 [6.9%] Hispanic, 49 518 [69.4%] non-Hispanic White, and 8461 [11.9%] other or multiple races or ethnicities), 5223 were born in 1950 to 1969, 12 226 in 1970 to 1979, 22 086 in 1980 to 1989, 23 894 in 1990 to 1999, and 7912 in 2000 to 2005. The mean (SD) age at menarche decreased from 12.5 (1.6) years in 1950 to 1969 to 11.9 (1.5) years in 2000 to 2005. The number of individuals experiencing early menarche increased from 449 (8.6%) to 1223 (15.5%), the number of individuals experiencing very early menarche increased from 31 (0.6%) to 110 (1.4%), and the number of individuals experiencing late menarche decreased from 286 (5.5%) to 137 (1.7%). For 61 932 participants with reported time to regularity, the number reaching regularity within 2 years decreased from 3463 (76.3%) to 4075 (56.0%), and the number not yet in regular cycles increased from 153 (3.4%) to 1375 (18.9%). The magnitude of the trend toward earlier menarche was greater among participants who self-identified as Asian, non-Hispanic Black, or other or multiple races (vs non-Hispanic White) ($P = .003$ for interaction) and among participants self-rated with low (vs high) socioeconomic status ($P < .001$ for interaction). Within a subset of 9865 participants with data on BMI at menarche, exploratory mediation analysis estimated that 46% (95% CI, 35%-61%) of the temporal trend in age at menarche was explained by BMI.

CONCLUSIONS AND RELEVANCE In this cohort study of 71 341 individuals in the US, as birth year increased, mean age at menarche decreased and time to regularity increased. The trends were

(continued)

Key Points

Question In the US, what are the temporal trends in age at menarche and time from menarche to cycle regularity?

Findings This cohort study of 71 341 US female individuals born between 1950 and 2005 found significant trends toward earlier menarche and longer time to regularity over time, and these trends were more pronounced among those who were non-Hispanic Black, Asian, or of other or multiple races (compared with non-Hispanic White individuals) and among low socioeconomic status groups. Body mass index at menarche partially mediated the trend for menarche.

Meaning These findings suggest that early-life menstrual characteristics have been trending in directions that indicate higher risk of later adverse health outcomes, which may contribute to health disparities.

+ Invited Commentary

+ Supplemental content

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Abstract (continued)

stronger among racial and ethnic minority groups and individuals of low self-rated socioeconomic status. These trends may contribute to the increase in adverse health outcomes and disparities in the US.

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Introduction

Menarche is the culmination of a complex sequence of events involving the maturation of the reproductive axis.[1,2] Early menarche is associated with increased risk of adverse health outcomes, such as cardiovascular diseases, cancers, spontaneous abortion, and premature death,[3-9] whereas late menarche is associated with increased risk of fractures.[10,11] Studies have found trends toward earlier menarche during the past 5 to 10 decades in the US as well as globally.[12-19] In the US, studies have additionally evaluated whether this trend varied by sociodemographic factors.[13,20-26] Some of them[13,21-23,25] showed significant racial and ethnic differences, whereas others[20,24,26] did not, and most[13,20,22,24] were limited to non-Hispanic Black vs White comparisons. Furthermore, most studies[20,21,23,24,26] focused on mean age at menarche, with the frequency of early or late menarche rarely evaluated. Notably, obesity is a risk factor for early-onset puberty,[27-31] and the prevalence of childhood obesity has increased in the US,[32,33] leading to hypotheses on the potential role of obesity in the trends toward earlier menarche. However, whether obesity is the primary factor underlying the trends in menarche remains debatable.[34] Whether and to what extent the trend in menarche is attributable to changes in early-life body mass index (BMI) remains to be determined.[28]

The menstrual cycle is a vital sign.[35] The maturation of the reproductive axis, measured as the time from menarche to established cycle regularity, is another important but understudied hallmark of early-life menstrual health. Within 1 to 2 years after menarche, irregular cycles are considered a normal process of pubertal transition.[36,37] Full maturation of the reproductive axis leads to more regular menstrual function.[38] Longer time to regularity has been associated with lower fecundability, longer menstrual cycles, and increased risk of metabolic conditions and all-cause mortality.[39-42] Whereas the trends in time to regularity (influenced by environmental pollutants)[43,44] were evaluated in Japanese[14] and French[45] cohorts, it is not known whether it has also changed during the past several decades in the US.

In this study, we used data from a large, mobile application–based cohort of adults in the US to evaluate temporal trends in menarche and time to regularity among members of a racially and ethnically diverse study population born between 1950 and 2005. We analyzed overall temporal trends and whether observed trends differ by sociodemographic factors. Additionally, we explored whether BMI at menarche might mediate the observed temporal trends.

Methods

Study Population

The Apple Women's Health Study is a prospective digital cohort study in the US. Users of the Apple Research app on their iPhone were eligible if they had ever menstruated at least once in life, live in the US, were at least 18 years old (19 years in Alabama and Nebraska and 21 years in Puerto Rico), and were able to communicate in English. Eligibility also required sole use of an iCloud account and an iPhone. Enrollment began on November 14, 2019, and is ongoing. Participants provided written informed consent at enrollment. This study was approved by the institutional review board at Advarra. Details were described previously.[46] On enrollment, participants were asked to complete surveys of demographics as well as reproductive and medical history. For this analysis, we included participants who reported female sex assigned at birth, who were enrolled until March 20, 2023, and

who provided age at menarche information. We excluded those born in 1931 to 1949 due to potential survival bias and too few individuals representing this group. A conceptual model is shown in eFigure 1 in Supplement 1. The final study population included 71 341 participants; data analysis was limited to subsets who answered the relevant questions (eFigure 2 in Supplement 1). This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline.

Birth Year and Age at Menarche

We grouped self-reported year of birth as 1950 to 1969 (n = 5223), 1970 to 1979 (n = 12 226), 1980 to 1989 (n = 22 086), 1990 to 1999 (n = 23 894), and 2000 to 2005 (n = 7912). Participants were asked the question, "At what age did you have your first menstrual period? It's okay to estimate," with the following response options: "7 years old or younger," integer options between 8 and 15 years old, "16 years old or older," "I don't know," or "I prefer not to answer." Those who indicated they did not know or preferred not to answer or did not respond were excluded. We derived the following measures: (1) age at menarche (in years) (we assigned the value of 7 to those aged ≤7 years [196 (0.3%)] and the value of 16 to those aged ≥16 years [2447 (3.4%)]); (2) early menarche (yes/no) (age at menarche <11 years[47]); (3) very early menarche (yes/no) (age at menarche <9 years[48]); and (4) late menarche (yes/no) (age at menarche ≥16 years).[49]

Time to Cycle Regularity

Participants were asked, "After your first menstrual cycle, how long did it take for your cycle to become regular?" with the following response options: "less than 1 year," "1-2 years," "3-4 years," "more than 5 years," "after using hormones (eg, birth control pills)," "They're not yet regular," "I don't know," or "I prefer not to answer." Those who indicated don't know or prefer not to answer or who did not respond were considered missing. We further excluded 224 individuals with potentially inaccurate time-to-regularity information (eMethods in Supplement 1). For the remaining 61 932 participants, we categorized time to regularity as 2 years or less, 3 to 4 years, more than 5 years, not yet regular, or regular after using hormones.

Covariates

We considered the following self-reported variables to evaluate whether the temporal trends in age at menarche or time to regularity differ by sociodemographic factors: (1) self-identified race and ethnicity (Asian, Hispanic, non-Hispanic Black, non-Hispanic White, and other and multiple races (including American Indian or Alaska Native, Middle Eastern or North African, Native Hawaiian or other Pacific Islander, "None of these fully describe me," and self-identified with >1 option)[50]; (2) subjective socioeconomic status (SES) at enrollment based on the MacArthur Scale of Subjective Social Status[51] (categorized as 0-3 [low], 4-5 [medium], and 6-9 [high]), which was used as a surrogate for premenarche SES; and (3) geographic location (based on state of residence and categorized as Northeast, Midwest, South, and West).

In addition, among a subset of 9865 participants (13.8%) who retrospectively reported weight and height at menarche, we derived BMI (calculated as weight in kilograms divided by height in meters squared) for age *z* scores, percentiles, and categories at menarche using the Centers for Disease Control and Prevention Growth Chart.[52-54] We considered BMI at menarche as a potential mediator of temporal trends in age at menarche or time to regularity.

Statistical Analysis

We calculated means (SDs) for continuous variables and reported numbers (percentages) for binary or categorical variables, overall and stratified by birth year categories (χ^2 tests were performed to identify differences in time to regularity by birth year categories). We summarized the percentages of time to regularity by age at menarche. We used generalized linear regression (gaussian or binomial

distributions for continuous or binary categorical variables), with birth year as the exposure variable to generate *P* values for temporal trends.

To understand how temporal trends differ by sociodemographic factors, we performed analyses stratified by each covariate. A test of trend was performed within each level of the covariate by including birth year as the exposure variable in regression models. We also tested whether the slope of trends differed by covariates by including an interaction term between each covariate and birth year in the regression models and performing a type 3 test for significance.

We evaluated trends over time in the subset of 9865 participants with data on BMI at menarche. We performed an exploratory causal mediation analysis[55,56] with nonparametric bootstrap (500 simulations) to quantify the proportions (95% CIs) of temporal trends in menarche or time to regularity mediated by BMI *z* score at menarche. We evaluated these temporal trends as a secondary analysis after stratifying by BMI categories at menarche or adjusting for BMI at menarche *z* scores.

To evaluate the robustness of our results, we performed sensitivity analyses, including evaluating the temporal trends in time to regularity when further adjusted for age at menarche, using models that mutually adjusted for race and ethnicity and SES and using multinomial logistic models for the categorical time-to-regularity variable, with 2 years or less as the referent group. Analyses were conducted in Python, version 3.6 (Python Software Foundation) and R, version 4.1.2 (R Project for Statistical Computing). All statistical tests were 2-sided with 95% CIs. $P < .05$ was considered statistically significant.

Results

The **Table** shows the characteristics of the 71 341 participants. Among them, 2228 (3.1%) self-identified as Asian, 4918 (6.9%) as Hispanic, 3665 (5.1%) as non-Hispanic Black, 49 518 (69.4%) as non-Hispanic White, and 8461 (11.9%) as other or multiple races. A total of 21 561 (30.2%) had a high subjective SES level. The mean (SD) age at menarche was 12.2 (1.6) years, and 9174 (12.9%) had early menarche (aged <11 years). A total of 38 524 (62.2%) reached regularity within 2 years after menarche, whereas 6950 (11.2%) did not establish regularity. Characteristics of the 9865 participants with weight and height information at menarche are given in eTable 1 in Supplement 1. Compared with the full study population, these participants tend to have earlier birth years, be non-Hispanic White, and have high subjective SES.

Figure 1 shows the temporal trends of age at menarche and time to regularity. The mean (SD) age at menarche decreased from 12.5 (1.6) to 11.9 (1.5) years comparing those born in 1950 to 1969 vs 2000 to 2005 ($P < .001$ for trend) (Figure 1A and Table). The number of individuals experiencing early menarche increased from 449 (8.6%) to 1223 (15.5%), the number of individuals experiencing very early menarche increased from 31 (0.6%) to 110 (1.4%) for very early menarche, and the number of individuals experiencing late menarche decreased from 286 (5.5%) to 137 (1.7%) ($P < .001$ for trend) (Figure 1B and Table). From the 1950 to 1969 birth years to the 2000 to 2005 birth years, the number reaching regularity within 2 years decreased from 3463 (76.3%) to 4075 (56.0%), and the number not yet in regular cycles increased from 153 (3.4%) to 1375 (18.9%) ($P < .001$ for trend) (Figure 1C and Table). The mean (SD) time to regularity among those who spontaneously established regularity increased from 1.27 to 1.40 years ($P < .001$ for trend) (Table). eFigure 3 in Supplement 1 shows lower percentages of time to regularity less than 2 years among those with either early or late menarche (inverse U-shaped association). Further adjusting for age at menarche resulted in similar distributions of time to regularity (eFigure 4 in Supplement 1).

The temporal trends stratified by race and ethnicity are presented in **Figure 2** (estimates in eTable 2 in Supplement 1). Participants who were Asian, Hispanic, non-Hispanic Black, or of other or multiple races or ethnicities had consistently earlier mean age at menarche than non-Hispanic White participants. All racial and ethnic groups had temporal trends toward earlier menarche ($P < .001$ for trend), but when compared with non-Hispanic White participants, the magnitude of decrease in

mean age at menarche across birth year categories was larger among those self-identified as non-Hispanic Black, Asian, and other or multiple races or ethnicities (P = .003 for interaction). All racial and ethnic groups showed a decreasing proportion of time to regularity within 2 years and an increased proportion of not establishing regularity (P < .001 for trend) (eFigure 5 and eTable 2 in Supplement 1), although there was no interaction between race and ethnicity and birth year. The temporal trends stratified by SES are presented in **Figure 3** (estimates in eTable 3 in Supplement 1). Compared with those with high SES, those with low SES had earlier menarche, lower proportion of time to regularity within 2 years (eFigure 6 in Supplement 2), and larger magnitude of decrease in age at menarche. The heterogeneity by race and ethnicity for the trend toward earlier menarche remained when further adjusted for SES and vice versa (eTable 4 in Supplement 1). There was no interaction between geographic region and birth year when adjusting for race and ethnicity (eTable 5 in Supplement 1).

Table. Characteristics of the 71 341 Apple Women's Health Study Participants, Overall and by Birth Year Category[a]

Characteristic	Total (N = 71 341)	Birth year				
		1950-1969 (n = 5223)	1970-1979 (n = 12 226)	1980-1989 (n = 22 086)	1990-1999 (n = 23 894)	2000-2005 (n = 7912)
Race and ethnicity						
Asian	2228 (3.1)	86 (1.6)	311 (2.5)	668 (3.0)	908 (3.8)	255 (3.2)
Hispanic	4918 (6.9)	176 (3.4)	750 (6.1)	1511 (6.8)	1861 (7.8)	620 (7.8)
Non-Hispanic Black	3665 (5.1)	283 (5.4)	720 (5.9)	1194 (5.4)	1088 (4.6)	380 (4.8)
Non-Hispanic White	49 518 (69.4)	4131 (79.1)	8862 (72.5)	15 505 (70.2)	16 088 (67.3)	4932 (62.3)
Other or multiple races[b]	8461 (11.9)	392 (7.5)	1245 (10.2)	2481 (11.2)	3057 (12.8)	1286 (16.3)
Geographic region						
Northeast	11 300 (15.8)	898 (17.2)	1830 (15.0)	3408 (15.4)	3898 (16.3)	1266 (16.0)
Midwest	15 787 (22.1)	996 (19.1)	2444 (20.0)	4627 (20.9)	5680 (23.8)	2040 (25.8)
South	26 343 (36.9)	1851 (35.4)	4650 (38.0)	8239 (37.3)	8675 (36.3)	2928 (37.0)
West	17 527 (24.6)	1418 (27.1)	3208 (26.2)	5686 (25.7)	5549 (23.2)	1666 (21.0)
SES scale						
Low (0-3)	18 131 (25.4)	658 (12.6)	2237 (18.3)	5242 (23.7)	7280 (30.5)	2714 (34.3)
Medium (4-5)	29 031 (40.7)	1768 (33.9)	4924 (40.3)	9231 (41.8)	10 017 (41.9)	3091 (39.1)
High (6-9)	21 561 (30.2)	2635 (50.4)	4726 (38.7)	6874 (31.1)	5667 (23.7)	1659 (21.0)
Age at menarche, mean (SD), y	12.2 (1.6)	12.5 (1.6)	12.4 (1.6)	12.2 (1.6)	12.1 (1.6)	11.9 (1.5)
Menarche						
Early (age <11 y)	9174 (12.9)	449 (8.6)	1234 (10.1)	2826 (12.8)	3442 (14.4)	1223 (15.5)
Very early (age <9 y)	795 (1.1)	31 (0.6)	92 (0.8)	236 (1.1)	326 (1.4)	110 (1.4)
Late (age ≥16 y)	2447 (3.4)	286 (5.5)	498 (4.1)	850 (3.8)	676 (2.8)	137 (1.7)
Time to cycle regularity[c]	61 932	4538 (7.3)	10 327 (16.7)	18 611 (30.0)	21 183 (34.2)	7273 (11.7)
≤2 y	38 524 (62.2)	3463 (76.3)	7254 (70.2)	11 818 (63.5)	11 914 (56.2)	4075 (56.0)
3-4 y	3980 (6.4)	262 (5.8)	609 (5.9)	1100 (5.9)	1427 (6.7)	582 (8.0)
>5 y	3613 (5.8)	266 (5.9)	766 (7.4)	1249 (6.7)	1149 (5.4)	183 (2.5)
Not yet regular	6950 (11.2)	153 (3.4)	559 (5.4)	1857 (10.0)	3006 (14.2)	1375 (18.9)
Regular after hormones	8865 (14.3)	394 (8.7)	1139 (11.0)	2587 (13.9)	3687 (17.4)	1058 (14.5)
Time to cycle regularity (among those who established cycle regularity at enrollment not due to hormone use), mean (SD), y[d] (N = 46 117)	1.43 (1.5)	1.27 (1.4)	1.40 (1.5)	1.45 (1.5)	1.48 (1.5)	1.40 (1.3)

Abbreviation: SES, socioeconomic status.

[a] Data are presented as number (percentage) of participants unless otherwise indicated. Numbers may not add up to the total number or 100% due to missingness.

[b] Other includes American Indian or Alaska Native, Middle Eastern or North African, Native Hawaiian or Pacific Islander, or none of these categories can fully describe the participant. Multiple races correspond to those who selected more than 1 race and ethnicity category.

[c] Details of inclusion and exclusion of the 61 932 individuals who provided information on time to regularity are described in the eMethods in Supplement 1.

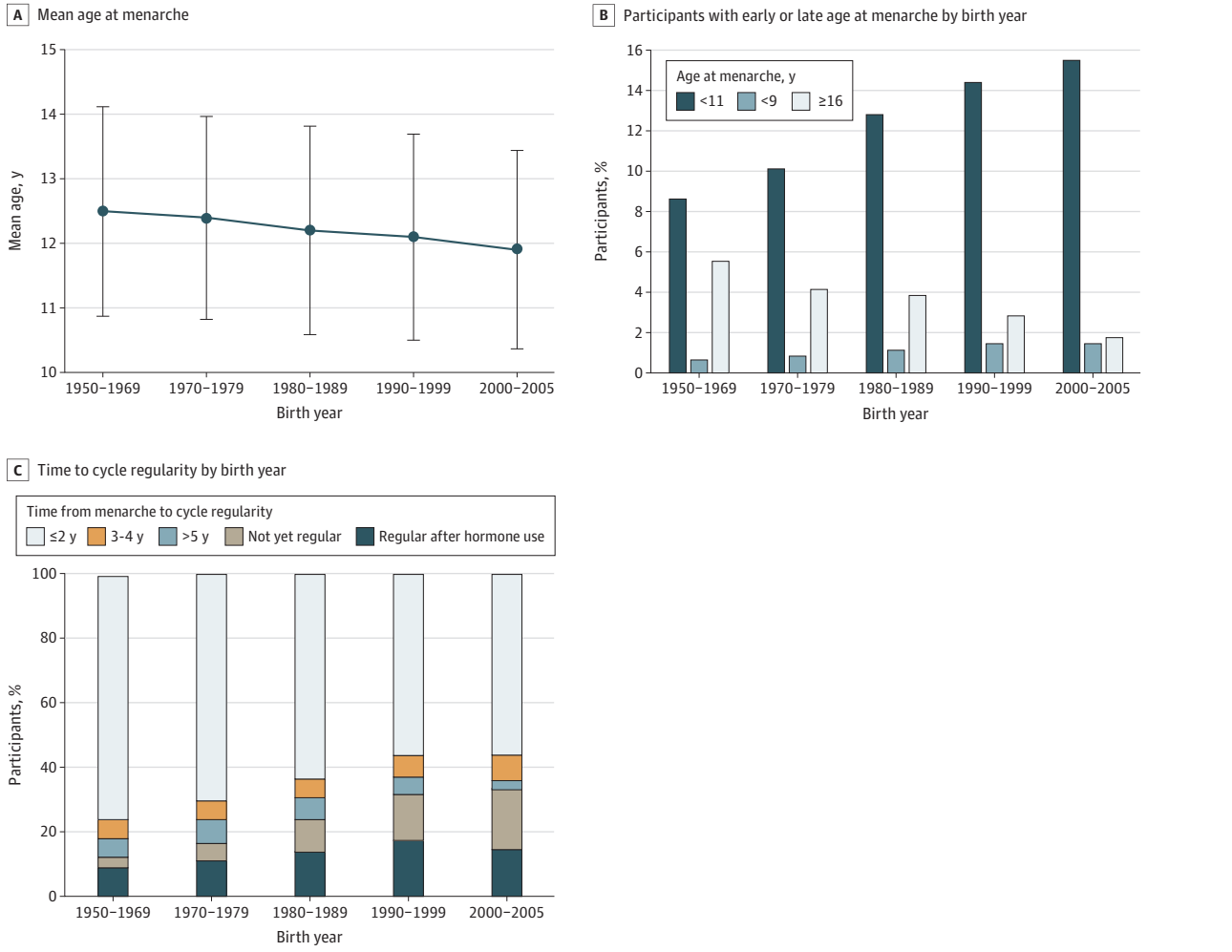
[d] Among the 46 117 participants who reported reaching cycle regularity at enrollment (not due to hormone use), we assigned the following values to each category of response: 0.5 years for those who reached cycle regularity at less than 1 year, 1.5 years for those who reached cycle regularity at 1 to 2 years, 3.5 years for those who reached cycle regularity at 3 to 4 years, and 5.5 years for those who reached cycle regularity at more than 5 years.

Overall, using multinomial logistic regressions yielded *P*-for-trend values of <.001 for each category of time to regularity compared with ≤2 years. Among the 9865 participants who provided weight and height at menarche, the BMI *z* score, percentile, and prevalence of obesity increased across birth year categories (eFigure 7 and eTable 1 in Supplement 1). An exploratory mediation analysis showed that the proportion of the temporal trends toward earlier menarche mediated by BMI *z* score at menarche was 46% (95% CI, 35%-61%) (**Figure 4**). When stratified by BMI categories at menarche, the healthy and underweight group still showed a trend toward earlier menarche (eTable 6 in Supplement 1). When adjusted for BMI *z* scores, a trend toward earlier menarche remained (eTable 6 in Supplement 1), as did heterogeneity by race and ethnicity (eFigure 8 in Supplement 1). There was no evidence of significant mediation by BMI at menarche for the temporal trends in time to regularity (eTable 7 in Supplement 1).

Discussion

This cohort study of 71 341 participants born between 1950 and 2005 in the US found temporal trends toward earlier menarche (earlier mean age, higher percentage of early menarche, and lower percentage of late menarche) and longer time from menarche to cycle regularity (lower percentage

Figure 1. Temporal Trends of Age at Menarche and Time to Cycle Regularity Among 71 341 Apple Women's Health Study Participants



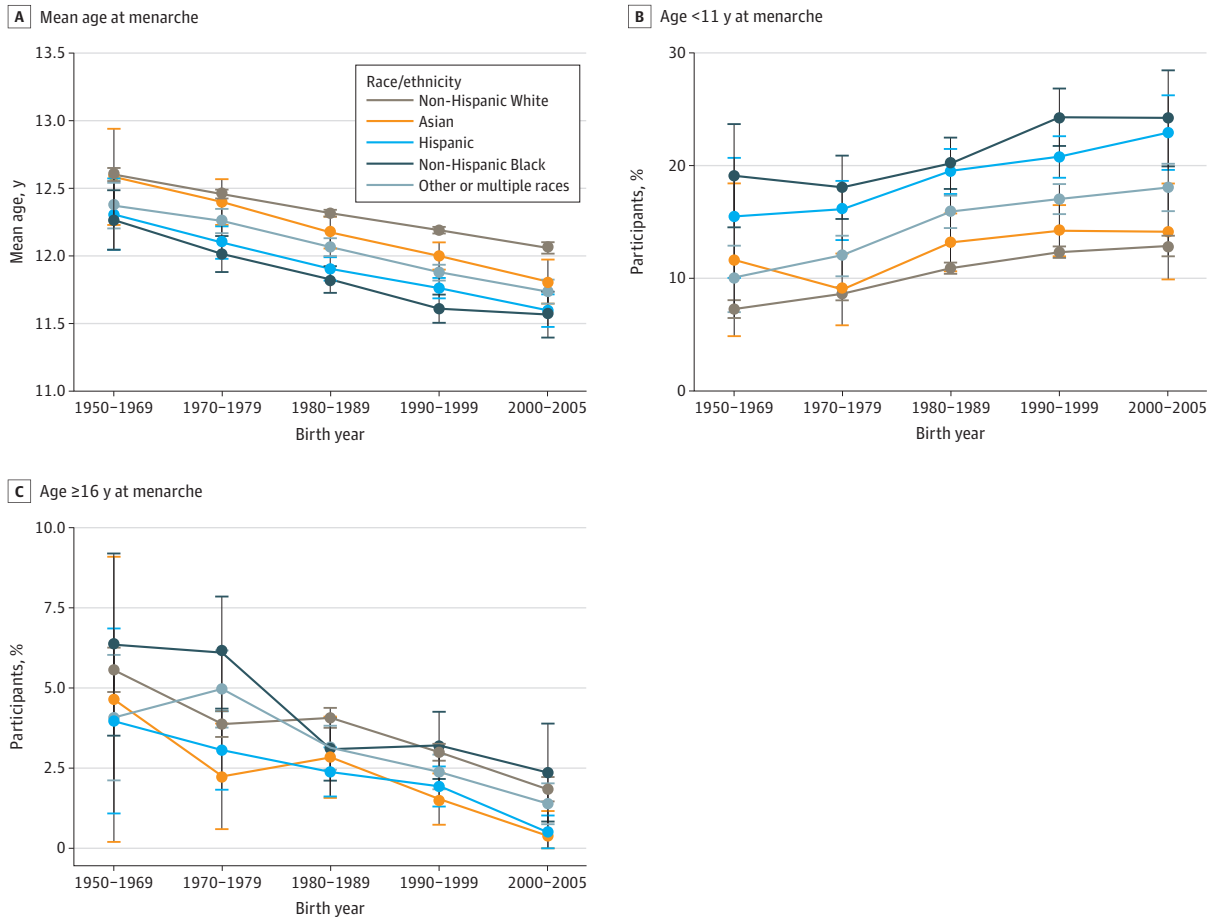
Error bars indicate SDs.

of time to regularity within 2 years, higher percentage of time to regularity within 3-4 years, and higher percentage of not establishing regularity). These trends remained across all sociodemographic groups but were stronger among certain non-White (specifically, Asian, non-Hispanic Black, and other or multiple races or ethnicities) and low SES groups. In an exploratory analysis, BMI at menarche may explain a significantly large proportion of the temporal trends toward earlier menarche.

Our findings of a temporal trend toward earlier menarche are consistent with some US-based studies, with similar magnitude of changes.[12,13,16] Other studies indicated that age at menarche stabilized during the past 50 years, whereas evidence that the median decreased by 2.5 to 4 months in the past 25 years remains,[20,57] consistent with a change from 12.2 to 11.9 years of age for those born in 1980 to 1989 vs 2000 to 2005 in our study. Despite a relatively small magnitude of change in mean age, our study is among the first to show that the percentages of early and very early menarche have also increased by almost 2-fold across birth years from 1950 to 2005, raising concerns that more individuals may be vulnerable to adverse health outcomes related to early menarche.[3-6] Late menarche has decreased, which may have other health implications, such as the decreasing rates of fractures.[58,59]

We found that non-Hispanic Black participants had consistently earlier mean age at menarche than White participants, also similar to prior US-based studies.[13,20-26] We also found that

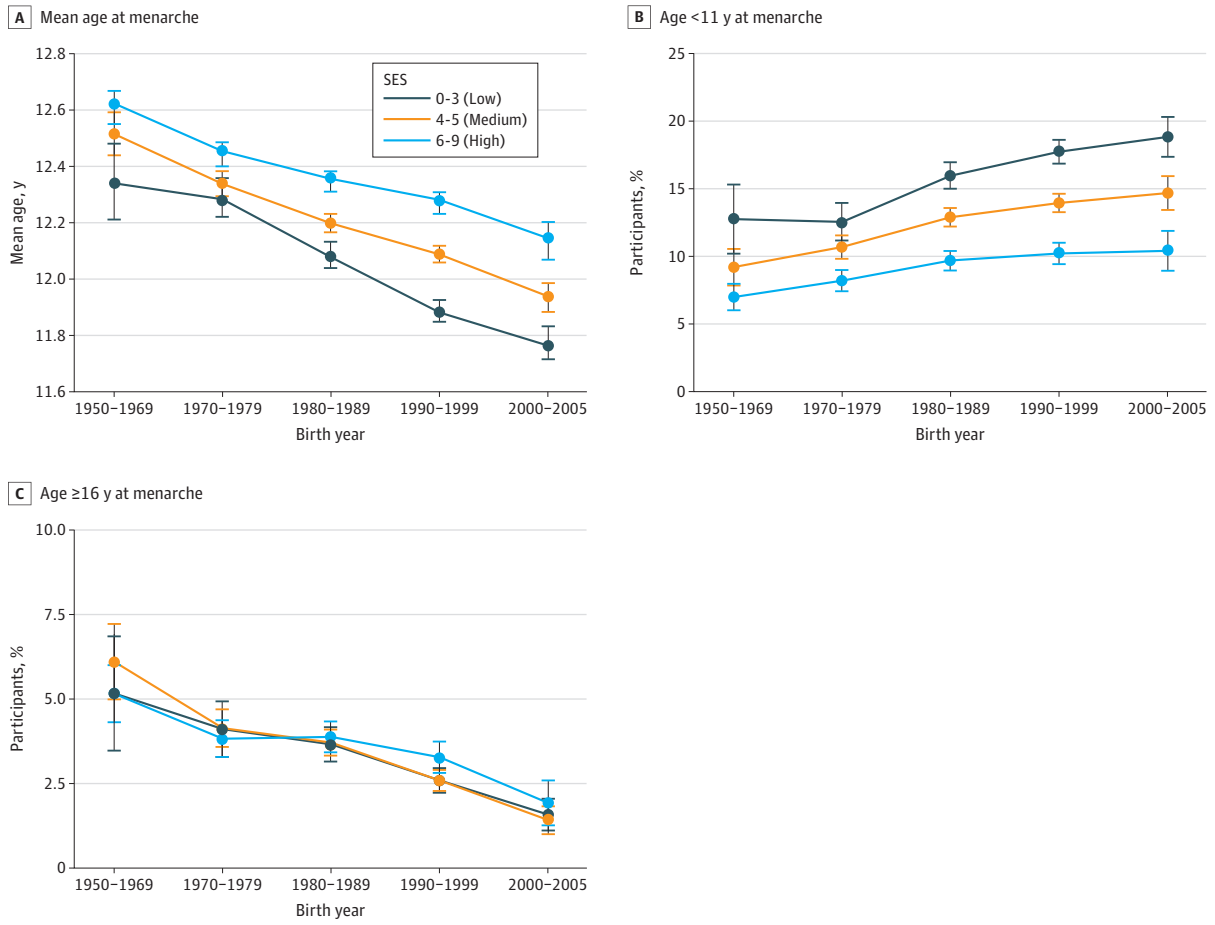
Figure 2. Temporal Trends of Age at Menarche by Birth Year, Stratified by Race and Ethnicity



Other includes American Indian or Alaska Native, Middle Eastern or North African, Native Hawaiian or other Pacific Islander, or none of these categories can fully describe the participant. Multiple races correspond to those who self-identified as more than 1 race and ethnicity category. All trends were statistically significant at $P < .05$. Error bars indicate 95% CIs.

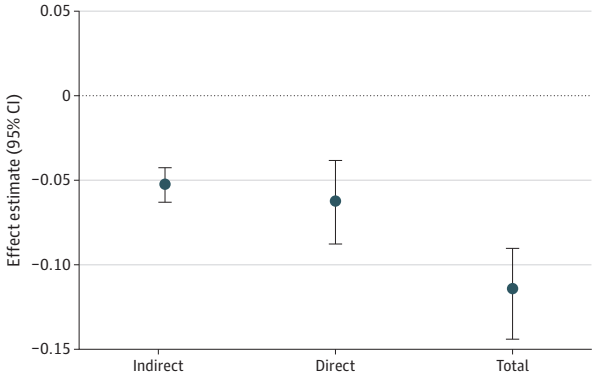
non-Hispanic Black participants had a larger magnitude of change toward earlier menarche across birth year categories compared with non-Hispanic White participants. Similarly, we found other groups (Asian and other or multiple races), rarely evaluated in previous studies of menarche, also had consistently earlier mean ages and larger magnitudes of change toward earlier menarche than non-Hispanic White participants. We found similar patterns for self-rated low SES (compared with

Figure 3. Temporal Trends of Age at Menarche by Birth Year, Stratified by Socioeconomic Status (SES)



All trends were statistically significant at $P < .05$. Error bars indicate 95% CIs.

Figure 4. Exploratory Causal Mediation Among 9865 Participants With Body Mass Index (BMI) *z* Score at Menarche



The exploratory mediation analysis estimated that 46% (95% CI, 35%-61%) of the temporal trend in age at menarche was explained by BMI at menarche. Total effect represents the overall change in age at menarche per 10-year lapse in birth year, direct effect represents the proportion of this change that is independent of BMI *z* score at menarche, and indirect effect represents the proportion of this change mediated through BMI *z* score at menarche. Error bars indicate 95% CIs.

high SES). The factors driving this widening gap of disparities remain to be explored; transethnic genome-wide association studies indicated that these disparities are unlikely to be attributed to genetic variations, suggesting they may be driven by other environmental or contextual factors that may, through racism, impact different pathways, leading to earlier menarche.[60]

Onset of menarche is closely related to attainment of adequate body fat via pathways such as increased insulin-like growth factor 1 and leptin that stimulate gonadotropin-releasing hormone.[61] In our exploratory analysis, we found that BMI at menarche may explain 46% of the temporal trends in menarche. This finding suggests that childhood obesity, a risk factor for earlier puberty,[27-30,62] which has increased in the US,[32,33] could be a contributing factor to the trend toward earlier menarche. However, the remaining 54% remain unclear. Our exploratory analysis also showed that BMI may have contributed to earlier menarche among non-Hispanic White, Black, and other or multiple races, whereas the trend among Asian and Hispanic individuals remains to be further explored. Previous studies also showed that the biggest decrease in age at menarche occurred before the obesity epidemic in the US,[34] suggesting that other factors need to be explored to explain these trends and disparities, including environmental factors (eg, endocrine-disrupting chemicals, metals, or air pollutants could impact pubertal timing,[63-65] with disproportionally higher exposure among certain racial and ethnic minority groups),[66-68] dietary patterns (eg, sugar intake via insulin-mediated pathways),[69-71] psychosocial stress,[72] and adverse childhood experiences.[73]

Our findings of temporal trends toward longer time to regularity and higher proportion of never establishing regularity in the US have not been previously reported. Because longer time to regularity has been associated with adverse outcomes,[39-42] it may serve as an early-life vital sign. These temporal trends may be driven by longer time to maturation of the reproductive axis (eg, impacted by endocrine disruptors)[74] or increasing ovulation disorders[75] that impact cycle regularity. Although earlier studies suggest that regular menstruation should be established within 1 to 2 years after menarche,[37,38,76,77] evidence remains limited on whether delays beyond 2 years warrant clinical or lifestyle intervention.[78] In our study, the mean time to regularity among those who spontaneously established regularity was 1.2 to 1.5 years within the 2-year window. However, the proportions taking 3 to 4 years or never establishing regularity were increasing. A French cohort born between 1935 and 1950 showed a decrease from 64% to 53% for time to regularity within 1 year, but data are limited for the US.[45] We also found differences by race and ethnicity (eg, Hispanic individuals reported a higher rate of not establishing regularity compared with their non-Hispanic White peers, consistent with a study[79] showing that Hispanic individuals having the highest risk of cycle irregularity in adulthood). Our findings suggest the necessity of further studies on the postmenarche years and the need for early intervention during relevant time windows. Continued research on the association of BMI and other factors on reproductive development is needed, and findings should be conveyed to health professionals.

Strengths and Limitations

This study has several unique strengths. First, a large study size of 71 341 participants in a heterogeneous population allowed for sufficient statistical power to detect racial and ethnic differences, even for groups that were previously understudied. Second, we evaluated temporal trends in the percentages of early or late menarche in addition to mean age. Third, our study is the first, to our knowledge, to evaluate and report a temporal trend toward longer time to regularity, suggesting future research directions on this understudied early-life marker of menstrual health. Fourth, our study is the first, to our knowledge, to use digital observational cohort data evaluating BMI at menarche as a potential contributor to the observed temporal trends.

Our study also has limitations. First, the retrospective self-report may induce recall bias and misclassification, likely differential across birth year categories. However, previous validation studies[80-82] showed moderate to high correlations between recalled and original age and body size at menarche. Second, BMI at menarche was only available among a subset of participants with demographic distributions different from the full study population. Third, data are limited for

additional early-life factors that may contribute to these trends. Fourth, our results may not be generalizable to all US individuals who menstruate or to other populations. Potential selection bias may arise due to self-selection into the study that may be impacted by sociodemographic characteristics.

Conclusions

In this US cohort study of 71 341 individuals born between 1950 and 2005, we observed temporal trends toward earlier menarche and longer time to regularity. These trends appeared across all sociodemographic groups but were stronger among certain racial and ethnic groups (Asian, non-Hispanic Black, or other and multiple races or ethnicities) and low subjective SES groups. Body mass index at menarche mediated a significantly large proportion of the trends toward earlier menarche. Further awareness among health care practitioners and researchers is needed to understand the reasons for these trends and their health implications.

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REFERENCES

1. Forman MR, Mangini LD, Thelus-Jean R, Hayward MD. Life-course origins of the ages at menarche and menopause. *Adolesc Health Med Ther*. 2013;4:1-21. doi:10.2147/AHMT.S15946

2. Heffner LJ, Schust DJ. *The Reproductive System at a Glance*. Vol 23. John Wiley & Sons; 2010.

3. Lee JJ, Cook-Wiens G, Johnson BD, et al. Age at menarche and risk of cardiovascular disease outcomes: findings from the National Heart Lung and Blood Institute-sponsored Women's Ischemia Syndrome Evaluation. *J Am Heart Assoc*. 2019;8(12):e012406. doi:10.1161/JAHA.119.012406

4. Apter D, Vihko R. Early menarche, a risk factor for breast cancer, indicates early onset of ovulatory cycles. *J Clin Endocrinol Metab*. 1983;57(1):82-86. doi:10.1210/jcem-57-1-82

5. Fuhrman BJ, Moore SC, Byrne C, et al. Association of the age at menarche with site-specific cancer risks in pooled data from nine cohorts. *Cancer Res*. 2021;81(8):2246-2255. doi:10.1158/0008-5472.CAN-19-3093

6. Cooper GS, Ephross SA, Weinberg CR, Baird DD, Whelan EA, Sandler DP. Menstrual and reproductive risk factors for ischemic heart disease. *Epidemiology*. 1999;10(3):255-259. doi:10.1097/00001648-199905000-00011

7. Boden JM, Fergusson DM, Horwood LJ. Age of menarche and psychosocial outcomes in a New Zealand birth cohort. *J Am Acad Child Adolesc Psychiatry*. 2011;50(2):132-140.e5. doi:10.1016/j.jaac.2010.11.007

8. Liestøl K. Menarcheal age and spontaneous abortion: a causal connection? *Am J Epidemiol*. 1980;111(6):753-758. doi:10.1093/oxfordjournals.aje.a112953

9. Sandler DP, Wilcox AJ, Horney LF. Age at menarche and subsequent reproductive events. *Am J Epidemiol*. 1984;119(5):765-774. doi:10.1093/oxfordjournals.aje.a113797

10. Canoy D, Beral V, Balkwill A, et al; Million Women Study Collaborators. Age at menarche and risks of coronary heart and other vascular diseases in a large UK cohort. *Circulation*. 2015;131(3):237-244. doi:10.1161/CIRCULATIONAHA.114.010070

11. Zhu J, Chan YM. Adult consequences of self-limited delayed puberty. *Pediatrics*. 2017;139(6):e20163177. doi:10.1542/peds.2016-3177

12. Worthman CM, Trang K. Dynamics of body time, social time and life history at adolescence. *Nature*. 2018;554(7693):451-457. doi:10.1038/nature25750

13. Krieger N, Kiang MV, Kosheleva A, Waterman PD, Chen JT, Beckfield J. Age at menarche: 50-year socioeconomic trends among US-born black and white women. *Am J Public Health*. 2015;105(2):388-397. doi:10.2105/AJPH.2014.301936

14. Hosokawa M, Imazeki S, Mizunuma H, Kubota T, Hayashi K. Secular trends in age at menarche and time to establish regular menstrual cycling in Japanese women born between 1930 and 1985. *BMC Womens Health*. 2012;12(1):19. doi:10.1186/1472-6874-12-19

15. Cho GJ, Park HT, Shin JH, et al. Age at menarche in a Korean population: secular trends and influencing factors. *Eur J Pediatr*. 2010;169(1):89-94. doi:10.1007/s00431-009-0993-1

16. Herman-Giddens ME. Recent data on pubertal milestones in United States children: the secular trend toward earlier development. *Int J Androl*. 2006;29(1):241-246. doi:10.1111/j.1365-2605.2005.00575.x

17. Hoshi H, Kouchi M. Secular trend of the age at menarche of Japanese girls with special regard to the secular acceleration of the age at peak height velocity. *Hum Biol*. 1981;53(4):593-598.

18. Brix N, Ernst A, Lauridsen LLB, et al. Timing of puberty in boys and girls: a population-based study. *Paediatr Perinat Epidemiol*. 2019;33(1):70-78. doi:10.1111/ppe.12507

19. Rosenberg M. Menarcheal age for Norwegian women born 1830-1960. *Ann Hum Biol*. 1991;18(3):207-219. doi:10.1080/03014469100001532

20. Euling SY, Herman-Giddens ME, Lee PA, et al. Examination of US puberty-timing data from 1940 to 1994 for secular trends: panel findings. *Pediatrics*. 2008;121(suppl 3):S172-S191. doi:10.1542/peds.2007-1813D

21. Anderson SE, Must A. Interpreting the continued decline in the average age at menarche: results from two nationally representative surveys of U.S. girls studied 10 years apart. *J Pediatr*. 2005;147(6):753-760. doi:10.1016/j.jpeds.2005.07.016

22. Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS; Bogalusa Heart Study. The relation of menarcheal age to obesity in childhood and adulthood: the Bogalusa Heart Study. *BMC Pediatr*. 2003;3:3. doi:10.1186/1471-2431-3-3

23. Chumlea WC, Schubert CM, Roche AF, et al. Age at menarche and racial comparisons in US girls. *Pediatrics*. 2003;111(1):110-113. doi:10.1542/peds.111.1.110

24. Slyper AH. The pubertal timing controversy in the USA, and a review of possible causative factors for the advance in timing of onset of puberty. *Clin Endocrinol (Oxf)*. 2006;65(1):1-8. doi:10.1111/j.1365-2265.2006.02539.x

25. Martinez GM. Trends and patterns in menarche in the United States: 1995 through 2013-2017. *Natl Health Stat Report*. 2020;(146):1-12.

26. Walvoord EC. The timing of puberty: is it changing? does it matter? *J Adolesc Health*. 2010;47(5):433-439. doi:10.1016/j.jadohealth.2010.05.018

27. Currie C, Ahluwalia N, Godeau E, Nic Gabhainn S, Due P, Currie DB. Is obesity at individual and national level associated with lower age at menarche? evidence from 34 countries in the Health Behaviour in School-aged Children Study. *J Adolesc Health*. 2012;50(6):621-626. doi:10.1016/j.jadohealth.2011.10.254

28. Ahmed ML, Ong KK, Dunger DB. Childhood obesity and the timing of puberty. *Trends Endocrinol Metab*. 2009;20(5):237-242. doi:10.1016/j.tem.2009.02.004

29. Wei S, Schmidt MD, Dwyer T, Norman RJ, Venn AJ. Obesity and menstrual irregularity: associations with SHBG, testosterone, and insulin. *Obesity (Silver Spring)*. 2009;17(5):1070-1076. doi:10.1038/oby.2008.641

30. Elizondo-Montemayor L, Hernández-Escobar C, Lara-Torre E, Nieblas B, Gómez-Carmona M. Gynecologic and obstetric consequences of obesity in adolescent girls. *J Pediatr Adolesc Gynecol*. 2017;30(2):156-168. doi:10.1016/j.jpag.2016.02.007

31. Bratke H, Bruserud IS, Brannsether B, et al. Timing of menarche in Norwegian girls: associations with body mass index, waist circumference and skinfold thickness. *BMC Pediatr*. 2017;17(1):138. doi:10.1186/s12887-017-0893-x

32. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity and trends in body mass index among US children and adolescents, 1999-2010. *JAMA*. 2012;307(5):483-490. doi:10.1001/jama.2012.40

33. Anderson PM, Butcher KF, Schanzenbach DW. Understanding recent trends in childhood obesity in the United States. *Econ Hum Biol*. 2019;34:16-25. doi:10.1016/j.ehb.2019.02.002

34. McDonald JA, Eng SM, Dina OO, Schooling CM, Terry MB. Infection and pubertal timing: a systematic review. *J Dev Orig Health Dis*. 2016;7(6):636-651. doi:10.1017/S2040174416000313

35. Committee on Adolescent Health Care. ACOG Committee Opinion No. 651: menstruation in girls and adolescents: using the menstrual cycle as a vital sign. *Obstet Gynecol*. 2015;126(6):e143-e146. doi:10.1097/AOG.0000000000001215

36. Mansfield MJ, Emans SJ. Adolescent menstrual irregularity. *J Reprod Med*. 1984;29(6):399-410.

37. Teede HJ, Misso ML, Costello MF, et al; International PCOS Network. Recommendations from the international evidence-based guideline for the assessment and management of polycystic ovary syndrome. *Hum Reprod*. 2018;33(9):1602-1618. doi:10.1093/humrep/dey256

38. Zhang K, Pollack S, Ghods A, et al. Onset of ovulation after menarche in girls: a longitudinal study. *J Clin Endocrinol Metab*. 2008;93(4):1186-1194. doi:10.1210/jc.2007-1846

39. Wesselink AK, Wise LA, Hatch EE, et al. Menstrual cycle characteristics and fecundability in a North American preconception cohort. *Ann Epidemiol*. 2016;26(7):482-487.e1. doi:10.1016/j.annepidem.2016.05.006

40. Wise LA, Mikkelsen EM, Rothman KJ, et al. A prospective cohort study of menstrual characteristics and time to pregnancy. *Am J Epidemiol*. 2011;174(6):701-709. doi:10.1093/aje/kwr130

41. Lozano-Esparza S, Jansen EC, Hernandez-Ávila JE, Zamora-Muñoz S, Stern D, Lajous M. Menarche characteristics in association with total and cause-specific mortality: a prospective cohort study of Mexican teachers. *Ann Epidemiol*. 2021;62:59-65. doi:10.1016/j.annepidem.2021.06.007

42. Jansen EC, Stern D, Peterson KE, Lajous M, López-Ridaura R. Early menstrual factors are associated with adulthood cardio-metabolic health in a survey of Mexican teachers. *Matern Child Health J*. 2019;23(3):356-368. doi:10.1007/s10995-018-2650-7

43. Mahalingaiah S, Missmer SE, Cheng JJ, Chavarro J, Laden F, Hart JE. Perimenarchal air pollution exposure and menstrual disorders. *Hum Reprod*. 2018;33(3):512-519. doi:10.1093/humrep/dey005

44. Dossus L, Kvaskoff M, Bijon A, et al. Determinants of age at menarche and time to menstrual cycle regularity in the French E3N cohort. *Ann Epidemiol*. 2012;22(10):723-730. doi:10.1016/j.annepidem.2012.07.007

45. Clavel-Chapelon F; E3N-EPIC Group. Evolution of age at menarche and at onset of regular cycling in a large cohort of French women. *Hum Reprod*. 2002;17(1):228-232. doi:10.1093/humrep/17.1.228

46. Mahalingaiah S, Fruh V, Rodriguez E, et al. Design and methods of the Apple Women's Health Study: a digital longitudinal cohort study. *Am J Obstet Gynecol*. 2022;226(4):545.e1-545.e29. doi:10.1016/j.ajog.2021.09.041

47. Warp ML, Grindstad T, Magnus MC, et al. Early or late menarche is associated with reduced fecundability in the Norwegian Mother, Father and Child Cohort Study. *Hum Reprod*. 2024;39(4):812-821. doi:10.1093/humrep/deae011

48. Yüce Ö, Bideci A, Çelik N, Çamurdan O, Cinaz P. Diagnostic value of urinary luteinizing hormone levels in the monitoring of precocious puberty treatment. *Arch Endocrinol Metab*. 2020;64(2):121-127. doi:10.20945/2359-3997000000212

49. Lacroix AE, Gondal H, Shumway KR, Langaker MD. Physiology, Menarche. In: *StatPearls*. StatPearls Publishing; 2023.

50. Li H, Gibson EA, Jukic AMZ, et al. Menstrual cycle length variation by demographic characteristics from the Apple Women's Health Study. *NPJ Digit Med*. 2023;6(1):100. doi:10.1038/s41746-023-00848-1

51. Moss RH, Kelly B, Bird PK, Pickett KE. Examining individual social status using the MacArthur Scale of Subjective Social Status: findings from the Born in Bradford study. *SSM Popul Health*. 2023;23:101463. doi:10.1016/j.ssmph.2023.101463

52. Kuczmarski RJ, Ogden CL, Guo SS, et al. 2000 CDC Growth Charts for the United States: methods and development. *Vital Health Stat 11*. 2002;(246):1-190.

53. Wei R, Ogden CL, Parsons VL, Freedman DS, Hales CM. A method for calculating BMI z-scores and percentiles above the 95th percentile of the CDC growth charts. *Ann Hum Biol*. 2020;47(6):514-521. doi:10.1080/03014460.2020.1808065

54. National Center for Health Statistics. Growth Charts—CDC extended BMI-for-age growth chards. December 21, 2022. Accessed August 30, 2023. https://www.cdc.gov/growthcharts/extended-bmi.htm

55. Tingley D, Yamamoto T, Hirose K, Keele L, Imai K. mediation: R package for causal mediation analysis. *J Stat Softw*. 2014;59:1-38. doi:10.18637/jss.v059.i05

56. Imai K, Keele L, Tingley D. A general approach to causal mediation analysis. *Psychol Methods*. 2010;15(4):309-334. doi:10.1037/a0020761

57. Sørensen K, Mouritsen A, Aksglaede L, Hagen CP, Mogensen SS, Juul A. Recent secular trends in pubertal timing: implications for evaluation and diagnosis of precocious puberty. *Horm Res Paediatr*. 2012;77(3):137-145. doi:10.1159/000336325

58. Elhakeem A, Frysz M, Tilling K, Tobias JH, Lawlor DA. Association between age at puberty and bone accrual from 10 to 25 years of age. *JAMA Netw Open*. 2019;2(8):e198918. doi:10.1001/jamanetworkopen.2019.8918

59. Leslie WD, Lix LM, Yogendran MS, Morin SN, Metge CJ, Majumdar SR. Temporal trends in obesity, osteoporosis treatment, bone mineral density, and fracture rates: a population-based historical cohort study. *J Bone Miner Res*. 2014;29(4):952-959. doi:10.1002/jbmr.2099

60. Fernández-Rhodes L, Malinowski JR, Wang Y, et al. The genetic underpinnings of variation in ages at menarche and natural menopause among women from the multi-ethnic Population Architecture using Genomics and Epidemiology (PAGE) Study: a trans-ethnic meta-analysis. *PLoS One*. 2018;13(7):e0200486. doi:10.1371/journal.pone.0200486

61. Hall JE. Neuroendocrine control of the menstrual cycle. In: *Yen and Jaffe's Reproductive Endocrinology*. Elsevier; 2019:149-166. doi:10.1016/B978-0-323-47912-7.00007-X

62. Kershaw EE, Flier JS. Adipose tissue as an endocrine organ. *J Clin Endocrinol Metab*. 2004;89(6):2548-2556. doi:10.1210/jc.2004-0395

63. Binder AM, Corvalan C, Calafat AM, et al. Childhood and adolescent phenol and phthalate exposure and the age of menarche in Latina girls. *Environ Health*. 2018;17(1):32. doi:10.1186/s12940-018-0376-z

64. Lee JE, Jung HW, Lee YJ, Lee YA. Early-life exposure to endocrine-disrupting chemicals and pubertal development in girls. *Ann Pediatr Endocrinol Metab*. 2019;24(2):78-91. doi:10.6065/apem.2019.24.2.78

65. Anastasiadis X, Matsas A, Panoskaltsis T, Bakas P, Papadimitriou DT, Christopoulos P. Impact of chemicals on the age of menarche: a literature review. *Children (Basel)*. 2023;10(7):1234. doi:10.3390/children10071234

66. James-Todd TM, Chiu YH, Zota AR. Racial/ethnic disparities in environmental endocrine disrupting chemicals and women's reproductive health outcomes: epidemiological examples across the life course. *Curr Epidemiol Rep*. 2016;3(2):161-180. doi:10.1007/s40471-016-0073-9

67. Mohai P, Lantz PM, Morenoff J, House JS, Mero RP. Racial and socioeconomic disparities in residential proximity to polluting industrial facilities: evidence from the Americans' Changing Lives Study. *Am J Public Health*. 2009;99(suppl 3):S649-S656. doi:10.2105/AJPH.2007.131383

68. Perry MJ, Arrington S, Freisthler MS, et al. Pervasive structural racism in environmental epidemiology. *Environ Health*. 2021;20(1):119. doi:10.1186/s12940-021-00801-3

69. Soliman A, De Sanctis V, Elalaily R. Nutrition and pubertal development. *Indian J Endocrinol Metab*. 2014; 18(suppl 1):S39-S47. doi:10.4103/2230-8210.145073

70. Mueller NT, Jacobs DR Jr, MacLehose RF, et al. Consumption of caffeinated and artificially sweetened soft drinks is associated with risk of early menarche. *Am J Clin Nutr*. 2015;102(3):648-654. doi:10.3945/ajcn.114.100958

71. Carwile JL, Willett WC, Spiegelman D, et al. Sugar-sweetened beverage consumption and age at menarche in a prospective study of US girls. *Hum Reprod*. 2015;30(3):675-683. doi:10.1093/humrep/deu349

72. Glass DJ, Geerkens JT, Martin MA. Psychosocial and energetic factors on human female pubertal timing: a systematized review. *Evol Hum Sci*. 2022;4:e28. doi:10.1017/ehs.2022.24

73. Zhang L, Zhang D, Sun Y. Adverse childhood experiences and early pubertal timing among girls: a meta-analysis. *Int J Environ Res Public Health*. 2019;16(16):2887. doi:10.3390/ijerph16162887

74. Amir S, Shah STA, Mamoulakis C, et al. Endocrine disruptors acting on estrogen and androgen pathways cause reproductive disorders through multiple mechanisms: a review. *Int J Environ Res Public Health*. 2021;18(4):1464. doi:10.3390/ijerph18041464

75. Liu J, Wu Q, Hao Y, et al. Measuring the global disease burden of polycystic ovary syndrome in 194 countries: Global Burden of Disease Study 2017. *Hum Reprod*. 2021;36(4):1108-1119. doi:10.1093/humrep/deaa371

76. Legro RS, Lin HM, Demers LM, Lloyd T. Rapid maturation of the reproductive axis during perimenarche independent of body composition. *J Clin Endocrinol Metab*. 2000;85(3):1021-1025. doi:10.1210/jc.85.3.1021

77. UpToDate. Normal puberty. Accessed September 21, 2023. https://www.uptodate.com/contents/normal-puberty?csi=1ba24be4-9f95-4311-85d5-5d6f291e3550&source=contentShare

78. Carlson LJ, Shaw ND. Development of ovulatory menstrual cycles in adolescent girls. *J Pediatr Adolesc Gynecol*. 2019;32(3):249-253. doi:10.1016/j.jpag.2019.02.119

79. Nobles J, Cannon L, Wilcox AJ. Menstrual irregularity as a biological limit to early pregnancy awareness. *Proc Natl Acad Sci U S A*. 2022;119(1):e2113762118. doi:10.1073/pnas.2113762118

80. Must A, Phillips SM, Naumova EN, et al. Recall of early menstrual history and menarcheal body size: after 30 years, how well do women remember? *Am J Epidemiol*. 2002;155(7):672-679. doi:10.1093/aje/155.7.672

81. Lundblad MW, Jacobsen BK. The reproducibility of self-reported age at menarche: the Tromsø Study. *BMC Womens Health*. 2017;17(1):62. doi:10.1186/s12905-017-0420-0

82. Koprowski C, Coates RJ, Bernstein L. Ability of young women to recall past body size and age at menarche. *Obes Res*. 2001;9(8):478-485. doi:10.1038/oby.2001.62

SUPPLEMENT 1.

eMethods. Detailed Exclusion of Individuals With Potentially Inaccurate Time to Regularity Information
eFigure 1. Conceptual Model of the Research Question and Potential Mechanisms
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SUPPLEMENT 2.
Data Sharing Statement