

Secular Trend of Age at Menarche in Chinese Adolescents Born From 1973 to 2004

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abstract

OBJECTIVES: To estimate secular trend and factors influencing the age at menarche for Chinese girls born from 1973 to 2004.

METHODS: Data were collected from the China Health and Nutrition Survey, a prospective open cohort and an ongoing nationwide health and nutrition survey, consisting of 3199 apparently healthy Chinese girls aged 6 to 18 years at entry from 1991 to 2011. Average age at menarche and its 95% confidence interval were estimated by weighted means of Kaplan-Meier survival analysis. Cox proportional hazard models were applied to identify the independent predictive factors of age at menarche.

RESULTS: The age at menarche declined from 14.25 in Chinese girls born before 1976 to 12.60 in girls born after 2000, with an estimated decline of 0.51 years per decade ($P < .001$). The downward trend of age at menarche for rural girls was greater than for urban girls (0.62 vs 0.35 years per decade; $P < .001$). Girls living in urban areas, living in central areas, with high BMI, and with high-energy diets had a high risk of early menarche, whereas girls living on the east coast who had high-carbohydrate diets had a low risk of early menarche.

CONCLUSIONS: The authors of this study found a continuous downward secular trend of age at menarche for Chinese girls in both urban and rural areas born from 1973 to 2004. Among all variables, urban residency, BMI, and energy intake are negatively associated with age at menarche, whereas carbohydrate intake is positively associated with age at menarche.



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WHAT'S KNOWN ON THIS SUBJECT: Age at menarche for girls around the world has been decreasing, although the rate is slowing in industrialized countries.

WHAT THIS STUDY ADDS: There is a continuing downward trend in age at menarche for Chinese girls born from 1973 to 2004, which is greater in rural girls.

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Previous studies have found that the average age at menarche has decreased from ~16 to 13 years over the past 180 years, with some variation across different countries.¹ Although this trend toward earlier menarche may be slowing in industrialized countries,¹⁻³ it is still more significant in other countries.⁴⁻⁷ Little is known about the trends in menarche in China. China changed dramatically during the past few decades in many aspects, especially socioeconomic status, an important influencing factor of the onset of puberty.^{3,5,8}

The objectives of this study were to evaluate trends in the average age at menarche in China and to explore the demographic, socioeconomic, nutritional, and lifestyle characteristics associated with age at menarche in a large sample of Chinese girls born over the past 3 decades.

METHODS

China Health and Nutrition Survey

The China Health and Nutrition Survey (CHNS) is an ongoing open cohort established in 1989 and updated in 1989, 1991, 1993, 1997, 2000, 2004, 2006, 2009, 2011, and 2015.⁹ It is an international collaborative project between the Carolina Population Center at the University of North Carolina at Chapel Hill and the National Institute for Nutrition and Health at the Chinese Center for Disease Control and Prevention. Briefly, a 7-day period using a multistage, random cluster design was employed to obtain nationally representative information, taken from interviews and direct examinations, on the health and nutritional status of the Chinese population.⁹ Details of the CHNS have been described elsewhere.¹⁰⁻¹²

Sample

Girls aged 6 to 18 years were asked, “Have you ever had a menstrual period?” to define their menstrual status, and postmenarcheal girls were then asked, “How old were you when the periods started?” to identify the age of their first period. The questionnaires for girls aged 6 to 10 years were completed by a parent or guardian. Girls aged 11 to 18 years completed the questionnaires by themselves.

The outcome of interest was the attainment of menarche and the age at menarche assessed as month and year. The data were obtained from the aforementioned questions. To reduce potential misclassification, only the first reported ages at menarche in the panel data were used.

The survey included 8638 households with 35 703 participants among 15 provinces. With the exclusion of the surveys in 1989 and 2015 (because the data of 1989 on menarche were not contained and the data of 2015 were not yet available), 3483 girls aged 6 to 18 years were included. Among them, 284 girls with missing information on menarche were excluded. A total of 3199 Chinese girls born between 1973 and 2004 remained in the analyses. Birth years from 1973 to 1976 were combined because the total number of subjects included in the final analyses was small. Birth years from 2000 to 2004 were combined because <10% of girls born after 2000 had menarche during the interview,¹³ and statistical power was low if analyzed separately. On the basis of the birth years, girls were categorized in 5 groups, that is, 1973 to 1980, 1981 to 1985, 1986 to 1990, 1991 to 1995, and 1996 to 2004 (hereinafter referred to as “5 birth-year groups”).

Predictors of Age at Menarche

BMI was categorized as 4 levels on the basis of the age-specified BMI

standard for Chinese teenagers,^{14,15} in which girls with different ages had different criteria.

Total energy and macronutrient (carbohydrate, protein, and fat) intake per day were estimated by using 3 24-hour recalls and by directly weighing food consumed during the survey^{9,10} and were categorized as high, normal, or low according to the Dietary Reference Intakes for Chinese teenagers.¹⁶ The carbohydrate and fat intakes are adequate when the supplying energy accounts for 50% to 65% and 20% to 30% of total energy,¹⁶ respectively. The standards of energy (kilocalories) and protein (grams) intakes are different for girls with different ages.¹⁶

As presented in Table 1, other variables (ethnicity, region, rural or urban residency, household income per person, parental education, living with parents, and exercise) were all assessed as categorical variables. The household income per person was divided into 4 categories by quartile. Region was categorized as central area (Henan, Hubei, Hunan), east coast (Beijing, Jiangsu, Shandong, Shanghai), northeastern area (Liaoning, Heilongjiang), and western area (Chongqing, Guangxi, Guizhou). Teenagers' physical activity was estimated by using the summary of exercise frequency at school and outside of campus, and was categorized into 3 categories (≤ 2 times per week, 3–7 times per week, ≥ 8 times per week).

Statistical Analysis

To address the complex sampling design, weights for the examination sample were used in all tests. Kaplan-Meier cumulative probabilities were used to estimate the restricted mean and SEs of age at menarche for each birth year and each category of predictors. Trends in age at menarche over birth year (years per decade) were estimated by

TABLE 1 Univariate and Multivariate Cox Proportional Hazard Models of Age at Menarche

Characteristics	Total	Mean Age at Menarche ^a	Unadjusted HR (95% CI)	Adjusted HR (95% CI) ^b
Total	3199	13.56		
Demographic variables				
Year of birth				
1973–1980	596	14.06	1.00	1.00
1981–1985	697	14.06	0.85 (0.75–0.96)*	0.77 (0.67–0.88)**
1986–1990	762	13.48	1.26 (1.15–1.38)**	1.12 (0.99–1.27)
1991–1995	482	13.00	1.69 (1.53–1.86)**	1.51 (1.33–1.71)**
1996–2004	662	12.75	2.13 (1.87–2.41)**	1.92 (1.70–2.17)**
<i>P</i> trend ^c			<.001	<.001
Region				
Northeastern area	491	13.45	1.00	1.00
East coast	664	13.66	0.91 (0.80–1.03)	0.83 (0.72–0.96)*
Central area	1096	13.47	1.03 (0.94–1.13)	1.13 (1.03–1.25)*
Western area	948	13.66	0.95 (0.84–1.08)	1.02 (0.91–1.15)
Ethnicity				
Han	2710	13.52	1.00	1.00
Minority	452	13.80	0.93 (0.83–1.05)	0.99 (0.87–1.12)
Missing	37	14.50	0.41 (0.17–0.94)*	0.35 (0.17–0.72)*
Socioeconomic variables				
Rural or urban residency				
Rural	2289	13.68	1.00	1.00
Urban	910	13.20	1.32 (1.18–1.48)**	1.26 (1.15–1.38)**
Household income per person				
Q1	785	14.03	1.00	1.00
Q2	786	13.60	1.19 (1.06–1.32)**	1.06 (0.94–1.20)
Q3	786	13.48	1.32 (1.19–1.47)**	1.03 (0.92–1.16)
Q4	784	13.12	1.59 (1.40–1.80)**	0.96 (0.82–1.13)
Missing	58	12.92	1.95 (1.40–2.73)**	1.55 (1.09–2.20)*
<i>P</i> trend ^c			<.001	.301
Paternal education (y)				
≤6	599	13.91	1.00	1.00
7–9	1240	13.58	1.18 (1.06–1.31)*	0.96 (0.86–1.06)
10–12	713	13.48	1.30 (1.12–1.52)**	0.98 (0.84–1.13)
≥13	67	13.37	1.38 (1.22–1.55)**	0.85 (0.72–1.00)*
Missing	171	13.12	1.53 (1.34–1.74)**	0.85 (0.63–1.16)
<i>P</i> trend ^c			<.001	.239
Maternal education (y)				
≤6	1101	13.87	1.00	1.00
7–9	1116	13.40	1.30 (1.18–1.43)**	1.09 (0.97–1.22)
10–12	512	13.42	1.39 (1.21–1.59)**	1.16 (1.02–1.32)*
≥13	161	13.10	1.55 (1.28–1.89)**	1.02 (0.80–1.29)
Missing	309	13.28	1.37 (1.17–1.61)**	0.72 (0.51–1.03)
<i>P</i> trend ^c			<.001	.231
Living with parents				
Without parents	180	12.87	1.00	1.00
Father or mother	295	13.26	0.78 (0.63–0.97)*	0.67 (0.47–0.95)*
Father and mother	2704	13.61	0.66 (0.54–0.79)**	0.55 (0.31–0.98)*
Missing	20	13.70	0.60 (0.39–0.92)*	0.79 (0.50–1.25)
<i>P</i> trend ^c			<.001	.072
Nutritional and lifestyle variables				
BMI				
Underweight	280	14.06	1.00	1.00
Normal	2290	13.54	1.40 (1.21–1.62)**	1.41 (1.23–1.61)**
Overweight	133	12.76	2.13 (1.66–2.72)**	2.05 (1.63–2.57)**
Obese	63	12.63	2.71 (1.83–4.01)**	2.33 (1.58–3.42)**
Missing	433	13.66	1.28 (1.04–1.57)*	1.30 (1.06–1.59)*
<i>P</i> trend ^c			<.001	<.001
Energy intake (kcal/d)				
Low	1563	13.48	1.00	1.00
Normal	982	13.61	0.91 (0.82–1.00)	1.04 (0.91–1.20)
High	534	13.51	1.04 (0.94–1.14)	1.29 (1.11–1.50)**
Missing	120	14.19	0.67 (0.53–0.85)**	0.69 (0.48–1.01)

TABLE 1 Continued

Characteristics	Total	Mean Age at Menarche ^a	Unadjusted HR (95% CI)	Adjusted HR (95% CI) ^b
<i>P</i> trend ^c			.856	.005
Protein intake (g/d)				
Low	856	13.51	1.00	1.00
Normal	652	13.68	0.91 (0.80–1.04)	0.93 (0.83–1.05)
High	1571	13.49	1.02 (0.93–1.16)	0.99 (0.88–1.10)
Missing	120	14.19	0.68 (0.54–0.86)*	—
<i>P</i> trend ^c			.444	.921
Fat intake (%)				
Low	931	14.01	1.00	1.00
Normal	957	13.33	1.52 (1.40–1.66)**	1.15 (0.97–1.36)
High	1191	13.28	1.62 (1.48–1.78)**	1.02 (0.82–1.27)
Missing	120	14.19	0.95 (0.74–1.23)	—
<i>P</i> trend ^c			<.001	.542
Carbohydrate intake (%)				
Low	638	13.18	1.00	1.00
Normal	1260	13.29	0.95 (0.87–1.04)	1.01 (0.90–1.13)
High	1181	13.93	0.62 (0.57–0.68)**	0.77 (0.63–0.94)*
Missing	120	14.19	0.56 (0.45–0.71)**	—
<i>P</i> trend ^c			<.001	.033
Exercise (times/wk)				
≤2	2057	13.72	1.00	1.00
3–7	734	13.26	1.26 (1.13–1.41)**	1.10 (0.99–1.23)
≥8	400	13.16	1.38 (1.21–1.58)**	1.06 (0.93–1.21)
Missing	8	13.39	1.14 (0.69–1.87)	1.32 (0.69–2.53)
<i>P</i> trend ^c			<.001	.176

Calculated with application of weights for the CHNS sample.

^a From Kaplan-Meier survival probabilities.

^b Adjusted for other covariates in the table.

^c Calculated by using the median value of each category as a single ordinal variable in the Cox regression model.

* $P < .05$.

** $P < .01$.

using the slope of linear regression model with mean age at menarche as the dependent variable and year of birth as the predictor. The trends of age at menarche were stratified and compared between rural and urban girls and Han and minority ethnicities. The statistical significance of these trends was determined by using tests for linear trends for year of birth in multivariate Cox proportional hazard models.

Cox proportional hazard models were used to examine the association of age at menarche with each predictor. Dummy variables were set for each predictor because all covariates were transferred into categorical data. Unadjusted and adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated by using univariate and multivariate Cox proportional hazard models, respectively. Additionally, ties were handled by using the

Breslow method. The proportional hazards assumption in the Cox regression model was tested by using Schoenfeld residuals. Linear trends of HRs were tested by using the median value of each category as a single ordinal variable in the Cox regression model. Analyses were conducted with the statistical software Stata 13.1 (StataCorp, College Station, TX). Two-sided tests were used, and $P < .05$ was considered statistically significant.

RESULTS

The Age at Menarche

All the characteristics and other results are presented in Table 1. The weighted percentiles in the 5 birth-year groups for girls who had attained menarche in the last survey were 64.98, 34.68, 62.54, 72.71 and 31.81, respectively. Additionally, the weighted percentiles in the age groups of 6 to 9, 10 to 18, and 14

to 18 for girls who had attained menarche were 0.78, 40.32, and 81.72, respectively. Forty-seven percent girls had not had menarche.

Overall, for girls born during the 30-year period, the weighted mean age at menarche was estimated at 13.56 years. Age at menarche decreased substantially from 14.25 to 12.60 years, with an estimated decline of 0.51 years per decade ($P < .001$) (Fig 1). The results were also compared with other countries in Fig 2.

On average, during the 30-year period, urban girls had menarche 5.76 months (0.48 years) earlier than rural girls (at 13.20 vs 13.68 years). Although there were downward secular trends of age at menarche for both rural and urban girls, these 2 trends were significantly different ($P < .001$). The weighted mean age at menarche decreased by ~2.67 years for rural girls versus 1.34 years for urban girls (Fig 3). During the

30-year period, the mean age at menarche for rural girls decreased substantially from 14.51 years in the birth year of 1976 to 11.84 years in the birth year of 2000 (0.62 years per decade; $P < .001$). In contrast, the downward secular trend for urban girls was mild, with the mean age initially decreasing from 13.39 to 12.05 years (0.35 years per decade; $P < .001$). Besides, a significant difference between rural and urban girls born in the 1980s was found in mean age at menarche (14.00 vs 13.38 years), whereas mean ages were similar for those born after 1995 (12.75 vs 12.73 years).

On average, Han girls had menarche 3.36 months (0.28 years) earlier than minority girls (at 13.52 vs 13.80 years). The secular trends of age at menarche were not significant between Han girls (13.93–12.55 years; 0.52 years per decade, $P < .001$) and minority girls (14.33–11.80 years; 0.39 years per decade, $P < .001$).

Predictors of Age at Menarche

Results of Cox proportional hazard models are presented in Table 1. All variables in the models satisfy the proportional hazards assumption (all $P > .05$). After multivariate adjustment, the association of early menarche with household income per person, parental education, fat intake, exercise, and living with parents would lose statistical significance, whereas the association with girl's birth year, rural or urban residency, BMI, and carbohydrate intake remained significant. Although energy intake and region were not associated with age at menarche in univariate models, the associations changed after covariates' inclusion in multivariate model.

In detail, the risks of early menarche for girls born late (Fig 4) and girls with high BMI or high energy intake were higher, whereas the risks for

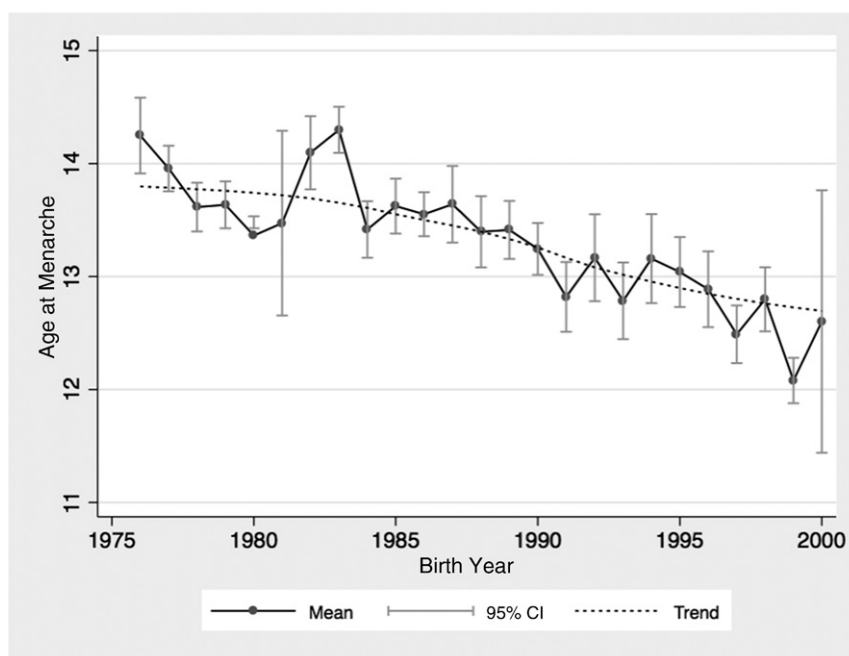


FIGURE 1 Mean age at menarche by year of birth in Chinese girls aged 6 to 18 born between 1973 and 2004.

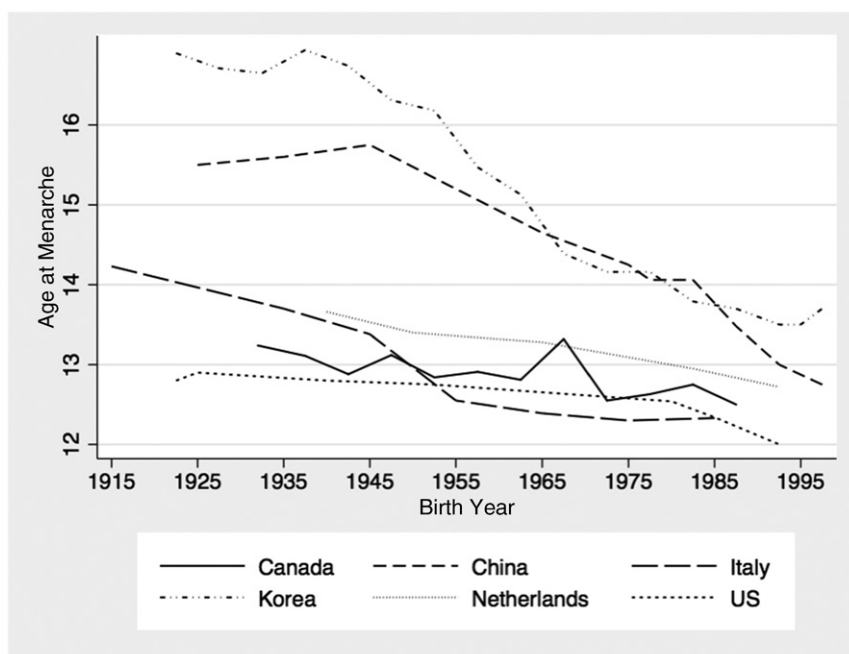


FIGURE 2 Secular trends of age at menarche in 6 countries.^{8,17–23} Ages at menarche in the Netherlands and the United States were calculated as median age, whereas others were calculated as mean age.

girls with high carbohydrate intake was lower (all P trend $< .05$). Girls living in urban areas had a higher risk of early menarche (HR: 1.26, 95% CI: 1.15–1.38). The hazard of early menarche was significantly higher for

girls living in the central area (HR: 1.13, 95% CI: 1.03–1.25) and lower for girls living in the east coast area (HR: 0.83, 95% CI: 0.72–0.96) when compared with girls living in the northeastern area.

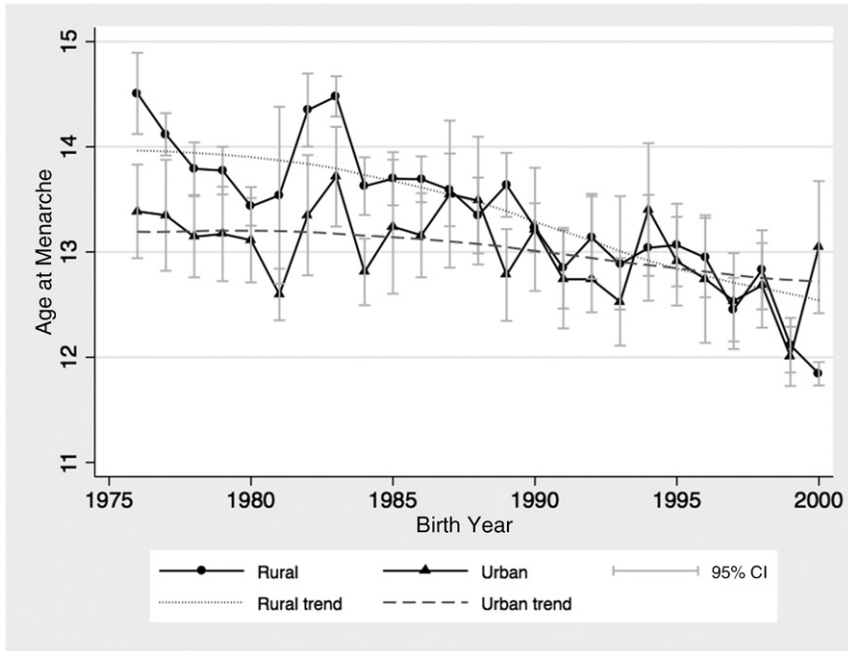


FIGURE 3 Mean age at menarche by year of birth in Chinese girls aged 6 to 18 born between 1973 and 2004, stratified by rural or urban residency.

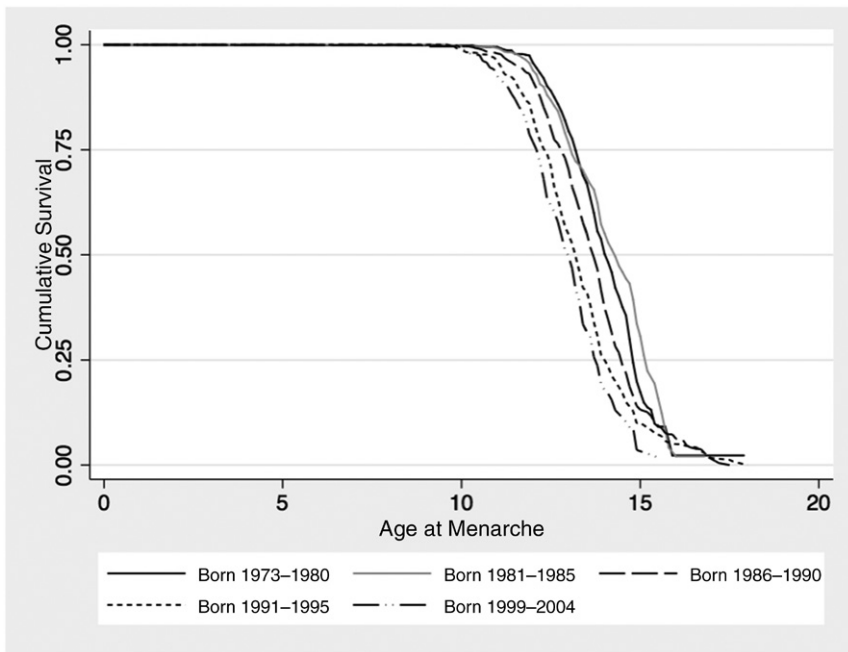


FIGURE 4 Kaplan-Meier survival probability of age at menarche among Chinese girls aged 6 to 18 born between 1973 and 2004.

DISCUSSION

This study of a national cohort confirms a continuous downward secular trend of age at menarche through birth years of 1973 to 2004

among Chinese girls. Mean age at menarche declined from 14.25 to 12.60 years during the 30-year period, with an average decline of 0.51 years per decade. Moreover, the mean age at menarche for rural

girls decreased markedly (0.62 years per decade), but urban girls showed a smaller decrease (0.35 years per decade). However, secular trends of mean age at menarche between Han girls (0.52 years per decade) and minorities (0.39 years per decade) were not significant.

As presented in Fig 2, the downward trend was common around the world, although the average ages at menarche were different.^{8,17-23} Anderson et al^{24,25} found the mean age at menarche for US girls decreased from 12.75 years in 1963 through 1970 to 12.54 years in 1988 through 1994, and then to 12.34 years in 1999 through 2002. And the age at menarche for Western European girls declined by ~3 to 4 months per decade from 1830 to 1980.²⁶ Hosokawa et al²⁷ concluded that the mean age at menarche for Japanese girls had decreased by 1.6 years over the 50-year period since 1930, from 13.8 to 12.2 years. During the past decade, several researchers reported similar results on age at menarche for Chinese girls. Song et al^{28,29} analyzed a national sample of girls aged 9 to 18 years from the National Survey on the Constitution and Health of Chinese Students. They reported a decreased trend of mean age at menarche from 13.41 years in 1985 to 12.47 years in 2010²⁸ and a difference in mean age at menarche between rural and urban girls (12.92 vs 12.60 years).²⁹ Another retrospective study¹⁹ based on China Kadoorie Biobank found that mean age at menarche decreased from 15.5 years for girls born in 1925 to 14.2 years for girls born in 1978. Although the downward secular trend of age at menarche has recently slowed in Japan, the Netherlands, Germany, and Bulgaria,^{27,30} and remained stable in Belgium and Norway,³⁰ it has continued to decline in China, in both urban and rural areas.

The differences in age at menarche between urban and rural areas well establish that urban girls reach

menarche earlier than rural girls.^{30,31} Our study has also revealed a significant difference between urban and rural girls in age at menarche. A faster downward trend in age at menarche for rural girls is also evident. It is believed that urbanization influences the evolution of age at menarche, probably through increasing BMI.³¹ Studies^{28,32,33} have shown a continuous decrease in the magnitude of the association between age at menarche and rural or urban residency coinciding with the urbanization of China over the past 30 years. According to the official statistics, the rate of urbanization increased from 23.71% in 1985 to 29.04% in 1995 and, in addition, to 49.68% in 2010.^{28,33}

Our study has found that a high BMI was a risk factor of early menarche. Many researchers explained this by an effect of increased body fat on the hypothalamic-pituitary-gonadal axis.^{20,34–36} However, some researchers reported the limited influence of BMI on age at menarche in high-BMI groups¹⁸ and explained it by hyperandrogenism in girls with obesity.^{37–39} Tchernof and Després,⁴⁰ however, indicated that high plasma estradiol levels and low sex hormone binding globulin levels because of puberty were associated with adiposity, which meant that the high BMI resulted from the beginning of menarche. Previous studies have shown that higher energy, protein, and fat intake are positively associated with early menarche, and higher carbohydrate intake is negatively associated with early menarche.^{36,41–47} As shown by our results, high energy intake was positively associated with early menarche, and high carbohydrate intake was positively related to late menarche. The fact that energy intake was associated with age at menarche in multivariate analysis but not in univariate analysis can be explained by the effect of birth time. The association becomes significant

($P < .001$) when only adjusted for birth year. Ages at menarche are different among regions. Girls living in the central area have the biggest risk of early menarche, whereas girls living in the east coast region had menarche latest.

Additionally, the associations of early menarche with socioeconomic factors except rural or urban residency lose statistical significance after adjustment. This suggests that general social and economic status influence age at menarche through other covariates and that these covariates play a more minimal role in influencing the sexual maturation of Chinese girls. It supports the notion that socioeconomic factors are not independent predictors of age at menarche in well-developed countries.^{7,17,18}

Human evidence exists that exposure to endocrine-disrupting agents such as lead and polybrominated biphenyls can induce an earlier onset of menarche.^{39,48,49} However, neither exposure was available for analysis in our multivariate model, despite recognition that minority populations may have higher environmental contaminant exposure. It is possible that girls born late might be more likely to be exposed to these agents and, as a result, had menarche earlier than girls born early.

Strengths of the study are as follows. Firstly, this research used data from a national representative sample with a diverse population and a prospective follow-up study design; thus, the results are more likely to be generalizable to the China population. Secondly, compared with other studies around the world, not only demographic and socioeconomic variables but also nutritional and lifestyle variables were included as factors. And this study used convincing BMI and nutrition category standards formulated by the Chinese government. Thirdly, differing from other cross-sectional studies, our study was conducted in a birth

cohort, which reduced recall bias and increased accuracy.

Several limitations should be kept in mind when interpreting our findings. First, analysis of retrospective data might bring recall bias to our study. Height, weight, and other variables were collected a period after the menarche. The second concern is the large amount of missing data. Approximately half of the girls failed to record their age at menarche because they were too young to have their menarche at last survey or didn't want to answer the questions. Approximately one-fourth of girls were last surveyed before 12 years old. Additionally, some of the factors this study wanted to analyze had missing data. To address this concern, this study generated new categories containing missing data for each variable and calculated the HRs and 95% CIs of the missing groups; however, it still might bring bias to our study.

CONCLUSIONS

Data from the CHNS indicated that the average age at menarche for Chinese girls born from 1973 to 2004 both in urban and rural areas had a continuous downward secular trend. In general, both the downward trend and average age at menarche for rural girls are greater than for urban girls. Additionally, urban residency, BMI, and energy intake are negatively associated with age at menarche, whereas carbohydrate intake is positively associated with age at menarche. Additional studies are warranted to elucidate factors, particularly nutrition and exposure to endocrine-disrupting agents, which may account for the downward secular trend in age at menarche.

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ABBREVIATIONS

CHNS: China Health and Nutrition Survey
HR: hazard ratio
CI: confidence interval

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