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Age at Menarche in Relation to Adult Height

The EPIC Study

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In the last two centuries, age at menarche has decreased in several European populations, whereas adult height has increased. It is unclear whether these trends have ceased in recent years or how age at menarche and height are related in individuals. In this study, the authors first investigated trends in age at menarche and adult height among 286,205 women from nine European countries by computing the mean age at menarche and height in 5-year birth cohorts, adjusted for differences in socioeconomic status. Second, the relation between age at menarche and height was estimated by linear regression models, adjusted for age at enrollment between 1992 and 1998 and socioeconomic status. Mean age at menarche decreased by 44 days per 5-year birth cohort ($\beta = -0.12$, standard error $= 0.002$), varying from 18 days in the United Kingdom to 58 days in Spain and Germany. Women grew 0.29 cm taller per 5-year birth cohort (standard error $= 0.007$), varying from 0.42 cm in Italy to 0.98 cm in Denmark. Furthermore, women grew approximately 0.31 cm taller when menarche occurred 1 year later (range by country: 0.13–0.50 cm). Based on time trends, more recent birth cohorts have their menarche earlier and grow taller. However, women with earlier menarche reach a shorter adult height compared with women who have menarche at a later age.

body height; Europe; menarche

Abbreviations: EPIC, European Prospective Investigation into Cancer and Nutrition; SD, standard deviation.

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Several risk factors for breast cancer have been identified, including age at menarche and adult height. Studies have consistently shown that women having their menarche at an earlier age have an increased risk for breast cancer compared with women who had their menarche at a later age (1–6). A decrease of 9 percent in premenopausal breast cancer risk was found for each additional year menarche occurred later. This decrease was approximately 4 percent when breast cancer was diagnosed after menopause (6). A recent pooled analysis of seven prospective cohort studies investigating the role of height as a risk factor for breast cancer showed a significant increased risk of breast cancer with increasing height in postmenopausal, but not in premenopausal, women (7).

Since the early 19th century, secular changes have been described for age at menarche as well as for adult height. In Europe, age at menarche has decreased, although the results from the past 50 years are less consistent (8). In several countries, age at menarche remained stable or has even started to increase since the mid 20th century (9–11), whereas in other countries the downward trend still continues (12, 13). In the same period, height has increased by about 0.3–3.0 cm per decade over the last century (8, 9, 14). Hauspie et al. (8) claim that the secular trend in height has slowed down since World War II, but others (14) could not confirm this finding. Secular trends in these established risk factors for breast cancer may also predict changes in breast cancer incidence and are therefore important to monitor. Although on an ecologic (population) level women seem to have their menarche earlier and to grow taller, several studies show that women with earlier menarche reach a shorter adult height compared with women who have menarche at a later age (1, 12, 15–19).

The aim of this paper is to describe secular trends in age at menarche and height in the past century and to investigate whether adult height is related to the age at which menarche occurs. For this purpose, we used individual data on 286,205 women who participated in the European Prospective Investigation into Cancer and Nutrition (EPIC). The large number of women included and the fact that we have data from nine different European countries participating in this cohort give us the opportunity to investigate trends in age at menarche and adult height in different countries, as well as the relation between these two characteristics.

MATERIALS AND METHODS

Subjects

The EPIC study is a multicenter prospective study carried out in 23 study centers from 10 European countries. In the present study, only data from the female EPIC participants of nine countries were used ($n = 307{,}081$). At the time of the current analysis, data from Norway had not yet been included in the central database. A detailed description of the study population and data collection of the EPIC study has been published elsewhere (20). In short, the study includes 307,081 women, aged 35–70 years. Women were recruited between 1992 and 1998, and information was collected through a nondietary questionnaire on lifestyle variables and through a dietary questionnaire addressing usual diet. Anthropometric measurements were obtained, and blood samples were taken. The EPIC study was not intended to include a representative study population of each country, and the selection of study populations in each country was influenced by practical considerations of obtaining adequate participation and ensuring long-term follow-up.

Assessment of age at menarche, height, and leg length

In all countries, age at menarche was obtained from the general lifestyle questionnaire. In Sweden, Italy, the Netherlands, United Kingdom, and Greece, age at menarche was asked in years (open question). In other countries (Denmark, Spain, Germany, France), age at menarche was asked in predefined categories ($\leq$8, 9, 10, . . ., 19, or $>$19 years). Age at menarche was missing for 0.1–4.3 percent of women per country. An exception was Sweden, where 44 percent of the subjects had missing values on age at menarche because one of the two centers did not obtain this information for its participants.

Trained observers using standardized methods measured height to the nearest 10 mm in Spain, Sweden, the Oxford, United Kingdom, subcohort, and Denmark; to the nearest 5 mm in the Netherlands, France, the Norfolk, United Kingdom, subcohort, and three of the Italian cohorts; and to the nearest 1 mm in two Italian subcohorts, Greece, and Germany. In global France and in the Oxford, United Kingdom, subcohort, height was self-reported by participating women and measured only in a subsample (29 percent in France and 40 percent in the United Kingdom). Self reported height is generally overestimated, especially in shorter subjects (21). By use of a method designed by Haftenberger et al. (21), we calculated measured height from the self-reported values for those women from the Oxford, United Kingdom, subcohort for whom only self-reported height was available. The formula was obtained through comparison of the women for whom self-reported height and measured height were both available (1,464 women). The following formula was used: measured height (cm) = (27.096 + (0.853 $\times$ self-reported height) − (0.069 $\times$ age)). For the French women with both self-reported and measured data, the time interval between self-reports and measurements varied between less then 1 month and 6 years. The maximum time interval considered necessary by Haftenberger et al. (21) to allow for a reasonable comparison of self-reported and measured values was 3 months. Because of an insufficient number of eligible women in this time interval, prediction equations from self-reports were not determined (21). In this paper, we therefore present self-reported values for the French women. For 1,857 women, only measured height (not self-reported height) was available in France. These women were not included in the analyses on trends in height and in the analyses on the relation between height and age at menarche.

Sitting height was measured in Italy, Spain, the Utrecht cohort from the Netherlands, Greece, Germany, Denmark, and the subsample from France in which height was measured as well, while participants were seated on a chair.

Sitting height was then measured from the head to the seat of the chair to the nearest 10 mm in France and Greece and to the nearest 1 mm in all other cohorts. Because the onset of ovarian estrogen production (at menarche) is thought to affect the growth of the long bones in particular (18, 19), the use of leg length might be more appropriate to describe the effect of menarche on growth. Therefore, we estimated leg length by subtracting the sitting height from the total body height (leg length = height − sitting height). Data on height were missing for 0.1–1.7 percent of women per country.

Statistical analysis

The analyses were restricted to women who had nonmissing data on height as well as menarche and who had their menarche at a physiologic age, which we defined as menarche from age 8 until 18 years ($n = 286{,}205$).

For the description of trends, mean age at menarche and height were plotted in 5-year birth cohorts. The oldest cohort includes women born from 1915 to 1919, and the youngest women were born from 1960 to 1964. Because socioeconomic status varied considerably among countries and, especially, mean height varied considerably along the different categories of socioeconomic status, we plotted the socioeconomic status-adjusted mean values of menarche and height. We used the highest school level reached as a proxy for the socioeconomic status of a woman in her youth. Women with no education or only primary school education were classified as "low," women who completed secondary school or technical/professional school were classified as "intermediate," and women with a university degree were classified as having a "high" socioeconomic status. Trends were tested using a linear regression model in which the 5-year birth cohort was entered continuously as the independent variable, and either age at menarche (in years) or height (in cm) was entered as the dependent variable; p values are reported. Linearity was assessed by plotting the partial residual plots. Again, the analyses were adjusted for socioeconomic status. For three countries (the Netherlands, Germany, and France), the plots showed that trends for height were only linear starting from the 1935–1939 birth cohort, and the linear trend was, therefore, tested only from this birth cohort until the last.

We calculated the difference between the r^2 of the full model omitting age at menarche and the r^2 of the full model in order to estimate the percentage of the total variation in height explained by variation in age at menarche.

Since we believe that the worsened living conditions during World War II had a marked influence on age at menarche (22) and on height (23), we decided to analyze the relation between age at menarche and adult height separately for women born before 1945 and from 1945 onward. By use of this cutoff point, we ensure that the latter group is not exposed to the effects of World War II at any time in their life, whereas these effects could influence the relations found in the first group. In order to see whether the relations differed in different countries, we stratified the analyses by country.

RESULTS

The reported mean age at menarche in Europe varies from 12.5 (standard deviation (SD): 1.5) years in Italy to 13.6 (SDs: 1.4 and 1.5) years in Sweden and Denmark (table 1). In all participating European countries, a statistically significant downward trend in the mean age at menarche per 5 years is observed (figure 1). The linear regression coefficients (βs) ranged from −0.05 in the United Kingdom to −0.16 in Spain and Germany ($p < 0.0001$ in all countries). For example, a β coefficient of −0.05 means that, for each subsequent 5-year birth cohort, menarche occurs 0.05 year (≈18 days) earlier. From figure 1, a stabilization or even a slight increase in the age at menarche of the younger birth cohorts can be observed in the United Kingdom, Germany, Italy, and Spain.

In France, Germany, and the Netherlands, a sharp increase in the mean age at menarche was seen in women born between 1920 and 1934. From 1935 onward, the mean age at menarche started to decline in these countries as well (the Netherlands: $\beta_{1935-1964} = -0.11$, $p < 0.0001$; France: $\beta_{1935-1964} = -0.09$, $p < 0.0001$; Germany: $\beta_{1935-1964} = -0.16$, $p < 0.0001$).

For height, too, there is a large variation in Europe, with Dutch women being the tallest (mean height (cm): 164.4, SD: 6.3) and Greek women being the shortest (mean height (cm): 156.1, SD: 6.4) (table 1). Figure 2 shows that the mean height for women has increased in all nine European countries, with a range by country from 0.42 cm in Italy to 0.98 cm in Denmark per 5-year birth cohort. For the birth cohort 1920–1924, the tallest women (the Netherlands) and the shortest women (Greece) were on average 162.2 cm and 153.3 cm, respectively. For younger women in the birth cohort 1960–1964, the mean adult height ranged from 166.0 cm for Dutch women to 158.6 cm for Spanish women. In several countries (the Netherlands, Greece, Spain, and Sweden), the increase in mean height appears to be leveling off in the younger birth cohorts.

To exclude any effects of World War II, we analyzed the relation between age at menarche and adult height stratified into two birth cohorts (women born before 1945 or from 1945 onward) and separately for each country (table 2). In general, we found that women who had their menarche at a later age reached a taller adult height; for example, for France, a delay of menarche by 1 year increased the adult body height by approximately 0.41 cm. For most countries except for the United Kingdom, Sweden, and Greece, this association was somewhat clearer in women born in 1945 or later. In Greece, a much weaker relation was found between age at menarche and adult height for the women born in 1945 or later ($\beta_{<1945} = 0.31$ (95 percent confidence interval: 0.23, 0.38) vs. $\beta_{\geq 1945} = 0.13$ (95 percent confidence interval: 0.02, 0.24)). In Sweden and the United Kingdom, the relation between age at menarche and adult height was similar over both strata of birth cohorts. Overall, the age at menarche explained about 1 percent of the variation in height. Most of the variation in height was explained by country of residence (13 percent). Age at intake and socioeconomic status explained 0.02 percent and 2 percent of the variation in height, respectively.

TABLE 1. Population characteristics by European country for women born between 1915 and 1964

Country	No.*	Birth years included	Median age in years at recruitment (range)	Mean age in years at menarche (SD†)	Mean height in cm (SD)	Mean leg length in cm (SD)	Socioeconomic status	
							Level	%
France	70,913	1921–1956	51 (36–72)	12.84 (1.40)	161.77 (5.65)	76.69 (4.70)	Low	12
							Intermediate	51
							High	37
Italy	31,559	1920–1962	51 (35–74)	12.54 (1.46)	158.48 (6.15)	73.51 (4.31)	Low	30
							Intermediate	57
							High	13
Spain	25,241	1925–1961	47 (35–69)	12.91 (1.56)	156.74 (5.82)	74.10 (4.97)	Low	79
							Intermediate	11
							High	10
United Kingdom	44,025	1918–1963	51 (35–74)	12.89 (1.54)	162.51 (6.00)		Low	27
							Intermediate	43
							High	31
The Netherlands	25,414	1924–1962	54 (35–70)	13.28 (1.56)	164.42 (6.26)	77.31 (4.59)	Low	20
							Intermediate	62
							High	18
Greece	14,428	1920–1964	54 (35–74)	13.19 (1.52)	156.13 (6.44)	72.25 (4.47)	Low	65
							Intermediate	24
							High	11
Germany	29,669	1926–1963	48 (35–70)	13.16 (1.48)	163.27 (6.22)	77.31 (4.23)	Low	30
							Intermediate	43
							High	27
Sweden	16,699	1923–1950	56 (44–73)	13.59 (1.41)	163.65 (6.04)		Low	39
							Intermediate	46
							High	15
Denmark	28,257	1929–1947	56 (50–65)	13.56 (1.53)	164.11 (6.05)	77.52 (4.25)	Low	31
							Intermediate	62
							High	7
Total	286,205	1918–1964	52 (35–74)	13.03 (1.52)	161.53 (6.53)	75.64 (4.88)	Low	31
							Intermediate	47
							High	23

* Number of women with nonmissing data on height and age at physiologic menarche, defined as menarche from age 8 to age 18 years.
† SD, standard deviation.

The effect of age at menarche on leg length was similar to the relation between age at menarche and total body height (table 2).

DISCUSSION

The study presented here has several advantages. Never has there been a study on age at menarche and adult height as large as this one, including individual data on almost 300,000 women. Furthermore, the EPIC is unique in its design and size, covering nine European countries with a high degree of standardization in measuring anthropometric characteristics. There is also a large overlap of time periods and cohorts covering each country. Therefore, in this study, we were able to compare trends among several European populations from north to south over several birth cohorts.

In all the nine European countries included in the present study, the mean age at menarche has been decreasing in women born since 1935. For several countries, the mean age at menarche had already started to decline from 1920 onward. Hauspie et al. (8) found a decrease in mean age at menarche of 4.5 months per decade in the years 1910–1970, which is slightly more compared with our findings (1–4 months per decade). Okasha et al. (12) reported a decrease in menarche in the United Kingdom of 6 months in women born between 1920 and 1951, which is also more than the

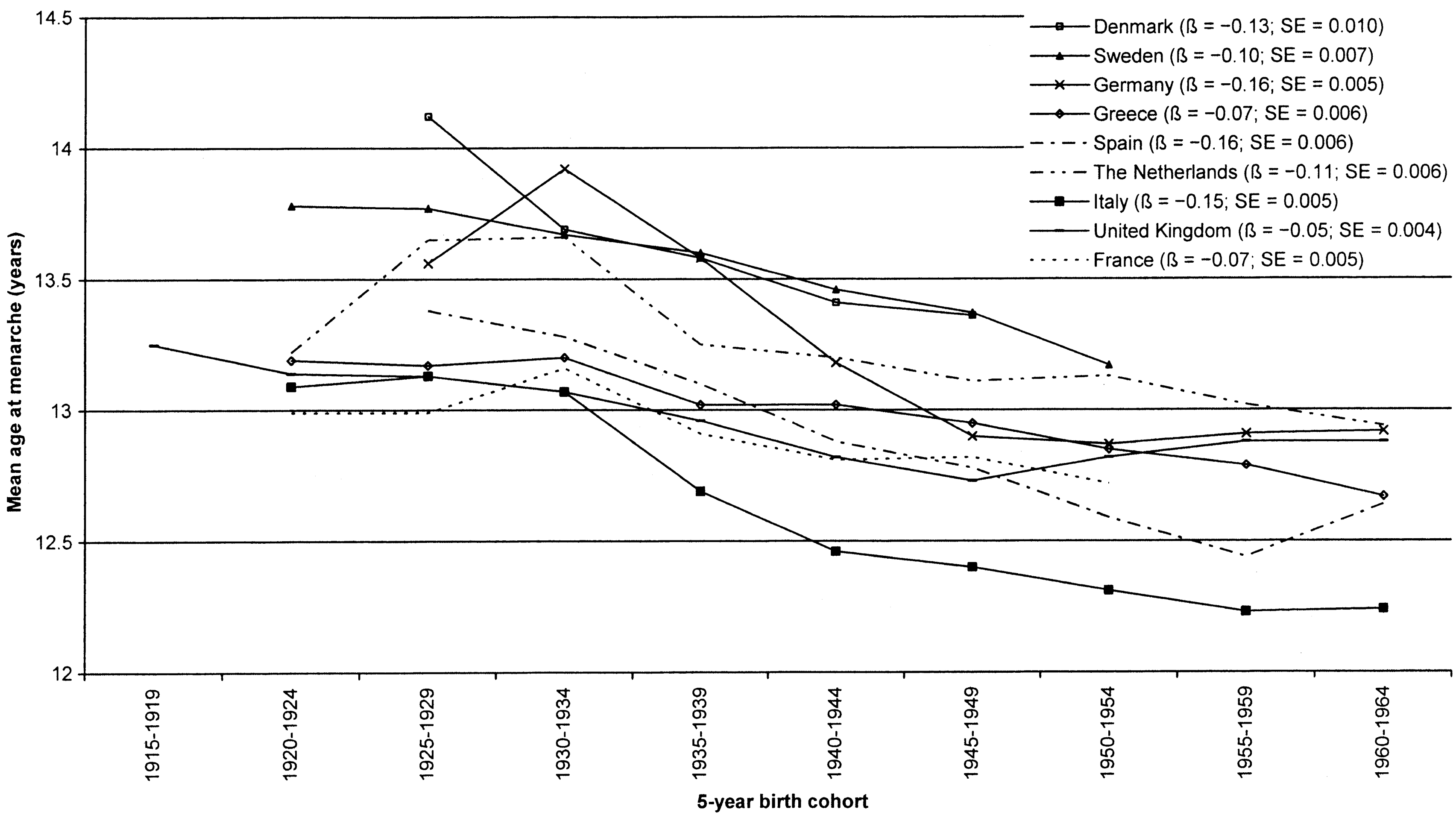

FIGURE 1. Mean age at menarche of women born between 1915 and 1964, adjusted for socioeconomic status, for 5-year birth cohorts for each participating country (Denmark, Sweden, Germany, Greece, Spain, the Netherlands, Italy, United Kingdom, and France). β is the country-specific regression coefficient from linear regression models, in which the independent variable is 5-year birth cohort and the dependent variable is age at menarche. $p_{trend} < 0.0001$ for all countries. SE, standard error.

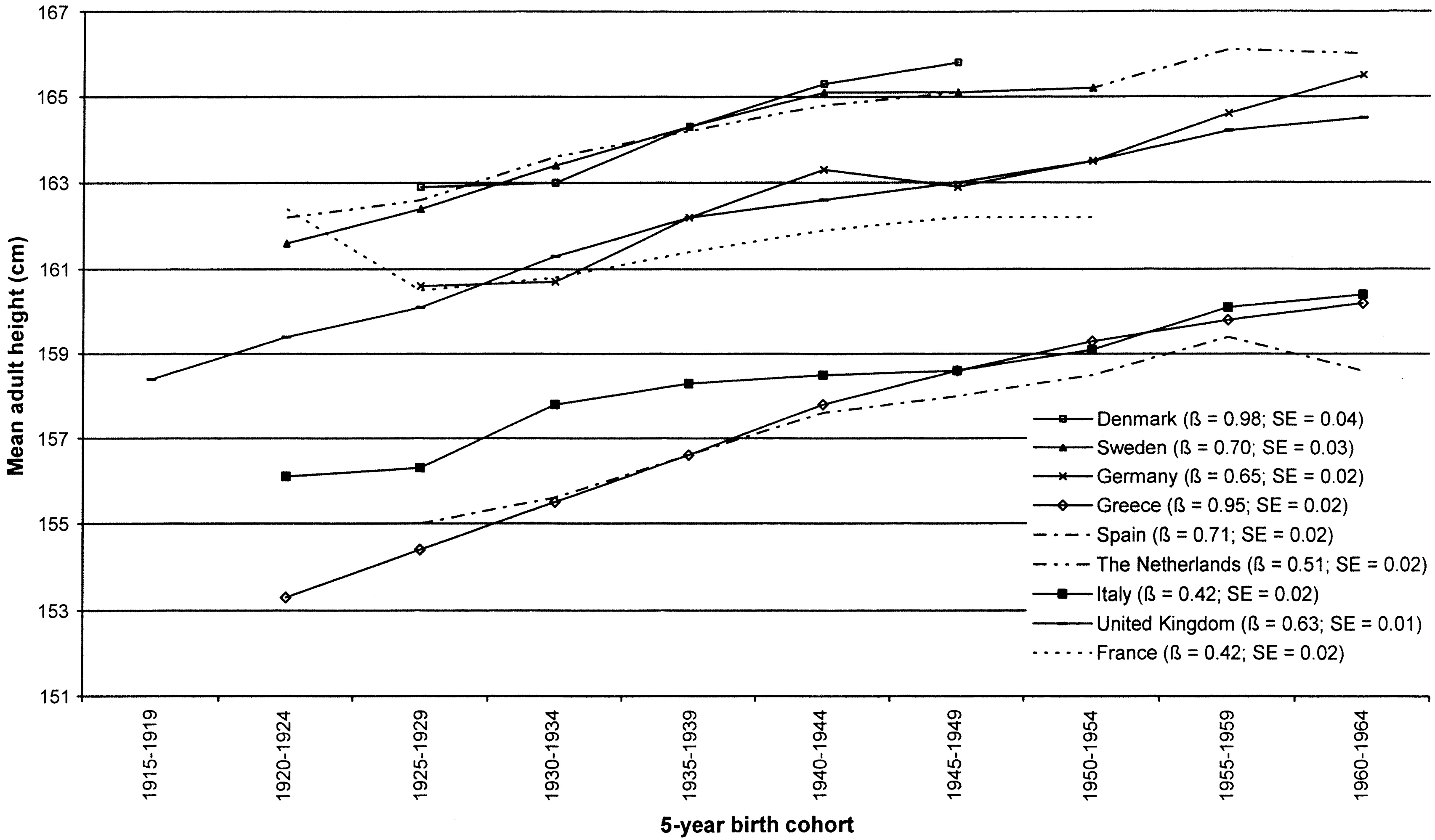

FIGURE 2. Mean height of women born between 1915 and 1964, adjusted for socioeconomic status, for 5-year birth cohorts for each participating country (Denmark, Sweden, Germany, Greece, Spain, the Netherlands, Italy, United Kingdom, and France). β is the country-specific regression coefficient from linear regression models, in which the independent variable is 5-year birth cohort and the dependent variable is height. $p_{trend} < 0.0001$ for all countries. SE, standard error.

TABLE 2. Regression coefficients for the association of adult height and leg length with age at menarche, adjusted for age at intake and socioeconomic status, stratified by European country and by the two birth cohorts before 1945 and from 1945 to 1964

	<1945		1945–1964	
	β coefficient*	95% confidence interval	β coefficient	95% confidence interval
France				
Height	0.41	0.37, 0.44	0.44	0.39, 0.49
Leg length	0.41	0.36, 0.47	0.47	0.39, 0.55
Italy				
Height	0.36	0.30, 0.43	0.50	0.43, 0.57
Leg length	0.36	0.32, 0.41	0.47	0.42, 0.52
Spain				
Height	0.21	0.14, 0.28	0.43	0.36, 0.49
Leg length	0.27	0.21, 0.33	0.42	0.37, 0.48
United Kingdom				
Height	0.36	0.31, 0.41	0.37	0.32, 0.43
The Netherlands				
Height	0.19	0.13, 0.25	0.37	0.28, 0.46
Leg length	0.22	0.17, 0.27	0.24	0.12, 0.36
Greece				
Height	0.31	0.23, 0.38	0.13	0.02, 0.24
Leg length	0.29	0.23, 0.35	0.18	0.10, 0.26
Germany				
Height	0.32	0.25, 0.38	0.37	0.30, 0.43
Leg length	0.27	0.22, 0.32	0.37	0.32, 0.41
Sweden				
Height	0.28	0.21, 0.35	0.26	0.12, 0.41
Denmark				
Height	0.29	0.24, 0.34	0.37	0.23, 0.51
Leg length	0.30	0.26, 0.33	0.30	0.20, 0.40
Total				
Height	0.31	0.30, 0.33	0.39	0.36, 0.41
Leg length	0.30	0.28, 0.31	0.38	0.36, 0.41

* β coefficient showing the number of centimeters taller in height or longer in leg length per year later at menarche.

3 months' decrease in 30 years that we found in our study for the United Kingdom.

We found that height has been increasing by approximately 0.7 cm per 5-year birth cohort in women born between 1915 and 1965. Hauspie et al. (8) reported an increase in adult stature of between 0.3 and 1.3 cm per decade in European countries since 1950, which is slightly lower compared with our findings. However, the time periods included in the study of Hauspie et al. were not birth years, which makes their results difficult to compare with ours.

The observed trends in age at menarche and adult height are probably caused by changes in the nutritional, hygienic, and health status of Western populations (8, 9, 24, 25). Nutrition, in particular, appears to play an important role in the onset of menarche. There is a vast amount of literature reporting that girls with higher body weight, higher body mass index, more body fat, and greater height reach their menarche earlier (15, 26–31). Furthermore, it has been suggested that girls need to reach a critical weight or height for menarche to occur and that changes in dietary habits as observed in children may have caused this critical weight to be reached at an earlier age (1, 8, 29, 32). Up to now it is unclear, however, whether energy intake or specific nutritional components play a role, or whether nutrition affects menarche through its effect on accumulation of adipose tissue (29–31, 33).

The present study suggests that the trend in age at menarche has leveled off or has even reversed, as was found in other studies (8, 9, 11). Moreover, in some countries, the secular trend in height has started to level off in our data. This was also seen in other studies, although not as clearly as in the present study (8, 9, 14).

Our results support the general belief that women who reach their menarche at a later age will eventually grow taller compared with women who reach their menarche at an earlier age. This relation may be explained by the earlier closure of epiphyseal growth disks because of the increase in ovarian estrogens (18, 19). A delay in menarche allows more growth of the long bones before the epiphyses unite and results in a taller adult height. Therefore, the menarcheal age probably has its main effect on height in the long bones. Leg length might, therefore, be a more appropriate outcome than total body height, even more since leg length is stable even if shrinkage appears in older women. Our results confirm this, as the effect of age at menarche on leg length is comparable to the effect on total body height. So, for each year of delay in when a woman reaches menarche, she will grow approximately 0.35 cm taller in total body height. This increase is fully caused by an increase in leg length, which was also approximately 0.35 cm.

Although the association between age at menarche and adult height is quite strong in this study, only a small part of the variation in height is explained by the variation in menarcheal age (about 1 percent in this study). Most of the variation in height was explained by country of residence (13 percent).

In all participating countries, age at menarche decreased over time, and the adult height increased. In addition, in all participating countries, the adult height increased with each additional year that menarche occurred later. Despite these similarities, there were also some differences among the participating countries. Historical differences, such as war influences, may play a role. All countries participating in this study, except Spain and Sweden, were involved in World War II, but only the Netherlands and Germany (after the latter's capitulation) suffered from severe famine as a result of the war. Our data show a strong increase in age at menarche for women aged approximately 10–20 years during World War II in the Netherlands and a few years later in Germany and France. Others already showed that World War II postponed age at menarche (22) and led to shorter adult height (23). As a result of this influence, the relation between age at menarche and adult height might be obscured. We, indeed, found a weaker relation between age at menarche and height for women born before, compared with women born during or after, 1945.

The linear relation between age at menarche and adult height was smaller in Greek women born during or after 1945 compared with women born before 1945. We do not have a clear explanation for this exception. During World War II and the Greek Civil War, which immediately followed World War II, Greece suffered from severe famine and poverty that lasted until 1949. It might be that women exposed to this period of famine and poverty had later menarche and remained smaller. This would dilute the relation between age at menarche and adult height.

In Spain, the Civil War that took place from 1936 to 1939 also resulted in famine in the years after the war (1940–1952). In this study, we see no clear effects of this war, which may be explained by the fact that only parts of Spain were involved in the war.

Furthermore, in France, height was self-reported instead of measured. It is known that women tend to overestimate their height (21). Overestimation of height is more common in shorter and in older women. With aging, women tend to lose height, mainly because of changes in the spinal vertebral bodies and disk spaces (34). We observed that the oldest women were the shortest. In case older women have overestimated their height, their measured height will in reality be even shorter, and observed trends in France will then be stronger than those observed in this study.

As already noted in the paragraphs above, in most countries the relation between age at menarche and height was stronger for younger than for older women. Apart from famine influences, we also have to consider misclassification as an explanation for this phenomenon. One may argue that younger women may report menarcheal age more accurately, because the event was more recent. In the French cohort, there are data on 549 women who answered the question on age at menarche twice with an 18-month interval. Of these women, 70.7 percent reported an identical age at first menstruation, and 98.5 percent reported an age at menarche within a year of that initially reported. These percentages did not differ for older compared with younger women (13). Must et al. (35) were able to compare the actual measured age at menarche and the reported age 33 years later. They showed that the actual mean age at menarche did not differ from the recalled mean age at menarche (12.93 years (95 percent confidence interval: 12.81, 13.06) vs. 12.85 years (95 percent confidence interval: 12.69, 13.00)). Moreover, any misclassification was not dependent on the age at menarche (35). Although misclassification of age at menarche in our study is likely, these reports do not support the existence of age-dependent differential misclassification.

Analyses were adjusted for age at intake and socioeconomic status. Unfortunately, the EPIC does not have information on childhood nutrition. Nutrition may influence the onset of menarche as well as height, and information would have made it possible to more thoroughly study the associations. We used socioeconomic status as an approximation for childhood nutrition. In fact, we used "highest education" as a proxy for socioeconomic status in childhood. Whether highest education reflects socioeconomic status correctly may depend on the age of a woman as well as on country. Therefore, we also analyzed trends without adjustment for socioeconomic status. For height, all countries showed more pronounced trends. For age at menarche, trends were on average quite similar, with the exceptions of Greece, where the trend was more pronounced ($\beta = -0.12$ vs. $\beta = -0.07$), and of the Netherlands, where the trend was less pronounced ($\beta = -0.06$ vs. $\beta = -0.11$).

In summary, we found that the mean age at menarche has decreased from 1920 onward by approximately 0.1 year per 5-year birth cohort in nine Western European countries. The mean adult height has increased by approximately 0.7 cm per 5-year birth cohort during the same period. For both age at menarche and adult height, we found that the trends are leveling off in some countries. An increase in adult height and a decrease in age at menarche will probably partly explain increases in breast cancer incidence in several countries.

Despite the inverse relation on an ecologic (population) trend level, the analyses show that earlier age at menarche in individuals is related to shorter adult height. The latter may appear contradictory to the known effects of age at menarche and height on breast cancer risk. It is likely, however, that these risk factors affect breast cancer risk through different pathways. Early menarche may lead to an increased lifetime exposure to endogenous sex hormones, which may cause an increased risk of breast cancer (36–38). Taller adult height, on the other hand, is positively associated with high levels of growth hormone and insulin-like growth factor I and might be a reflection of increased growth hormone/insulin-like growth factor I activity during childhood, which is also hypothesized to increase breast cancer risk (32, 39, 40).

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